

Seroprevalence of Hepatitis A virus markers in Eastern Saudi Arabia

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ABSTRACT

Objectives: To record and update the sero-epidemiological status of Hepatitis A virus in Eastern Saudi Arabia. To investigate the main viral etiology of clinical hepatitis in children and discuss the possibility of introducing a Hepatitis A virus vaccine in this Province.

Methods: Examining serum specimens by Enzyme Linkage Immuno-Sorbet Assay technique for these parameters: Immunoglobulin M anti-hepatitis A virus, total immunoglobulin anti-hepatitis A virus, and in selected cases we checked for hepatitis B surface antigen and anti-hepatitis C virus. The study was carried out in the Virology Diagnostic Labs, of Dammam Regional Laboratories & Blood Bank, Dammam. A total of 12,357 serum samples were collected from 5876 healthy children, 5798 healthy adults, and 683 from clinically diagnosed hepatitis in children. The period of study was 12 years from February 1987 to January 1999.

Results: Hepatitis A virus prevalence showed 3% for pre-school age, 80% in older children and 93% in adults, while total prevalence was 86%. Breaking down the prevalence among children showed 3% in the <6 years age group, 62% in the 6 - <8 years age group, 71% in the 8 - <10 years age group, 83% in the 10 - <12 years age group

and 93% in the 12 - <18 years age group. While the grand total among children was 78%. The prevalence of hepatitis B viruses causing clinical hepatitis in children showed: 65% for hepatitis A virus, 21% for hepatitis B virus, 7% for hepatitis C virus, 2% for double infection of hepatitis B virus + hepatitis C virus and 5% for non A, non B, non C.

Conclusion: Hepatitis A virus infection starts dramatically high in school-age children, and then rises gradually with an increase in age. This reflects that our region is of pattern I class. There is no difference in the prevalence due to seasons of year, climate or sex. Hepatitis A virus is the leading cause of clinical hepatitis in children, followed by hepatitis B virus and hepatitis C virus. There is a possibility of starting to introduce hepatitis A virus vaccine among pre-school age children, as well as among hepatitis A virus negative adults that live in a higher socioeconomic environment within the country, which can be considered as islands of pattern II among pattern I areas.

Keywords: Hepatitis A virus, vaccination.

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Hepatitis A virus (HAV) is a picorna virus, which was discovered by Feinstone in 1973.¹ Hepatitis A virus is a non-enveloped virus, 25-28 nm in diameter, containing single stranded ribonucleic acid, and usually described as Enterovirus type 75.² Hepatitis A virus is primarily transmitted through fecal contamination of food or drink by the oral route. However, although post transfusion hepatitis A is uncommon, it has been increasingly documented

in recent years, often as a source of nosocomial outbreaks in hospitals.³⁻⁵ Nevertheless, this mode of infection is unusual as long term HAV carriage has not been demonstrated and the viraemic phase is relatively short around 7-10 days with a maximum of two weeks.^{6,7} Hepatitis A virus occurs endemically all over the world, independent of the climate.² The exact incidence of HAV infection is difficult to estimate due to the high proportion of asymptomatic,

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anicteric infections, difference in the surveillance and in the different patterns of the HAV disease. Hence, the degree of under reporting is known to be very high. However, analyzing data from the prevalence rates in different parts of the world revealed the presence of the following epidemiological patterns.⁸ Pattern I, occurs in developing poor countries with low socioeconomic conditions and with prevalence rate of up to 99% of the adult population. Pattern II, usually starts by middle age, while infants and children are less exposed than in pattern I. This pattern appears in many developed countries in Europe and the United States of America (USA) due to the high standards of hygiene and sanitation, such groups show a high number of non-immune young adults. Pattern III occurs in areas which are not exposed to the HAV during the early stage of life and the disease is usually acquired later with travel to endemic countries. This pattern is seen in highly developed countries with very high standards in sanitation and hygiene, as in Northern European countries such as Sweden.⁸ Despite massive information about HAV infectivity, its epidemiology is constantly changing throughout the world due to improving water supplies and sanitation conditions.^{6,8} People are actually shifting from pattern I to II, and those of pattern II are moving to pattern III. This means that the young populations (infant and children) will be less exposed to HAV during their childhood, while the older ones become more susceptible. Diagnosis of HAV infection has been readily established by the detection of anti-HAV IgM and anti-HAV IgG in the blood serum of the affected individual, and correlating them with the clinical picture.^{9,10} It is a well known debate about the cytopathic effect of the HAV on hepatocytes, some authors suggest that the HAV infection pathology is due to a T-cell mediate immunological mechanism, while others related it to the direct cytopathic effect of the virus itself.^{11,12} There is also a possibility of a relationship between HAV and the development of insulin-dependent Diabetes Mellitus, though this theory is not yet settled.¹³ Many worldwide studies have been published on HAV infection and all the international data has stated that HAV prevalence is closely related to poor hygiene conditions, and low socioeconomic status.¹⁴⁻²⁴ Some studies⁸ have predicted the possibility of eradication of HAV infection after the successful introduction of HAV vaccines in developed countries, and they are looking to see the eradication of this virus infection in the same way as the Poliomyelitis virus after the expanded vaccination program of polio-vaccines. The aim of our study is to record the new epidemiological status of HAV in this part of the world, and the possibility of the introduction of an HAV vaccine in certain groups of the population, especially in those with high cultural and socioeconomic status in Saudi Arabia, as a result of

