

The epidemiology of hepatitis A infection in Palestine: a universal vaccination programme is not yet needed

K. YASSIN¹*, R. AWAD², A. TEBI³, A. QUEDER³ AND U. LAASER¹

¹ *Section of International Public Health, School of Public Health, University of Bielefeld, Postfach 100131, 33501 Bielefeld, Germany*

² *Management Information System, Ministry of Public Health, Palestinian National Authority, Palestine*

³ *Department of Primary Health Care, Ministry of Public Health, Palestinian National Authority, Palestine*

(Accepted 17 April 2001)

SUMMARY

In Palestine, there has been an increase in the reported incidence of acute hepatitis A virus (HAV) infection since 1995. Since overt clinical disease occurs only among adults, questions were raised whether or not a shift in the epidemiology of HAV has occurred. This is generally characterized by a decrease in the overall incidence rate and a shifting in the mean age of infection towards adolescence and early adulthood. The need for a vaccination programme is being discussed. To resolve this issue, we examined the prevalence of anti-HAV in a representative sample of 396 school children in the Gaza Strip. The prevalence of anti-HAV was 93·7% (95% CI: 91·3, 96·1%). Stratifying the prevalence by age showed that 87·8% (95% CI: 78·6, 97%) were HAV antibody positive by the age of 6. By the age of 14, almost 98% (95% CI: 92·7, 100%) were HAV antibody positive. This means that the majority of HAV infection is still taking place in early childhood, when it is usually asymptomatic and of little clinical significance. The results refuted the shifting epidemiology theory and we recommend that a vaccination programme against HAV infection is not yet needed. Alternative explanations for the increase in reported cases are discussed.

INTRODUCTION

Hepatitis A virus (HAV) infection is one of the most common infectious diseases and the leading cause of acute viral hepatitis worldwide [1–3]. Conservative estimates indicate that at least one and half million new infections worldwide occur annually [4] and that the seroprevalence in several of the economically developing countries in Africa [5–11], Asia [12–16] and Latin America [17–18] approaches 100%. In those countries where HAV is highly endemic, most infections occur by 5 years of age and the majority of these infections are asymptomatic. As a result, reported disease rates in these countries are low and outbreaks of disease seldom occur [1, 2]. By contrast, the seroprevalences in several industrialized countries

were shown to be less than 5%. Infection in these countries is usually acquired during adolescence and early adulthood and accompanied with significant morbidity [1, 3].

Several countries in the Middle East have been reporting a decline in the seroprevalence of HAV during the past two decades [5, 19–24]. This is attributed to improved sanitary and hygienic conditions in these countries. Paradoxically, this decline has been accompanied by a significant increase in the incidence of acute clinical disease, partly because a significant proportion of infections are currently occurring in older age groups and partly because case finding and reporting has improved [1].

The epidemiology of HAV infection in the general population in Palestine is not known as seroprevalence studies are lacking. However, a controversial debate is

* Author for correspondence.

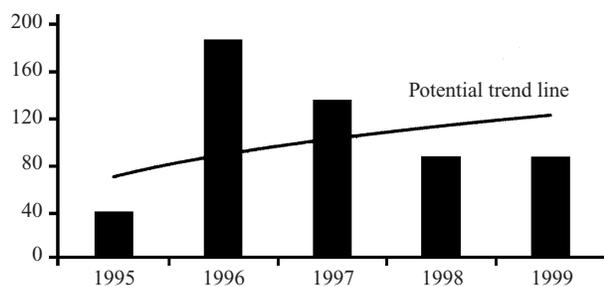


Fig. 1. Reported incidence rates (per 100,000 population) of HAV infection in Palestine since 1995.

currently being raised over whether or not Palestine is experiencing a shifting epidemiology of HAV infection. The reported incidence rates of HAV infections showed that since 1995 there has been an increase in the incidence of overt clinical cases with a shift in the peak age of infection from childhood to adulthood (Fig. 1). This shifting epidemiology has been reported in several regions in the world [5, 15, 17, 25]. This is suggested to be accompanied by a decline in the overall incidence rate of HAV infection in the community. The need for a vaccination programme is accordingly being discussed.

Opponents of the shifting epidemiology theory claim that the differences in the reported cases of HAV infection reflects inconsistencies in diagnosis and irregularities in reporting. They suggest therefore that an immunization strategy is not needed since most infections are still acquired in early childhood. In this age group, infection is usually asymptomatic and of little clinical significance.

This study is the first in Palestine to examine the seroprevalence of HAV among school children. The logic behind it was that defining the seroprevalence in this age group would be decisive in resolving the controversy. If anti-HAV is universal in these children, then the shifting epidemiology theory is refuted and a vaccination programme is not needed.

