Clinical Decision Support System for the Diagnosis, Analysis and Management of Hepatitis C

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Abstract

CLINICAL DECISION SUPPORT SYSTEM FOR DIAGNOSIS, ANALYSIS AND MANAGEMENT OF HEPATITIS C

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Diagnosing, analyzing and managing hepatitis C is an important task for physicians. Traditional diagnosis of chronic disease, like Hepatitis C, is time consuming and expensive. In order to understand the complete analysis of Hepatitis, an understanding of the overall impact of Hepatitis C Length of Stay in the hospital, total charges of the treatment, procedures, mortality rate, morbidity and how Hepatitis effects the liver so that an early diagnose of Hepatitis C Virus must be achieved. The research is divided into two parts, first part is data analysis of hepatitis and liver diseases, and the second part is Clinical Decision Support System (CDSS) for the diagnosis of Hepatitis C is proposed.

The objective of this study is to examine the hospitalization outcomes of total charges, length of stay in the hospital, cost of the treatment, died during hospitalization, procedures, for gender, race/ethnicity, Insurance type, income level, location of the hospital, age, region of the hospital, destination after discharge, admission source, mortality, morbidity, and admission to the hospital. The study focusses on the facts about the Hepatitis C and other Liver Diseases. A variety of statistical analysis are performed based on the NIS data from 2007 to 2012.

This study utilized the National (Nationwide) Impatient Sample (NIS) for the years 2007 to 2012. The data source is an inpatient dataset produced every year. The NIS is a publicly available all-payer inpatient health care dataset with national estimates of inpatient stays. NIS is a Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality (AHRQ). The current study includes the estimation of Length of Stay, total charges of the treatment, total charges of the procedures and other elements using the SPSS statistical analysis software.

The study revealed several significant factors related to the Hepatitis and other Liver diseases. Hepatitis C cases remained highest among other categories of Hepatitis as Hepatitis A+E and Hepatitis B+D, Cirrhosis remained highest among Chronic Hepatitis and Hepatocellular Carcinoma for the entire period of analysis. Hepatitis C Virus was found highest among the age groups of 21 to 51 years old and males, and low-income population for the year 2007. In average Hepatitis C was found highest among the age group 52-65 years throughout the years 2008 to 2012. The White population had highest number of Hepatitis C patients, followed by the Black population and then the Hispanic population. The Medicaid and Medicare coverage were highest for hepatitis C patients among Private insurance, Self-Pay, No Charge and Other. Hepatitis C was highest in the Northeast region per 100,000 normalized populations as compared to any other region. Urban location noticed higher number of patients reported with Hepatitis C infection. Hospital Emergency admission was highest for Hepatitis C patients. Admission Source for the Hepatitis C patients showed highest from Emergency Department throughout the entire period of analysis. Destination after discharge showed that most of the patients stayed to home self-care after they discharged from the hospital, followed by short term

hospital transfer and home health care. An average Length of stay for Hepatitis C patient for the entire period of analysis was around 5.73 days to 6.01 days each year. Trauma center charged most to Hepatitis C patient throughout the entire period of the analysis as compared to Elective, Urgent and emergency treatment centers. Cirrhosis shows the highest number of deaths in the hospital followed by Hepatitis C. Number of patients die of Hepatitis C is highest for age group 52 to 65 years. Biopsy Procedure is performed highest followed by Liver Transplant and Destruction of tissue throughout the entire period of the analysis. The highest number of biopsy procedures was performed for Cirrhosis patients followed by Chronic Liver disease and then Hepatitis C. The cost of Liver Transplant remained the most expensive procedure followed by Repair of Liver and Removal of Lobe throughout year 2007-2012. The results of the analysis help to determine national estimates of incidence, prevalence inpatient mortality, morbidity, severity of illness, reference for resources allocation, hospital utilization, and policy changes related treatment of Hepatitis C Virus and other liver diseases.

For the 2nd part, a new Clinical Decision Support System (CDSS) was developed using Exsys Corvid for expert analysis. CDSS is algorithmic method of data analysis to help healthcare providers make decision, improve diagnostic probabilities, patient care and reduce overall treatment expenses. Clinical Decision Support System was successfully developed for Hepatitis C diagnostics. This CDSS is medically accurate and can guide healthcare professionals through the diagnostic process. Corvid Exsys rule-based system is used for building automated expert systems. The software utilizes backward and forward chaining technique. Selected variables had been entered in decision making flow to get the final diagnosis outcome of the analysis.

The analysis is performed using Corvid Exsys software and the following variables were used in the analysis: Patient Age, Duration of disease, blood Transfusion year, Disease Symptom, liver related diseases, blood-borne reason for hepatitis, potential reason of disease by drugs, hepatitis due to other diseases and Test Performed.

Input variables: Age- “numeric”, Blood Transfusion- “More or equal to 15 years” or “Less than 15 years”, Disease symptoms- Static list with values “fatigue, weight loss, Joint/Belly pain, loss of appetite, dark urine, itchy skin/sour muscle, abdominal swelling, fever, nausea, fluid retention, confusion, jaundice, and metabolic problem.”

The symptoms include Hepatitis Free, Hepatitis Present or Inconclusive results. Confidence variable decides if hepatitis is present or not or more detailed test was needed. All the questions asked by the system during the diagnosis process are based on the clinical literature. The system can guide a clinician through the diagnostic process to achieve hepatitis results and decision-making expert system was successfully developed.

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CHAPTER I – INTRODUCTION

1.1 Introduction

Diagnosing, analyzing, and managing a disease is very challenging component in the medical field. Hepatitis is one of the many diseases which are very difficult to diagnose due to the fact that most people don't have symptoms, despite they are infected with it for a while. The hepatitis C virus (HCV) infection is often associated with chronic liver disease including fibrosis, cirrhosis and liver cancer, liver transplant, and liver failure. HCV establishes chronic infections in 71 million people of the world's population and 3.5 million people in the US [1].

Hepatitis C is a disease caused by a virus that infects the liver. Over time, it could lead to fibrosis – is the beginning stage of liver scarring, cirrhosis, hepatocellular carcinoma, liver cancer, liver transplant and liver failure. In fact, many people don't even know that they have hepatitis C until they have some liver damage. This can take many years. Most people who are infected with this virus could develop long-term or another name is chronic hepatitis C. People who get hepatitis C for a short time and then get better, is called to have an acute hepatitis C.

HCV is classified in the Hepaciviral genus of the Flaviviridae family. Patients with this disease are more likely suffer from fatigue and depression, jaundice, loss of appetite (anorexia), weight loss, pain in the upper part of the abdomen, fever, nausea, vomiting, dark Urine, pale stool, skin rashes, joint pains (Polyarthritis), muscle pain, malaise (feeling of being sick), swelling of the legs (edema) and swelling of the abdominal (ascites) these occur if there is a liver failure; Early and precise diagnosis, analysis, and management of virus is very important step to reduce the mortality, morbidity and inconvenience to the

patient. Health care costs are increasing with illnesses. As a society we need to shift our focus to preventive care. An annual Healthcare spending in America is 2 trillion dollars [2]. More than 75 percent of this cost is spending on over all chronic illnesses including hepatitis [3]. One would think about taking the help of technology to reduce the overall cost. Clinical Decision Support Systems (CDSS) have been proposed and are one of the best alternatives to reduce cost of the treatment, avoid misdiagnosis, and mismanagement. CDSS has been shown over the time as improved care for illnesses by providing reminders and alerts for best practices and guideline at the right time [2].

Clinical decision support (CDSS) systems provide clinicians, staff, patients, and providers with knowledge and person-specific information, intelligently filtered and presented at appropriate times, to enhance treatment options and cost of treatment. The Institute of Medicine has long recognized problems with health care quality in the United States for more than a decade. It has advocated using health information technology (IT) which includes electronic CDS, to improve quality of service and time to cure of critical diseases.

A properly-designed CDSS is an interactive software-based system intended to help decision makers compile useful information from raw data, documents, personal knowledge and/or business models to identify and solve problems and make decisions. CDSS belong to an environment with multidisciplinary foundations, including database research, artificial intelligence, human computer interaction, simulation methods, software engineering and telecommunication.

Decision support systems constitute a class of computer-based information systems including knowledge-based systems that support decision making activities. Making the

right decision in business is usually based on the data quality and the ability to shift through and analyze the data to find trends that can create strategies resulting in optimal solution to complex problem. Decision support systems are created to help people make decisions by providing access to information and analysis tools. It is a way to model data and make quality decisions based on it.

The function of clinical decision support systems is to analyze and process the data that is collected over a period of time and makes decisions based on some analysis. An active decision support system actually processes data and explicitly shows solutions based upon that data. A cooperative decision support system is when data is collected, analyzed and then is provided to a human component which helps the system revise or refine it. It means that both a human component and computer component work together to come up with the best solution.

The best way to reduce the mortality rate, misdiagnosis and mismanagement of Hepatitis C virus, it is suggested the use of clinical decision support system (CDSS). With the help of CDSS one can diagnose hepatitis at the early stage and reduce treatment cost and time. CDSS will be used as a risk assessment tool to alert the risk levels for hepatitis. Recognizing the symptoms and alarming with the risk factors will further help in the diagnosis and treatment options.

Clinical decision support system also helps us in fulfilling protocols set for the healthcare system improvement [4], known as "S-T-E-E-E-P" goals

- Safety (reducing medical injuries to patients);
- Timeliness (reducing waits and delays);
- Effectiveness (increasing the reliability of evidence-based care);

- Efficiency (reducing the cost and care);
- Equity (closing racial and social economic gaps in health status);
- Patient centeredness (giving patients competence in self-management) [5].

The presence of ineffectiveness and inefficiency in service is a very serious obstacle for better health, which CDSS will help us to overcome these obstacles [6].

1.2 Significance of the Research Study

Hepatitis C virus (HCV) is a viral infection that attacks the liver. The virus can cause both acute and chronic hepatitis. HCV acute stage is asymptomatic; few people are diagnosed during the acute phase. In those people who develop chronic HCV infection, the infection is also often undiagnosed because the infection remains asymptomatic until decades after infection when symptoms develop secondary to serious liver damage. Chronic HCV leads to fibrosis, cirrhosis, hepatocellular carcinoma, liver cancer, liver transplant and liver failure.

Hepatitis C virus (HCV) is a blood-borne virus. Most people get infected by injecting drug or reuse of medical equipment, especially syringes and needles in healthcare settings; the transfusion of unscreened blood and blood products; sexually transmission; infected mother to child during birth. Globally an estimated 71 million people have chronic hepatitis C infection and approximately 399,000 people die each year from Hepatitis C virus, mostly from cirrhosis and hepatocellular carcinoma [7]. In the United States approximately 3.5 million people have chronic hepatitis C virus infection and about 19,000 of these people die each year from cirrhosis or liver cancer [8].

HCV treatment is improving, but more improvement is needed. In 2015, of the 71 million persons living with HCV infection globally, 20% (14 million) knew their diagnosis.

7.4% of those diagnosed (1.1 million) were started on treatment in 2015. In 2016, 1.76 million people were additionally treated in bringing the global coverage of hepatitis C curative treatment to 13%. Much more needs to be done in order for the world to achieve the 80% treatment target by 2030 [7].

In 2011, the annual economic burden associate with chronic HCV infection in the US was $6.5 billion dollars and it will peak in 2024 at $9.1 billion dollars. The lifetime cost of an individual infected with HCV in 2011 was estimated at $64,490 [9].

Medicine is quite expensive. The table 1 below highlights the average cost of treatment for one person the combination Direct-acting antivirals (DAAs) currently available. Most of these drugs take at least 12 weeks to cure HCV, while the most recently approved drug Mavyret takes 8 weeks to cure. Most of these individual drugs are effective for specific strains, or genotypes, of HCV. However, some newer combination medications, which contain two or more drugs, work for all genotypes. DAAs may be used alone or, very often, in combination with other drugs. Most are available in pill form. Typically, these pills have far fewer side effects than previous treatment options.

Generic Name	Brand Name	Manufacturer	Date of FDA Approval	Approximate cost for 12 week Therapy	approximate cost for 8-week therapy
Glecaprevir/pibrentasvir	Mavyet	Abbvie Inc.	8/17	NA	$26,400
Elbasvir/grazoprevir	Zepatier	Merck Sharp & Dohme	1/16	$55,700	
Sofosbuvir/Velpatasvir	Epclusa	Gilead Sciences, Inc.	6/16	$75,000	
sofosbuvir/Velpatas/vir/voxilaprevir	Vosevi	Gilead Sciences, Inc.	7/17	$75,600	
Ombitasvir/paritaprevir/ritonavir	Technivie	Abbvie Inc.	7/15	$78,100	
Dasabuvir/ombitasvir/paritaprevir/ritonav	Viekira Pak	Abbvie Inc.	12/14	$83,300	
Ledlpascir/sofosbuvir	Harvoni	Gilead Sciences, Inc.	10/14	$94,800	

Figure 1.1: Average cost of treatment per person for different years [8].

Many researches and reports have shown evidence that chronic hepatitis c virus has high infection rate and very high treatment cost. People who end up with cirrhosis or liver cancer have to be on medication throughout their lives, which also means even higher cost. Because HCV is asymptomatic, lack of symptoms during the early stage creates a challenge for early detection too. Symptoms are often presented during the advance stage of the virus; sometimes light symptoms like feeling nausea, poor appetite or weight loss can be easily mistaken for a non-life-threatening illness and result could end up with misdiagnose or delay in diagnosis.

Catching the HCV infection at a very early stage that can bring down or eliminate the cost of treatment. People who are at high risk test them regularly and give them high priority for treatment so that they do not end up with lifelong diseases. A method for early diagnosis is crucial, hence the significance of this study. Clinical decision support System

(CDSS) comes into the picture. The CDSS is to identify the risk levels of the individuals and to point them in the direction of screening to eliminate chronic diseases. The ultimate goal is to discover the disease sooner than later.

1.3 Background of the problem

Diagnosing, analyzing and managing hepatitis is an important task for physicians. In order to supply a complete therapy to a patient, a correct diagnosis is not enough. For clinicians, one of the most important works in the health examinations is to interpret the health examination results. Manually interpreting numerous health examination results is complex and error-prone. The diagnosis is subjective at times and error prone because of this a delay can be generated. A health examiner not only provides useful information for early diagnosis of diseases but also supplies the recommendation for self-health management.

Both clinicians and health examiner receive benefit by the comprehensive health examination results. A detailed health examination package may compose of multiple examination items such as physical examinations, histories of laboratory tests, radiological studies, endoscopies and others. For clinicians, one of the most important works is to generate a comprehensive report after interpreting the health examination results. The results gathered from distributed sources have to be simultaneously and entirely interpreted to get the whole picture of health conditions. The manual interpretation of multiple examination items is complex and error-prone [10]. Computer based decisions can make diagnosis easy, robust and consistent. Also, it reduces errors.

The Institute of Medicine has long recognized problems with health care quality in the United States. It took some time to adopt clinical decision support system (CDSS), to

improve quality since 2004. The Federal Government promoted the importance of electronic medical records (EMRs). There has been a slow but increasing adoption of health IT [11]. A working definition has been proposed by Dr. Robert Hayward of the Centre for Health Evidence; "Clinical Decision Support Systems link health observations with health knowledge to influence health choices by clinicians for improved health care". This statement has simplified Clinical Decision Support to a functional concept. It is a major topic of artificial intelligence in medicine. Further, although EMRs with computerized provider order entry (CPOE) can improve accessibility and legibility of information, it is unlikely that there will be major improvements in the quality and cost of care from the use of health IT without proper implementation and use of CDSS.

The most common use of CDSS is for addressing clinical needs, such as ensuring accurate diagnoses, screening in a timely manner for preventable diseases, or spotting adverse drug events (ADE) [12]. CDSS can also lower costs, improve efficiencies and reduce patient inconveniences. CDSS can address all of these areas simultaneously—for example, by alerting clinicians to potentially duplicative testing.

For more complex cognitive tasks, such as diagnostic decision making, the aim of CDSS is to assist, rather than to replace the clinician. The new methodology of using CDSS to assist forces the clinician to interact with the CDSS utilizing both the clinician's knowledge and the CDSS to make a better analysis of the patients' data than either human or CDSS could make on their own.

Typically, the CDSS would make suggestions of outputs or a set of outputs for the clinician to look through and the clinician officially picks useful information. There is growing recognition that CDS, when well-designed and implemented, holds great potential

to improve health care quality and possibly even increase efficiency and reduce health care costs.

Real challenge is to configure the proposed Clinical decision support system to get the best result for the optimal and accurate care. Ultimately, we are trying to use CDSS to identify the Hepatitis C virus sooner than later.

Many researchers have used the knowledge-based systems and collective intelligence methods to provide computer-assistance and decision support for the medical field. These "intelligent and expert" system all of them supply the same principal to develop flexibility and the possibility to reuse the knowledge over and over again [13-17].

1.4 Objectives and Goals of the study

The objective of this research has been divided into two parts. The part - I is data analysis and knowledge discovery of hepatitis and liver diseases. The part – II is design and develop a Clinical Decision Support System for Hepatitis C. The research examines the trends and analyzes a number of records for patients with Hepatitis C virus and liver diseases from the year 2007 to 2012. Data was taken from the National Inpatient Sample (NIS), which is part of the Healthcare Cost and Utilization Project (HCUP). HCUP is associated with the Agency for Healthcare Research and Quality (AHRQ). HCUP brings together the data from State data organizations and hospital associations.

Data for hepatitis and liver diseases have been analyzed. The following categories have been used: Patient with the length of stay, total charges of treatment, how many died in the hospital, their Income status, age, race, gender, sex, location after the discharge, hospital location, hospital region, the payment methods, admission type,

admission source and procedures performed on these patients, mortality rate and morbidity rate of Hepatitis C and other liver diseases.

The purpose of selecting Hepatitis A, B, C, D, E, Hepatitis Carrier, Cirrhosis, Chronic hepatitis, Chronic Liver Disease, Disorder of Liver, Hepatocellular Carcinoma (HCC), Procedures performed and procedure cost on these diseases is to compare Hepatitis C with other liver diseases, which is very crucial for the study to determine various impact.

Although it is well understood that hospitalization cost is a large portion of the total medical cost, the hospitalization cost for patients with Hepatitis C and other liver diseases have not been thoroughly examined by various researchers. The research includes this critical factor along with understanding the impact of Hepatitis C Virus and other liver diseases has on total charges of treatment, length of stay, total charges of procedure. This large sample size data allows analyzing at a large national scale, nothing has been published to view Hepatitis C in a much broader way with other liver diseases. This study will help to fill the literature gap by providing the results. These results help to shed light on healthcare cost because patients that are discharged to other facilities such as skilled nursing or short-term hospitals are likely to incur additional cost and impose more substantial care burdens on the healthcare system when compared with a patient that discharges routinely.

The main objectives of the study include:

(i) Understand the impact of other variables such as patients died in the hospital, income level status, hospital location, hospital region, age, race, gender, location after the discharge, the payment methods, admission type, and admission source;

(ii) Identify mortality, morbidity rate among Hepatitis and liver disease patients;

(iii) Analyze the charges of the Procedure for the Hepatitis C and other liver diseases;

(iv) Identify if there is a difference in the length of stay for patients with Hepatitis and other liver diseases;

(v) Analyze the hospital charges of Hepatitis C and Other Liver diseases.

The other part of the objective is to design and develop a Clinical Decision Support System for Hepatitis C. The CDSS was developed using the software Exsys Corvid version 6.1.0. It uses Java applets, allowing flexibility for the user. It is designed so it can be accessed from any location and any device that can connect to the Internet using a web browser. Exsys Corvid directly delivers knowledge as opposed to information [18].

One of the major areas of medical error is the improper administration of a disease. Medical errors are globalized disasters over the past decade. Every day so many patients suffer and even die of different types of misdiagnose. According to the study conducted by the Institute of Medicine (2006), around 1.5 million people are injured and 7,000 died each year in the United States because of misdiagnose [19].

The main objective of this research is to develop a Clinical Decision Support System (CDSS). The key objectives are summarized below:

(i) Create rules for diagnosis of the hepatitis. Find the differences in hepatitis A, hepatitis B and hepatitis C. The system will develop particularly for hepatitis C.

(ii) Develop a Clinical Decision Support System for Diagnosing, analyzing and managing hepatitis.

(iii) Develop Corvid Expert System frame work to create a rule-based CDSS. Knowledge base of the system will be developed using rules. These rules will be obtained by the practicing experts in their field, from evidence-based guidelines, and from knowledge-base.

(iv) The rules will base on forward and backward chaining.

(v) Design the system in a way that it can be scaled by adding new and more rules to the knowledge base. With time new knowledge must be included into the rule base. Corvid framework helps on adding new variables, rules and logic blocks at any point and time to expand the application.

(vi) Patient management for monitoring the state of treatment to do accurate diagnosis of various hepatitis (A, B and C particularly).

(vii) Develop a systematic approach for CDSS to do proper diagnosis and monitoring patients.

(viii) System to develop a program and configure it for an earlier diagnosis of Hepatitis.

(ix) To minimize the medical errors in diagnosing, analyzing and during the treatment process of hepatitis. In addition, it also improves treatment outcome, saves time and cost.

(x) Friendly user interface, fast and easy to use and which provides up-to-date information at the point -of-care.

Clinical Decision Support System can evaluate several considerations that are compulsory to make the right decisions. System makes sure that all the important criteria are evaluated before a treatment plan is recommended. CDSS will ask questions to the user about patient's age, gender and symptoms, medical records, lifestyle factors, family history and utilize this information by built-in-knowledge, clinical evidence and facts and a set of logic rules to calculate /analyze the answers before generating the overall risk factor score and or suggesting a course of action to the user.

The proposed CDSS will be an interactive system that can be launched from any place. This system can also be used for training purposes for undergraduate students or inexperience clinicians or in a classroom scenario. System can be launched remotely through interactive login that will enable students to learn at their own pace and at their own time.

1.5 Research Hypothesis

The research hypothesis has been divided into two parts. First part is data analysis and knowledge discovery of hepatitis and liver diseases. The second part is to design and develop a Clinical Decision Support System for Hepatitis C.

This data analysis methodology can be utilized by the general public and healthcare providers to achieve the following:

Hypothesis 1: Find the correlation between mortality and morbidity among the following categories age, gender, race, payment methods, died during hospital stay,

Income-Level, admission type, admission source, hospital region, hospital location, and destination after discharge. These criteria will be investigated. **Expectation** is mortality to be higher with older, low income, black male population. Fewer patients to die in hospital stay.

Hypothesis 2: To examine the association between the Hepatitis & liver diseases and Length of stay. **Assumption** is hepatitis cause liver disease or they are closely related. More severe the condition of patient, longer time patient to say in the hospital.

Hypothesis 3: To determine the Cost of procedures with age group. **Expectation** is older patient should have higher cost of procedure.

Hypothesis 4: To examine the association between the Hepatitis & Liver diseases and total charges of treatment. **Assumption** is they are closely related. Sever the symptom, higher the cost of treatment.

The other part is to design and develop a Clinical Decision Support System for Hepatitis C. Clinical Decision support System is about storing, codifying and modeling the human expertise and knowledge into processing rules and logic for further problem solving. Thus, knowledge asset is the heart of Decision Support System [20].

Hypothesis 5: Develop CDSS for faster detection and treatment options. **Expectation** is to implement best possible statistical model for HCV detection and treatment.

Hypothesis 6: Develop methodologies for early diagnosis of hepatitis – focus on HCV. **Expectation** is to detect early and treat early – reduce overall cost and avoid become chronic.

Hypothesis 7: Build medical information and knowledge base. **Assumption** is to help faster and cost-effective treatment using the knowledge base, which will help faster detection and treatment.

Hypothesis 8: Eliminate the diagnosis errors and have a better patient management. **Expectation** CDSS is implemented for efficient diagnostics and patient management.

Hypothesis 9: Develop CDSS for faster detection and treatment options. **Expectation** is to implement rules-based knowledge management system for clinicians, existing literature, and evidence-based guidelines.

1.6 Thesis Outline

This thesis is composed of six chapters. Chapter 1 provides the background and motive of this research. An academic review which identifies the level of understanding and degree of knowledge acquisition and modeling in Clinical Decision support System. In Chapter 2. Furthermore, the knowledge of Liver, Hepatitis, Liver diseases, and Clinical Decision Support system. In CDSS its existing practices in medical diagnosis of Hepatitis C Virus, and technologies and techniques for such decision support are also discussed. In chapter 3, the research methodology for the Hepatitis, Liver diseases and Clinical Decision Support system is presented. In chapter 4 discusses a detail results of the descriptive statistical analysis. The results from the analysis provides an overall summary of the study. This analysis helps to identify hospitalization outcome, procedure performed, procedure cost, total charges and admission type, disposition and mortality, morbidity and incidence of various types of hepatitis and liver diseases. A variety of statistical analysis was performed based on the NIS data for 2007 to 2012. In chapter 5

Corvid Exsys rule-based system is used for building automated expert systems. It is the bridge between rules that people can read and understand, and rules that the computer can use effectively. The system is based on historical data and clinical diagnosis methods. Corvid systems software is use for clinical decision support system development. Finally, a conclusion is drawn in chapter 6 to summarize this research study and some suggestions for further study are also discussed.

CHAPTER II – HEPATITIS AND BASICS OF CDSS

2.1 Introduction

This chapter discusses an overview of the liver, its function, its diseases, different types of hepatitis and Clinical Decision Support System. Hepatitis like Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D and Hepatitis E, its mortality rate, morbidity, complications it can cause to the liver, causes of Hepatitis, risk factors, immunization, control and who should be tested for Hepatitis.

In the United States the most common viruses are HAV, HBV and HCV. All three of these independent viruses can produce acute illness and are asymptomatic. HBV, HCV or (HBV and HDV) together can be a chronic disease that remains asymptomatic that is the reason people infected with HBV, HCV or coinfected (HBV and HDV) are unaware that they are infected. This silent infection can remain in the blood for decades and continue to damage the liver [21]. Lack of symptoms early in the disease creates problem [22].

Symptoms shows up during the advanced stage of the disease usually 65% of cases are asymptomatic, few adults might feel light symptoms [23,24]. Most of the symptoms can be easily mistaken for a non-life-threatening illness like weight loss and poor appetite or abdominal pain, fatigue, fever, nausea, but the initial belief may be of something minor. The patient might ignore the signs for a while or go for medical checkup later rather than immediately; perhaps, because the initial symptoms are manageable and mostly associated with other minor health issues. Other reason can be a concern of being thought of being over reacting especially if after getting medical attention it turns out to be nothing serious [22].

Chronic hepatitis B virus (HBV) and Hepatitis C virus (HCV) is the most common cause of chronic liver disease that can lead to liver fibrosis, liver cirrhosis, liver cancer (hepatocellular carcinoma), liver transplant, and liver failure [25]. Delay in the treatment of chronic hepatitis causes severe liver damage or cirrhosis; before you receive hepatitis treatment, you will continue to have an increased chance of liver cancer even after treatment [26]. Advanced fibrosis and cirrhosis support a role for severe inflammatory responses in the development of hepatocellular carcinoma (HCC) [25].

Globally an estimated 130–150 million people live with hepatitis C virus [27]. A significant number of people with HCV will progress to chronic disease, hepatocellular carcinoma, and death [27]. Estimated 75% of acute HCV infections become chronic virus and chronic HCV infection increases the risk of liver disease [28]. Approximately 80 million people live with chronic HCV infection, and in 2013 an estimated 700,000 people died from HCV. More than 80% of the HCV burden is in low- and middle-income countries. Since there is no vaccine for HCV, prevention strategies rely on limiting exposure to the virus [27].

It is estimated that 1.47 million will develop liver cirrhosis, 350,000 will develop liver cancer, and almost 900,000 will die from HCV-related complications. HCV infected patients puts intense burden on healthcare resources in the United States. Between the years 2001through 2010, HCV infected individuals accounted for almost 3 million outpatient, inpatient, and emergency department visits in the United States [28].

In the world, liver cancer remains the third most frequent cause of cancer-related deaths and the fifth most common cancer [29]. Diagnosis and treatment of Hepatitis B and

Hepatitis C disease depends on the Fibrosis Stage which could be from F0-no damage to F4-cirrhosis [30].

Patients with cirrhosis needs complex treatment, medications and hospitalization that leads to an overall annual cost of over $2.5 billion in the United States alone [31].

For year 2011 an estimated cost of treatment for Hepatitis was $ 6.5 billion dollars, by 2024 it will reach to $ 9.1 billion dollars. This cost is for approximately 8 to 12 weeks therapy only [8]. In 2007, mortality from HCV infection surpassed human immunodeficiency virus (HIV) [28].

A clinical decision support system is a health information technology system. The main purpose of CDSS is to assist physicians, clinicians and other health professional to analyze and reach a diagnosis based on patient data [2]. Corvid provides an environment for web-enabled knowledge automation Expert System for decision-making problems. Corvid allows the logical rules like If Then Else statements to make a decision as logical rules are easy to create, read, understand and maintain to produce diagnosis, recommendations and advice [18].

2.2 Basics of Hepatitis

In Greek, the word Hepato means “liver,” while “itis” means “inflammation.” Hence, “hepatitis” deals with the inflammation of the liver [32]. Liver weights around three pounds. Blood is constantly flowing through this organ to process useful nutrients and to get rid of toxins. Liver performs more than 500 functions that make our body work properly. Liver’s job is to manufacture proteins, storing certain vitamins, iron and other minerals and sugar; it regulates the transport of fat stores and controls the production and

excretion of cholesterol. Liver also regulates blood clotting, producing bile essential to the proper digestion of food (fat) in the small intestine [33].

Liver purifies the blood by neutralizing and destroying poisonous substances out of the body, it metabolizes alcohol and other drugs. In addition, liver maintains hormone balance, it forms blood before birth, protects the body from infection by producing immune factors and removing bacteria from the blood stream, above all it regenerates its own damaged tissue [33]. Anything that makes liver inflamed is called hepatitis [33].

Liver can get hepatitis inflammation by toxic matter and viruses [33]. Viral hepatitis signals those infections whose main tissue tropism is the liver. There are five distinct viruses like that [34]; which are known as Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, and Hepatitis E. So, one can conclude that Hepatitis deals with deterioration of liver cells caused by contaminated water, feces, sharing used needles, illegal drugs, alcohol, smoking and other chemical compounds.

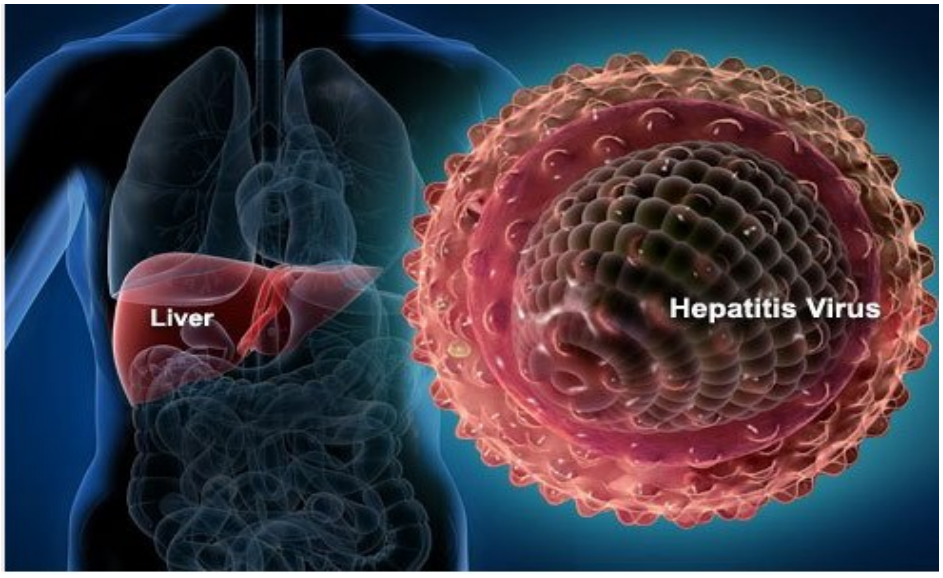

Figure 2.1: Image of liver and hepatitis virus in the human body [35].

2.2.1 Hepatitis A

HAV is the least dangerous of all viral forms of hepatitis. Hepatitis A virus is an infection of the liver. It inflames the liver. This virus is asymptomatic in few cases HAV shows some symptoms. HAV remains in acute stage and it heals itself. It is spread through oral contact with feces, contaminated food and infected drinking water/ swimming pool water [36,37]. Hepatitis A virus is a vaccine-preventable virus of the liver caused by hepatitis A virus (HAV).

Globally there are an estimated 1.4 million cases of HAV every year [38]. Figure 2.2 shows the incidence of hepatitis A in the United States of America from 2006 to 2016. As shown in the graph in the year 2006 there were 3,579 incidences and in the year 2016 there were 2,007 incidences. HAV incidences have gone down that shows that the prevention with vaccine is working. But, still numbers of incidence are too high.

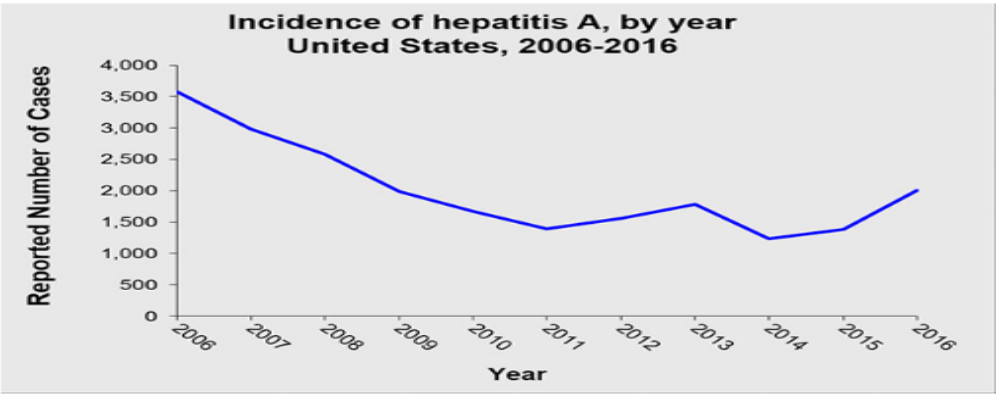

Figure 2.2: Incidence of hepatitis A in the US from 2006 to 2016 [39].

Hepatitis, A virus is a small non-envelop and has a single strand of RNA- a chemical containing the virus's genes, or the blueprint for reproducing new virus to

multiply [39, 40]. Hepatitis A virus replicates inside the hepatocytes and interferes with liver function. This leads to an immune response, thus leading to liver inflammation.

In HAV 50-70% of cases will show mild symptoms like nausea, vomiting, malaise, and diarrhea; 30-50% of pediatric cases will show fever and dark urine [36]. Approximately 75% of infected adults will develop fever, Jaundice (yellow of the eyes and skin), dark urine, and pain in the belly, loss of appetite, Nausea, diarrhea, and fatigue [36,37].

Hepatitis A virus signs and symptoms last for less than 2 months, in some cases 10-15% of cases could last up to 6 months [41]. Hepatitis A virus can be spread about two weeks before the symptoms appear and during the first week of symptoms show up. HAV is not spread by casual contact in the office, school, or factory, but it is spread by drinking water/ice and foods contaminated by infected feces or through contact with infected water in swimming pools. Circulation of HAV occurs with household contact within families and by sexual contact. A household contact comes through the direct touching with the feces, for example changing infant's diaper [39] or preparing food by an individual who was contaminated with HAV and did not wash their hands after using the bathroom [42]. Indirect way of transmission of HAV is by eating shell fish that grew in water contaminated with sewage, [43,44] or eating strawberries that were picked up by the farmer who may have been infected with HAV [45,46]. Hepatitis A can also be transmitted by men who have sex with men- oral-anal sexual encounter played a major role in transmission of this virus [47,48,49]. Using contaminated water and shared equipment or drugs in injection drug users for intravenous drug use and close personal contact with a person who is infected with the virus, international travelers- who were staying with overly crowded living conditions, and or poor sanitation.

Humans are the only host for hepatitis A. During the initial period the virus is present in blood and excreted via the biliary system-is a fluid made by the liver to helps digest fat, and releases it into the small intestine into the feces. As viral replication begins to wane, symptoms begin to appear [50].

There is no treatment for hepatitis A virus. Once you get it just make yourself comfortable, get enough rest, hydration and nutrition. Let the illness run its course. The patient should be educated to avoid hepatotoxins such as alcohol and acetaminophen. But once it goes away, you are immune. Better hygiene and proper sanitation have reduced rates of HAV in United States. To control and to prevent spreading hepatitis A virus relies heavily on clean environment and personal hygiene [43,51]. The best way to prevent hepatitis A virus is also to get vaccinated.

There are 2 Hepatitis A vaccines that are licensed in the United States of America. After giving 2 doses of Hepatitis A vaccine, the protection power was 94% as measured by the presence of anti-HAV, protection power increases to 99% after getting 1-year booster [52].

2.2.2 Hepatitis B

Hepatitis B virus (HBV) infection is a very serious global public health problem. Hepatitis B is a potentially life-threatening liver infection. It can cause chronic infection and puts people at high risk of death from cirrhosis and liver cancer. It is estimated for 257 million people are living with hepatitis B virus infection worldwide [38]. In the year 2015 it was reported that there were 887,000 deaths, mostly from complications with liver-like cirrhosis and hepatocellular carcinoma (HCC) worldwide [1]. HBV is one of the

most common chronic infections, and the leading cause for hepatocellular carcinoma (HCC) worldwide [53]. Patients with HBV 10-20% of them develops Hepatocellular carcinoma [54]. Chronic hepatitis B (CHB) is associated with high mortality 15–40% in 10–25 years [55], with about 880,000 deaths per year due to complications of chronic hepatitis B virus (WHO 2017).

Approximately 20-30% of adult individuals with chronic hepatitis B infections will develop progressive liver disease, including cirrhosis, liver cancer, and liver failure [38]. Less than 5% of otherwise healthy persons who are infected as adults will develop chronic infection. 90% of infants infected during birth will develop chronic Hepatitis B virus and 30-50% of children infected before the age of 6 years will develop chronic infections [38,56].

Figure 3 shows the condition of the liver with chronic hepatitis, cirrhosis and hepatocellular carcinoma.

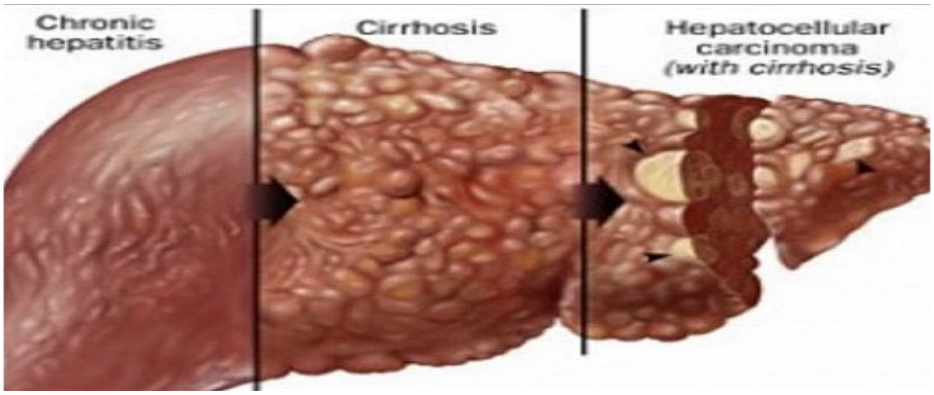

Figure 2.3: Liver with Chronic Hepatitis [57].

Hepatitis B virus is transmitted through parenteral- something that located outside the digestive tract for example injection of drugs, blood transfusion, organ transplant, medical, surgical and dental procedures, acupuncture, sharing of tooth brush or razors, needle piercing such as use of needles in the hospitals or through tattoos, drug abusers

through sharing of needles and syringes either in health care or individual who inject drugs. Other ways of transmission are sexual intercourse, particularly in unvaccinated men who have sex with men and heterosexual persons with multiple sex partners or contact with sex workers, semen, saliva, menstrual, vaginal cervical secretions; and perinatal-immediately before and after birth [40,83,84]. Hepatitis B virus can be transmitted to other individuals regardless of the symptoms are present or not [85].

Transmission of Hepatitis B from mother to a child occurs at the time of delivery of the baby when it comes in contact with the mother's blood. Infection can occur while the baby is in the womb and as pregnancy progresses so are the chances of hepatitis infection increases too. Infected mothers who are breastfeeding their babies cannot transmit the infection unless the nipples are cracked and bleeding. Mothers who go through the treatment of Hepatitis B virus should not breastfeed the child at the same time [38]. Figure 4 shows how people get infected by HBV including infants.

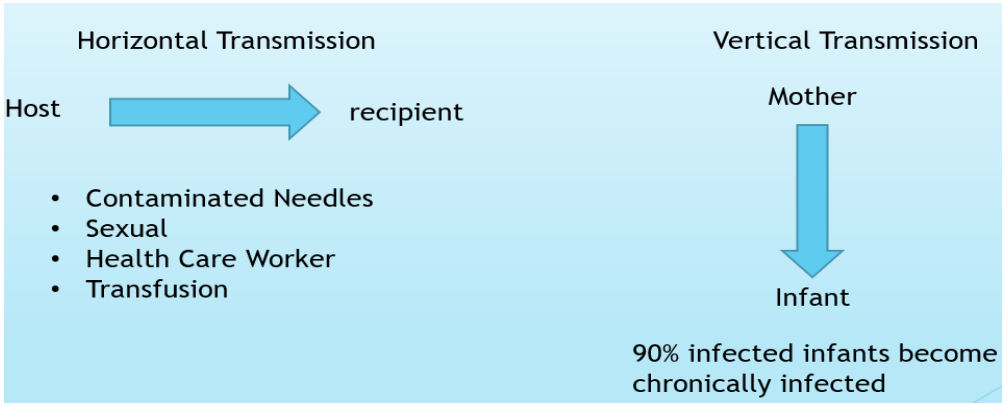

Figure 2.4: Transmission of HBV [57].

Hepatitis B virus cannot be spread by coughing, hugging, holding hands, using the same dishes or eating food together. Kissing does not transmit HBV unless

the saliva is contaminated with blood. Hepatitis B virus can only be spread when blood comes in contact with the blood of an infected person [43-46].

The incubation period of the hepatitis B virus is from 30 days to 180 days. The virus may be detected within thirty to sixty days. The hepatitis B virus can be acute infection or chronic infections. Its initial stage of infection, which lasts from two months to four months, but no more than six months, this short-term is called acute stage. Hepatitis B virus which lasts more than six months is consider chronic HBV or long-term infection [23].

Acute Hepatitis B is not treated with medications. Normally the disease will heal itself in 4 to 8 weeks period. Getting lots of rest, eat a fat-free diet, and prohibit from drinking alcohol or taking drugs, these precautions will help heal HBV faster. If the virus has been in the blood for more than 6 months, it is considered a permanent (or chronic) hepatitis B infection. Chronic hepatitis B, if left untreated, can cause serious liver injury and increases the chance of liver cancer.

Patients with chronic hepatitis B virus may be asymptomatic for several years before showing any signs of infection [58]; usually 65% of cases are asymptomatic, few adults might feel light symptoms [23,24]. If symptoms do appear, they will start showing after two to three months after the exposure to the hepatitis B virus had happened; these symptoms will last from two weeks to several months [58]. Symptoms are jaundice, fatigue, loss of appetite, weight loss, pain in the upper part of the abdomen, fever, nausea, vomiting, dark urine, pale stool, skin rashes, joint pain, malaise, swelling of legs and muscle pain.

The fatality rate is high among sixty years and older individuals. Some patients who are chronically infected with HBV may eventually suffer from different diseases like cirrhosis, fibrosis and hepatocellular carcinoma (HCC) [59]. Chronically infected patients have 100-time higher risk of HCC than noncarrier [60]. Each year millions of people die due to HBV-induced diseases [61].

In endemic areas HBV is often receive by vertical and horizontal transmission with the chronicity rate of more than 90%, while in areas of low prevalence for example high income countries, it is usually transmitted horizontally especially sexual and parenteral route with the chronicity rate of more than 90% of acute infection [62]. Parenteral route means- something that located outside the digestive tract for example injection of drugs, blood transfusion, organ transplant, medical, surgical and dental procedures, acupuncture, sharing of tooth brush or razors, needle piercing such as use of needles in the hospitals or through tattoos, drug abusers through sharing of needles and syringes either in health care or individual who inject drugs. Other ways of transmission are sexual intercourse, particularly in unvaccinated men who have sex with men and heterosexual persons with multiple sex partners or contact with sex workers, semen, saliva, menstrual, vaginal cervical secretions; and perinatal-immediately before and after birth [38,63,64]. Hepatitis B virus can be transmitted to other individuals regardless of the symptoms are present or not [65].

The term Occult HBV (O-HBV), this means HBV reactivation toward advanced liver fibrosis and cirrhosis, and hepatocellular carcinoma is possible. Patients with immune suppression due to chemotherapy, organ transplantation, corticosteroids and uncontrolled HIV infection can lead to reactivation of HBV [66,67].

HBV can cause HCC in the absence of cirrhosis in 0.1% per year. The family history of HCC and metabolic syndrome are risk factors for HCC development in the absence of cirrhosis [25]. However, 70% - 90% of cases HCC develops in cirrhotic livers [68]. It is known that HBV infection and HCC have similar geographical distribution--as many as 85% of HCC cases are found in endemic HBV population, such as those in China or Africa [62].

Many factors increase the risk of HCC among HBV carriers and those risks are Demographic like male gender, older age, ethnicity, family history of HCC; Viral like high viral load, genotype, longer duration of infection, co-infection with HCV, HIV or Hepatitis D Virus (HDV); Clinical for example cirrhosis; Environmental like exposure to aflatoxin, heavy alcohol abuse or cigarette smoking [62].

HBV infection causes HCC despite the availability of a vaccine. Although global vaccination is available but, mother-to-child transmission is hard to prevent [25]. If mother is not vaccine or treated on time then, the child born from that mother must get the hepatitis. This is the reason treatment must start on time.

To diagnose and monitor hepatitis blood tests are available. The hepatitis B vaccine is the key part in prevention of HBV. In 1992 the WHO recommended implementation of universal childhood vaccination. In this program all infants receive the hepatitis B vaccine as soon as possible after birth. The birth dose should be followed by 2 or 3 doses to complete the primary series. All children and adolescents younger than 18 years and not previously vaccinated should receive the vaccine. The following group of people should also get vaccinated and they include [38]:

- People who frequently require blood or blood products, dialysis patients, recipients of solid organ transplantation;
- People interned in prisons;
- Persons who inject drugs;
- Household and sexual contacts of people with chronic HBV infection;
- People with multiple sexual partners;
- Healthcare workers and others who may be exposed to blood and blood products through their work;
- Travelers who have not completed their HB vaccination series

There is no specific treatment for acute hepatitis B; care is aimed at maintaining comfort and adequate nutritional balance, including intake of lot of fluids to replace liquids lost from vomiting.

For chronic hepatitis B treatment, a common approach is viral suppression. Treatment can slow the progression of cirrhosis, reduce incidence of liver cancer and improve long term survival. But the problem is with such treatment that it has to be continued for several years or even lifelong, because the risk of recurrence after discontinuation is very high; that is why current guidelines recommend therapy [69]. There is a risk for HBV rebound and reactivation after discontinuation of therapy, which might be higher among people who inject drugs with sudden inability to adhere to treatment [70]. Since reactivation can be very serious and fatal than the primary infection, antiviral treatment should be considered also for this reason [71].

Many people are diagnosed only when they already have advanced liver disease. Among the long-term complications of HBV infections, cirrhosis and hepatocellular carcinoma cause a large disease burden. Liver cancer progresses rapidly, and since treatment options are limited, the outcome is in general poor. In low-income settings, most people with liver cancer die within months of diagnosis. In high-income countries, surgery and chemotherapy treatment is buying them more time to live. Liver transplantation is sometimes used in people with cirrhosis in high income countries, with varying success [38].

The CDC [58] recommends routine hepatitis B screening for the following populations:

- person with behavioral exposures to HBV, such as injection drug users (IDU) and men who have sex with men (MSM);
- persons receiving immunosuppressive therapy (e.g., chemotherapy);
- persons with liver disease of unknown etiology
- donors of blood, plasma, organs, tissues, or semen;
- hemodialysis patients;
- pregnant women;
- infants born to HBsAg positive mothers;
- persons who are in occupations in which they are at increased risk for HBV exposure, such as health care and public safety workers;
- HIV-infected persons.

2.2.3 Hepatitis C

Hepatitis C is a liver disease caused by the hepatitis C virus. Hepatitis C virus is a viral infection that causes liver inflammation. This virus sometimes leads to a serious

liver damage. The hepatitis C virus (HCV) spreads through contaminated blood. Its symptoms are same as Hepatitis B virus.

The virus can be acute-short lived less than six months, or chronic- life long illness more than 6 months. HCV is asymptomatic in 80%. About 15-45% of infected persons clear the virus within 6 months without any treatment. The remaining 60-80% will develop chronic HCV infection. Of those with chronic HCV infection, the risk of cirrhosis of the liver is between 15–30% within 20 years. Worldwide in 2015, there were 1.75 million new HCV infections cases [72].

Hepatitis c virus is a blood-borne virus that infects the liver [28]. Most people who are infected with hepatitis C-even people who have been infected for a while-usually don't have symptoms. If symptoms do develop, they may include Fatigue; Joint pain; Belly pain; Itchy skin; Sore muscles; Dark urine; Jaundice (WHO 2018). Patients with Hepatitis C virus are more likely suffer from fatigue and depression than patients with liver disease of other etiology [73].

About 2.3 million people of the estimated 36.7 million living with HIV globally have serological evidence of past or present HCV infection. Among all HIV-infected persons, the prevalence of anti-HCV was 6.2%. Liver diseases represent a major cause of morbidity and mortality among persons living with HIV [72].

HCV is transmitted via parenteral routes-outside the digestive track. In industrialized countries via intravenous drug abuse or by invasive sexual practices and is rarely transmitted from mother to child. Transmission has been limited by improving hygienic standards.

It is commonly transmitted through parenteral routes:

- Injecting drug through the sharing of injection needle;
- The reuse of medical equipment, especially syringes and needles in healthcare settings;
- The transfusion of unscreened blood and blood products;
- Invasive sexually practices;
- Infected mother to child during birth is rare [74].

HCV acute stage is asymptomatic; few people are diagnosed during the acute phase. In those people who develop chronic HCV infection, the infection is also often undiagnosed because the infection remains asymptomatic until decades after infection when symptoms develop secondary to serious liver damage. The incubation period for hepatitis C is 2 weeks to 6 months [38].

After a person has been diagnosed with chronic hepatitis C infection, they should get an assessment of the degree of liver damage (fibrosis and cirrhosis) [21].

Populations at increased risk of HCV infection include:

- people who inject drugs;
- people who use intranasal drugs;
- recipients of infected blood products or invasive procedures in health-care facilities with inadequate infection control practices;
- children born to mothers infected with HCV;
- people with sexual partners who are HCV-infected;

- people with HIV infection;
- prisoners or previously incarcerated persons;
- People who have had tattoos or piercings.

There is no vaccine for hepatitis C but there is a treatment. Prevention of HCV infection depends upon reducing the risk of exposure. The following list provides recommendation of prevention [21]:

- hand hygiene: including surgical hand preparation, hand washing and use of gloves;
- safe and appropriate use of health care injections;
- safe handling and disposal of sharps and waste;
- provision of comprehensive harm-reduction services to people who inject drugs including sterile injecting equipment;
- testing of donated blood for hepatitis B and C (as well as HIV and syphilis);
- training of health personnel; and
- Promotion of correct and consistent use of condoms.
- immunization with the hepatitis A and B vaccines to prevent coinfection from these hepatitis viruses and to protect their liver;
- Regular monitoring for early diagnosis of chronic liver disease [21].

When treatment is necessary, the cure rate depends on several factors including the strain of the virus and the type of treatment given. Access to HCV treatment is improving, but remains limited. In 2015, of the 71 million persons living with HCV infection globally, 20% (14 million) knew their diagnosis. 7.4%

of those diagnosed (1.1 million) were started on treatment in 2015. In 2016, 1.76 million people were additionally treated in bringing the global coverage of hepatitis C curative treatment to 13%. Much needs to be done in order for the world to achieve the 80% treatment target by 2030 [72].

2.2.4 Hepatitis D

Hepatitis D virus (HDV) also known as "delta" virus. It causes a liver infection. Hepatitis D is not common in the United States. Hepatitis D only occurs in people who are infected with the hepatitis B virus because HDV is an incomplete virus that requires the help of HBV to replicate, and for transmission [75].

HDV can be an acute-short-term infection or a long-term- chronic infection. Hepatitis D is transmitted when infected body fluids like blood, saliva, semen and vaginal fluid touches the body tissues under the skin for example through needle puncture or broken skin or through the mucosal membranes- is the thin moist lining of many parts of the body like mouth, throat and genital area with infectious blood or body fluids [26]. HDV can be acquired either as a coinfection-at the same time with HBV or as superinfection-infection occurring after or on top of an earlier infection, especially following treatment in people with HBV infection. There is no vaccine for hepatitis D, but it can be prevented by hepatitis B vaccination. Vertical transmission-passage of a disease-causing agent from mother to baby during the period immediately before and after the birth, is possible but rare [38].

HDV replicates in the liver and significantly increases the amount of liver damage relative to that caused by an infection with HBV alone [57]. HDV-HBV co-infection is

considered the most severe form of chronic viral hepatitis, it causes more rapid liver related death and hepatocellular carcinoma [21].

There is no vaccine for HDV. The hepatitis B vaccine can prevent hepatitis D by preventing hepatitis B [26].

The following people are at increased risk for HDV

- Chronic HBV carriers;
- People who are not immune to HBV either by natural disease or immunization with the hepatitis B vaccine;
- Persons who inject drugs (PWID) suggest that injecting drug use is an important risk factor for HDV co-infection;
- High-risk sexual activity (e.g. sex worker) is also an increased risk for HDV infection.

For treatment guidelines recommend medication for at least 48 weeks irrespective of on-treatment response patterns. Liver transplantation may be considered for cases of severe hepatitis and end-stage liver disease.

Prevention and control of HDV infection requires:

- prevention of HBV transmission through hepatitis B immunization;
- blood safety;
- injection safety;

2.2.5 Hepatitis E

Hepatitis E is a liver infection caused by the Hepatitis E virus (HEV). Hepatitis E is a self-limited disease that does not result in chronic infection. It is rare in the United States but, HEV is common in many parts of the world. It is transmitted from ingestion of fecal matter, even in microscopic amounts, and is usually associated with contaminated water supply in countries with poor sanitation. There is currently no FDA-approved vaccine for Hepatitis E [38].

Hepatitis E is most common in developing countries with inadequate water supply and environmental sanitation. People living in refugee camps or overcrowded temporary housing after natural disasters can be particularly at-risk.

Hepatitis E virus is usually spread by the fecal-oral route. The most common source of HEV infection is fecal contaminated drinking water. There is a possibility of zoonotic spread- a disease that can be transmitted from animal to humans. That is why consumption of uncooked/undercooked pork, deer, boar meat and shellfish from infected animals.

The symptoms of Hepatitis E are similar to those of other types like hepatitis B or Hepatitis C. Symptoms usually develop in 15 to 60 days after exposure. HEV excretion in stool has been demonstrated from one week prior to onset up to 30 days after the onset of jaundice [38].

Most people with Hepatitis E recover completely. However, for pregnant women, Hepatitis E can be a serious illness with mortality reaching 20%–25% in their third trimester of pregnancy [40]. Hepatitis E could also be serious among persons with preexisting chronic liver disease resulting in decompensated liver disease and death. Similarly, high mortality occurs solid organ transplant recipients on immunosuppressive therapy.

Diagnosis can be confirmed only by testing for the presence of antibody against HEV or HEV RNA in blood and/or stool. No serologic tests to diagnose HEV infection have been approved by FDA for use in the United States [38].

Hepatitis E usually resolves on its own without treatment. There is no specific antiviral therapy for Hepatitis E. Patients are typically advised to rest, get adequate nutrition and fluids, and avoid alcohol. Hospitalization is sometimes required in severe cases and should be considered for pregnant women.

Prevention of Hepatitis E relies on good sanitation such as hand washing with safe water especially before handling food and of clean drinking water. Travelers to developing countries can reduce their risk for infection by not drinking unpurified water; boiling of water will inactivate HEV. Avoiding raw or undercooked meat can reduce the risk of HEV transmission [76].

2.2.6 Hepatitis Carrier

A carrier is an individual who is not able to get rid of the hepatitis B or hepatitis C virus. Carriers keep the virus for the rest of their lives and can give it to others. A small number of adults and many children younger than 5 years infected with the hepatitis B virus will become carriers. Inactive carriers make the largest group in chronic infected patients. There are roughly 300 million individuals are inactive carriers of hepatitis [77].

2.2.7 Chronic Hepatitis

Chronic hepatitis C can be a lifelong infection with the hepatitis C virus if left untreated. Left untreated, chronic hepatitis C can cause serious health problems, including liver damage, cirrhosis (scarring of the liver), liver cancer, and even death. Others regard chronic hepatitis C as having a variable outcome, the majority of infected

persons not dying from the disease, but more likely from the comorbid conditions that so often accompany infection by this agent, or from more common medical conditions [78].

Chronic hepatitis is hepatitis that lasts more than 6 months. The most common causes of chronic hepatitis are Hepatitis B virus; Hepatitis C virus; Alcoholic hepatitis: inflammatory condition of the liver caused by heavy alcohol consumption and Autoimmune hepatitis: is a disease in which the body's immune system attacks liver cells. This immune response causes inflammation of the liver, also called hepatitis [26].

2.3 Liver Diseases

2.3.1 Cirrhosis

Liver fibrosis is the excessive accumulation of extracellular matrix (ECM) proteins including collagen that happens in most types of chronic liver diseases. Advanced liver fibrosis results in cirrhosis [79].

Cirrhosis is a condition in which the liver slowly with time breaks down and is unable to function normally. Scar tissue replaces healthy liver tissue and partially blocks the flow of blood through the liver. As cirrhosis gets worse, the liver begins to fail [56].

Cirrhosis has symptoms, such as fatigue and severe itchy skin. They may not appear until the liver is badly damaged. Causes of cirrhosis include alcoholic liver disease, nonalcoholic fatty liver disease, chronic hepatitis C, and chronic hepatitis B [26].

Liver Cirrhosis is a critical stage of chronic liver disease caused by hepatitis C virus (HCV); 67% to 91% of Patients with HCV related causes like cirrhosis, hepatocellular carcinoma (HCC) and liver failure die of liver related diseases [80].

Approximately 370,000 people die each year with HCV and liver related causes each year [81].

HCV-related liver disease can progress over several decades, liver cirrhosis and hepatocellular carcinoma (HCC) are advanced forms of diseases. In 20% to 30% of chronically infected with HCV will develop Cirrhosis in 15 to 25 years later in their lives [80,81]. In the absence of treatment 67%-91% of patients die because of liver-related causes like HCC or hepatic failure. Liver cirrhosis also occurs due to HBV, alcohol abuse, and nonalcoholic steatohepatitis (NASH) [80].

In a systematic review found that in HCV – infected patients with liver cirrhosis 2.8%-11.7% develops hepatic decompensation, 1.8%-8.3% develops HCC, and 2.7%-6.7% die or go through liver transplant each year [80,82].

2.3.2 Chronic Liver Disease

The virus with chronic liver disease can cause both acute and chronic hepatitis, ranging in severity from a mild illness lasting a few weeks to a serious, lifelong illness. Hepatitis C is a major cause of liver cancer. Because chronic liver disease may develop many years after acute hepatitis C virus (HCV) infection, the past incidence of acute infections is a major determinant of the future burden of HCV associated complications [83].

