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RAPID COMMUNICATION

Changing patterns of hepatitis A prevalence within the Saudi population over the last 18 years

Faleh Al Faleh, Suliman Al Shehri, Saleh Al Ansari, Mohammed Al Jeffri, Yaqoub Al Mazrou, Ahmad Shaffi, Ayman A Abdo

Faleh Al Faleh, Ayman A Abdo, Department of Medicine, College of Medicine, King Saud University, Riyadh 11461, Saudi Arabia
Suliman Al Shehri, Saleh Al Ansari, Ministry of Education, Riyadh, Saudi Arabia
Mohammed Al Jeffri, Yaqoub Al Mazrou, Ministry of Health, Riyadh, Saudi Arabia
Ahmad Shaffi, Department of Community Medicine, College of Medicine, King Saud University, Riyadh 11461, Saudi Arabia
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Correspondence to: Ayman A Abdo, Department of Medicine, College of Medicine, King Saud University, PO Bob 2925(59), Riyadh 11461, Saudi Arabia. aabdo@ksu.edu.sa
Telephone: +966-1-4671215 Fax: +966-1-4671217
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Abstract

AIM: To determine the seroprevalence of Hepatitis A (HAV) amongst Saudi children and compare it with previously reported prevalence data from the same population.

METHODS: A total of 1357 students were randomly selected between the ages of 16 and 18 years (689 males and 668 females) from three different regions of Saudi Arabia (Madinah, Al-Qaseem, and Aseer) and tested for anti-HAV-IgG.

RESULTS: The overall prevalence of anti-HAV-IgG among the study population was 18.6%. There was no difference between males and females but there was a significant difference in the seroprevalence (P = 0.0001) between the three different regions, with Madinah region showing the highest prevalence (27.4%). When classified according to socioeconomic status, lower class students had a prevalence of 36.6%, lower middle class 16.6%, upper middle class 9.6%, and upper class 5.9% (P = 0.0001). Comparing the current study results with those of previous studies in 1989 and 1997 involving the same population, there was a marked reduction in the overall prevalence of HAV from 52% in 1989, to 25% in 1997, to 18.6% in 2008 (P < 0.0001).

CONCLUSION: Over the last 18 years, there has been a marked decline in the prevalence of HAV in Saudi children and adolescents. The current low prevalence rates call for strict adherence to vaccination policies in high-risk patients and raises the question of a universal HAV vaccination program.

Key words: Hepatitis A; Saudi Arabia; Epidemiology; Prevalence; Serology

Peer reviewer: Sammy Saab, MD, MPH, AGAF, Departments of Medicine and Surgery, Pfleger Liver Institute, 200 UCLA Medical Plaza, Suite 214, Box 957302, Los Angeles, CA 90095-7302, United States

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INTRODUCTION

Hepatitis A (HAV) is a major health problem worldwide and, like other enteric infectious diseases, is classically an infection of childhood. Although acute infection commonly passes unnoticed, a significant proportion of patients may have fulminant liver failure, especially patients with liver cirrhosis or immune deficiencies. Generally, its prevalence pattern varies from one population to the other and is closely related to the socioeconomic conditions of sanitation and hygiene. An improvement in sanitation and living standards in many areas of the world has caused the epidemiology of HAV to rapidly evolve. As such, with an improvement in living conditions, more clinical cases are being diagnosed owing to the increased age of those susceptible, which is paradoxical to childhood infection where the majority of infections are subclinical[1-5]. The availability of safe and efficacious vaccines against HAV has made it

increasingly important to understand the epidemiology of HAV in a given area before a strategy for the use of the vaccine is advised or implemented[6-8]. In particular, the epidemiological data from the previous decade may no longer be valid now.

Understanding the epidemiological shift in HAV seropositivity is of strategic importance to a nation's healthcare system. In countries that dramatically improve their socioeconomic status and standards of living, the susceptible pool may increase rapidly to such an extent that HAV becomes a major public health concern. The epidemiology of HAV in developed countries is characterized by low prevalence rates among children with a large group of susceptible adults being negative for anti-HAV.