improved hygiene that shifts pattern I category (in some selected areas) to pattern II or even pattern III. The aim of this study is also extended to investigate the main etiology of hepatitis as a clinical disease among children.

Methods. Subjects. For 12 years (February 1987 to January 1999) a total of 12,357 samples of serum were obtained from the following subjects: 5876 samples were collected from healthy children (<6 - <18 years, mean age 12 years) of both sexes, from Primary Health Care facilities, Dammam Central Hospital, and Maternity and Children Hospital in Dammam. These subjects were chosen at-random. Five thousand, seven hundred and ninety eight samples were collected from healthy adult male blood donor's from Dammam Regional Blood Bank, and from healthy pregnant woman attending antenatal care facilities in Primary Health Care Centers, Dammam. The age group was (18 - < 50 years, mean age 34 years) for both groups. Six hundred and eighty three specimens from children clinically diagnosed as having hepatitis, these patients were diagnosed in Dammam Central Hospital and other hospitals in the Dammam vicinity, the mean age was 12 years for both sexes. All of the 12,257 samples were tested for IgM anti-HAV and total anti-HAV on the day of collecting or otherwise kept frozen at -20°C, and thawed before being tested.

Kits used for these parameters. Enzyme immunoassay for the detection of IgM antibody to HAV and enzyme immunoassay for the detection of Total anti-HAV; Abbotts Diagnostics Division Labs., North Chicago, USA. All the initially reactive specimens were confirmed by repeat Enzyme Linkage Immuno-Sorbent Assay (ELISA) testing, and the repeated reactive (RR) specimens were considered as positives. We also tested the 683 specimens from clinically diagnosed hepatitis children for Hepatitis B surface antigen (HBsAg) and for anti-hepatitis C virus (HCV) in addition to the anti-HAV tests. These tests for hepatitis B virus (HBV) and HCV were carried out according to the instructions.²⁵ All the methods and techniques of this study followed the manufacturers instructions.

Results. The results were statistically analyzed to get the 95% Confidence Interval (CI) for the prevalence estimation.²⁶ In this study, we considered subjects who were only positive for total anti-HAV to have remote infection, immune to HAV, and cannot be reinfected again.²² The specimens who were positive for IgM anti-HAV to have been recently infected. The specimens from clinically diagnosed hepatitis in children who are positive for HBsAg, or anti-HCV, or both, were considered as having HBC or HCV, or both while those negative to HAV, HBV and HCV were diagnosed as non A, non

B, non C hepatitis. Table 1 shows HAV prevalence according to age group of a healthy population. Table 2 shows total anti-HAV among healthy Saudi children. Table 3 shows clinically diagnosed hepatitis and sero-diagnosis of HAV, HBV, and HCV among 683 children.

Table 1 - Age dependence prevalence of hepatitis A virus among the healthy Saudi population.

Age group (years)	Number of subjects	Positive (%)	95% Confidence Interval
< 6	78	2 (3.0)	-0.945 - 6.06
6 - <18	5798	4634 (80.0)	789.98 - 99.99
18 - \geq 50	5798	5393 (93.0)	92.35 - 93.67
TOTAL	11674	10029 (86.0)	85.27 - 86.53

Table 2 - Total anti-hepatitis A virus among healthy Saudi children.

Age group (years)	Number of subjects	Positive (%)	95% Confidence Interval
<6	78	2 (3.0)	-0.945 - 6.06
6 - <8	892	522 (62.0)	58.69 - 65.07
8 - <10	1487	1045 (71.0)	68.22 - 72.86
10 - <12	1581	1316 (83.0)	81.39 - 85.07
12 - <18	1838	1717 (93.0)	92.27 - 94.54
TOTAL	5876	4636 (79.0)	77.85 - 79.93

Table 3 - Clinically diagnosed hepatitis and serodiagnosis of hepatitis A virus, hepatitis B virus, hepatitis C virus and Non A, B, C, hepatitis among 683 children.

