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Revisão

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Association between Schistosomiasis mansoni and hepatitis C: systematic review

Associação entre esquistossomose mansônica e hepatite C: revisão sistemática

ABSTRACT

OBJECTIVE: To perform a systematic review of the prevalence of the HCV/*S. mansoni* co-infection and associated factors in *Schistosoma mansoni*-infected populations.

METHODS: The bibliographic search was carried out using the Medline, Lilacs, SciELO, Cochrane Library and Ibecs databases. The criteria for the studies' selection and the extraction data were based on systematic review methods. Forty five studies were found, with nine being excluded in a first screening. Thirteen articles were used for data extraction.

RESULTS: The HCV infection rates in schistosomiasis populations range from 1% in Ethiopia to 50% in Egypt. Several studies had poorly defined methodologies, even in areas characterized by an association between hepatitis C and schistosomiasis, such as Brazil and Egypt, which meant conclusions were inconsistent. HCV infection rates in schistosomotic populations were heterogeneous and risk factors for acquiring the virus varied widely.

CONCLUSIONS: Despite the limitations, this review may help to identify regions with higher rates of hepatitis C and schistosomiasis association. However, more studies are necessary for the development of public health policies on prevention and control of both diseases.

DESCRIPTORS: Comorbidity. Hepatitis C, epidemiology. Schistosomiasis, epidemiology. Review.

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RESUMO

OBJETIVO: Realizar revisão sistemática sobre a prevalência da confecção do vírus da hepatite C e *Schistosoma mansoni* e os fatores de risco associados a indivíduos com esquistossomose.

MÉTODOS: Revisão realizada nas bases de dados Medline, Lilacs, SciELO, Biblioteca Cochrane e Ibecs. Os critérios de seleção e a obtenção dos dados foram baseados em métodos de revisão sistemática. Foram encontradas 45 referências relevantes, das quais nove foram excluídas na primeira triagem, 14 na leitura dos resumos e nove na leitura completa. Treze artigos foram selecionados para análise.

RESULTADOS: A prevalência da associação entre vírus da hepatite C e *Schistosoma mansoni* variou de 1% na Etiópia a 50% no Egito. Alguns estudos apresentam metodologias pouco definidas, mesmo em áreas caracterizadas pela associação entre vírus da hepatite C e *S. mansoni*, como Brasil e Egito, o que não permitiu conclusões consistentes. As taxas de infecção pelo VHC em populações esquistossomáticas foram heterogêneas e os fatores de risco para adquirir o vírus foram variáveis.

CONCLUSÕES: Apesar das limitações, esta análise pode ajudar a identificar regiões com maiores taxas dessa associação. Outros estudos serão necessários para o desenvolvimento de políticas públicas de prevenção e controle dessas doenças.

DESCRITORES: Comorbidade. Hepatite C, epidemiologia. Esquistossomose, epidemiologia. Revisão.

INTRODUÇÃO

Schistosomiasis is the second most important parasitic infection after malaria and affects more than 200 million people in 74 countries.[56] It is endemic, with high prevalence and morbidity rates in many countries, especially those in Africa, such as Egypt,[18] Kenya[9] and Sudan,[27,44] and in South America, mainly Brazil.[38,a]

The prevalence of schistosomiasis ranged from 15 to 45% in Egypt and Brazil.[18,38,a] In this country, six to eight million people are infected with *Schistosoma mansoni* and about 30 million people live under risk of infection.[a] The prevalence of Schistosomiasis mansoni (SM) can reach up to 27% of the population in some areas of Northeastern Brazil,[38] turning this country into a major schistosomiasis endemic area in the world.

The diverse clinical patterns observed for this disease depend on many factors, including parasite strain, host genetic background, host nutritional and immunological state, and co-infections.[9,10,16,31,35] Schistosomiasis may progress to the most advanced stage of disease, the hepatosplenic form (HS). This clinical form is observed in endemic areas and is characterized by portal hypertension that may cause digestive hemorrhage.[28,42,48] When SM comes combined with other hepatic disease, especially the Hepatitis C Virus (HCV) infection, the progression of hepatic fibrosis into cirrhosis and hepatocellular carcinoma (HCC) can occur within a few years.[29,40] Concomitant SM and HCV infection is observed with high frequency in Egypt[2,7,47] and Brazil.[39]

Hepatitis C is also considered an important public health issue throughout the world, with approximately 3% of people (about 170 million) being infected with the HCV.[1,2] It is also the most important cause of liver disease and HCC in developed countries, including the

[a] Maciel RCR. Enzimas caniculares na forma hepatoesplênica da esquistossomose mansoni [dissertação de mestrado]. Recife: Universidade Federal de Pernambuco; 2006.