METHODS

Study population

The study population consisted of school children aged 6–14 years in the Gaza strip. A sample of 396 children was randomly enrolled in the study from 47 schools, all primary and preparatory schools in the strip. These schools included 28 governmental schools affiliated to the Palestinian National Authority and 19 schools affiliated to the United Nation's Relief and Work Association. The sample was chosen using a

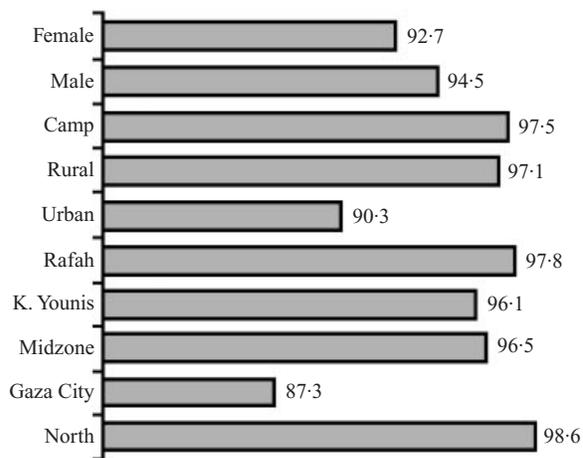


Fig. 2. Prevalence of anti-HAV by governorate, residence and sex in school children in Palestine.

multistage technique without replacement of drop-outs. Initially, a sample size of 400 children was planned. The sample size was calculated to keep the probability of α -error and β -error less than 5% and 20%, respectively and to compensate for an expected drop out in the order of 10%. A sample was taken from each school according to its size (percentage of students in the school in relation to all students in the Gaza strip). In each school, children were selected using a simple random technique.

Blood sampling and serologic testing

A 5 ml blood sample was obtained from each child by a trained nurse in a vacutainer plain tube and immediately transported to the central laboratory of the Ministry of Health. There, sera were separated from the cellular blood components, coded and stored at -20°C . Serum testing for total anti-HAV was carried out using a closed-system Abbott Enzyme Immunoassay (Abbott Laboratory).

Personal information

Information about the age, sex and the residence of children enrolled in the study was obtained from the school records and confirmed by interviewing the children before obtaining the blood sample.

RESULTS

Demographic characteristics

Children were enrolled from all schools in the five governorates in Gaza, 35.4% from Gaza city, 18.7%

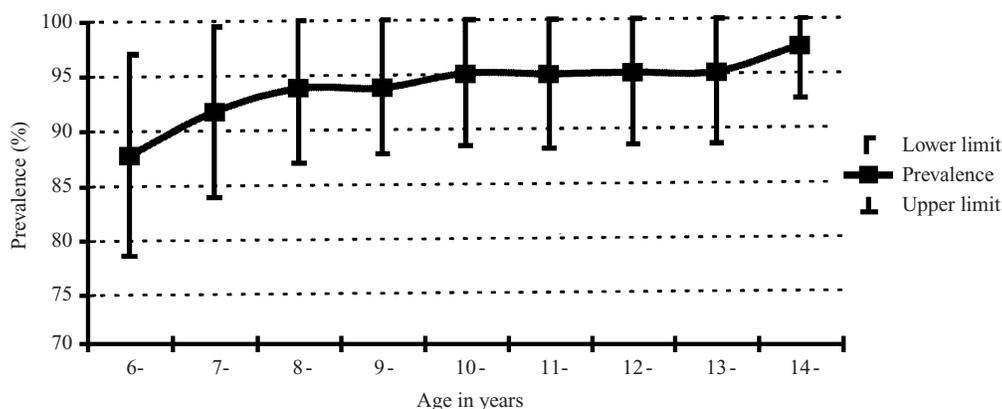


Fig. 3. 95% Confidence interval for the age-specific prevalence of anti-HAV in school children in Palestine.

from North Gaza, 14.6% from Gaza Midzone, 19.2% from Khan Younis and 11.6% from Rafah. With respect to residential type, 52% were from urban areas, 17.7% from rural areas and 30.3% from refugee camps. The sex distribution of participants showed that 50.5% were male and that 49.5% were female; 48.7% were enrolled from primary schools (6–10 years old) and 51.3% from preparatory schools (11–15 years old).