Two decades ago, studies performed in Saudi Arabia indicated the HAV prevalence rate to be in the range of 90%-100% amongst the adult population[9-13]. However, later studies showed a consistent decline in anti-HAV prevalence rate[14,15]. In the years 1989 and 1997, community-based studies revealed that the overall prevalence rate of HAV infection among children of age 1-12 years had reduced dramatically from 52% (1989) to 25% (1997)[16,17].

We aimed to evaluate the epidemiological shift in HAV serostatus within the adolescent population of three predefined regions of Saudi Arabia and compare it to previously published data.

MATERIALS AND METHODS

Study population

We selected our sample from a population of 10-12th grade school students (corresponding to the age of 16-18 years) in three regions. These regions were as follows: (1) The Aseer region: school population of 25 512, 13 996 males and 11 516 females; (2) Madinah: school population of 23 852, 12 133 males and 11 719 females; and (3) The Al-Qaseem region: school population of 16 067, 7974 males and 8093 females. These regions were selected because they represented low, medium, and high prevalence rates in our previous studies. The sample was selected using a stratified random sampling technique where the Kingdom was stratified into three strata according to the previous endemicity of infection. The proportional allocation method was used to determine the recruited number of students in each stratum. Within the stratum, the sample was proportionally allocated according to gender. In every region, schools served as the sampling units. From the list of schools in the region, one or more male schools and one or more female schools that satisfied the required sample size were randomly selected.

A total of 1357 students (689 males, 668 females) from these three regions of the Kingdom of Saudi Arabia (KSU), were randomly selected. The socioeconomic status of this population was also stratified (low, middle and high class). King Abdulaziz City for Science and Technology approved the protocol of this study, and informed consent was obtained from the parents as well as from the students participating in the study.

Data collection, blood sampling and testing

Fieldwork for this study was undertaken in December 2007 and January 2008. Demographic data were recorded, and a venous blood sample (5-10 mL) was taken from each student. Serum was separated by centrifugation, coded, and stored at -70℃ until tested. Blood samples were tested for anti-HAV-IgG using EIA kits ADVIA Centaur system.

The socioeconomic status of each student was taken to be representative of that of the father and/or the mother and classified using a socioeconomic status 3-point scoring system derived according to the type of house (mud-built = 1, apartment or ordinary house = 2, villa = 3), number of rooms in the house (1-2 rooms = 1, 3-4 rooms = 2, 5 and more = 3), number of family members (4 or less = 3, 5 = 3, 6 = 2, 7 or more = 1), father and mother education (primary grade or less = 1, secondary/high school = 2, university or equivalent = 3), parent occupation (laborer = 1, farmer or office clerk = 2, trader = 3). An overall score of less than 10 from a maximum of 21 was classified as representative of a low socioeconomic status, 10-15 as low middle, 15-17 as high middle and above 17 as high class.

Statistical analyses

Data was entered in MS Excel and analyzed using SPSS Pc+ version 16.0 statistical software. Descriptive statistics (proportional) were used to summarize the categorical variables. χ^2 test followed by analysis of residuals was used to calculate the statistical association between two categorical variables. χ^2 test for trend was used to calculate the significance of proportions of categorical variables at different time points. P value of < 0.05 was considered statistically significant.

RESULTS

The blood samples of 1357 students (aged 16 to 18 years; 689 males and 668 females) were collected and analyzed. The overall prevalence rate of anti-HAV-IgG among the population study was 18.6%.

Association between anti-HAV-IgG values and gender

A significant association between gender and anti-HAV serostatus was seen. The proportion of males who were anti-HAV positive (21%) was significantly higher when compared with females (16.2%) ($P = 0.021$). The adjusted residuals of the frequencies were also statistically significant when compared with the 5% standard normal deviate value (1.96) (Table 1).