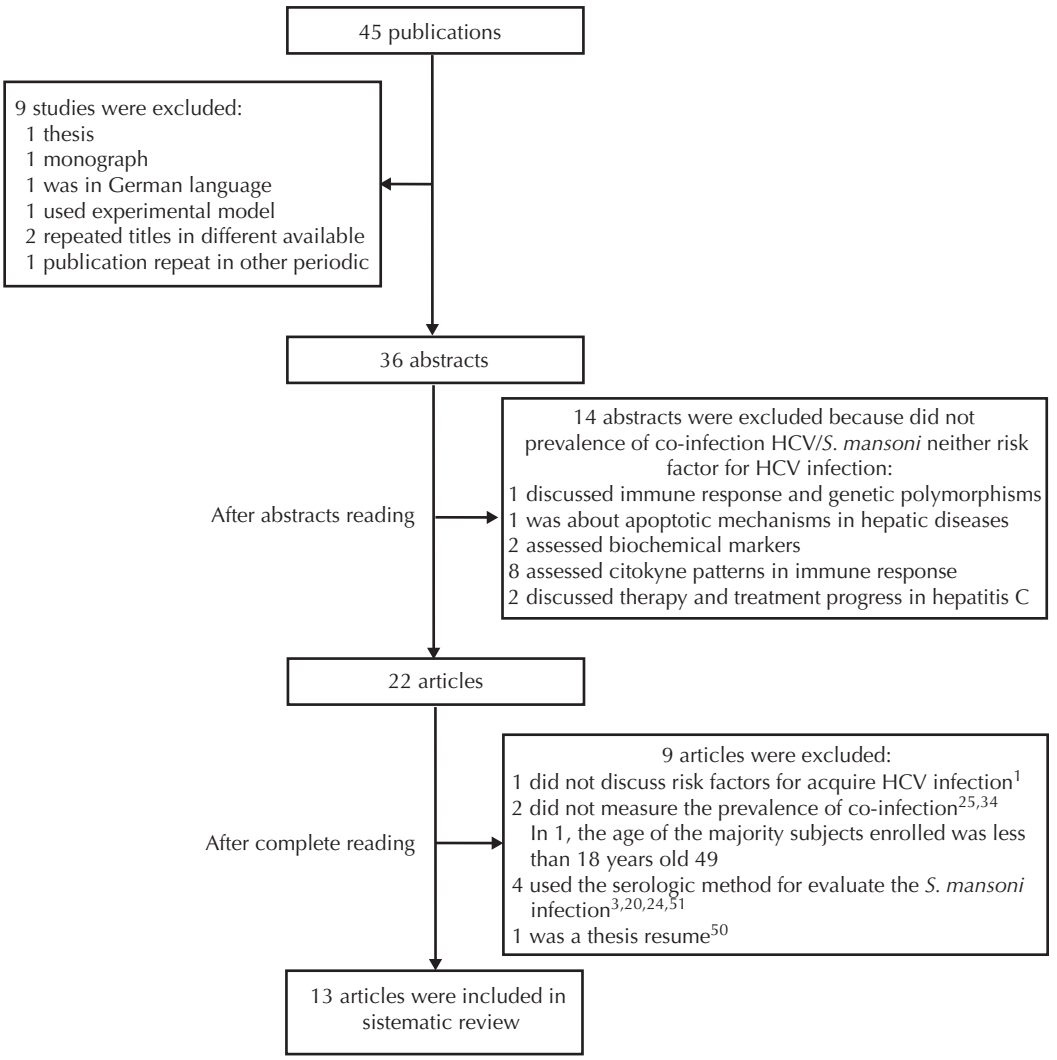

Figure. Flowchart of the systematic review results of selected publications.

