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Hepatitis A in the Eastern Mediterranean Region: A Review on the Prevalence

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Context: Hepatitis A continues to be a major health problem worldwide with 1.5 million symptomatic cases annually. As a result of improved sanitary conditions, several studies have reported a shifting epidemiological pattern for this viral infection from various parts of the world. Considering that most of Eastern Mediterranean countries have been known endemic for HAV, this review was performed to make its current magnitude more clarified in this area.

Evidence Acquisitions: This review summarizes the publications on HAV epidemiology in EMRO countries. A relatively complete search was performed in MEDLINE and EMBASE to identify the most relevant manuscripts published from 1980 to 2010.

Results: Besides some studies illustrated a down sloping prevalence in some countries, still there are some areas with intermediate and high seropositivity of HAV in EMRO. Additionally, considering the ever-increasing relationships between different countries and nations following globalization, there are a large number of HAV susceptible people from nonendemic and low endemic regions who travel to EMRO countries each year. This heterogeneous HAV exposure profile among population should be considered as a serious threat which makes HAV outbreaks happening more probable in EMRO.

Conclusions: Regarding the heterogeneity of HAV prevalence in different regions shown here, more accurate prevalence data should be obtained from the whole area to be able to design more efficient protective strategies against HAV in EMRO.

Keywords: Hepatitis A; Epidemiology; Prevalence; Vaccine

1. Context

Approximately 1.5 million symptomatic cases of hepatitis A virus (HAV) infection happen in the world each year (1). Hepatitis A virus was first isolated in 1973 (2). It is a small, nonenveloped RNA virus that belongs to Picornaviridae family (3) and causes 75% of all cases of hepatitis worldwide (4). Since then, investigations have been performed to clarify HAV structure (5), the process of getting infected, and to find an efficient way of preventing hepatitis A among populations (6-8). Replication of HAV occurs in liver; it is secreted to bile, and is highly found in stool, especially during the late incubation period and the first week of symptomatic phase of disease (9). This infection can be easily transmitted through fecal-oral route, by close contact with infected person, and contaminated food and water and even blood products (10). Prevalence of HAV infection is not the same in different parts of the world (varies between 15% and 100%), and depends on geographic area, sanitary levels and socioeconomic conditions (11-14). Meanwhile, a shifting epidemiological pattern from high to intermediate and low seropositivity has been shown in many countries, some of which are underdeveloped and developing countries (4, 7, 15-18). Although this change seems desirable, it can lead to a higher risk of outbreaks among adult population who have not been exposed to HAV in their life and are not immune against it (7, 19). Superimposing of HAV in patients with chronic liver disease during epidemics can end in many deaths (20-22). In addition, hepatitis A is often asymptomatic in childhood and its morbidity and fatality increase by age (7, 23, 24). To protect these nonimmune people, or at least, to evaluate if it is necessary to protect them, estimating HAV epidemiology in areas like EMRO countries which are known as HAV endemic regions seems necessary.

Actually, clarify of epidemiological pattern of HAV infection can be helpful in further planning to keep it under control and impede outbreaks. In this review, epidemiological investigations from this geographic zone, mostly those based on the accumulated data from 1980 to 2010, were studied to more clarify the HAV current magnitude in Eastern Mediterranean Regional Organization (EMRO) countries.

Implication for health policy/practice/research/medical education:
Epidemiology of hepatitis A infection has changed during the recent years, and health policy makers and infectious specialists as well as other specialties should know about the situation in their community.