- Alcoholic Fatty liver: liver cannot break down fat properly. This can cause fat to build up, which is known as alcoholic fatty liver. Alcoholic fatty liver disease is the earliest stage of alcohol-

related liver disease.

- Alcoholic liver damage: is caused by damage to the liver from excessive drinking.

- Chronic non-alcoholic disease: is the accumulation of extra fat in liver cells that is not caused by alcohol [26].

2.3.3 Disorder of Liver

Over years, HCV infection can cause major damage to the liver. Over time, inflammation in the liver causes scarring and permanent damage. HCV attacks the liver. Many people develop a chronic infection after initial infection with HCV. Chronic HCV infection slowly causes inflammation and damage the liver. Sometimes the condition may not be diagnosed for 20 or 30 years. The liver damage due to the virus begins with fibrosis, the build-up of scar tissue in the liver which can then lead to cirrhosis, where areas of the liver cease to function. The liver can only compensate for so much of the liver ceasing to function. This leads to decompensated cirrhosis also called end stage liver disease (ESLD) when the liver ceases to function [84]. Some of the other problems can occurs and those problems are as follows:

- Congestion of Liver: liver dysfunction due to venous congestion, usually due to congestive heart failure;

- Hepatic infarction: can occur when there is both hepatic arterial and portal vein flow compromise;

- Hepatopulmonary Syndrome: When the liver is not functioning properly, blood vessels in the lungs may dilate. If this is intense then the lungs can lose their ability to effectively transfer oxygen to the body [33].

2.3.4 Hepatocellular Carcinoma (HCC)

This is the most common form of liver cancer in adults [26]. Hepatocellular Carcinoma begins in the liver cell called hepatocyte. Cancer that begins in other organs of the body like the colon, lung or breast and then spreads to the liver is called metastatic cancer rather than liver cancer. It is higher if the liver is scarred by an infection like Hepatitis B or Hepatitis C. HCC is more common in people who drink alcohol and have accumulated fat in the liver. Hepatocellular carcinoma also occurs in people with chronic liver diseases, such as cirrhosis which is caused by hepatitis B or hepatitis C infection (Mayo Clinic 2019).

Hepatocellular carcinoma (HCC) is the most prevalent malignant tumor of the liver. It appears that the HCC increases as the severity of the underlying liver disease increases [85]. It is the fifth most common cancer in men worldwide and the seventh among women, and the third leading cause of cancer-related death [86,87,88]. HCC is rare in patients under the age 40 years and chances increases in those patients over the age 65 years, chances are highest in those patients at age 75 years or higher [62].

The rate of HCC progression varies from person to person and this is probably due to the existence of a complex interplay between host and environmental factors. Host-older age, longer duration of infection, male sex or alcohol consumption > 50 g/day, severity of fibrosis stage; environmental factors- viral genotype/subtype or viral load, geographic variability [89-93]. All these factors have been identified as predictors of progression from Hepatitis to HCC.

While HBV is the main cause of HCC in the high incidence HCC areas like Africa and East Asia, and HCV is the major cause in low incidence HCC areas, like Western Europe and North America [81,93-95].

HCC is more common in middle-income and low-income countries than in developed ones. The disease burden is highest in areas where HBV infection prevalence is high like 8% or more, such as in sub-Saharan Africa and especially in Eastern Asia (70% of all new HCCs worldwide), with incidence rates of over 20 per 100,000 individuals. China by itself, with the highest HCC incidence worldwide 395,000 cases per year, accounts for 55% of liver cancer deaths each year [96,97,98]. Mediterranean countries such as Italy, Spain, and Greece and Eastern and Southeastern Europe have intermediate incidence rates of 10-20 per 100,000 individuals, while the Americas and Great Britain have a relatively low incidence (< 5 per 100,000 individuals) [88,96].

The most important risk factors for HCC are as follows:

- Viral hepatitis which includes chronic hepatitis B Virus (CHB) and chronic hepatitis C virus (CHC);
- Toxic- consumption of alcohol and exposition to aflatoxin B1;

- Metabolic-diabetes and non-alcoholic fatty liver disease and hereditary haemochromatosis- Iron overload indicates accumulation of iron in the body from any cause. Organs most commonly affected by haemochromatosis is the liver and two other parts , Haemochromatosis presents with the Chronic liver disease and cirrhosis of the liver;
- Immune- primary biliary cirrhosis and autoimmune hepatitis. Primary biliary cirrhosis is a progressive disease of the liver which is caused by a buildup of bile within the liver. Whereas autoimmune hepatitis is a disease in which the body's own immune system attacks the liver and causes it to become inflamed. Autoimmune hepatitis can lead to cirrhosis and liver failure;
- The geographical variability in the incidence of HCC has been distribution of HBV and hepatitis C virus (HCV) infections. It has been estimated that HBV is responsible for 50-80% of cases for the development of HCC and HCV are responsible for 10-25%, of cases for the development of HCC cases worldwide [85,99].

The symptoms for HCC are similar to Hepatitis B Virus and Hepatitis C Virus. There is a treatment for it. Treatment that is good for the patient will depend on the size and location of hepatocellular carcinoma, how well the liver is functioning, and overall health. Hepatocellular Carcinoma treatments include:

- **Surgery-**Surgery to remove the cancer and a margin of healthy tissue that surrounds the infected area. This option is for early-stage liver cancers who have normal liver function.

- **Liver transplant surgery-** Surgery to remove the entire liver. This option is good for healthy people whose liver cancer is within the liver.
- **Destroying cancer cells with heat or cold.** Ablation procedures to kill the cancer cells in the liver using extreme heat or cold. This procedure is recommended for who can't undergo a surgery.
- **Delivering chemotherapy or radiation directly to cancer cells.** Using a catheter that's passed through blood vessels and into the liver.
- **Radiation therapy.** Radiation therapy using energy from X-rays or protons. This option is good if surgery is not an option.
- **Targeted drug therapy.** Targeted drugs attack particular weaknesses in the cancer cells, and this helps to slow down the progression of the disease with advanced liver cancers.
- **Immunotherapy.** Immunotherapy drugs uses body's germ-fighting immune system to attack the cancer cells. This option is good for treating advanced liver cancer.
- **Clinical trials.** Clinical trials give a chance to try new liver cancer treatments.

2.3.5 Liver Transplant

Liver transplantation due to hepatitis C (HCV)-related liver disease occurs among Americans born between 1941 and 1960. Findings in the December issue of Liver Transplantation, a journal published by Wiley on behalf of the American Association for the Study of Liver Diseases (AASLD), suggest that continuing increase in demand for the liver transplantation is due to the development of liver cancer in baby boomers with HCV

patients, but this demand may decrease as patients born in this time period continue to grow older.

HCV is the most common blood-borne infection and cause of liver disease requiring transplantation in the U.S., chronically infecting more than one percent of Americans. Previous studies show that among patients living with chronic HCV, 10% to 20% will develop cirrhosis and up to 5% will progress to liver cancer (hepatocellular carcinoma; HCC). Further evidence implicates HCV as the primary risk factor for developing HCC in up to 47% of cases of patients with HCC. The highest U.S. HCV prevalence of 4% occurred in those born from 1940 to 1965, who were 20 to 30 years of age during 1979 to 1989, when HCV infection risk was at its peak [100].

Over the coming decade the aging of those infected with HCV will challenge the transplant community to reconsider current treatment plans given the projected increase in liver transplantation demand, particularly from patients with HCV and liver cancer. With the aging of the population of patients with HCV, many of these patients may not be healthy enough for transplantation and the number of liver transplants in patients with HCV may decrease [101].

2.4 CDSS in Clinical Diagnosis and Decision Support System

There are several advantages of implementing Clinical Decision Support System for the diagnosis of Hepatitis. One can use CDSS from remote location. Decisions are not consistent; it has lot of errors; system provides efficiency and for the efficacy. CDSS improved the patient care and workflow in the health care setting. It provides more advance techniques for the comfort, safety and long-Gevity of the patient while treatment is in progress. System has the ability to generate fast and reliable diagnosis and patient

management report within a short period, based on the built-in-rules and knowledge base. System has the ability to store a large data (patient records) without any memory loss or confusion about one patient for another. System eliminates medical errors because it cannot combine medical records of more than one patient to make a decision. CDSS system can be portable and cannot get overwhelm to produce wrong decision. Decision is not based on feelings, instincts, appearance, race and color. System is following pure protocols of built-in-rules [102-107].

Many clinical trials and pilot studies showed a positive impact in Hepatitis patient care and a reduction in the cost of health care [103]. Clinical decision support system is useful (incorporating professional development and patient presence), facilitate conditions (incorporate workflow, training and integration), ease of use and reliability in the knowledge base [104].

In another study showed that CDSS decreases the malpractice payments because of its known benefits for the quality and safety [105]. The overall reports about the usability and safety of the system is positive through the alerts and reminders and decision output [106], another study showed that providers using CDSS without any assistance needs only seconds for recommendations of abnormal finding. CDSS results in a problem-solving tool at the expert level, educating users to perform at this clinical level, but also assists actual experts in arriving at an accurate diagnosis[107].

Implementation of the CDSS for the diagnosis of Hepatitis allows easy communication among providers within the organization or different clinical settings, if availability of the system is authorized in that location, this will result in immediate

change in the patient record without any delay which could be vital in the diagnostics and treatment outcome for a patient [102-107].

2.5 Corvid in Clinical Decision Support System

The CDSS was developed using the software Exsys Corvid version 6.1.0, which uses Java applets, allowing flexibility for the user, where it can be accessed from any location and any device that can connect to the Internet using a web browser. Exsys Corvid directly delivers knowledge as opposed to information [18].

There are three components for Exsys Corvid Core system: the user interface, the knowledge base and the inference engine. The user interface provides online access to the decision support system and allows users to interact with it through any web browser. It also allows the user to view the final system outcome and get the advice. The second component is knowledge base that retains all the knowledge needed for the decision-making. The knowledge is built in the system in the form of heuristic rules. A decision-making knowledge base is derived from variables. The third component is the inference engine, that analyzes the heuristic rules from the knowledge base and produces the advice for the problem [18].

There are two inference methods that are used in running any decision support system and those are the Backward chaining and the forward chaining. Backward chaining is one of the most powerful features of the Corvid Inference Engine and is the main reason it is much easier to solve complex problems with IF/THEN rules in Corvid than using IF/THEN statements in a programming language.

Backward chaining is conceptually quite simple. If the Corvid Inference Engine need a particular value for the backward chaining logic currently doing, it will check all the rules to see if there are any rules that could tell it selected condition is valid. If it finds a rule, it will suspend what it is currently doing and try to evaluate the new rule. Once it has gotten the value it needs, it will return to what it was originally doing. This happen recursively, so if the new rule required a value that could be obtained from other rules, those would be tested, etc. People do it all the time when making decisions. If you are diagnosing a machine that is not working, you might think: "Maybe it is the power supply", but if you saw the lights were still on, you would know it was getting power. You don't consciously think, "If the lights are on, then the machine is getting power", but if asked "How do you know the machine is getting power?" the answer would be the "lights". In a Corvid system there could be a rule:

IF The machine's lights are on THEN The machine is getting power.

This is a typical "heuristic" rule that describes a specific fact that might be used in making the decision. Backward chaining is often referred to as "Goal Driven" and it can be thought of as a "To Do" list. A system will start with the top To Do list item being something like "Generate a report" or "Find the most likely diagnosis". The Corvid Inference Engine always tries to do whatever is at the top of the list. If the top item on the list requires some value that is not known, getting that value becomes the new top item on the list, pushing down the previous goal. The Inference Engine now focuses on that item, but it too may require other values that become the top values. As values are obtained from the rules, the items are removed from the To Do list, and the item below again becomes the top item. This continues with items being added and removed until all the items are

removed and the system is done. This may sound complicated, but it is all done automatically by the Inference Engine. All the developer has to do is provide the rules that will tell the system how to derive the values it needs. The order of the rules is not particularly important, since the Inference Engine will find whatever rules are appropriate when it needs them. This makes for a very "free-form" approach to writing the rules, which is very different from the highly order dependent way the logic has to be coded in a computer language.

Forward chaining inference method is data-driven. It starts with available data and uses inference rules to extract more data, either from rules or the user, to reach to the conclusions. The name "forward chaining" comes from the fact that the computer uses logic in the rules to analyze it, and reasons its way to come to the answer.

The advantages of forward chaining are that the availability of new data leads to new inferences, which could be faster for some dynamic problems in which conditions are likely to change. However, backward chaining is better suited for clinical decision-making problems where all required data may not be available up front [108].

2.5.1 Types of Variables

Variables are the building blocks which are used in corvid. Variables are used to define the logic in the Logic Blocks, to hold user data during a session and to define the goals of how the system will run.

There are 7 variable types that can be input into the system and those variables are as follows:

- Static list – is a multiple-choice list with defined values during the CDSS development for example – presence of a diagnostic symptoms, asking a

question, the day of the week, state of an item like (on/off), and set up a static list value like (high/medium/low).

- Dynamic list – It is a multiple-choice list with the values defined during runtime of the system. The values come from external sources such as spreadsheets or it can be set by the logic of the system. For example, a selection of options that change frequently and are not known at time of system development [18].
- Numeric – Any numeric value used in expressions. For example: temperature, pressure, stock price, interest rate.
- String – A string value that can hold any text string for examples: name, social security number.
- Date – a date value that can be used in testing various comparison data like future/past dates for example birth dates, or maturity date [18.]
- Collection – a list of strings as values. Any string or Variable can be added to the Collection for examples “best" products, configuration, overall comments, and selections from a database.
- Confidence – a variable that is assigned a confidence value for a degree of certainty. Many formulas can be used to combine the values to an overall confidence for the Variable. For example, likelihood that a product is appropriate for the user [18].

There are restrictions for the variable names. Variables can contain any character, including non-English characters, but the following characters cannot be used: ~! @ ^ & * ( ) - + = " ' ? > < . , / : ; { } | \ `[ ]

* For my diagnosis of Hepatitis C Virus, I will be using static list and confidence variable.

The Exsys Corvid software has a confidence system that allows to create a rule for symptoms that are the possibilities based on knowledge from clinical literature. A rule will be included to cover the patients who may be asymptomatic during the time of assessment or has inactive Hepatitis C virus, where a patient shows no symptoms or has minor symptoms, yet their serology is positive for the Hepatitis virus. With the rate of underdiagnosis, this inclusion plays an important role. A confidence variable system within the inference engine makes it possible [18].

Variables can be added and edited to the system. There are two ways to add a variable. First way is to add a variable from the Manu Item select "Variables". Second way is by clicking directly on the Variable icon. To add a new variable, click the "New" button. That will show the new variable window and then enter a valid variable name, select a type and click OK. Figure 2.5 shows an image of the new variable window.

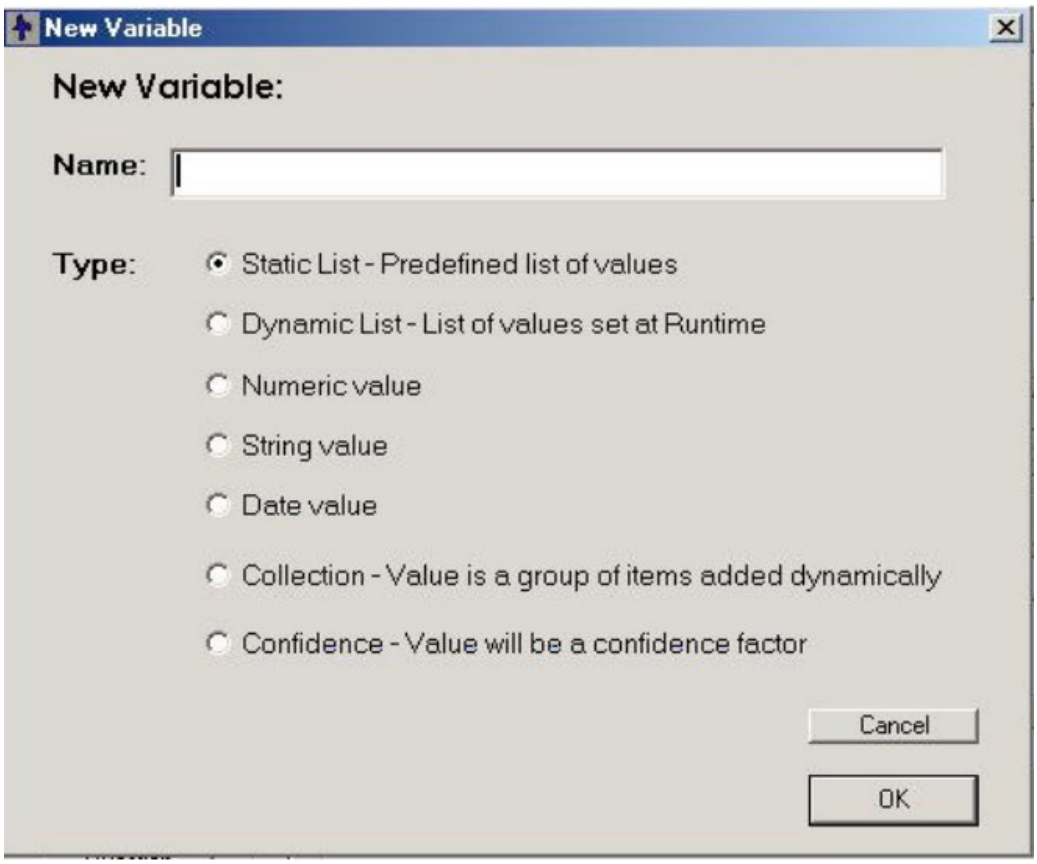

Figure 2.5 New Variable [18].

2.5.2 Make Rules for Corvid

Clinical Decision Support system is a rule-based system. Rules are in the form of IF Then Else form [2]. Exsys Corvid represents a way to define, organize and structure rules into logically blocks. These Logic Blocks are blocks that are made up of rules that can be defined by tree diagrams or stated as individual rules. Each block can contain multiple rules [184]. Following is an example of a multiple rule [18].

IF Bulb goes out

AND The lights in the room stay on

THEN Change Bulb

IF Bulb goes out

AND Other Light in the room go out

THEN

IF Bulb goes out

AND Other lights in the room go out

AND Other light in the house stay on

THEN Fix circuit

IF Bulb goes out

AND Other Lights in the room go out

AND Other lights in the house go out

Then Call the power company

2.5.3 Logical Block

Exsys Corvid uses Logic Blocks. A Logic Block can be any combination of rules and decision trees. A block can be from an entire knowledge base to a single rule. The logic block is in the form of an If/Then rule, which makes it easy to read and understand. A Logic Block is added to a system by clicking on the Logic Block icon, or by choosing "Logic" from "Block" under the "Windows" menu. This will display a Logic Block editing window. Figure 2.6 displays The Logic Block Window.

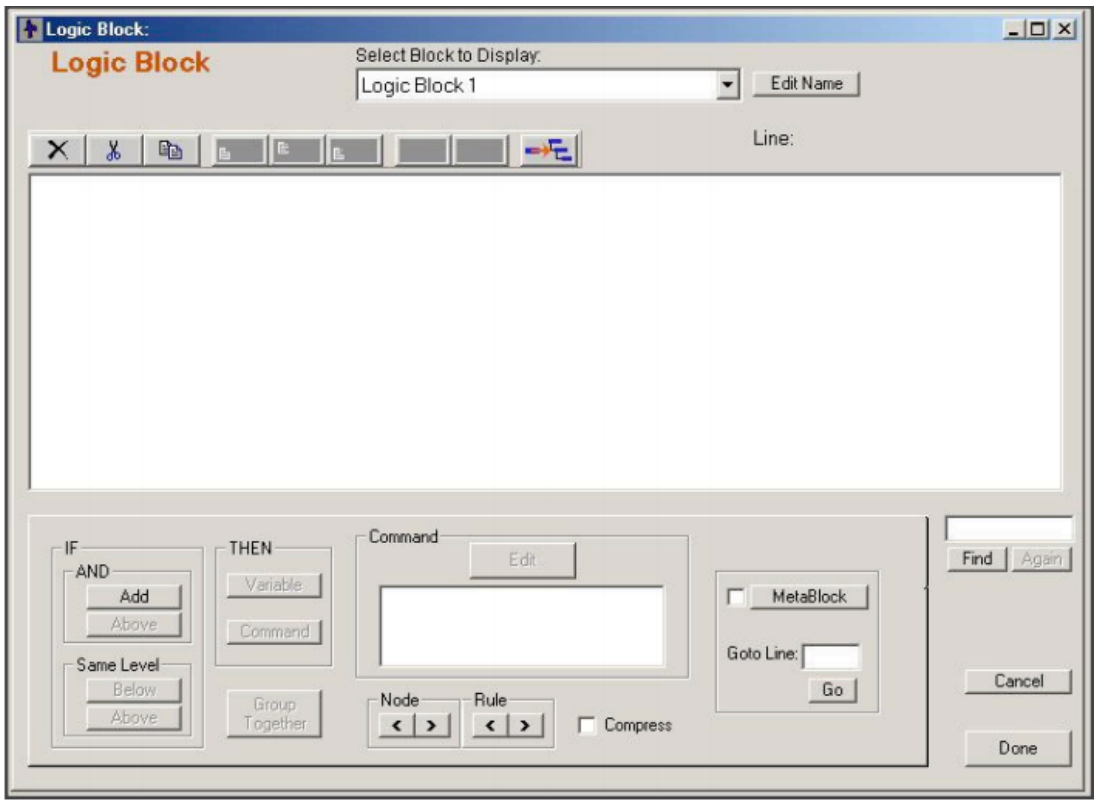

Figure 2.6 Logic Block Window [18].

Logic Blocks are made up of nodes that describe the logic of the system. Each node represents the IF and THEN conditions to build an If and Then rule. Logic Blocks provide a very convenient way to use a group of related rules from within the expert system. In the Corvid Logic Block window blocks are created and edited. Figure 2.7 shows the Logic block view of the rule used in section 2.5.2.

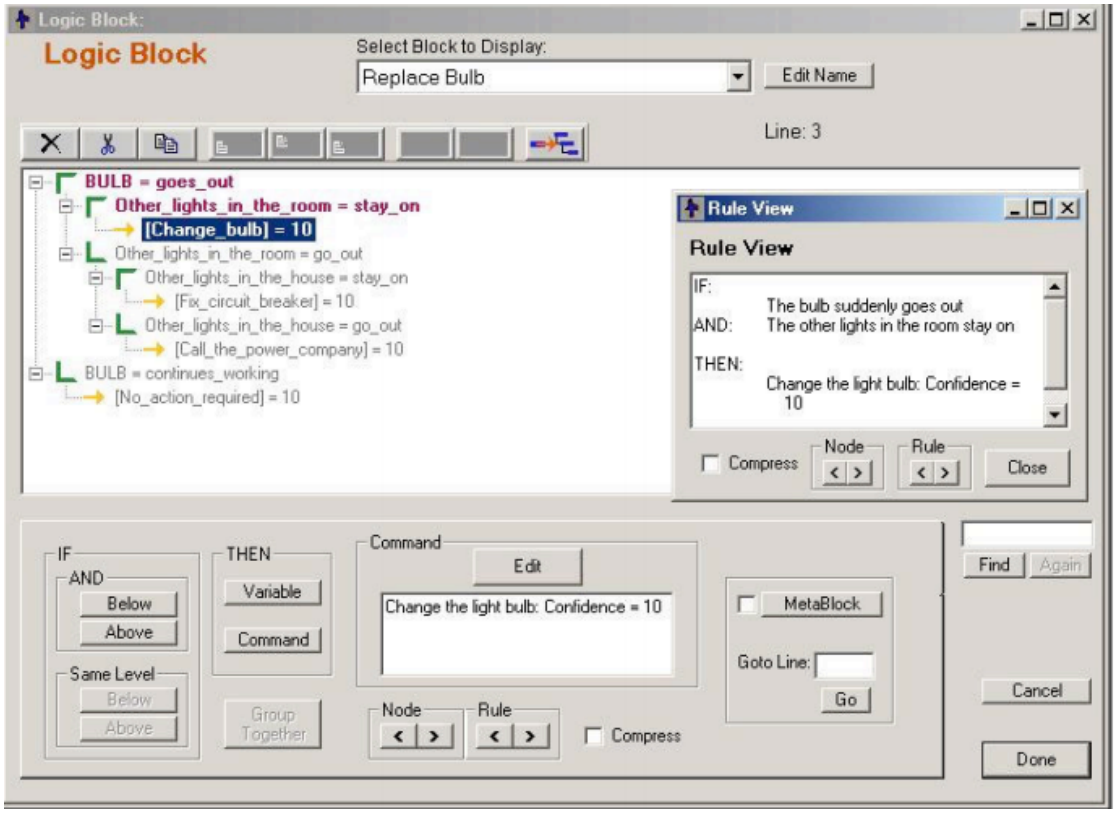

Figure 2.7 Logic Block with Rule [18].

Each line in the Corvid tree is a node. Green square brackets indicate the IF nodes. The brackets mark a group of nodes that use the same Corvid variable but have different values. THEN nodes are marked with an arrow. When an IF node is indented under another IF node, the nodes are combined with a logical AND - meaning both nodes must be true.

2.5.4 System Output

Confidence Variables gets "confidence values" in the rules. A variable may assign a value by many rules. Then, these values are combined from all the rules to determine the overall confidence value for the variable by just adding them up. The sum determines if that variable is the best recommendation. One can think of the value as

"points" added to or points taken away from the “score” for the item. In a rule, the Confidence Variables are assigned a value only in the THEN part. This is indicated in the rule by an " = " sign followed by the value to assign. For example, if a system is trying to decide what to wear, and it has a Confidence Variable "Jacket", there could be rules:

IF it is below 50 degrees
THEN Jacket =10
IF it is raining
THEN Jacket=15

The first rule means that if it is below 50 degrees, give "Jacket" 10 points. Likewise, the second rule would add another 15 points. If the system used both rules, the overall confidence for "Jacket" would be 10+15 or 25 points. If there were more rules that assigned a value to "Jacket", their values would also be added to the overall sum. There could also be a rule like:

IF it is below 10 degrees
THEN Jacket= -100
AND Coat=50

which would mean if it is below 10 degrees, then a jacket is not appropriate, so it is given a large negative value of -100 to greatly reduce its overall confidence. This would be a deduction of 100 points. At the same time, another Confidence Variable "Coat" is given a value of 50. At the end of a run, the Confidence Variable with the highest overall point score will be displayed in the results as the "Best" option based on the input.

The actual values to assign can be any number. These numbers should be scaled relative to each other. If a rule increases the likelihood of a particular Confidence Variable, it can give few points. If rule is a significant factor, then it could increase by many points. Rules that shows that a Confidence Variable is not appropriate then, that rule should assign similar negative values to decrease its likelihood. Adding a value of hundred will assure that a variable is in the recommendations, and large negative values will eliminate a variable from the results.

To complete the example from section 2.5.3, Corvid's Rule View window shows the full text of the rule. The output would look something like figure 2.8, that shows the system output with the confidence=10, which means it is recommended to change the light bulb

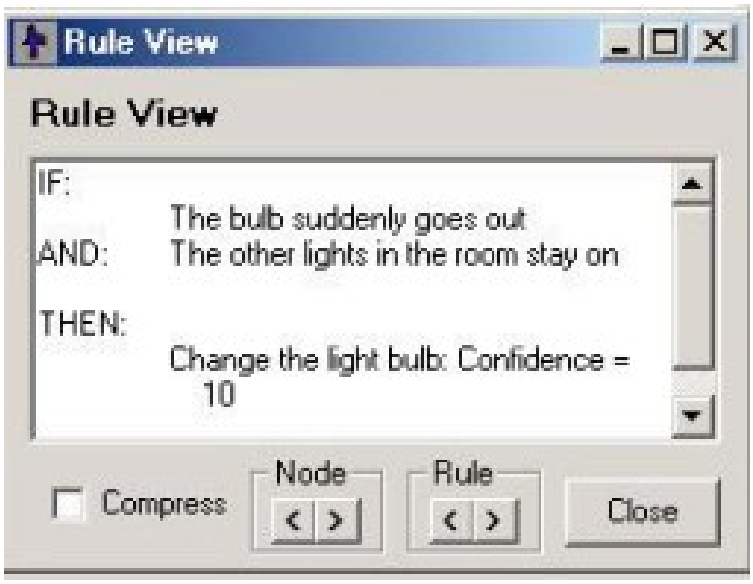

Figure 2.8 System Output [18].

2.6. Conclusion and Discussion

This chapter covers background and detail of Hepatitis, Liver Diseases, Clinical Decision support system (CDSS) and Exsys Corvid. There are five types of Hepatitis A, B, C, D, E, Carrier and Chronic Hepatitis. HAV, HBV, HDV and HEV have already preventive vaccine developed. There is no vaccine for HCV. Acute stage (<6 months duration) of HAV, HBV, HCV, HDV and HEV are self-healing. Any virus which lasts more than six months is considered to be a chronic hepatitis. HAV and HEV occur due to contaminated food and water. HBV spreads through body fluids like urine, saliva, vaginal fluids, semen, needle puncture, broken skin or through the mucosal membranes- the thin moist lining of many parts of the body like mouth, throat and genital area with infectious blood or body fluids. HCV spreads via exposure to the contaminated blood. HDV is an incomplete virus and occurs in person who is infected with the HBV. HDV can be acquired either as a coinfection or as superinfection-infection after or on top of an earlier infection, especially after treatment of HBV. HDV-HBV co-infection is considered the most severe form of chronic viral hepatitis. It causes more rapid liver related death and hepatocellular carcinoma.

Liver diseases like Cirrhosis, chronic liver disease, disorder of liver and Hepatocellular Carcinoma (HCC). Hepatitis causes cirrhosis. Cirrhosis is a condition in which the liver slowly breaks down and is unable to function normally. Chronic Liver Disease refers to disease of the liver which lasts more than six months. It is an alcoholic hepatitis where inflammation in the liver due to heavy alcohol consumption or liver

cannot break down the fat properly. Disorder of liver is a liver dysfunction due to the heart or blood vessels in the lungs may dilate. Then the lungs can lose their ability to transfer oxygen to the body. Hepatocellular carcinoma (HCC), a liver cancer, is also caused due to Hepatitis. It begins in the liver cell. HCC is higher if the liver is scarred by an infection like Hepatitis B or Hepatitis C. HCC is more common in people who drink alcohol and have accumulated fat in the liver. The symptoms for HCC are similar to Hepatitis B Virus and Hepatitis C Virus.

Clinical Decision Support system (CDSS) and Exsys Corvid is also part of this chapter. A clinical decision support system is a health information technology system. The main purpose of CDSS is to assist physicians, clinicians and other health professional to analyze and conclude a diagnostic based on patient data. The CDSS was developed using the software Exsys Corvid version 6.1.0, which uses Java applets, allowing flexibility for the user, where it can be accessed from any location and any device that can connect to the Internet using a web browser. Exsys Corvid directly delivers knowledge as opposed to information.

CHAPTER III- LITERATURE REVIEW

3.1 Introduction

This chapter contains previous research related to areas of various types of hepatitis and liver diseases, diagnosis, treatment and management. Also, CDSS for managing hepatitis has been reviewed. The literature review is divided into two parts, first part is data analysis of hepatitis and liver diseases, and second part is Clinical Decision Support System (CDSS) implementation to manage hepatitis patients. In the data analysis section review has been done in the areas to mortality, morbidity, races, various age groups, and treatments. Research has been reviewed in the last 10-15 years. The study includes research done by researchers in the area of CDSS, and managing aspects of managing disease, medications, treatment plans, hospital infections, reducing mortality, co-infections of hepatitis and liver diseases, and other factors related Hepatitis and liver diseases. Content also includes work done by other researchers on hepatitis and liver diseases.

3.2 Hepatitis C and Cirrhosis

This section includes historical review of cirrhosis in relation with hepatitis C by different researchers.

The research by (Ikeda, Kenji et al., 2006 [109]) included study on 183 patients between the years 1974 and 1990 with assessed for carcinogenesis rate and risk factors. Predicted carcinogenesis rates were using a cohort from the same hospital between the years 1991 and 2003 (n=302) and an external cohort between the years 1975 and 2002 (n=205). Diagnosis of the disease found the carcinogenesis rates in the primary cohort

were 28.9% at the 5th year and 54.0% at the 10th year. A proportional hazard model identified alpha-fetoprotein (>=20 ng/ml, hazard ratio 2.30, 95% with confidence interval 1.55-3.42), age (>=55 years), gender (male), and platelet count (<100,000 counts/mm3) as independently associated with carcinogenesis. When carcinogenesis rates were simulated in 16 conditions according to four binary variables, the 5th- and 10th-year rates varied from 9-64%, and 21-93%. Actual carcinogenesis rates in the internal and external validation cohorts were similar to those of the simulated curves. Simulated carcinogenesis rates were suitable to patients with HCV-related cirrhosis. Since, hepatocarcinogenesis rates varied among patients depending on the background features, we should consider stratifying them for cancer screening and cancer prevention programs. However, no work has been done on introducing race and region of the patients.

The research by (Toshikuni, Nobuyuki et al., 2009 [110]) included multivariate analyses using the Cox proportional hazard model for a total of 227 patients (75 alcoholic and 152 HCV-infected patients) with compensated cirrhosis patients were enrolled. The median follow-up period was 4.9 years. The cumulative rates of hepatocellular carcinoma (HCC) development were significantly lower in the alcoholic patients than in the HCV-infected patients (6.8% vs 50.3% at 10 years, P = 0.0003), while the cumulative rates of hepatic decompensation (37.4% vs 51.7% at 10 years) and survival (53.8% vs 47.4% at 10 years) did not differ between the two groups (Kaplan-Meir analysis). The risk of HCC was lower in alcoholic cirrhosis than in HCV-related cirrhosis (hazard ratio (HR), 0.46). The main causes of death were hepatic failure and non-hepatic diseases in the alcoholic patients and HCC and hepatic failure in the HCV-infected patients. While the risk of

hepatic decay and mortality was the same. Predictors of decreased survival were non-abstinence (HR, 2.53) in the alcoholic patients and low serum albumin level (1.58) in the HCV-infected patients. The study concluded that absence from alcohol was important for improving the survival of patients with alcoholic cirrhosis. However, no work has been done on introducing age and gender of the patients.

The study by (Bruno et al., 2009 [111]) included a study 352 patients with compensated hepatitis C virus (HCV) induced cirrhosis, continuously observed between the years 1989 and 1992. The model for end-stage liver disease (MELD) score was calculated with information collected at enrollment. Baseline predictors and inter-current events associated with mortality were achieved using the Cox regression model. During a median follow-up of 14.4 years, 194 subjects received an individual course of interferon monotherapy, 131 patients developed decay (ascites, bleeding, hepatic encephalopathy), 109 patients had hepatocellular carcinoma (HCC), 9 had liver transplant, and 158 died. Liver-related death (Hazard Ratio, 2.27), HCC occurrence increased the risk of decompensation fivefold. The research concluded with the results that the development of HCC during follow-up strongly accelerate the occurrence of decompensation, which is the main determinant of death. Patients with a MELD score ≤10 at study entry had a lengthy life expectancy. Hepatic and overall mortality hazard ratios were 8. and 3.80, respectively. However, no work has been done to introducing age range of the patients.

The study by (Toshikuni et al., 2014 [112]) found that in the absenteeism of antiviral therapy, 67%-91% of patients with HCV-related Liver Cirrhosis patients die of liver-related causes, hepatocellular carcinoma (HCC) and liver failure. Standard therapy with

pegylated interferon and ribavirin makes a sustained virological response (SVR) in 25% of HCV genotype 1-infected patients and in 69% of patients infected with genotypes 2 and 3. An interferon-free therapy called direct-acting antiviral agent attains sustained virological response in more than 50% of patients with HCV genotype 1 Liver Cirrhosis. However, no work has been done to introducing age range, gender, region or income level of the patients. As a result, no clear model has been laid out.

The study by (Barritt et al., 2019 [113]) states that trends in inpatient charges among patients with cirrhosis to find the drivers of healthcare expense. The study shows that it was a hypothesis that alcoholic cirrhosis (AC) was a contributor to overall expense. The study used the method to perform analysis of the Health Care Utilization Project Nationwide Inpatient Sample Database from the year 2002–2014 (annual cross-sectional data) and New York and Florida State Inpatient Databases from the year 2010–2012 (longitudinal data). Adult patients with cirrhosis of the liver were categorized as Alcoholic Cirrhosis and patient characteristics were analyzed using ordinary least squares regression modeling. A random effects model was used to evaluate 30-day readmissions. The study shared the results in total, 1,240,152 patients with cirrhosis were admitted between the year 2002 and 2014. Of these, 567,510 (45.8%) had a diagnosis of Alcoholic Cirrhosis. The study states that the total charges for Alcoholic Cirrhosis increased by 95.7%, accounting for 59.9% of all inpatient cirrhosis-related charges for the year 2014. Total aggregate charges for Alcoholic Cirrhosis admissions were $28 billion and increased from $1.4B in the year 2002 to $2.8B by the year 2014. In the NIS and SID, patients with Alcoholic Cirrhosis were younger, white and male. Study shows that the readmission rates at 30, 60, and 90 days were all higher among Alcoholic Cirrhosis

patients. The study concluded that the inpatient charges for cirrhosis care are high and constantly increasing. Alcohol-related liver disease is responsible for more than half of these charges due to the volume of admissions and readmissions of the same patients. The study suggested the alcohol addictions therapy might be the most cost-effective way to reduce inpatient cirrhosis care expenditures. However, no work has been done to introducing region and income status of the patients.

The study by (Alazawi, et al., 2010 [114]) states that the most studies states that the chronic hepatitis C virus (HCV) natural history have taken the development of cirrhosis as an end-point. The purpose of this paper is to establish the outcome of HCV cirrhosis. The study states that the methods they mention in this paper was that a systematic literature review was performed. In that data regarding HCV mono-infected patients were included. Weighted mean annual percentage rates for death/transplantation, decompensation of cirrhosis and development of HCC were calculated. The study mentioned the results, the data relating to 2386 patients. In compensated HCV cirrhosis, the estimated annual rate of death/transplantation is 4.58%, that of decompensation is 6.37% per and that of HCC, 3.36%. When compared with studies of untreated patients, studies that included treated patients reported lower mean annual percentage rates of HCC (2.52% vs. 4.79%, P = 0.02), but not decompensation (5.34% vs. 7.88%, P = 0.026) and death/transplantation (3.79% vs. 4.62%, P = 0.25). The study concluded with that the results brings the attention that there is a need for continued vigilance for the occurrence of HCC, while confirming the relatively slow progress of compensated HCV cirrhosis. These data may underestimate the rate of disease progression, particularly HCC

development. However, no work has been done to introducing age, gender, or race of the patients.

The study by (Serfaty, et al.,1998 [115]) states that this study supposed to assess the incidence of decompensation (ascites, jaundice, variceal bleeding, and encephalopathy), hepatocellular carcinoma (HCC) and death or liver transplantation in patients with compensated hepatitis C virus (HCV)-related cirrhosis, taking into account the viral genotype and interferon (IFN) therapy. Between the years1989 and 1994. 668 patients with no clinical evidence of decompensation were referred to the department for liver biopsy because of positivity for anti-HCV antibodies and elevated aminotransferase activity; 103 of these patients had cirrhosis. The median follow-up was 40 months. Fifty-nine patients were treated with IFN for a mean duration of 11+/-6 months; 3 (5%) had a prolonged biochemical and virological response. Baseline characteristics of IFN-treated and untreated patients were not significantly different. HCV genotypes (InnoLiPa) were predominantly 1b (48%) and 3a (20%). During follow-up, complications of cirrhosis occurred in 26 patients, HCC in 11 patients, and decompensation not related to HCC in 19 patients. Sixteen patients died, 94% of liver disease. Three patients were transplanted for liver failure. The 4-year risk of HCC was 11.5% (annual incidence 3.3%) and that of decompensation was 20%. Survival probability was 96% and 84% at 2 and 4 years. The study states that in patients with compensated HCV-related cirrhosis, complications of cirrhosis were frequent, with whatever the viral genotype; and the severity of cirrhosis and the absence of IFN therapy were independently predictive of bad outcome. The study shows that the absence of IFN therapy was the only independent factor predictive both for HCC and decompensation. A low albumin level at entry and the absence of IFN

therapy were the two independent factors predictive of death or liver transplantation. Probability of survival rate at 2 and 4 years was very different between IFN-treated and untreated patients (respectively 97% and 92% vs 95% and 63%, P < .0001). However, no work has been done to introducing age, race and gender of the patients.

A study by (Gramenzi, A et al. 2001 [116]) states that the aim to evaluate the effect of interferon on the clinical course of compensated hepatitis C virus related cirrhosis where 72 cirrhotic patients treated with interferon and 72 untreated controls matched treated patients with for quinquennia of age, sex, and Child-Pugh's score were enrolled in a non-randomized controlled trial. Treated patients received leucocytic interferon alfa, with an escalating schedule for 12 months. The incidence and risk (Cox regression analysis) of clinical complications (hepatocellular carcinoma, ascites, jaundice, variceal bleeding, and encephalopathy) and death rate were calculated. Over median follow up periods of 55 months for treated and 58 for untreated subjects, seven and nine patients, respectively, died, and 20 and 32, respectively, developed at least one clinical complication (ns). Hepatocellular carcinoma developed in 6 treated and 19 untreated patients (p=0.018). Seven treated patients showed sustained aminotransferase normalization and none died or developed complications. Clinical complications were significantly associated with low albumin, bilirubin, and prothrombin activity while hepatocellular carcinoma was related to no treatment with interferon, esophageal varices, and high alpha fetoprotein levels. By stratified analysis, the beneficial effect of interferon was statistically evident only in patients with baseline alpha fetoprotein levels > or =20 ng/ml. The study concluded with that the interferon does not affect the overall or event free survival of patients with hepatitis C virus related cirrhosis, it seems to prevent the

development of hepatocellular carcinoma. Patients who achieved sustained aminotransferase normalization survived and did not develop any complications during follow up. However, no work has been done to introducing race and income status of the patients.

The study by (Giovanna et al., 2002 [117]) states that the aim of this study was to compare the prognosis of patients with hepatitis B surface antigen (HBsAg) positive and those with antibody to hepatitis C (anti-HCV) positive cirrhosis. The study used the method where 297 untreated Western European patients with compensated viral cirrhosis (Child class A; 161 patients with hepatitis type B and 136 with type C) who were followed for a median period of 6.6 yr. The study states the results that at diagnosis, median age was lower (48 vs 58 year, in HBsAg-positive cirrhotic patients. The Kaplan-Meier 5-year probability of hepatocellular carcinoma (HCC) was 9% and 10% in HBsAg and anti-HCV-positive cirrhotic patients, respectively; the corresponding figures for decompensation unrelated to HCC were 16% and 28% and for survival were 86% and 84%, respectively. Patients with HBV infection may present with cirrhosis about 10 years earlier than those with HCV infection. HCV infection tends to be associated with a higher risk of decompensation, and mortality was 1.53 (CI = 0.81-2.89), 0.59 (CI = 0.37-0.94), and 1.44 (CI = 0.85-2.46) respectively, in HBsAg-positive patients compared with anti-HCV-positive cirrhotic patients. Among HBsAg-positive cirrhotic patients, the risk for HCC, decompensation, and mortality was 0.89 (CI = 0.30-2.63), 4.05 (CI = 1.09-15.1), and 5.9 (CI = 1.64-21.3), in HBV-DNA positive (HBeAg positive or negative) compared with HBV-DNA negative (HBeAg negative) patients. The study concluded with patients with HBV infection may present with cirrhosis about 10 year earlier than

those with HCV infection. HCV infection associate with a higher risk of decompensation, but these data should take into consideration the heterogeneity of HBV-related cirrhosis in terms of viremia levels and risk of hepatic failure. Survival shows no differences to HBV or HCV etiology in Western European cirrhotic patients. However, no work has been done to introducing age, race and gender of the patients.

The study by (Van der Meer, A J et al., 2014 [118]) analyzed international multicenter cohort of consecutively treated patients with HCV genotype 1 infection and cirrhosis. The number needed to treat (NNT) to prevent death or clinical disease progression (any cirrhosis-related event or death) in one patient was resolved with the adjusted survival among patients without sustained virological response and adjusted hazard ratio of sustained virological response. Overall, 248 patients were followed for a median of 8.3 years. Fifty-nine (24%) patients obtained sustained virological response. Patients without sustained virological response, the adjusted 5-year survival and event-free survival were 94.4% and 80.0%. At 50% sustained virological response to be expected with triple therapy, the estimated number that was needed to treat was 43. The number needed to treat to prevent clinical disease progression in one patient in 5 years was 302, 18 and 13 at 2%, 35% and 50% sustained virological response. In conclusion, the number needed to treat to prevent clinical endpoints among the cirrhotic patients with HCV genotype 1 has declined significantly with the development of antiviral therapy. Sustained virological response was affiliated with reduced all-cause mortality and clinical disease progression. The number needed to treat to prevent one death in 5 years declined from 1052 at 2% to 61 at 35%. However, no work has been done to introducing age range, and gender of the patients.

The study by (Tapper, B Elliot and Neehar D Parikh, 2018 [119]) took the population data from the US Census Bureau compiled by the Center for Disease Control and Prevention's Wide-ranging Online Data for Epidemiologic Research for their study. Their study found that annual cirrhosis death Increased by 65% to 34,174, while HCC death doubled to 11,073 between the years 1999 and 2016. One subgroup of Asians and Pacific Islanders experienced an improved mortality from hepatocellular carcinoma where the death rate decreased by 2.7% (95% confidence interval 2.2% to 3.3%, P< 0.001) per year. A yearly increase in cirrhosis related mortality were most noticeable for Native Americans (called as an "American Indians" in the census database) (4.0%, 2.2% to 5.7%, P=0.002). The age adjusted death rate due to hepatocellular carcinoma increased yearly by 2.1% (1.9% to 2.3%, P<-.001); deaths due to cirrhosis began increasing in by the year 2009 through 2016 by 3.4% (3.1% to 3.8%, P<0.001). During the year 2009-16 people aged between 25-34 years experienced the highest average annual increase in cirrhosis related mortality (10.5%, 8.9% to 12.2%, P <0.001), this conclusion was driven entirely by alcohol related liver disease. During the year 2009-16, mortality due to peritonitis and sepsis- infection from bacteria due to cirrhosis increased, with respective annual increases of 6.1% (3.9% to 8.2%) and 7.1% (6.1% to 8.4%). Only Maryland, showed improvements in mortality (−1.2%, −1.7% to −0.7% per year), while many, concentrated in the south and west, observed disproportionate annual increases: Kentucky 6.8% (5.1% to 8.5%), New Mexico 6.0% (4.1% to 7.9%), Arkansas 5.7% (3.9% to 7.6%), Indiana 5.0% (3.8% to 6.1%), and Alabama 5.0% (3.2% to 6.8%). No state showed improvements in hepatocellular carcinoma related mortality, while Arizona (5.1%, 3.7% to 6.5%) and Kansas (4.3%, 2.8% to 5.8%) experienced the most severe

annual increases. Research concluded by stating that the mortality due to cirrhosis has increased in the US since the year 2009. Deaths due to alcoholic cirrhosis for people aged between 25 and 34 had experienced the greatest increase in mortality. White Americans, Native Americans, and Hispanic Americans experienced the greatest increase in deaths from cirrhosis. Mortality due to cirrhosis improved in Maryland but worst in Kentucky, New Mexico, and Arkansas. The rapid increase in death rate among young people was due to the alcohol. However, no work has been done to introducing gender of the patients.

3.3 Cirrhotic Hepatitis C and Hepatocellular Carcinoma

This section includes historical review of Cirrhotic Hepatitis C and Hepatocellular Carcinoma by different researchers.

The study by (Shiratori, Yasushi et al., 2005 [120]) analyzed 345 patients with chronic hepatitis C and cirrhosis enrolled in previous trials. 271 patients received 6 to 9 million U of interferon 3 times weekly for 26 to 88 weeks; 74 received no treatment. Blood tests and abdominal ultrasonography were done to detect hepatocellular carcinoma. In 119 patient's hepatocellular carcinoma was detected during a 6.8-year follow-up: 84 (31%) in the interferon-treated group and 35 (47%) in the untreated group. Accumulative incidence of hepatocellular carcinoma among interferon-treated patients was lower than in untreated patients, especially sustained virologic responders. In total 69 patients died during follow-up: 45 (17%) in the treated group and 24 (32%) in the untreated group. Interferon-treated patients survived better than the untreated group. The study concluded that the interferon therapy for cirrhotic patients with chronic hepatitis C,

in whom the infection had been cured, guarded the development of hepatocellular carcinoma and improved survival. However, no work has been done to introducing gender, age and race of the patients.

The research by (Papatheodoridis, G V et al. 2001 [121]) included the pooled odds ratio (OR) and 95% confidence intervals (CI) were calculated from the raw study data. 2178 patients and 7 studies were found to fulfil our inclusion criteria. Hepatocellular carcinoma development was more frequent in untreated (21.5%) than in interferon-treated patients (8.2%; OR: 3.0, 95% CI: 2.3-3.9). The studies reporting hepatocellular carcinoma incidence in patients with and without supportive response to interferon, hepatocellular carcinoma was detected at a much higher rate in patients without (9%) than with a sustained response (0.9%; OR: 3.7, 95% CI: 1.7-7.8). Moreover, hepatocellular carcinoma developed more frequently in the untreated patients than in the non-sustained responders (OR: 2.7, 95% CI: 1.9-3.9). The benefit from the interferon therapy on the hepatocellular carcinoma incidence was not influenced by the study type (prospective or retrospective), the follow-up duration, or the study origin. The study concluded with the finding of interferon therapy significantly reduces the hepatocellular carcinoma risk in patients with hepatitis C virus cirrhosis. Hepatocellular carcinoma development becomes almost insignificant among sustained responders, but a reduction in hepatocellular carcinoma incidence is also achieved even in the non-sustained responders. However, no work has been done to introducing gender, or age of the patients.

The study by (Singal, Ashwani K et al., 2010 [122]) included systematic review and meta-analysis. 4700 patients (Twenty studies) were analyzed that compared untreated patients with those given interferon (IFN) alone or ribavirin. Risk ratios (RRs) determined effect size using a random effects model. Pooled data showed reduced HCC risk in the treatment group (RR, 0.43; 95% confidence interval [CI], 0.33-0.56), although the data were heterogeneous. Meta-regression analysis showed that studies with follow-up durations of more than 5 years contributed to heterogeneity. Analysis of 14 studies (n = 3310) reported sustained virologic response (SVR) rates with antiviral treatment showed reduction in HCC risk in patients with an SVR, as compared with nonresponses. The greatest benefits were observed in patients treated with ribavirin-based regimens. Meta-analysis of 4 studies assessing the role of maintenance IFN in non-responders didn't show HCC risk reduction. No publication bias was detected by the Egger test analysis. The study concluded with the finding that the risk of HCC is reduced among patients with HCV who achieve an SVR with antiviral therapy. Maintenance therapy with IFN does not reduce HCC risk for the patients who do not respond to initial therapy. However, no work has been done to introducing gender, or age of the patients.

The research by (Moon, Chansoo et al., 2010 [123]) included a total of 463 Chronic Hepatitis C patients who underwent pegylated interferon alfa and ribavirin therapy were classified as sustained virological response (SVR) or non-sustained virological response based on response to the antiviral therapy. They investigated disease progression to cirrhosis in non-cirrhotic patients, development of cirrhosis-related complications such as ascites, variceal bleeding, and hepatic encephalopathy in patients with cirrhosis, and development of the hepatocellular carcinoma (HCC) disease. Three hundred patients

accomplished sustained virological response, and 163 were classified into the non-sustained virological response group. The overall sustained virological response rates were 64.8 %, and multivariate analysis showed that younger age, non-cirrhosis, HCV genotype 2 or 3, lower HCV RNA level (<800,000 IU/mL), and lower body weight were independent factors associated with SVR (all $P < 0.05$). During a median follow-up of the patient 36.1 months, non-cirrhotic patients with sustained virological response had a lower risk of progression to cirrhosis as compared with patients with non-SVR ($P < 0.001$). Moreover, sustained virological response was related to a reduced risk of HCC development ($P = 0.017$). The study concluded with finding of SVR resulted in significantly more favorable long-term outcomes, such as lower risk of progression to cirrhosis and HCC occurrence compared with non-SVR. However, no work has been done to introducing gender, region or race of the patients.

The research by (Degos, F et al., 2000 [124]) included analysis from January 1987-1997, 416 patients (240 male, median age 57 years) with uncomplicated Child-Pugh. A Hepatitis C Virus related cirrhosis were followed in two Paris area centers from diagnosis of cirrhosis until death or reference date June 1, 1998. The analysis used a three-state disability model generalizing the Cox model. Of the 416 patients, 60 developed HCC with a five-year rate of 13.4% (95% confidence interval (CI) 9.0-17.8%). By multivariable analysis, time to HCC relied on age (hazard ratio (HR) 1.05 per year; p=0.0005), male sex (HR 2.13; p=0.01), oesophageal varices (HR 2.36; p= 0.008), decreased platelet count (HR 0.99; p=0. 03), and bilirubin level (HR 1.01; p=0.003), while death after HCC was related to tobacco consumption (HR 1.04; p=0.0006). In contrast, death free of HCC was dependent on age (HR 1.04; p=0.01), oesophageal

varices (HR 2.75; p=0.001), low platelet count (HR 0.99; p=0.006), and albumin level (HR 0.90; p=0.0001). 83 died (including 34 patients with HCC), with a five-year death rate of 15.3%. The incidence rate of HCC and mortality rate should be higher in these patients than previously stated, and prediction of HCC and death are closely related to age and symptoms of portal hypertension. The study concluded with the incidence of HCC and mortality should be higher in these patients than previously stated, and prognostic factors of HCC and death are closely related with age and symptoms of portal hypertension. However, no work has been done to introducing race, region and income level of the patients.

The research study by (Fan et al., 1995 [125]) states that the safety of hepatectomy for hepatocellular carcinoma (HCC) associated with cirrhosis and the selection criteria for surgery in terms of hospital mortality. Major hepatectomy for HCC in the presence of cirrhosis is considered dangerous as mortality rate is high (26% to 50%). The study states that some previous workers recommended that only selected patients with Child's A status or indocyanine green (ICG) retention at 15 minutes of less than 10% undergo major hepatectomy. A survey was made of our patients with HCC and cirrhosis undergoing major hepatectomy between 1989 and 1994. The preoperative, intraoperative, and postoperative data of 54 patients with cirrhosis were choose who had major hepatectomy. Patients were compared with those of 25 patients with underlying chronic active hepatitis and 22 patients with normal livers undergoing major hepatectomy for HCC. The study states that major hepatectomy, defined as resection of two or more liver segments by Goldsmith and Woodburn nomenclature, was performed on all the patients. The study main outcome was to measure the hospital mortality, which was

defined as death within the same hospital admission for the hepatectomy. The research paper shared the results that preoperative liver function in patients with cirrhosis was worse than in those with normal livers. The intraoperative blood loss was higher (*P*=.01), but for patients with cirrhosis, chronic active hepatitis, and normal livers, the hospital mortality rates (13%, 16%, and 14%) were similar. The hospital mortality rate for patients with cirrhosis in the last 2 years of the study was only 5%. Patients with cirrhosis could tolerate up to 10 L of blood loss and survive the major hepatectomy. By discriminant analysis, an ICG retention of 14% at 15 minutes was the cutoff level that could maximally separate the patients with cirrhosis with and without mortality. The study concluded with that the major hepatectomy for HCC in the presence of cirrhosis is associated with a mortality rate that is similar to the rate for patients with normal livers. An ICG retention of 14% at 15 minutes would serve as a better selection criterion than the 10% previously used**.** However, no work has been done to introduce age, race, gender of the patients and no comparison of the number of deaths in the hospital among hepatectomy patients or non-hepatectomy patients.

3.4 Hepatitis C and Hepatocellular Carcinoma

The research by (Naoumov, N V et al., 1997 [126]) 1438 patients with histologically proven cirrhosis were examined. The presence of HCV RNA, anti-HCV and characterization of virus genotypes were found in 72 cases who developed hepatocellular carcinoma after a median follow-up of 5.3 years (range 1 to 16) and compared to 72 controls who had cirrhosis only, after a median follow-up of 4.8 years (range 1 to 16). Patients in the hepatocellular carcinoma group and results were matched, one to one, for age, sex, nationality, HBsAg seropositivity, duration of follow-up and etiology of

cirrhosis. HCV RNA was found in 31 of 72 (44%) patients who developed hepatocellular carcinoma, significantly more frequently than in 17 of 72 (23%) controls with cirrhosis (odds ratio 2.4, 95% confidence interval 1.2 to 5.0; p = 0.013). When cirrhosis of different etiologies was revealed the results showed that the hepatitis C virus replication was more often detected in patients developing hepatocellular carcinoma in association with cryptogenic cirrhosis (p = 0.007), alcoholic cirrhosis (p = 0.043) and hepatitis B virus seronegative cirrhosis (p = 0.05). Hepatitis C virus genotypes 1b and 4 were the most common. Genotypes 1b and 4 were found in 53% and 25%, of the patients studied, but were equally distributed between cirrhosis progressing to hepatocellular carcinoma and controls. The research concluded with hepatitis C virus replication is closely associated with hepatocellular carcinoma development in cirrhosis, and there is no special role of hepatitis C virus genotypes. However, no work has been done to introducing region and income level of the patients.

The research by (Caselmann, W H, and M Alt., 1996 [127]) longitudinal studies showed that 16 of 62 anti-HCV antibody (ab)-positive patients developed hepatocellular carcinoma (HCC) within 5 yr. The frequency of anti-HCV antibody in HCC patients has been as high as 72% in Spain, 49-62% in Italy and 58% in France. It ranges between 9 and 36% in the USA and is about 26% in Germany. In HBV-endemic areas like South East Asia and Equatorial Africa, HCV-related HCCs plays an insignificant role. The risk of developing of HCC was elevated (up to 69.1-fold) for anti-HCV antibody-positive patients as compared to anti-HCV antibody-negative controls in almost all geographic areas. There is some data for an increased risk of developing HCC when hepatitis B virus (HBV) coinfection is present. Cirrhosis is likely to represent an additional risk

factor for the development of HCC in anti-HCV antibody-positive patients. Blood transfusions are the source of infection in barely one third of anti-HCV antibody-positive HCC patients. There was no significant difference in age or gender between anti-HCV antibody-positive and antibody-negative HCC patients. On the molecular level, HCV replication intermediates have been detected in HCC tissue and point mutations within the p53 gene have been demonstrated. Hepatocellular Carcinoma deaths were significantly ($p = 0.01$) higher in Swedish anti-HCV antibody-positive patients than in anti-HCV antibody-negative controls (18 vs. 4%). However, no work has been done to introducing income level of the patients.

The study by (Reddy, Arvind et al., 2013 [128]) 185 cirrhotic patients with HCC who had hepatitis C virus antibody (HCV Ab) (+) and HBsAg(-). These patients were at Wayne State University between 1999 and 2008. 108 patients had HCV polymerase chain reaction confirmation of viremia while the remaining (77) had Chronic Hepatitis C on the basis of a positive HCV Antibody and the absence of any other cause of liver disease. Data was taken from institutional database of 356 HBsAg (-) age, race and gender matched patients with HCV RNA-confirmed Chronic Hepatitis C and without HCC. There was another subgroup of controls included 118 matched patients with liver cirrhosis. χ^2 test and t test were used for data analysis. 77% of patients in all 3 groups were African Americans. Patients with HCC had a higher body mass index ($P = 0.03$), a higher rate of co-infection with human immunodeficiency virus (HIV) ($P = 0.05$) and a higher rate of alcohol abuse ($P = 0.03$) than the controls. More patients with HCC had Hepatitis B than controls (78% vs 39%, $P = 0.01$). 63% of patients with HCC were both hepatitis B surface antigen (HBsAb) (-) and HBcAb (+) compared to 23% of controls (P

< 0.01). When compared to cirrhotic controls, the frequency of HBcAb (+) remained higher in patients with HCC (78% vs 45%, P = 0.02). Patients with HCC were likely to be both HBsAb (-) and HBcAb (+) than the cirrhotic controls (63% vs 28%, P = 0.01). 100% of Chronic Hepatitis C and HIV co-infected patients with HCC (n = 11) were HBcAb (+) when compared to controls (44%; n = 9). Data showed that suppressed Hepatitis B occurs at a higher frequency in patients with Chronic Hepatitis C and HCC than in patients with Chronic Hepatitis C without HCC. However, no work has been done to introducing income level of the patients.

