

## Hepatitis A Virus: Is Vaccination Necessary in Middle East?

Mehdi Saberifiroozi<sup>1\*</sup>

1. Digestive Disease Research Center (DDRC) and Department of Internal Medicine, Shariati Hospital, Tehran University of Medical Sciences, Tehran, I. R. Iran

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Hepatitis A virus (HAV) infection is a self-limiting disease caused by a 27-nm RNA virus from the picorna virus family. Its' transmission is primarily via the fecal-oral route. The disease is usually mild and anicteric in children, however the rate of the icteric form, severity, and mortality increase in adult life. The estimated case-fatality rate in age over 40 years is approximately 2%, while this rate is less than 0.1% in the pediatric age group. Improvements in sanitation and hygiene will decrease the rate of infection and subsequent acquired immunity in the pediatric population which will increase the susceptibility to infection. Therefore the burden of disease will be increased in young age and adulthood.

Three strategies can be implemented for prevention of this infection such as personal hygiene and enteric isolation, passive immunoprophylaxis by injection of human serum immunoglobulin, and vaccination. The most effective, durable strategy is vaccination, which can be done before exposure or in early post-exposure period.<sup>1,2</sup> Both inactivated and attenuated HAV vaccines are effective and safe. The efficacies of inactivated and attenuated vaccines are around 86% and 95% respectively.<sup>3</sup>

In this issue of Middle East Journal of Digestive Disease, Rabiee et al. have reported the prevalence of HAV infection in students of Tehran University of Medical Sciences. The rate of positive IgG anti-HAV serology was 53.5% in this group of students whose mean age was 20.73 years. Although not a random sample of our population, however they can be a representative sample of young Iranian educated people because they come from different parts of the country. According to this report, at least half were susceptible to HAV infection, which could be an important issue for health care providers.<sup>4</sup>

According to previous reports, as other Middle Eastern countries, Iran was labeled as a high prevalence area. In the last three decades the hygienic conditions, sanitation, and education levels improved significantly.<sup>5</sup> So researchers could predict a decreased rate of enterically transmitted viral hepatitis such as HAV.

Multiple studies have been performed in Iran regarding the preva-

\* **Corresponding Author:**

Mehdi Saberifiroozi, MD  
Professor of Medicine and Gastroenterology,  
Digestive Disease Research Center, Shariati  
Hospital, Tehran University of Medical Sci-  
ences, Tehran, Iran  
Tel: + 98 21 82415104  
Fax: + 98 21 82415777  
Email: saberifm@ams.ac.ir  
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lence of HAV infection. These studies were from different areas of the country had different designs and different results. In a study from Fars Province in southern Iran, out of 1050 participants, 88.2% were positive for anti-HAV. Of participants, a positive serology was documented in 79.3% of participants greater than 20 years of age and in 99% of those greater than 30 years of age ( $p=0.01$ ). The rate of positive serology was more in rural regions (95.9%) compared to urban areas (85.1%). Family crowding was associated with higher antibody levels.<sup>6</sup>

In multiple studies which have been done in Iran, the rates of HAV exposure range from 8.6% to 98.6% in different studies.<sup>7-20</sup> Due to the high fatality rate of HAV infection in patients with chronic liver disease, some researchers reported a 59.4% to 95% exposure rate in this group.<sup>21-24</sup> Vaccination of susceptible persons rather than mass vaccination was proposed in patients with chronic liver disease.

In some Asian and Middle Eastern countries such as Saudi Arabia and Lebanon, which are undergoing an epidemiologic transition of HAV from a hyper-endemic to an intermediate or hypo-endemic pattern, a similar trend is evident. There is a crucial discussion regarding a national vaccination program for the prevention of HAV infection and its sequel.<sup>25-28</sup>

According to our clinical experience, there are an increasing number of severe, acute HAV infections with high rates of morbidity and mortality in adults.<sup>29-31</sup>

Previous studies reported greater than a 90% exposure rate to HAV in the community, however recent studies have reported an exposure rate of less than 50% in the young age group. By considering the high rate of HAV infection in our region, implementation of adequate, suitable and cost-effective preventive strategies is mandatory.<sup>32</sup> In addition to enteric isolation and personal hygiene, other strategies particularly pre- or post-exposure vaccinations for susceptible persons or high-risk group should be seriously considered.