United Kingdom and USA,[5,41,53,54] and in developing countries, such as Egypt[2,25,26] and Brazil.[6,39,45]

In Egypt, eight to ten million are infected and 68 million people have been exposed to HCV[52] (a prevalence of 10 to 60%), mainly in rural areas.[15,17,21] The prevalence of HCV infection is lower in Brazil than in Egypt and varies from 2.5% to 4.9%, corresponding to approximately 3.9 to 7.6 million people.[11]

HCV may be implicated as a factor influencing the severity of schistosomiasis in developing countries. Likewise, an influence of SM on HCV severity has been suggested by some authors.[29,33,39]

There are many contradictory data about the prevalence of HCV/*S. mansoni* co-infection in SM endemic areas and the risk factors associated with increased susceptibility for HCV infection in a *S. mansoni*-infected person, especially in the HS form.[2,4,7,49]

The worldwide relevance of the hepatitis C and schistosomiasis association as a public health issue is mainly due to the severe clinical patterns and high morbidity associated with it, especially in developing countries. This study aimed to perform a systematic review of the prevalence of the HCV/*S. mansoni* co-infection in SM-infected population living in endemic areas and associated factors.

METHODS

The bibliographic search was performed through a systematic search covering the 1990s and up to May 2011. The terms "Schistosomiasis mansoni" and "Hepatitis C" were utilized to search the Medline, Lilacs, SciELO, Cochrane Library and IBECS databases. These databases fulfill the minimum criteria search to conduct a systematic review, in accordance with the literature.[22]

Forty-five publications were obtained through the website search described and a first screening was performed. The criteria adopted for inclusion were:

- Studies in scientific article formats published on or after 1989, the year in which HCV was discovered;
- Titles published in English, Spanish or Portuguese with available abstracts;
- Studies performed with human populations.

Nine studies were excluded because they utilized experimental models, were presented as thesis or monograph or were redundant in different databases (Figure).

A second screening was done by analyzing the 36 selected abstracts. Fourteen studies were excluded because they did not contain information about the prevalence of HCV/*S. mansoni* association or the risk factors associated with HCV infection in a schistosomiasis population (Figure).

A total of 22 articles were selected for complete reading. This step was carried out by a pair of reviewers where each one, independently, filled a table with the criteria relevant to the articles selected for data extraction.[14,22] There was no discordance between the two reviewers in regard to the articles selected, with *kappa* index = 1 ($p < 0.05$). The inclusion criteria adopted in this step were:

- Population: subjects of both sexes infected by *S. mansoni* and living in endemic areas;
- Age group: > 18 years old;
- Measurement of HCV/*S. mansoni* association: studies that described the methods utilized to measure the prevalence of HCV and *S. mansoni* infections;
- Risk factors: studies that reported the risk factors associated with HCV infection and if there is a correlation with schistosomiasis.

Studies that used only serologic methods to evaluate the prevalence of *S. mansoni* infection were excluded because the distinction between past and present infection is not possible, raising doubts about the confirmed SM diagnosis.[20]

Of the 22 articles selected for the last step, 13 filled all inclusion criteria and offered data required to analyze the prevalence of hepatitis C and schistosomiasis association in SM endemic areas. The exclusion of the nine articles in the last screening are described in Figure.[1,3,20,24,25,34,49-51]

RESULTS

Table 1, 2 and 3 list the 13 articles that were analyzed.

The prevalence of HCV/*S. mansoni* association ranged from 0.8[37] to 50.0% among the studies, with the highest ranges in Egypt (10 to 50%).[2,9,19,29,30]

Among the 13 articles included in the final step of the review, ten were cross-sectional studies,[8,9,19,29,30,36,37,39,40,45] one was a retrospective cases series,[6] one was a prospective cases series[2] and the other was a cases series with an external control group.[32] Five studies[6,32,39,40,45] were conducted in Brazil, five in Egypt,[2,9,19,29,30] two in Sudan,[36,37] one in Ethiopia[8] and one in Kenya.[9] A higher prevalence of HCV infection was found in the SM population of Egypt, compared to the other countries (Table 1).

Eight studies[2,6,19,32,36,37,40,45] sought to determine the serologic prevalence of HCV infection in an SM population and one study proposed to verify any epidemiologic relationship of schistosomiasis and HBV and HCV serologic markers.[30] Six studies[6,9,29,37,39,40] aimed to evaluate the severity of hepatic lesions and morbidity of hepatitis C when associated with SM and to correlate this with serologic markers. The mean age of humans enrolled in these studies was 33.7 years and in four articles subjects were > 40 years[6,29,32,36] (Table 2).

