

REDUCTION IN THE PREVALENCE OF ANTIBODY TO HEPATITIS A VIRUS AMONG YOUNG SAUDI ADULTS: IMPLICATIONS FOR HEPATITIS A VACCINE

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تم فحص ١٣٣ مريضاً سعودياً خلال الفترة (من يوليو ١٩٩٣م إلى مايو ١٩٩٤م) لمعرفة أسباب إصابتهم بالتهاب الكبد الوبائي. وُجد أن ٥١ مريضاً (٣٨٪) منهم كانوا مصابين بالحمى (١) وأن ٣٠, ٢٠٪ بالحمى (ج) ثم (ب) (٨, ١٢٪)، وأخيراً الحمى المضخمة للخلايا (٢, ٣٪). كما لم يتم اكتشاف أي من مؤشرات هذه الحمى ولاحمى ابشتاين بار لدى ٣, ٢٦٪ من المصابين بالتهاب الكبد الوبائي. وبتحليل نتائج المرضى المصابين بالتهاب الكبد الوبائي (١) وجد أن الأغلبية الساحقة (٢, ٨٨٪) كانوا من الأطفال الذين تتراوح أعمارهم ما بين ١ - ١٢ سنة. أما المرضى الباقين ٦ (٨, ١١٪) فهم من البالغين (١٥-٢٤ سنة). أما بالنسبة للمرضى المصابين بالتهابات الكبد الوبائية ج، ب فأكثرهم من البالغين ٧٤٪ و٨٢٪ على التوالي.

وتشير النتائج إلى أن هناك تغييراً وبائياً فيما يخص الإصابة بالحمى (١) حيث إنه بعد فحص عينات ٦٣٠ شخصاً ما بين ١ - ٣٠ سنة في عام ١٩٩٤م وجد أن نسبة التعرض لمستضدات حمى (١) ٢, ٦٠٪ مقارنة بنسبة ٥, ٧٦٪ في دراسة أجريت عام ١٩٨٦م على ٥٨٧ شخصاً. ونتيجة لذلك نرى أهمية إجراء دراسات على مستوى المملكة لإثبات هذا التغير وحصص الأشخاص المعرضين للإصابة بحمى (١) فربما يستفيدون من التحصين ضد حمى (١).

Viral etiology was investigated in 133 Saudi patients with acute hepatitis seen in King Khalid University Hospital, Riyadh, between July 1993-May 1994. Out of the 133 patients, 51 (38.3%) were diagnosed as having acute hepatitis due to hepatitis A virus (HAV). Hepatitis C virus (HCV) was the second most common etiological agent (20.3%). There were 35 patients with acute hepatitis (26.3%) in whom no viral marker for HAV, HBV, HCV, CMV or Epstein-Barr virus (EBV) was detected. Among the 51 patients with acute hepatitis due to HAV, the majority (88.2%) were children (1-12 years) and only 6 (11.8%) were adults (15-24 years). This is in contrast to patients with HCV or HBV infection where the majority were adults: 74.1% and 82.3% respectively. The diagnosis of acute hepatitis due to HAV in Saudi adults, an observation not seen earlier, indicated a change in the epidemiological pattern of HAV infection in the Saudi population. This change was confirmed by the significant reduction in the prevalence of anti-HAV in 630 Saudi subjects (1-30 years old) (50.2%) investigated in 1994 compared to that of 587 subjects of the same age group investigated in 1986 (76.5%) ($P < 0.005$). In the light of these results, a nation-wide survey is recommended to confirm this pattern in other areas. It is important that high-risk Saudi groups be identified and evaluated for their anti-HAV status as these groups are candidates for HAV vaccination. (Saudi J Gastroenterol 1995;1(2):93-96)

