

HEPATITIS E IN SINGAPORE - A SEROPREVALENCE STUDY

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ABSTRACT

The seroprevalence of anti-HEV IgG was determined in a hospital-based population in a general medical unit. Patients who were otherwise well but admitted for acute, non-hepatological conditions represent the "healthy" general population, and those admitted primarily with liver disorders were studied. The seroprevalence of anti-HEV IgG was found to be 10.5% in the "healthy" population and 14.7% amongst those with liver diseases. The lack of travel history and past history of jaundice suggests presence of local cases and subclinical manifestation in some of the infected patients.

There is an association between seroprevalence of hepatitis A and E, suggesting common predisposing factors for both infections. Anti-HAV IgG has a higher seroprevalence. Retesting of anti-HEV IgG in those who were initially positive found persistence of antibodies beyond twelve months. Both anti-HAV IgG and anti-HEV IgG were found more commonly in the older age groups.

Keywords: seroprevalence, anti-HEV IgG, hepatitis A, subclinical infection

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INTRODUCTION

Since the first documentation of hepatitis E as an enterically-transmitted non-A, non-B hepatitis (ET-NANB) epidemic in Kashmir Valley in 1980⁽¹⁾, it has been reported from the Soviet Union, Ethiopia, Nepal, Burma, Mexico, etc indicating its association with ingestion of contaminated water^(2,3). However, it is only recently recognised that people from the developed countries are not spared from the infection. Travellers from the UK⁽⁴⁾ and USA⁽⁵⁾ have been affected. A seroprevalence of up to 3% was found in patients with non-A, non-B, non-C hepatitis in the Netherlands⁽⁶⁾.

Until mid-1994, it is not our routine clinical practice to look for hepatitis E in our patients. This may be due to an assumption of its non-existence in this country. A seroprevalence study in therefore carried out to clarify this impression.

We would like to determine if our patient population is exposed to the hepatitis E virus and if so, to determine the persistence of the antibodies and thus their protection against reinfection. By determining the patients' travel history, we attempt to determine if there were any local cases of hepatitis E.

As both hepatitis A and E are transmitted by oro-faecal route, serological association of the two viruses are determined.

METHODOLOGY

As this is a hospital-based study and to minimise skewed data, we selected patients who have been previously well and admitted at the time of study for some acute illnesses to reflect as closely

as possible the healthy general population. We are also curious to know if the presence of one liver illness, particularly viral hepatitis, predispose the patients to develop another. Therefore, we also looked particularly into our population of patients who were admitted for liver diseases to determine if they have a higher seroprevalence of hepatitis E than the general population.

Two hundred and nineteen patients were randomly selected from two groups of patients admitted to the Department of Medicine II, Singapore General Hospital between June and September 1993. Group 1 consists of patients who were admitted for acute, non-hepatological conditions and who had been otherwise well. All of them do not have past history of significant medical illness other than a few who had simple illnesses which were previously managed by their primary health care providers in the community. They represent the "healthy" population. Patients with abnormal liver function tests results were excluded from this group. Group 2 consists of patients who were admitted to the hospital primarily for hepatological conditions.

All patients' sera were tested for anti-HEV IgG (ELISA, Genelab) and anti-HAV IgG (EIA, Abbott Laboratories). Those who tested positive were called back one year later for repeat testing of anti-HEV IgG. History of travel prior to admission to the hospital and past history of jaundice in the "healthy population" were specifically asked for.

RESULTS

Group 1 consists of 124 patients, 66 males and 58 females, aged between 14-95 years (median 50 years). Thirteen of them (10.5%) tested positive for anti-HEV IgG and 92 of them (74.2%) tested positive for anti-HAV IgG. All anti-HEV IgG positive patients also tested positive for anti-HAV IgG. Thirteen of the 92 patients (14.1%) who tested positive for anti-HAV IgG also tested positive for anti-HEV IgG. There was no statistically significant difference in the frequency of travel between the anti-HEV IgG positive (90%) and the anti-HEV IgG negative (71.6%) groups of patients. None of those who tested positive for anti-HEV IgG could recall any past history of jaundice.