The inclusion criteria used by the authors to choose subjects with schistosomiasis were mainly: people living in endemic areas with positive parasitological exams confirmed by the presence of *S. mansoni* eggs in stool samples or rectal biopsies (eight studies) and/or ultrasonography (US) compatible with periportal fibrosis (PPF) (six studies). The epidemiological history was considered in seven studies to compose diagnosis when in conjunction with one or both criteria mentioned above.

The main exclusion criteria adopted for the selected studies was if the person did not live at the study site. People with no history of contaminated water contact and/or with liver disease caused by alcohol consumption, autoimmune disorders or by Hepatitis viruses A, B, D or with others etiologies were also excluded from these studies. Six studies did not mention the exclusion criteria adopted.[2,9,19,30,32,36]

The most commonly chosen technique of HCV diagnosis was 3rd generation anti-HCV ELISA, utilized in five studies.[8,9,36,37,45] Four other studies utilized 2nd generation anti-HCV ELISA.[2,19,29,30] The quantification of the viral titers was performed by HCV RNA PCR in seven studies.[6,9,29,36,37,39,40]

Six studies made appropriate epidemiologic and statistical analyses to confirm the correlation between risk factors associated and HCV infection in SM

Table 1. Authors, type of studies and their objectives.

Author	Country	Type of study	Objective
Silva JLA et al[45] (2008)	Brazil	Cross-sectional	To obtain the serological prevalence for HCV in SM patients
Mudawi HM et al[36,a] (2007)	Sudan	Cross-sectional	To determine the prevalence of HCV and identify the most common genotype in patients with HSS
Mudawi HM et al[37,a] (2007)	Sudan	Population based cross-sectional	To determine the HCV prevalence and the risk factors associated, in a population living in SM endemic area
Berthe N et al[8] (2007)	Ethiopia	Population based cross-sectional	To elucidate determinants of morbidity in SM
Blanton RE et al[9] (2002)	Egypt and Kenya	Population based cross-sectional	To compare the severity of hepatic lesions and morbidity in co-infection in two populations with different epidemiological patterns for SM and hepatitis C
Pereira LMMB et al[40,a] (2001)	Brazil	Cross-sectional with an external control group	To analyze the frequency of HBV and HCV markers and to correlate this with severity of hepatic lesions in co-infected patients
Kamal S et al[29,a] (2000)	Egypt	Cross-sectional	To investigate the influence of SM on chronic hepatitis C with respect to the natural course of the disease and others parameters
Aquino RTR et al[6] (2000)	Brazil	Retrospective cases series	To evaluate the frequency and the consequences of the co-infection of hepatitis B and C in patients with HSS
El-Sayed HF et al[19,a] (1997)	Egypt	Cross-sectional	To determine the prevalence of HBV and HCV in a endemic area for SM and the risk factors associated with co-infection
Pereira LM et al[39] (1995)	Brazil	Cross-sectional with an external control group	To investigate the HCV participation in severity of hepatic lesions in SM patients
Abdel-Wahab MF et al[2] (1994)	Egypt	Prospective cases series	To estimate the prevalence and magnitude of HCV infection in Egypt
Kamel MA et al[30] (1994)	Egypt	Population based cross-sectional	To determine the epidemiological relationship between SM and HBV and HCV serologic markers
Lacerda CM et al[32,a] (1993)	Brazil	Cases series with an external control group	To study the HBV and HCV serologic markers in 50 patients with HSS and compare the results with 50 controls

[a] Authors used the logistic regression multivariate method to analyze the risk factors associated with HCV acquisition in an SM population.
HSS: Heaptocellular carcinoma; HCV: Hepatitis C Virus; SM: Shistosomiasis mansoni; HBV: Hepatitis B Virus

patients.[19,29,32,36,37,40] The other articles suggested possible risk factors without any statistical correlation found (Table 3).

Blood transfusion was cited by seven of them as a risk factor for HCV contamination.[2,6,29,32,39,40,45] The second most observed risk factor described in three studies was the antischistosomal mass treatment, due to the use of syringes and nosocomial equipments without proper sterilization.[2,19,29] Surgical procedures,[19,29] digestive endoscopy,[45] old age,[9,19] genetic background[9] and hemodialysis[2] were also cited as risk factors for HCV acquisition. Four studies did not find any association between SM infection and an increased risk of acquiring HCV.[8,30,36,37]

DISCUSSION

Schistosomiasis is an important public health issue associated with poverty and poor sanitary conditions.[13] All studies described were conducted in developing countries since the 1970s, especially in Egypt, Sudan, Ethiopia, Kenya and Brazil, confirming the impact of this disease in these countries.[13] The association between schistosomiasis and hepatitis C has been studied by many authors, showing the importance of research into this condition worldwide (Tables 1, 2 and 3).

