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Absence of relationship between *Schistosoma japonicum* and hepatitis B virus infection in the Dongting lake region, China

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SUMMARY

In order to determine whether infection with *Schistosoma japonicum* is related to a higher rate of infection with hepatitis B virus and/or to a higher probability of HBsAg chronic carriage, a population based survey was carried out in China in which HBV markers were studied in 112 subjects with long-lasting *S. japonicum* infection, and 93 subjects with no *S. japonicum* infection 37·5% of the cases and 40·9% of controls showed no markers of HBV infection. The prevalence rate of HBsAg was 12·5% in the cases and 12·9% in the controls. For anti-HBc and anti-HBs the figures were 59·8% and 59·8%, and 27·9% and 35·0%, respectively. These data do not support the hypothesis of an interaction between infection with hepatitis B virus and *S. japonicum*.

INTRODUCTION

Schistosomiasis japonica and hepatitis B virus (HBV) infection are two of the major causes of liver disease in China, where an estimated 11 million people are infested with *Schistosoma japonicum* and with an HBsAg carrier rate of 10·3% [1]. Whether there is a specific association between schistosomiasis and HBV infection is a subject of great controversy. A high frequency of co-infection of chronic type B hepatitis with schistosomiasis has been found in persons hospitalized in Brazil [2], Egypt (*Schistosoma mansoni*) [3, 4] and China (*S. japonicum*) [5, 6]. Patients with both diseases had a worse prognosis than those with schistosomiasis alone. However, field-based studies have failed to support an association between the two infections [7–10].

One idea that would resolve the difference between hospital based and field based studies is that schistosome infected patients may be more vulnerable to the severe consequences of HBV infection rather than more susceptible to infection *per se*. Since patients with schistosomiasis show some evidence of immunosuppression [11], it has been suggested that they may be especially vulnerable to liver injury with chronic hepatitis B infection [2, 12, 13]. This suggestion cannot be adequately examined in hospital studies of persons with decompensated liver disease, because such samples are biased toward inclusion of patients with advanced chronic hepatitis.

The specific aims of this study were to determine whether infection with *S. japonicum* is related to a higher rate of infection with HBV and/or to a different host response to this agent (higher probability of HBsAg chronic carriage). To test this hypothesis, we carried out a controlled population based survey in China.

MATERIALS AND METHODS

A village in the Dongting lake region, China, was selected. The mean egg count on 3 consecutive days was obtained using a modified Kato thick smear [14].

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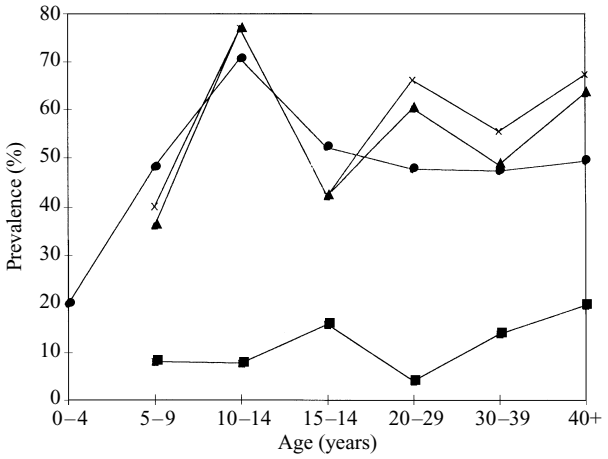

Fig. 1. Percentage prevalence of hepatitis B virus (HBV) serological markers and schistosomiasis in 205 subjects, the Dongting lake region, China: ●, positive for schistosomiasis; ■, carrying HBsAg; ×, exposed to HBV (positive for one or more markers); ▲, positive for anti-HBc.

S. japonicum infected study subjects described here did not receive mass-antischistosomal treatment during 1992–5, but all were free to seek treatment through the existing health services in or near their villages. All subjects were identified in house-to-house surveys; none were 'patients' in the sense that they sought medical care because of illness.

Intravenous blood was drawn, sera separated and kept frozen until the tests were performed. Sera were tested for HBsAg, anti-HBs and anti-HBc using the enzyme immunoassay kit (Hepanostika, Belgium) without knowledge of the parasitological status of the subjects. If the HBsAg test was positive, the sera was tested again by using HBsAg confirmatory reagents (Hepanostika). The data were analysed using epi-info6 software.

RESULTS

Prevalence of *S. japonicum* was highest in those aged 10–14 years and lowest in those aged 0–4 years (Fig. 1). The exposure rate to HBV (positivity of one marker or more) was 60·4%, the carrier rate of HBsAg was 12·7%. There was significant association between age and exposure. The carrier rate of HBsAg, expressed as the ratio of carrier : exposed, was high in the young (Fig. 1). The rate of exposure to HBV also reached a peak within the age range 10–14 years.

The pattern of HBV markers was similar in *S. japonicum* positive group and negative group. The absence of exposure to HBV as expressed by the negativity for the HBV serological markers was 37·5% in the cases and 40·9% in the controls. The prevalence rate of HBsAg was 12·5% in the *S. japonicum* positive subjects and 12·9 in the negative subjects. For anti-HBc and anti-HBs the figures were 59·8% and 59·8%, and 27·9% and 35·0%, respectively (Table 1).

DISCUSSION

The association of HBV and *S. japonicum* infection is an issue of concern of more severe morbidity and higher mortality may result compared with either infection alone [15]. In contrast to earlier assessments of the relationship between HBV markers and *S. japonicum* infection, which showed a strong association between them [5, 6], our study used a population based approach rather than starting with patients selected on the basis of disease manifestation. Our negative results provide useful evidence that *S. japonicum* infection is not an important risk factor for HBV infection and its evolution to chronicity. These findings are consistent with the reports investigating the relationship between HBV markers and *S. japonicum* [16], and *S. mansoni* [8, 9] using a similar study design.

Studies of hospital patients suffer from a potential bias because concurrent infection with schistosomes and hepatitis may produce medical care seeking behaviour. Another problem is lack of an appropriate control group [17]. The high prevalence rate of HBsAg found by others in *S. japonicum* cases associated with the most advanced form of the hepatic disease [5, 18] might only confirm the notion that HBsAg is a risk factor for chronic liver disease. It might seem obvious that if the periportal granulomatous lesions due to *S. japonicum* are associated with primary hepatocytic lesions due to HBV, the hepatic pathology and function would be worse than with the *S. japonicum* related lesions alone. This is also suggested by pathological studies done in West African subjects infected with *S. mansoni* [19]. One of the observations made in China has also suggested that prior parenteral treatment with antischistosomal drugs may be a major risk factor for acquisition of concomitant HBV infections [20]. Treatment of schistosomiasis is now based on oral drugs. There is now no risk of hepatitis through parenteral treatment.

Despite its limitations due to sample size, we believe the present study offers the strongest evidence to date that infections with *S. japonicum* and HBV do not interact with respect to infection rate.

Table 1. *Hepatitis B virus serological markers in* 205 *subjects classified by stool examination, the Dongting lake region, China*

	No. HBsAg positive	No. Anti-HBsAg positive	No. Anti-HBcAg positive
S. japonicum positive	14/112 (12·5%)	35/100 (35%)	67/112 (59·8%)
S. japonicum negative	12/93 (12·9%)	24/86 (27·9%)	49/93 (52·7%)
P-value	0·931	0·303	0·307

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