2. Evidence Acquisition

Potentially relevant studies were identified using an electronic search since 1980 up to 2010 in Medline, Embase, Scopus and ISI. The searches were performed using several predefined combinations of the following keywords and MESH terms or their equivalents without temporal limits: Hepatitis A, HAV, Prevalence, Epidemiology, Outbreak, and EMRO. The additive search was performed by the names of all countries in EMRO area separately (Afghanistan, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, The United Arab Emirates, Yemen). Additionally, Persian-specific databases including SID, EMR Medex, websites of Iranian universities, Iran Medex and MagIran were searched using the aforementioned keywords. The final list of obtained titles and abstracts was reviewed by the two authors, and eligible studies were ascertained and their full texts were obtained. Furthermore, bibliographies of included studies were screened to find other relevant studies. Included manuscripts should have been studies published in full, and the final decision on their eligibility has been made by consensus.

3. Results

Two hundred and ninety nine potentially relevant studies were imported to our Endnote library. Through title and abstract screening by the two authors, 82 more relevant studies were selected and their full texts were obtained. Finally, 33 studies were enrolled in our review on the epidemiology of HAV in EMRO countries. Iran, Saudi Arabia, Egypt, Lebanon and Pakistan had 9, 7, 5, 3 and two studies respectively. One study was found for each of Afghanistan, Kuwait, Morocco, Palestine, Somalia, Syria and the United Arab of Emirates. Unfortunately, no relevant study was found for Tunisia, Yemen, Sudan, Qatar, Oman, Libya, Jordan, Iraq, Djibouti, and Bahrain. Prevalence data obtained from previous epidemiological studies in EMRO countries are summarized in Table 1.

Table 1. HAV Prevalence in Different EMRO Countries

Authors	Publication Year	Target Population	Studied Population, No.	Age, y	HAV Prevalence, %
Afghanistan					
Carmoi et al. (25)	2009	Residents of the Kabul district who visited the French military field hospital	102	5-65	99
Egypt					
El-Karaksy et al. (26)	2008	Children with chronic liver diseases	172	< 5	62.1
Salama et al. (27)	2007	Children of different socioeconomic status (SES) in Cairo: Low SES	426	3-18	90
		High SES	142	3-18	50
Omar et al. (28)	2000	A group of socially and economically deficient preschool children of Alexandria	228	< 7	26.3
Darwish et al. (29)	1996	Residents of a semiurban village in the Nile River delta	155	1-67	100
Ramia (30)	1986	Egyptian blood donors in Saudi Arabia		20-35	91-94.5
Iran					
Merat et al. (31)	2010	General population of three Iranian provinces (Tehran, Golestan and Hormozgan)	1869	18-65	86
Ataei et al. (32)	2008	General population of urban and rural areas of Isfahan province	816	> 6	8.33
Roushan et al. (33)	2007	Hepatitis B chronically infected patients of Babol, a northern city	392	10-19	59.4
				20-29	89.8
				> 29	97.5
Ghorbani et al. (1)	2007	Army draftees in Tehran	800	19 ± 1	97.63
Alizadeh et al. (34)	2007	Chronically HBV infected patients in Hamedan province	83	10-77	85.5
		Chronically HCV infected patients in Hamedan province	39	30-49	92.3
Saberifiroozi et al. (35)	2005	Chronic liver disease patients in Shiraz city	204	ND [a]	98
Nassrolahei et al. (36)	2004	Healthy volunteers of Mazandaran province	374	3-81	30.9
Mehr et al. (37)	2004	Children visited in four major hospitals of Tehran	1018	0.5-14.9	22.3
Moghani-Lankarani et al. (38)	2004	Chronically HBV infected patients of Tehran Hepatitis Center	283	< 30	65.3
				30-49	80.4