Several countries have adopted universal or mass vaccinations for prevention of HAV, but the decision to implement national vaccinations in the

Middle East region needs additional evidence. The burden of HAV infection and vaccination costs are important considerations for decision-making, particularly in a low resource setting. There are multiple brands of HAV vaccine where the cost of each dose is between 15 to 65 USD. In comparison to other viral infections with greater disease burden and lower vaccination cost such as hepatitis B virus (HBV) infection, currently, there is no clear evidence for suggesting mass vaccination for HAV in our region.

At the present time we have a large proportion of susceptible young adults especially in urban regions. In the future if HAV vaccination is proven necessary, it can be a component of the routine vaccination program such as HBV for all neonates and children. A single combined HBV/HAV vaccine can also be injected at the time of entry into high school as a catch up vaccination for both viruses.<sup>33</sup>

If an outbreak of HAV infection occurs, we should vaccinate susceptible individuals. This method of prevention has been cost-effective in multiple studies. Implementation of accelerated vaccination needs adequate facilities for early diagnosis of an outbreak, identification of susceptible persons, and the feasibility of rapidly vaccinating the target population. In the setting of an outbreak, the injection of a vaccine during the pre- and post-exposure period is more effective than an immunoglobulin injection. In these settings, an accelerated vaccination can be performed for a more rapid effect. One trial studied the combined, accelerated HAV/HBV vaccination injected at 0, 7, 21 days and a booster dose a 12 months with good efficacy and safety.<sup>34</sup>

The World Health Organization has proposed routine vaccination for all children in addition to rapid outbreak diagnosis and control by accelerated vaccination in intermediate prevalence countries such as the Middle East if the burden of HAV infection is significant.<sup>35</sup>

Serologic susceptibility alone is not an adequate reason for implementing a national routine vaccination program. It should be documented that HAV infection is an important health problem in the com-

munity. The burden of HAV infection in the region should be determined along with documentation of the incident cases of acute hepatitis, fulminant liver failure, the rate of liver transplant due to HAV, and the rate of mortality by this infection at the national level.

The economic burden for routine vaccination in children should be calculated. The cost for each vaccine dose varies. In the US, the pediatric vaccine dose is approximately 15-30 USD; the adult dose is around 25-65 USD, and the adult type combined HAV/HBV is approximately 45-92 USD. Lower cost vaccines are available in India, Australia, and China, which can be used accordingly. This cost may equal the cost of an HBV vaccine; however the burden of HBV in the Middle East region is higher than HAV. A priority setting is necessary in each country compared to other national health problems. In some countries, for reducing the cost of mass vaccination, the dose of vaccine has been reduced to a single injection, which it seems to be effective.<sup>36-39</sup>

Currently there are no adequate and clear evidences for a national mass vaccination program for HAV infection. High risk groups should be identified. There should be simultaneous maintenance of good surveillance and control procedures by training health care providers, in addition to the design of a suitable health infrastructure, and determining the epidemiological data of infection, complications and death rate due to HAV.

Importantly there are a large number of persons susceptible to HAV, particularly in adults who reside in cities. These people are at risk for future infection and severe disease as possible outbreaks. The following strategies should be implemented for outbreak control such as determining the source of infection. Is there a common source of infection such as water, food, or a person-to-person source of infection? In addition there should be rapid identification of people who are at risk. Implementation of rapid vaccination, destruction of common source of infection, and maintaining adequate personal and community hygienic conditions should be undertaken.

## CONFLICT OF INTEREST

The author declares no conflict of interest related to this work.

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