The majority of articles were cross-sectional studies (Table 1) and aimed to determine the prevalence of HCV infection in a confirmed SM population. Cross-sectional studies are important in identifying regions in developing countries that need more attention from the government authorities for the implementation of public health policies in regards to treatment and control for both hepatitis C and SM. On this point, this review may help to identify regions where the association of these diseases and the risk factors associated with HCV infection are relevant, and to aid the implementation of prevention and control actions.

Table 2. Systematic review of results of Hepatitis C Virus and *Schistosoma mansoni* diagnosis and prevalence of Hepatitis C Virus/ *mansoni* association.

Population size	Population characteristics	HCV diagnosis	SM diagnosis	Prevalence of Association
184 subjects[45]	41.3% male	Anti-HCV ELISA 3rd generation	Not mentioned	11.9%
176 subjects[36]	81.3% male Mean age = 41.4	Anti-HCV ELISA 3rd generation HCV RNA PCR and genotype	Clinical and history examinations Ultrasonography (US) with periportal fibrosis (PPF)	4.5% for anti-HCV 2.3% for HCV RNA PCR
410 subjects[37]	45% male Mean age = 35 91% have SM infection	Questionnaire Anti-HCV ELISA 3rd generation HCV RNA PCR	Presence of ova in stool samples Epidemiological history	2.2%
2.451 subjects[8] 1.615 SM infected	52.1% male Mean age = 18.8	Anti-HCV 3rd generation	Kato-Katz Questionnaire US	21-30 years old = 1.6% 31-40 = 0.8% > 40 = 1%
237 Kenyans[9] 112 Egyptians	Mean age Kenyans: 33.1 Mean age Egyptians: 34	Anti-HCV ELISA 3rd generation RT-PCR	Parasitological exams US	Egyptians: 39.7% Kenyans: 11.3%
234 subjects[40] 50 controls	Mean age: 39 55.1% male; 44.9% female	Anti-HCV HCV RNA PCR	Clinical examination Presence of eggs in stools or rectal biopsy	20% for anti-HCV 12.4% for HCV RNA PCR
126 subjects[29]	84 men (66.6%) Mean age = 43 Group A (n = 33): HCV infection; mean age = 44.2 Group B (n = 30): Schistosomiasis; mean age = 38.2 Group C (n = 63): co-infection; mean age = 41.5	Anti-HCV ELISA 2nd generation HCV RNA PCR	Presence of eggs in stool or rectal biopsy Epidemiological history	50%
101 HSS patients[6]	Mean age: 40.31 42.6% male 75.8% Caucasian; 8.1% black; 16.2% mixed ethnicity	Anti-HCV HCV RNA PCR	History and clinical examinations Medical records	12.9%
506 subjects[19]	Mean age: 20 52% male; 48% female	Anti-HCV ELISA 2nd generation	Kato-Katz technique US	10.3% 28% in people more than 40 years old
215 patients[39] 50 controls	SM: 43 with HIS 173 with HSS 115 male (53.4%) Mean age = 38 Controls: 21 male (42%) Mean age = 45	Anti-HCV ELISA anti-core and NS3/ NS4 Nested PCR	History examination Presence of *Schistosoma* eggs in stools or rectal biopsy Liver biopsy	22% in patients 2% in controls
354 adults[2]	Patients admitted to Kasr El Aini Hospital, in Cairo, for chronic hepatic diseases evaluation	Liver function tests, liver biopsies Anti-HCV ELISA 2nd generation	History examination Liver function tests US Liver biopsies	32.9% 77% were male
1,550 subjects[30]	Mean age = 20.2	Anti-HCV ELISA 2nd generation in duplicate samples	Kato-Katz US compatible with PPF	15.3%
50 HSS patients (G1)[32] 50 controls (G2)	G 1: SM patients, 46% male; mean age = 41 G 2: 42% male; mean age = 44.4	Anti-HCV ELISA 1st generation	Medical records	20%

RT-PCR: real time – polymerase chain reaction; HCV: Hepatitis C Virus; SM: Schistosomiasis mansoni; HSS: Hepatosplenic schistosomiasis; HBV: Hepatitis B Virus; HCC: hepatocellular carcinoma; HIS: hepato intestinal schistosomiasis

Table 3. Risk factors, results and conclusion of studies selected.

