Coinfection of Schistosoma species with Hepatitis B or Hepatitis C Viruses

Table 1.4 Studies Comparing Subjects with Schistosomiasis and Subjects with Hepatitis C Virus

No	Reference	Location (Years)	Study Design (Objective) and Study Population	Exclusion Criteria	Diagnosis of Disease	Findings on Coinfection
1	Morais et al. 2006	Cidade University, Recife, Brazil (n.a.)	*Case Series* (comparative, immunology, severity): Case groups: 3 HSS, 23 HCV, and 11 HSS w HCV patients; Controls: presented in graphs, but nowhere described; *Note:* further details on patients n.a.	HIV, HBV	HCV: anti-HCV, HCV-RNA ; HSS(Sm): stool, ultrasound, liver biopsy	Coinfected patients had higher TNF-alpha levels than either mono-infected groups, while mono-HSS patients displayed higher TNF-Beta levels; IL-13 levels were similar between all patient groups; Results suggest that immunoregulation of coinfection differs from each disease in isolation.
2	Morais et al. 2010	Hospital dad Clinicas da Universidade Federal de Pernambuco, Recife, Pernambuco, Brazil (n.a.)	*Case Control* (comparative, severity, biomarkers): Case groups: 22 HSS, 39 HCV, and 19 HSS w/HCV, aged 18-65 years; Controls: 13 non HSS, non-HCV subjects, ages 21-57 years from non-endemic areas of Pernambuco	Other causes of liver disease, liver transplantation, prior interferon therapy, immunosuppressive therapy, HBV, HIV	HCV: anti-HCV w/HCV RNA; HSS (Sm): stool, ultrasound	There was no difference in fibrosis degree between coinfected subjects and mono HCV patients who were both anti-HCV+ w/HCV-RNA+, based on histology evaluation, or between coinfected subjects and mono HSS based on ultrasound; However, coinfected patients did display higher fibrosis markers such as AP, bilirubin and gamma-globulin, compare to either mono-infected patient group; best indicators for distinguishing between mind and severe fibrosis varied by group, with TNF-alpha and alkaline phosphatase best for mono HCV subjects, while total bilirubin was the best

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						indicator for coinfected patients; no bio marker was identified for mono HSS subjects, as 91% presented with severe fibrosis according to ultrasonography.
3	Kamal et al 2000	Liver Unit, Ain Shams University Hospital, Cairo, Egypt (1992-1999)	*Cohort* (comparative, risk factors, disease progression): <u>Patient groups</u>: 30 Sm, 33 HCV and 63 Sm w/HCV subjects; mean group ages 38-44 years, 67% male; <u>*Note*</u>*:* all Egyptians from rural and urban areas in Cairo, Nile delta, and Upper Egypt- areas; Patients followed for 72-76 months	Serological evidence of active HAV,HBV,HDV infection, autoimmune hepatitis, cytomegalovirus, Epstein Barr virus, or other hepatic parasites.	<u>HCV:</u> anti-HCV w/HCV RNA; <u>Sch(Sm,Sh):</u> history or current infection, stool, urine, rectal biopsy, ultrasound; Note: all patients had active HCV infection.	Compared with mono HCV patients, coinfected patients had higher HCV titers and longer duration of HCV infection (9 vs. 13 years), with greater clinical signs of liver disease, including cirrhosis, at the start of study; over the observation period, coinfected patients had greater progression of disease, resulting in higher liver-related mortality (48%) compared with mono HCV (12%) and mono Sm (3%); the development of HCC was only observed in coinfected patients (11%), not in either mono infected group; HCV Genotype 4 observed in 62% mono infected HCV subjects vs. 92% in the coinfected subjects; On average, coinfected patients had acquired HCV infection at a younger age than those infected with HCV alone (aged 19 vs. age 30); PAT was associated with HCV in coinfected patients, whereas blood transfusion was