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Introduction

Hepatitis continues to be a major health problem in developing and tropical countries (1). This is particularly true for hepatitis A virus (HAV) where infection occurs during early life leading to nearly 100% prevalence of antibody to HAV (anti-HAV) in individuals above 10 years of age (2-4). The clinical course of HAV infection is largely dependent on age. For example, in day-care centers more than 90% of children infected below the age of 5 years remain asymptomatic and only fewer than 10% develop typical illness with icterus (5). On the other hand, 70-80% of infected adults develop icteric hepatitis (6). Since HAV spreads by the fecal-oral route, chiefly after contamination of food and water by fecally excreted virus from infected individuals, the incidence and prevalence of HAV infections are closely connected with hygienic conditions. During the past decades, there has been a dramatic change in the epidemiology of HAV mainly in developing countries in transition, with rapid socioeconomic improvements (7-9). This situation applies to Saudi Arabia which is highly endemic for hepatitis A (10). The recent documentation of acute HAV infections in Saudi adults at our hospital prompted us to reinvestigate the seroepidemiology to HAV after 9 years of our initial report (10).

Materials and Methods

Patients

A total of 133 jaundiced patients presenting with symptoms of acute hepatitis were seen at King Khalid University Hospital (KKUH) in Riyadh between July 1993 and May of 1994. After a complete clinical examination, specimens were sent to the laboratory for full blood counts, liver function tests and serological investigations. A patient was considered recently infected by HAV, cytomegalovirus (CMV) or Epstein-Barr virus (EBV) by demonstrating anti-HAV IgM, anti-CMV IgM or anti-EBV IgM (VCA), respectively. A fourfold rise in the titre of antibody to hepatitis C virus (anti-HCV) between the acute or convalescent sera or the presence of anti-HCV IgM was diagnostic of acute HCV infection. Diagnosis of acute hepatitis B virus (HBV) infection was based on the presence of HBsAg and anti-HBcIgM. If

the serum sample was negative for all the above markers, the etiology was considered as non-A, non-B, non-C (NANBNC).

Prevalence of anti-HAV

For evaluating the rate of exposure to HAV among the Saudi population, 379 Saudis (206 males, 173 females) from one to 30 years of age from the Riyadh area, Central Province were tested for anti-HAV IgG. Individuals over 16 years of age were blood donors, medical students and hospital employees, while those between 10 and 16 years of age were patients admitted to KKUH without symptoms suggesting liver disease and for whom none of the above-mentioned viral markers have been requested. Children 1-10 years old were investigated in another research project regarding the epidemiology of hepatitis E virus (HEV) infection in Saudi Arabia. The sampling strategy of these children has already been detailed (11).

Serological investigations

Anti-HAV IgG, anti-HAV IgM, HBsAg, HBeAg, Anti-HCV IgG were detected by the commercially available enzyme-linked immunosorbant assay (ELISA) kits from Organon Tecknicka. Anti-HBcIgM, anti-HCV IgM were detected by ELISA kits available from Abbott Laboratories. Confirmation of anti-HCV IgG-positive samples was performed by recombinant immunoblot assay (RIBA) from Ortho Diagnostics. Anti-CMV IgG and anti-EBV IgM (VCA) were detected by VIRGO-ELISA test from Electronucleosis Inc. Data was analyzed using the Chi-square test.

Results

Results of the serologic investigations of 133 patients admitted to KKUH with acute hepatitis are shown in Table 1. Out of the 133 patients, 51 patients were diagnosed as having acute hepatitis due to HAV. HCV was the second most common etiological agent (20.3%) followed by HBV (12.8%) and CMV (2.3%). There were 35 patients with acute hepatitis (26.3%) in whom no viral marker for HAV, HBV, HCV, CMV or EBV was detected. Among the 51 patients with acute hepatitis due to HAV, the majority (88.2%)

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Table 1. Etiology of icteric hepatitis in Saudi patients from June 1993 - May 1994 at King Khalid University Hospital, Riyadh.