The research by (Albeldawi, Mazen et al., 2012 [129]) patients with confirmation HCC between the year 1994 and 2007 (404 patients). A case-control design (four controls for each case with non-cirrhotic HCC) were chosen to compare the characteristics and survival of HCV in HCC patients without (cases) and with (controls) cirrhosis. This study used logistic regression analysis to identify association with HCV in non-cirrhotic HCC. 87 patients with non-cirrhotic HCC were identified, six (7 %) had HCV infection in comparison with 107 of 317 (55.7 %) with cirrhotic HCC (P < 0.001). Compared with the HCV-associated HCC cirrhotic group, patients with HCV-associated HCC in the absence of cirrhosis were more likely to present with a single nodule (100 vs. 66.7 %), larger nodule size (>5 cm) (100 vs. 16.7 %), and macrovascular invasion (66.7 vs. 17.4 %) at the time of diagnosis. Four out of six patients with HCV-associated HCC in the absence of cirrhosis where alive at three years all of them had resection, which was better survival than for HCC arising in cirrhotic livers of HCV-infected individuals (66.7 vs. 39.1 %). Paper concluded with the statement that HCV is responsible for a small minority of non-cirrhotic HCC cases representing an uncommon and poorly defined subgroup of HCC.

However, no work has been done to introducing age, gender and race/ethnicity of the patients.

The research by (Nash, Kathryn L et al., 2010 [130]) states that over a 2-year period, patients with chronic hepatitis C infection without cirrhosis with HCC were diagnosed.

Six patients (five males, one female) with chronic hepatitis C infection without cirrhosis and with HCC. Out of six patients, five patients were treated by surgical resection and one patient had liver transplantation. After the evaluation results were confirmed that the presence of HCC and the absence of cirrhosis were in all cases. The degree of fibrosis of the background liver was showed as mild (n = 1), moderate (n = 4) or bridging fibrosis (n = 1). Review of the clinical case revealed that all cases had an additional risk factor for the development of HCC (four had evidence of past hepatitis B virus infection; two had a history of excessive alcohol consumption; a further patient had exposure to immune suppression). The research concluded that HCC does occur in patients with non-cirrhotic HCV infection who have other risk factors for hepatocarcinogenesis. However, no work has been done to introducing age, race/ethnicity of the patients.

The research by (Fujioka, Shin-Ichi et al., 2003 [131]) states that the hepatitis B virus (HBV) gene has been detected in hepatocellular carcinoma (HCC) tissue negative for the hepatitis B surface antigen and positive for the hepatitis C virus (HCV) antibody. Eleven patients were diagnosed with HCV-positive chronic liver disease; these patients developed HCC; they were assigned to group A. HBV DNA was detected in 8 of the 11 patients (73%). Twenty-five patients, which did not develop HCC, these patients were

selected as group B. Six of the group B patients were classified as DNA-positive (24%). The HBV DNA in liver tissue was found to be highly related to HCC development ($P < 0.01$). The study concluded, that the presence of the HBV gene in patients with chronic HCV associated-liver injury appears to develop hepatocarcinogenesis. However, no work has been done to introducing age and gender of the patients.

The study by (Michielsen, P et al., 2012 [132]) states that 25% of hepatocellular carcinoma (HCC) is related to HCV, being the main cause in Western Europe, North America and Japan. HCV can be suspected in the development of HCC in an indirect way through induction of chronic inflammation, or directly by means of viral proteins activating several signaling pathways. Patients with clinically significant hepatic fibrosis there is widespread agreement that antiviral therapy is indicated in order to eliminate the virus. It is generally accepted that sustained virologic response (SVR), i.e. undetectable HCV RNA at 24 weeks after treatment withdrawal, is associated with resolution of liver disease in patients without cirrhosis. Results of treatment for chronic hepatitis C have improved drastically. The current standard of care is a combination of pegylated interferon and ribavirin for 24 to 48 weeks, depending on the genotype. In the near future, this standard of care will include addition of directly-acting antivirals. In the year 2011 two protease inhibitors (boceprevir and telaprevir) have been registered for use in adults with genotype 1 chronic hepatitis C, increasing the SVR rates from less than 50% to about 70% in patients treated with a triple combination. There is very limited evidence for the role of interferon-based therapy in primary, secondary and tertiary prophylaxis of HCC in patients with chronic Hepatitis C. The study concluded by stating that most studies were designed to assess the antiviral effect of treatment and not the long-term

impact on the natural history of the disease. Current study must be using the more successful emerging treatments of chronic hepatitis C are must be conducted to evaluate the risk of HCC. However, no work has been done to introducing age and gender of the patients.

The study by (Tanaka, H et al., 2000 [133]) states that 594 patients with chronic hepatitis C who received interferon-alpha therapy (Interferon group) and 144 patients with chronic hepatitis C who did not receive interferon (Control group). The patients in the Interferon group were categorized into the following three groups, which was based on the response of the serum aminotransaminase level of the patient during and after completion of the therapy protocol: sustained responders (n = 175), transient responders (n = 165), and non-responders (n = 254). The age, sex, serum aminotransaminase level, platelet count, histological staging, hepatitis C virus (HCV) subtype, and HCV concentration at baseline were adjusted with the Cox proportional hazards model. The length of follow-up for the risk for developing hepatocellular carcinoma (HCC) was 57.2 +/- 13.9 months in the Interferon group and 67.7 +/- 28.7 months in the Control group. Multivariate analysis showed that interferon therapy decreased the risk for developing HCC by 48% as compared with that in the Control group (P = 0.064). The older the age, being male, having a low platelet count, and higher histological stage were independent factors associated with the development of HCC. The hazard rate ratio for development of HCC in the sustained responders, transient responders, and non-responders was 0.16 (95% confidence interval [CI]: 0.04-0.62), 0.27 (95% CI: 0. 09-0.79), and 0.74 (95% CI: 0.37-1.48). Study further states that 18 patients during the follow-up in the Interferon group died (10 from liver-related diseases) and 17 patients in the Control group died (10

from liver-related diseases). No sustained responder or transient responder in the Interferon group died of liver-related disease. The cumulative survival rates of the Interferon and Control groups were nearly identical during the first 5 years following diagnosis. Thereafter, the cumulative survival rate of the Control group declined, resulting in an 8-year survival rate in the Interferon and Control groups of 97% and 81% (P = 0. 061). Study states that the similar trends were seen in the survival analysis of those who had died of liver disease: the 8-year survival rates of the Interferon and Control groups were 98% and 88%, respectively (P = 0. 32). The study concluded with that interferon therapy lowered the incidence of HCC among patients with chronic hepatitis C for those who showed sustained normalization and among those patients who showed normalization of the serum aminotransferase level after completion of interferon therapy. The survival analyses and determination of the cause of the death suggested that interferon therapy improves the long-term survival of chronic hepatitis C patients who respond to this therapy, possibly by decreasing mortality from liver-related diseases. However, no work has been done to introducing race, region or salary level of the patients.

3.5 Clinical Decision Support System for Hepatitis C Virus

The study by (Fathauer, L and J. Meek, 2012 [134]) states that the Clinician compliance with clinical guidelines in the treatment of Hepatitis C (HCV) patients has been reported very low (as low as 18.5%). Treatment is complex and patient compliance is often inconsistent. Due to this an active clinician surveillance and support is important. A clinical decision support system (CDSS) embedded within an electronic health record can provide reminders, summarize key data, and make the process easy to coordinate

with patient care. The paper describes the implementation and evaluation of a CDSS to support HCV treatment. It includes the design, implementation, and initial evaluation of an HCV-specific CDSS. Design and implementation processes by representing the reporting on the impact of the CDSS on quality indicator, and comparing the pre-CDSS group to the post-CDSS group, were the part of this study. The CDSS was successfully designed and implemented for diagnosis of HCV. Pilot testing of the clinical outcomes acknowledged high rates of quality indicator completion in both the pre- and post-CDSS. The post-CDSS group received a higher frequency of reminders (4.25 per patient) than the pre-CDSS group (.25 per patient). The study concluded with the case report documented processes used to successfully design and implement an HCV CDSS. Results did positively demonstrate the feasibility of comparing quality indicator completion rates of pre-CDSS and post-CDSS successfully. This research paper suggests that the future studies must include a larger sample size data size across multiple providers with expanded outcomes, staff satisfaction, and time studies to calculate efficiency and cost effectiveness of the CDSS. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients as well as no HCV data analysis was done.

A study by (Loftus, Dani et al., 2019 [135]) states that hepatitis C Virus (HCV) is classified as a contagious liver disease that can be either acute or chronic, and the illness ranges in severity from mild to lifelong. It is estimated that 2.7 million people in the United States (US) have HCV, but only half are diagnosed. The CDC recommends testing by birth-cohort, focusing on adults born between 1945 and 1965. Three main objectives for this project included implementation of a clinical decision support system

(CDSS), increasing HCV screening by providing education to the support staff, in primary care clinics of a local hospital, and sharing resource information with patients diagnosed with HCV about the available treatments. Because a CDSS was not established, in-services by clinic educators regarding HCV and screening were conducted. Education about HCV and the hospital-based HCV clinic were shared with local health departments and the Red Cross. The study shared the results regarding the hospital-based HCV clinic utilization, there was a 48% increase in patients referred following the implementation. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

A study by (Oleimanian Gharehchopogh F, Mousavi S K., 2019 [136]) states that Clinical Decision Support Systems (CDSS) are designed in the form of computer programs that help medical professionals make decisions about disease diagnosis. The main aim of these systems is to assist physicians in diagnosing diseases, a physician can interact with the system and use them to analyze patient data, diagnose diseases, and other medical activities. The study states that this is a descriptive-analytic study. The datasets include 768 records of diabetes with 8 features and 155 records of hepatitis with 19 features, which were provided by the Global Website of UCI. In this study, the Particle Swarm Optimization (PSO) algorithm was used for Feature Selection (FS) and the Firefly Algorithm (FA) was used to classify diabetes and hepatitis into two healthy and unhealthy classes. 80% of the data was used for training and the remaining (20%) was used for testing. The experiments results showed that the accuracy of the PSO and FA for the diabetes dataset was 84.41% and 82.08%. Also, the accuracy of the PSO and

FA for the hepatitis dataset was 81.84% and 80.34%. The accuracy of the proposed model for the diabetes and hepatitis datasets was 95.38% and 94.09%. The study concluded with that according to the results, the proposed model had a lower error rate in diagnosis compared to the PSO and FA. The results of this study can help doctors in timely diagnosis of diabetes and hepatitis. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

A study by (Sara Sweidan et al., 2016 [137]) states that using of clinical decision support systems (CDSSs) may improve chronic disease management, which can be expensive and requires recurrent visits to multiple health professionals, ongoing disease control, treatment monitoring, and patient behavior modification. The objective of this survey is to determine if CDSSs can improve the processes of chronic care including diagnosis, treatment, and monitoring (management) of diseases. The survey covers articles extracted from relevant databases. It uses search related to information technology and viral hepatitis which are published between 2000 and 2016. The study shows the results that 80% of studies asserted the benefits provided by information technology (IT); 75% of studies asserted the benefits concerned with medical domain;25% of studies do not clearly define the added benefits due IT. The CDSS current state requires many improvements to support the management of liver diseases such as HCV, liver fibrosis, and cirrhosis. The study concluded that the number of health applications with DSS has been increased. Accurate diagnosis is the most important problem of medicine. Understanding the relationship between diagnosis and finding the clinical protocols is affected in healthcare. This survey provided a very important

knowledge related to clinical domain from several search studies in different medical specialties for helping in the development, implementation and evaluation of CDSS systems for long life management. The study states that there is a limitation in managing HCV disease. The study further states that future work proposes a new framework in CDSS to diagnosis HCV patient to choose appropriate protocol for treatment. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

3.6 CDSS and Liver Diseases

The study by (El-Sappagh et al., 2018 [138]) states that diagnosis of liver fibrosis, is very crucial. Clinical decision support systems (CDSSs) based on patient's historical medical data and accurate Artificial Intelligence (AI) techniques can aid physicians in their decision-making process. The task of arriving at an accurate decision, and in a timely diagnosis decision is extremely complex because of the dynamic, vagueness, and uncertainty associated with this disease. Fuzzy logic can handle these issues. Two of the most interesting techniques are a fuzzy analytical hierarchy process (FAHP) and an adaptive neuro-fuzzy inference system (ANFIS). The FAHP is very popular for dealing with uncertainty in multi-criteria decision-making, and the ANFIS is popular in learning fuzzy inference system from data based on artificial neural networks. These two methods have not been used to model CDSSs in fibrosis stage detection domain. This study developed a CDSS based on a case comparison of the effectiveness of the FAHP and the ANFIS in the medical diagnosis of the fibrosis disease. This study states that design and implementation of two frameworks was based on these two techniques. Diagnostic real data of 119 cases infected by chronic viral hepatitis C from the Liver Institute at

Mansoura University are used to train and test both the FAHP and ANFIS. Criteria and sub criteria weights are based on opinions of two domain experts. The ANFIS model is designed using trial and error based on the analysis of various experiments. Results are later compared with the diagnostic conclusions of medical expert. The results show that two techniques can successfully be employed in designing a diagnostic CDSS system for fibrosis diagnosis. The two techniques achieve a classification accuracy of 93.3%. The results confirm the effectiveness of both methods. That is why both the FAHP and ANFIS are possible approaches in modeling CDSS for diagnosis of a liver fibrosis stage. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

The study by (Keltch, B., Lin, Y. & Bayrak, C., 2014 [139]) states that globally one in twelve people have the Hepatitis B or Hepatitis C virus. Diagnosis and treatment of this disease is guided by liver biopsies where a small amount of tissue is removed to determine the fibrosis stage from F0 (no damage) to F4 (cirrhosis). Biopsies are expensive. Non-invasive techniques for determining fibrosis stage have been developed. Non-invasive methods have utilized serum markers, imaging test, and genetic studies. Clinical decision support systems (CDSS) use decision support system theory and technology to assist clinicians in the diagnosis and treatment process. Using historical clinical data and the Artificial Intelligence (AI) techniques to aid physicians in their decision-making process is the goal of CDSS. The CDSS provides a large number of medical support functions to help clinicians make the reasonable diagnosis and choose the best treatment possibilities. This paper uses four artificial intelligence predictive techniques to publicly available data on 424 Hepatitis B and Hepatitis C patients.

Demographic and standard serum markers are utilized to predict fibrosis stage and then compare these predictions to known biopsy results. A final decision tree evaluation is applied to make a final prediction. The author states that a publicly available web application can be used as a prototype for presenting AI predictive results in a CDSS environment based on these models. The study concluded that this technique along with others could mitigate the need for some liver biopsies in more than 500 million Hepatitis B and C patients worldwide with additional validation and verification. However, no work has been done to diagnose Hepatitis C virus and test performed to confirm the disease of the patients.

The study by (Sweidan et al., 2018 [140]) states that clinical decision support system become a part of daily life. Accurate diagnosis of liver cirrhosis helps in avoiding medical problems which may lead to death. The study states that the aim of the study is to build a fuzzy expert system for the diagnosis of liver fibrosis-stage (DLFS). This study uses the method where the system uses machine learning tools and data mining statics to discover fuzzy rules, which help physicians to give a fast and accurate diagnosis. The experiment has been performed on real dataset from clinical data sheets for 119 patients infected by chronic HCV. Study shared the results that the system identifies liver fibrosis-stage with high degree of accuracy 95.7% and may decrease the need for liver biopsy. The study concluded with a new knowledge-based system for liver fibrosis stage prediction using fuzzy reasoning technique. This study used entropy to generate the fuzzy rules to be used in the knowledge-based system of fuzzy rule-based reasoning method for the disease classification. The study has evaluated the knowledge-based system on real test dataset of 119 HCV patient cases. The results of our

experiments on the dataset indicated that the proposed system achieved good prediction accuracy 95.7% for liver fibrosis stage. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

The study by (Chevrier et al., 2011 [141]) states that the objective of this work was to create a self-working computerized clinical decision support system (CDSS) which should be able to analyze liver function tests (LFTs) in order to provide diagnostic suggestions and helpful care support to clinicians. The study states that an expert system that processes clinical information to provide diagnostic dealing with abnormal Liver Function Tests, therefore we created a drug-disease causality assessment tool to include drugs in the differential diagnosis. The CDSS will guide clinicians in the care process where system offers them case-specific support in the form of guidelines, order sets and references to recent articles. The CDSS will be implemented in University Hospitals clinical information system (CIS) during the year 2011. The study discussed the results where preliminary tests have been conducted on case reports chosen randomly on PubMed. Considered as medical challenges, case reports were nevertheless processed correctly by the program to the extent that 18 cases out of 20 were diagnosed accurately. The study concluded with the statement that the system was able to find the precise cause of Analyze Liver Function Tests and to guide the clinician towards the right set of diagnosis. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

The study by (Acharya et al., 2016 [142]) states that fatty liver disease (FLD) is known by the abnormal retention of large vacuoles of neutral fat in the liver cells, due to

alcoholism or metabolic syndrome. Fatty Liver Disease can lead to severe liver diseases such as hepatocellular carcinoma, cirrhosis and hepatic inflammation but it is a reversible disease if diagnosed early. This is why paper states that computer-aided diagnostic tools-clinical decision support system (CDSS) play a very important role in the automation of diagnosis of Fatty Liver Disease. This paper focuses on the detection of fatty liver disease by using ultrasound images. The information from the image is extracted using GIST descriptor models. Marginal Fisher Analysis (MFA) integrated with Wilcoxon signed-rank test helps to eliminate the trivial features and provides the distinctive features for qualitative classification. The study states that the clinically important features are used using classifiers such as decision tree (DT), support vector machine (SVM), adaBoost, *k*-nearest neighbor (*k*NN), probabilistic neural network (PNN), naïve Bayes (NB), fuzzy Sugeno (FS), linear and quadratic discriminant analysis classification of normal and abnormal liver images. The study states that the results showed that probabilistic neural network classifier can diagnose fatty liver disease with an average classification accuracy of 98%, 96% sensitivity, 100% specificity and Area Under Curve (AUC) of 0.9674 correctly. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

The study by (Zia et al., 2015 [143]) states that rule based and case-based reasoning technique both are two complementary alternatives to Clinical decision support system (CDSS). In this study case-based reasoning technique was used for medical data diagnosis & treatment suggestion for liver disease. Case-Based reasoning technique is a method to explore in a medical context where symptoms represent the problem, and diagnosis and treatment represent the solution. The study states that similarity

measurement is the major weakness in executing the case-based reasoning technique accurately and adequately. The study proposes a similarity algorithm by using Average Weighted Euclidian distance method which calculates distance between the new case and stored cases and then using similarity function to retrieve closely related cases from the case repository. Once the case is retrieved, re-instantiation strategy of case adaption phase is used for adapting the suggesting way out of the current problem. Then proposed solution of the problem is revised by the medical expert in the revise phase of the case-based reasoning technique. Then, the revised solution is updated into the case repository as a new case. The study concluded with if there is an absence of the similar stored cases with respect to a new input case in a case repository, then the study states that the system needs an automated rules-based reasoning system that will generates the solution for the new input case without the supervision of expert. For this purpose, hybrid reasoning approach will be used to solve this type of issues. This research performed data analysis on the Indian Liver Patient dataset from UCI Machine Learning Repository was used for diagnosis & classification. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

The study by (Donnan et al., 2007 [144]) states that liver function tests (LFTs) are routinely performed in primary care, and are the gateway to further invasive and expensive investigations to diagnosis a disease. Very little is known of the consequences in people with an initial abnormal liver function (ALF) test in primary care and with no obvious liver disease. Further investigations may be expensive for Health Services. This study determines the natural history of abnormalities in liver function test before liver

disease presents in the population and identify those who require minimal further investigations for reduction in costs. The study uses a population-based retrospective cohort study that will follow up all those who have had an incident liver function test (LFT) in primary care to subsequent liver disease or mortality over a period of 15 years (approx. 2.3 million tests in 99,000 people). The study takes place in Primary Care (pop approx. 429,000) between the year 1989 and 2003. The target population consists of patients with no recorded clinical signs or symptoms of liver disease and registered with a general practitioner. The health technologies being assessed are liver function test, viral and auto-antibody tests, ultrasound, CT, MRI and liver biopsy. The study will use the Epidemiology of Liver Disease (ELD) database to find the outcomes of liver disease. These are based on hospital admission data (Morbidity Record 1), dispensed medication records, death certificates, and examination of medical records. A sample of patients (n = 150) with recent initial abnormal liver function tests or invitation to biopsy will complete questionnaires to obtain quality of life data and anxiety measures. Cost-effectiveness and cost utility Markov model analyses will be performed from health service. The results will also be used to develop a computerized clinical decision support tool (CDSS). The aim of this paper was to give information rather than the research, there was no special algorithm used or special data analysis done. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

3.7 Conclusion

Around 40 literatures in the area of hepatitis, and liver diseases using clinical decision support system (CDSS) had been reviewed expanding last several years. Under

the data analysis section of the review, hospital, treatment, management, cost and mortality, associated with hepatitis and liver disease were covered. The research included evidence of indirect burden of illness and relationship between HCV infection, impact on productivity and impact on healthcare benefits/cost. The literature review was divided into five categories (i) Hepatitis C related cirrhosis, (ii) Cirrhotic Hepatitis C and Hepatocellular Carcinoma (HCC), (iii) Hepatitis C and Hepatocellular Carcinoma, (iv) Clinical Decision Support System (CDSS) and Hepatitis C, and (v) CDSS and Liver Diseases.

The category Hepatitis C related Cirrhosis discusses research papers about alcohol related liver disease and how it was a major factor on the treatment charges, abstinence from alcohol was important for improving the survival of patients with alcoholic cirrhosis, alcohol addictions therapy was suggested to reduce the expense of Alcoholic Cirrhosis, the absence of Interferon (IFN) therapy was responsible for HCC and decompensation, interferon does not seem to affect survival of patients with Hepatitis C Virus related Cirrhosis while it seems to prevent the development of hepatocellular carcinoma, treated patients reported significantly lower rates of HCC, patients with HBV infection may present with cirrhosis about 10 years earlier than those with HCV infection, HCV infection tends to be associated with a higher risk of decompensation, deaths due to alcoholic cirrhosis for people aged between 25 to 34 had experienced the greatest increase in mortality. However, no work has been done regarding this category on introducing age and gender of the patients.

In the category regarding Cirrhotic Hepatitis C and Hepatocellular Carcinoma (HCC), it analyzes research papers about interferon therapy for cirrhotic patients with

chronic Hepatitis C especially for; those patients who had been cured interferon therapy prevents the development of hepatocellular carcinoma (HCC) and improved survival but, a reduction of HCC is also achieved even in the non-sustained responders, the risk of HCC is reduced among patients with HCV who achieve a sustained virological response (SVR) with antiviral therapy, maintenance therapy with Interferon (IFN) therapy does not reduce HCC risk among patients who do not respond to initial therapy, SVR resulted in significantly more favorable long-term outcomes-such as lower risk of progression to cirrhosis and HCC occurrence, the incidence of HCC and mortality should be higher in patients with higher age. However, no work has been done regarding this category on introducing race and region of the patients.

In category Hepatitis C and Hepatocellular Carcinoma discusses research papers about interferon therapy significantly lowered the incidence of HCC among patients with chronic hepatitis C, interferon therapy improves the long-term survival of chronic hepatitis C patients who respond to this therapy, possibly by decreasing mortality from liver-related diseases, the presence of the HBV gene in patients with chronic HCV associated-liver injury appears to develop hepatocarcinogenesis, HCC does occur in patients with non-cirrhotic HCV infection who have other risk factors for hepatocarcinogenesis, HCV is responsible for a small minority of non-cirrhotic HCC cases representing an uncommon and poorly defined subgroup of HCC, latent Hepatitis B occurs at a significantly higher frequency in patients with Chronic Hepatitis C and HCC than in patients with Chronic Hepatitis C without HCC. However, no work has been done regarding this category on introducing age, gender, race and region of the patients.

In the category Clinical Decision Support System (CDSS) and Hepatitis C discusses research papers about successfully design and implement an HCV CDSS results did positively demonstrate the feasibility of comparing quality indicator completion rates pre-CDSS and post-CDSS, implementation of a clinical decision support system (CDSS) for providers, increasing HCV screening by providing education to the support there was a 48% increase in patients referred following implementation, the proposed model had a lower error rate in diagnosis, 80% of studies asserted the benefits provided by CDSS; 75% of studies asserted the benefits concerned with medical domain;25% of studies do not clearly define the added benefits due CDSS, and the CDSS current state requires many improvements to support the management of liver diseases such as HCV, liver fibrosis, and cirrhosis. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

In the category Clinical Decision Support System (CDSS) and Liver Diseases discusses research papers about two techniques fuzzy analytical hierarchy process (FAHP) and an adaptive neuro-fuzzy inference system (ANFIS) both achieved a classification accuracy of 93.3%. The results confirm the efficiency and effectiveness of both methods, the evaluation results showed that the system identifies liver fibrosis-stage with high degree of accuracy 95.7%, probabilistic neural network classifier can diagnose fatty liver disease with an average classification accuracy of 98%, fuzzy expert system for the diagnosis of liver fibrosis-stage (DLFS). This study uses the method where the system uses machine learning tools and data mining statics to discover fuzzy rules, which help physicians to give a fast and accurate diagnosis, and the CDSS offers case-specific

support in the form of guidelines. However, no work has been done to diagnose Hepatitis C virus and test performed using backward and forward chaining to confirm the disease of the patients.

In essence, CDSS has been studied for liver disease treatment, and management. Basic information has been provided by researches; actual data from HCUP or other providers were used for statistical analysis and CDSS. The papers analyzed above lacked discussion on the impact of race, region, gender or age of the disease.

There is no comprehensive study into the hospitalization characteristics of patients pertaining to their length of stay, total charges of treatment, Procedure performed, household income, age, sex, hospital location, hospital region, payment methods, and race for Hepatitis and Liver diseases patients. There are no studies analyzing the Hepatitis and liver diseases. In addition to that is to develop Clinical Decision Support System to diagnose Hepatitis C using backward and forward chaining. I have covered these gaps in my research.

CHAPTER IV- ANALYSIS AND RESULTS

4.1 Introduction

This chapter provides a detail results of the descriptive statistical analysis. The results from the analysis provide overall summaries of the study. This analysis helps to identify hospitalization outcome, procedure performed, procedure cost, total charges and admission type, disposition and mortality, morbidity and incidence of various types of hepatitis and liver diseases. A variety of statistical analysis was performed based on the NIS data for 2007 to 2012.

4.2 Data Source

The aim of this study is to analyze the Hepatitis C Virus. For this chapter, data was taken from the National Inpatient Sample (NIS), which is part of the Healthcare Cost and Utilization Project (HCUP). HCUP is associated with the Agency for Healthcare Research and Quality (AHRQ). HCUP brings together the data from State data organizations and hospital associations. HCUP combines both private and state organization data, including the Federal government. Researchers have been able to utilize this database for research on a broad range of healthcare policies. The NIS is the publicly available database. This database is used by researchers and policymakers to identify, track, and analyze national trends in health care utilization, access, charges, quality, medical practice patterns and outcomes of treatments [145].

4.3 Data Elements

The Healthcare Cost and Utilization Project (HCUP) data was given by Rutgers University department of Health Professionals. The data was in the format of SPSS. SPSS is an IBM Statistics software version 26. For analysis purpose IBM-SPSS

statistical analysis software and Microsoft Excel was used. The data was recoded for all yearly Hepatitis and Liver disease diagnosis and procedure cases in a general category and then subcategorized for more detail analysis. Yearly filters were used to fetch out the yearly results.

Table 4.1 Data Elements

HCUP Data Elements	Descriptive Title
AGE	Age in years at admission
ASOURCE	Admission source
ATYPE	Admission type
DIED	Died during hospitalization
DISPUNIFORM	Disposition of patient
MALE/FEMALE	Sex of patient
HOSP_LOCATION	Location (urban/rural) of hospital
HOSP_REGION	Region of hospital
LOS	Length of stay
PAY1	Insurance type
RACE	Race
TOTCHG	Total charges
ZIPINC_QRTL	Median household income for patient
PROCEDURES	Procedure Code

NIS description of Data elements, HCUP [145]. January 2020

Table 4.1 show the data elements that were used to analyze the Hepatitis C virus. The data elements that were used to analyze Hepatitis C virus were age, admission source, admission type, died in the hospital, disposition of patient, sex, hospital location (urban/rural), hospital region, length of stay, payment methods, race, total charges of treatment, household income and Procedure performed.

Table 4.2 Independent Variable and Codes

Full Name	Independent Variables	ICD-9-CM Codes
Hepatitis A Virus, Hepatitis E Virus	Hep A+E	0700, 0701, 07043,07053
Hepatitis B Virus, Hepatitis D Virus	Hep B+D	0702,0703, 07020-07023, 07030-07033,07042,07052
Hepatitis C Virus	Hep C	0704, 0705, 07041, 07044, 07051, 07054, 07070, 07071, 07049, 07059
Hepatitis Carrier	Hepatitis Carrier	V0260-V0269
Cirrhosis	Cirrhosis	5715, 5716, 5712
Chronic Hepatitis	Chronic Hepatitis	5714, 57140, 57141, 57142, 57149
Chronic Liver disease	Chronic Liver Disease	571, 5710,5711, 5713, 5718, 5719
Disorder of liver	Disorder of Liver	5730, 5731-5735, 5738
Hepatocellular Carcinoma	HCC	1550, 1551
Procedure	Procedure of Hepatitis	5011, 5012, 5013, 5014, 5019, 501, 5021,5022, 5023, 5024, 5025, 5026, 5029, 502, 503, 5051, 5059, 505, 504, 500, 5061, 5069, 506, 5091, 5092, 5093, 5094, 5099, 509, 9101-9106, 9109, 9202

ICD-9-CM Codes, December 2019 [146]

Table 4.2 shows Independent variables that are used for analysis of Hepatitis C virus are Hepatitis A+B, Hepatitis B+D, Hepatitis C, Hepatitis Carrier, Cirrhosis, Chronic Hepatitis, Chronic Liver disease, disorder of Liver and Hepatocellular Carcinoma (HCC). The independent variables for Procedures performed are Biopsy, Destruction of Tissue, Removal of Lobe, Liver Transplant, Repair of Liver, Other Procedures and Liver Scan. HCUP provided ICD-9-CM for diagnosis and ICD-9-PR for procedure codes which are shown in the table [146].

4.4 Data Analysis

This research focuses on the analysis of the number of records of patients with Hepatitis C virus from the year 2007 to 2012. Hepatitis C virus patient with the length of stay, total charges of treatment, how many died in the hospital, their Income status, hospital region, age, race, gender, sex, disposition, hospital location, the payment methods, admission type, admission source and Procedures performed on these patients.

The purpose of selecting Hepatitis A, Hepatitis B, Hepatitis C, Hepatitis D, Hepatitis E, Hepatitis Carrier, Cirrhosis, Chronic hepatitis, Chronic Liver Disease, Disorder of Liver, Hepatocellular Carcinoma (HCC), Procedures performed and procedure cost on these diseases is to compare Hepatitis C with other liver diseases. Hepatitis C effects the liver and give rise to other liver diseases. A comparison and overview are very crucial.

The large sample size data allows to analyze at a large national scale, nothing has been published to view Hepatitis C in a much broader way with other liver diseases. This

study will help to fill the literature gap by providing the results. This analysis helps to identify hospitalization outcome, procedure performed, procedure cost, total charges and admission type, disposition and mortality, morbidity and incidence of various types of hepatitis and liver diseases.

Table 4.3 Incidence of Hepatitis A, B and C

Year	Hep A+E	Hep B+D	Hep C
2007	1,670	14,794	102,015
2008	1,734	15,707	105,304
2009	1,529	14,973	112,519
2010	1,758	15,751	118,646
2011	1,684	15,367	130,617
2012	1,516	14,476	122,988

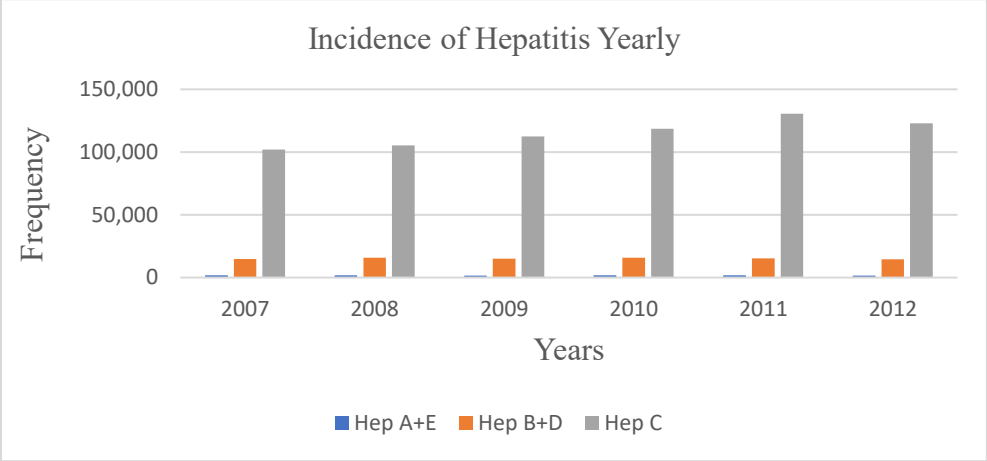

Figure 4.1 Incidence of Hepatitis yearly

The result from table 4.3 and figure 4.1 provides the overall summary of the study for Hepatitis A+E, Hepatitis B+D and Hepatitis C from 2007 to 2012. For Hepatitis C

the number of cases increased each year. Hepatitis C cases remained the highest among Hepatitis A+E and Hepatitis B+D. 2011 had the largest increase of 10%. Hepatitis A+E cases were lowest as compared to Hepatitis B+D and Hepatitis C. Hepatitis A+E remained constant. Hepatitis B+D cases remained higher than Hepatitis A+E and lower than Hepatitis C.

- **Summary for Hepatitis C Categorized by Age Group**

Table 4.4 Hepatitis C Utilization Characteristics

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Length of Stay, mean days	5.95	0.5%	5.75	50.1%	6.24	40.3%	6.44	7.6%	6.56	1.6%
Died during Hospital Stay	7	0.2%	1,092	33.9%	1,581	49.1%	427	13.3%	110	3.4%
Total charges of Treatment, mean charges	$31,980	0.5%	$30,979	50.1%	$39,427	40.3%	$43,161	7.6%	$38,303	1.6%

Table 4.4 show that age group 66- 80 years stayed in the hospital for 6.44 days. Age group 21-51 years stayed in the hospital for 5.75 days and 50.1% patients stay was of that length. Death rate during the hospital stay is high among 52-65 years age group. Age group 66-80 years stayed longer and total charges of the treatment were high too for this group.

Table 4.5 Total mean charges of Procedure Performed on Hepatitis C patients

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Total mean Charges of Procedure										
Biopsy	$93,750	0.9%	$71,094	39.3%	$89,084	47.7%	$65,190	10.8%	$90,554	1.2%
Destruction of Tissue	$0	0.0%	$62,378	16.8%	$48,302	59.6%	$49,780	19.3%	$33,916	4.3%
Removal of Lobe	$0	0.0%	$49,143	16.7%	$63,167	60.0%	$44,450	20.0%	$70,632	3.3%
Liver Transplant	$387,399	0.7%	$334,921	30.3%	$316,436	62.6%	$318,459	6.5%	$0	0.0%
Repair of Liver	$0	0.0%	$75,062	41.2%	$334,937	41.2%	$63,644	17.6%	$0	0.0%
Other Procedures	$372,136	0.7%	$81,647	19.4%	$80,893	62.6%	$48,623	15.8%	$39,612	1.4%
Liver Scan	$27,260	0.6%	$56,107	54.7%	$67,734	36.5%	$64,826	7.7%	$62,182	0.6%

Table 4.5 shows that 47.7% biopsies procedure, 59.6% destruction of tissue, 60% removal of

lobe, 62.6% liver transplant 41.2% repair of liver, 62.6% of other procedure and 36.5 % of liver

scan done on age group 52-65 years old.

Table 4.6 Race/Ethnicity of Hepatitis C Patients

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Race/Ethnicity										
White	203	0.4%	23,601	51.5%	17,853	39.0%	3,262	7.1%	898	2.0%
Black	40	0.2%	8,194	43.5%	9,144	48.5%	1,258	6.7%	221	1.2%
Hispanic	61	0.6%	5,665	51.4%	4,168	37.8%	998	9.1%	127	1.2%
Asian or Pacific Island	10	0.9%	288	27.2%	356	33.7%	329	31.1%	74	7.0%
Native American	5	0.6%	454	54.7%	307	37.0%	51	6.1%	13	1.6%
Others	8	0.4%	1,136	50.9%	817	36.6%	240	10.8%	29	1.3%

Table 4.6 shows that 39.0% were white and age group 52-65 years old, 48.5% of black and age group 52-65 years, 51.4% of Hispanic and age group 21-51, 33.7% of Asian or Pacific Island and age group 52-65 years, 54.7% of Native American and age group 21-51 years age group and 50.9% of others and age group 21-51 years old group with Hepatitis C virus.

Table 4.7 Gender of Hepatitis C Patients

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Sex										
Male	176	0.3%	30,706	48.3%	28,038	44.1%	3,978	6.3%	738	1.2%
Female	284	0.7%	20,297	53.2%	12,939	33.9%	3,716	9.7%	905	2.4%

Table 4.7 shows Hepatitis C was highest among male and female age group 21-51 years old.

Table 4.8 Insurance Type of the Hepatitis C Patients

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Primary Payer										
Medicare	16	0.1 %	10,321	33.8 %	12,294	40.2 %	6,487	21.2 %	1,441	4.7%
Medicaid	208	0.7 %	18,044	60.8 %	11,065	37.3 %	306	1.0%	57	0.2%
Private Insurance	148	0.7 %	9,051	44.1 %	10,527	51.3 %	685	3.3%	121	0.6%
self-Pay	54	0.5 %	8,017	70.6 %	3,218	28.3 %	56	0.5%	11	0.1%
No Charge	7	0.5 %	978	65.0 %	492	32.7 %	26	1.7%	2	0.1%
Other	27	0.3 %	4,455	56.2 %	3,297	41.6 %	130	1.6%	19	0.2%

Table 4.8 shows that highest Medicare frequency was with age group 52-65 years, Medicaid frequency was highest among age group 21-51 years. This group also belongs to low income group, highest self-pay is among 21-51 age group and highest other type of payment also belongs in the 21-51 years age group. Private Insurance was used to pay by 51.3% with age group 52-65 years.

Table 4.9 Income Level of the Hepatitis C

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Income Level										
$1-38,999	156	0.4%	20,487	52.3%	15,582	39.8%	2,499	6.4%	421	1.1%
$39,000-47,999	127	0.5%	12,157	50.7%	9,581	40.0%	1,709	7.1%	381	1.6%
$48,000-62,999	69	0.4%	9,370	48.4%	7,919	40.9%	1,606	8.3%	378	2.0%
$63,000+	88	0.6%	6,028	43.4%	5,729	41.3%	1,594	11.5%	441	3.2%

Table 4.9 describes that age group 21-51 years 52.3% belong to income level of $1-38,999, 50.7% belong to income level of $39,000-47,999, 48.4% belongs to income level of $48,000-62,999 and 43.4% belongs to the income level of $63,000+.

Table 4.10 Location of the Hospital

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Location										
Rural	57	0.7 %	4,667	56.8 %	2,837	34.5 %	537	6.5 %	115	1.4 %
Urban	403	0.4 %	46,302	49.5 %	38,107	40.8 %	7,154	7.7 %	1,534	1.6 %

Table 4.10 describes highest count for the age group of 21-51 years with hospital location in the rural and urban locations.

Table 4.11 Admission to the Hospital

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Admission to the Hospital										
Emergency	220	0.4%	30,079	50.6%	24,076	40.5%	4,153	7.0%	947	1.6%
Urgent (Patient Appointment)	106	0.8%	7,328	55.1%	4,821	36.3%	852	6.4%	184	1.4%
Elective (waiting list admission)	92	0.7%	6,757	50.5%	5,180	38.7%	1,143	8.5%	201	1.5%
Trauma Center	1	0.7%	89	58.9%	48	31.8%	10	6.6%	3	2.0%
Other	0	0.0%	17	47.2%	16	44.4%	2	5.6%	1	2.8%

Table 4.11 shows highest emergency admission, urgent, elective, trauma, and others were among age group 21-51 years.

Table 4.12 Admission Source of the Patient

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Admission Source										
Emergency Department	201	0.3%	29,105	49.8%	23,778	40.7%	4,338	7.4%	978	1.7%
From Different Hospital	15	0.4%	1,572	46.2%	1,426	41.9%	319	9.4%	72	2.1%
Other	191	0.7%	14,467	51.0%	11,044	38.9%	2,237	7.9%	426	1.5%

Table 4.12 shows patient's admission source shows highest among 21-51 years age group with emergency admission, patient came from different hospital, other health facilities, court/law enforcement and others.

Table 4.13 Hospital Region

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Region										
Northeast	86	0.4%	10,138	52.2%	7,330	37.7%	1,493	7.7%	379	2.0%
Midwest	81	0.5%	8,770	49.6%	7,110	40.2%	1,447	8.2%	291	1.6%
South	200	0.5%	20,386	51.6%	15,780	39.9%	2,587	6.5%	547	1.4%
West	93	0.4%	11,728	46.6%	10,767	42.7%	2,169	8.6%	434	1.7%

Table 4.13 shows that age group 21-51 years had the highest count at the Northeast, Midwest, south and west region.

Table 4.14 Destination after Discharge

Hepatitis C Virus 2007	1-20 Years		21-51 Years		52-65 Years		66-80 Years		81+ Years	
Categorized by Age Group	Numbers	%	Numbers	%	Numbers	%	Numbers	%	Numbers	%
Destination After Discharge										
To Home Self Care	374	0.5%	38,435	54.1%	27,559	38.8%	4,077	5.7%	644	0.9%
Transfer to Short-Term hospital	47	0.3%	5,890	39.5%	6,510	43.7%	1,894	12.7%	565	3.8%
To Home Health Care	13	0.2%	2,734	33.1%	3,990	48.3%	1,197	14.5%	324	3.9%
Left Against Medical Advice	19	0.5%	2,807	66.9%	1,274	30.4%	88	2.1%	6	0.1%
Died	7	0.2%	1,092	33.9%	1,581	49.1%	427	13.3%	110	3.4%
Discharge	0	0.0%	40	34.8%	60	52.2%	13	11.3%	2	1.7%

Table 4.14 shows that highest count that goes to home self-care, to home health care, left against medical advice is among age group 21-51 years after discharge from the hospital. Transfer to short-term hospital, died in the hospital, and discharged is high among age group 52-65 years.

4.4.2 Chronic Diseases of the Liver under Hepatitis Virus Influence

Table 4.15 Hepatitis has effect on other Diseases

Year	Cirrhosis	HCC	Chronic Hepatitis
2007	89,358	9,451	4,178
2008	93,982	11,950	4,407
2009	98,978	11,380	4,348
2010	104,860	12,242	4,594
2011	120,019	13,425	5,208
2012	115,229	12,913	4,511

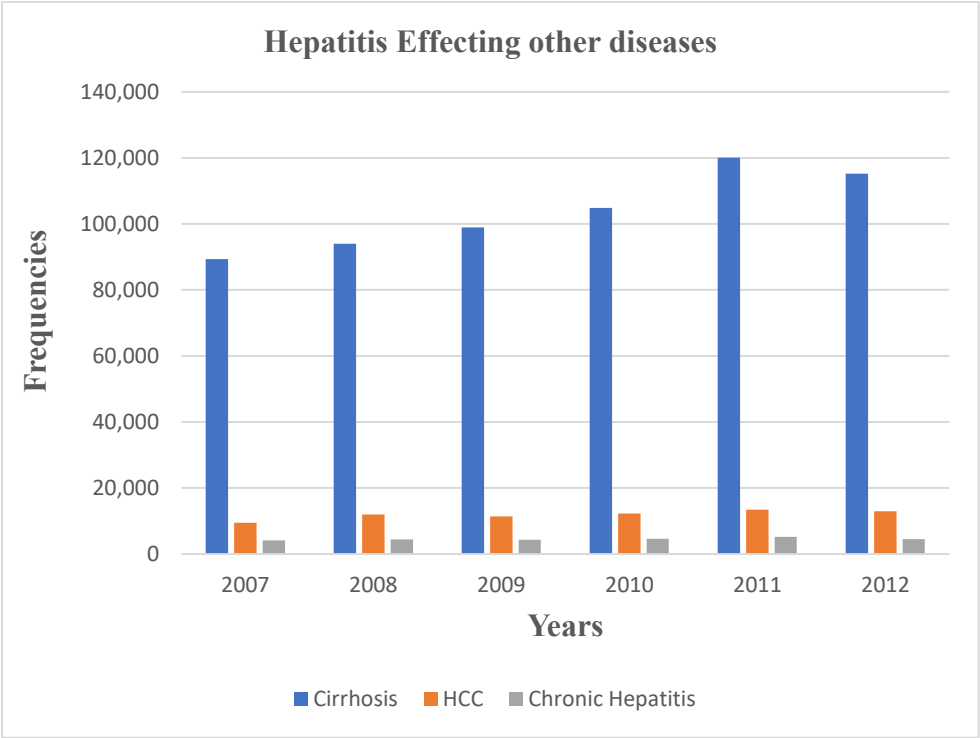

Figure 4.2 Hepatitis effects other diseases

The result from table 4.15 and Figure 4.2 provides the overall summary of the study for Cirrhosis, Hepatocellular Carcinoma (HCC) and Chronic Hepatitis. All three diseases are cause by Hepatitis B and Hepatitis C viruses. Cirrhosis is highest as compared to other disease. For cirrhosis the number of cases increased each year. Hepatocellular Carcinoma (HCC) is caused by Hepatitis B and Hepatitis C. Biggest increase was in 2008 of 26%. Chronic Hepatitis had highest increase of 13% and highest decrease of 13% too. It did not fluctuate a lot. In summary cirrhosis increased by 29%, HCC increased by 37% and Chronic Hepatitis increased by 8% from 2007 to 2012.

- Incidence of Liver Diseases

Table 4.16 Effect of Hepatitis on Liver

Year	Hepatitis Carrier	Chronic Liver Disease	Disorders of liver
2007	6,870	45,787	24,696
2008	5,970	56,189	26,237
2009	5,948	61,784	28,423
2010	5,897	69,023	28,265
2011	3,616	78,280	30,420
2012	3,930	75,329	28,075

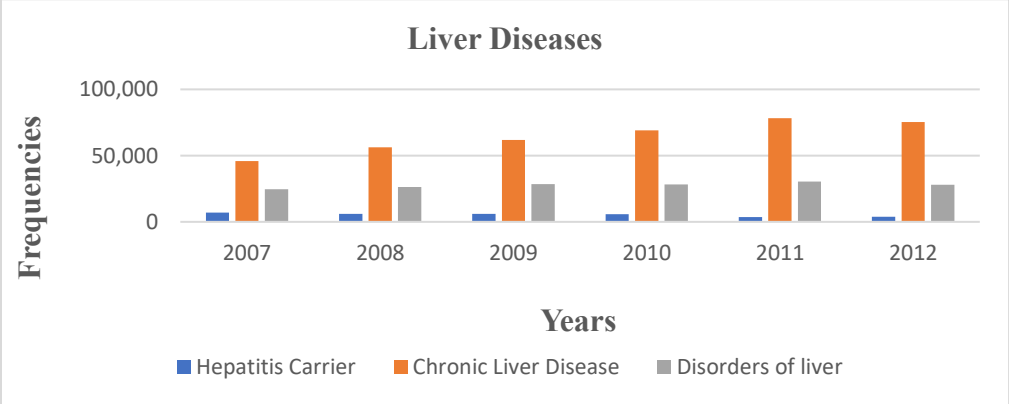

Figure 4.3 Effect of hepatitis on Liver diseases

The result from table 4.16 and Figure 4.3 provides the overall summary of the study for Hepatitis Carrier, Chronic Liver disease and Disorders of liver. Hepatitis Carrier cases decrease each year. Largest increase was 9% and largest decrease was 39%. Chronic Liver disease is caused by Hepatitis B and Hepatitis C virus. Chronic liver disease is the highest among Hepatitis Carrier and disorders of liver. 2008 had the highest increase. In

2007 it was 45,787 and in 2012 cases were 75,329. Disorders of liver are not caused by Hepatitis. In 2007 it was 24,696. Disorders of lever had the highest increase of 8% and lowest decrease of 8%. In summary Hepatitis carrier decreased by 43%, chronic liver disease increased by 65% and Disorders of liver increased by 14% from 2007 to 2012.

4.4.3 Incidence of Hepatitis and Liver Diseases

Table 4.17 Liver Diseases

Year	Hep A+E	Hep B+D	Hep C	Cirrhosis	HCC	Chronic Hepatitis	Hepatitis Carrier	Chronic Liver disease	Disorders of Liver
2007	1,670	14,794	102,015	89,358	9,451	4,178	6,870	45,787	24,696
2008	1,734	15,707	105,304	93,982	11,950	4,407	5,970	56,189	26,237
2009	1,529	14,973	112,519	98,978	11,380	4,348	5,948	61,784	28,423
2010	1,758	15,751	118,646	104,860	12,242	4,594	5,897	69,023	28,265
2011	1,684	15,367	130,617	120,019	13,425	5,208	3,616	78,280	30,420
2012	1,516	14,476	122,988	115,229	12,913	4,511	3,930	75,329	28,075
Sum	9,891	91,068	692,089	622,426	71,361	27,246	32,231	386,392	166,116

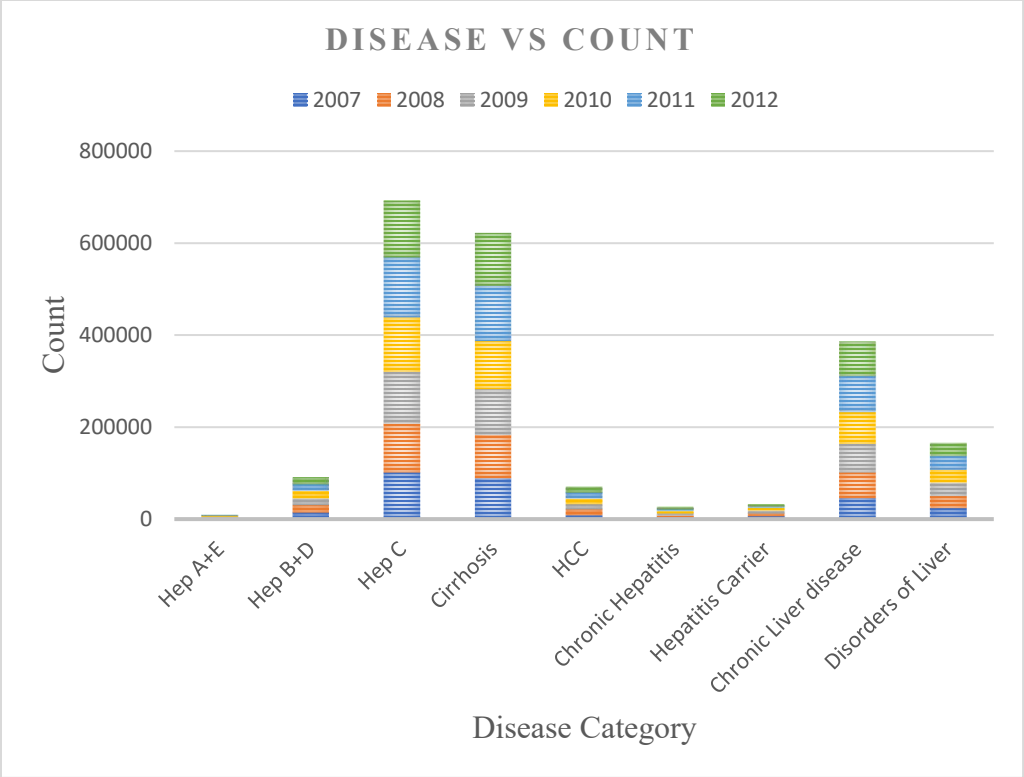

Figure 4.4 Disease Vs Count

The result from the table 4.17 and figure 4.4 shows the summary of all liver diseases from 2007 to 2012. Summary of the highest cases to the lowest cases are shown below. Hepatitis C – 692,089; Cirrhosis - 622,426; Chronic Liver disease - 386,392; Disorder of Liver - 166,116; Hepatitis B+D – 91,068; HCC – 71,361; Hepatitis Carrier – 32,231; Chronic Hepatitis – 27,246; Hepatitis A+E – 9,891.

4.5 Disease Characteristics

4.5.1 Incidence of Disease by the Age, Sex and Race/Ethnicity

- **Incidence of Disease by Age Group**

- For the Year 2007

Table 4.18 Incidence of diseases by Age Group

Age 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
1-20 years	70	178	460	85	265	220	610	1,001	244
21-51 years	682	7,872	51,022	4,002	27,361	1,326	22,997	7,415	1,350
52-65 years	483	4,749	40,987	1,823	36,856	1,214	14,312	6,237	3,775
66-80 years	308	1,570	7,696	531	20,187	1,102	5,591	6,222	3,039
81+	126	372	1,651	144	5,004	314	1,238	3,680	1,022

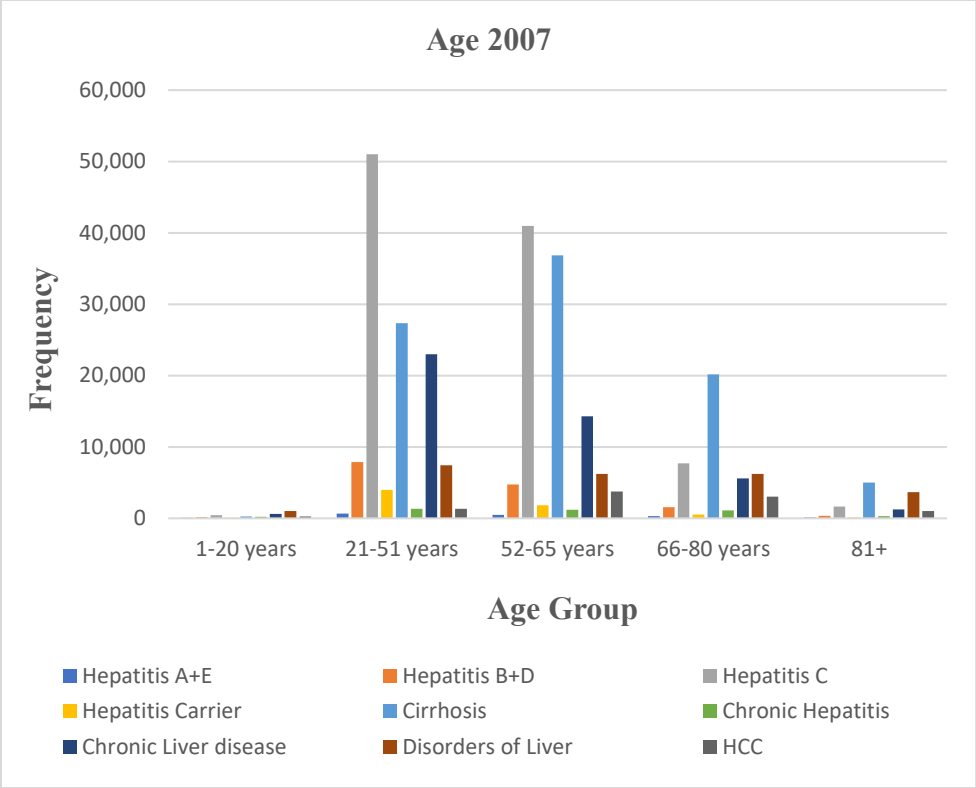

Figure 4.5 Incidence of diseases by Age Group 2007

The above table and figure indicate that Hepatitis C virus was highest, 2nd highest was cirrhosis and 3rd highest was Chronic Liver disease among 21-51 years old group. The bar graph shows that with age Hepatitis cases went down for 2007.

- For the Year 2008

Table and figure were omitted as lot of data was missing.

- For the Year 2009

Table 4.19 Incidence of Diseases by Age Group

Age 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
1-20 years	46	115	520	52	252	196	773	1,002	282
21-51 years	591	7,178	48,790	3,296	27,233	1,377	29,169	7,638	1,454
52-65 years	486	5,409	51,785	1,816	43,593	1,251	20,112	7,315	4,814
66-80 years	277	1,816	9,013	372	21,754	1,184	8,574	7,522	3,567
81+ Years	127	381	1,912	113	5,418	329	1,681	4,742	1,175

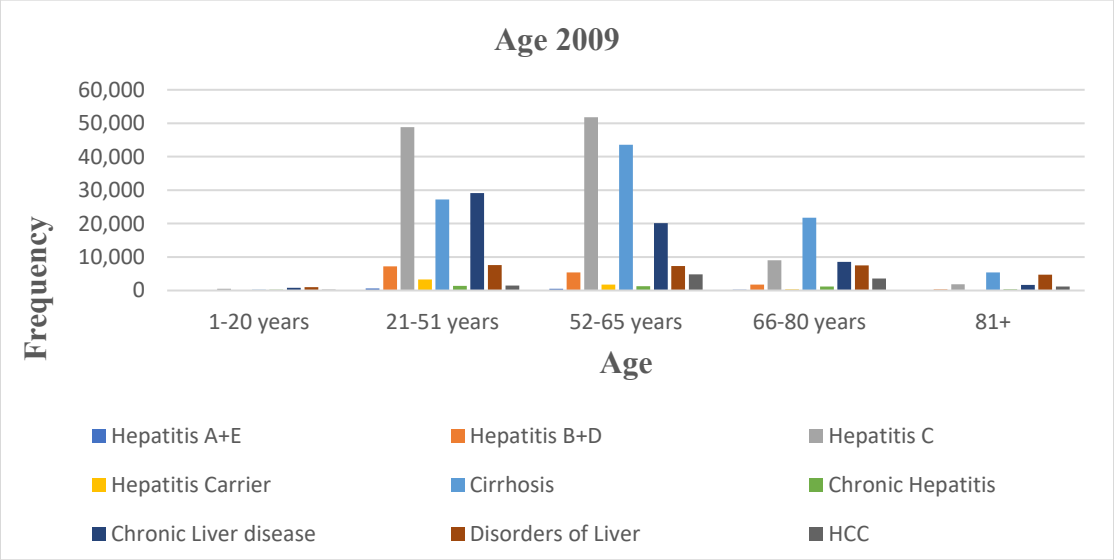

Figure 4.6 Incidence of diseases by Age Group 2009

Table 4.19 and Figure show that Hepatitis C and Cirrhosis was high for age group 52-65 years. Chronic Liver disease was higher that Cirrhosis among 21-51 years old for the year 2009.