Group 2 consists of 95 patients, 68 males and 27 females, aged 18 - 87 years (median 52 years). Seventeen had acute hepatitis, 48 were hepatitis B carriers and 30 had other liver diseases. Of the 95 patients, 14 (14.7%) were found to be anti-HEV IgG positive (Table I) and 71 (74.7%) tested positive for anti-HAV IgG. Ten patients had IgG antibodies for both hepatitis A and E. The majority of the patients had history of travel - 88.9% and 78.7% in the anti-HEV IgG positive and negative

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Table I – Seroprevalence of anti-HEV IgG in patients presenting primarily with hepatic disorder (ie Group 2 patients)

Diagnosis of various subgroups	No. of patients	No. with positive anti-HEV IgG(%)
Acute hepatitis	17	3 (17.6%)
Hepatitis B related disease	48	5 (10.4%)
Other chronic liver diseases	30	6 (20%)

* No statistically significant difference in seroprevalence of anti-HEV IgG was found in various subgroups.

patients respectively (NS).

We managed to trace 10 of the anti-HEV IgG positive patients, including one who had acute NANBNC hepatitis, for repeat study after a lapse of 12 months. Nine remained strongly positive for anti-HEV IgG and 1 tested weakly positive for the antibody.

DISCUSSION

Our study has shown significant seroprevalence rate of anti-HEV IgG in our population. While it is a study that is confined to the hospital population, it is probably representative of the Singapore population as the seroprevalence of anti-HAV IgG obtained in this study is similar to that found by Yap et al⁽⁷⁾. So far, while we cannot be certain of where our patients acquired the infection, the fact that anti-HEV IgG was found in some patients who had no history of travel would suggest that there could be cases of locally-acquired infection. It is interesting to note that none in Group 1 who tested positive for hepatitis E had past history of jaundice or acute hepatitis, suggesting the possibility of subclinical infection.

The co-existence of anti-HEV IgG and anti-HAV IgG in our "healthy" population is interesting. Looking at the results, we can conclude that the seroprevalence rate of anti-HEV IgG is 13.7% amongst the patients who had hepatitis A but 0% in those who never had hepatitis A ($p < 0.05$). This may indicate common predisposing factors in both diseases which are known to be transmitted by oro-faecal route. Hepatitis A is, however, a commoner condition in Singapore with a higher seroprevalence rate. The predilection of anti-HEV IgG exclusively in the anti-HAV IgG positive population is however not seen in patients with any history of liver diseases. Other factors, therefore, may be involved in rendering this group of patients susceptible to hepatitis E. For example, seroprevalence of anti-HEV IgG is highest in the subgroup of patients with "other liver diseases", where 60% were made up of patients with alcoholic liver diseases. It is well-known that alcoholics are prone to develop various medical conditions. The commonly associated poor social condition in this group of patients may be a contributing factor, as hepatitis E is transmitted by contaminated water and is prevalent in places with poor sanitary condition.

As in the case of hepatitis A, positive serology for hepatitis E tends to occur in the older age group (Fig 1a and b), suggesting that its prevalence may be related to the socio-economic development and sanitary condition of a country. Therefore, like hepatitis A, we would expect to see fewer local cases of acute hepatitis E. Nevertheless, hepatitis E will remain as a condition of concern to us as Singaporeans travel more frequently and to more exotic places where the standard water supply is suboptimal.