Prevalence of anti-HAV

The prevalence of anti-HAV is shown in Fig. 2 and in all students was 93.7% (95% CI: 91.3, 96.1). The prevalence was very high in all governorates: 98.6% in North Gaza (95% CI: 95.9, 100), 87.3% in Gaza city (95% CI: 81.8, 92.8), 96.5% in Gaza Midzone (95% CI: 91.8, 100), 96.1% in Khan Younis (95% CI: 91.7, 100) and 97.8% in Rafah (95% CI: 93.6, 100). Likewise, the prevalence was very high in all residential types and did not statistically differ between urban areas, rural areas or refugee camps. The prevalence was 90.3% (95% CI: 86.3, 94.3), 97.1% (95% CI: 93.2, 100) and 97.5% (95% CI: 94.7, 100) for the three residential type respectively. Gender was not shown to have a significant association with the prevalence of anti-HAV. The prevalence was 94.5% in males (95% CI: 91.3, 97.7) and 92.9% in females (95% CI: 89.3–96.5).

The age-specific prevalence of anti-HAV showed that by the age of 6, 87.8% of children had already acquired the infection (95% CI: 78.6–97) (Fig. 3). The prevalence increased gradually but linearly with age so that 97.5% of children were positive for anti-HAV by the age of 14 (95% CI: 92.7–100).

DISCUSSION

There are some data in Palestine suggesting that there has been an increase in the reported clinical cases of acute hepatitis A infection among adults in recent years. This has raised a question about whether or not there has been a shifting epidemiology of HAV which might necessitate the establishment of a vaccination programme. Our study of the prevalence of anti-HAV in a representative sample from school children in Palestine provides substantive evidence that such a shift is not occurring. It revealed that infection with HAV is still basically occurring in early childhood. In our sample, 87% of children were positive for anti-HAV by the age of 6 and 97.5% were positive by the age of 14. Since infection in early life is generally asymptomatic and does not lead to chronic infection, we believe that HAV does not constitute a serious public health problem in Palestine.

Likewise, the change in the trend of reported cases of overt clinical infection cannot be explained by the claimed shifting epidemiology of HAV. Instead, it can be attributed to several other factors that can alone or in combination affect the incidence or the reporting of HAV infection. Firstly, there has been a significant improvement in diagnosis and reporting of infectious diseases since the foundation of the Ministry of Public Health in 1995. Diagnostic kits, both serological and biochemical, have been made available to hospitals and health centres by the Ministry. This has presumably enabled physicians to diagnose cases of acute HAV infection which were not diagnosed previously. Furthermore, the Management Information System within the Ministry of Public Health has been encouraging physicians to report these cases which were not reported otherwise.

There has also been an influx of Palestinian returnees to the Gaza strip since the Palestinian National Authority was established in 1994. A proportion of these returnees came from countries where HAV is not endemic or where HAV is declining. Therefore, a percentage of these individuals carry the risk of acquiring the infection when they return to Palestine. Since infection in adolescence and adulthood is usually manifested as an overt clinical disease and associated with considerable morbidity, it is likely these cases are diagnosed and notified, leading to an increase in the reported incidence rate of HAV infection.

A shifting epidemiology of HAV infection might have been taking place in the Palestinian areas in the West Bank, which lie in close proximity to Israel. In Israel, there has been a substantial decline in the incidence of HAV infection with a shift in the mean age of infection towards early adulthood. This has led to significant morbidity, especially among recently recruited army soldiers. Israel has launched a successful surveillance and prophylaxis programme to control HAV infection in the army. The programme achieved a considerable decline in the seroprevalence over a relatively short period [26–31]. Whether or not the West Bank has witnessed similar developments in the epidemiology of HAV is an issue for further research.

In conclusion, HAV infection is endemic and highly prevalent in the Gaza Strip. Infection occurs overwhelmingly in early childhood, passes unnoticed in the majority of cases and does not result in chronic complications. These results refute the notion that there has been a shifting epidemiology of HAV infection and provides substantial evidence that a vaccination programme against HAV is not yet needed.