- For the Year 2010

Table 4.20 Incidence of Diseases by Age Group 2010

Age 2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
1-20 years	62	127	594	71	393	226	1,002	1,078	334
21-51 years	637	7,439	49,340	3,118	28,679	1,454	32,125	7,692	1,486
52-65 years	598	5,803	57,059	1,902	47,093	1,409	22,486	7,558	5,501
66-80 years	328	1,903	9,297	411	22,226	1,136	9,604	7,144	3,676
81+	129	410	1,826	122	5,620	362	1,937	4,695	1,188

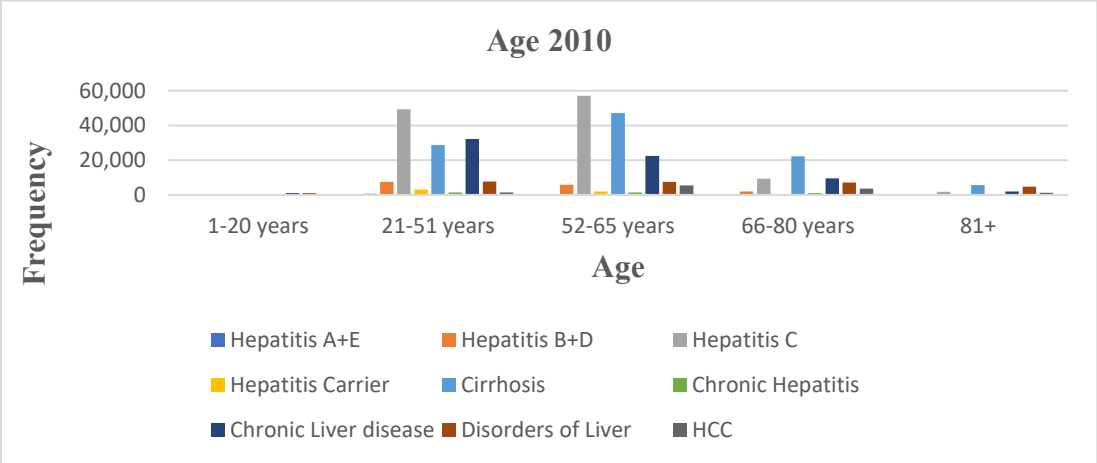

Figure 4.7 Incidence of Diseases by Age Group

Table 4.20 and Figure 4.7 show that Hepatitis C virus showed highest in 52 -65 years group age. In age group 66-80 Cirrhosis frequencies goes up.

- For the Year 2011

Table 4.21 Incidence of Diseases by Age Group

Age 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
1-20 years	69	93	611	44	319	191	941	845	391
21-51 years	566	6,715	50,496	1,895	29,838	1,584	34,437	7,706	1,511
52-65 years	549	6,033	65,177	1,139	55,664	1,592	26,747	8,405	5,996
66-80 years	358	1,994	11,354	332	26,256	1,415	11,625	8,131	4,176
81+	141	443	2,245	93	6,751	416	2,407	5,124	1,235

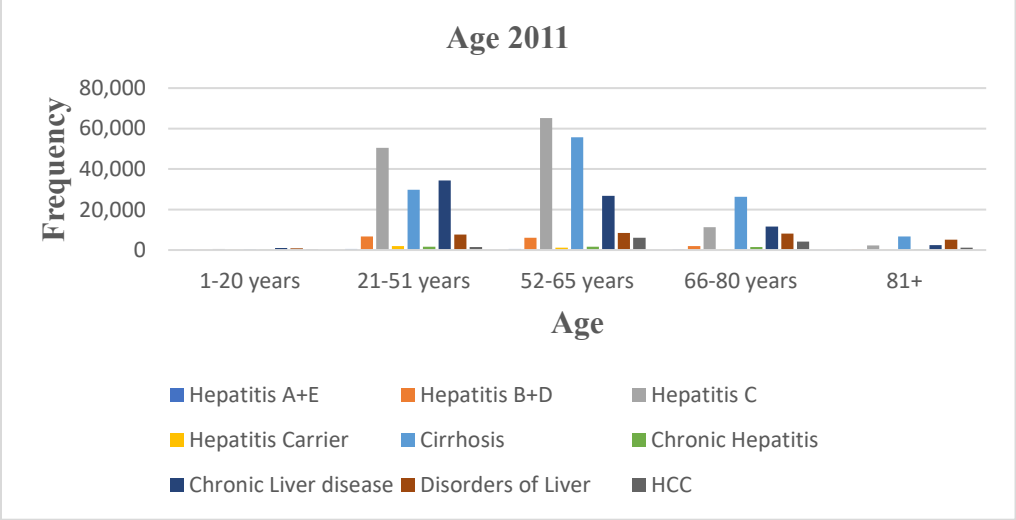

Figure 4.8 Incidence of Diseases by Age Group 2011

Table 4.21 and Figure 4.8 show that Chronic Liver disease diminishes with age. Age group 66-

80 years Cirrhosis remains elevated. Age group 81+ Cirrhosis remains with a patient.

- For the Year 2012

Table 4.22 Incidence of Diseases by Age Group

Age 2012	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
1-20 years	53	93	533	31	336	247	941	966	368
21-51 years	511	6,210	46,170	2,114	27,928	1,353	32,796	7,105	1,367
52-65 years	506	5,631	62,809	1,269	54,521	1,342	25,875	7,851	5,998
66-80 years	322	2,010	10,832	307	25,095	1,191	11,286	7,365	3,875
81+	120	451	1,892	91	6,164	370	2,331	4,544	1,236

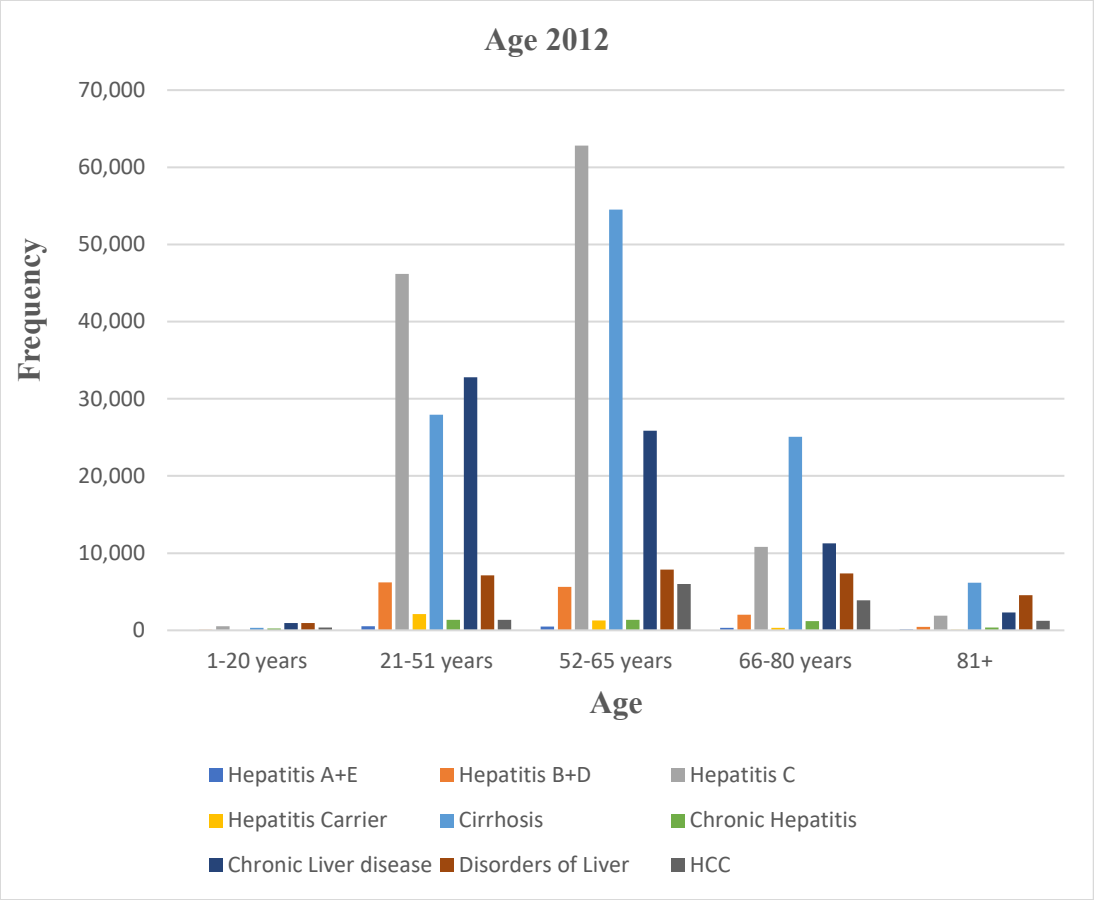

Figure 4.9 Incidence of Diseases by Age Group 2012

Table 4.22 and figure 4.9 show occurrences of Hepatitis C remained highest, 2nd highest is Cirrhosis and 3rd place is Chronic Liver disease from the years 2007 to 2012. Hepatitis C occurrences remained elevated from age group 21 to 65 years. Cirrhosis was highest among 66-80 years age group. Chronic Liver disease showed highest among 21-51 years age group.

- **Incidence of the disease by the Sex**
- For the Year 2007

Table 4.23 Gender Frequency by Disease Type 2007

Sex 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Males	846	8,988	63,636	3,581	55,183	1,193	25,565	11,284	6,524
Females	819	5,749	38,141	3,002	34,469	2,982	19,165	13,251	2,898

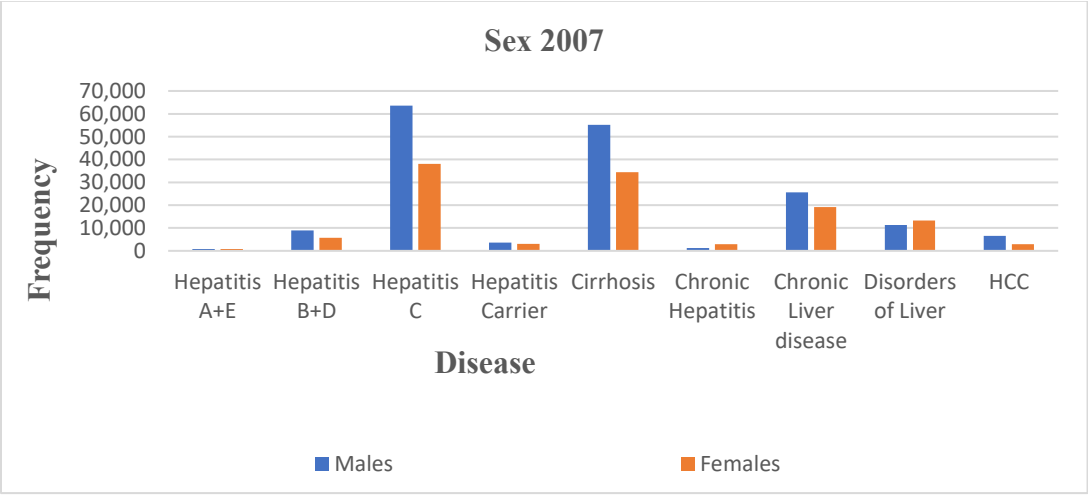

Figure 4.10 Gender Frequency by Disease Type 2007

Table 4.23 and figure 4.10 indicates that Hepatitis A+E shows equal amount of infection between males and females. All other diseases show High males' incidence for the year 2007.

- For the Year 2008

Table 4.24 Gender Frequency by Disease Type 2008

Sex 2008	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver Disease	Disorders of Liver	HCC
Males	936	9,866	65,154	3,016	57,207	1,209	30,572	11,907	8,207
Females	795	5,769	39,812	2,651	36,216	3,195	24,384	14,159	3,719

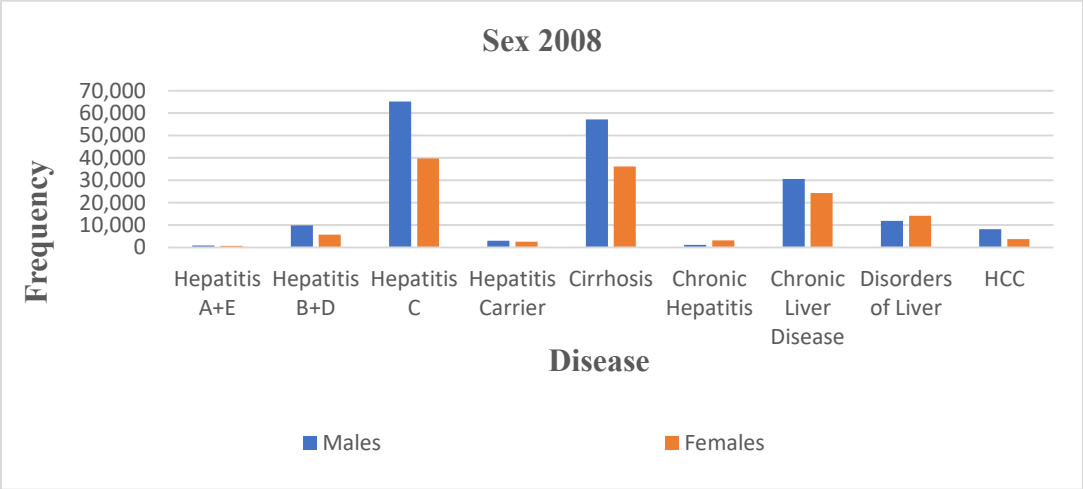

Figure 4.11 Gender Frequency by Disease Type 2008

Table 4.24 and Figure 4.11 show that Hepatitis C has highest count of males' incidence, 2nd highest is male incidence in Cirrhosis and 3rd highest is male incidence in Chronic Liver disease for the year 2008.

- For the Year 2009

Table 4.25 Gender Frequency by Disease Type 2009

Sex 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Males	777	9,278	69,862	3,181	60,043	1,152	33,364	13,092	7,680
Females	745	5,606	42,133	2,468	38,195	3,183	26,934	15,113	3,600

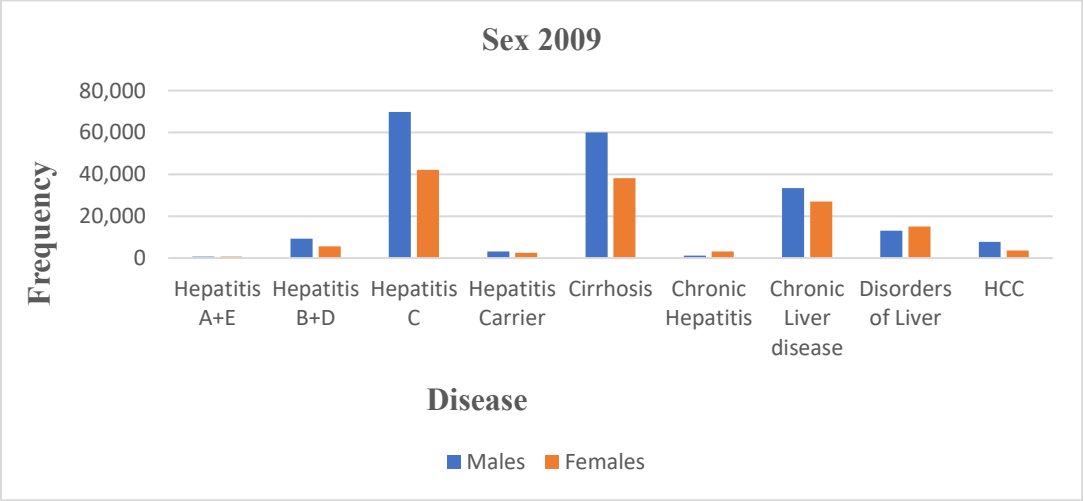

Figure 4.12 Gender Frequency by Disease Type 2009

Table 4.25 and Figure 4.12 show no significance difference between the year 2008 and 2009 for sex frequency with diseases.

- For the Year 2010

Table 4.26 Gender Frequency by Disease Type 2010

Sex 2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Males	937	9,771	73,790	2,985	64,078	1,222	36,601	13,149	8,284
Females	817	5,906	44,301	2,639	39,923	3,362	30,539	15,002	3,900

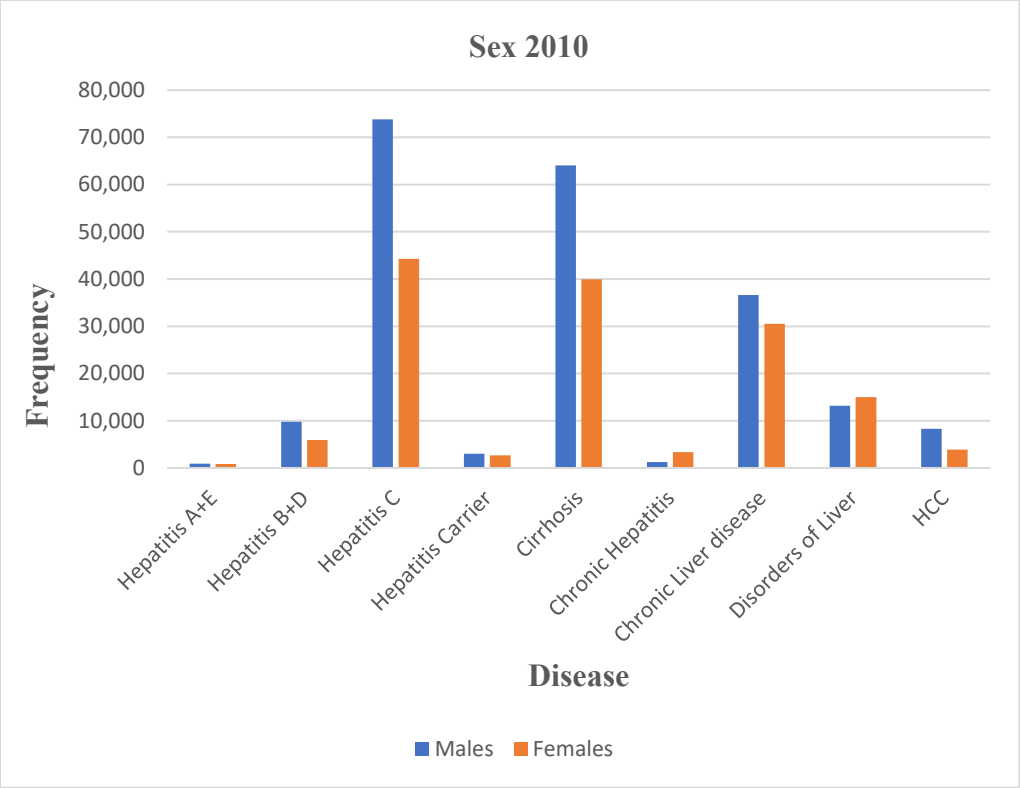

Figure 4.13 Gender Frequency by Disease Type 2010

Table 4.26 and Figure 4.13 show no significance difference for the year 2010. Males count is higher than Female count.

- For the Year 2011

Table 4.27 Gender Frequency by Disease Type 2011

Sex 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Males	826	9,511	80,597	1,616	72,010	1,365	41,205	14,106	9,289
Females	854	5,762	49,272	1,887	46,817	3,830	34,937	16,094	4,017

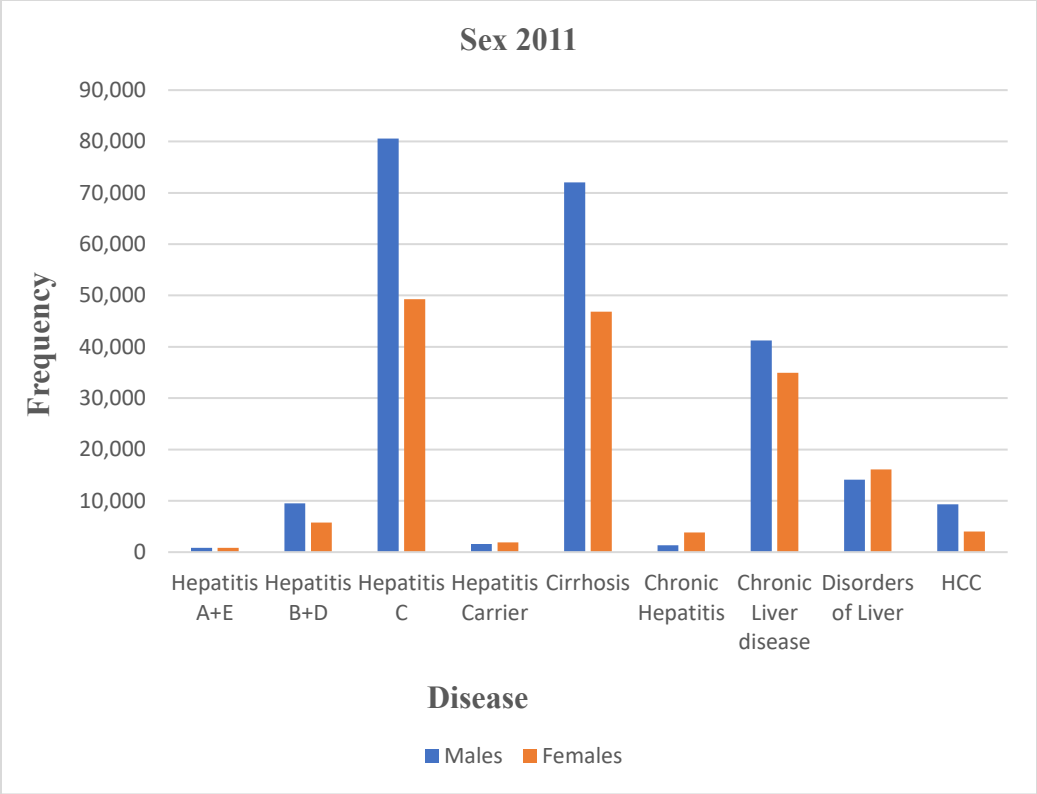

Figure 4.14 Gender Frequency by Disease Type 2011

Table 4.27 and figure 4.14 show equal distribution of males and Females for Hepatitis A+E

occurrences whereas all other diseases show high occurrence for males.

- For the Year 2012

Table 4.28 Gender Frequency by Disease Type 2012

Sex 2012	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Males	776	8,771	75,528	1,848	69,567	1,204	39,153	13,308	8,842
Females	736	5,624	46,702	1,964	44,474	3,299	34,071	14,520	4,001

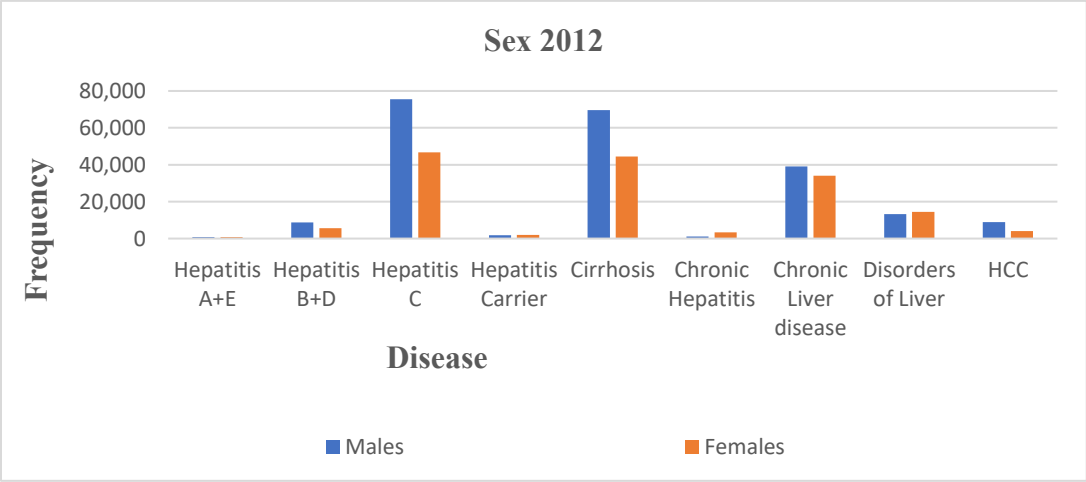

Figure 4.15 Gender Frequency by Disease Type 2012

Table 4.28 and Figure 4.15 show that males are showing high occurrence rate. Highest number of frequencies is for Hepatitis C, 2nd highest is cirrhosis and 3rd highest are for Chronic Liver Disease. The ratio from men to women for Hepatitis A+E shows strikingly similar for the years 2007 to 2012.

- **Incidence of disease by the Race/Ethnicity**
- Absolute Numbers of Hepatitis C Cases

Table 4.29 Race/Ethnicity Occurrences

Normalized Race Per 100,000 Occurrences	White	Black	Hispanic	Asian or Pacific Islander	Native American	Others
2007	15	6	4	0	0	1
2008	18	6	4	1	0	1
2009	19	7	4	1	0	1
2010	20	8	4	0	0	1
2011	22	9	5	0	0	1
2012	22	8	5	0	0	1

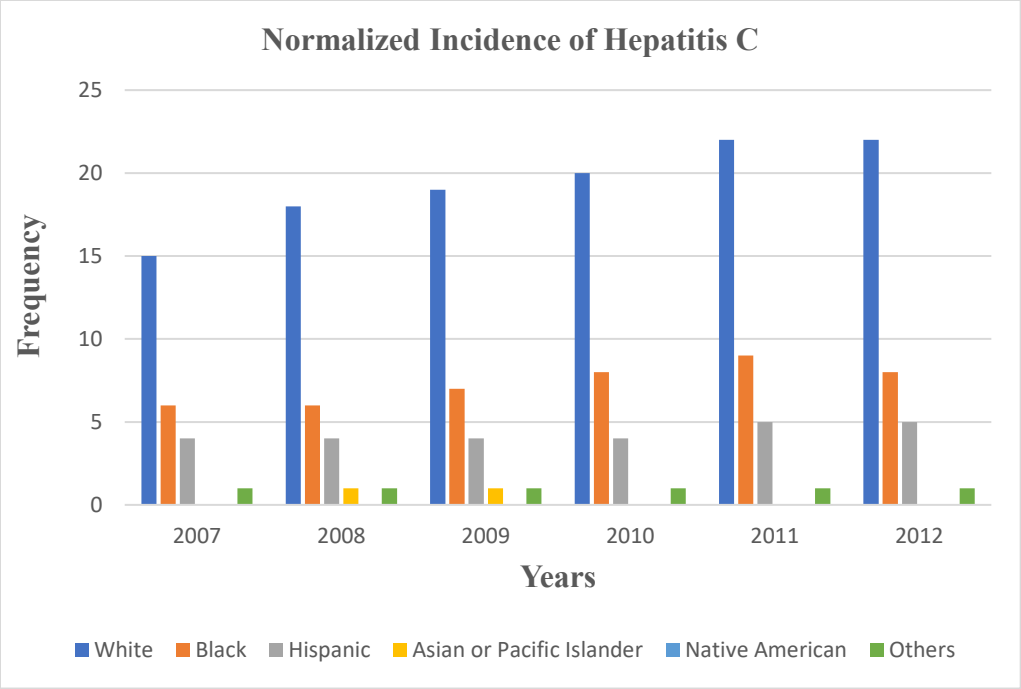

Figure 4.16 Race/Ethnicity Occurrences

Table 4.29 and figure 4.16 show that white population with Hepatitis C is highest. Curve shows that White population increased each

year from the year 2007 to 2012. This Normalized population is per 100, 000 occurrences.

4.5.2 Insurance Type

- For the Year 2007

Table 4.30 Occurrences of Payment Methods 2007

Payment Methods 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Medicare	563	4,378	30,559	1,478	38,306	1,792	11,231	10,677	4,407
Medicaid	297	4,244	29,680	2,598	18,451	621	7,061	3,023	1,385
Private Insurance	519	3,476	20,532	1,579	20,254	1,390	16,815	7,958	2,883
Self-Pay	174	1,528	11,356	704	7,040	188	6,372	1,677	312
No Charge	11	206	1,505	61	757	29	586	190	42
Other	100	854	7,928	157	4,668	140	2,575	974	374

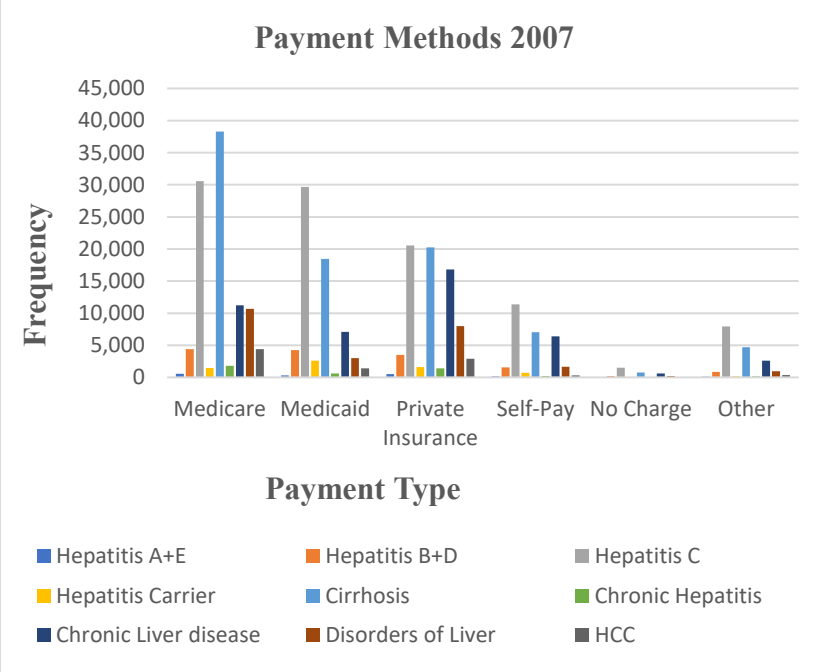

Figure 4.17 Occurrences of Payment Methods 2007

Table 4.30 and figure 4.17 show Medicare which is a federal program that covers health coverage if an individual age is 65+ or under 65 years of age and have a disability, regardless of the income level. Medicaid is a state and federal program that provides health coverage to individuals with very low-income status. Hepatitis C is very common among low income group who are receiving Medicaid. Cirrhosis is highest among Medicare group who are above 65 years old.

- For the Year 2008

Table 4.31 Occurrences of Payment Methods 2008

Payment Methods 2008	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Medicare	635	5,021	32,321	1,102	39,113	1,901	13,639	11,256	5,283
Medicaid	292	4,384	32,045	2,674	19,900	648	8,606	3,323	1,942
Private Insurance	553	3,852	22,019	1,244	22,632	1,537	21,613	8,583	3,870
Self-Pay	148	1,371	10,129	325	6,503	154	7,129	1,787	373
No Charge	13	207	1,535	61	905	36	822	182	32
Other	89	781	6,738	264	4,218	121	3,037	916	417

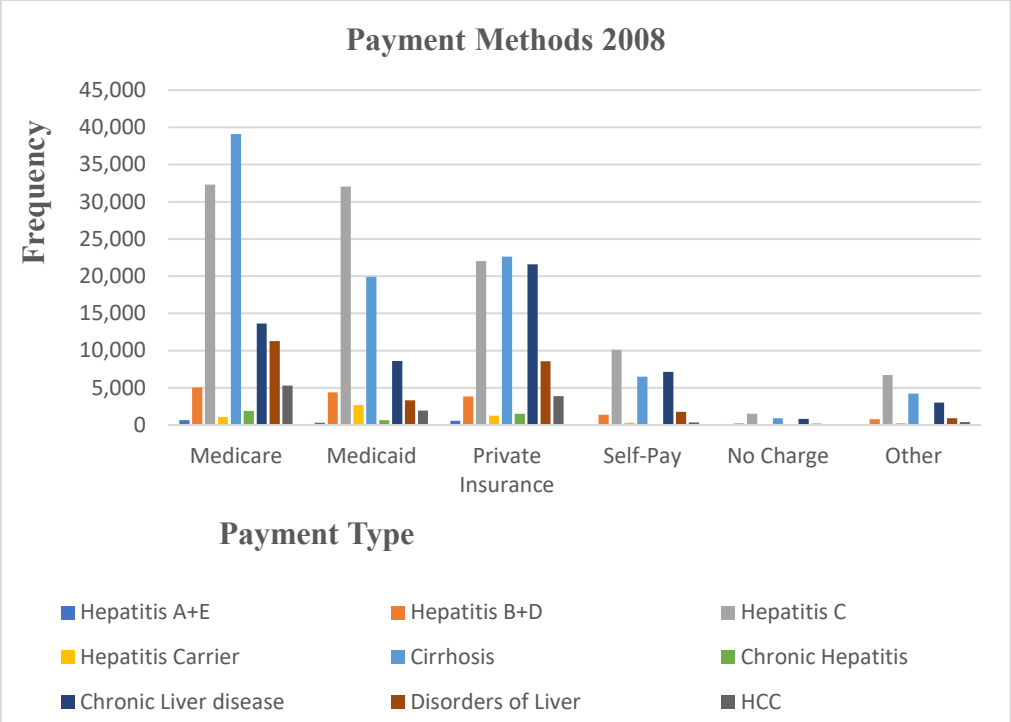

Figure 4.18 Occurrences of Payment Methods 2008

Table 4.31 and Figure 4.18 show that very few patients were using private insurance. Patients in private insurance group had almost same occurrence rate for Hepatitis C, Cirrhosis and Chronic Liver Disease.

- For the Year 2009

Table 4.32 Occurrences of Payment Methods 2009

Payment Methods 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Medicare	523	4,825	34,509	1,228	41,599	1,872	16,289	13,112	5,049
Medicaid	325	4,581	36,734	2,626	21,575	636	9,684	3,598	1,863
Private Insurance	455	3,032	20,074	1,086	21,805	1,462	21,544	8,514	3,404
Self-Pay	143	1,525	12,129	440	8,184	207	8,599	1,811	507
No Charge	21	186	1,626	44	889	14	804	176	26
Other	58	722	6,736	219	4,012	136	3,226	935	431

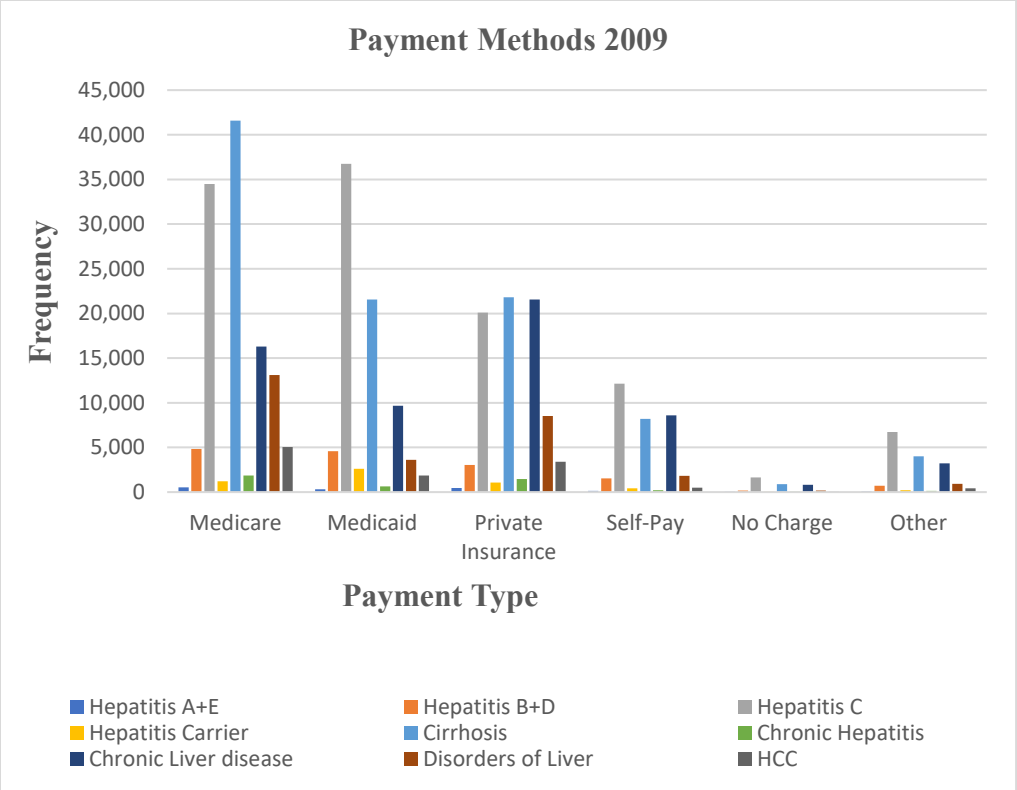

Figure 4.19 Occurrences of Payment Methods 2009

Table 4.32 and Figure 4.19 show Cirrhosis is highest in Medicare group and Hepatitis C is highest in Medicaid group.

- For the Year 2010

Table 4.33 Occurrences of Payment Methods 2010

Payment Methods 2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Medicare	609	5,073	37,267	1,353	43,730	1,982	18,551	12,722	5,475
Medicaid	363	4,975	39,098	2,625	23,711	719	11,795	3,981	2,140
Private Insurance	495	3,065	20,521	1,088	22,403	1,489	23,111	8,297	3,623
Self-Pay	162	1,697	12,495	381	8,301	233	9,220	1,977	453
No Charge	26	202	1,648	30	973	23	954	194	73
Other	93	626	6,654	144	4,631	136	3,351	936	403

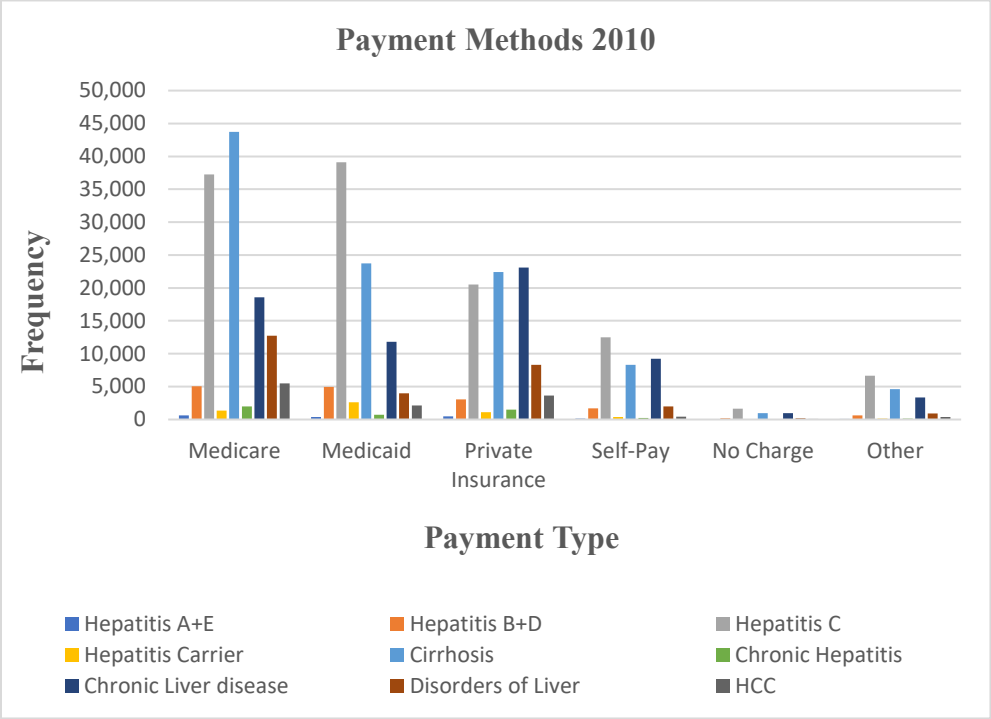

Figure 4.20 Occurrences of Payment Methods 2010

Table 4.33 and Figure 4.20 show that Hepatitis C and Medicare patients increased by 7.99% and Medicaid patients increases by 6.43% from the year 2009 to 2010.

- For the Year 2011

Table 4.34 Occurrences of Payment Methods 2011

Payment Methods 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Medicare	661	5,340	43,591	915	52,177	2,416	22,641	14,620	6,181
Medicaid	361	4,839	43,610	1,298	25,843	736	12,762	3,836	2,346
Private Insurance	429	3,121	21,441	934	25,379	1,649	25,681	8,625	3,663
Self-Pay	129	1,161	12,309	168	8,844	222	10,150	1,895	455
No Charge	21	163	1,880	19	1,288	39	1,101	186	99
Other	80	619	6,512	165	4,864	125	5,323	965	502

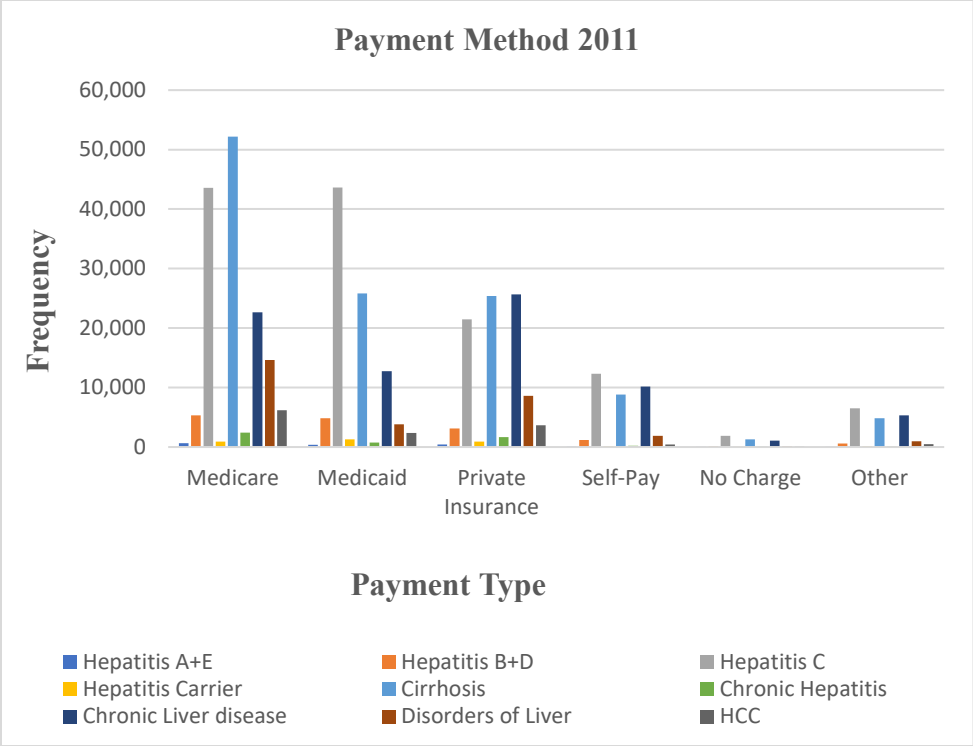

Figure 4.21 Occurrences of Payment Methods 2011

Table 4.34 and Figure 4.21 show that Hepatitis C and Medicare patients increased by 4.91% and Medicaid patients increases by 11.54% from the year 2010 to 2011.

- For the Year 2012

Table 4.35 Occurrences of Payment Methods 2012

Payment Methods 2012	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Medicare	608	5,006	41,773	906	51,271	2,103	22,439	13,393	6,055
Medicaid	316	4,454	40,533	1,712	25,060	628	12,891	3,930	2,236
Private Insurance	395	2,830	19,266	869	22,615	1,359	23,606	7,557	3,517
Self-Pay	121	1,296	12,218	212	8,992	219	9,620	1,751	472
No Charge	12	132	1,283	9	702	25	795	164	39
Other	57	644	6,794	102	5,087	156	3,672	984	475

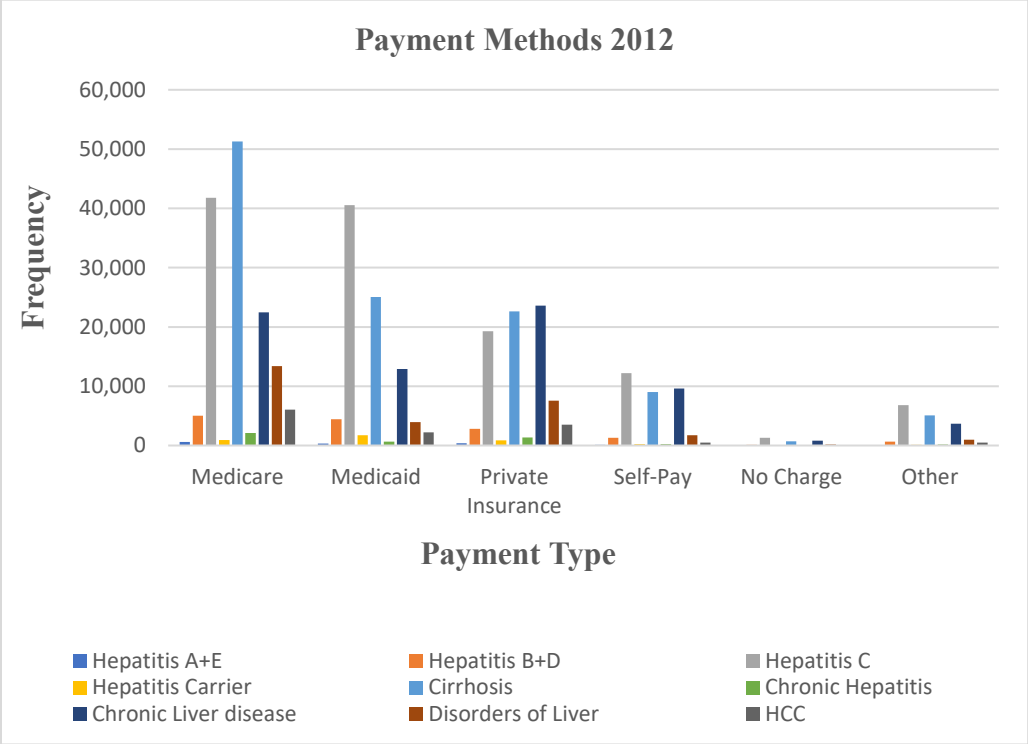

Figure 4.22 Occurrences of Payment Methods 2012

Table 4.35 and Figures 4.22 show that Hepatitis C and Medicare patients decreased by 4.17%

and Medicaid patients decreased by 7.05% from the year 2011 to 2012.

4.5.3 Incidence of Disease by the Income Level

- For the Year 2007

Table 4.36 Income Status of Patients 2007

Income 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
$ 1-38,999	492	5,570	39,145	1,455	29,256	1,124	12,229	6,946	2,467
$ 39,000-47,999	393	3,263	23,955	1,260	22,976	1,061	11,068	6,068	2,129
$ 48,000-62,999	378	2,654	19,342	1,744	19,175	1,009	10,632	5,520	2,172
$ 63,000+	342	2,492	13,880	1,432	14,954	864	9,415	5,357	2,343

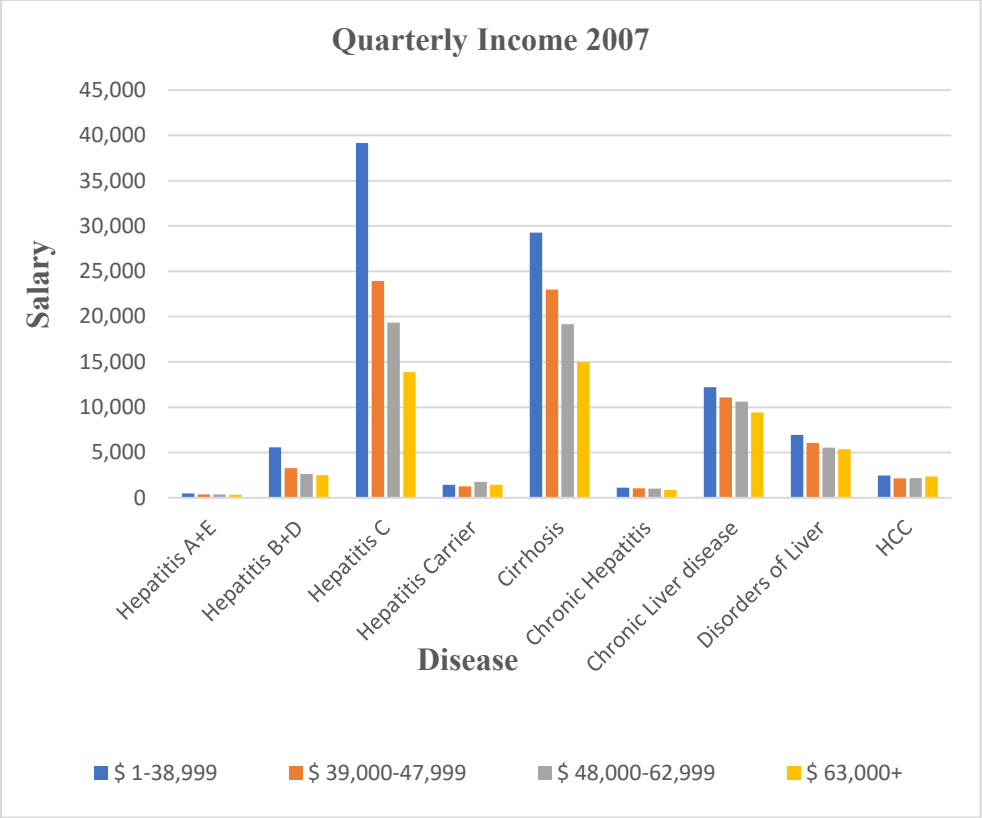

Figure 4.23 Income Status of Patients 2007

Table 4.36 and Figure 4.23 shows that 39,145 patients of Hepatitis C Virus fall under income less than $38,999. Only 23,955 patients fall under $39,000 to $48,000. Lastly 13,880 patients fall under above $63,000+ income range.

For the Year 2008

Table 4.37 Income Status of Patients 2008

Income 2008	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
$1-38,999	498	5,253	37,359	2,061	28,510	1,311	14,216	7,050	3,091
$39,000-48,999	424	3,704	26,900	852	25,182	1,183	14,720	6,701	2,968
$49,000-63,999	393	2,944	20,212	832	19,839	894	12,741	5,962	2,619
$64,000+	354	2,892	15,048	970	16,537	928	11,664	5,750	2,895

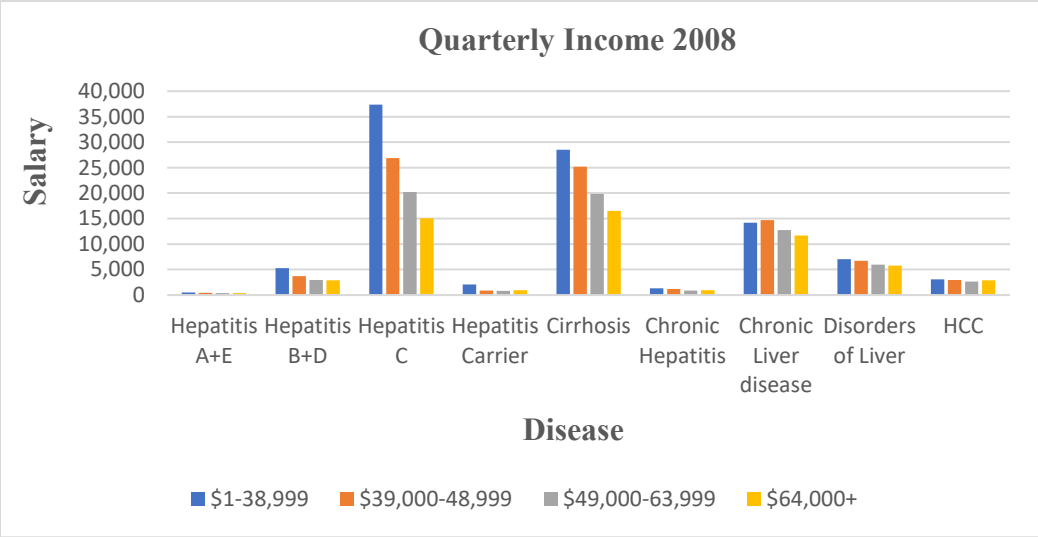

Figure 4.24 Income Status of Patients 2008

Table 4.37 and Figure 4.24 show that 28,510 patients of Cirrhosis fall under income less than $38,999. Only 25,182 patients fall under $39,000 to $48,000. Lastly 16,537 patients fall under above $64,000+ income range.

- For the Year 2009

Table 4.38 Income Status of Patients 2009

Income 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver Disease	Disorders of Liver	HCC
$1-39,999	418	5,097	41,012	1,574	30,474	1,157	15,519	7,327	3,074
$40,000-49,999	343	3,253	26,602	1,054	25,243	1,094	15,378	6,977	2,722
$50,000-65,999	337	2,797	21,652	879	21,912	1,031	14,707	6,772	2,637
$66,000+	319	2,519	14,319	987	16,530	917	12,669	6,379	2,482

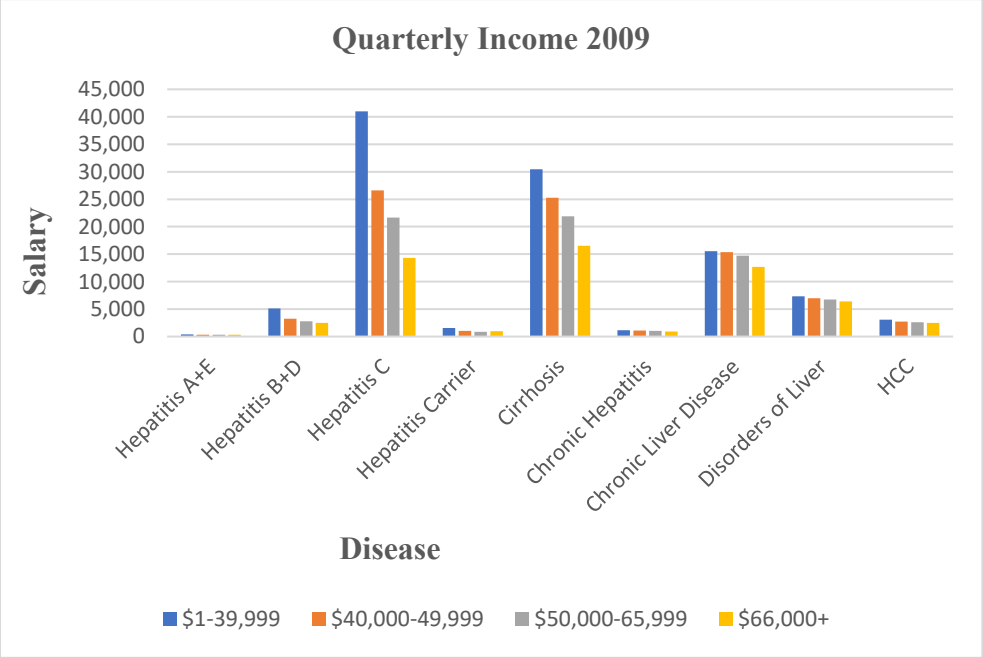

Figure 4.25 Income Status of Patients 2009

Table 4.38 and figure 4.25 show that 15,519 patients of Chronic Liver disease fall under less than $40,000 income salary.

- For the Year 2010

Table 4.39 Income Status of Patients 2010

Income 2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
$1-40,999	536	6,044	44,746	1,142	33,169	1,295	17,566	7,585	3,346
$41,000-50,999	420	3,332	27,441	961	25,964	1,117	16,538	6,784	2,845
$51,000-66,999	381	2,799	23,377	1,436	23,392	1,072	16,264	6,740	2,904
$67,000+	351	2,414	15,175	973	17,407	993	14,694	6,329	2,688

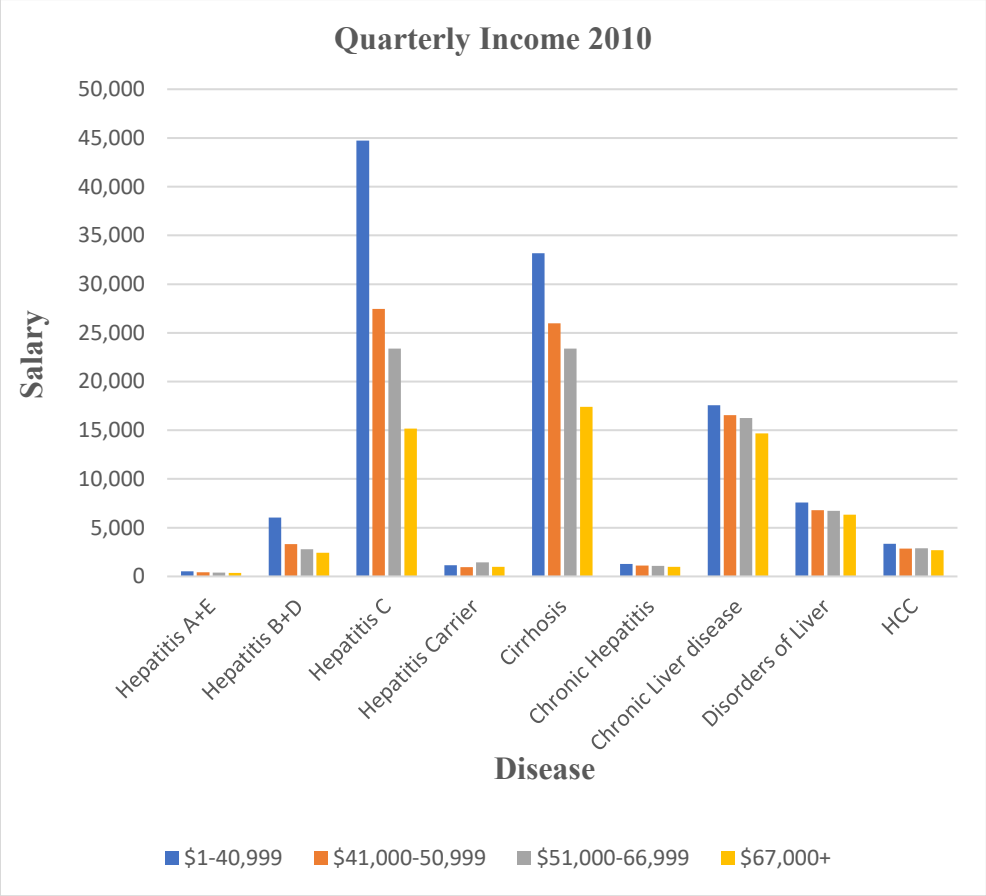

Figure 4.26 Income Status of Patients 2010

Table 4.39 and Figure 4.26 show that lower income level patient has higher # of Hepatitis C due to less medical coverage. The same pattern is true for other diseases too for the year 2010.

- For the Year 2011

Table 4.40 Income Status of Patients

Income 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver Disease	Disorders of Liver	HCC
$1-38,999	497	5,515	50,565	931	38,553	1,420	20,398	8,206	3,974
$39,000-47,999	400	3,348	30,372	714	29,232	1,282	18,253	6,875	3,052
$48,000-63,999	400	2,993	26,103	752	28,193	1,332	19,378	7,755	3,271
$64,000+	315	2,460	16,491	757	19,724	1,045	16,177	6,779	2,694

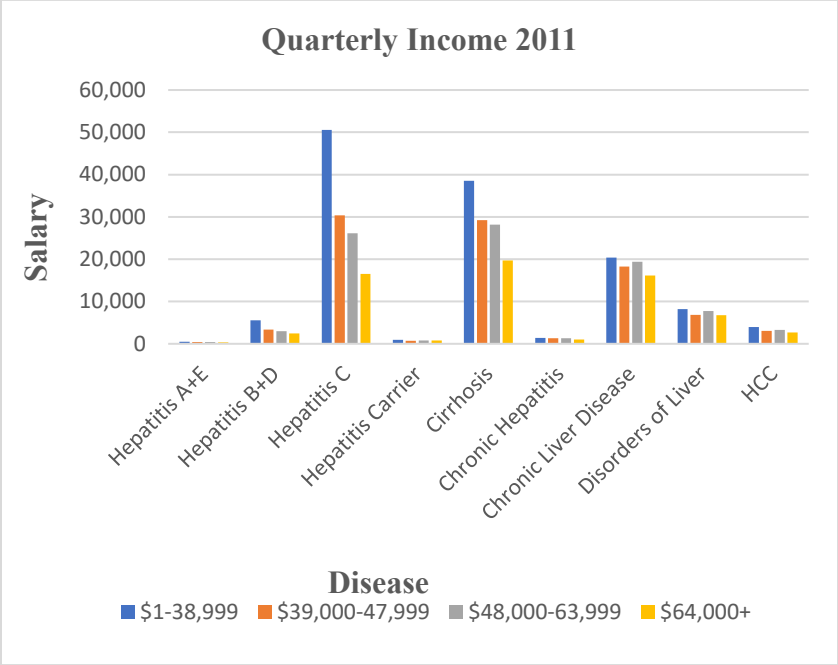

Figure 4.27 Income Status of Patients 2011

Table 4.40 and Figure 4.27 show that lower income level patient has higher # of Hepatitis C due to less medical coverage. The same pattern is true for other diseases too for the year 2011.