While we managed to demonstrate that the anti-HEV IgG can persist for a minimum of at least one year, it is worth noting that the seroprevalence rate in our study dips after the fifth decade. This may support the observations that the anti-HEV IgG may

Fig 1a - Percentage of patients who were positive for anti-HEV IgG in each age group (Group 1/"healthy" patients)

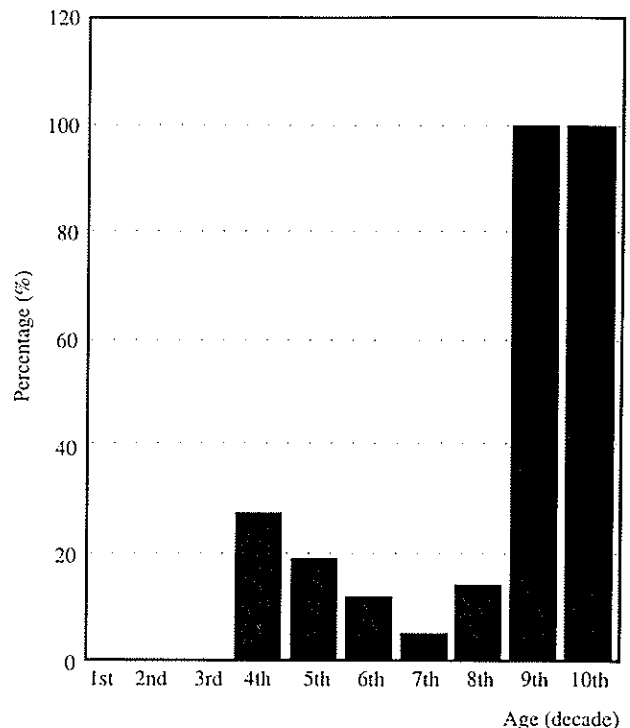
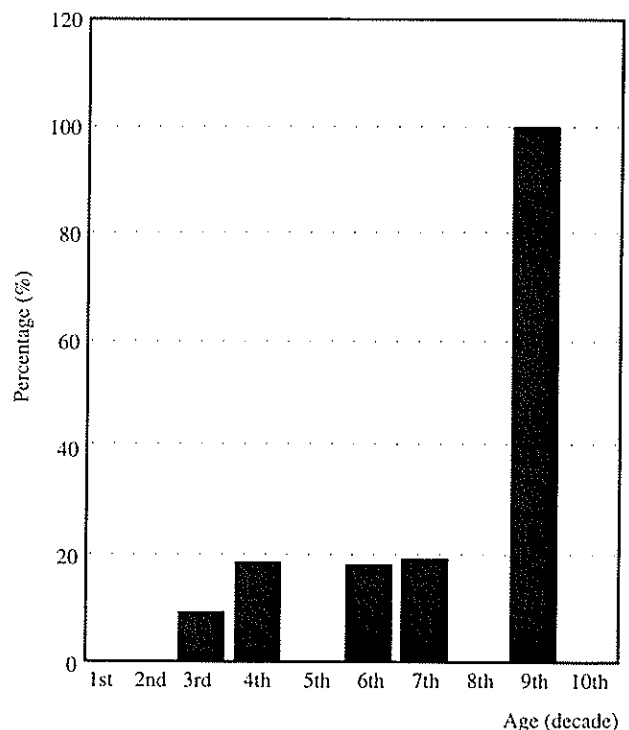


Fig 1b – Percentage of patients who were positive for anti-HEV IgG in each age group (Group 2/liver disease patients)



be lost some time after the infection and hence unable to provide protection against reinfection^(8,9). Further study will need to be carried out in this aspect.

CONCLUSION

The seroprevalence rate of anti-HEV IgG in our population is about 10% to 15%. There is no statistical significant difference in the seroprevalence between the healthy population and those

with underlying liver disease, though the predisposing factors for infection may differ. In those who have no underlying liver disease, susceptibility to hepatitis A is associated with susceptibility to hepatitis E. Whereas, if the patients have a history of liver disease, the risk of acquiring hepatitis E may be independent to that of hepatitis A, and it is likely to be more so in those with alcoholic liver disease.

There may be local cases of hepatitis E and the infection may be subclinical. This will require verification in subsequent studies.

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