Infection Diseases Section *Review Article*

A Global Perspective on the Intrafamilial Transmission of Hepatitis B Virus Infection

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Abstract

The major transmission route of HBV virus is contact with the blood or other body fluids of an infected person. Apart from parenteral, sexual and vertical transmission, HBV may be transmitted through child to child or household personal contact- but not casual contact, and spread of the infection has been reported through household contacts. This review article aims to evaluate the epidemiology of intrafamilial transmission of HBV infection in different parts of the world.

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Introduction

In a global perspective, hepatitis B virus (HBV) infection characterizes a major health problem with almost 2 billion people representing serological evidence of a HBV infection; and about 350 million live people with chronic infection whose estimated annual mortality comprises to 600,000 persons, due to the acute or chronic consequences of HBV infection [1,2].

The conventional transmission route of HBV virus is contact with the blood or other body fluids of an infected person. Apart from parenteral, sexual and vertical transmission, HBV may be transmitted through child to child or household personal contact- but not casual contact [3]. So, it would not be surprising if several members of the same household represent evidence of HBV infection. In these cases, viral transmission is thought to occur through intrafamilial contact, resulting in clustering of HBV infection within family groups [4-6] .On the other hand, genetic factors as well as maternal or sexual transmissions are not supposed to play major roles in the intrafamilial HBV spread. So, the precise mechanisms of intrafamilial spread of HBV remain to be established in each area, to help health authorities in order to develop preventive strategies [7,8]. For this purpose, one firstly needs to conduct epidemiological studies in different regions to well understand associations of intrafamilial HBV transmission [9]. Until now, several studies from various countries have reported intrafamilial spread of HBV. In this article, we aim to review the existing literature to determine the epidemiology and patterns of HBV transmission between the family members of different regions of the world, and to identify the best preventive strategies, as the best and most cost-effective method, which can be undertaken in all countries of high or low financial resources, to minimize this health dilemma throughout the globe [10].

Literature Search Method

A comprehensive search of the literature was conducted to find all reports on the intrafamilial spread of HBV infection in different world

regions. Search engines used for this purpose were Google Scholar, Thomson Reuters and Medline. Keywords employed for the literature search included “intrafamilial transmission of hepatitis B virus infection”, “hepatitis B virus transmission + children”, “hepatitis B virus transmission family members”, “hepatitis B virus horizontal transmission”, “hepatitis B virus vertical transmission”. All the search terms were repeated using HBV instead of “hepatitis B virus”. In all the reviewed articles, only HBsAg was considered for determining co-infection.

Prevalence of Familial HBV Infection

The prevalence of HBsAg among family members of Iranian HBV carriers has been reported from 11% in a study from Nahavand [11] to over 20% in Hamadan province, and to over 25% in Charmahal O Bakhtiari Province [12,13]. In Turkey, this rate is up to 38%, which is quite an alarming percentage [14]. This high rate of infection in Turkey should also alert Iranian health authorities, because the studied Turkish province is near the Iranian border. In Greece, the HBsAg positive rate was about 16% among family members of carriers [15] and in Bosnia and Herzegovina, this prevalence was about 12% [16]. Due to a relatively diverse cultural behavior and living style in different regions of Iran, this wide range of intrafamilial prevalence of HBV reflects more dangerous behaviors in specific regions of the country, highlighting the relevance of education to develop preventive strategies. Moreover, the significant higher frequency of illiterate people representing positive HBsAg emphasizes on the importance of education.

Perinatal Transmission

Perinatal transmission of HBV infection is of crucial importance because it is associated with a substantial risk of getting chronic; and heavy preventive orders have been suggested to break this transmission route [17]. It is speculated that the HBsAg carrier rate increases rapidly between the first and second years of age; but does not substantially change during the subsequent years [18].

In the Middle East, perinatal transmission of HBV has been proposed not to play major roles [19]. Studies from Turkey have suggested that perinatal HBV transmission is not a common route of intrafamilial infection spread [14,20,21]. Another report from turkey showed that fathers of the index cases had a higher level of antigen positivity than mothers (61% vs. 47%) [22]. In a Western Brazilian population, offsprings represented the least rate of HBsAg positivity compared to other family members [23]. Similar observation has been reported from Nahavand in Iran, where mothers of the index cases did not represent high prevalence of HBV infection in this region [11], although in another study from Charmahal O Bakhtiari Province of Iran, higher rate of co-infection has been reported for mothers of the index cases, highlighting the importance of perinatal transmission route in this country area [12]. Studies from other countries also suggest perinatal transmission of HBV as a major virus spread way [24]. In Greece, mothers of the infected index cases were at the same risk of being HBsAg positive to that of fathers; but offsprings of the infected mothers were at over 3 times larger risk of HBsAg positivity [15]; similar to a report from Brazil [25], in a report from Bosnia and Herzegovina, mothers represented the highest rate of coinfection to the index cases [16]; a Tunisian study [26] showed that 21% of the children born to infected mothers were HBsAg positive which is higher than that of an Iranian report [12]; the same study showed that being HBeAg positive for a mother increases the carrier rate of the born children to 73%. A study from India, as well, showed that offsprings of the carrier mothers represent the highest rate of co-infection [27]; although these disparities might be able to suggest the perinatal transmission of HBV as an important route, due to a lack of time sequence determination, one can argue that this does not essentially show a vertical transmission in the perinatal period, and might be simply related to afterward contacts between mothers – who are obviously at higher contact to their offsprings than fathers - and children.