REFERENCES

- Koff RS. Hepatitis A. *Lancet* 1998; **351**: 1643–9.
- Feinstone SM. Hepatitis A: epidemiology and prevention. *Eur J Gastroenterol Hepatol* 1996; **8**: 300–5.
- Shapiro CN, Margolis HS. Worldwide epidemiology of hepatitis A virus infection. *J Hepatol* 1993; **18**: S11–4.
- Hadler SC. Global impact of hepatitis A virus infection changing patterns. In: Hollinger FB, Lemon SM, Margolis HS, eds. *Viral hepatitis and liver disease*. Baltimore: Williams & Wilkins, 1991; 14–20.
- Tufenkeji H. Hepatitis A shifting epidemiology in the Middle East and Africa. *Vaccine* 2000; **18**: S65–7.
- Ajdukiewicz A, Mosley JW. Hepatitis A antibody in West Africa. *Lancet* 1980; **ii**: 695.
- Willcox M, Brohult J, Olsson I, Bengtsson E. Antibody to hepatitis A virus in Liberians. *Trans R Soc Trop Med Hyg* 1980; **74**: 690.
- Ayoola EA. Antibody to hepatitis A virus in healthy Nigerians. *J Natl Med Assoc* 1982; **74**: 465–8.
- Barin F, Denis F, Chotard J et al. Sero-epidemiological study of hepatitis A infection in Senegalese children. *Ann Pediatr* 1980; **27**: 539–42.
- Gebreselassie L. Prevalence of specific markers of viral hepatitis A and B among an Ethiopian population. *Bull WHO* 1983; **61**: 991–6.
- Baylet R, Lemaire JM, Ridet J. Sero-epidemiology of hepatitis A. Results obtained in Senegal. *Pathol Biol* 1981; **29**: 217–21.
- Joshi N, Yr NK, Kumar A. Age related seroprevalence of antibodies to hepatitis A virus in Hyderabad, India. *Trop Gastroenterol* 2000; **21**: 63–5.
- Kunasol P, Cooksley G, Chan VF, et al. Hepatitis A virus: declining seroprevalence in children and adolescents in Southeast Asia. *Southeast Asian J Trop Med Publ Hlth* 1998; **29**: 255–62.
- Kalayanarooj S, Vaughn DW, Snitbhan R, Ariyasriwatana C. Age-specific prevalence of hepatitis A antibody in Thai children. *Southeast Asian J Trop Med Publ Hlth* 1995; **26**: 709–11.
- Barzaga BN. Hepatitis A shifting epidemiology in South-East Asia and China. *Vaccine* 2000; **18**: S61–4.
- Arankalle VA, Tsarev SA, Chadha MS, et al. Age-specific prevalence of antibodies to hepatitis A and E viruses in Pune, India 1982 and 1992. *J Infect Dis* 1995; **171**: 447–50.
- Tanaka J. Hepatitis A shifting epidemiology in Latin America. *Vaccine* 2000; **18** Suppl 1: S57–60.
- Tapia-Conyer R, Santos JI, Cavalcanti AM, et al. Hepatitis A in Latin America: a changing epidemiologic pattern. *Am J Trop Med Hyg* 1999; **61**: 825–9.
- Andre F. Hepatitis B epidemiology in Asia, the Middle East and Africa. *Vaccine* 2000; **18** Suppl 1: S20–2.
- Papaevangelou G. Epidemiology of hepatitis A in Mediterranean countries. *Vaccine* 1992; **10** Suppl 1: S63–6.
- Dal-Re R, Garcia-Corbeira P, Garcia-de-Lomas J. A large percentage of the Spanish population under 30 years of age is not protected against hepatitis A. *J Med Virol* 2000; **60**: 363–6.
- Marinho RT, Valente AR, Ramalho FJ, de Moura MC. The changing epidemiological pattern of hepatitis A in Lisbon, Portugal. *Eur J Gastroenterol Hepatol* 1997; **9**: 795–7.
- el-Hazmi MA. Hepatitis A antibodies: prevalence in Saudi Arabia. *J Trop Med Hyg* 1989; **92**: 427–30.
- Kremastinou J, Kalapothaki V, Trichopoulos D. The changing epidemiologic pattern of hepatitis A infection in urban Greece. *Am J Epidemiol* 1984; **120**: 703–6.
- Cianciara J. Hepatitis A shifting epidemiology in Poland and Eastern Europe. *Vaccine* 2000; **18** Suppl 1: S68–70.
- Gdalevich M, Gillis D, Mimouni D, Grotto I, Shpilberg O. Trends in epidemiology of hepatitis in the Israel

- Defense Forces – direction over several years. *Harefuah* 2000; **138**: 755–7.
27. Gillis D, Yetiv N, Gdalevich M et al. Active versus passive immunization against hepatitis A in the Israel defence forces: a cost–benefit analysis. *Vaccine* 2000; **18**: 3005–10.
 28. Gdalevich M, Grotto I, Mandel Y, Mimouni D, Shemer J, Ashkenazi I. Hepatitis A antibody prevalence among young adults in Israel – the decline continues. *Epidemiol Infect* 1998; **121**: 477–9.
 29. Karenyi YV, Mendelson E, Shlyakhov E, et al. Prevalence of antibodies against hepatitis A virus among new immigrants in Israel. *J Med Virol* 1995; **46**: 61–5.
 30. Green MS, Tsur S, Slepon R. Sociodemographic factors and the declining prevalence of anti-hepatitis A antibodies in young adults in Israel: implications for the new hepatitis A vaccines. *Int J Epidemiol* 1992; **21**: 136–41.
 31. Kark JD, Camhy NA, Shany SB. Reduction in hepatitis A antibody prevalence among young adults in Israel. *Public Hlth Rev* 1992; **20**: 31–40.