Risk factors for HCV	Results	Conclusion
Blood transfusion[45] Digestive endoscopy	90.5% of co-infected had HSS form 54.5% received blood transfusion	Blood transfusion and endoscopy history are associated with the increase of HCV prevalence in HSS form.
No risk factor[36,a]	Genotype 4 was the most prevalent in HS patients. The parenteral therapy was not associated with co-infection	The HCV prevalence in HS patients is considered low (4.5%) and the genotype 4 is the most common in Sudan.
No risk factor[37,a]	91% had SM 11.2% had anti-HCV+, only 2.2% were HCV RNA PCR+ Between 21 and 40 years old, the anti-HCV reactivity was 7.8%	HCV infection has low prevalence in Sudan and the anti-SM parenteral therapy cannot be associated with co-infection.
No risk factor[8]	65.9% were positive for SM 1.3% subjects with SM were positive for HCV The highest prevalence was found among children	It is necessary to integrate helminth control targeting school-aged children to reduce the risk of PPF in future.
Age older[9] Genetic background	OPG mean was higher among the Kenyans than Egyptians The PPF pattern was higher among Egyptians Hepatitis C is 3 times more prevalent among Egyptians	Geographical differences are observed in relation to PPF patterns among the two populations. HCV is associated with active infection only among Egyptians, who present more severity and morbidity for co-infection.
Blood transfusion[40,a]	57% were positive for HBV or HCV or both	HCV infection may contribute to severity of liver damage when the subject has the HSS form.
Anti-SM therapy (76%)[29,a] Blood transfusion (22.2%) Nosocomial exposure	The mortality in group C was 48% after 6 years in comparison with group A (12%) and B (3%). HCC is most frequent in co-infected (33%) patients than mono-infected. Mortality was not affected by age, HCV RNA titer or genotype virus	Patients co-infected are characterized by more advanced liver disease, higher HCV RNA titers, predominance of HCV genotype 4, higher inflammatory activity, incidence of cirrhosis and HCC with much higher mortality rate.
Blood transfusion[6]	84.6% of anti-HCV+ had HCV RNA PCR+ with high aminotransferases, more cell decompensation and high rate of chronic hepatitis	The rate of hepatitis B and C markers in HSS patients is higher than control group and it is responsible for a high frequency of liver damage.
History of surgeries[19,a] Anti-SM parenteral treatment	Anti-HCV was positive in 10.3% of subjects and 5% was positive for anti-HBV and anti-HCV	Hepatitis B and C are the major public health problems in Egypt. Studies about epidemiology, natural history, risk factors and modes of transmission are necessary.
No significance between groups was found for blood transfusion[39]	The HCV prevalence in co-infected group was higher (22%) than in control group (2%). 61.7% of co-infected had HCV-RNA circulating with high levels of liver enzymes, especially in HSS decompensated form	Co-infection is a major factor contributing to the severity of liver disease in chronic SM and active replication of the virus in the liver or at extra-hepatic sites is strongly associated with severe liver disease.
Blood transfusions[2] Hemodialysis Anti-SM parenteral treatment	The prevalence of anti-HCV was 46% in renal chronic patients, 22.1% in soldiers and 47.2% in chronic hepatic diseases	HCV infection prevalence is high in Egypt, especially among patients with liver disorders. More studies are necessary to confirm this transmission route.
No risk factors[30]	About 1550 samples examined by Kato-Katz technique, 49.1% were positive for SM. The anti-HCV was + in 15,9%, and increases with age	No relationship among HBV or HCV and *S. mansoni* infection is found in those living in endemic area for SM, with statistical significance.
Blood transfusion[32,a] Sporadic contamination	Prevalence of HCV serologic marker was 20% in group 1 and 4% in group 2. Among 10 HSS patients, 7 had received blood transfusion	A high prevalence for anti-HCV markers is found in SM patients in comparison with healthy people.