- For the Year 2012

Table 4.41Income Status of Patients 2012

Income 2012	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
$1-38,999	504	5,386	48,645	1,222	38,850	1,214	21,114	8,110	3,788
$39,000-47,999	343	3,024	28,328	620	27,722	1,141	17,498	6,490	2,840
$48,000-62,999	330	2,747	23,554	748	24,747	1,075	17,388	6,527	3,034
$63,000+	277	2,445	15,696	786	19,045	983	15,256	6,031	2,799

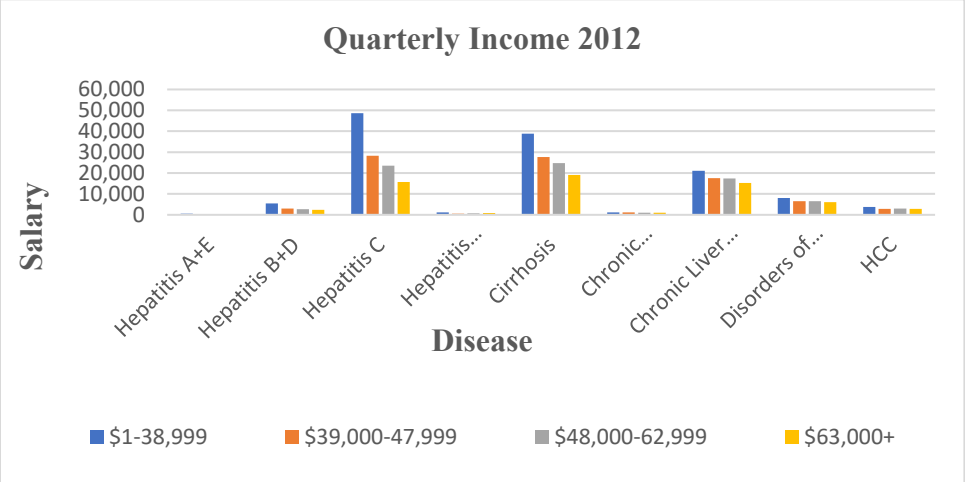

Figure 4.28 Income Status of Patients 2012

Table 4.41 and Figure 4.28 show that lower income level patient has higher # of Hepatitis C due to less medical coverage for the year 2012.

4.6 Hospital Location by Region and Hospital Type

- **Region of the Hospital**

Absolute Numbers for Hepatitis C Cases

Table 4.42 Hospital Region

Normalized Region Incidence by 100,000 Occurrences	Northeast	Midwest	south	West
2007	186	154	92	146
2008	191	158	93	148
2009	203	168	98	156
2010	214	177	102	163
2011	235	194	111	177
2012	202	167	95	151

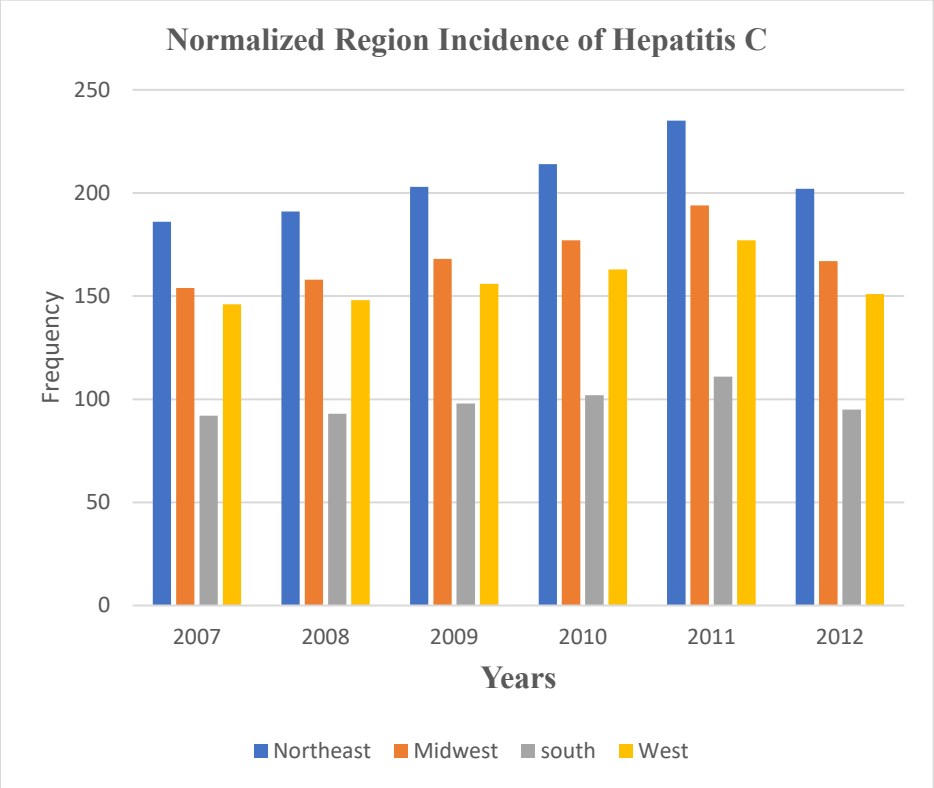

Figure 4.29 Hospital Region

Table 4.42 and Figure 4.29 show that HCV was highest in Northeast region.

Normalized population is per 100,000 population. **Area of the Hospital Rural/Urban**

- For the Year 2007

4.43 Hospital Location 2007

Hospital Location 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Rural	133	805	8,213	398	9,586	489	5,115	2,916	617
Urban	1,535	13,925	93,500	6,187	79,960	3,682	39,580	21,595	8,803

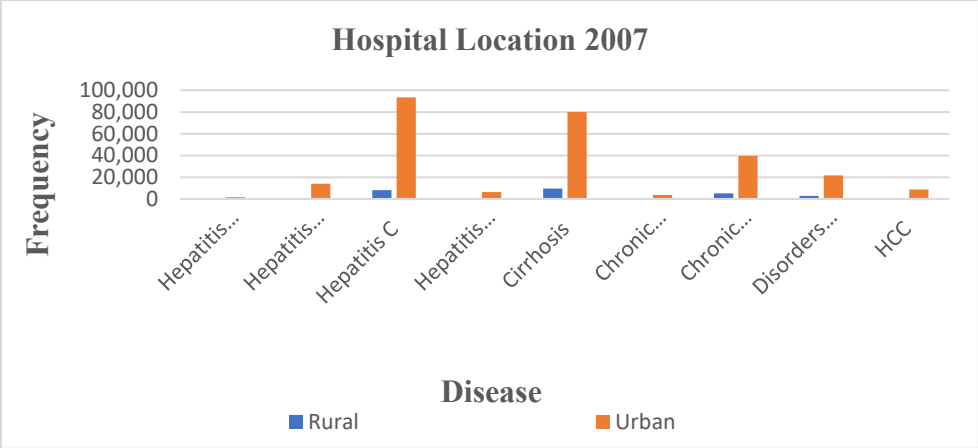

Figure 4.30 Hospital Location 2007

Table 4.43 and figure 4.30 show that HCV occurrences are significantly High in Urban areas for the year 2007.

- For the Year 2008

Table 4.44 Hospital Location 2008

Hospital Location 2008	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Rural	174	775	7,512	192	9,088	434	5,484	2,970	648
Urban	1,558	14,856	97,432	5,479	84,248	3,972	49,407	23,096	11,275

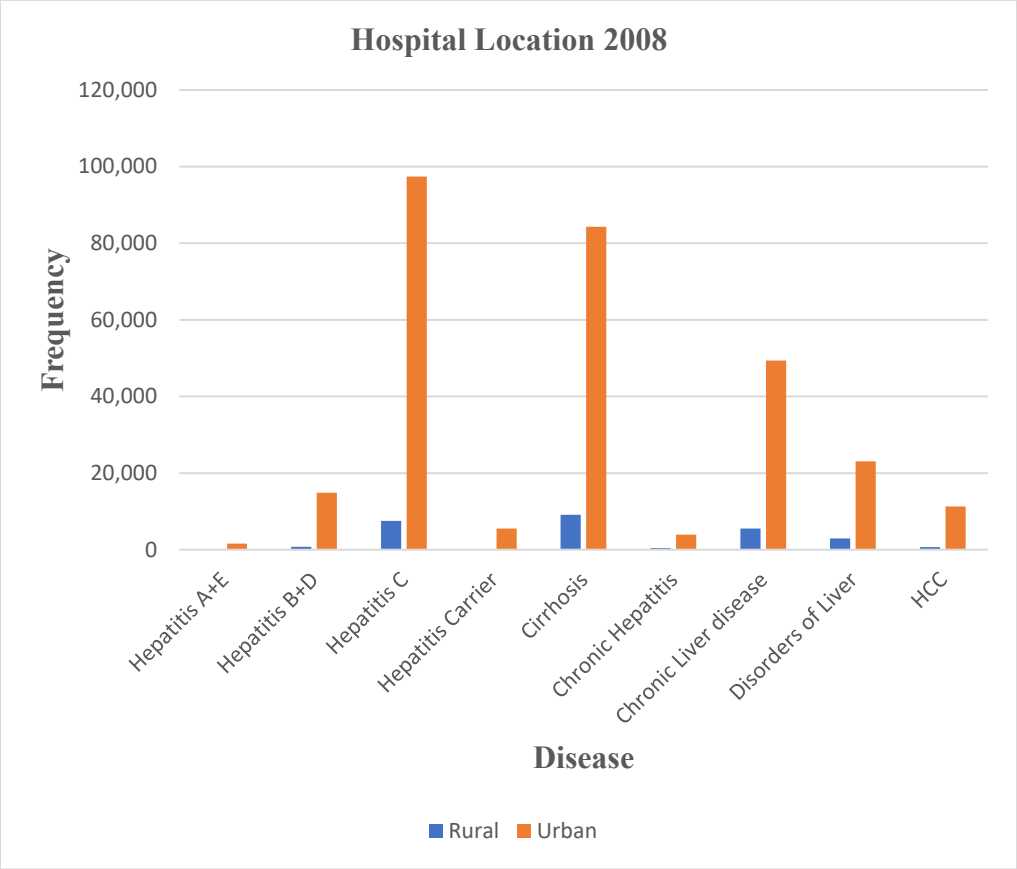

Figure 4.31 Hospital Location 2008

Table 4.44 and figure 4.31 show that HCV occurrences are significantly High in Urban areas for the year 2008. 2nd highest occurrences are Cirrhosis in the Urban area too.

- For the Year 2009

Table 4.45 Hospital Location 2009

Hospital Location 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Rural	111	694	7,800	147	8,576	402	5,983	2,969	642
Urban	1,382	13,754	102,103	5,452	87,922	3,848	53,420	24,717	10,410

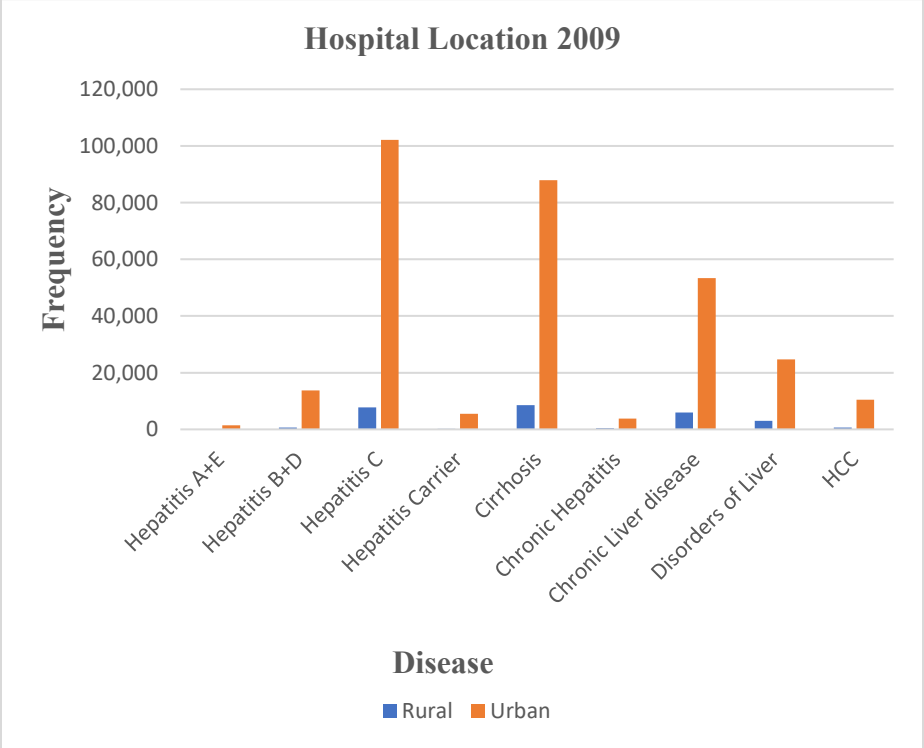

Figure 4.32 Hospital Location 2009

Table 4.45 and Figure 4.32 show that HCV occurrences are significantly high in Urban areas for the year 2007.

- For the Year 2010

Table 4.46 Hospital Location 2010

Hospital Location2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Rural	162	789	8,620	256	10,112	475	7,116	2,968	755
Urban	1,577	14,752	108,351	5,356	92,947	4,060	59,353	24,904	11,312

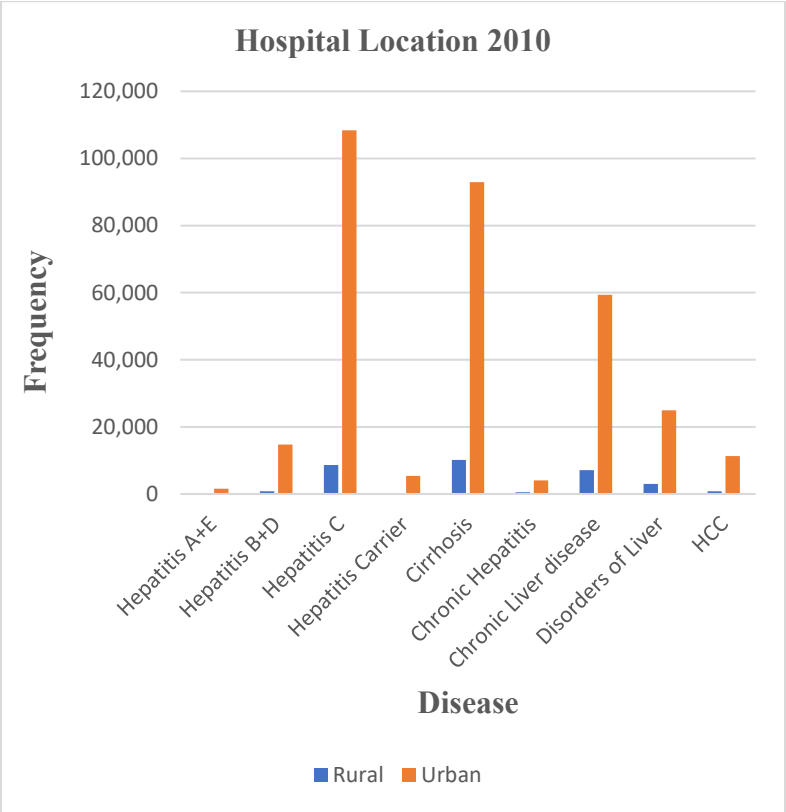

Figure 4.33 Hospital Location 2010

Table 4.46 and Figure 4.33 show that Hepatitis C Virus occurrences are significantly high in Urban areas for the year 2010.

- For the Year 2011

Table 4.47 Hospital Location

Hospital Location 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Rural	150	753	8,289	190	9,807	460	7,056	2,864	577
Urban	1,513	14,304	118,304	3,302	107,012	4,689	68,056	27,019	12,503

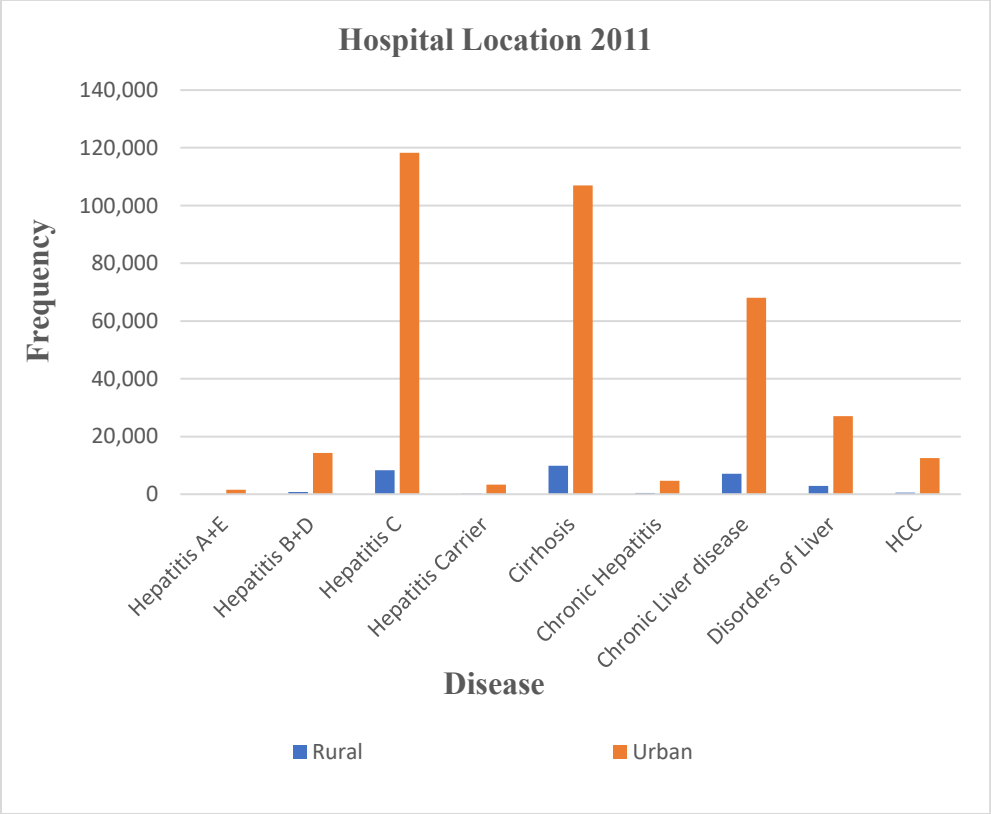

Figure 4.34 Hospital Location 2011

Table 4.47 and Figure 4.34 show that Hepatitis C Virus occurrences are significantly high in Urban areas for the year 2010. Highest occurrence is for Hepatitis C followed by Cirrhosis and Chronic Liver Disease for the year 2011.

4.7 Patient Admission and Discharge Statistics

- **Admission Type in the Hospital**
    - For the Year 2007

Table 4.48 Admission Type 2007

Admission Type 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	807	8,166	59,475	3,427	54,074	2,224	26,957	13,929	4,397
Urgent	224	2,082	13,291	1,261	11,870	731	5,928	3,720	1,308
Elective	389	2,096	13,373	1,447	9,191	752	5,630	3,648	2,074
Newborn	1	5	4	13	2	0	13	76	0
Trauma Center	0	10	151	1	71	3	50	38	2
Other	1	5	36	0	20	0	7	8	0

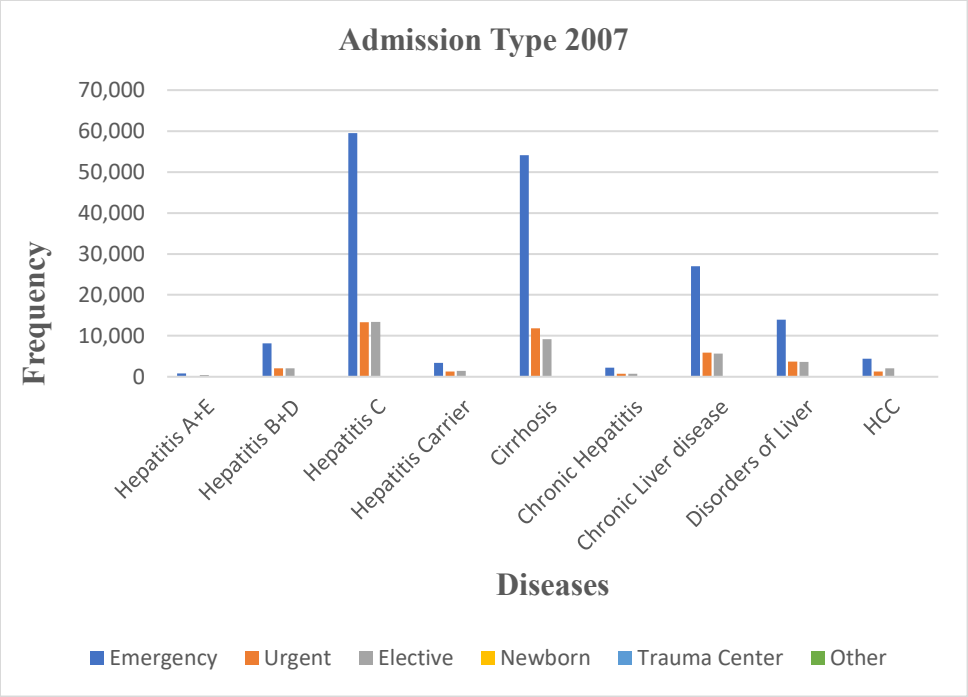

Figure 4.35 Admission Type 2007

Table 4.48 and Figure 4.35 show that Hepatitis C showed the highest emergency visits. 2nd highest is Cirrhosis 3rd highest is chronic liver disease. Emergency visit for Hepatitis C for 2007 is 59,475. Emergency visit for Cirrhosis for 2007 is 54,074. Emergency visit for chronic liver disease for 2007 is 26,957. Urgent- not life threatening is highest for Hepatitis C. 2nd highest is Cirrhosis. 3rd highest is Chronic Liver disease. Urgent for Hepatitis C for 2007 is 13,291. Urgent for Cirrhosis for 2007 is 11,870. Urgent for Chronic Liver disease for 2007 is 5,928. Elective-patient choose to come because feeling uncomfortable is highest for Hepatitis C. 2nd highest is Cirrhosis. 3rd highest is Chronic Liver disease. Elective for Hepatitis C is 13,373. Elective for Cirrhosis is 9,191 and elective for chronic liver disease is 5,630.

- For the Year 2008

Table 4.49 Admission Type 2008

Admission Type 2008	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	889	8,617	62,326	3,579	57,255	2,365	33,033	14,978	5,216
Urgent	260	1,952	14,290	632	13,270	756	7,713	4,100	1,602
Elective	369	2,239	13,026	951	9,177	730	7,753	3,715	2,790
Newborn	1	5	9	11	6	1	11	76	1
Trauma Center	5	34	294	5	210	6	138	82	5
Other	3	26	169	0	23	2	35	15	1

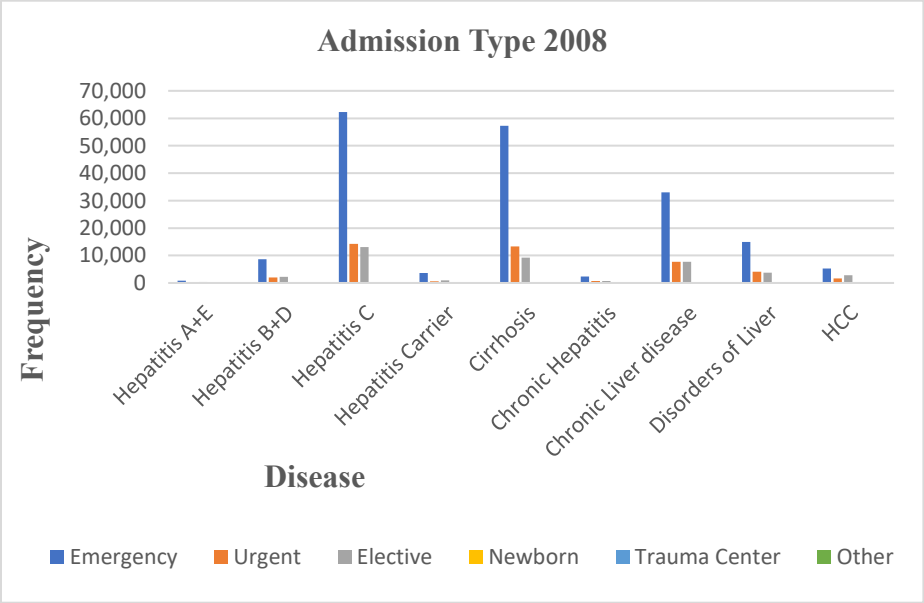

Figure 4.36 Admission Type 2008

Table 4.49 and figure 4.36 show that Emergency cases are high for Hepatitis C, 2nd highest is for Cirrhosis and 3rd highest are Chronic Liver Disease. Urgent cases were highest for Hepatitis C, 2nd highest is for Cirrhosis and 3rd highest is Chronic Liver disease. Urgent and Elective are almost similar for Chronic Liver Disease.

- For the Year 2009

Table 4.50 Admission Type 2009

Admission Type 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	800	8,239	65,525	3,433	58,040	2,262	36,462	16,009	5,155
Urgent	223	2,310	16,705	716	14,959	792	8,892	4,712	1,891
Elective	284	1,833	12,571	997	9,307	659	7,196	3,418	1,915
Newborn	0	1	8	11	4	0	13	109	0
Trauma Center	2	28	316	12	184	2	125	84	4
Other	2	6	12	0	10	0	8	1	1

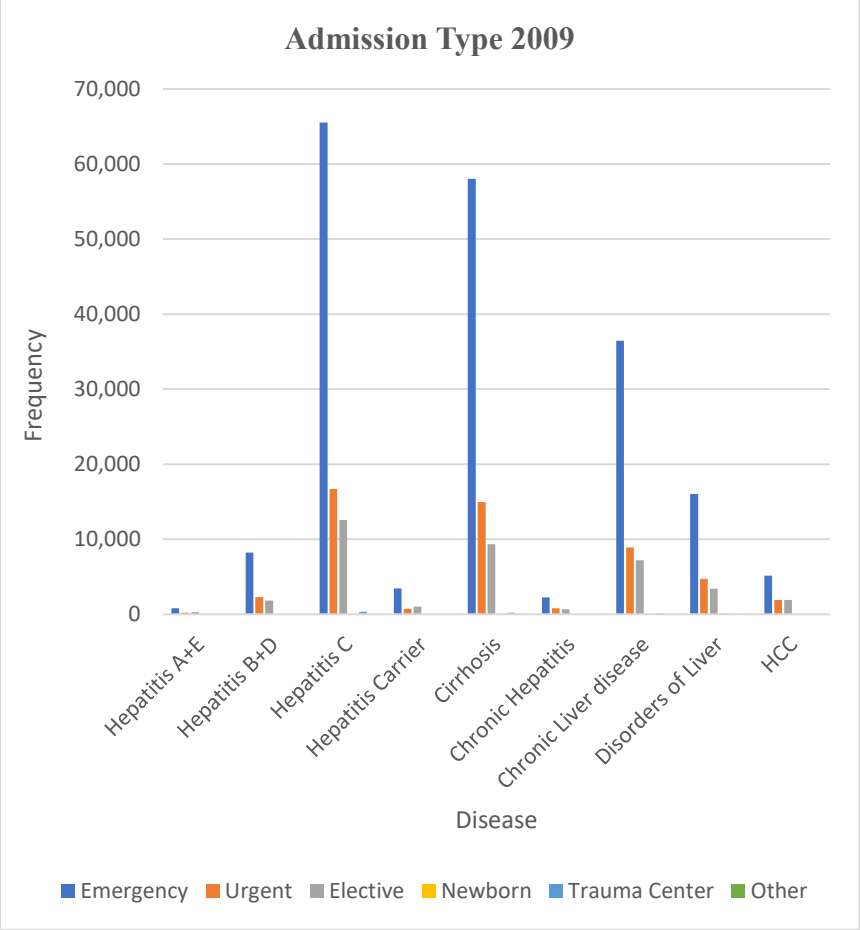

Figure 4.37 Admission Type 2009

Table 4.50 and Figure 4.37 show that Emergency cases are highest for the Hepatitis patients, 2nd highest are Cirrhosis, 3rd highest is Chronic Liver disease, 4th highest is Disorders of Liver.

- For the Year 2010

  Table 4.51 Admission Type 2010

Admission Type 2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	914	8,852	69,345	2,957	62,157	2,423	39,277	15,730	5,597
Urgent	269	2,138	16,324	1,112	15,529	796	9,987	4,653	1,974
Elective	361	2,258	15,511	1,073	10,573	775	8,805	3,921	2,535
Newborn	1	7	7	14	7	1	19	142	1
Trauma Center	5	37	457	5	321	6	158	107	14
Other	1	9	76	0	4	0	0	8	1

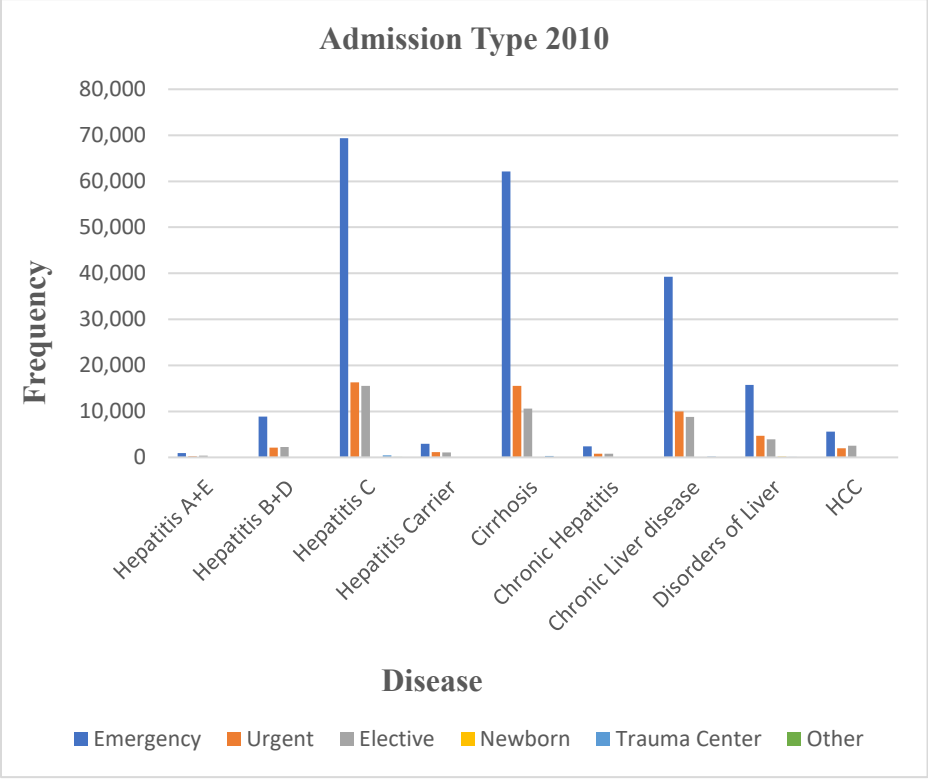

Figure 4.38 Admission Type 2010

Table 4.51 and Figure 4.38 show that Emergency admission is highest for HCV followed by Cirrhosis and Chronic Liver Disease.

- For the Year 2011

Table 4.52 Admission type 2011

Admission Type 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	864	8,519	78,326	1,729	73,250	2,860	46,984	17,969	6,448
Urgent	258	2,190	17,380	627	16,690	889	9,568	4,579	2,256
Elective	334	2,120	15,893	761	11,587	796	8,806	3,672	2,613
Newborn	0	1	6	7	1	0	14	135	0
Trauma Center	3	52	565	13	400	7	197	143	21
Other	4	50	425	1	21	0	24	2	1

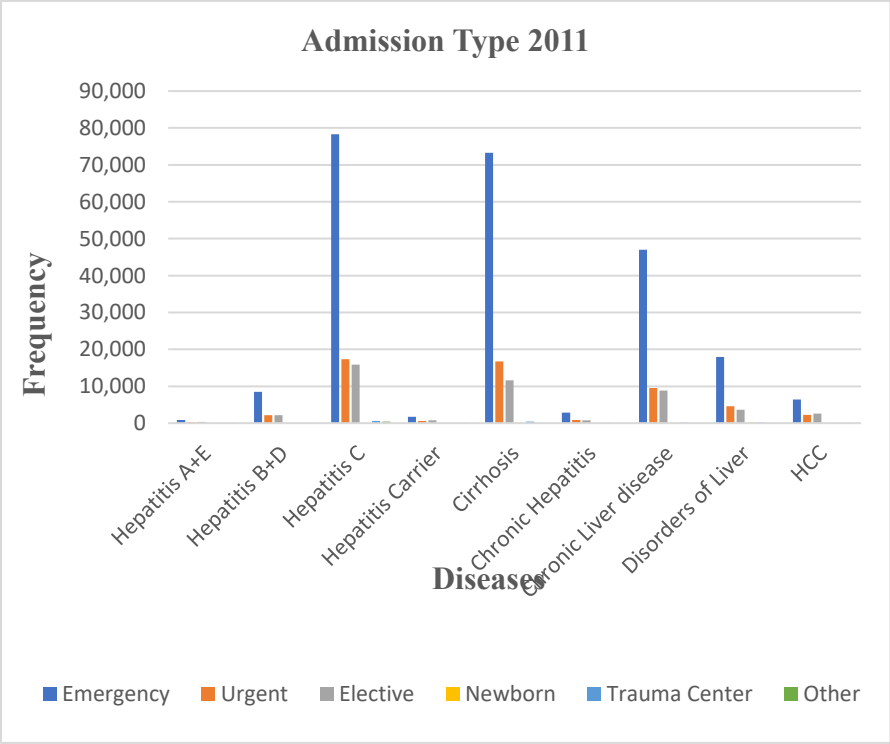

Figure 4.39 Admission Type 2011

Table 4.52 and Figure 4.39 show that Emergency admission is highest for Hepatitis C, 2nd highest is for Cirrhosis and the 3rd highest is for Chronic Liver Disease, 4th highest is Disorders of Liver.

- Summary for the Admission Type: Hepatitis C, Cirrhosis and Chronic Liver Disease
- **For Hepatitis C**

Table 4.53 Admission Type Hepatitis C

Admission Type for Hepatitis C	Emergency	Urgent	Elective
2007	59,475	13,291	13,373
2008	62,326	14,290	13,026
2009	65,525	16,705	12,571
2010	69,345	16,324	15,511
2011	78,326	17,380	15,893

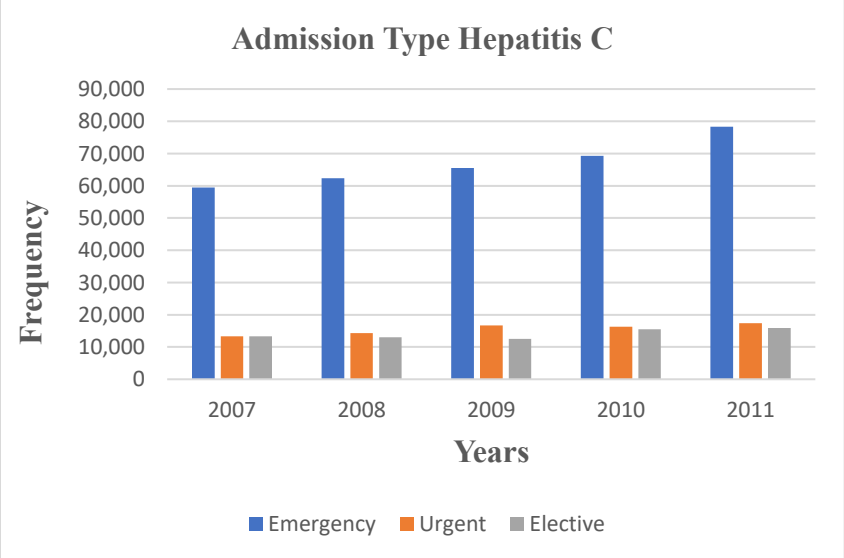

Figure 4.40 Admission Type Hepatitis C

Figure 4.40 Admission Type Hepatitis C. Table 4.53 and Figure 4.40 show high emergency admission to the hospital for the Hepatitis C virus for the analysis. Emergency Admission shows highest for the year 2011.

Table 4.54 Admission Type Cirrhosis

Admission Type for Cirrhosis	Emergency	Urgent	Elective
2007	54,074	11,870	9,191
2008	57,255	13,270	9,177
2009	58,040	14,959	9,307
2010	62,157	15,529	10,573
2011	73,250	16,690	11,587

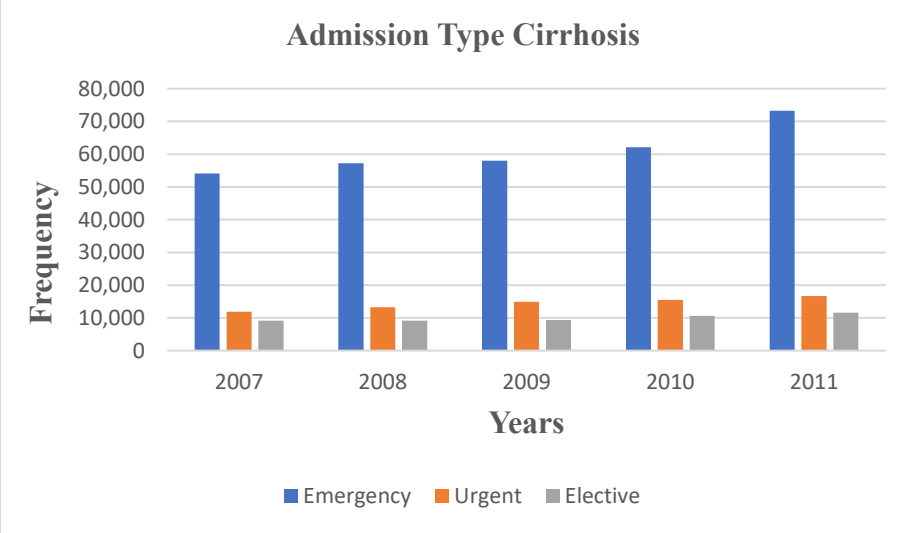

Figure 4.41 Admission Type Cirrhosis

Table 4.54 and Figure 4.41 shows that Emergency cases are high for Cirrhosis from 2007 to 2011 and the highest Emergency cases were found in the year 2011.

- For the Chronic Liver Disease

Table 4.55 Admission Type Chronic Liver Disease

Admission Type Chronic liver disease	Emergency	Urgent	Elective
2007	26,957.00	5,928.00	5,630.00
2008	33,033.00	7,713.00	7,753.00
2009	36,462.00	8,892.00	7,196.00
2010	39,277.00	9,987.00	8,805.00
2011	46,984.00	9,568.00	8,806.00

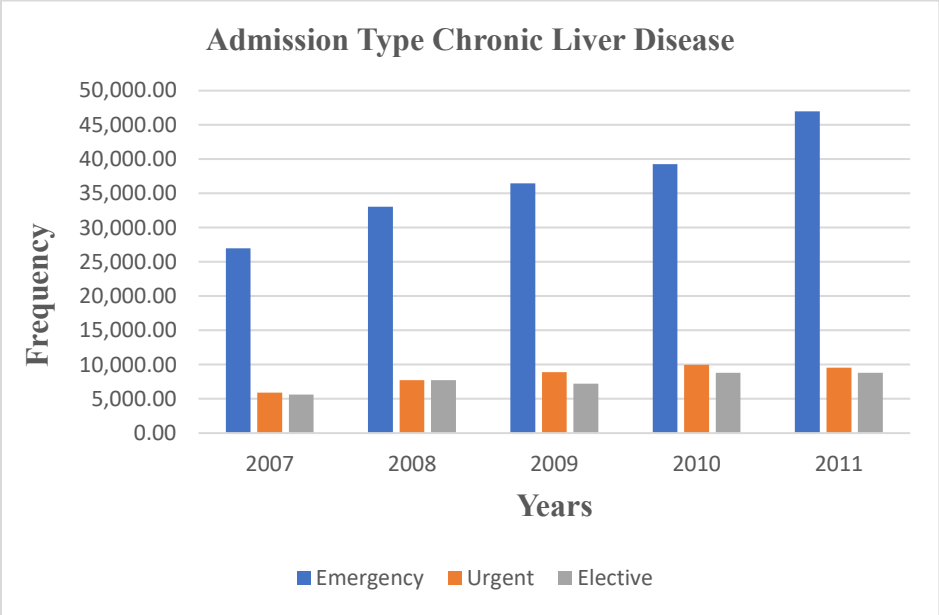

Figure 4.42 Admission Type Chronic Liver Disease

Table 4.55 and Figure 4.42 shows that Emergency cases are high For Chronic Liver Disease

from 2007 to 2011. Emergency cases are highest for the year 2011.

- **Admission Source of the Patient**

- For the Year 2007

Table 4.56 Admission Source of the Patient 2007

Admission Source 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency Department	780	7,823	58,400	2,960	56,468	2,183	27,285	13,799	4,320
From Different Hospital	67	501	3,404	99	3,368	170	1,064	887	385
Other	618	4,751	28,365	2,785	19,605	1,345	11,435	7,031	3,597

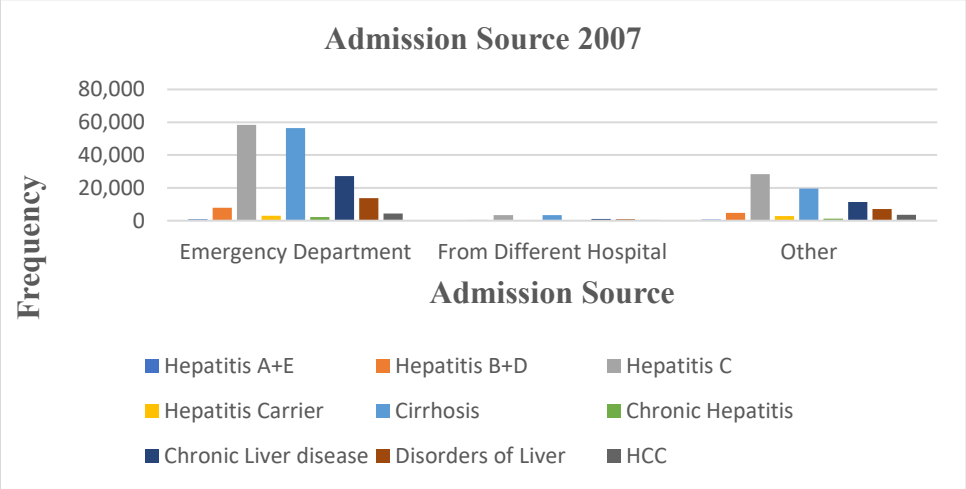

Figure 4.43 Admission Source of the Patient 2007

Table 4.56 and figure 4.43 show that Hepatitis C patients frequently need to go to the emergency department.

- For the Year 2008

Table 4.57 Admission Source of the Patient 2008

Admission Source 2008	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency Department	381	4,481	30,305	1,412	27,629	1,046	14,715	6,848	2,537
Another Hospital	37	261	1,779	63	1,647	92	639	455	191
Other	292	2,790	15,323	900	8,911	585	7,130	3,367	2,029

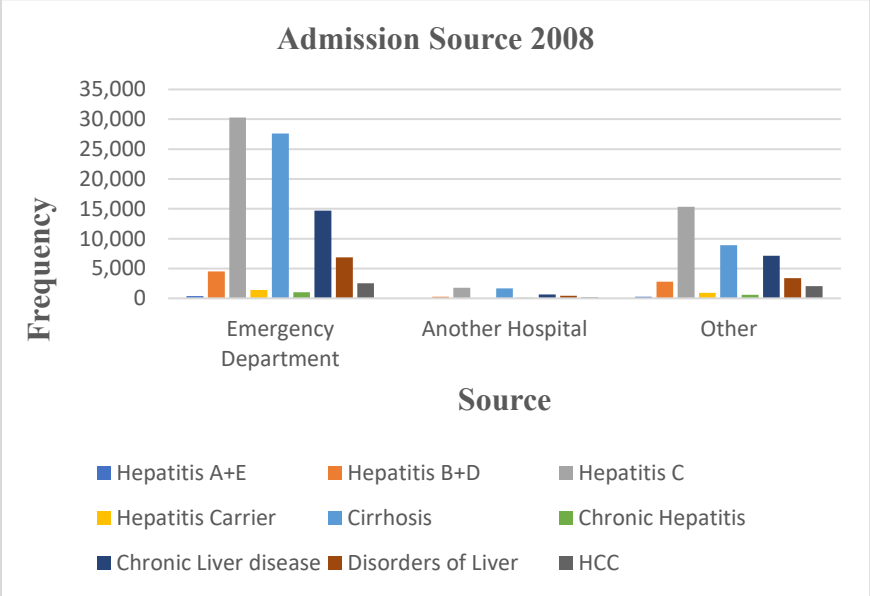

Figure 4.44 Admission Source of the Patient 2008

Table 4.57 and Figure 4.44 show that Hepatitis C patients frequently need to go to the emergency department. 2nd highest admission rate is for Cirrhosis to the emergency department for the year 2008.

- For the Year 2009

Table 4.58 Admission Source of the Patient 2009

Admission Source 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency Department	251	2,958	22,225	1,602	18,261	592	9,714	4,051	1,661
From Different Hospital	26	260	1,610	42	1,476	85	558	375	209
Other	147	1,606	9,474	754	5,636	319	4,718	2,423	1,438

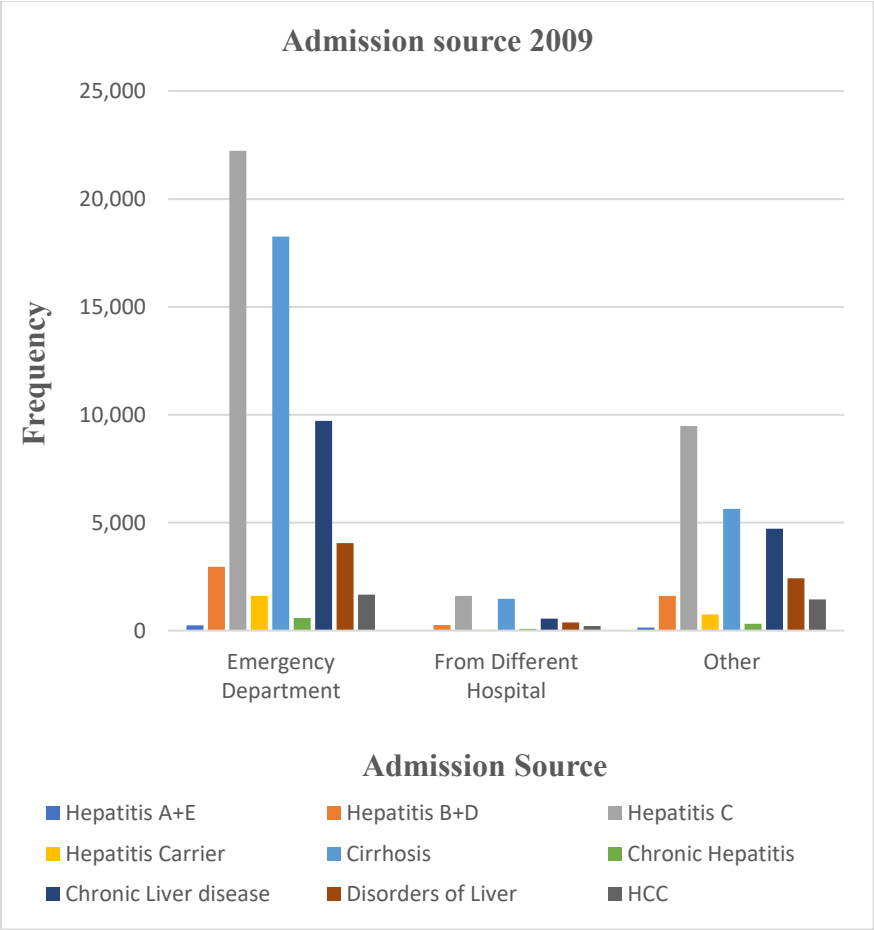

Figure 4.45 Admission Source of the Patient 2009

Table 4.58 and Figure 4.45 show that Hepatitis C patients frequently need to go to the emergency department. 2nd highest admission rate is for Cirrhosis to the emergency department for the year 2009.

- For the Year 2010

Table 4.59 Admission Source of the Patient 2010

Admission Source 2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency Department	196	2,302	17,870	1,020	16,294	548	9,133	3,507	1,796
From Different Hospital	15	207	1,496	32	1,217	56	560	313	166
Other	193	1,822	13,822	846	7,322	381	6,631	2,544	1,410

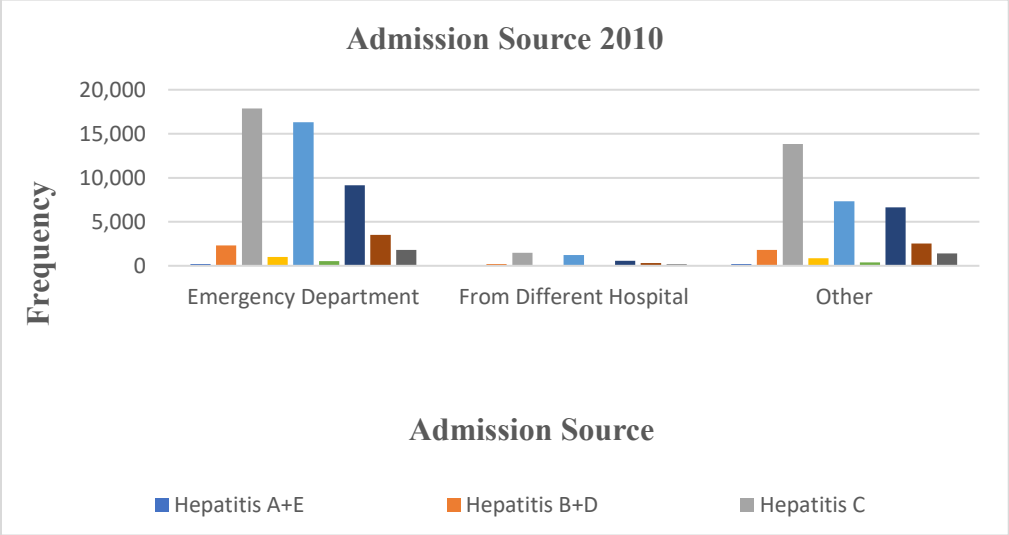

Figure 4.46 Admission Source of the Patient 2010

Table 4.59 and Figure 4.46 shows insignificant numbers of patients came from different hospital.

- For the Year 2011

Table 4.60 Admission Source of the Patient 2011

Admission Source 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency Department	151	1,775	14,773	189	14,931	507	8,947	3,139	1,238
From Different Hospital	17	210	1,451	32	1,217	53	622	355	145
Other	223	2,239	15,276	540	8,592	464	8,202	3,032	1,635

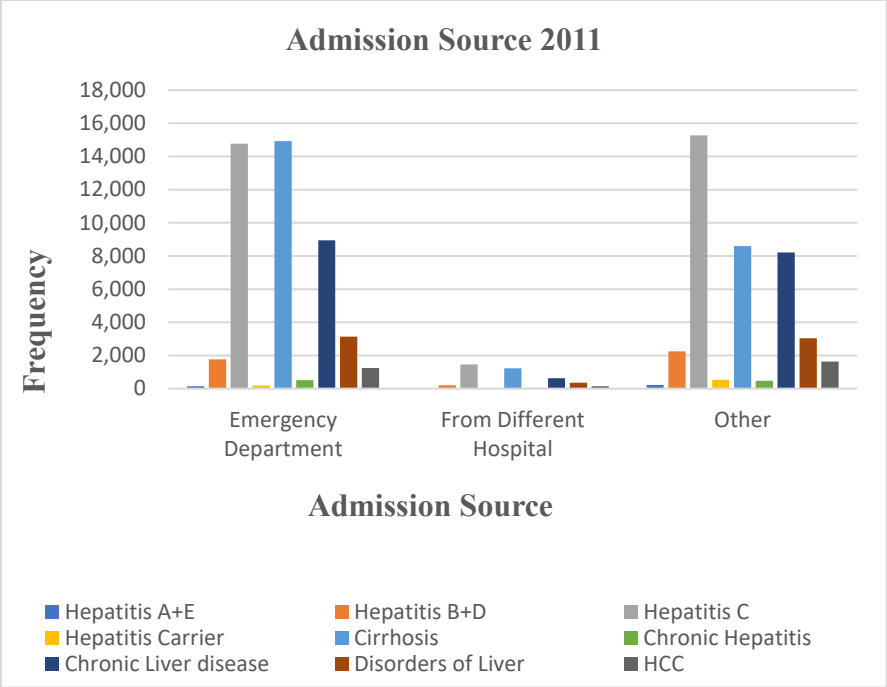

Figure 4.47 Admission Source of the Patient 2011

Table 4.60 and Figure 4.47 shows almost same amount of Hepatitis C patients and Cirrhosis patients need emergency department for the year 2011.

- Summary for the Admission Source for Hepatitis C, Cirrhosis and Chronic Liver Disease

Hepatitis C

Table 4.61 Admission Source Hepatitis C

Admission Hepatitis C Results	Emergency	Other
2007	58,400	28,365
2008	30,305	15,323
2009	22,225	9,474
2010	17,870	13,822
2011	14,773	15,276

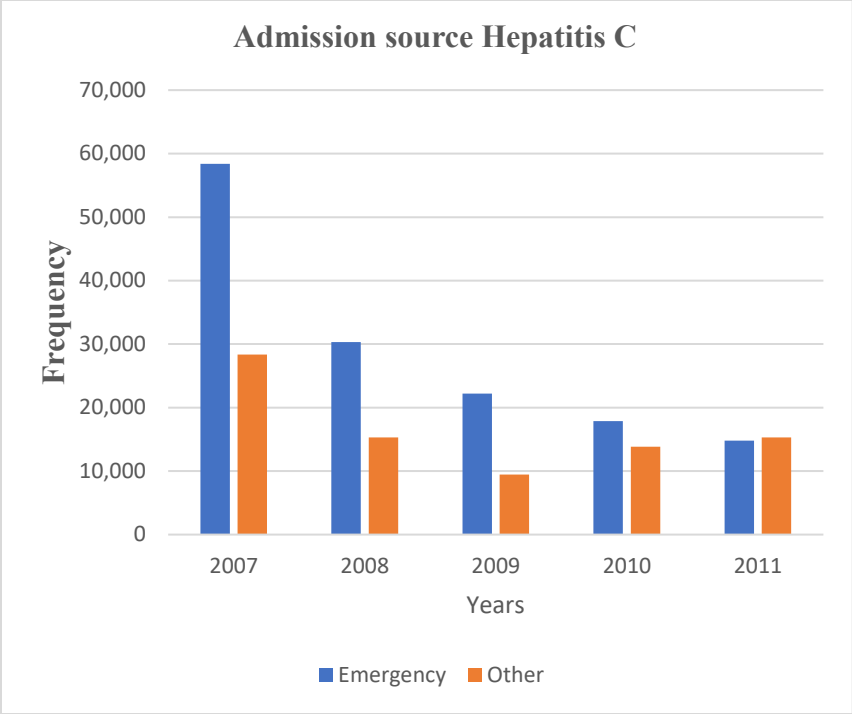

Figure 4.48 Admission Source Hepatitis C

Table 4.61 and Figure 4.48 show the trend for Hepatitis C patients, with years number of emergency source getting less. For the year 2011 emergency and other sources of patients became almost same.

- Cirrhosis

Table 4.62 Admission Source Cirrhosis

Admission Cirrhosis Results	Emergency	Other
2007	56,468	19,605
2008	27,629	8,911
2009	18,261	5,636
2010	16,294	7,322
2011	14,931	8,592

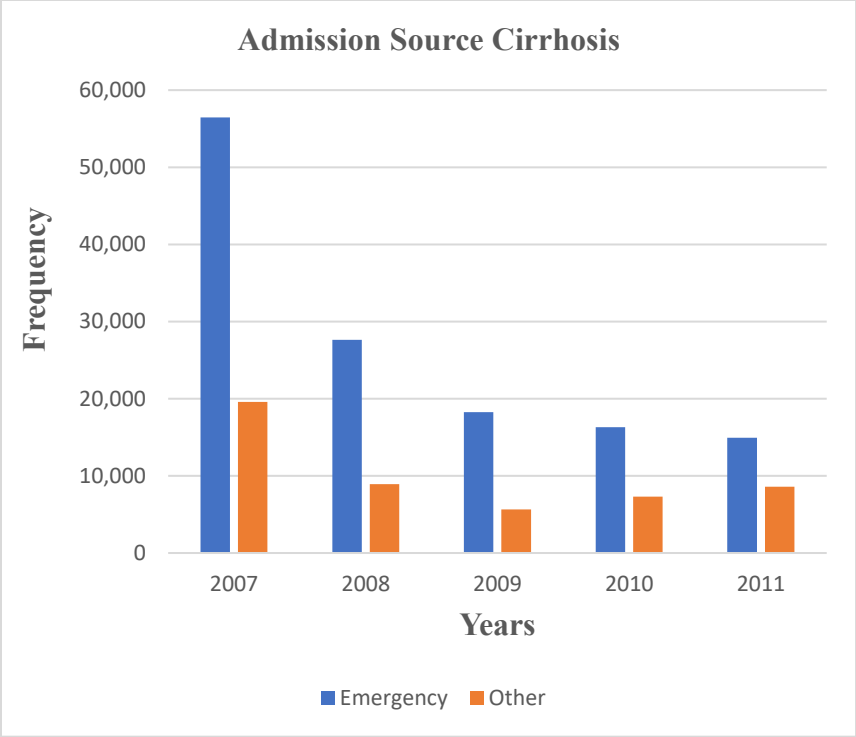

Figure 4.49 Admission Source Cirrhosis

Table 4.62 and Figure 4.49 show the trend for Cirrhosis patients, with years number of emergency source getting less. For the year 2011 emergency source for Cirrhosis patients were 73.55% less than the year 2007.

- Chronic Liver Disease

Table 4.63 Admission Source Chronic Liver Disease

Admission Chronic Liver Disease	Emergency	Other
2007	27,285	11,435
2008	14,715	7,130
2009	9,714	4,718
2010	9,133	6,631
2011	8,947	8,202

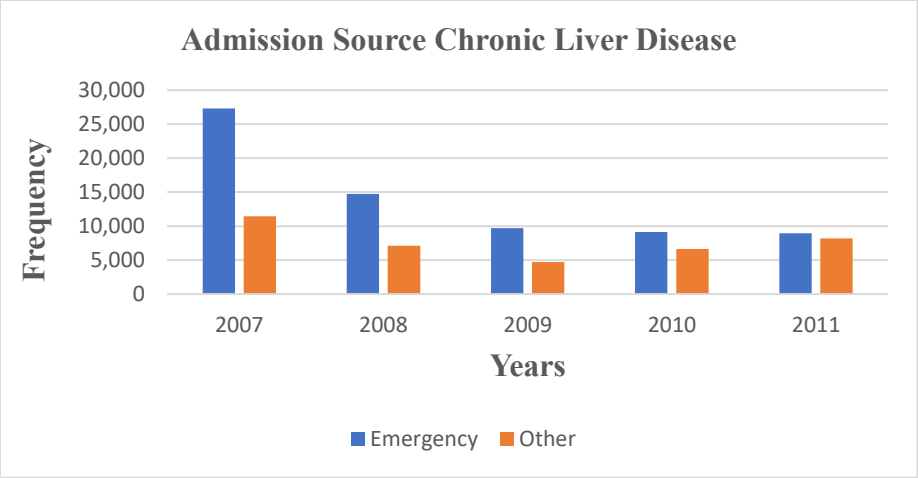

Figure 4.50 Admission Chronic Liver Disease

Table 4.63 and Figure 4.50 show that the trend for Chronic Liver Disease with emergency admission is getting less. Curve shows by the year 2011 67.20% reduction in emergency source.