Sexual Transmission between Sex Partners

Sexual relationship is one of the confirmed routes of HBV transmission among the human populations and therefore, husbands and wives as well as sex partners have always been of particular interest, because due to the very high rate of interpersonal sexual relations in the young population, a transmissible infection will have a high chance of rapid spread in the society. In the

Middle East, sexual contact has been reported a significant path of HBV spread. A study from Hamadan, Iran reported a 32% HBsAg positivity for the spouses of the index carriers [13]. In Turkey, husbands of the infected wives were at a substantial risk of co-infection (70% vs. 22% for their female counterparts) [14]. Similar to the study from Greece [15], in an Iranian study from Nahavand, this rate was equal to that of wives, but in another one [12], wives represented the predominant sexual partners to be coinfected to the index case. In Bosnia and Herzegovina, although the percentage of the infected husbands (to the index cases) was low (1/13(7.7%)), this rate was 0% (0/36) among wives. Putting together, it is surprising to conclude that according to the existing evidence, male sex partners (husbands) seems to be at a higher risk for getting the HBV infection, than their female counterparts (wives) .

Non-sexual Horizontal Transmission

Coinfection between siblings probably provides the best evidence for non-sexual horizontal transmission of HBV infection between members of a family. In the Turkish study [14], after husbands and offsprings of the carrier mothers, siblings were the predominated family members representing co-infection to the index cases, with the same rate for the two genders (about 40%). However, in the study from Nahavand, Iran, brothers had the highest rate of infection than all other types of family relations (25%) including sisters (10%). Similar to Nahavand, a Greek report also indicated brothers as having the highest rate of coinfection (60%). The condition in Bosnia and Herzegovina was similar to that in Nahavand, with a 25% rate of coinfection for brothers which represented the second highest rate of HBsAg positivity after mothers. An Iranian study from Charmahal O Bakhtiari Province reported 15% rate of coinfection for siblings, with no special report for the gender groups. For Brazil, controversial reports exist with one study reporting 75% of infection rate for the siblings [23], while another one reports a low rate of only 4% for the same group [25]. In an Indian report, siblings represented the highest HBsAg positivity rate among all family members [27]. On the other hand, direct evidence for non-sexual horizontal transmission methods of HBV have been reported in some populations. A study from Brazil [23] showed that shared used of toothbrush was a significant factor playing role in the spread of HBV between family members in this country; the same study reported nail clippers as a facilitating tool for infection spread; although significance level was not achieved. Other non-hygienic behavious including contact during play, exposure of open wounds, sharing towels and razors, and exchange of chewing gum and candies have also been accused in promoting infectious rate in the populations especially in children [28,29]

Cultural and Behavioral Issues

Traditional transmission routes have been reported in several reports from different regions of the world. Imani et al. [12] in an Iranian study found that in non-vaccinated study participants, ear piercing, phlebotomy and rural life still play significant roles in these families which have previously been reported as strong risk factors for HBV transmission in Iran and other regional countries [30]. This finding is very important and shows that co-infections in particular families does not essentially show transmission of the infection between family members and shows that the higher incidence of HBV infection in these families might be due to higher incidences of risky behaviors in these families. Moreover, it signifies the relevance of HBV vaccination, as an overwhelmingly confirmed effective preventive strategy [31,32], in order to decrease the risk of infection spread. Despite the overall decreasing curve for the epidemiology of HBV infection in Iran [33], the significant role for the rural life also alerts us that health measures and preventive methods are not well maintained in these societies, and should be considered as an urgent health obstacle to issue. On the other hand, the HBsAg positive rate of 12% for vaccinated patients reported in an Iranian study [12] is not surprising and can be explained either by vaccination after getting the infection or vaccine inefficiency due to several things including not maintaining the cold chain [34].

Conclusion

Compared to the general population, the substantially large share of the HBV infection rate among family members of virus carriers shows that intrafamilial transmission of HBV infection

is a very important spread path for the HBV, which can be simply prevented through education and adherence to hygienic precautions. On the other hand, the high rate of risky behaviors as well as higher rate of illiteracy in these families reported by different studies emphasizes on the importance of promoting education and hygienic precautions in these societies. Unfortunately most of the publications in the current literature are cross-sectional, and the number of prospective studies is very limited. The time sequence of transmission among family members in cross-sectional studies is vague, and so, there is no warrant that the carrier labeled as the index case is actually the first infected member of the family. Therefore, determination of the index cases was arbitrary in these studies. So, we recommend conducting prospective studies of large populations, especially in families who only have one HBV carrier case, and other members have been confirmed negative for HBV at the entrance to the study.

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Conflict of Interests
None Declared.

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