[a] Authors who used the logistic regression multivariate method to analyze the risk factors associated with Hepatitis C Virus acquisition in a Schistosomiasis mansoni population.
PCR: polymerase chain reaction; HCV: Hepatitis C Virus; SM: Schistosomiasis mansoni; HSS: Hepatosplenic schistosomiasis; HBV: Hepatitis B Vírus; HCC: hepatocellular carcinoma; HS: hepato schistosomiasis; PPF: periportal fibrosis; HSS: Hepatosplenic schistosomiasis

A few studies pointed to a correlation between diseases with morbidity patterns, progression of liver damage[29,39] and risk factors[2,6,9,19,29,30,36,37,39,40,45] in acquiring HCV. It could be useful to understand the clinical course of this particular condition and for treatment choices (Tables 2 and 3). When schistosomiasis and hepatitis C association is established, the clinical course develops into severe hepatocellular damage. Viral persistence and hepatic cirrhosis can develop faster than in mono-infected people.[6,29]

The high percentage of HCV infection in schistosomiasis populations of different countries caught the attention of the scientific community for the variable prevalence of disease association rates.[8,19,36,37,40,45] The rates ranged from 10 to 50% in Egypt,[2,9,19,29,30] mainly due the mass treatment of the schistosomiasis infected population in the 1970s. This public policy was not adopted in other countries and similar prevalence rates cannot be observed.[8,36,37] There is a lack of a relationship between the high prevalence of HCV infection in schistosomiasis endemic areas and risk factors, although many of them were.

Disease association rates in Brazil, although not as high as in Egypt, can be considered relevant due to the high morbidity when HCV is present. When the study was conducted with hospital patients in Brazil, disease association rates were up to 20%.[32,39,40] Conflicting results among studies on HCV/*S. mansoni* association in Brazil,[6,40,45,46,b] reinforce the need for further studies of this condition, especially with appropriate methodologies for prevalence and risk factor evaluations. Methodological issues are the main problem of the majority of studies worldwide, suggesting the inadequacy of study designs.

The serologic method was the most commonly used method of evaluating HCV infections, including recently developed techniques adapted from the older versions. The 3rd generation ELISA is performed by many research groups, since it is a fast and relatively cheap technique.[8,9,36,37,45] Some authors reject this method because, in *S. mansoni*, infection could produce auto-antibodies against HCV epitopes, mimicking HCV infection.[3] However, this immunoglobulin (Ig) production is not well defined in the literature and the auto-Ig's ratios are low, which can be differentiated from HCV infection by increasing the cut-off point. As for schistosomiasis diagnosis, the method of choice continues being Kato-Katz test, based on the presence of *S. mansoni* eggs in stool samples or in rectal biopsies, and US patterns to evaluate the periportal fibrosis.[43,55] This review confirms that no significant diagnosis methods have been developed for either disease over the last decades.

The current systematic review also considered risk factors associated with an increased chance of acquiring HCV infection when the subject has SM.[19,29,32,36,37,40] These data may be useful to direct monitoring and treatment campaigns for both diseases and may contribute to lower prevalence and morbidity rates in the future.

Blood transfusion was the risk factor most cited[6,32,39,40,45] in Brazil and the anti-schistosomiasis parenteral mass therapy,[2,19,29] in Egypt. Poorly sterilized syringes and equipment used during these campaigns[21,26] may be the key to increased chances of acquiring HCV.

In the HS schistosomiasis form, common in endemic areas, the subject presents esophageal varices in most cases as a consequence of periportal hypertension and disease severity in SM.[43] Disruption of these veins can cause digestive bleeding and blood transfusion may be required for patient survival.[b]

The serological screening in Brazilian blood banks did not include anti-HCV markers before 1993, in spite of the recent discovery of HCV. Blood transfusion before this year can be considered as a risk factor for HCV acquisition.[12] The lack of proper sterilization of equipment and reused syringes during anti-schistosomiasis parenteral mass therapy[21,23] increases the chance of HCV infection in SM patients in Egypt. The causes of HCV infection are different among the countries and in most cases the public policies are adopted as a reflex.

In most articles, the risk factors were based on patient reports and epidemiological history, without significant statistical analyses. More studies are needed to clarify HCV transmission routes and risk factors for HCV/*S. mansoni* association. The last study on this issue was published in 2008, pointing to the lack of research in this area.

In conclusion, this revision shows the lack of well-designed studies with appropriate methodology for evaluating the prevalence of this condition in areas of endemic schistosomiasis. Despite the limitations of this study, the results may help to identify regions with higher HCV/*S. mansoni* association rates. New public health policies attempting to reduce the current high prevalence and morbidity rates observed in hepatitis C and schistosomiasis could be proposed, especially in SM endemic regions.

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