- **Destination of the Patient after Discharge from the Hospital**
- For the Year 2007

Table 4.64 Destination After Discharge 2007

Destination After Discharge 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
To Home Self Care	1,225	10,360	71,089	4,613	53,184	2,899	34,244	16,665	5,305
Transfer to Short Term Hospital	225	2,086	14,906	1,091	17,349	656	5,113	4,060	1,436
To Home Health Care	155	1,206	8,258	435	10,438	440	2,945	2,572	1,560
Left Against Medical Advice	26	496	4,194	382	2,053	29	1,507	359	57
Died	37	574	3,217	62	6,494	149	906	870	1,035

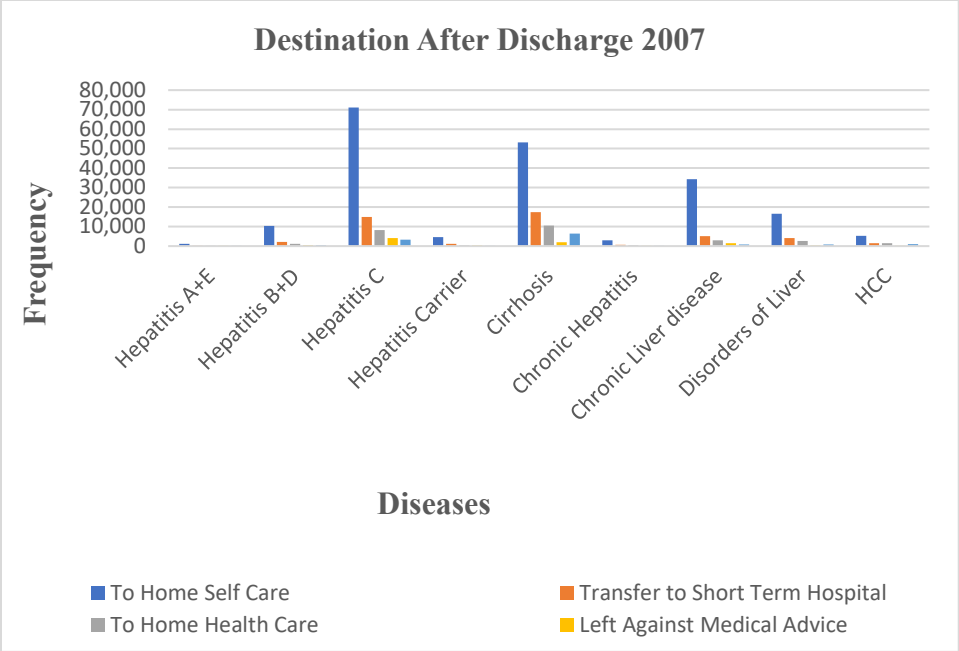

Figure 4.51 Destination After Discharge 2007

Table 4.64 and Figure 4.51 shows that highest number of the patients stayed to home self-care after patents left the hospital. 2nd highest number of the patients transfer to short term hospital and the 3rd Highest number of the patients to home health care for the year 2007

- For the Year 2008

Table 4.65 Destination After Discharge 2008

Destination After Discharge 2008	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
To Home Self Care	1,207	10,653	73,750	4,254	56,434	3,062	42,064	17,812	6,828
Transfer to Short Term Hospital	244	2,277	14,276	472	17,525	636	6,132	4,178	1,706
To Home Health Care	192	1,595	9,408	344	11,260	529	3,983	2,917	2,079
Left Against Medical Advice	28	439	4,296	552	2,112	37	1,608	351	78
Died	56	645	3,030	47	5,912	140	1,110	799	1,206

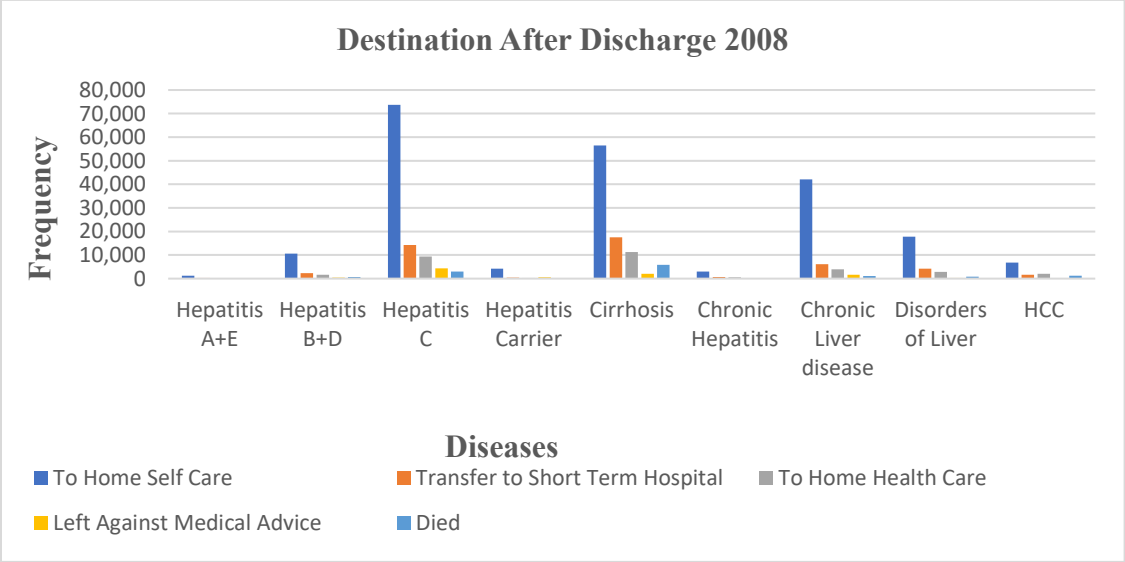

Figure 4.52 Destination After Discharge 2008

Table 4.65 and Figure 4.52 shows that highest number of the patients stayed to home self-care after patents left the hospital. 2nd highest number of the patients transfer to short term hospital and the 3rd Highest number of the patients to home health care for the year 2008

- For the Year 2009

Table 4.66 Destination After Discharge 2009

Destination After Discharge 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
To Home Self Care	1,024	10,121	77,501	4,136	58,327	2,925	45,314	18,412	6,282
Transfer to Short Term Hospital	254	2,189	16,124	572	19,044	715	7,283	4,995	1,734
To Home Health Care	164	1,453	10,078	439	11,964	493	4,433	3,254	1,982
Left Against Medical Advice	32	476	4,419	430	2,162	34	1,695	307	75
Died	48	597	3,518	59	6,478	161	1,503	1,176	1,144

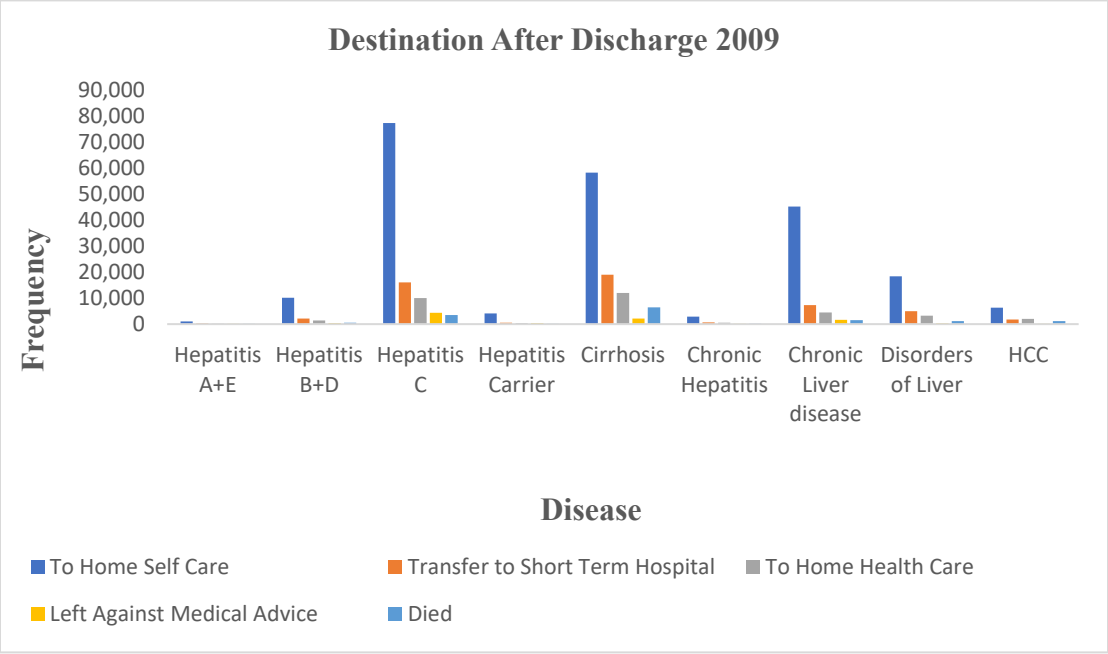

Figure 4.53 Destination After Discharge 2009

Table 4.66 and Figure 4.53 shows that highest number of the patients stayed to home self-care after patients left the hospital. 2nd highest number of the patients transfer to

short term hospital and the 3rd Highest number of the patients to home health care for the year 2009.

- For the Year 2010

Table 4.67 Destination After Discharge 2010

Destination After Discharge 2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
To Home Self Care	1,196	10,620	79,691	4,063	61,138	3,054	50,280	18,290	6,595
Transfer to Short Term Hospital	278	2,343	17,884	739	20,285	708	8,018	4,962	1,922
To Home Health Care	210	1,565	11,484	437	13,582	589	5,462	3,324	2,374
Left Against Medical Advice	24	496	5,058	325	2,335	59	1,797	397	92
Died	41	611	3,590	58	6,392	170	1,507	1,157	1,144

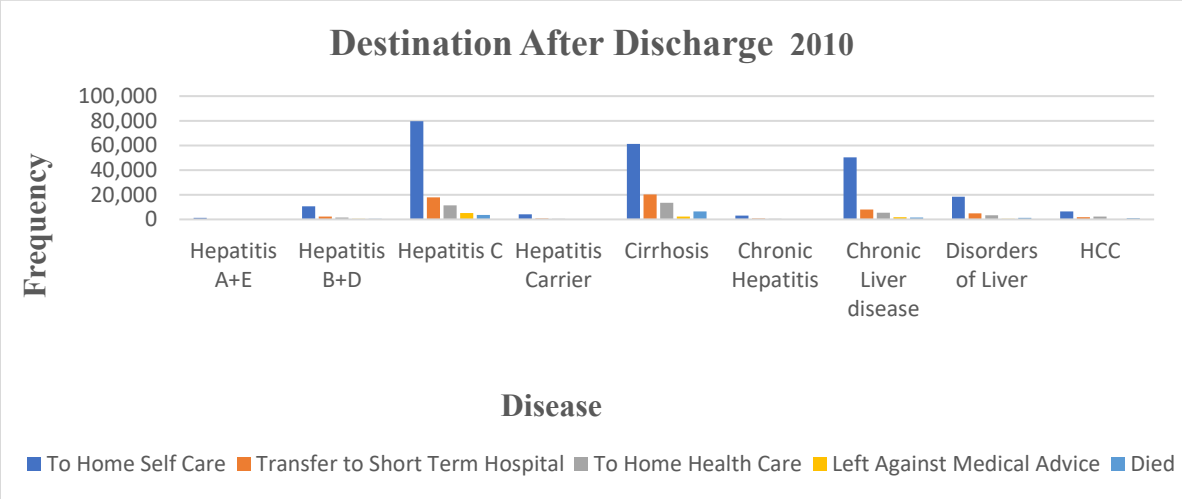

Figure 4.54 Destination After Discharge 2010

Table 4.67 and figure 4.54 show that highest number of the patients stayed to home self-care after patients left the hospital. 2nd highest number of the patients transfer to short term hospital and the 3rd Highest number of the patients to home health care for the year 2010.

- For the Year 2011

Table 4.68 Destination After Discharge 2011

Destination After Discharge 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
To Home Self Care	1,094	10,076	86,152	2,608	68,620	3,342	55,517	19,013	7,198
Transfer to Short Term Hospital	298	2,438	20,966	429	24,382	931	9,882	5,737	2,162
To Home Health Care	197	1,705	13,157	311	15,815	703	6,682	3,824	2,570
Left Against Medical Advice	41	482	5,498	116	2,599	39	2,092	350	86
Died	52	549	3,837	37	7,084	172	1,775	1,238	1,259

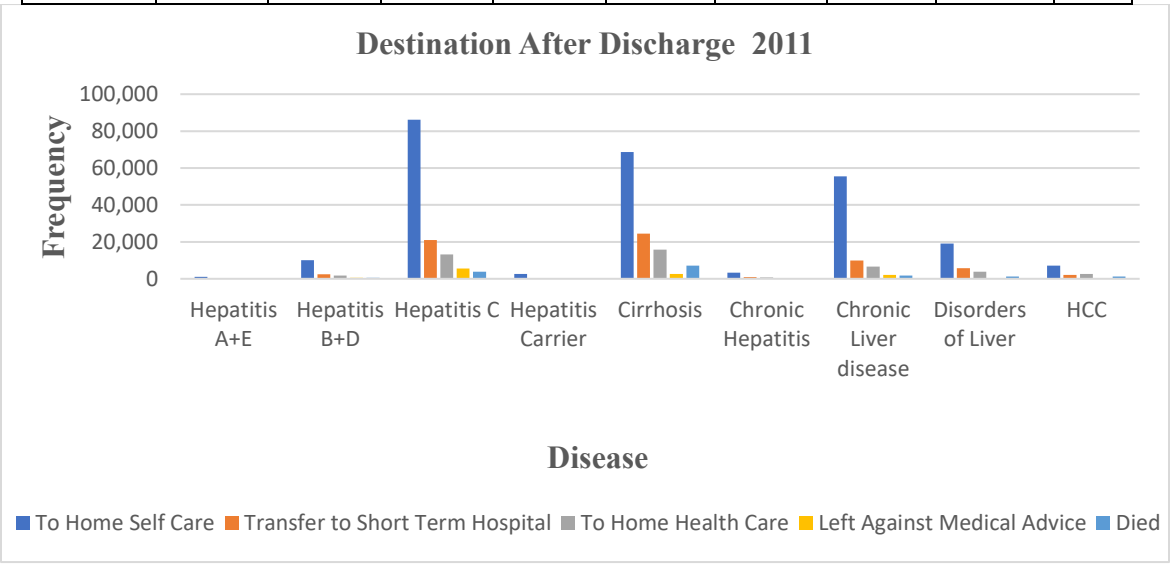

Figure 4.55 Destination After Discharge 2011

Table 4.68 and Figure 4.55 show that highest number of the patients stayed to home self-care after patients left the hospital. 2nd highest number of the patients transfer to short term hospital and the 3rd Highest number of the patients to home health care for the year 2009.

For the Year 2012

Table 4.69 Destination After Discharge 2012

Destination After Discharge 2012	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
To Home Self Care	995	9,563	81,797	2,804	66,403	2,925	53,666	17,634	7,027
Transfer to Short Term Hospital	256	2,210	18,915	459	22,677	749	9,468	5,070	2,128
To Home Health Care	180	1,674	12,629	279	15,421	612	6,440	3,639	2,426
Left Against Medical Advice	39	428	5,173	226	2,525	41	1,935	314	96
Died	42	507	3,530	43	6,849	170	1,671	1,139	1,119

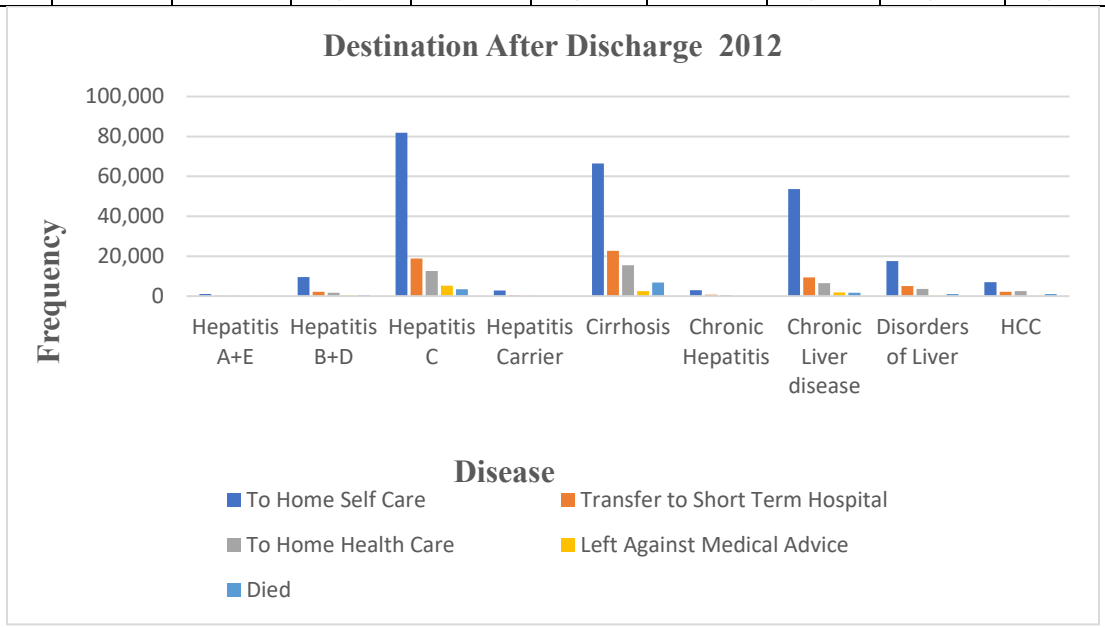

Figure 4.56 Destination After Discharge 2012

Table 4.69 and figure 4.56 show that Most of the patients stayed to home self-care after discharge from the hospital, followed by short term hospital transfer and home health care. Maximum number of patients died in hospital was highest for Cirrhosis followed by Hepatitis C for the year 2012.

4.8 Analysis of LOS, Hospital Charges, Admission Type and Mortality

- Incidence of Disease by the Length of Stay

Table 4.70 Weighted Average of Length of Stay

Weighted Average of Length of Stay	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorder of Liver	HCC
2007	5.80	6.51	6.01	5.24	6.59	6.17	5.14	6.82	6.08
2008	6.41	6.45	5.74	4.61	6.13	5.58	5.10	6.49	6.20
2009	6.70	6.25	5.79	5.41	6.28	5.96	5.44	7.24	6.01
2010	6.14	6.71	5.85	5.00	6.23	6.03	5.35	7.37	5.90
2011	6.31	6.46	5.85	4.79	6.15	5.95	5.39	6.91	5.83
2012	6.25	6.34	5.73	5.16	6.00	5.86	5.37	7.28	5.93

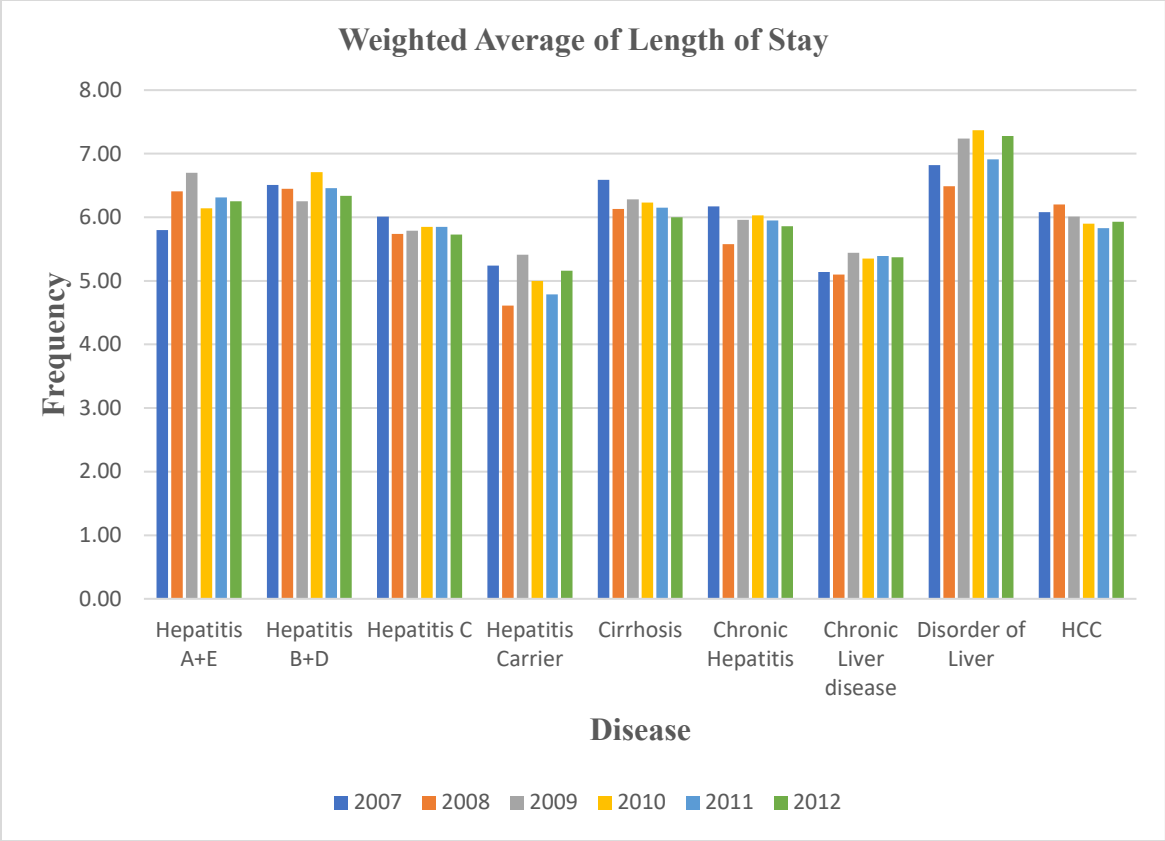

Figure 4.57 Mean Length of Stay

Table 4.70 and Figure 4.57 show that in 2007 Hepatitis C had the highest Length of stay of 6.01 days. After 2007 length of stay decreased to an average of 5.79 days from 2008 to 2012. Hepatitis Carrier has the shortest stay and Disorder of Liver has the longest stay.

- Below is an average length of stay for all diseases from 2007 to 2012

Hepatitis Carrier 5.03 days, Chronic Liver disease 5.29 days, Hepatitis C 5.82 days, chronic Hepatitis 5.92 days, Hepatocellular Carcinoma (HCC) 5.99 days, Cirrhosis 6.23 days, Hepatitis A+E 6.26 days, Hepatitis B+D 6.45 days, Disorder of Liver 7.01 days.

Disorder of Liver has the highest Length of stay an average of 7.01 days from 2007 to 2012.

- **Hospital Charges and Admission Type**
- For the Year 2007

*Emergency room provides medical treatment for the acute care of patients who comes to the hospital without prior appointment; either by their own or brought by an ambulance.

*Urgent is delivery or the doctor decides there is a clinical need to admit the patient in few days.

*Elective is booked admission or waiting list admission.

*Trauma Center treats injuries like fall, motor vehicle collisions, gunshot wounds, or burn.

*Other is Rehabilitation, Psychiatric (mental Health) admission.

Table 4.71 Mean Charges and Admission Type 2007

Mean Charges and Admission Type 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	$29,838	$35,745	$31,013	$25,957	$36,337	$34,874	$25,420	$35,535	$38,586
Urgent	$25,616	$30,859	$29,268	$13,799	$35,397	$38,831	$22,980	$38,241	$38,989
Elective	$27,628	$36,015	$32,331	$20,582	$39,364	$36,587	$29,639	$42,119	$44,513
Trauma Center	$0	$117,237	$58,476	$21,145	$74,544	$97,267	$57,334	$87,601	$25,290
Other	$39,338	$37,235	$37,879	$0	$28,928	$0	$5,691	$15,538	$0

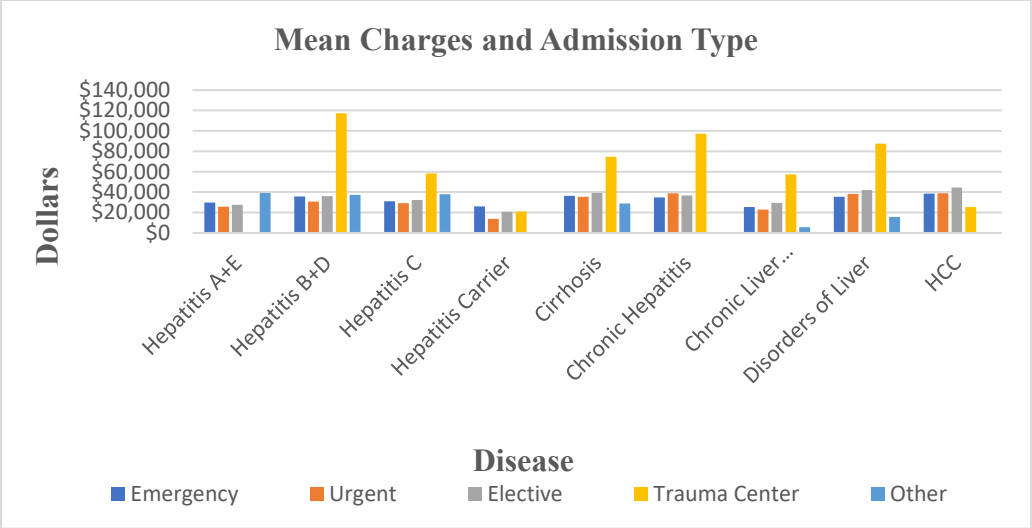

Figure 4.58 Mean Charges and Admission Type 2007

Table 4.71 and 4.58 show that Hepatitis A+E patients did not have any trauma center charges. Patients with Hepatocellular Carcinoma (HCC) had the lowest charges for the trauma center. Hepatitis B+D patients showed highest trauma charges, Chronic Hepatitis patients showed the 2nd highest trauma charges, and Disorders of Liver showed the 3rd highest Trauma Center charges.

- For the Year 2008

Table 4.72 Mean Charges and Admission Type 2008

Mean Charges and Admission Type 2008	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	$37,635	$38,158	$31,685	$20,940	$36,216	$34,902	$28,776	$35,225	$44,815
Urgent	$39,340	$38,224	$30,538	$19,919	$39,228	$45,360	$27,065	$37,139	$51,551
Elective	$48,008	$40,678	$36,991	$24,185	$42,316	$38,005	$32,992	$42,661	$49,761
Trauma Center	$71,550	$84,479	$59,879	$31,834	$59,735	$44,139	$56,729	$63,089	$24,765
Other	$13,590	$7,094	$7,776	$0	$25,527	$14,831	$10,133	$24,267	$0

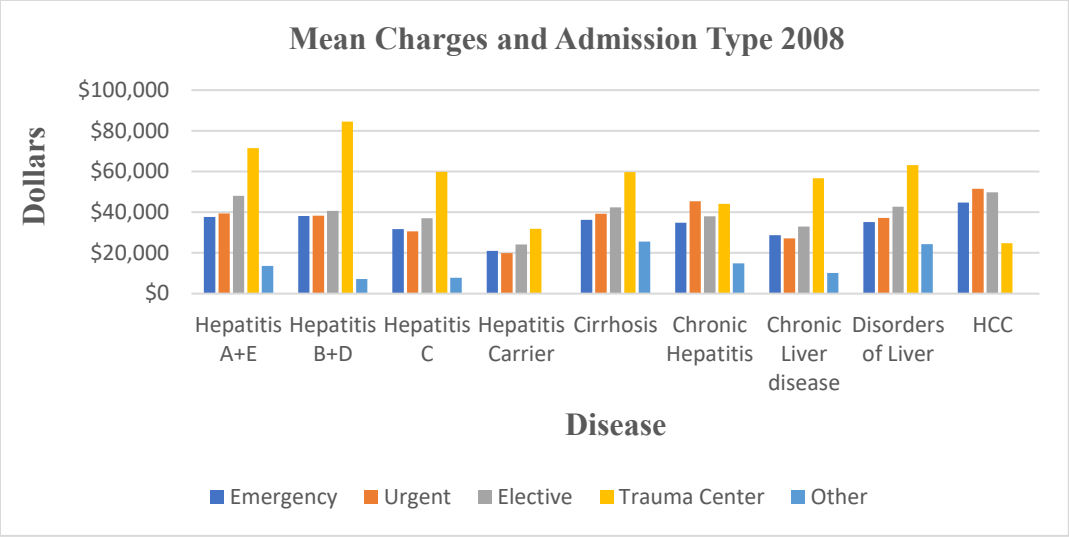

Figure 4.59 Mean Charges and Admission Type 2008

Table 4.72 and Figure 4.59 show that Hepatitis B+D patients had the highest charges for Trauma Center. Hepatitis A+E patients shows the 2nd highest charges and Disorder of Liver shows the 3rd highest charges for the Trauma Center. Hepatocellular Carcinoma (HCC) patients showed the lowest trauma Center charges for the year 2008.

- For the Year 2009

Table 4.73 Mean Charges and Admission Type 2009

Mean Charges and Admission Type 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	$40,465	$41,034	$35,327	$21,363	$39,377	$36,365	$32,801	$41,750	$43,282
Urgent	$45,727	$54,124	$40,046	$25,849	$42,552	$35,639	$32,927	$48,736	$50,316
Elective	$44,523	$46,002	$43,677	$31,790	$49,062	$40,162	$37,883	$51,645	$60,697
Trauma Center	$107,150	$59,821	$78,001	$41,609	$103,744	$28,109	$87,898	$66,344	$12,806
Other	$9,106	$19,937	$16,832	$0	$18,443	$0	$14,538	$4,816	$17,818

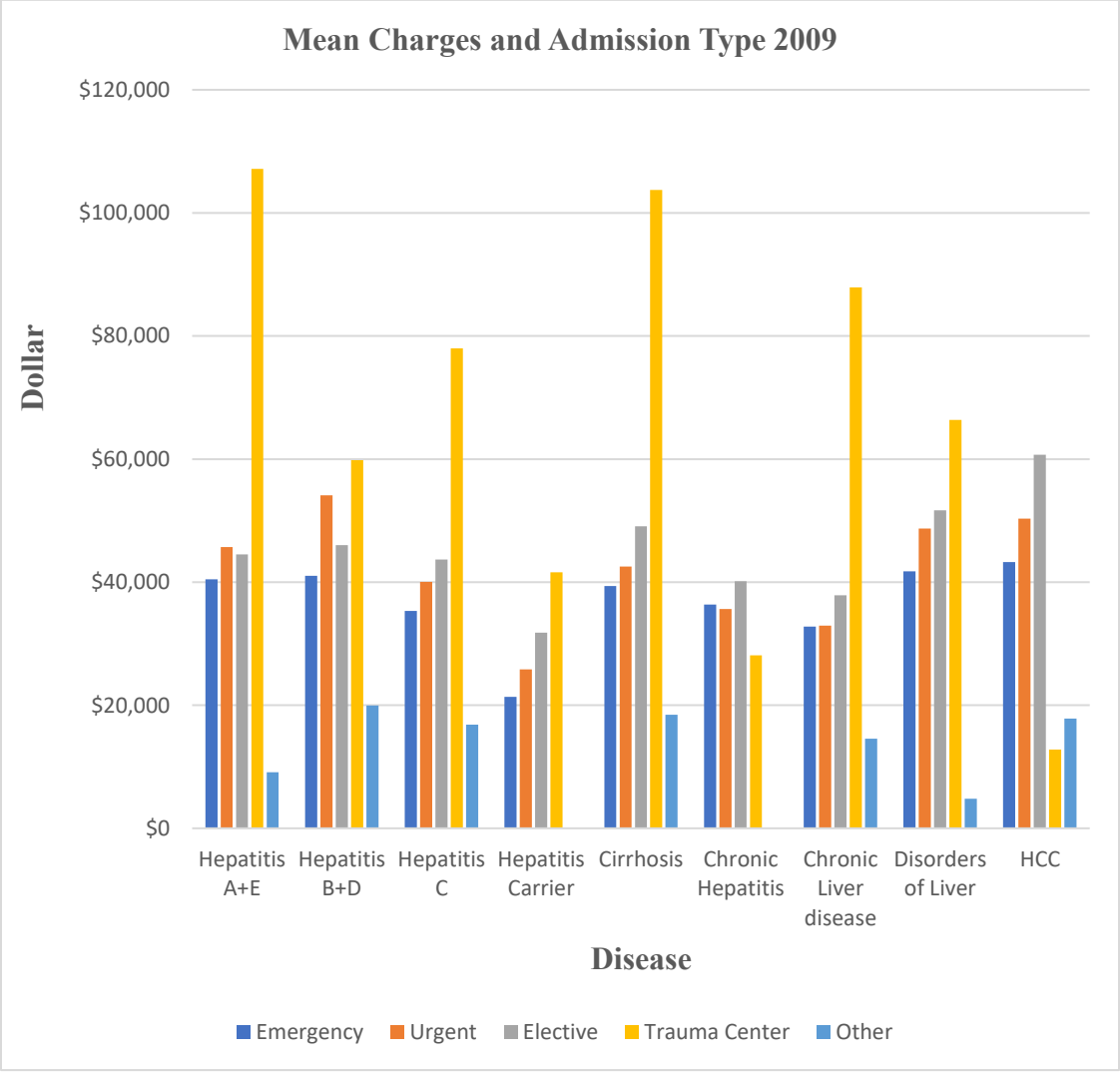

Figure 4.60 Mean Charges and Admission Type 2009

Table 4.73 and Figure 4.60 show that Hepatitis A+E patients shows the highest charges for the Trauma Center, Cirrhosis patients shows the 2nd highest charges and Chronic Liver Disease shows the 3rd highest charges for the Trauma Center. HCC has the lowest Trauma Center charges for the year 2009.

- For the Year 2010

Table 4.74 Mean Charges and Admission Type 2010

Mean Charges and Admission Type 2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	$41,921	$44,672	$36,338	$24,982	$40,542	$41,620	$34,407	$44,542	$44,777
Urgent	$40,876	$45,652	$39,269	$20,471	$46,030	$39,901	$35,760	$55,163	$48,176
Elective	$54,761	$51,360	$47,639	$24,553	$58,798	$54,909	$44,382	$58,228	$69,066
Trauma Center	$78,948	$104,974	$96,493	$60,878	$96,175	$148,360	$83,821	$88,112	$96,976
Other	$0	$6,266	$7,594	$0	$12,960	$0	$0	$13,533	$0

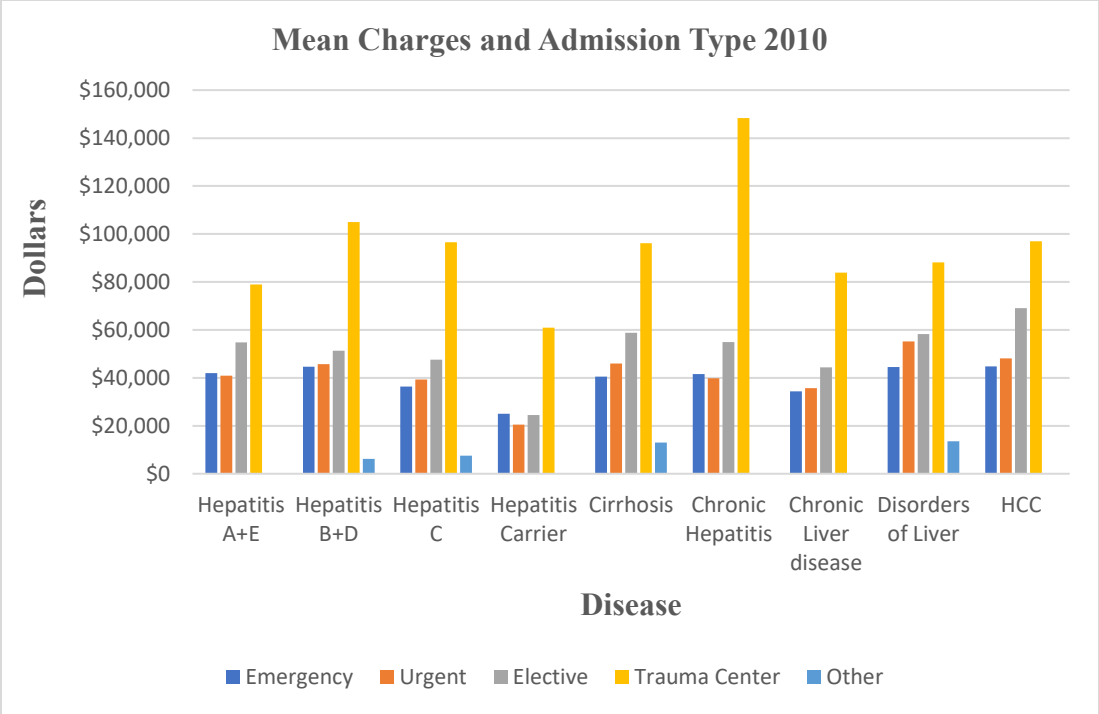

Figure 4.61 Mean Charges and Admission Type 2010

Table 4.74 and Figure 4.61 show that Chronic Hepatitis patients has the highest charges for the

Trauma Center, Hepatitis B+D shows the 2nd highest charges and HCC has the 3rd highest

Trauma Center charges for the year 2010.

- For the Year 2011

Table 4.75 Mean Charges and Admission Type 2011

Mean Charges and Admission Type 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
Emergency	$44,514	$47,395	$38,816	$32,280	$43,544	$43,439	$36,916	$45,735	$46,704
Urgent	$51,320	$66,006	$56,582	$31,490	$62,659	$63,905	$45,479	$61,269	$71,159
Elective	$55,137	$49,026	$47,772	$33,394	$57,679	$58,763	$45,602	$60,926	$67,704
Trauma Center	$56,386	$105,682	$103,710	$58,561	$96,068	$43,315	$84,325	$104,311	$60,604
Other	$34,971	$15,829	$11,833	$8,177	$19,758	$0	$24,859	$11,347	$41,951

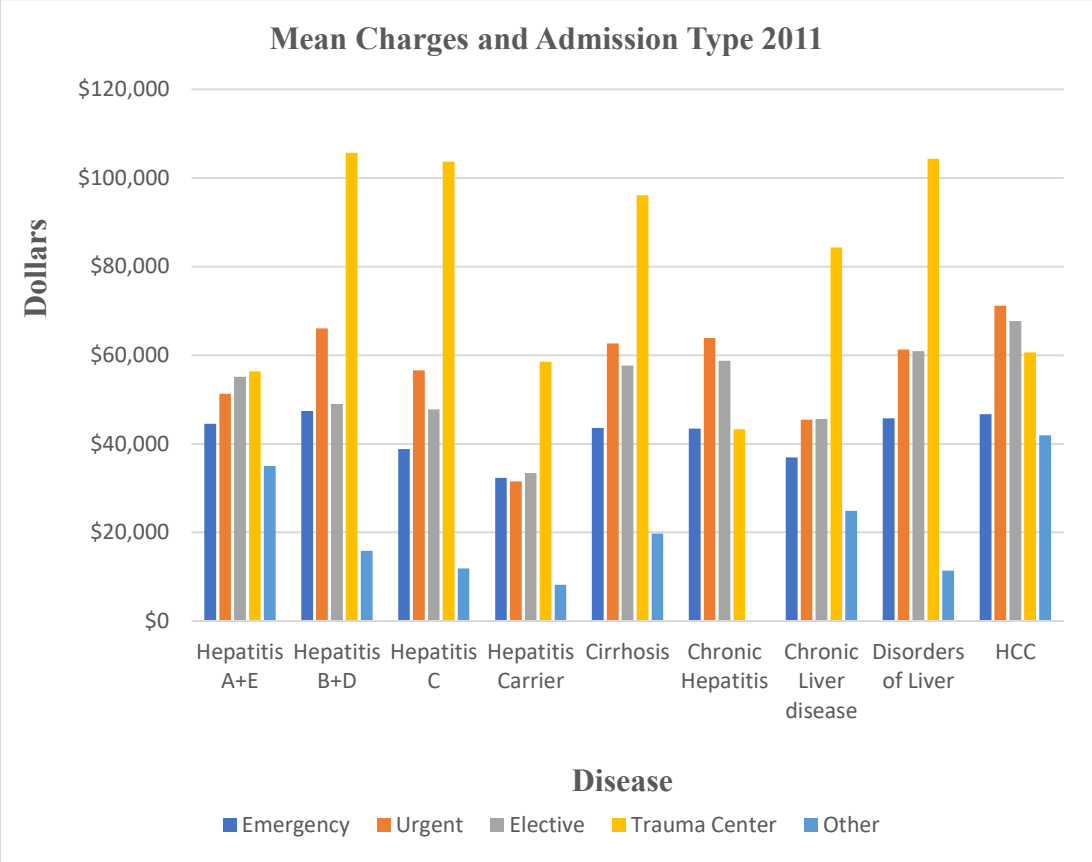

Figure 4.62 Mean Charges and Admission Type 2011

Table 4.75 and Figure 4.62 show that Hepatitis B+D has the highest trauma Center charges; Disorder of Liver shows the 2nd highest charges for Trauma Center and Hepatitis C patients has the 3rd highest Trauma Center charges.

- **Patients Died During the Hospital Stay**

Table 4.76 Number of deaths in the Hospital

Die in Hospital	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronic Hepatitis	Chronic Liver disease	Disorders of Liver	HCC
2007	37	574	3,217	62	6,494	149	906	870	1,035
2008	56	645	3,030	47	5,912	140	1,110	799	1,206
2009	48	597	3,518	59	6,478	161	1,503	1,176	1,144
2010	41	611	3,590	58	6,392	170	1,507	1,157	1,144
2011	52	549	3,837	37	7,084	172	1,775	1,238	1,259
2012	42	507	3,530	43	6,849	170	1,671	1,139	1,119
Total	276	3483	20722	306	39209	962	8472	6379	6907

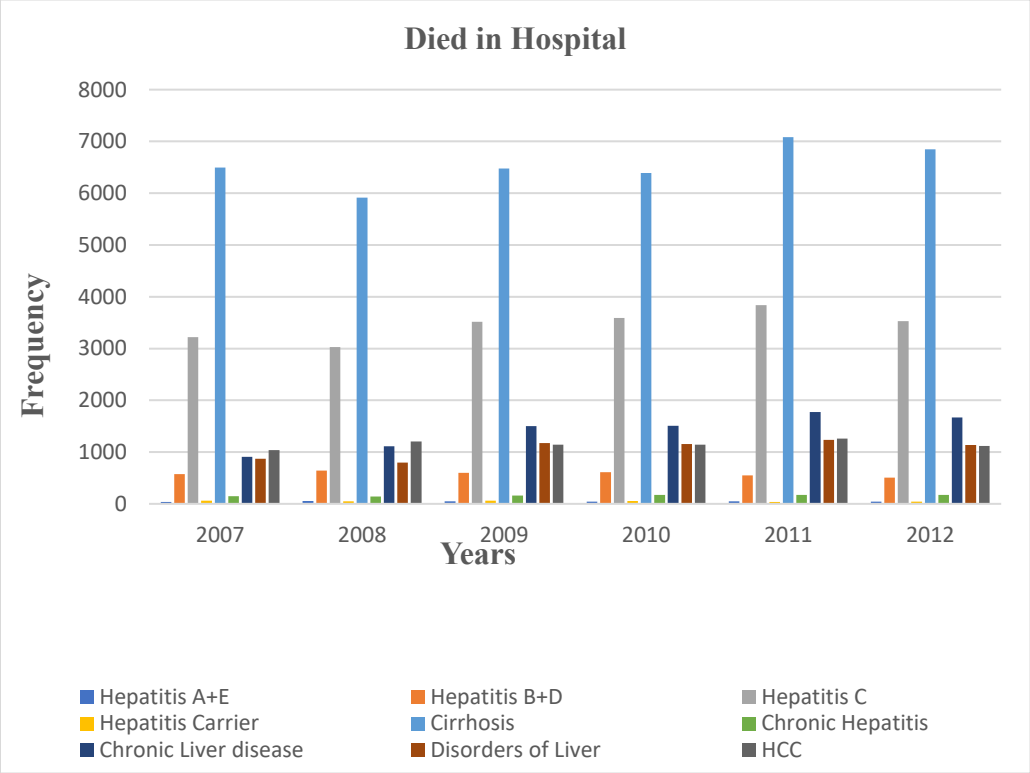

Figure 4.63 Number of deaths in the Hospital

Table 4.76 and figure 4.63 show that Cirrhosis has the highest number of death rate in the hospital. Cirrhosis death numbers increased by 5% from 2007 to 2012. The highest increase of death rate was in 2011 by 11%. Hepatitis C has the 2nd highest death rate in the hospital. Its death in hospital increases by 10% from 2007 to 2012. Chronic Liver

disease is the 3rd highest number of death rate in the hospital. It increased by 84% from 2007 to 2012.

4.9 Number of Procedures

- For the Year 2007

Table 4.77 Procedure Performed 2007

Procedure 2007	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronis Hepatitis	Chronic Liver Disease	Disorder of Liver	HCC
Biopsy	33	319	1,697	24	3,115	554	1,842	1,372	1,199
Destruction of Tissue	1	60	174	4	282	17	128	327	466
Removal of Lobe	0	25	30	1	50	5	29	37	162
Liver transplant	2	72	455	2	845	65	68	65	298
Repair of Liver	0	1	17	0	22	0	6	29	15
Other Procedures	1	38	144	0	154	3	21	265	277
Liver Scan	5	35	187	8	169	12	130	76	27

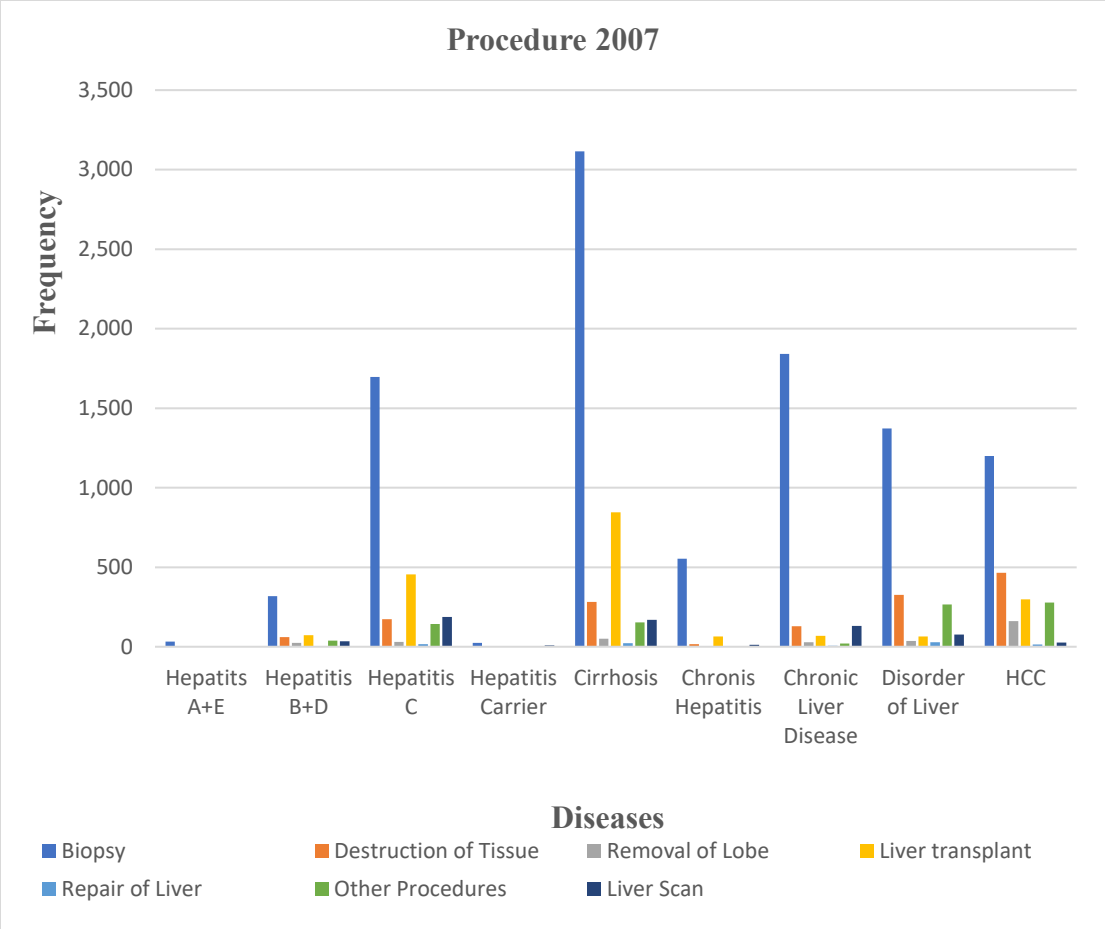

Figure 4.64 Procedure Performed 2007

Table 4.77 and Figure 4.64 show that highest number of Biopsy done on Cirrhosis, 2nd highest number of Biopsy done on Chronic Liver Disease, and 3rd highest Biopsy done on Hepatitis C for the year 2007. Cirrhosis patients shows highest number of Liver Transplant, Hepatitis C shows the 2nd highest number of Liver Transplant and Hepatocellular Carcinoma (HCC) shows the 3rd highest number of Liver Transplant. HCC shows the highest number of procedures done for Destruction of tissue. Disorder of Liver shows the 2nd highest and Cirrhosis shows the 3rd highest number of procedures done for Destruction of tissue.

- For the Year 2008

Table 4.78 Procedure Performed 2008

Procedure 2008	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronis Hepatitis	Chronic Liver Disease	Disorder of Liver	HCC
Biopsy	31	359	1,892	19	3,312	563	2,484	1,458	1,489
Destruction of Tissue	2	118	346	4	438	10	138	435	783
Removal of Lobe	0	40	46	1	55	3	26	51	283
Liver transplant	4	153	793	2	1,356	83	125	97	576
Repair of Liver	1	4	9	1	28	1	11	23	11
Other Procedures	5	49	204	0	235	11	3	187	351
Liver Scan	6	21	91	4	117	9	111	59	22

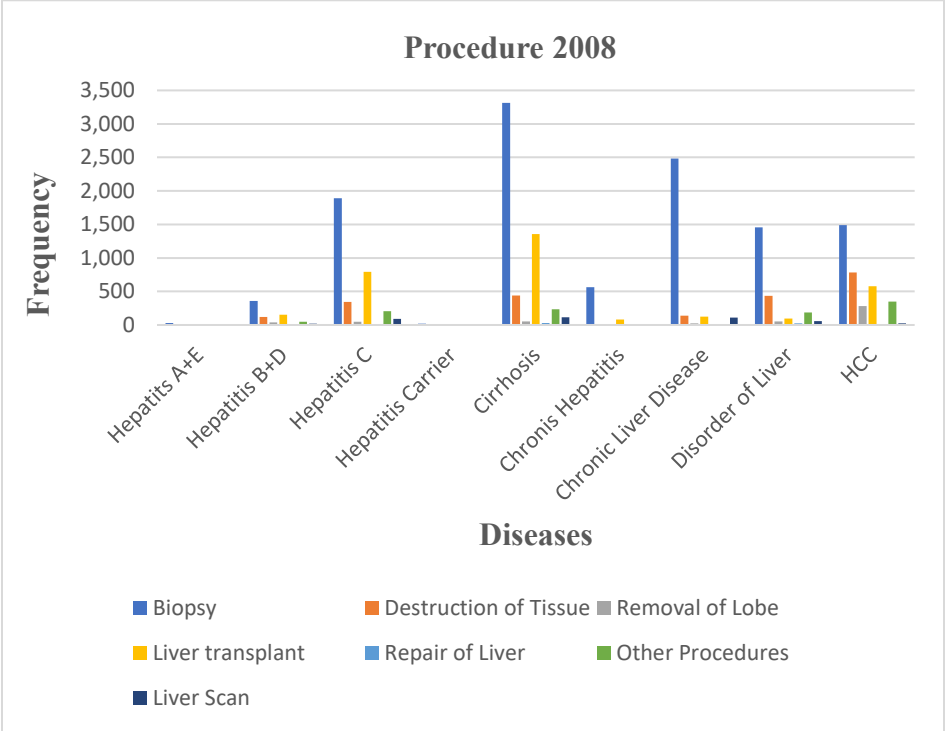

Figure 4.65 Procedure Performed 2008

Table 4.78 and Figure 4.65 show that Cirrhosis patients has the highest number of

Biopsy procedure done, Chronic Liver Disease shows the 2nd highest and Hepatitis C shows the 3rd highest Biopsy procedures done on these patients. Cirrhosis shows the highest number of Liver Transplant, Hepatitis C shows the 2nd highest, and HCC shows the 3rd highest Liver Transplant for the year 2008.

- For the Year 2009

Table 4.79 Procedure Performed 2009

Procedure 2009	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronis Hepatitis	Chronic Liver Disease	Disorder of Liver	HCC
Biopsy	40	372	1920	22	3285	505	2489	1401	1478
Destruction of Tissue	3	94	308	3	355	11	107	407	642
Removal of Lobe	1	21	47	1	34	3	16	43	200
Liver transplant	3	85	605	0	969	35	116	84	403
Repair of Liver	0	3	13	0	19	2	9	24	10
Other Procedures	4	34	128	3	166	1	22	173	246
Liver Scan	4	46	203	1	123	3	96	47	19

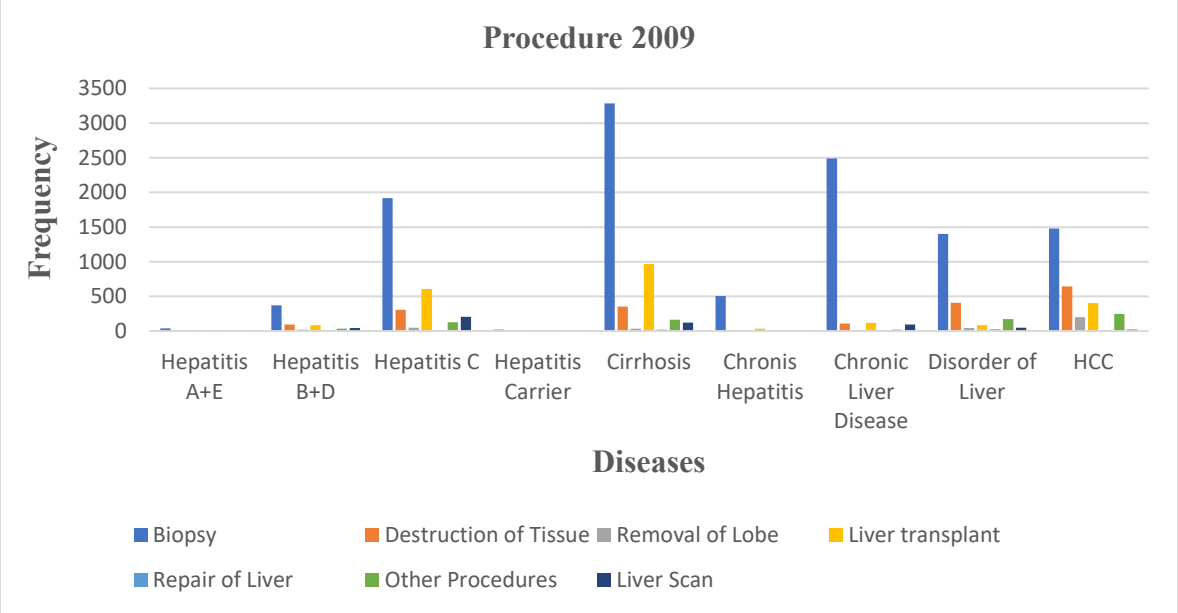

Figure 4.66 Procedure Performed 2009

Table 4.79 and Figure 4.66 show that Cirrhosis patients has the highest number of Biopsy procedure done, Chronic Liver Disease shows the 2nd highest and Hepatitis C shows the 3rd highest Biopsy procedures done on these patients. Cirrhosis shows the highest number of Liver Transplant, Hepatitis C shows the 2nd highest, and HCC shows the 3rd highest Liver Transplant for the year 2009.

- For the Year 2010

Table 4.80 Procedure Performed 2010

Procedure 2010	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronis Hepatitis	Chronic Liver Disease	Disorder of Liver	HCC
Biopsy	40	321	1878	25	3214	507	3053	1458	1364
Destruction of Tissue	4	71	271	5	345	12	126	434	641
Removal of Lobe	0	22	32	1	45	2	29	59	212
Liver transplant	4	64	544	0	963	57	80	74	383
Repair of Liver	0	3	14	0	21	0	14	12	14
Other Procedures	1	30	141	3	153	2	31	193	241
Liver Scan	6	28	111	6	149	8	146	65	19

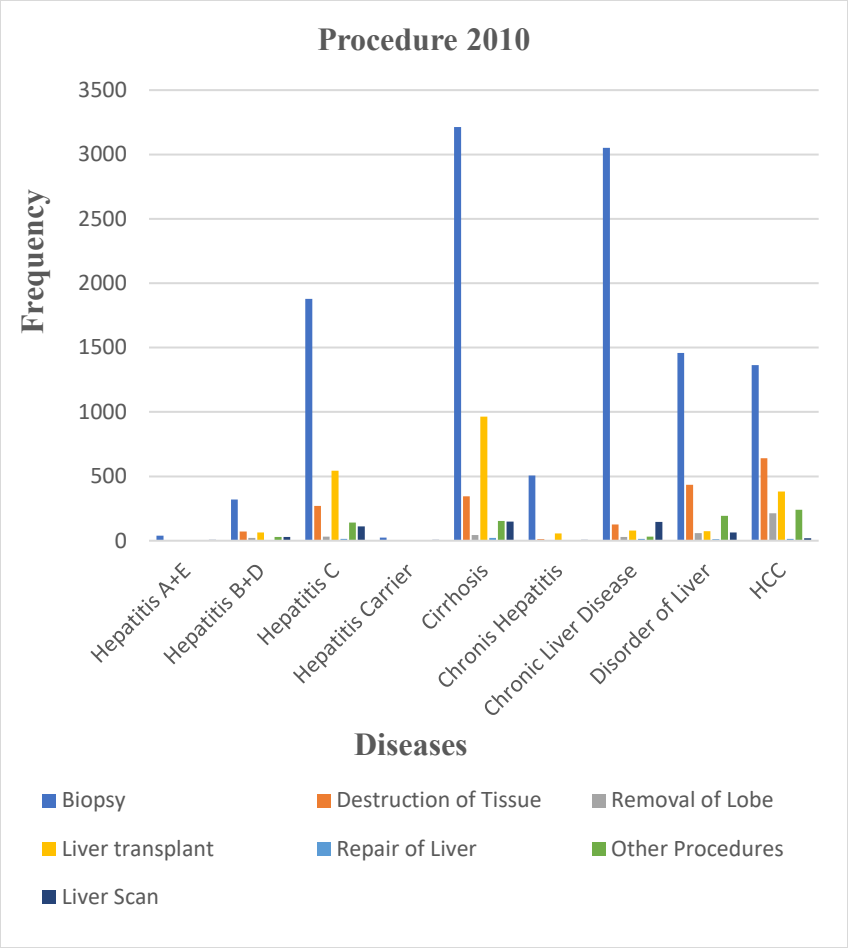

Figure 4.67 Procedure Performed 2010

Table 4.80 and Figure 4.67 show that Cirrhosis patients has the highest number of Biopsy procedure done, Chronic Liver Disease shows the 2nd highest, Hepatitis C shows the 3rd highest, Disorder of Liver shows the 4th highest and HCC shows the 5th highest Biopsy procedures done on these patients. Cirrhosis shows the highest number of Liver Transplant, Hepatitis C shows the 2nd highest, and HCC shows the 3rd highest Liver Transplant for the year 2010.