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						associated with mono HCV patients.
4	El-Kady et al. 2004	National Liver Institute, Minufiya University, El-Minufiya, Egypt (n.a.)	*Case Control* (comparative, immunology, complications, severity): <u>Case groups:</u> 15 Sm, 20 chronic HCV and 20 Sm w/chronic HCV patients, group mean ages 40-46 years, 66-75% male; <u>Controls:</u> 5 healthy subjects, matched for age and sex with no evidence of liver disease	n.a.	<u>Chronic HCV :</u> anti-HCV w/HCV-RNA; <u>Sch(Sm):</u> stool/rectal snip w/SchAb; <u>*Note:*</u> All Sm patients had ova in stool/rectum	Coinfected subjects had IL-4 and IL-10 levels that were comparable to or higher than mono Sm subjects, and IFN-gamma and IL-18 levels that were considerably lower than mono HCV subjects; This dominate Th2 cytokine profile suggests infection with Sm preceded HCV in coinfected subjects, and inhibits their ability to mount a HCV-specific Th1 response; Coinfected patients had high fibrosis scores, with high ALT and AST than other groups.
5	Kamal et al 2004	Ain Shams University, Cairo, Egypt (n.a.)	*Cohort* (comparative, immunology, disease progression): <u>Patient groups:</u> 23 acute HCV for 6-10 months, 20 HSS and 25 acute HCV w/HSS subjects; HCV groups matched by age, sex and duration of HCV infection (all genotype 4); HSS groups matched for duration of Sch infection <u>*Note:*</u> Patients were	No subject had received antiviral or immune-modulatory treatment before entry or during follow up; other causes of hepatitis ruled out.	<u>Acute HCV:</u> anti-HCV w/HCV-RNA, w/ ALT (GT 10 normal); <u>Sch(Sm):</u> stools/rectal biopsy, SchAb, liver biopsy	Coinfected subjects had accelerated liver fibrosis compared with mono-HCV subjects (0.58 vs. 0.1 units per year), despite similar baseline necroinflammatory scores and the absence of fibrosis; few mono-schistosomal subjects had progression of fibrosis; Coinfected subjects also had higher degrees of interface hepatitis, periportal necrosis and lower magnitude and breadth of intrahepatic HCV specific CD4+ T cell responses compared with subjects with mono HCV subjects; The enhancement of progression of

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			followed for 96 +/- 8.7 months.			liver fibrosis is associated with the failure to develop HCV-specific CD4+ Th1 response during the early phase of chronic infection favors the development of liver damage and progression of disease.
6	El-Kady et al 2005	National Liver Institute, Minufiya University, El-Minufiya, Egypt (n.a.)	*Case Control* (comparative, immunology, complications) Case groups: 15 Sm, 20 chronic HCV and 20 Sm w/chronic HCV patients, group mean ages 40-46 years, 66-75% male; Controls: 5 healthy subjects, matched for age and sex with no evidence of liver disease.	n.a.	Chronic HCV: anti-HCV w/HCV-RNA; Sch(Sm): stool/rectal snip w/SchAb; *Note:* All Sm patients had ova in stool/rectum	Coinfected subjects had cytokine profiles that were similar to mono-Sm subjects, with higher IL-4 and IL-10 and lower IFN-gamma and IL-18 levels; Coinfected patients had significantly higher HCV-RNA titers, with an inverse relationship between virus load and C4+ T- cell responses; Suggests dominance of the Th2 response may result in increased viral replication, resulting in more aggressive progression to fibrosis; ALT and AST levels were much higher in coinfected than other groups.
7	El-Masry et al. 2006	National Liver Institute, Minufiya University, El-Minufiya, Egypt (n.a.)	*Case Control* (comparative, severity): Case groups: 34 Sm, 58 chronic HCV and 68 Sm w/chronic HCV patients, mean group ages 25-40 years, 65% males; Controls: healthy controls, matched	Seromarkers for HAV, HBV, HDV infections, alcohol consumption, smoking	Chronic HCV: anti-HCV w/HCV-RNA, liver biopsy; Sch(Sm): stool/rectal snip w/SchAb; Note: All Sm patients had ova in stool/rectum	Coinfected patients had higher serum laminin concentrations than mono infected or control groups; This was positively correlated with fibrosis grading scores and highest in mono Sm patients, followed by coinfected patients; coinfected patients also had higher ALT and AST levels than all other groups.