| | HAV | HBV | HCV | CMV | NANBNC | TOTAL |
|------------|--------|--------|--------|-------|--------|-------|
| 1-12 years | 45 | 3 | 7 | 3 | 5 | 76 |
| >12 years | 6 | 14 | 20 | - | 30 | 57 |
| Total | 51 | 17 | 27 | 3 | 35 | 133 |
| (%) | (38.3) | (12.8) | (20.3) | (2.3) | (26.3) | (100) |

Table 2. Age-specific prevalence of anti-HAV in Saudis from Riyadh, Central Province.

| Age (years) | 1986 | | 1994 | | P |
|-------------|-----------------------------|--------|-----------------------------|--------|----------------------|
| | No. Positive/ No. tested | (%) | No. Positive/ No. tested | (%) | |
| 1-9 | 103/194 | (53.0) | 81/210 | 38.6 | 3.4×10^{-3} |
| 10-19 | 164/193 | (85.0) | 110/180 | 61.1 | 1×10^{-4} |
| 20-30 | 182/200 | (91.0) | 188/240 | 78.3 | 3×10^{-4} |
| Total | 449/587 | (76.5) | 379/630 | (60.2) | 1×10^{-4} |

*Data from reference 10.

were children (1- 12 years) and only 6 (11.8%) were young adults (15-24 years). This is in contrast to patients with HCV or HBV infection where the majority were adults: 74.1% and 82.3%, respectively.

Table 2 shows the results of the prevalence of anti-HAV IgG among Saudis of various age groups for 1994 compared with those published in 1986 (10). There was a significant reduction in the prevalence of anti-HAV in every age group investigated in 1994 compared to that of 1986. The overall prevalence of anti-HAV IgG in 1994 was 60.2% compared to 76.5% in 1986 and the reduction was statistically significant ($P < 0.005$).

Discussion

The results of this study confirm our earlier reports of the endemicity of HAV (10,12), HBV (13), and HCV (14) in Saudi Arabia. Among Saudi patients with acute icteric hepatitis, HAV was the major etiological agent (38.3%) followed by HCV (20.3%) and HBV (12.8%). Out of the 133 Saudi patients studied, 35 (26.3%) had no serological evidence of infection with the above-mentioned viruses. It is possible that HEV was the etiological agent for some of them (11) while others might be due to HCV but without detectable

circulating antibody at the time of presentation, or the disease was not of viral etiology. Unfortunately, HEV was not looked for in this study although it is endemic in Saudi Arabia.

In contrast to the situation with HBV and HCV infections, the majority (88.2%) of our icteric hepatitis patients due to HAV were children 1-12 years old, and only 11.8% were adults (15-24 years old). The documentation of acute icteric hepatitis due to HAV in Saudi adults, an observation not noted earlier, reflected a change in the epidemiologic pattern of HAV infection in the Saudi population. This change was further supported in the reduction in prevalence of antibody to HAV conducted recently compared to the one published 9 years earlier (10). The reduction was noted in all age groups investigated and was statistically significant. This finding points to a decline in the feco-oral transmission of HAV among Saudi children and reflects the marked improvement of hygienic conditions that took place in the Kingdom during the past decades. Similar shift in the epidemiology of HAV has recently been reported in other developing countries undergoing socioeconomic and hygienic improvements (7-9). For example, the transition from high to low endemicity to HAV in developing countries have led to explosive outbreaks due to viral cross-con-

tamination from endemic to nonimmune sectors of the population via food or water 915). Furthermore, in both developed and developing countries in transition, HAV is becoming an occupational hazard (16). Clinical illness due to HAV has been reported in pediatric wards, day-care centers, medical laboratories, and in travellers to less developed areas (16-17). It must be mentioned, however, that adults whose anti-HAV status was investigated in this study were mainly from the Riyadh area which is an urban area. Whether a similar reduction in exposure to HAV has also occurred in rural areas is still to be determined by a nationwide study. Such study is needed if application of HAV vaccine (18,19) is to be considered at this stage.

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