				> 50	93.1
Kuwait					
Alkhalidi et al. (39)	2009	Kuwaitis applying for new jobs	2851	ND [a]	28.8
Lebanon					
Bizri et al. (40)	2006	Students of 30 schools scattered all over Lebanon	902	14-18	71.3
Sacy et al. (41)	2005	General population	606	1-5	11
				6-10	28
				≥ 21	78
Shammaa et al. (42)	1982	General population	772	Adults	97.7
Morocco					
Bouskraoui et al. (43)	2009	Moroccan children	150	0.5-6	42.5
				7-14	70.3
Pakistan					
Aziz et al. (44)	2007	the pediatric age group of low socioeconomic urban communities of Karachi	380	≥ 14	100
Agboatwalla et al. (45)	1994	Healthy Pakistani children	258	< 5	94
Palestine					
Yassin et al. (46)	2001	School children of the Gaza strip	396	ND	93.7
Saudi Arabia					
Al Faleh et al. (47)	2008	Children from three different regions: Madinah, Al-Qaseem, Aseer	1357	16-18	18.6
Almuneef et al. (48)	2006	Newly hired employees of a care center in Riyadh	4006		67
		Children attending national guard schools	2399	> 8	7
				8-11	14
				12-15	30
				< 16	52
Fathalla et al. (49)	2000	Eastern Saudi Arabia	1167	Children and adults	86
Khalil et al. (50)	1998	Children presenting at clinics in Riyadh	592	≥ 6	13-20
				7-15	32-49
Al Rashed et al. (51)	1997	Saudi Arabian children	4375	Children	52.4
Arif (52)	1996	The populations of two areas of Saudi Arabia: Gizan (a rural area)	ND	ND	76.3
		Riyadh (an urban area with relatively good sanitation)	ND	ND	61.3
el-Hazmi (53)	1989	Male	ND	ND	96
		Female	ND	ND	95.1
Ashraf et al. (54)	1986	Hemodialysis patients	55	ND	100
Somalia					
Bile et al. (55)	1992	children from two residential institutions: Shebeli	596	ND	96
		Societe Organisation Sociale	76	ND	59
Syria					
Antaki et al. (56)	2000	General population	894	ND	89
The UAE					
Sharar et al. (57)	2008	Children who had nonhepatic related consultations in Abu Dhabi	367	< 12	20.1

[a] Abbreviation: ND, not determine

3.1. Epidemiology of Hepatitis A in EMRO Countries

Although HAV infection still seems endemic in number of EMRO countries, there is not enough data of current situation of this disease in the mentioned area. According to epidemiology of HAV infection, great differences exist among EMRO countries and also among various parts of the same country in some regions due to their sanitary and socioeconomic levels. Epidemiology of HAV infection in some of the Middle East countries and parts of Africa, most included in EMRO has been studied in 2000. Against scant data, HAV prevalence in Africa illustrated to be high in that manuscript and a shifting pattern from high to intermediate or low seropositivity has been reported in some of studied Middle East countries with remained high endemicity in others (15). According to table 1, declination in HAV seropositivity is apparent in parts of shown results. Vast range of HAV prevalence

in different parts or among different populations of the same country is also considerable (1, 36, 52, 58). This variety might be the result of different sanitary levels and hygienic improvements in various parts of countries.

3.2. HAV Prevalence in Children of EMRO Countries

IgG anti-HAV seropositivity of children has been investigated in a number of previous manuscripts. In a study from Egypt in 2000 anti-HAV seropositivity was reported to be 26.3% in children younger than seven years (28). In another study in 2007, 90% seropositivity was reported in children aging 3-18 years who were from low socioeconomic status, and 50% for those who were from high socioeconomic status of Cairo (27). On the other hand, Egyptian children with chronic liver disease were shown to have a seropositivity rate of 62.1% to 94.4% in 2008 (26). In a study on Saudi Arabian children, anti-HAV seropositivity was shown to be 52.4% in 1997 (51). Besides, in 1998, a seropositivity rate of 13-20% was reported for children younger than 6 years, and 32-49% for those aging 7-15 years who presented in Riyadh clinics for reasons other than hepatitis (50). Furthermore, Alumneef et al. investigated anti-HAV serostatus of children attending National Guard schools in 2006, and reported 7%, 14%, 30%, and 52% of seropositivity rates for children younger than 8 years, 8-11 , 12-15, and older than 16 respectively (48). Another study on 16-18 years old Saudi children in 2008 showed that 18.6% of them had anti-HAV (47).