Association between anti-HAV-IgG values and regions

A significant association was observed between the area (Aseer, Madinah, and Al-Qaseem) and anti-HAV serostatus. The proportion of subjects from Madinah who were anti-HAV positive (27.4%) was significantly higher compared with samples from other areas (Aseer: 13.5% and Al-Qaseem: 13.9%; $P < 0.0001$). The adjusted residuals of the frequencies of Madinah area (6.2)

Table 1 Prevalence of anti-HAV within the study population and its association with gender

Gender	Anti-HAV (%)		*P* value
	Positive	Negative	
Male (*n* = 689)	145 (21)	544 (79)	0.021
Female (*n* = 668)	108 (16.2)	560 (83.8)	

Table 2 Prevalence of anti-HAV and its association with the socioeconomic status of study population

Socioeconomic status	Anti-HAV(%)		*P* value
	Positive	Negative	
Low class (*n* = 239)	88 (36.8)	151 (63.2)	< 0.0001
Lower middle class (*n* = 880)	146 (16.6)	734 (83.4)	
Upper middle class (*n* = 136)	13 (9.6)	123 (90.4)	
High class (*n* = 102)	6 (5.9)	96 (94.1)	

were also statistically significantly higher when compared with the 5% standard normal deviate value (1.96) (Table 2).

Association between anti-HAV-IgG values and socioeconomic status

A significant association between social status of the sampled population and anti-HAV status was found. The proportion of low class subjects who were anti-HAV positive (36.8%) was significantly higher compared with subjects of other classes (lower middle class: 16.6%; upper middle class: 9.6% and high class: 5.9%; $P < 0.0001$). The adjusted residuals of the frequencies of low class (7.9) were also statistically significantly higher when compared with the 5% standard normal deviate value (1.96) (Table 3).

Comparison of anti-HAV-IgG of previous studies performed in 1989[16] and 1997[17], with the present study

There was a high statistically significant trend for decreased prevalence of HAV infection in all three areas over the three time points. Among the three areas (Al-Qaseem, Aseer and Madinah), the Al-Qaseem area had a significantly decreased prevalence of HAV infection (61.1% in 1989, 31.5% in 1997 and 13.8% in 2007-2008). The decrease in prevalence of HAV infection in Aseer area from 1997 to 2007-2008 was only 5.4% and in Madinah for the same period was only 1.2%, whereas in Al-Qaseem the decrease was 17.7% during the same period (Table 4).

DISCUSSION

The results of this study show a marked decline in the endemicity of HAV within the Saudi population in the age range of 16-18 years. This trend is highlighted by the dramatic linear decline from 53% in 1987 to 25% in 1997 and finally to 18.6% in the present study. Other studies from the region have shown a similar trend.

Table 3 Prevalence of anti-HAV and its association with the region of study population

Region	Anti-HAV(%)		*P* value
	Positive	Negative	
Aseer (*n* = 532)	72 (13.5)	460 (86.5)	< 0.0001
Al-Qaseem (*n* = 332)	46 (13.9)	286 (86.1)	
Madinah (*n* = 493)	135 (27.4)	358 (72.6)	

Table 4 Prevalence of HAV infection in KSA over the last 18 years (1989[16], 1997[17], and 2008)

Region	1989 prevalence (%)	1997 prevalence (%)	2007-2008 prevalence (%)	*P* value
Al-Qaseem	126/201 (61.1)	71/225 (31.5)	46/332 (13.8)	< 0.00001
Aseer	212/476 (44.5)	78/411 (18.9)	72/532 (13.5)	< 0.00001
Madinah	208/350 (59.4)	83/317 (26.2)	135/493 (27.4)	< 0.0001
Total	546/1027 (53.1)	232/953 (24.3)	253/1357 (18.6)	

Al Muneef and colleagues found a hepatitis A seroprevalence of 28.9% in 2399 Saudi children two years ago[18]. However, the present study which was performed on the same population cohort three times over the past 18 years showed a graded but dramatic decline in prevalence. In addition, this study was performed in three areas of different endemicity within the country, representing different levels of socioeconomic development.