- For the Year 2011

Table 4.81 Procedure Performed 2011

Procedure 2011	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronis Hepatitis	Chronic Liver Disease	Disorder of Liver	HCC
Biopsy	46	298	1878	12	3429	524	2762	1543	1525
Destruction of Tissue	0	68	271	0	344	12	140	452	650
Removal of Lobe	1	14	32	0	28	0	26	43	213
Liver transplant	3	53	544	0	931	60	104	53	389
Repair of Liver	0	5	14	0	26	1	12	17	22
Other Procedures	4	35	141	0	172	9	51	219	311
Liver Scan	2	11	111	3	120	9	129	59	12

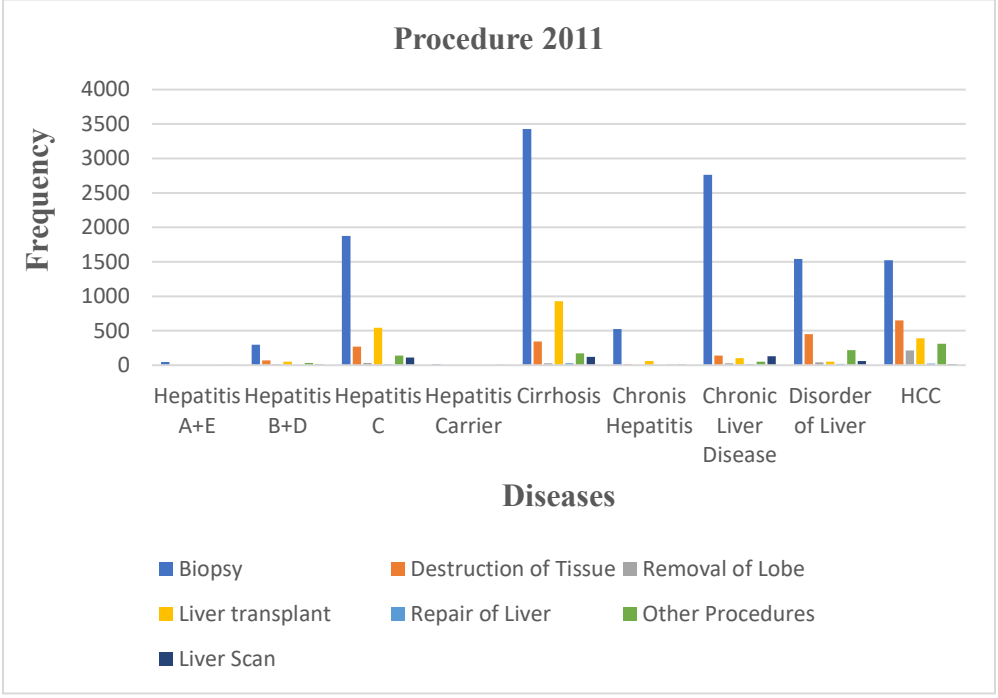

Figure 4.68 Procedure Performed 2011

Table 4.81 and Figure 4.68 show that Cirrhosis patients has the highest number of

Biopsy procedure done; Chronic Liver Disease shows the 2nd highest; and Hepatitis C shows the 3rd highest Biopsy procedures done on these patients. Cirrhosis shows the highest number of Liver Transplant, Hepatitis C shows the 2nd highest, and HCC shows the 3rd highest Liver Transplant for the year 2011. Patients with Hepatitis A+E and Hepatitis Carrier show insignificance number of procedures done on them.

- For the Year 2012

Table 4.82 Procedure Performed 2012

Procedure 2012	Hepatitis A+E	Hepatitis B+D	Hepatitis C	Hepatitis Carrier	Cirrhosis	Chronis Hepatitis	Chronic Liver Disease	Disorder of Liver	HCC
Biopsy	29	237	1,662	8	2,890	461	2,662	1,442	1,253
Destruction of Tissue	1	76	291	2	356	12	127	439	680
Removal of Lobe	0	21	41	0	53	1	20	37	214
Liver transplant	2	67	556	0	922	54	129	97	422
Repair of Liver	0	6	16	0	21	2	9	11	15
Other Procedures	3	39	153	1	154	3	55	199	253
Liver Scan	1	12	104	10	117	4	123	56	12

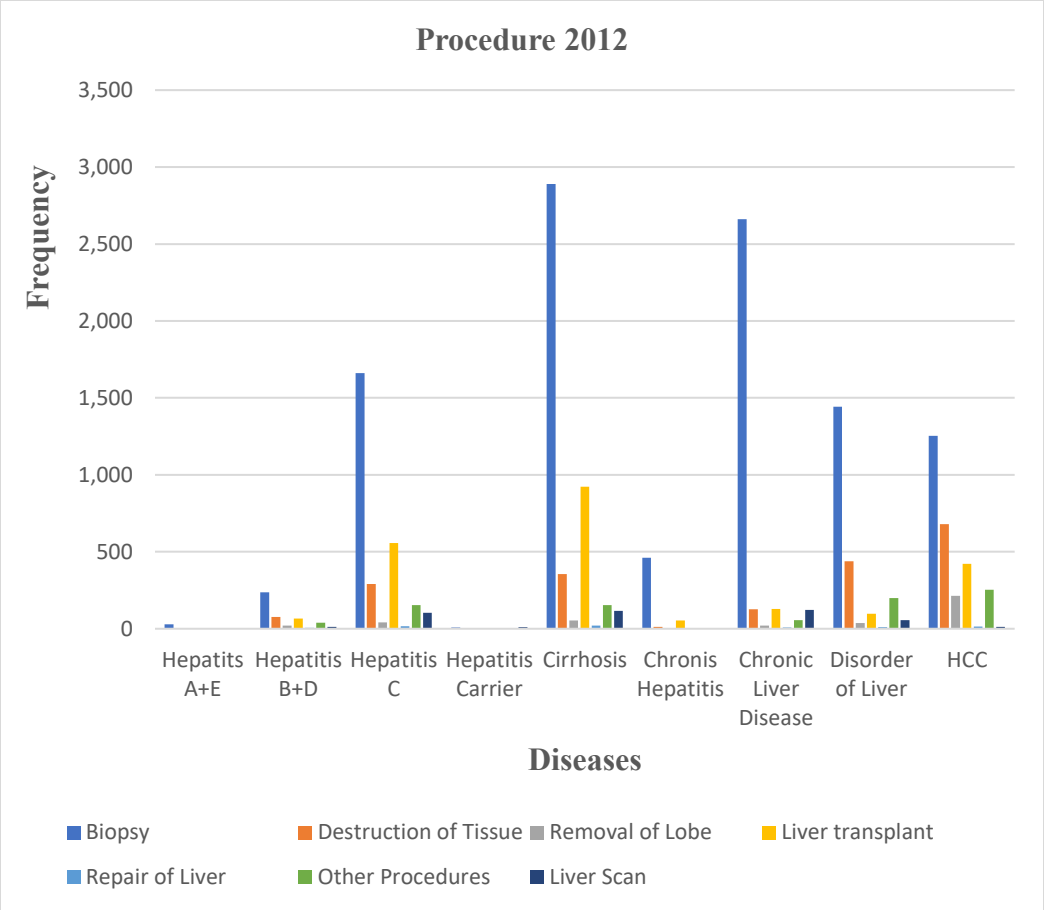

Figure 4.69 Procedure Performed 2012

Table 4.82 and Figure 4.69 show that Cirrhosis patients has the highest number of Biopsy procedure done, Chronic Liver Disease shows the 2nd highest, Hepatitis C shows the 3rd highest, Disorder of Liver shows the 4th highest and HCC shows the 5th highest Biopsy procedures done on these patients. Cirrhosis shows the highest number of Liver Transplant; Hepatitis C shows the 2nd Highest; and HCC shows the 3rd highest Liver Transplant for the year 2012. Hepatitis A+E and Hepatitis Carrier shows insignificance number of procedures done on these patients for the year 2012.

- **Yearly Procedures performed from 2007 to 2012**

Table 4.83 Yearly Procedure Performed

Yearly	Biopsy	Destruction of Tissue	Removal of Lobe	Liver Transplant	Repair of Liver	Other Procedures	Liver Scan
2007	10,155	1,459	339	1,872	90	903	649
2008	11,607	2,274	505	3,189	89	1,045	440
2009	11,512	1,930	366	2,300	80	777	542
2010	11,860	1,909	402	2,169	78	795	538
2011	12,017	1,937	357	2,137	97	942	456
2012	10,644	1,984	387	2,249	80	860	439

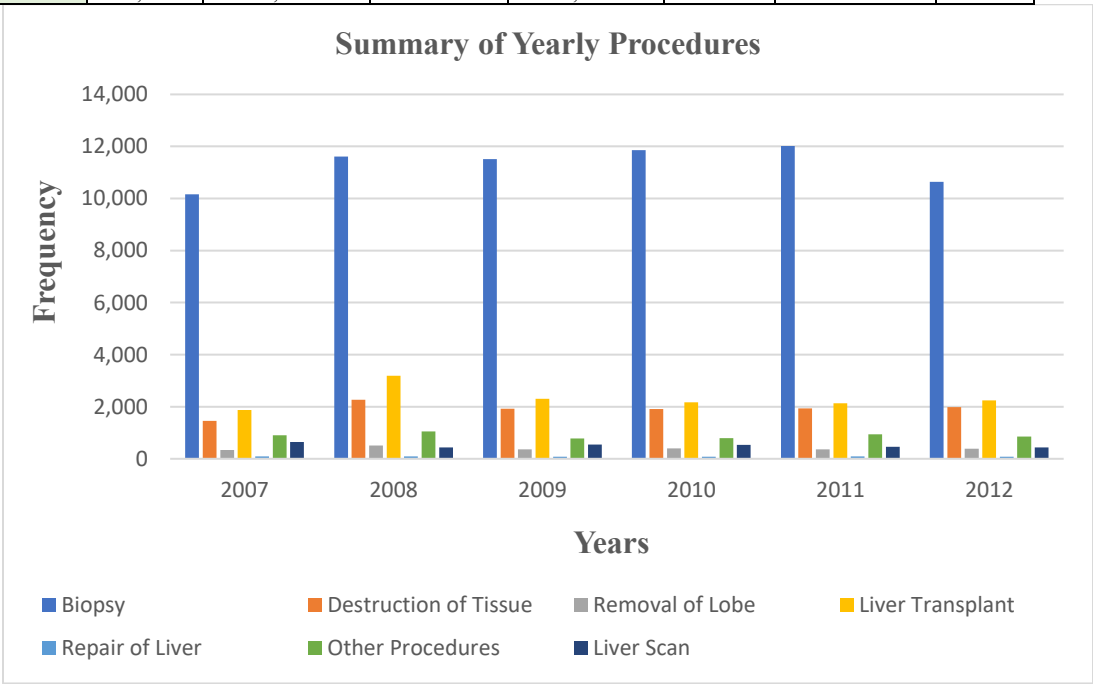

Figure 4.70 Yearly Procedure Performed

Table 4.83 and Figure 4.70 show that the Biopsy procedure is done more often than the other procedures. The curve shows that 18.33% increase occurred with Biopsy Procedure from the year 2007 to 2011 and a 11.42% decrease occurred with Biopsy Procedures from the year 2011 to 2012. Liver Transplant is highest for the year 2008; all other years it was consistent.

4.9.1 Mean Cost of Procedures for Hepatitis C Virus by Age Group

- For the Year 2007

Table 4.84 HCV Procedure Cost by Age Group 2007

HCV Procedure Cost by Age Group 2007	1-20 Years	21-51 Years	52-65 Years	66-80 Years	81+ Years
Biopsy	$93,750	$71,094	$89,084	$65,190	$90,554
Destruction of Tissue	$0	$62,378	$48,302	$49,780	$33,916
Removal of Lobe	$0	$49,143	$63,167	$44,450	$70,632
Liver Transplant	$387,399	$334,921	$316,436	$318,459	$0
Repair of Liver	$0	$75,062	$334,937	$63,644	$0
Other Procedures	$372,136	$81,647	$80,893	$48,623	$39,612
Liver Scan	$27,260	$56,107	$67,734	$64,826	$62,182

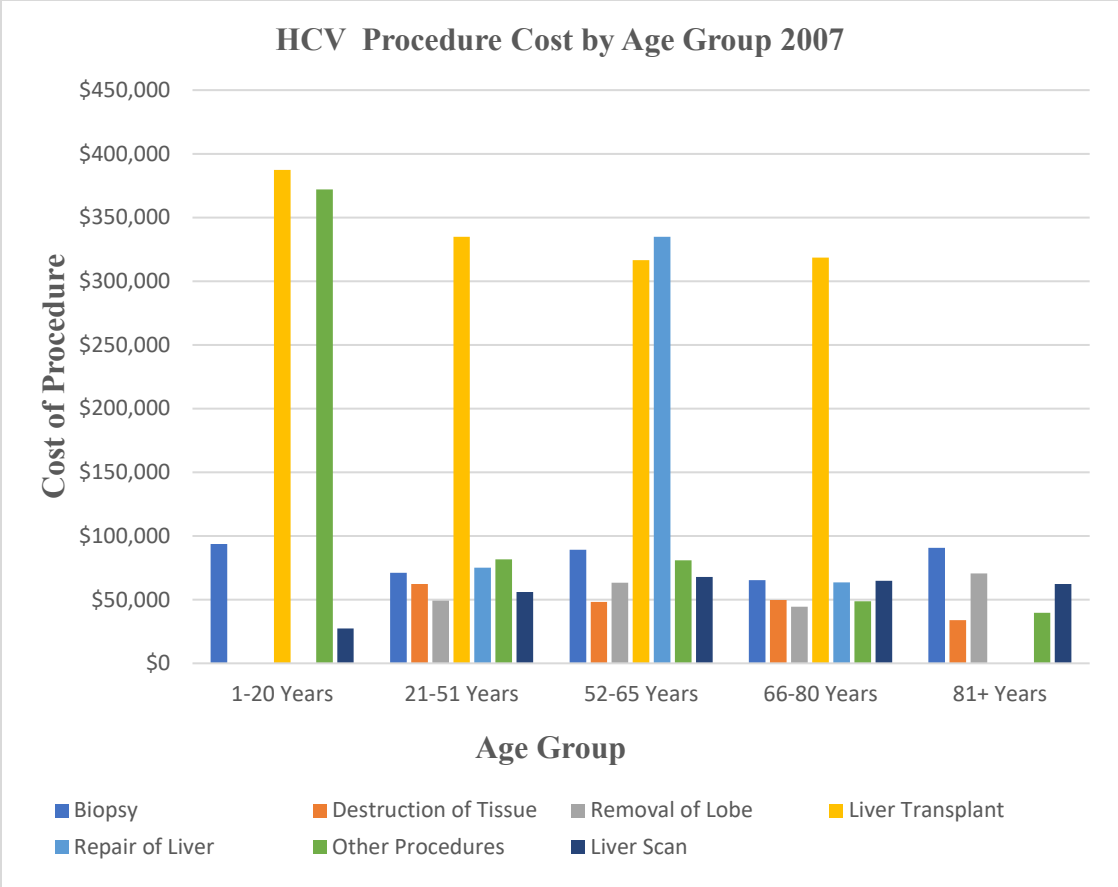

Figure 4.71 HCV Procedure Cost by Age Group 2007

Table 4.84 and Figure 4.71 show that for the age group '1-20 years' procedure category Other Procedure, Liver Transplant and Biopsy' mean cost is predominately highest. Age group '52-65 years' has the highest mean cost for the 'Repair of Liver.' Age group '81+ year' predominately has no evidence of 'Repair of liver' and 'Liver Transplant' for the year 2007 and Hepatitis C patients only.

- For the Year 2008

*Table 4.85 HCV Procedure Cost by Age Group and Figure 4.72 HCV Procedure Cost by Age Group were omitted as lot of data was missing.

- For the Year 2009

Table 4.86 HCV Procedure Cost by Age Group 2009

HCV Procedure Cost by Age Group 2009	1-20 Years	21-51 Years	52-65 Years	66-80 Years	81+ Years
Biopsy	$191,985	$105,228	$105,922	$110,583	$47,803
Destruction of Tissue	$0	$79,271	$87,234	$71,605	$36,611
Removal of Lobe	$0	$52,923	$137,388	$139,918	$279,389
Liver Transplant	$0	$431,329	$346,873	$421,998	$0
Repair of Liver	$0	$139,987	$232,623	$48,959	$0
Other Procedures	$0	$108,732	$67,651	$75,662	$67,487
Liver Scan	$111,452	$21,180	$30,646	$42,460	$34,002

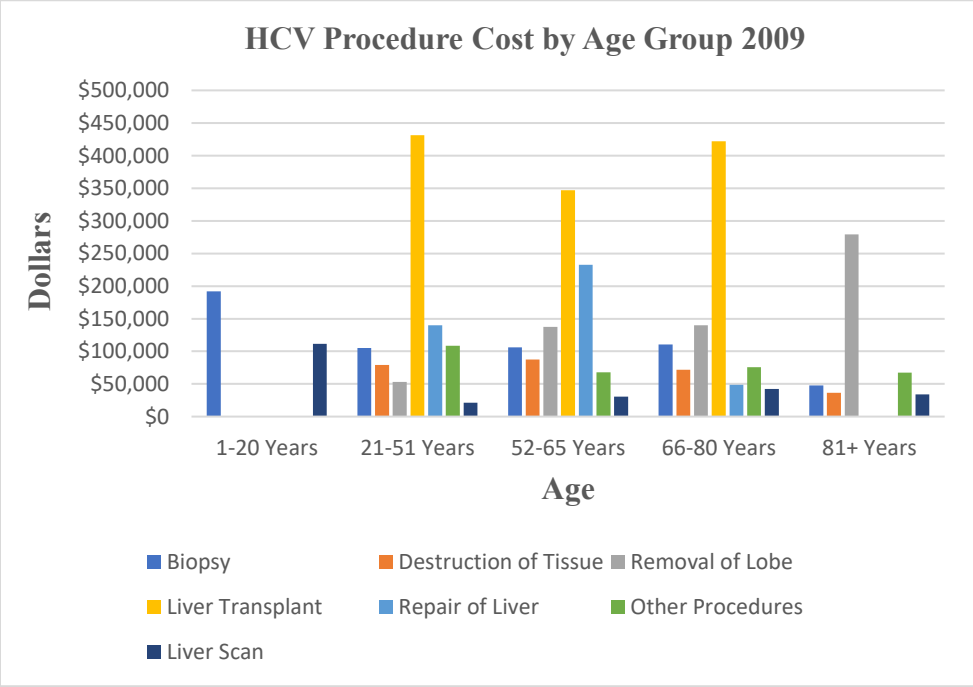

Figure 4.73 HCV Procedure Cost by Age Group 2009

Table 4.86 and Figure 4.73 show that for the age group '1-20 years' procedure category 'Biopsy and Liver Scan' mean cost is predominately highest for the year 2009. Age group '21-51 years' 'Liver Transplant' mean cost is highest for the year 2009. Age group '52-65 years' has the highest mean cost for the 'Repair of Liver.' Age Group '66-80 years' has the 2nd highest mean cost for the 'Liver transplant' Age group '81+ year' predominately shows highest mean cost for the 'Removal of Lobe' for the year 2009 and Hepatitis C patients only.

- For the Year 2010

Table 4.87 HCV Procedure Cost by Age Group 2010

HCV Procedure Cost by Age Group 2010	1-20 Years	21-51 Years	52-65 Years	66-80 Years	81+ Years
Biopsy	$55,752	$93,443	$116,244	$124,401	$61,296
Destruction of Tissue	$0	$63,235	$101,676	$81,793	$101,980
Removal of Lobe	$0	$123,922	$146,803	$71,049	$49,566
Liver Transplant	$230,161	$384,149	$371,446	$445,711	$153,153
Repair of Liver	$0	$90,645	$355,006	$0	$0
Other Procedures	$0	$79,208	$77,716	$73,384	$54,586
Liver Scan	$0	$27,619	$35,061	$103,752	$59,035

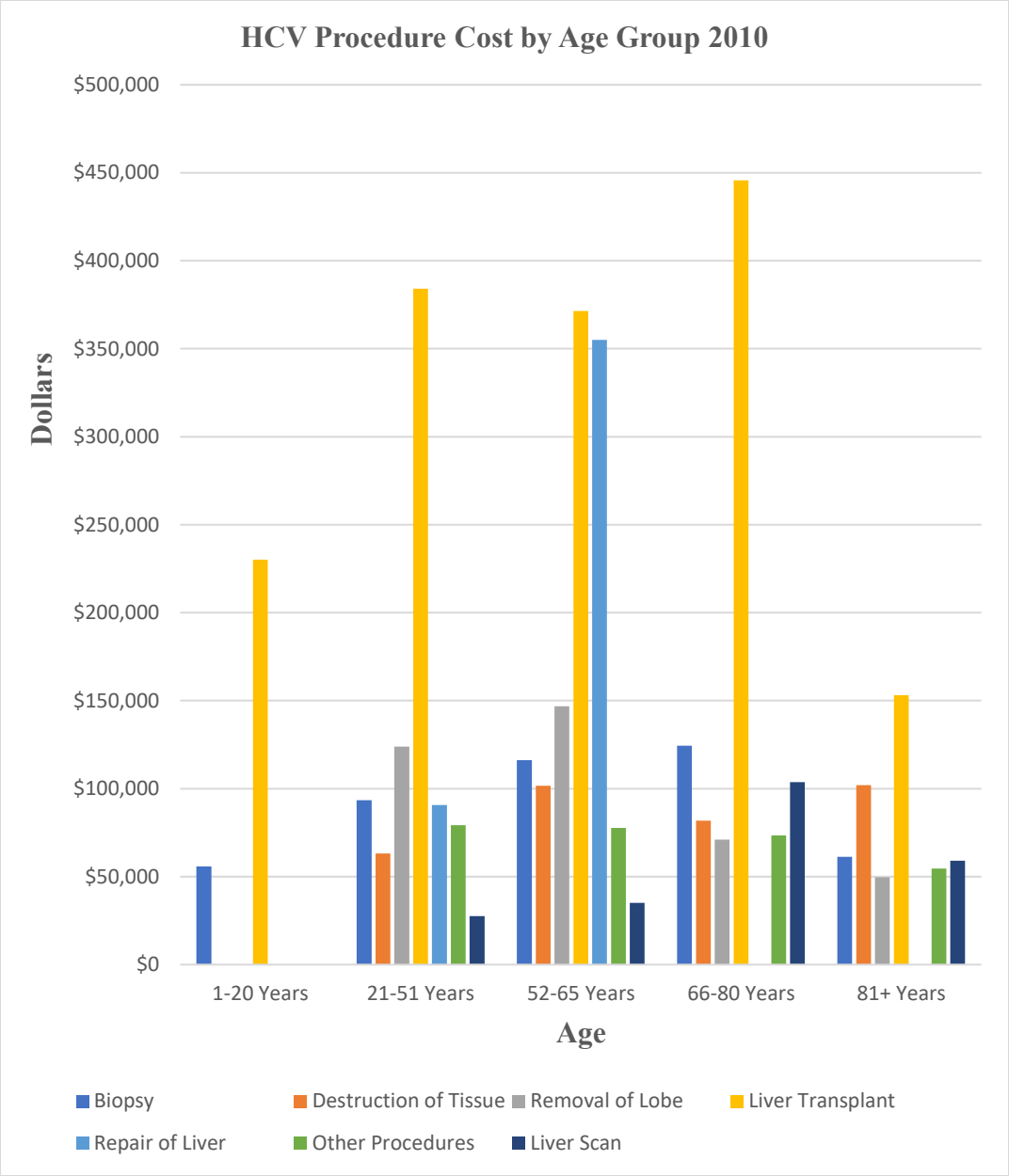

Figure 4.74 HCV Procedure Cost by Age Group 2010

Table 4.87 and Figure 4.74 show that for the age group '52-65 years' has the highest mean cost for the 'Repair of Liver.'

Age Group '66-80 years' has the highest mean cost for the 'Liver transplant'

Age group '81+ year' predominately shows no evidence of 'Repair of Liver' for the year 2010 and Hepatitis C patients only.

- For the Year 2011

Table 4.88 HCV Procedure Cost by Age Group 2011

HCV Procedure Cost by Age Group 2011	1-20 Years	21-51 Years	52-65 Years	66-80 Years	81+ Years
Biopsy	$41,352	$95,331	$124,312	$116,935	$63,483
Destruction of Tissue	$35,342	$160,901	$78,874	$108,961	$79,026
Removal of Lobe	$0	$166,328	$98,742	$314,618	$0
Liver Transplant	$0	$535,033	$383,592	$456,222	$295,217
Repair of Liver	$0	$240,828	$264,322	$345,467	$0
Other Procedures	$0	$57,698	$55,690	$50,912	$170,829
Liver Scan	$0	$33,303	$59,934	$220,133	$48,108

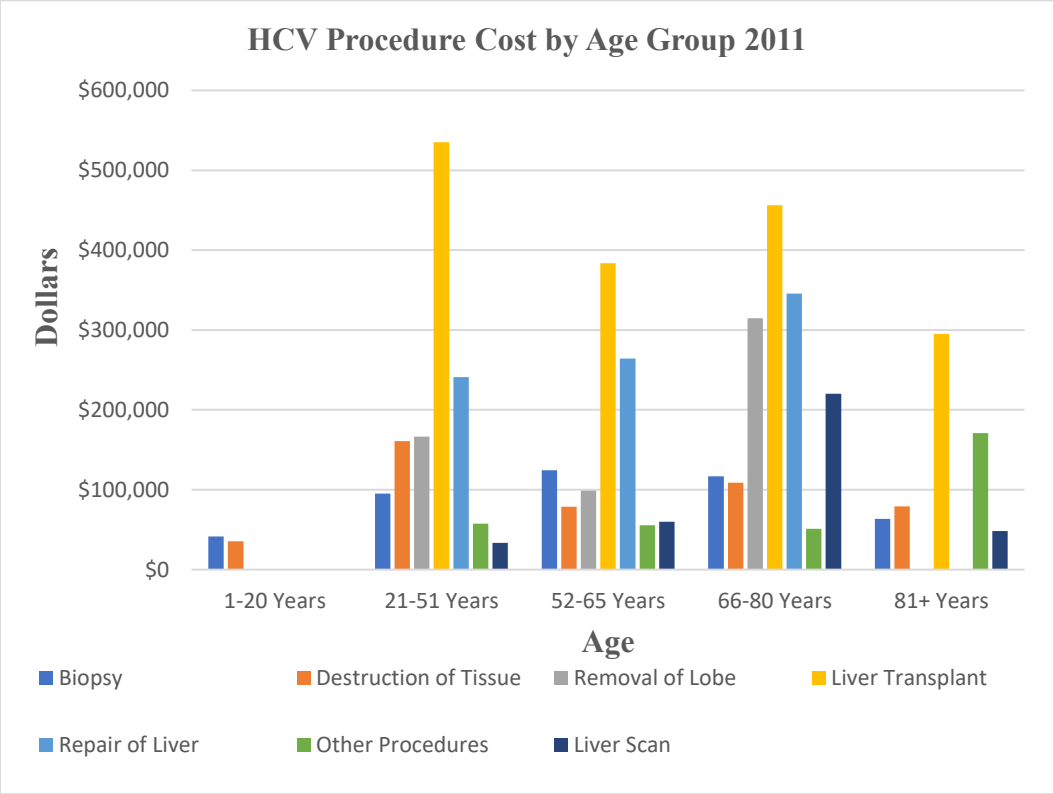

Figure 4.75 HCV Procedure Cost by Age Group 2011

Table 4.88 and Figure 4.75 show that for the age group '21-51 years' has the highest mean cost for the 'Liver Transplant.' Age Group '66-80 years' has the highest mean cost for the 'Repair of Liver' Age group '81+ year' predominately shows the highest mean cost for the 'Other Procedures' for the year 2011 and Hepatitis C patients only.

- For the Year 2012

Table 4.89 HCV Procedure Cost by Age Group 2012

HCV Procedure Cost by Age Group 2012	1-20 Years	21-51 Years	52-65 Years	66-80 Years	81+ Years
Biopsy	$95,940	$108,734	$124,757	$113,671	$121,659
Destruction of Tissue	$0	$105,525	$71,780	$100,526	$39,038
Removal of Lobe	$0	$87,333	$109,420	$104,882	$61,518
Liver Transplant	$0	$476,637	$421,093	$502,523	$209,494
Repair of Liver	$0	$85,155	$412,749	$0	$0
Other Procedures	$0	$83,224	$93,754	$135,797	$119,265
Liver Scan	$41,624	$48,654	$31,935	$49,329	$42,742

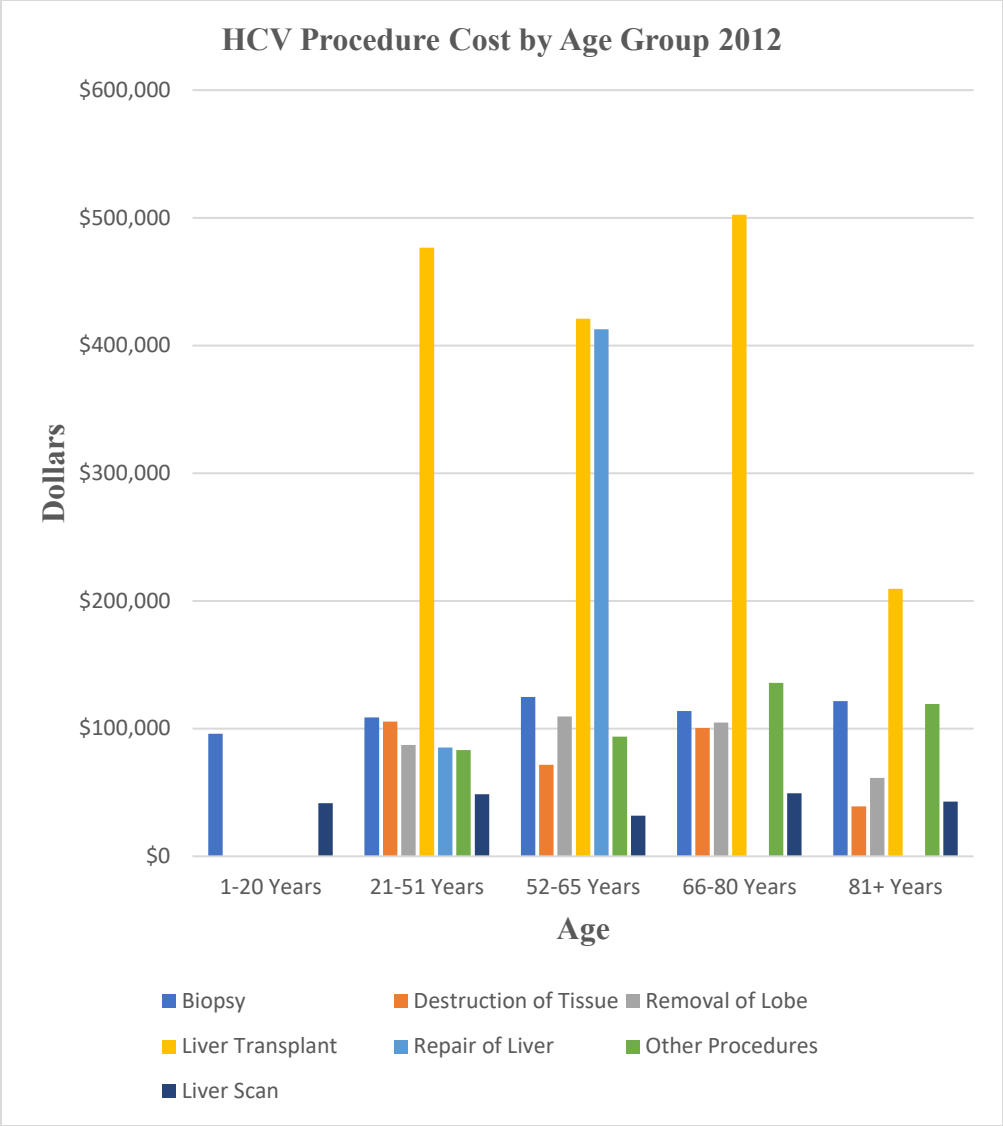

Figure 4.76 HCV Procedure Cost by Age Group 2012

Table 4.89 and Figure 4.76 show that for the age group '66-80 years' has the highest mean cost for the 'Liver transplant.' Age group '52-65 years' has the highest mean cost for the 'Repair of Liver.' Age Group '66-80 years' has the highest mean cost for the 'Other Procedures' Age group '81+ year' predominately shows no evidence of 'Repair of Liver' for the year 2012 and Hepatitis C patients only.

4.9.2 Yearly Total Cost of Procedures

Table 4.90 Yearly Average Cost of Procedure based on 9 diseases

Yearly Mean Cost of Procedure Based on 9 Diseases	2007	2008	2009	2010	2011	2012
Biopsy	$67,350	$77,376	$80,245	$83,964	$90,908	$93,576
Destruction of Tissue	$58,509	$66,392	$79,063	$79,168	$98,412	$95,043
Removal of Lobe	$93,746	$113,195	$131,758	$119,056	$143,642	$138,882
Liver Transplant	$314,685	$331,048	$356,339	$367,717	$443,887	$431,468
Repair of Liver	$148,362	$158,402	$148,361	$166,412	$238,182	$227,005
Other Procedures	$70,356	$80,040	$77,886	$80,737	$91,848	$92,909
Liver Scan	$61,309	$72,547	$39,748	$54,545	$60,660	$52,978

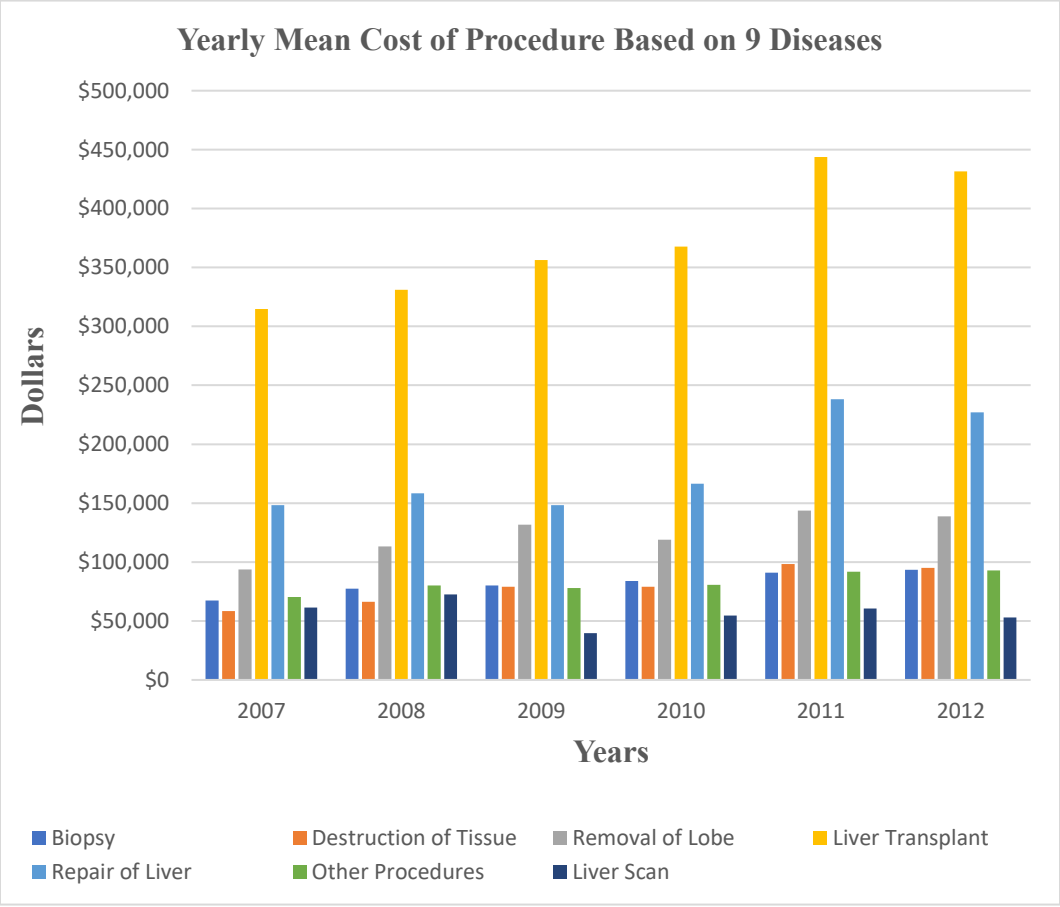

Figure 4.77 Yearly Mean Cost of Procedure Based on 9 diseases

*Mean Cost of Procedure is Based on 9 diseases and those diseases are Hepatitis A+E, Hepatitis B+D, Hepatitis C, Hepatitis Carrier, Cirrhosis, Chronic Hepatitis., Chronic Liver Disease, Disorder of Liver and HCC.

Significance Increase in Liver transplant from 2007 to 2012, the incremental was 37.11%. 2nd highest procedure done was of the Repair of Liver, which showed increment of 53%. 3rd highest procedure done was the Removal of Lobe, which showed increment of 48.14% between the years 2007 to 2012.

4.10 Interpretation of Race Analysis by Reference Population

Table 4.91 Hepatitis C Population of Different Races

Hepatitis C from the Total Population of Different Races	2007	2008	2009	2010	2011	2012
White	45,817	54,787	57,143	61,744	70,226	69,925
Black	18,857	19,201	22,300	26,385	29,697	26,177
Hispanic	11,019	11,184	12,727	13,956	15,331	14,871
Asian or Pacific Islander	1,057	1,603	1,713	1,440	1,425	1,357

Table 4.92 Hepatitis C Population of different Races by Percentage

Hepatitis C % of the Total population of Different Races	2007	2008	2009	2010	2011	2012
White	57.41%	60.87%	57.94%	57.64%	57.60%	59.48%
Black	23.63%	21.33%	22.61%	24.63%	24.36%	22.27%
Hispanic	13.81%	12.43%	12.90%	13.03%	12.58%	12.65%
Asian or Pacific Islander	1.32%	1.78%	1.74%	1.34%	1.17%	1.15%

2010	White	Blacks	Asians	Hispanics
US Population Distribution	62%	12%	5%	17%

Whites though making up 62 percent of the population only have on the average around 58 to 59 percent of Hep C cases. But Blacks while only constituting 12 percent of the population have on the average around 24 percent which immediately reveals that Blacks have greater predisposition to Hep C than Whites. On the contrary Asians (5 percent of population but having only 1.4% Hep C cases) and so Asians look like they are less predisposed to getting Hep C. Hep C Hispanics are also less in comparison to their population numbers.

4.11 Conclusion and Discussion

For this chapter, data was taken from the National Inpatient Sample (NIS), which is part of the Healthcare Cost and Utilization Project (HCUP). The Healthcare Cost and Utilization Project (HCUP) data was given by Rutgers University department of Health Professionals. The data was in the format of SPSS. SPSS is an IBM Statistics software version 26. For analysis purpose IBM-SPSS statistical analysis software and Microsoft Excel was used.

This research focuses on the analysis of the number of records of patients with Hepatitis C virus from the year 2007 to 2012. The data elements that were used to analyze Hepatitis C virus patient were as follows: length of stay, total charges of treatment, how many died in the hospital, their Income status, hospital region, age, race, gender, sex, disposition, hospital location (urban/rural), the payment methods, admission type, admission source and Procedures performed on these patients.

The disease selection that was used for analysis of Hepatitis C virus are Hepatitis A+E Virus, Hepatitis B+D Virus, Hepatitis C virus, Hepatitis Carrier, Cirrhosis, Chronic Hepatitis, Chronic Liver disease, disorder of Liver and Hepatocellular Carcinoma (HCC). The Procedures which were performed on the above diseases are as follows: Biopsy, Destruction of tissue, Removal of Lobe, Liver Transplant, Repair of Liver, Other Procedures and Liver Scan.

The following conclusions were drawn from the analysis:

Hepatitis C cases remained highest among Hepatitis A+E and Hepatitis B+D for the entire period of analysis as shown in Table 4.3 and Figure 4.1. Cirrhosis remained

highest among Chronic Hepatitis and HCC as shown in Table 4.15 and Figure 4.2. Chronic Liver disease remained highest followed by Disorders of Liver and Hepatitis Carrier as shown in Table 4.16 and Figure 4.3. It is observed that Hepatitis C cases remained highest among all the diseases as shown in Table 4.17 and Figure 4.4.

Hepatitis C Virus remained highest among the age groups of 21 to 51 years old, male population, and low-income population for the year 2007. Hepatitis C remained highest among the age group 52-65 for the years 2008 to 2012. The White population had highest number of Hepatitis C patients, followed by the Black population and then the Hispanic population as shown in Table 4.29 and Figure 4.16

The Medicaid and Medicare coverage were highest for hepatitis C patients among Private insurance, Self-Pay, No Charge and Other as shown in section Insurance Type.

Hepatitis C was highest in the Northeast region per 100,000 normalized population as compared to any other region as shown in Table 2.42 and figure 4.29. Urban location noticed higher number of patients reported with Hepatitis C infection as shown in Hospital Location by Region and Hospital Type section.

Hospital Emergency admission was highest for Hepatitis C patients. Admission Source for the Hepatitis C patients showed highest from Emergency Department throughout the entire period of analysis.

Destination after discharge showed that most of the patients stayed to home self-care after they discharged from the hospital, followed by short term hospital transfer and home health care.

Average Length of stay for Hepatitis C patient for the entire period of analysis was around 5.73 days to 6.01 days each year varied.

Trauma center charged most to Hepatitis C patient throughout the entire period of the analysis as compared to Elective, Urgent and emergency treatment centers. Other become lowest for all years of the study.

Cirrhosis shows the highest number of deaths in the hospital followed by Hepatitis C. Number of patients dies of Hepatitis C is highest for age group 52 to 65 years.

Biopsy Procedure is performed highest followed by Liver Transplant and Destruction of tissue throughout the entire period of the analysis. Curve shows that number of Biopsy procedures remained consistent throughout the period based on Table 4.83 and Figure 4.70. The highest number of biopsy procedures were performed for Cirrhosis patients followed by Chronic Liver disease and then Hepatitis C. The cost of Liver Transplant remained the most expensive procedure followed by Repair of Liver and Removal of Lobe throughout year 2007-2012, as shown on Table 4.90 and Figure 4.77.

CHAPTER V – CORVID IMPLEMENTATION FOR DIAGNOSIS

5.1 Overview of Proposed Technique

Expert system is used for the development of CDSS for the diagnosis of hepatitis and treatment options. The system is based on historical data and clinical diagnosis methods based by experts across various health institutions. Corvid systems software is use for CDSS development. CDSS is used to solve complex problems by reasoning about knowledge, and not by following the procedure of a developer as is the case in conventional programming [147,148]. The expert system has a unique structure, different from traditional computer programming. It is divided into two parts, one fixed, independent of the expert systems called the inference engine, and the other, the knowledge base. To run an expert system, the inference engine reasons using the knowledge base, like a human [1490]

In the 80s a third part appeared: a dialog interface to communicate with users. This ability to conduct a conversation with users was later called "conversational" [158]. Many companies began to market expert systems shells, some commercial developments of tools from universities, others written by venture capital backed startup companies. These claimed to allow rules to be written in plain language and thus, theoretically, allowed expert systems to be written without programming language expertise [151,152].

In this dissertation, Corvid Exsys rule-based system is used for building automated expert systems. The software utilized backward and forward chaining technique. It is the bridge between rules that people can read and understand, and rules that the computer can use effectively. User Interface (UI) provides ability to connect to external interfaces and databases, which can effectively be used for different analysis. There are many ways of

describing the heuristics for a decision-making process, but the one used by corvid is based on the rules the IF/THEN/ELSE rules. In the rules there is an IF part that can be assigned to be true or false based on the data for a specific case or situation. A confidence value between 1-100 can be assigned to the if part of the rule as well as the conclusions. When the IF part is true, the statements in the THEN part are also considered true. For example, a basic rule might be:

IF

You have yellowish eyes

THEN

You have Jaundice

A rule may have one or more IF conditions, and one or more THEN conditions. The IF condition is always Boolean tests that will evaluate "TRUE" or "FALSE". When there are multiple IF conditions, they are combined with AND & must all be true for the overall rule to be TRUE. There are also ways to build conditions with OR and other logical operators when needed. The THEN statements assign a value to a variable. This may be simply setting a value, adding content to a report, or adjusting a confidence (probability) value for a particular fact. When the IF conditions for a rule are TRUE, the assignments in the THEN statements are made, adding to the information the system has, or setting values that will be part of the results and system advice.

A case study of hepatitis using decision support system is done in this section. The hepatitis disease modeling starts with a simple flow diagram. Once modeling is finalized, a data flow diagram is plotted. The final outcome of data flow and modeling is prescription

of best treatment option for patient. The key parameters of the modelling includes: Patient age, Disease duration, Symptom of Disease (like fatigue, weight loss, joint and belly pain etc.), Past liver treatment, Blood transfusion or organ transplant related treatment, Drug and alcohol addiction, possibility of disease transmitted from Parents (HIV, HCV, Hemochromatosis or Hemodialysis) and EIA related symptoms. Probability and different combination of these parameters indicates present of specific disease category. This results in making decision on treatment options with suitable drug potency and duration.

Selected variables had been entered in Corvid (decision making flow) to get final outcome of the analysis and most effective treatment option for a patient. The efficient process flow of Fig. 5.1, 5.2 narrows down from a large # of combination of different variables to a defined path of diagnostics flow, which results in best diagnostics of HCV in shortest possible time and expense. This analysis could efficiently be used across any race and region in the world, which leads to consistent result. The treatment options depend on the location patient lives, cost of treatment, drug approved by regional governmental body and disease duration/intensity.

Detailed description of the flow diagram is mentioned in the section below. Based on various literature analysis (described in various section of this dissertation work and references), an initial scenario had been finalized. Various steps of diagnostics include (but not limited to).

5.2 Flow Chart for the Implementation

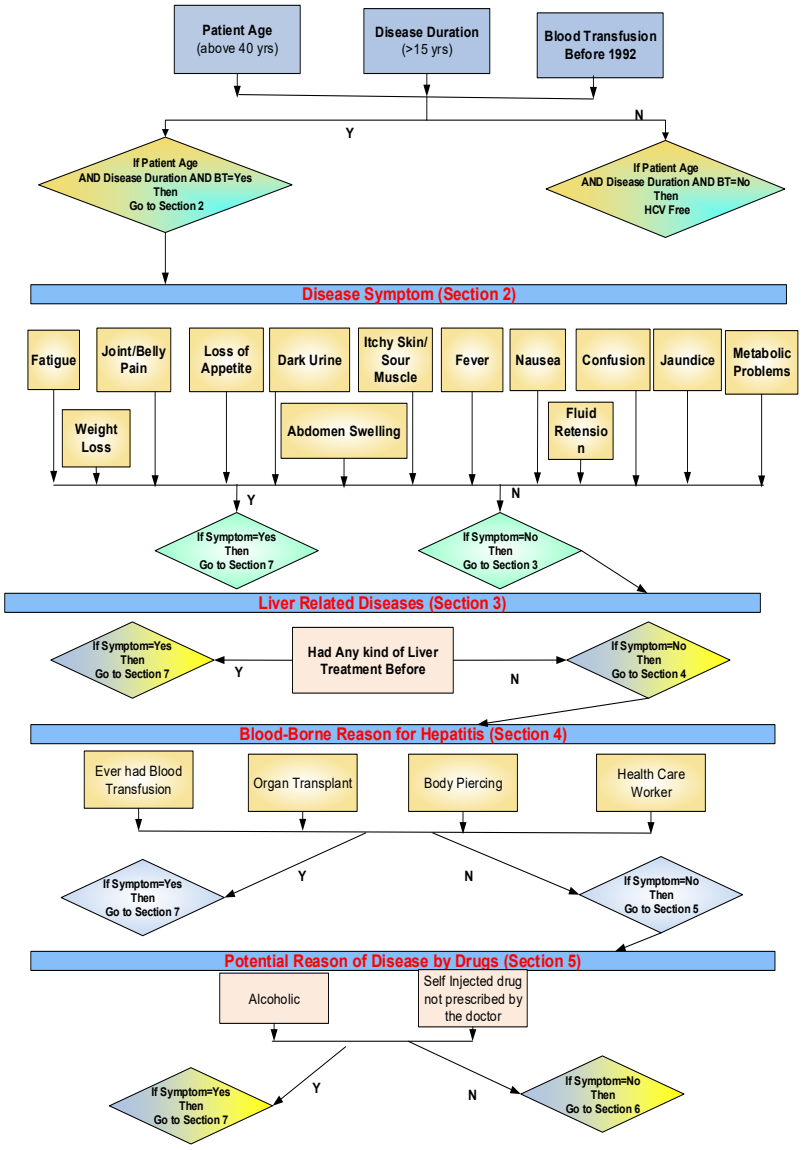

Figure 5.1 Hepatitis diagnostics steps for a Patient (Part 1)

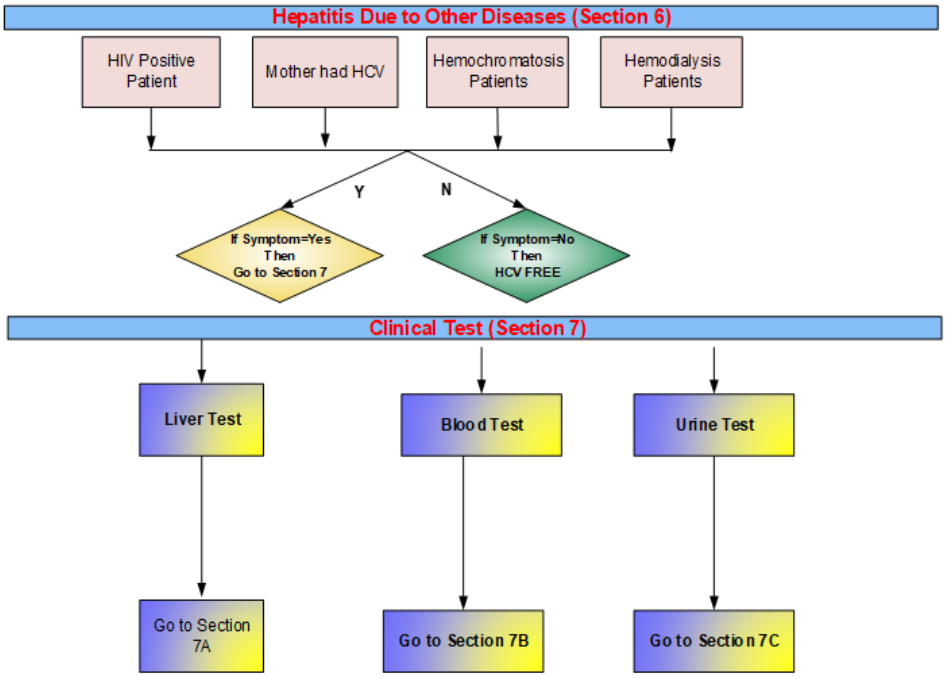

Figure 5.2 Hepatitis diagnostics steps for a Patient (Part2)

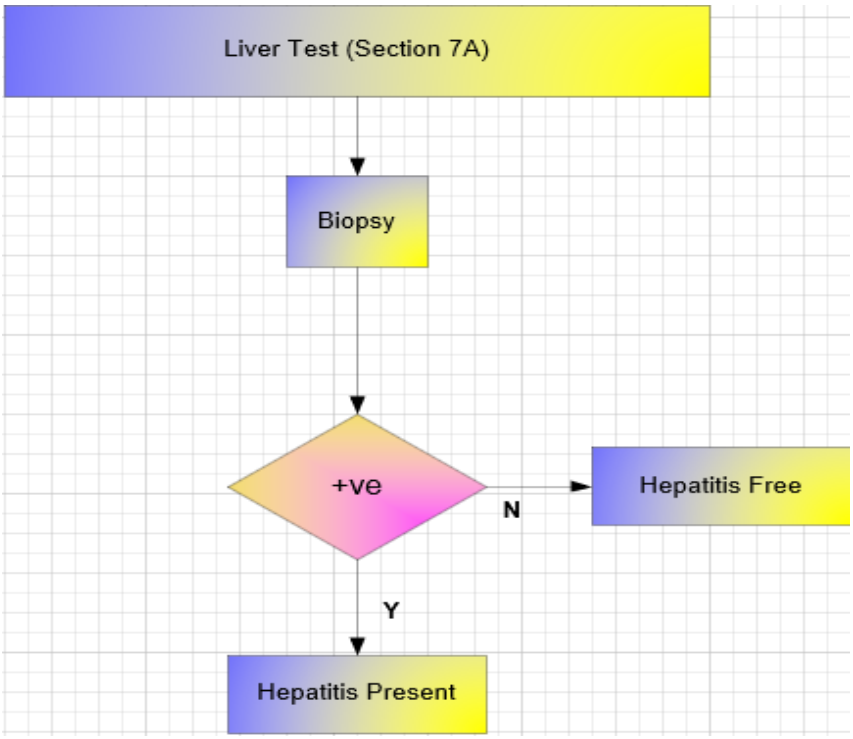

Figure 5.3 Liver Test (Section 7A)

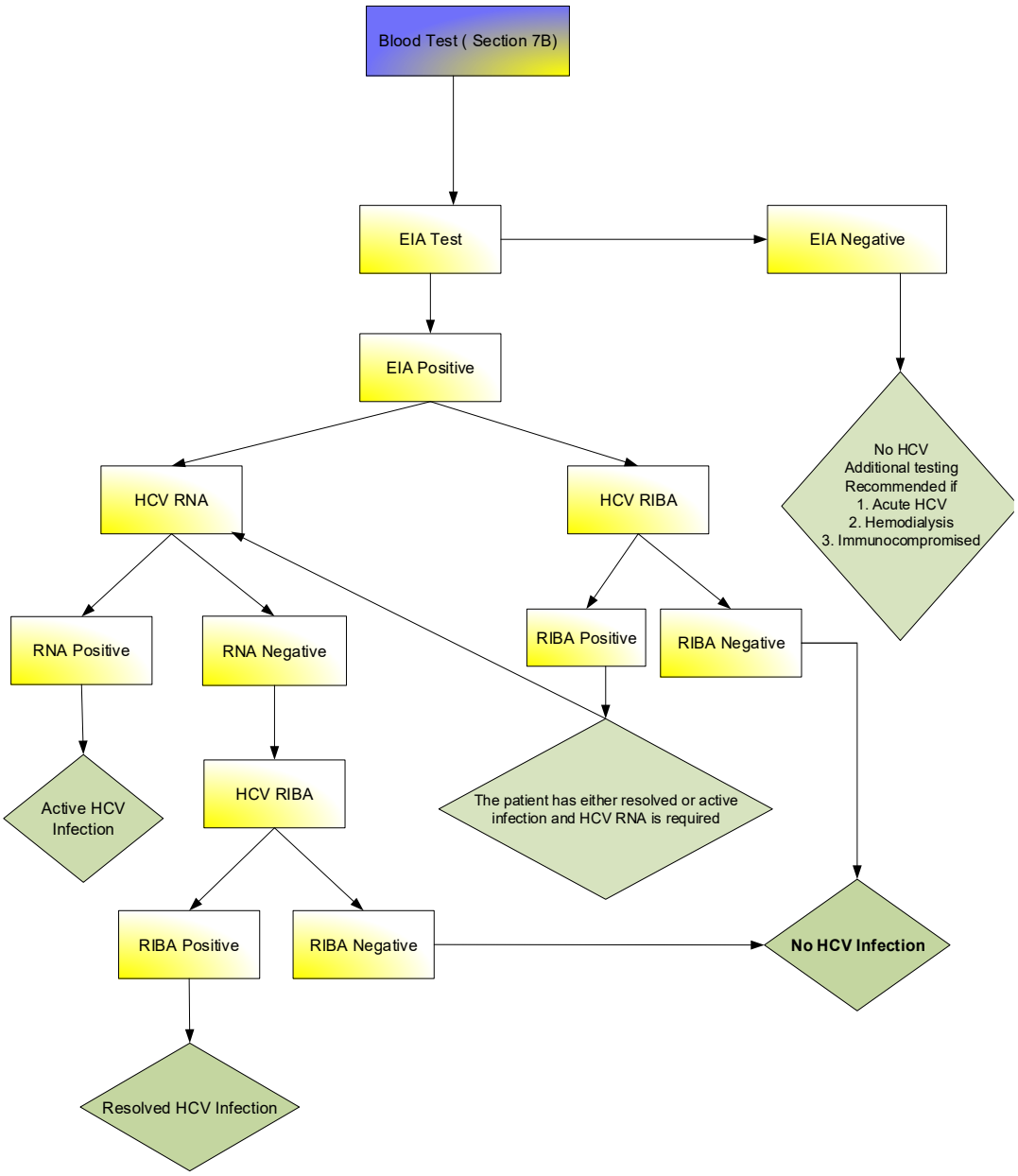

Figure 5.4 Blood Test (Section 7B)

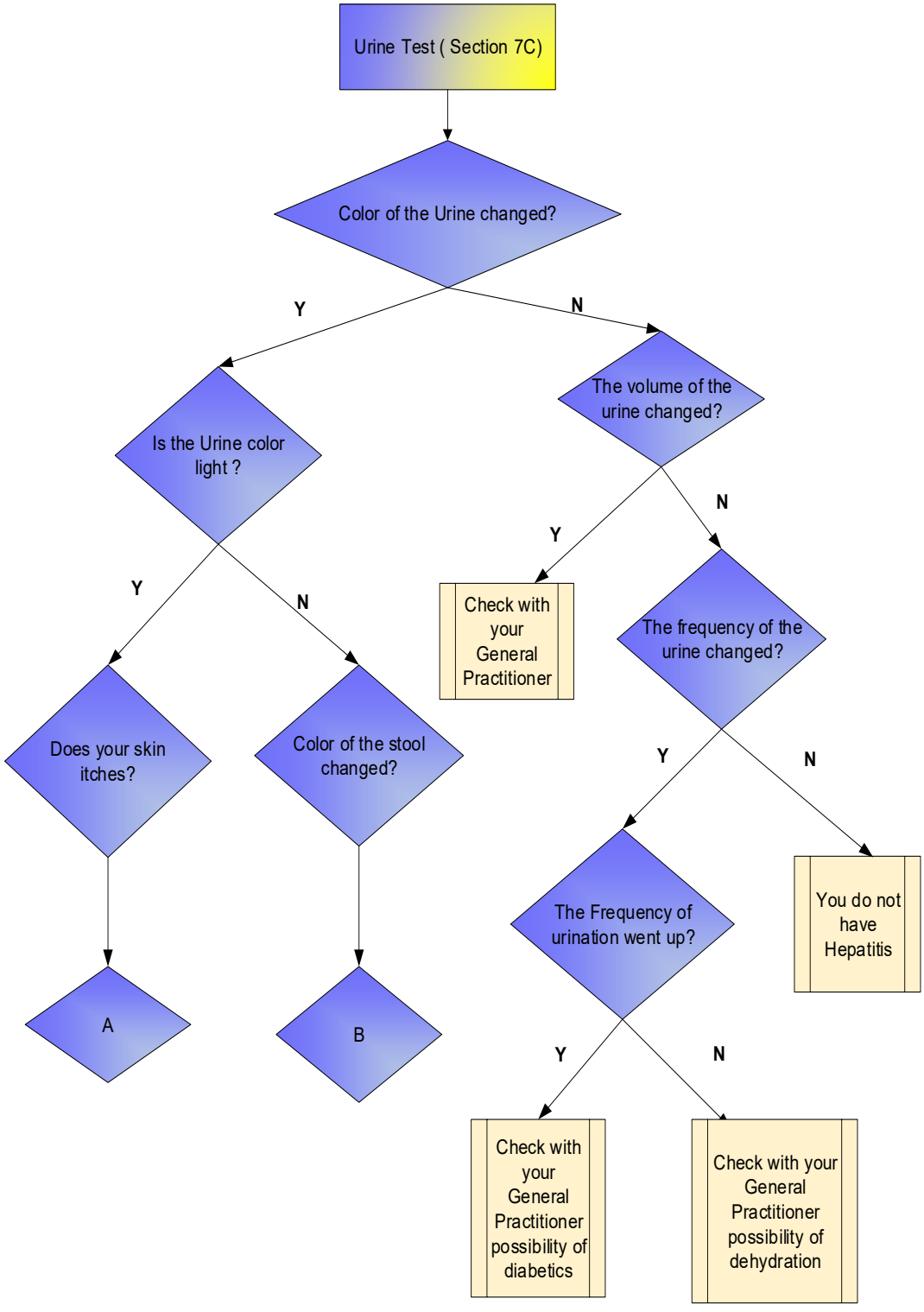

Figure 5.5 Hepatitis diagnostics for Urine Test

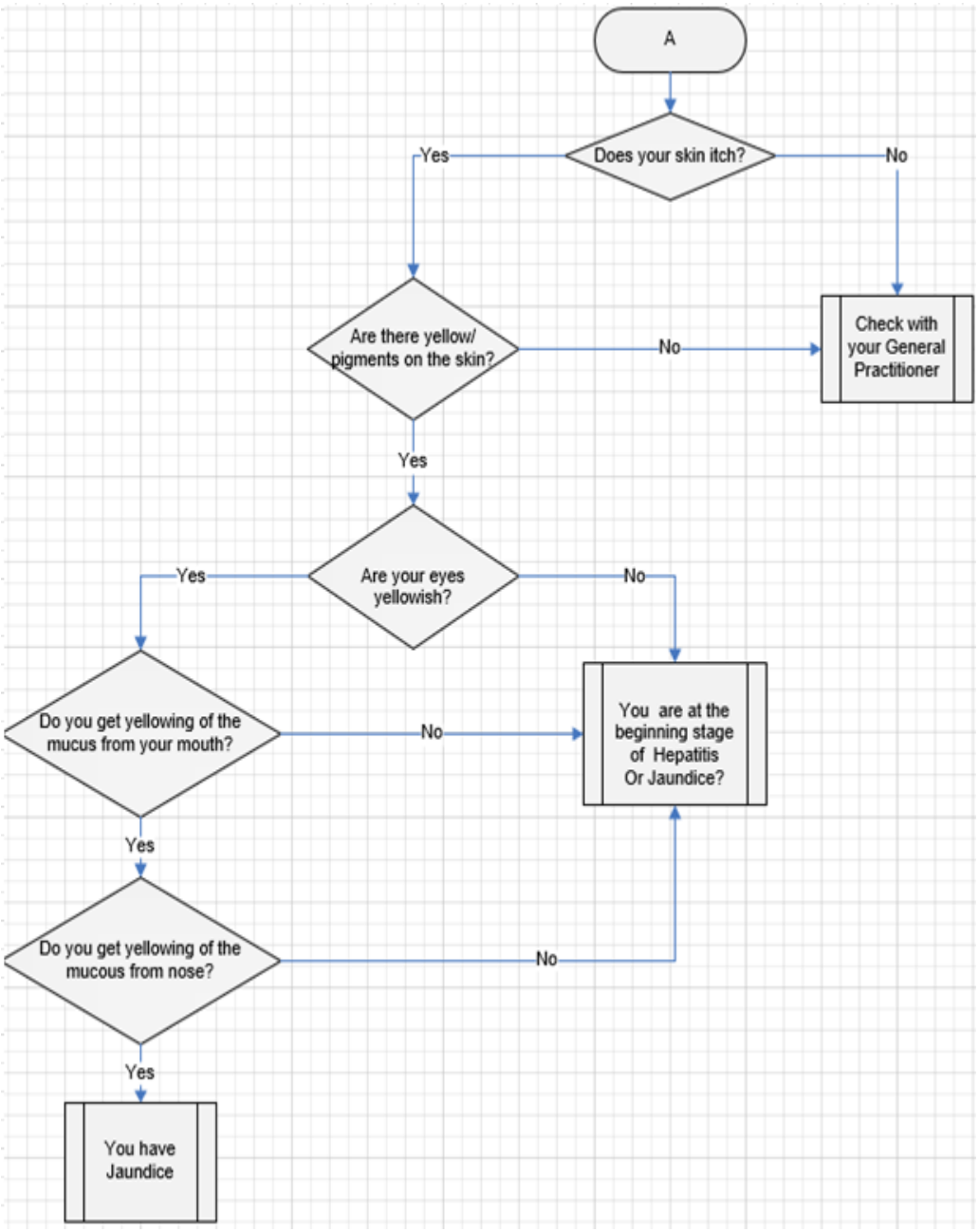

Figure 5.6 Hepatitis Diagnosis for Urine Test (A)

Figure 5.7 Hepatitis Diagnosis for Urine Test (B)

- **Patient Information**

Three major criteria for patient are taken into consideration for deciding if patient is suffering from hepatitis or not.