In a study from Lebanon in 2005, 11% of children between 1-5 years of age, and 28% of those between 6-10 years were anti-HAV seropositive (41). Besides, a seropositivity of 71.3% was reported for students from 30 schools scattered in Lebanon in 2006 (40).

Two studies from Pakistan in 1994 and 2007 showed a seropositivity rate of 94% for children younger than 5 years, and 100% for those older than 14 years respectively (44, 45).

A study from Iran in 2004 reported that 22.3% of children aging 0.5 to 14.9 years who attended four major hospitals in Tehran had positive results for anti-HAV (37). 42.5% and 70.3% of Moroccan children aging 0.5-6 and 7-14 years had positive results for anti-HAV respectively (43). Furthermore, a seropositivity of 93.7% was reported for Palestine children from Gaze strip in 2001 (46). Moreover, in a study from Somalia in 1992 which was performed in two residential regions, children were 59 to 96% anti-HAV seropositive (55). Finally, in a study from the United Arab Emirates on children younger than 12 years, 20% showed to be anti-HAV seropositive in 2008 (57). No direct data is available on the prevalence of HAV among children from other EMRO countries.

3.3. HAV Prevalence in Adults of EMRO Countries

100% of residents of Nile delta were shown to be anti-HAV seropositive in 1996 (29). Moreover, in a study on Egyptian blood donors in Saudi Arabia in 1986, 91-94.5% were anti-HAV seropositive (30). A study on residents of Kabul district visiting the French military field hospital showed a positive anti-HAV serostatus of 99% (25). In a recently published study on Iranian general population by Merat et al., 86% of the studied population aging 18-65 years were illustrated to be anti-HAV seropositive (31). Ghorbani et al. in 2007 showed that 97.63% of army draftees in Tehran, with the mean age of 19 years, were anti-HAV seropositive (1). Another study in 2008 from Isfahan province showed that 8.33% of population had positive results for anti-HAV (32), while 30.9% of studied population in Mazandaran province aging 3-81 years were reported to have positive results for anti-HAV (36).

In a study on newly hired employees of a care center in Riyadh in 2006, 67% were seropositive (48); whereas, 86% of seropositivity was shown by Fathalla et al. in 2000 among 11674 healthy population of Eastern Saudi (49) (Figure 1). 76.3% and 61.3% of studied population were shown to be anti-HAV seropositive by Arif in 1996 in Gizan and Riyadh respectively (52). In another study in 1989, 96% of males and 95.1% of females were reported have positive results (53). From the other side, 98.5% of Saudi patients with chronic liver disease were shown to have positive results for anti-HAV in 2009 (59). One study in 2005 from Lebanon showed that 78% of population older than 21 years had positive findings for anti-HAV IgG (41), while a seropositivity rate of 97.7% was reported in adults in 1982 (42). 89% of Syrians showed to be anti-HAV seropositive in 2000 by Antaki et al. (56), and 28.8% of Kuwaitis applying for new jobs were shown to have positive results in 2009 (39). Information about HAV prevalence in adults of other EMRO countries could not be obtained.

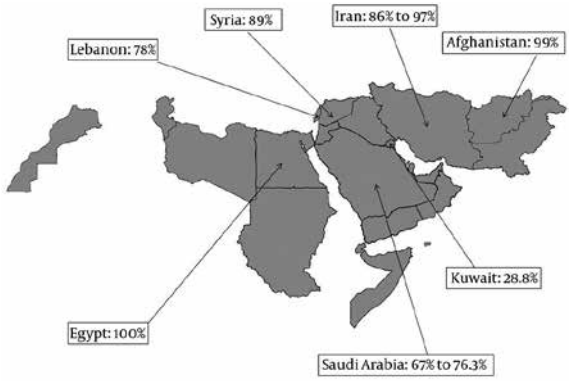

Figure 1. Distribution of HAV in EMRO Countries in adult group

4. Conclusions

In this review, the prevalence of HAV infection and its epidemiology in EMRO countries was studied. Although seroprevalence of HAV has decreased in many parts of the world, it is still high in a number of EMRO countries. For instance, it can be claimed that more than 70% of adult population still have positive findings for anti-HAV IgG in Egypt, Iran, Afghanistan, Lebanon, Morocco, Pakistan,