Hepatitis Virus	Number of Positive (%)	95% Confidence Interval
HAV (Igm anti-HAV)	441 (65.0)	60.98 - 68.16
HBV (HBsAg+ve)	146 (21.0)	18.29 - 24.44
HCV (anti HCV+ve)	48 (7.0)	5.11 - 8.95
HBV + HCV (HBsAg & anti -HCV+ve)	13 (2.0)	0.87 - 2.92
Non A, non B, non C	35 (5.00)	3.47 - 6.77
HAV - Hepatitis A virus; HBV - Hepatitis B virus; HCV - Hepatitis C virus; HBsAg - ?		

Discussion. More reliable international data exists about the prevalence of HAV past infection.^{17-21,27,28} Hepatitis A virus prevalence is closely linked to the socioeconomic status of the population and to the age of exposure to the virus. We presumed that the age of infection is linked to the socioeconomic factors. Many more young European/ North Americans (Pattern II & III) are seropositive to HAV than those of the same age group in Asia or Africa (Pattern I).^{15,17,18} From the mid 1980s, many Saudi studies have been published regarding HAV in Saudi Arabia, some have emerged from Jeddah, other from Riyadh and many from different regions of the Saudi Kingdom.²⁹⁻³⁹ All these studies gave prevalence rates that vary from 39% (among children), 91% (among adults),³² to 78% in different age groups,³⁹ and 87.5% among children.²⁹ However, these studies used a limited number of subjects that diverse from as low as 55 samples,³⁴ to a maximum of 1015 specimens.³² Here our trial used a large group of 12,357, all of Saudi nationality, from different age groups that starts from pre-school age to older than 50 years in both sexes. This study extended uninterrupted for 10 years, so we can claim that the current study could be the biggest one in the Eastern Province, and hence the outcome could represent the actual status of this problem in this part of the world. The seroprevalence of total anti-HAV for the age groups is shown in table 1, with a grand total prevalence of 86% (10,029 from 11,674). This high prevalence reflects the endemicity of HAV in our community. Several investigators have posited that HAV endemicity is due to poor hygiene conditions in most areas in the community. The current figures for children (Table 2) show that there is a dramatic rise of prevalence from school age children, with children more than 12 years old showing a prevalence almost equal to the prevalence in the adult group. Analyzing this data, the authors can state that in a given area almost everybody contracts HAV infection during childhood, as the HAV antibody rates increase markedly from pre-school to early-school age, such a picture puts this area among pattern I countries.

As patients of clinical hepatitis have more or less the same clinical signs and symptoms, despite the different etiological hepatitis viruses, we tried to study that problem among children (who are usually the main group to contract infection with HAV). The authors reached the conclusion that HAV is the most common cause of viral hepatitis among children in this Province. This study puts HAV, HBV and HCV as the 1st, 2nd and 3rd possibility in children clinically diagnosed hepatitis (Table 3).

It is well known that HBV and HCV usually cause both acute and chronic infection, and there are many HBC, HCV carriers among the worldwide population, while HAV is an acute only virus. However, recently some studies claimed that HAV

viraemia may extend from 12-16 months in the patient with HAV infection, though the usual period for the virus is only around 2 weeks in the body. Such status was termed (Relapsing HAV infection).⁸ Nevertheless, the question of chronic liver disease with HAV infection has been under debate, until it was reported recently that acute HAV infection appeared to trigger the onset of autoimmune chronic hepatitis in certain individuals who are genetically predisposed to develop autoimmune hepatitis.^{40,41} From the figures of the children's HAV prevalence, and due to the dramatic rise from the pre-school to the early school age group, we could recommend the introduction of HAV vaccine to the pre-school age children. The active immunization by inactivated vaccine could give a high seroconversion if given in 2 doses (360 U) one month apart, and one booster dose after 6-12 months, this can give a 96%-100% response, which could last for >10 years.⁴² Such a vaccine policy for pre-school children could place HAV along the track of eradication, as was the case with polio virus which belongs to the same Enterovirus family. So the eradication of HAV infection is no more a hope, but an imminent reality, in view of the public health and hygiene and the prosperous socioeconomic status in this part of the world. All these factors can change this area from pattern I to pattern II or even to pattern III as in European countries. The authors want to record that there was no difference in HAV prevalence in relation to sex, season of the year, or the climate, as the specimens were collected during the whole-year round. The only factors of importance were the age of the individual along with the socioeconomic status.

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