HAV endemicity is closely linked to improvements in sanitation and living conditions in the population. In the case of Saudi Arabia, the Saudi government's real-estate bank has helped to build 851 000 housing units through a government loan from 1974 to 2003[19].

According to the official human development report in 2003, the Saudi per Capita GDP increased from 1145 USD in 1970 to 10 853 USD in 2002 and the life expectancy at birth has changed from 53.9 years (1970-1975) to 70.9 in 2000[19].

We believe therefore, that the vast improvement in the socioeconomic status of the Saudi population is the factor most likely to be responsible for this decline. Furthermore, the overall reduction in illiteracy within the Saudi population from greater than 90% in the 1960s to 13.4% in 2007-2008 (7% in males and 19.8% in females)[20] is likely to have contributed to this decline.

A difference was also observed in the prevalence rates of anti-HAV between the three different regions of the KSA in our study, in effect reflecting the different stages of economic development of these regions. The role of socioeconomic status in the study population in determining the level of HAV prevalence was also demonstrated in this study (Table 3) similar to previous publications[16-17].

Previous community-based studies conducted in the Saudi population have shown differing gender-based results in HAV seropositivity. Al-Rashed showed no difference in the anti-HAV prevalence rates between male and female populations[17], while in another study, Khalil *et al*[21] showed a higher seropositivity for Saudi males. The dif-

ference between male and female prevalence rates among this age group is likely to be related to the greater exposure of the male population to HAV infection sources in the community. For instance, the eating habits of the Saudi male population are certainly more gregarious compared to the female population. Similarly, the local culture of less female co-habitation and social interaction may also play a role in reducing their exposure to infection sources.

Finally, this study indicated that more than 82% of the adolescent population of Saudi Arabia is susceptible to symptomatic HAV infection. This could occur either by exposure to infected persons, either where they live or upon travel to high endemic areas either within or outside the country. Outbreaks of symptomatic acute HAV infection have been recently reported within increasing pools of susceptible populations within the country[22-24]. This high susceptibility of the young population represents a continuous challenge to the healthcare system of the country.

Recently, an HAV vaccine has been introduced in many countries as part of an Extended Program of Immunization (EPI). Several studies have demonstrated the efficacy and safety of the vaccine[25-28] and some authorities have recommended its universal implementation in certain populations[29]. Therefore, the recent decision by the Saudi Ministry of Health to introduce the HAV vaccine as part of the EPI program starting from 2008, to children of 18-24 mo of age is certainly timely. The effect of this strategy needs to be studied in future community-based studies, where the results of the present study could well serve as a reference point for comparative analysis.

COMMENTS

Background

Hepatitis A (HAV) is a major health problem worldwide. Generally, its prevalence pattern varies from one population to the other and is closely related to the socioeconomic conditions of sanitation and hygiene. An improvement in sanitation and living standards in many areas of the world has caused the epidemiology of HAV to rapidly evolve.

Research frontiers

This research group took blood samples from school students aged 16-18 years in three different regions of the country after consent of the parents and students. It was found that the prevalence of hepatitis A in this population was 18.6% compared to 25% in 1997 and 52% in 1989. There was also a link between hepatitis A and socioeconomic status with children from a lower socioeconomic status having a higher prevalence.

Innovation and breakthroughs

This study confirmed the findings of other studies in Saudi Arabia and other developing countries showing a reduced rates of hepatitis A with improved socioeconomic status.

Applications

This study is important because it compares current prevalence rates with previous rates from the same community. The reported low rates in the current study calls for strict adherence to vaccination policies in high-risk patients and raises the question of a universal HAV vaccination program.

Peer review

HAV infection is an important topic, and continues to be a source of morbidity and mortality. Al Faleh elegantly describes how the HAV seroprevalance has decreased in Saudi Arabia, and appropriately raises concerns about an increasingly susceptible population.

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