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			for age and sex.			
8	Fahmy et al. 2006	Zagazig University Hospitals, Egypt (2005-2006)	*Case Control* (comparative, immunology): Case groups: 9 active Sm, 13 active HCV and 12 active Sm w/active HCV patients, group age range 27 to 61 years, 53% male; Controls: 10 apparently healthy non-Sm, non HCV subjects, aged 32-57 years, 50% male, drawn from University	Hepatitic infections other than HCV, parasitic infections other than Sm	Active HCV: anti-HCV w/HCV RNA w/elevated ALT; Active Sch(Sm): stool/rectal snip w/SchAb; *Note:* All Sm patients had ova in stool/rectal snip	Th2 cytokines (IL-4 and IL-10), were highest in all groups compared with controls, with coinfected patients displaying the highest levels of IL-4 levels; both coinfected and mono Sm infected patients had high levels of IL-10; Mono HCV infected patients displayed the highest levels of Th1 response cytokines (IL-2 and IFN-gamma), while coinfected subjects displayed levels lower than that observed in apparently healthy controls or mono Sm subjects; coinfection of Sm with HCV results in a strong Th2 response that leads to suppression of the Th1 response needed to control HCV infection.
9	Ahmed et al 2008	Al Azhar University, Cairo, Egypt (n.a.)	*Case Control* (comparative, liver functions, severity): Case groups: 16 Sm, 20 Sm w/HCV, and 19 HCV patients, aged 28-60 years, 64% male; Controls: 20 healthy subjects, aged 21-55, 80% male	n.a.	HCV: HCV-RNA; Sch(Sm): stool, SchAb; *Note:* All Sm Patients had ova in stool	All groups had higher mean ALT, AST and alpha-Glutathione-S-Transferase compared with controls; relative to one another; Mono Sch patients had the highest mean values, mono HCV patients had the lowest, with coinfected patients in between; ALT was more strongly correlated with fibrosis in subjects than other biomarkers.

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10	ElSammak et al 2008a	Medical Research Institute Teaching Hospital, Alexandria University, Egypt (n.a.)	*Case Control* (comparative, immunology, severity): Case groups: 22 SHF, 22 HCV and 22 SHF w/HCV patients, mean group ages 48-54 years, 60-64% males; Controls: 22 non-Sch, non HCV, mean age 49 years, 41% male	HBV infection, autoimmune liver disease, alcohol consumption, use of certain medications including contraceptives, malignancy, hypo-thyroid disease, pregnancy and other concomitant acute infection	HCV: anti-HCV w/HCV-RNA; Sch(Sm,Sh): stool, urine, SchAb, SHF/LD: ultrasound; *Note:* Sm ova found in 10 patients, no Sh ova detected; All patients had active HCV infection.	All patients had enlarged liver/spleen; Coinfected subjects had IL-4 levels that were higher than mono-Sm subjects, High IL-4 levels were correlated with greater portal vein diameter, more pronounced fibrosis and portal hypertension; Increased IL-4 secretion may down-regulate Th1 cell-mediated immune effecter mechanisms important in the host defense against HCV infection; Coinfected patients also had higher AST and ALT levels compared with other groups.
11	ElSammak et al. 2008b	Medical Research Institute Teaching Hospital, Alexandria University, Egypt (n.a.)	*Case Control* (comparative, pathology, genetics): Case groups: 22 SHF, 22 HCV, 22 SHF w/HCV, mean group ages 50-54 years, 53% male; Controls: 22 apparently healthy subjects, mean age 51 years, 64% male	HBV, auto-immune hepatitis, metabolic liver disease, Wilson's disease, history of alcohol consumption and malignancy	HCV: anti-HCV, HCV-RNA, Sch(Sm): stool, SchAb, ultrasound; Note: Sm ova found in 10 patients, no Sh ova detected	All patients had enlarged liver/spleen; only 10 subjects found to be excreting Sm eggs, all light infections; Patients with mono HCV had a higher frequency of homozygote Lymphotoxin-alpha (LT-alpha) mutant, while coinfected patients had a higher frequency of LT-alpha heterozygote mutants compared; Lymphotoxin-alpha is a member of the TNF superfamily which may be associated with susceptibility; Patients with mono SHF had a higher frequency of wild-type LT-apha genotype, as did controls; Overall, LT-alpha

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						polymorphisms may play a role in the susceptibility to HCV, but is do appear to affect susceptibility to Sch infection; Additional data is needed on coinfection.