Somalia and Syria (Table 1). Although data from Somalia and Syria is not that recent, they are the only available data on the discussed issue. Aforementioned points clarify that the results of studies performed in other parts of the world, especially in developed countries, cannot be generalized to EMRO area which includes a considerable number of underdeveloped and developing countries. As it is illustrated in Table 1, most EMRO countries can still be categorized as HAV endemic regions. Nonetheless, there are countries such as Saudi Arabia and Lebanon which show an obvious down sloping prevalence of HAV among their population. In addition, a low HAV prevalence of 28.8% was reported in Kuwaitis applying for new jobs in 2009 (39). A low HAV prevalence was reported for children of the United Arab Emirates as well (57), but this result cannot be attributed to general population of UAE considering the fact that HAV prevalence increases dramatically by age. On the other hand, heterogeneity of HAV prevalence in different areas of the same country has been reported frequently in EMRO area which is a result of nonequivalent hygienic improvements. This heterogeneity can be seen obviously between different parts of Iran, Egypt, and Somalia in table 1. However, differences among studies' design and studied population should be kept in mind as other influencing factors as well. Touristic spots of EMRO area attract a large number of people from all over the world annually. Thousands of Muslim pilgrims who attend Hajj in Mecca, Saudi Arabia, can be mentioned as an example, and hajji peoples are at a higher risk of acquiring the blood born and other viruses (60). Many of these travelers are not immune against HAV, because they come from the countries in which HAV prevalence is low. Moreover, as EMRO area is an unrest military zone, almost always there exist a number of western soldiers who are not immune against HAV. This daily spread number of nonimmune people should be emphasized as a serious threat of happening HAV outbreaks. Regarding so many influencing factors, in many situations, it would be very difficult to choose the most appropriate prevention strategy in EMRO area. One of the most significant influencing factors is HAV epidemiology which should be included in all decision making programs. It can be inferred that the first step in designing protection ways is to gain more accurate data of HAV current prevalence in the world, especially in the discussed area.

To make a decision about the best prevention strategy other influencing factors like the annually incidence of fulminant hepatitis following Hepatitis A in each country, accurate HAV seropositivity in different age groups, costs of these patients hospitalization and treatment, and costs of HAV vaccine, in addition to Gross National Income (GNI) should be considered (10). However, vaccination has been mentioned as an effective preventive measure which decreases the incidence of fulminant hepatitis (13, 61). Cost effectiveness studies will help us analyze all the aforementioned variables together, and draw a robust conclusion about HAV mass vaccination (10). Unfortunately, although the risk of HAV outbreaks is really high in EMRO area, accurate prevalence data from many of these countries cannot be found. On the other hand, there are other countries such as Iran, Saudi Arabia and Egypt located in EMRO, in which a number of epidemiological studies on the prevalence of HAV have been performed.

In conclusion, according to available data, HAV vaccination should be considered as a crucial issue in Saudi Arabia and Kuwait concerning their low HAV prevalence, while this issue needs to be investigated more thoroughly in Iran, Egypt, Pakistan, Lebanon, Afghanistan, and Morocco. Precise epidemiological data are required to be able to give an opinion about the necessity of HAV mass vaccination in other EMRO countries.

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Authors' Contribution

Dr. Nastaran Mahboobi did the search in the literature and prepared the first manuscript, Dr. Seyed Moayed Alavian helped in completion the search in the literature and finalizing the manuscript.

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