(a) Patient Age: From 1992 till today hepatitis C is a mandatory test performed for any disease, which are related to patient blood sample. This disease was not well known before the year 1992 and not a mandatory test requirement. Diagnostics of disease was not available in earlier time. Based on these criteria, patient age for positive diagnostics has been decided as 40 + years because from the year 2020 – 1992 is 28 years plus adding 15 years for HCV to develop liver disease ends up with 40 + years.

(a) Blood Transfusion: Before 1992, hepatitis C was not tested mandatorily before blood transfusion. If donor carries this disease, recipient should have got Hepatitis C, due to blood transfusion (a very common cause of spread of hepatitis C). Blood transfusion is considered as one of the decision-making criteria to diagnose hepatitis C.

(b) Disease Duration: If the disease symptom is found in patient, which can be traced back to approx. more than 15 years, there are very high chances that hepatitis C virus is present in patient's body.

- **Symptom of Disease**

The major symptom, which can indicate Hepatitis infection are as following:

(a) Fatigue: Fatigue is not tiredness, exhaustion, restlessness, but it is a symptom of overworked heart. Fatigue can be alleviated by taking rest. Fatigue can be Physical or Mental. Physical fatigue is a temporary, inability of a muscle to

maintain optimal physical performance, and is made more severe by intense physical exercise [148,153]. Mental fatigue is a brief decrease in maximal cognitive performance resulting from prolonged periods of cognitive activity. It can manifest as sleepiness, lethargy, or directed attention fatigue [154].

(b) Weight Loss: Consistently losing weight without any reason (like dieting). The loss of wait could directly relate to malfunction of liver, which is a strong relation in diagnosis of HCV.

(c) Joint/Belly Pain: Complains about stomach pain and pains on various joints. It is difficult to move freely. Pain may feel in more than half side of the belly. This is more typical for a stomach virus, indigestion, or gas. If the pain becomes more severe and frequent with no usual symptom, it may be caused by short term disorders or serious disease such as hepatitis (lever inflammatory).

(d) Loss of Appetite: When one has a reduced desire to eat, or no desire to eat at all. Continued loss of appetite is of major concern. With continued loss of appetite and decreased food and beverage intake, problems such as malnutrition (loss of nutrients), dehydration, wasting (extreme weight loss), vitamin and mineral deficiencies, and diarrhea. The most common medical conditions indicated by the symptoms decreased appetite, fatigue and weight loss (unintentional) including Depression in Adult, Hyperthyroidism, hepatitis and Multiple sclerosis.

(e) Dark Urine: The normal color of urine ranges from light yellow to dark amber, depending on the concentration of solutes in the urine [155]. Other urinary complaints may accompany like urinary urgency-having to hurry to get to the bathroom, frequent urination, burning pain with urination also known as "dysuria" which can suggest infection due to hepatitis or tumor, or colicky pains-stones [156].

(f) Itchy Skin/Sour Muscle: Itch is type of a sensory experience. Modern science shows that itch has many similarities to pain, and while both are unpleasant sensory experiences, their behavioral response patterns are different. Pain creates a withdrawal reflex while itch leads to a scratch reflex [157]. Hepatitis symptoms also shows similar kind of signs to human body.

(g) Abdominal Swelling: Abdominal swelling is a general condition in which the abdomen is enlarged. Abdominal swelling can be because of a sensation of fullness, bloating, stretching, or pain. Liver cancer can cause swelling of the abdomen. This could be due to the liver gets bigger from the growing cancer, and causes swelling on the right side of the abdomen. The cancer increases pressure in the liver causing blood to back up in the vessels.

(h) Fever: According to the Centers of Disease Control and Prevention (CDC), up to 80 percent of those with acute hepatitis C will not experience symptoms. In some cases, people will experience mild fever.

(i) Nausea: HCV infection is associated with an increased risk of nausea. The strong association between abdominal pain and nausea gives a clue of HCV patients.

(j) Fluid retention: This fluid retention can cause the abdomen to become quite swollen and uncomfortable. Conditions that cause fluid retention include heart failure, cirrhosis of the liver, and kidney failure.

(k) Confusion: Hepatitis C is a virus that affects the liver. The liver is responsible for removing harmful substances from your blood. When the liver doesn't function properly, it can affect the entire body, including the brain. Symptoms of brain fog, remembering things, maintaining concentration, and confusion are more likely to occur in people with advanced hepatitis C or cirrhosis of the liver.

(l) Jaundice: Jaundice is when the skin and the whites of the eyes turn yellow. This happens when there's too much bilirubin (yellow pigment) in the blood. Jaundice is a symptom of hepatitis C and cirrhosis and needs to be treated in the timely manner.

(m) Metabolic problem: It is possible that HCV infection causes fatty liver disease. Metabolic syndrome is highly prevalent among hepatitis C virus infected

patients. Metabolic syndrome is associated with hypertension, insulin resistance, increased abdominal fat, and overweight [158].

- **Liver Related Diseases**

The major symptom, which can indicate Hepatitis infection on a patient.

(a) Had Any Liver Treatment Before: Had patient gone through liver treatment in past like treatment for Cirrhosis, Chronic Hepatitis, HCC, Chronic Liver Disease? Because Hepatitis causes few symptoms, so most of them don't know that they have Hepatitis. Treatment depending on how damaged your liver is and other health conditions of a patient.

- **Blood-Borne Reason for Hepatitis**

The major symptom, which can indicate hepatitis infection on a patient are listed below:

(a) Blood transfusion: Hepatitis C is a blood borne virus. It is spread when blood from a person infected with the Hepatitis C virus enters the body of someone who is not infected. Hepatitis C virus is spread through blood transfusions and organ transplants.

(b) Organ Transplant: Hepatitis C infection in kidney transplant candidates and recipients. Hepatitis C virus (HCV) causes disease in transplanted kidneys. Most HCV-infected transplant recipients are infected prior to transplant, while on dialysis. The transmission of HCV through kidney transplantation is rare due to screening of donors [159].

(c) Body Piercing: Transmission of Hepatitis C is possible when poor infection-control practices are used during tattooing or piercing by visiting an unlicensed piercing facility. Hepatitis C exposure and infection can occur if the needle being used is not properly cleaned and sterilized.

(d) Health Care Worker: HCV transmission via blood splash to the eye have been reported, avoiding occupational exposure to blood is the primary way to prevent transmission of blood-borne illnesses among health care personnel. All health care personnel must practice standard precautions. Standard precautions include the appropriate use of personal protective equipment like gloves, masks, and protective eyewear.

- **Potential Reason of Disease by Drugs**

The major symptom, which can indicate hepatitis infection in a patient are listed below:

(a) Alcohol: Excessive alcohol use and infection from HCV can cause significant liver damage. It can lead to permanent scarring of the liver. The alcohol intake of more than 50 grams a day (approximately 3.5 drinks per day) leads to an increased risk of fibrosis and ultimate cirrhosis [160].

(b) Self-injected drugs: People who inject drugs (PWID) are at high risk for Hepatitis B virus (HBV) and Hepatitis C virus (HCV) infection by sharing needles and

equipment. In addition, outbreaks of Hepatitis A infection also have been reported among PWIDs group such outbreaks occurs through both percutaneous and fecal-oral routes [161].

- **Hepatitis Due to Other Diseases**

The major symptom, which can indicate hepatitis infection on a patient are listed as:

(a) HIV Positive Patient: The Hepatitis C virus (HCV) infection in HIV-infected patients shows a significant increase in liver disease progression, high rates of end-stage liver disease, and shortened lifespan [162].

(b) Mother had HCV: Active drug use and HIV coinfection increase the risk for HCV vertical transmission. Hepatitis C is rarely passed from a pregnant woman to her baby. The risk becomes greater if the mother has both HIV infection and Hepatitis C virus.

(c) Hemochromatosis Patients: Hemochromatosis is associated with iron overload in the body. Patients with elevated serum iron markers have more active chronic hepatitis with more liver fibrosis [163].

(d) Hemodialysis Patients: Hemodialysis, is a process of purifying the blood of a person whose kidneys are not working normally. Hepatitis C virus infection is

a significant cause of mortality in hemodialysis (HD) patients and kidney transplant recipients. In addition to screening for anti-HCV antibodies, liver biopsy is particularly valuable for assessing the stage of liver damage in HCV-infected patients [164].

- **Clinical Tests**

Diagnosis of Hepatitis is done via a series of clinical tests. There are 3 kinds of tests in this section Liver Test, Blood Test and Urine test.

- Liver Test (Section 7A): There are seven types of tests in this section that can be use. Those tests are Biopsy, Destruction of Tissue, Removal of Lobe, Liver Transplant, Repair of Liver, Other Procedures, and Liver Scan. If any result is positive that means there has been infection with hepatitis C in the past, if the result is negative then there has not been infection with hepatitis C Virus.

- Blood Test (Section 7B): Enzyme Immunoassay (EIA) is the most common testing kit used for HCV clinical testing. The blood test that looks for the genetic material (RNA) of the virus that causes hepatitis or for the proteins (antibodies) the body makes against HCV is performed in this study. The hepatitis C recombinant immunoblot assay (RIBA) is the confirmation test for the hepatitis C antibody. If the result of the HCV RIBA is positive, this confirms that the detection of a hepatitis C antibody (anti-HCV) was a true positive, meaning that there has been infection with hepatitis C in the past. If the HCV RIBA result is negative, it means that there

has not been infection with hepatitis C. If an earlier hepatitis C antibody (anti-HCV) test had been positive, then this was a false positive.

Other things to keep in the diagnostics of HCV:

- Even if the HCV RIBA result is positive, only the test of HCV RNA (viral load) can detect whether the hepatitis C virus is still present in the body.
- HCV RIBA is not a test that is needed for most patients. Usually, it is performed by blood banks to check for hepatitis C in people who donate blood.

This test may be the RIBA test or another test, called HCV RNA, which directly measures the virus. The RIBA test (which stands for Recombinant Immunoblot Assay) uses a different approach to finding hepatitis C antibodies in your blood. If this test is positive, you probably have been infected with hepatitis C. It's important to realize that antibody tests usually can't distinguish between past or current infection. Doctors must use clinical information (such as medical history, signs and symptoms) or other tests to determine active or past infection.

In summary of blood test diagnosis to Hepatitis C:

i. Negative RIBA = No hepatitis C antibodies found in blood. Patient is probably not infected with HCV.
ii. Positive RIBA = Hepatitis C antibodies were found in patient's blood using a very sophisticated lab test. Patient probably has been infected with hepatitis C.
iii. Negative HCV RNA = No active HCV infection.

iv. Positive HCV RNA = Active HCV infection.

- Urine Test (Section 7C): There are a few possible causes of dark urine and those causes are Jaundice, Hepatitis B Virus, hepatitis C Virus, and Cirrhosis of the liver.

5.3 Variables Used

The analysis is performed using Corvid Exsys software. Following variables are used for the analysis:

- **Patient Age** - Static variable and values - <=40; >40;

- **Duration of Disease** - Static variable and values - <=15 years;>15 years;

- **Blood transfusion year** (if any) - Static variable and values - Before 1992; in or after 1992;

- **Disease Symptom** - Fatigue; Joint/Belly Pain; Loss of Appetite; Dark Urine; Itchy Skin/sour Muscle, Fever, Nausea, Confusion, Jaundice, Metabolic Problems, Weight Loss, Abdomen Swelling and Fluid Retention;

- **Test Performed** - Collection variable and values – Liver Test; Blood Test; Urine Test

The Logical flow of the diagnostics is written as:

Input Variables Types:

(a) Age – Numeric

(b) Blood Transfusion - Static list with values “Before or on 1992”; “After 1992”.

(c) Disease Duration – Static list with values “More or equal to 15”; “Less than 15”.

(d) Disease Symptom – Static list with values “Fatigue”; “Joint/Belly Pain”; “Loss of Appetite”; “Dark Urine”; “Itchy Skin/Sour Muscle”; “Fever”; “Nausea”; “Confusion”; “Jaundice”; “Metabolic Problems”; “Weight Loss”; “Abdomen Swelling”; “Fluid Retention”; “None”.

- Screen to add new variables for the system

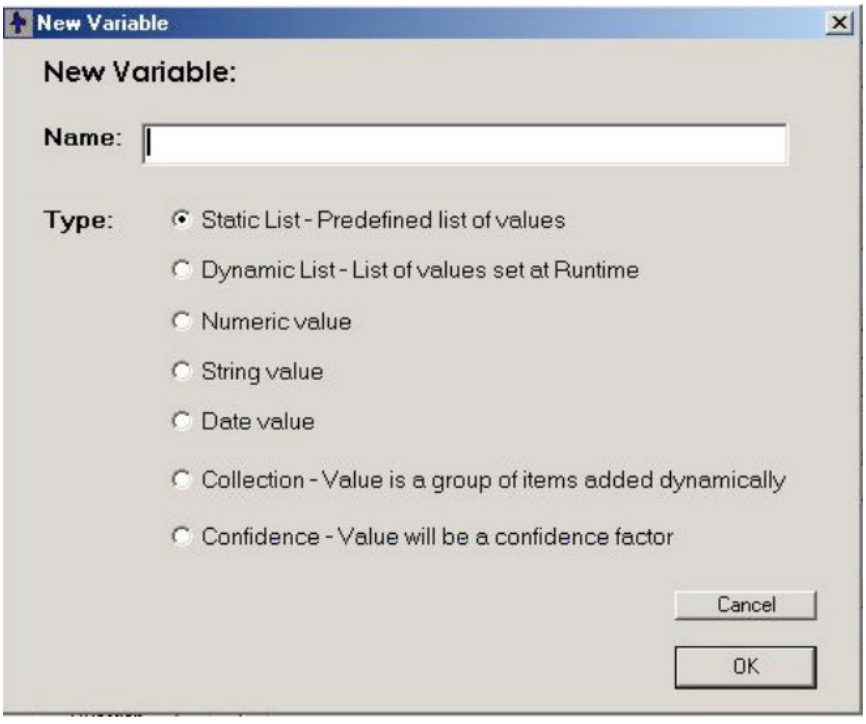

Figure 5.8 New Variable [18].

- System screen to add variables for the system

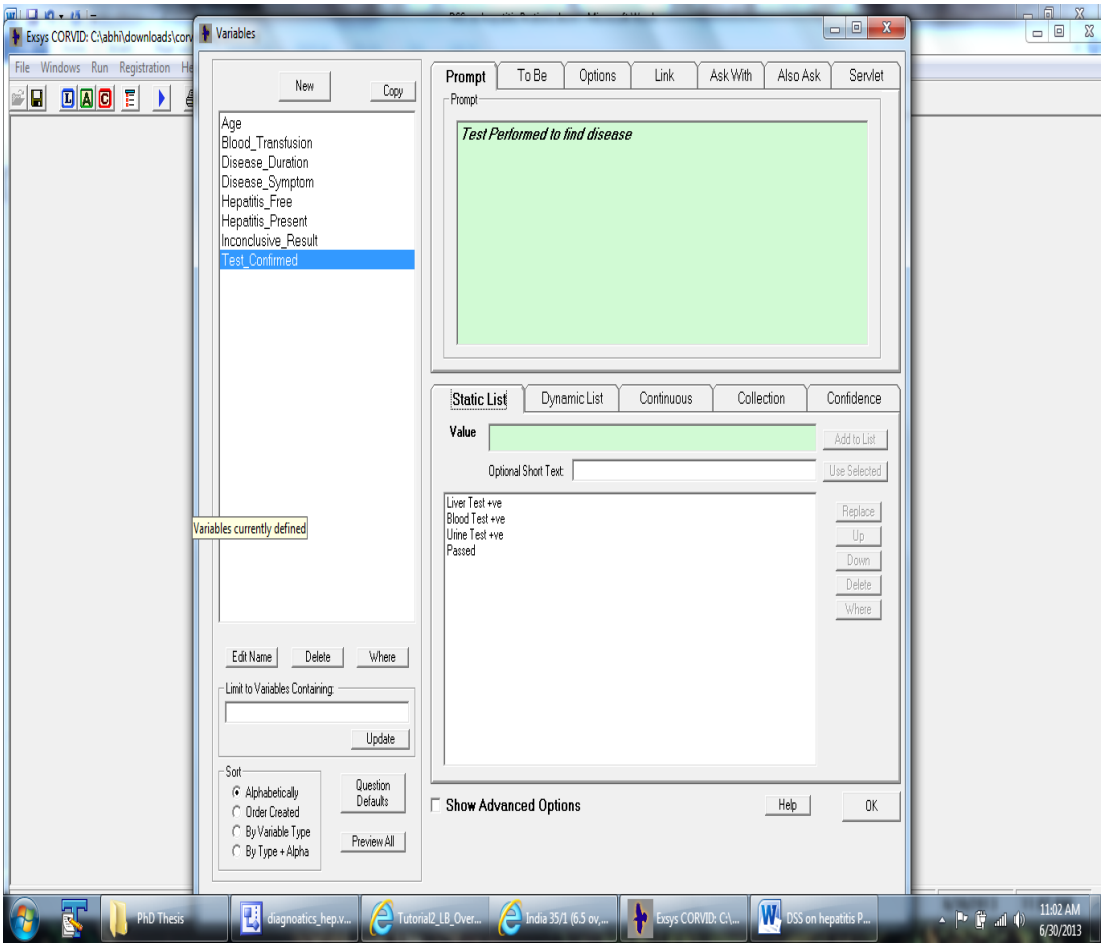

Fig 5.9 Exsys Variable Definition & Selection for the Diagnosis

5.4 Proposed Rules for the Diagnosis of Hepatitis

IF Age >=40 years;

AND Blood Transfusion is before 1992;

AND Disease Duration is more than 15 years;

IF the answer is No THEN you are HCV Free;

IF the answer is Yes THEN Go to Disease Symptoms (Section 2);

Do you have any symptoms of the disease like Fatigue, Joint and Belly pain, loss of appetite, dark urine, itchy skin/sour muscle, fever, nausea, confusion, Jaundice, Metabolic Problems, weight loss, abdomen swelling or fluid retention?

IF the answer is Yes THEN Go to Clinical Test (Section 7);

IF the answer is No THEN Go to Liver Related Diseases (Section 3);

You had any kind of Liver Treatment before?

IF the answer is Yes THEN Go to Clinical Test (Section 7);

IF the answer is No THEN Go to Blood-Borne Reason for Hepatitis (Section 4);

Did you ever have blood transfusion?

Did you ever have Organ Transplant?

Did you ever have Body Piercing?

Are you a Health Care Worker?

IF the answer is Yes THEN Go to Clinical Test (Section 7);

IF the answer is No THEN Go to Potential Reason of Disease by drug (Section 5);

Did you ever inject drugs or take non prescribe drug?

Do you drink?

IF the answer is yes then how often?

IF it is every day then are you an alcoholic?

IF the answer is Yes THEN Go to Clinical Test (Section 7);

IF the answer is No THEN Go to Hepatitis Due to Other diseases (Section 6);

Are you a HIV positive patient?

Does your mother have HCV?

Are you a Hemochromatosis patient?

Are you a Hemodialysis patient?

IF the answer is Yes THEN Go to Clinical Test (Section 7);

IF the answer is No THEN you are Hepatitis C virus Free;

Take Liver Test (Section 7A);

Take Biopsy test?

IF the result was -ve THEN Patient is Hepatitis Free.

IF the result was +ve THEN Patient has Hepatitis.

Take Blood Test (Section 7B);

Take EIA Test?

IF the result was EIA Negative THEN No Hepatitis;

IF the result was EIA Positive THEN take HCV RIBA OR HCV RNA;

IF took HCV RIBA THEN

IF the RIBA was Negative THEN No HCV Infection

IF HCV RIBA was Positive THEN The patient has either resolved or active infection and HCV RNA is required;

IF HCV RNA is Positive THEN Active HCV Infection.

IF RNA is Negative THEN must take HCV RIBA;

IF HCV RIBA is Positive THEN Resolved HCV Infection.

Take Blood Test (Section 7C);

Did the color of the Urine change?

IF the answer is No THEN

Did the volume of the urine change?

IF the answer is yes THEN Check with your General Practitioner;

If the answer is No THEN

Did the frequency of the urine change?

IF the answer is No THEN you do not have Hepatitis.

IF the answer is Yes THEN;

The frequency of the urination went up?

IF the answer is No THEN Check with your general practitioner possibility of dehydration.

IF the answer is Yes THEN check with your general practitioner possibility of diabetics.

Did the color of the Urine changes?

IF the answer is Yes THEN

Is the urine color light?

IF the answer is No THEN Go to “B”

Does color of the stool change?

IF the answer is No THAN Go to section C

IF the answer is Yes THEN

Does color of the stool is pale color?

IF the answer is Yes THAN You have Jaundice.

IF the answer is No THAN

Is there any weight loss?

IF the answer is no THAN

Do you have nausea?

IF the answer is no THAN You need to see general Practitioner;

IF the answer is yes THAN

Are you on dieting?

IF the answer is Yes THAN You need to see General Practitioner;

IF the answer is No THAN

Are you vomiting?

IF the answer is Yes THAN go to D;

IF the answer is NO THAN go to E;

Is there any weight loss?

IF the answer is yes THAN

Are you on dieting?

IF the answer is yes THAN You need to see General Practitioner;

IF the answer is no THAN

Are you vomiting?

IF the answer is Yes THAN go to D;

IF the answer is NO THAN go to E;

Is the Urine color light?

IF the answer is yes THAN

Does your skin itches? Go to “A”

IF the answer is no THAN Check with your general Practitioner;

IF the answer is yes THAN

Are there yellow pigments on the skin?

IF the answer is no THAN Check with your general Practitioner;

IF the answer is yes THAN

Are your eyes yellowish?

IF the answer is no THAN You are at the beginning stage of Hepatitis or Jaundice?

IF the answer is yes THAN

Do you get yellowing of the mucus from your mouth?

IF the answer is no THAN You are at the beginning stage of Hepatitis or Jaundice?

IF the answer is yes THAN

Do you get yellowing of the mucous from nose?

IF the answer is no THAN You are at the beginning stage of Hepatitis or Jaundice?

IF the answer is yes THAN You have Jaundice.

5.5 Corvid Based CDSS Design and Logic Blocks

- Logic block used for the implementation of rules, for diagnosis of Hepatitis

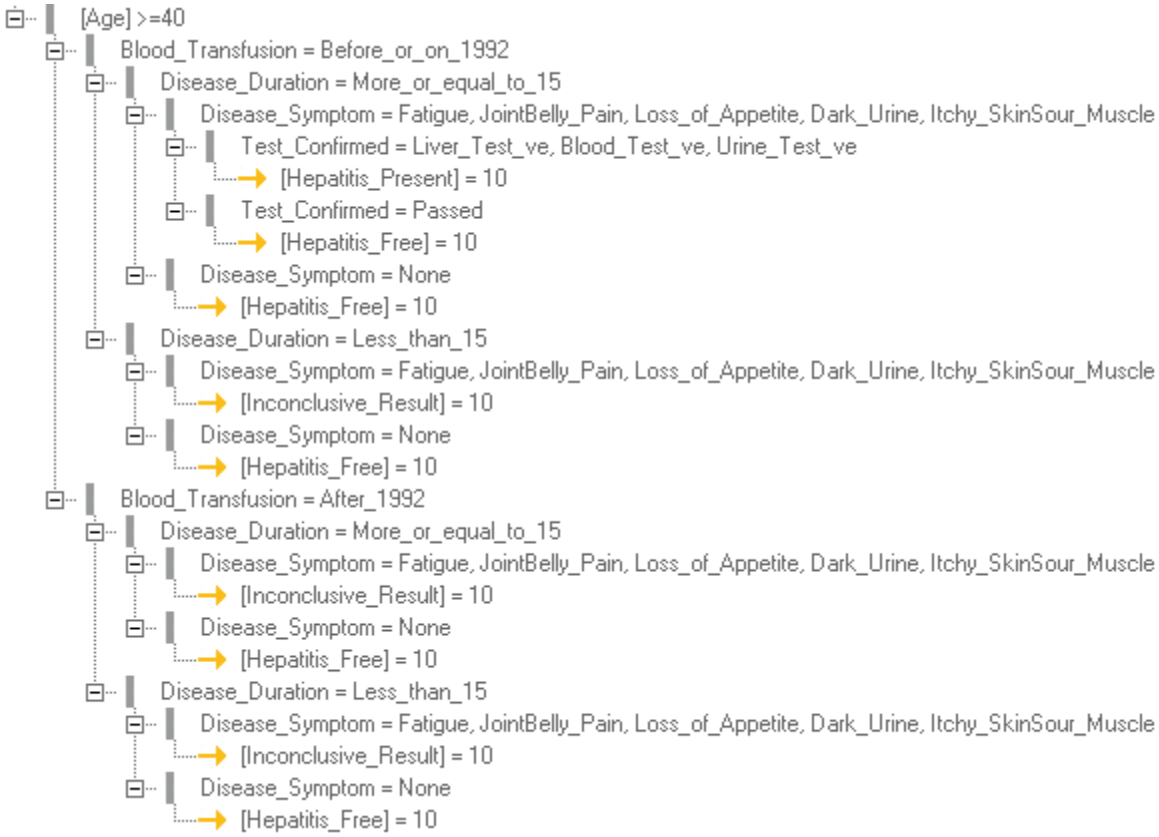

Fig 5.10 Logical Flow for Diagnostics

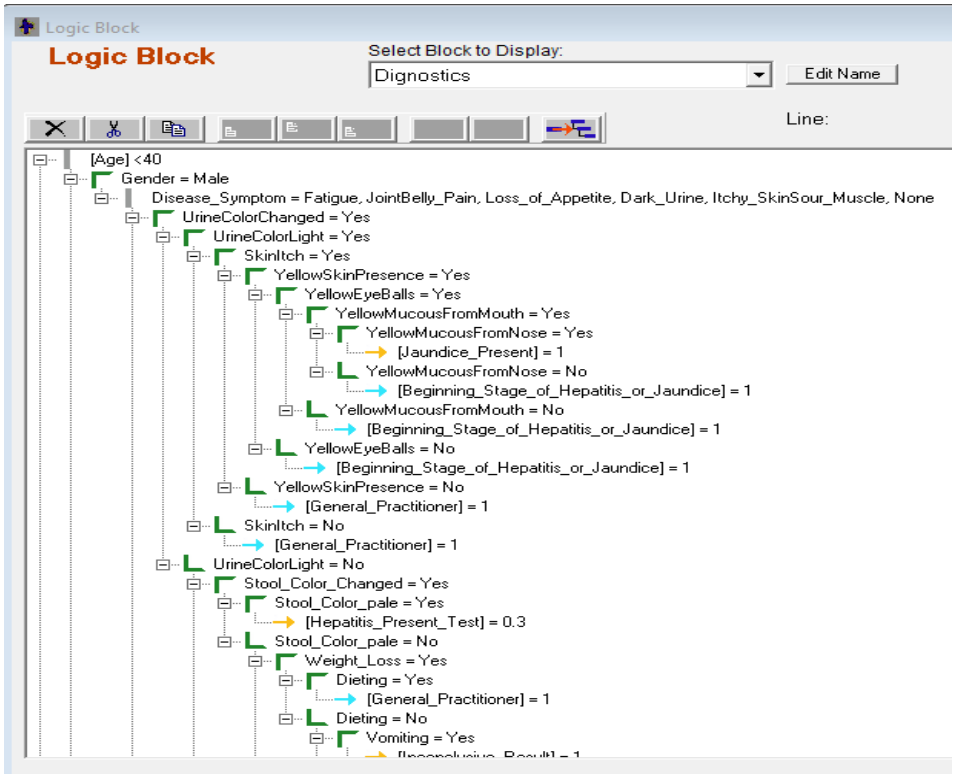

Figure 5.11 Logic Flow for the Complaint of Dark Urine

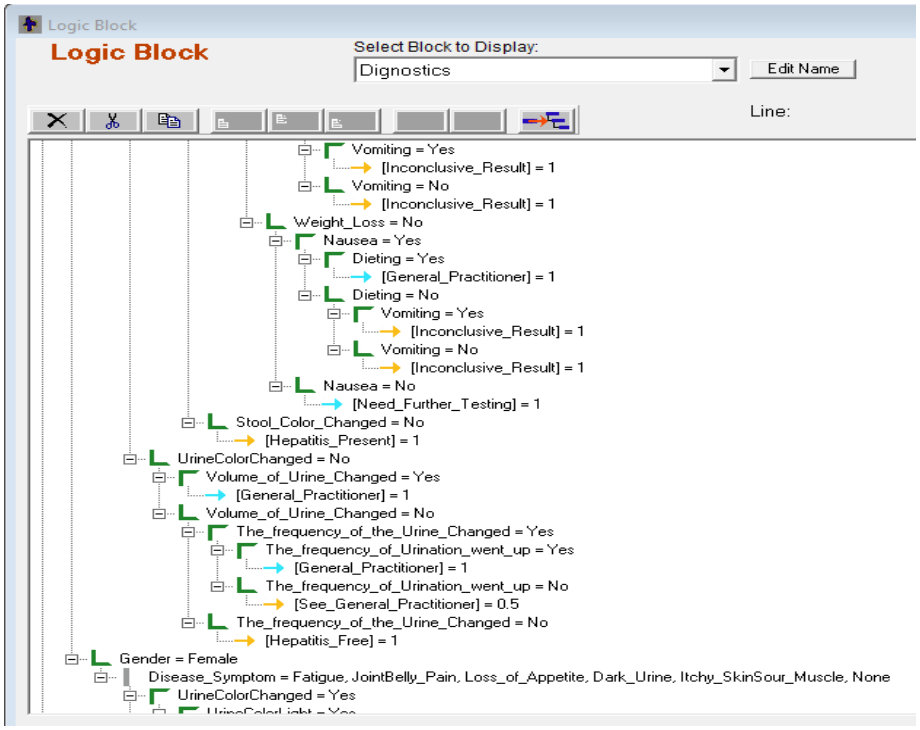

Figure 5.12 Logic Flow for the Complaint of Dark Urine B

5.6 CDSS Implementation Using Corvid

The Exsys software Java Run Time environment (applet or web component) is used for diagnosis of the symptom. Please find a series of flow for checking presence/absence of hepatitis in a patient via Corvid Exsys.

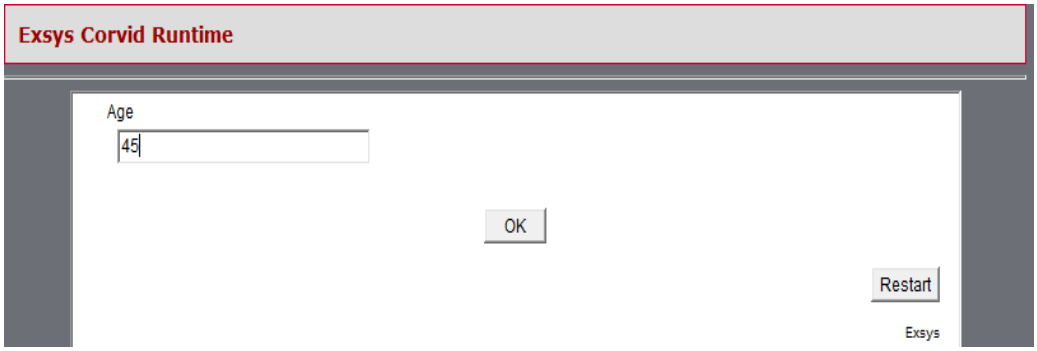

Figure 5.13 Enter value of variable Age and click “OK”

Exsys Corvid Runtime requesting Input from the clinician for the age of the patient.

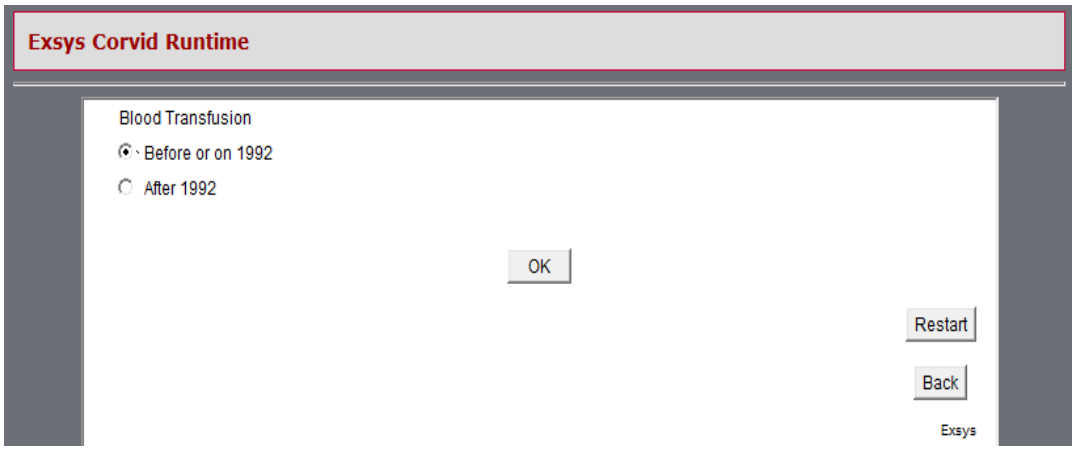

Figure 5.14 Select Year for Blood Transfusion and click “OK”

System is asking questions about the blood transfusion if blood transfusion occurred before or in 1992 or the 2nd choice of after the year 1992.

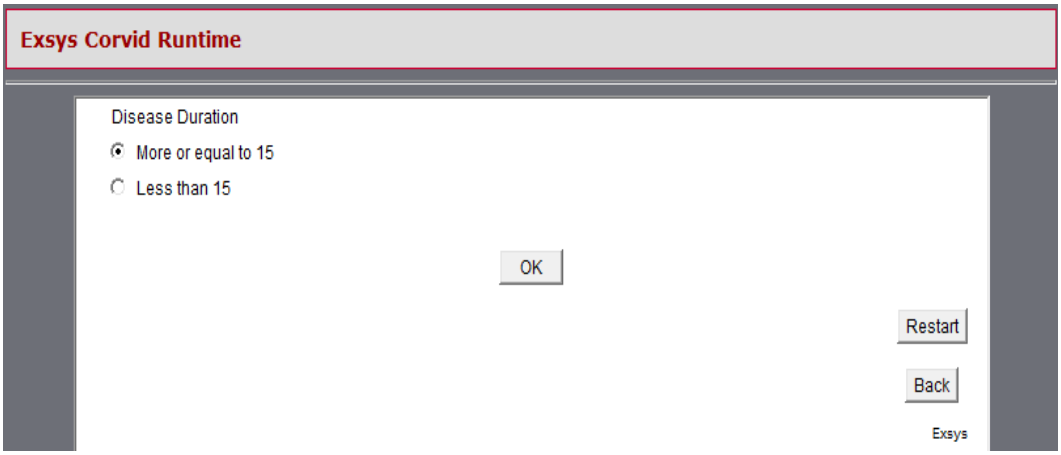

Figure 5.15 Select Disease Duration and Click “OK”

System is asking the next question of the “Disease Duration”. Must pick one choice if disease duration is more or equal to 15 years or disease duration is less than 15 years.

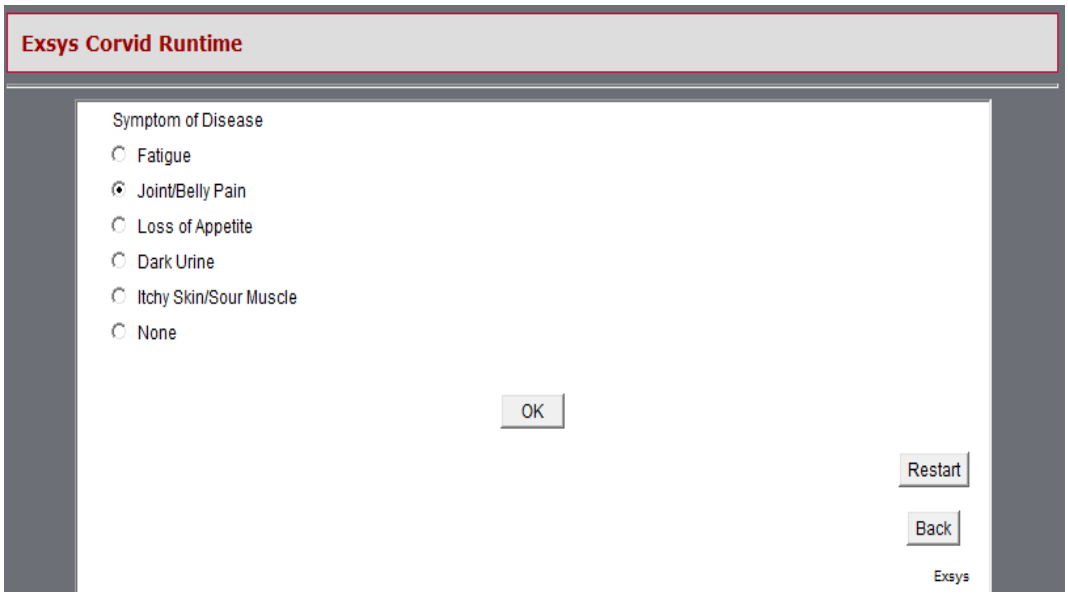

Fig 5.16 Select Disease Symptom and Click “OK”

In this screen system is asking for “Symptoms of Disease”. Must pick one from the choices provided. 1st choice is “Fatigue”, 2nd choice is “joint/Belly Pain”, 3rd choice is “Loss of Appetite”, 4th choice is “Dark Urine”, 5th choice is “Itchy Skin/sour Muscle”, and the 6th choice is “None”.

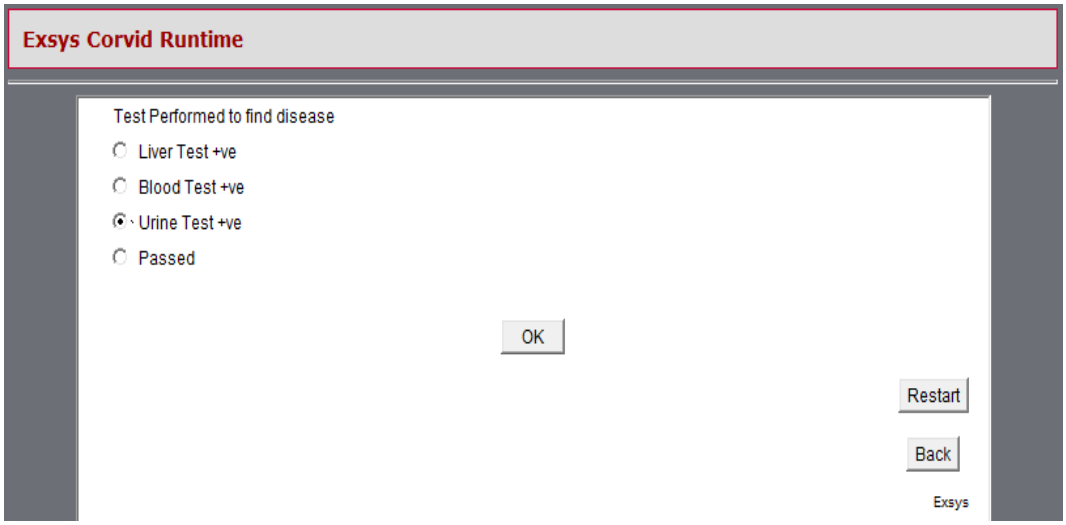

Figure 5.17 Select Test Performed and Click "OK"

In this screen system is asking for which test performed "Test Performed to find the disease" 1st choice is "Liver Test +ve", 2nd choice is "Blood Test +ve" and the 3rd choice is "Urine Test +ve" select one and click "OK".

5.7 CDSS Sample Input/output Screenshots

- Hepatitis Free – Confidence variable; decided if hepatitis is present or not.
- Hepatitis Present – Confidence variable; decided if hepatitis is present or not.
- Inconclusive Result – Confidence variable; not conclusive for present of symptom and more detailed test is needed.
- Test confirmed – Static list with values "Liver Test +ve"; "Blood Test +ve"; Urine Test +ve"; "Passed".

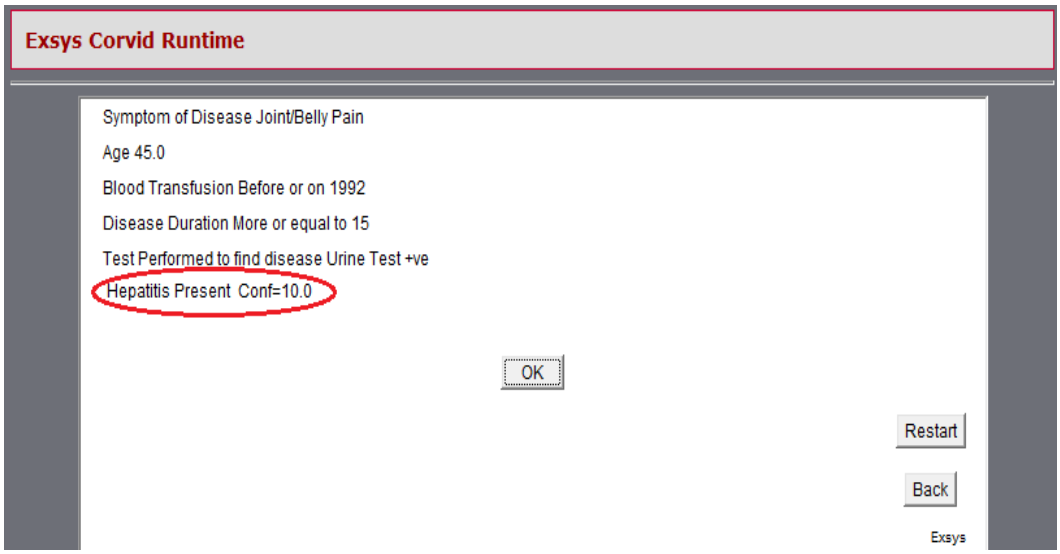

Figure 5.18 Confirmation of Disease

This screen shows the confirmation of Hepatitis as confidence level is maximum.

5.8 Conclusion and Discussion

Created Clinical Decision Support System for the Diagnosis of Hepatitis C virus. System is successfully developed to diagnose a disease. It is created for medical professionals with a guarantee that it is functioning accurately and the system is ready to guide the healthcare professionals to diagnose Hepatitis Virus. The goal is to make the CDSS easily accessible and user friendly. This system is capable of guiding a clinician through the steps to diagnose hepatitis virus, by asking accurate and precise disease symptoms, questions about other liver related diseases, blood-borne reason for the hepatitis, potential other reasons of disease by drugs, hepatitis due to other diseases and clinical tests. All the questions asked by the system during the diagnosis process were based on the clinical literature. The system is accurate and this system can guide a clinician through the diagnostic process to achieve the diagnosis of hepatitis results.

After achieving the diagnosis in a timely manner, with that the system proves that there is a need for the system.

CHAPTER VI- CONCLUSIONS AND DISCUSSIONS

6.1 Introduction

The chapter includes overall achievements on clinical decision support system for diagnostics, treatment and management of disease related to Hepatitis C using NIS and HCUP data sources. The conclusion is divided into two parts. The first part is data analysis of hepatitis and liver diseases, and the second part is Clinical Decision Support System (CDSS) for the diagnosis of Hepatitis C virus. The analysis is performed using SPSS and Corvid software. Further study should include more and current global data sources for diversified pattern of the disease analysis, early detection and treatment. The study should also integrate patient information stored in hospital database for a better prediction. Artificial Intelligence and deep learning methodologies using neural network could effectively be modelled for future research.

6.2 Conclusions

The current research is based on 9 hypotheses. These hypotheses are covered in the chapter I. The entire hypotheses have been proved correct based on the analysis performed on NIS and HCUP data using CDSS methodologies on HCV. SPSS and Corvid based systems are successfully developed to analyze data and confirm the hypotheses made in the earlier section of the thesis. The research focused on the data collected for 5 years between 2007 and 2012. The data has large range of diagnostics parameters, from which a selected set of data are used for the current research. The data is able to diagnose HCV and related disease and guide health care professionals to make best possible treatment and recovery decision. The analysis also includes diverse range of parameters such as, age, race, sex, providers, region, historical treatment and hospital stay

to establish best treatment option with optimal cost. The rich dataset taken from NIS and HCUP for the study precisely diagnose HCV related symptom and treatment options.

CDSS is implemented for data analysis to guide the healthcare professionals to diagnose Hepatitis C Virus. The process implemented in the thesis is capable of guiding a clinician through the steps to diagnose HCV by asking accurate and precise disease symptoms, questions about other liver related diseases, blood-borne reason for the hepatitis, potential other reasons of disease by drugs, hepatitis due to other diseases and clinical tests. All the questions asked by the CDSS system during the diagnosis process were based on the clinical literature.

The key findings include as Hepatitis C cases were highest among other categories of Hepatitis (A, B, D & E). HCV is highest among age group 21 to 51 for the year 2007. In average Hepatitis C was found highest among the age group 52-65 years throughout the years 2008 to 2012. Highest number of procedures performed and highest number of deaths is reported for the age group 52 to 65. Length of stay and treatment charges of Hepatitis C was highest for age group of 21 to 51. Number of patients dies of Hepatitis C is highest for age group 52 to 65. Male below 81 years of age, surpassed female population infected with Hepatitis C. Medicaid coverage was highest amount population aging below 51 and Medicare above 51 for Hepatitis C treatment insurance coverage. Maximum number of patients died in hospital was highest for Cirrhosis followed by Hepatitis C. Also, the greatest number of procedures was performed for Cirrhosis patients followed by Hepatitis C. Hepatitis C were highest in the Northeast region per 100,000 normalized populations as compared to any other region. Urban location noticed higher number of patients reported with Hepatitis C. Destination after discharge showed that

most of the patients stayed to home self-care, followed by short term hospital transfer and home health care. Average Length of stay for Hepatitis C patient was around 5.73 days to 6.01 days. Trauma center charged most to Hepatitis C patient as compared to elective, urgent and emergency treatment centers. Biopsy Procedure is performed highest followed by Liver Transplant and Destruction of tissue for Hepatitis C patients. The cost of Liver Transplant was most expensive procedure followed by repair of liver and removal of lobe throughout the study.

Hepatitis C diagnostics is performed using CDSS methodology. Corvid and SPSS statistical software are used for the analysis. 26 forward/backward chaining rules are applied for diagnostic of HCV. For a given scenario, maximum 11 rules are executed to come to a conclusion about confirmation of the HCV disease. Non-presence of disease can be achieved by execution of 6 rules. The diagnostics result discovered using SPSS and Corvid software is easily accessible and user friendly. This system is capable of guiding a clinician through the steps to diagnose hepatitis virus, by asking accurate and precise disease symptoms, questions about other liver related diseases, blood-borne reason for the hepatitis, potential other reasons of disease by drugs, hepatitis due to other diseases and clinical tests. All the questions asked by the system during the diagnosis process were based on the clinical literature. The system is accurate and can guide a clinician through the diagnostic process to achieve the diagnosis of hepatitis disease.

The Hepatitis C cases found the highest among rest of the categories of Hepatitis A+E and Hepatitis B+D from the data collected for the study. Length of stay and treatment charges of Hepatitis C was highest for mid age group of people. Number of patients dies of Hepatitis C is highest for older age group. The procedure to treat

Hepatitis C was highest for older age group. White population had highest number of patients of Hepatitis C for all age groups. Medicaid coverage was highest amount population aging below 51 and Medicare above 51 for Hepatitis C treatment insurance coverage. Trauma center changed most to Hepatitis C patient as compared to emergency and urgent treatment centers. Urban location noticed higher number of patients reported with Hepatitis C infection. Emergency hospital admission recoded as highest as compared of any other scheduled treatment or diagnostics for Hepatitis C. Hospitals in Southern region recoded maximum number of Hepatitis C patients as compared to any other reigns. West, Northeast and Midwest followed the reported Hepatitis C patients. Most of the patients stayed to home self-care after disposition, followed by short term hospital transfer and home health care. Maximum number of patients died in hospital was highest for Cirrhosis followed by Hepatitis C. Also, the greatest number of procedures was performed for Cirrhosis patients followed by Hepatitis C.

6.3 Discussion

NIS and HCUP data set is used for analysis of HCV disease. These data sets are selected as they are most comprehensive and nationwide hospitalization records are present in the data set. The data is very comprehensive and covers entire aspect of disease investigation and treatment options. Statistical software is used to analyze NIS and HCUP data. The research focuses on the analysis of the number of records of patients with Hepatitis C virus from the year 2007 to 2012. The SPSS and Corvid systems are successfully developed to diagnose Hepatitis C disease. Hepatitis causes cirrhosis. Cirrhosis is a condition in which the liver slowly breaks down and is unable to function

normally. HCV also spreads via exposure to the contaminated blood, blood transfusion and previous presence of lever diseases.

The key input parameters used for HCV analysis are age, sex and duration of disease. The other important parameters include the year blood transfusion took in place, disease symptom, liver related disease, drug abuse, region and parental history of the disease. The measure of disease progression represents a key challenge in any of the different stages of chronic liver disease. Indeed, a correct and reliable measure of the stage of the disease has relevant implications for assessing the effectiveness of the current therapeutic regimens and predicting the occurrence of complications. Accordingly, a current major effort is directed at evaluating minimally invasive procedures to be employed to substitute or integrate the standard invasive methods, that is, liver biopsy or the measurement of HCV. The key HCV clinical tests include Liver, Blood and Urine tests. The Procedures which were performed on the above diseases are as follows: Biopsy, Destruction of tissue, Removal of Lobe, Liver Transplant, Repair of Liver, Other Procedures and Liver Scan. All the questions asked by the system during the diagnosis process are based on the clinical diagnostics procedures used across hospitals and health care providers. The SPSS and Corvid systems are created for medical professionals with a guarantee of accuracy to diagnose Hepatitis C Virus.

Decision support system (DSS) is a powerful statistical analysis methodology, which is widely used across a number of industries like health care, manufacturing, financial etc. Decision support systems like SPSS and Corvid, are widely used to analyze larger volume of data to find a pattern and make appropriate decision resulted in best possible outcome. Decision support systems include human cognitive decision by

integrating various sources of information, providing intelligent access to relevant knowledge, aiding the process of structuring and optimizing the decisions. Decision support system in analyzing Hepatitis C (HCV) do not replace physicians but rather augment diagnostics and best possible treatment with optimal cost. In the agreement with the hypotheses discussed in the introduction section, the results of the current study show that a highly significant relationship exists with the HCV and the parameter used in the study (age, sex, race, symptom etc.). The thesis has been proved correct after analyzing NIS and HCUP data. During the actual study, collected data were sorted and checked for errors and completeness. HCV infections are serious public health problems that can have consequences in terms of psychological and occupational diseases.

6.4 Hypothesis Findings

Hypothesis 1: Find the correlation between mortality and morbidity among the following categories age, gender, race, payment methods, died during hospital stay, Income-Level, admission type, admission source, hospital region, hospital location, and destination after discharge. These criteria will be investigated. **Expectation** is mortality to be higher with older, low income, black male population. Fewer patients to die in hospital stay. **Finding** of the research is that this expectation is confirmed.

Hypothesis 2: To examine the association between the Hepatitis & liver diseases and Length of stay. **Assumption** is hepatitis cause liver disease or they are closely related. More severe the condition of patient, longer time patient to say in the hospital. **Finding** of the research is that this assumption is confirmed.

Hypothesis 3: To determine the Cost of procedures with age group. **Expectation** is older patient should have higher cost of procedure. **Finding** of the research is that this expectation is confirmed.

Hypothesis 4: To examine the association between the Hepatitis & Liver diseases and total charges of treatment. **Assumption** is they are closely related. Sever the symptom, higher the cost of treatment. **Finding** of the research is that this assumption is confirmed.

Hypothesis 5: Develop CDSS for faster detection and treatment options. **Expectation** is to implement best possible statistical model for HCV detection and treatment. **Finding** is it can be use in remote location to train health care providers.

Hypothesis 6: Develop methodologies for early diagnosis of hepatitis – focus on HCV. **Expectation** is to detect early and treat early – reduce overall cost and avoid become chronic. **Finding** of this expectation has been met.

Hypothesis 7: Build medical information and knowledge base. **Assumption** is to help faster and cost-effective treatment using the knowledge base, which will help faster detection and treatment. **Finding** of this assumption has been met.

Hypothesis 8: Eliminate the diagnosis errors and have a better patient management. **Expectation** CDSS is implemented for efficient diagnostics and patient management. **Finding** of this assumption has been met.

Hypothesis 9: Develop CDSS for faster detection and treatment options. **Expectation** is to implement rules-based knowledge management system for clinicians, existing literature, and evidence-based guidelines. **Findings** of this expectation has been met.

6.5 Future Direction of Research

The future direction of research is divided into two parts. The first part is data analysis of hepatitis and liver diseases, and the second part is Clinical Decision Support System (CDSS) for the diagnosis of Hepatitis C virus.

Future research for data analysis is as follows:

- Since this data analysis is limited to a U.S. based population only, a global perspective of the hospitalization characteristics of Hepatitis and Liver Disease patients is recommended.
- Since this data analysis is done on Hepatitis and Liver diseases, it is recommended that data analysis of hospitalization characteristics and treatment cost should be done on other diseases.

Future research for CDSS is as follows:

- More rules will be generated for differential diagnosis where two or more conditions share similar signs or symptoms for example HCV and HIV;
- Effectiveness and the doses of medication will be added in the knowledge-Base;
- Identify any adverse reaction or ineffectiveness of medication;
- We will create many more parameters for overall patient management within and outside the hospital;

- Expand the CDSS to include various types of Hepatitis including Hepatitis A and Hepatitis B;

- Further corvid will be performed for the treatment monitoring and drug interactions.

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APPENDIX- A

Rules for diagnosis:

(a) Condition when Age < 40 years (Probability is very less for hepatitis, but good to perform test)

Blood transfusion after 1992

Disease duration less than 15 years

Liver; Blood; Urine test +ve → *Inconclusive result. High possibility that patient doesn't have Hepatitis, but more test is needed*

Liver; Blood; Urine test -ve → *Patient is Hepatitis Free*

Blood transfusion before 1992

Disease duration more than 15 years

Liver; Blood; Urine test +ve → ***Patient has Hepatitis***

Liver; Blood; Urine test -ve → *Patient is Hepatitis Free*

(b) Condition when Age >= 40 years

Blood transfusion after 1992

Disease duration less than 15 years

Liver; Blood; Urine test +ve → *Inconclusive result. High possibility that patient doesn't have Hepatitis, but more test is needed*

Liver; Blood; Urine test -ve → *Patient is Hepatitis Free*

Blood transfusion before 1992

Disease duration more than 15 years

Liver; Blood; Urine test +ve → ***Patient has Hepatitis***

Liver; Blood; Urine test -ve → *Patient is Hepatitis Free*