

Original Article

Family Members have Greater Risk of Hepatitis B due to Horizontal Transmission

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Abstract

Introduction: Hepatitis B virus (HBV) infection is found worldwide. Its prevalence and predominant mode of transmission vary among geographic regions. The mode of horizontal transmission is important especially in household contacts of HBV living in an endemic area. The aim is to assess the predominant mode of HBV transmission among family members of index persons positive for hepatitis B surface antigen (HBsAg).

Methods: 100 subjects positive for HBsAg and their family members were tested for the markers of HBV infection by ELISA following the manufacturers' methodology. Their state of infection and rate of exposure in various age groups, occupational groups and in particular risk groups were analyzed to assess over the mode of transmission of HBV in the families.

Results: A total of 100 families, including a total of 532 subjects (age: 25.98 ± 15.66 years, mean \pm SD; sex (male/female): 280/253 were studied of whom 506 (95%) were obligate family members, 161(30.3%) had previous history of jaundice, 121(22.7%) had history of surgery and 63 (11.9%) had history of blood transfusion. Most of the subjects ($n=252$) belonged to the wide age groups of 5-60 years. 191(35.9%) were students followed by 112 (21.1%) housewives, 105 (19.7%) service holders, 42 (7.9%) businessmen, 10 (1.9%) health care personnel and 68 (12.8%) had no particular occupation. Overall 309 (58.1%) subjects were exposed to HBV. Exposure was more among house wives (68.8%), service holders (66.7%), businessmen (64.3%), health care personnel (60.0%) and students (48.2%). Though there was a male preponderance (53.4%) to HBV exposure than females (46.6%), frequencies for exposure were higher in females in the preschool age group (male vs. female: 20.0% vs. 80.0%), school age group (44.4% vs. 55.6%) and in young adults (47.8% vs. 52.2%). Chronic infection was observed in 110 (20.6%), acute infection in 30 (5.6%) and 115 (21.6%) had recovered after exposure while 53 (10.0%) showed atypical serology. Among the risk groups, 37% of the HBV exposed had history of jaundice, 23.7% had history of surgery and 8.1% had history of blood transfusion.

Conclusion: Results of this study suggests a high rate of HBV infection in the family members of persons with positive HBV markers. Horizontal transmission due to repeated contacts among the family members may be an important mode of transmission of the HBV.

Key words: HBV infection, Family contact, Horizontal transmission

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Introduction

Hepatitis B virus (HBV) infection is one of the major health problems in all geographical areas of the globe. In Bangladesh, there is paucity of information on the prevalence of HBV infections among general population and majority of the previous studies were conducted in selected group of people with higher risk factors such as blood donors, drug addicts, commercial sex workers (CSWs) or hospitalized patients.^{1,8} However, a recent report showed 5.5% HBsAg positivity among the general population living in Savar, a semi-urban area on the outskirts of Dhaka.⁹ Although HBsAg is the most reliable biological biomarker of HBV infection, and the anti-HBc antibody is an important marker for surveying the burden of HBV infection as it persists even after resolution of infection, and thus identifies both past and current HBV infection.¹⁰ Among the different modes of transmission, horizontal transmission of the HBV is important for an endemic area like Bangladesh which has not yet been investigated in the country. Horizontal transmission is not attributable to sexual contact, parenteral contact with blood or blood products, or to vertical transmission from mother to child, but to small wounds, wound exudates, saliva or by other means.¹¹ This way of transmission is important in household contacts of HBV carriers, in

institutions for the mentally handicapped persons and to lesser extent in nursery schools. It occurs especially in preadolescent children in an endemic area. However, the mechanisms of horizontal transmission are not clear. Children acquiring the disease under the age of 5 years usually become chronic carrier.¹² In most cases, they acquire the disease from infective mothers but may also be infected from other family members as well as from playmates.¹² These carrier children usually remain unknown following subclinical infections and serve as a major source of infection. Thus an initial perinatal transmission ultimately leads to multiple horizontal transmissions. In low endemic areas, HBV infection is acquired usually in adult life, most often through parenteral or sexual contact and is common only in certain high risk groups (e.g. intravenous drug abusers, promiscuous homosexual, health care personnel etc).¹³ In contrast, in endemic areas like Southeast Asia, the infection is often acquired at or near the time of birth from a carrier mother, more often the infection occurs later in childhood, in the absence of identifiable maternal, sexual or parenteral exposure to the virus.¹³ However, perinatal transmission of the disease is reported to be the most important mode of transmission in Southeast Asian countries.¹³ Hepatitis B virus infection is a major cause of morbidity and mortality related to chronic

liver diseases.¹⁴ Asymptomatic carriers are considered to be the commonest source of infection with hepatitis B virus.¹⁴ As carriers of hepatitis B is a potent source of infection in a family, all the member live in his contact are at risk of acquiring the disease. Even after identification of an acute or chronic cases of hepatitis B, attending physicians only concentrate to the management of the diseased individual ignoring the potential hazard of transmission of the disease to other family members. Most of the adult patients recover after an infection but during the disease period, the younger family members may acquire the disease and they are more prone to develop a chronic carrier state. Therefore, prevention of the infection should be considered equally important. Unless the risk potential is studied and documented, awareness among the clinician may not be achieved. We have experienced that just after knowing a family member positive for hepatitis B surface antigen (HBsAg), apprehensive relatives run for vaccination. Usually they undergo prevaccination screening for HBsAg and get vaccinated. In some cases, even the vaccination is done without prior screening. But it is not realized that the known HBsAg positive individual may be the first or only exposed or infected person in that family. There may be one or more infective carriers within the family and the known positive

person might have acquired the disease from the apparently healthy carrier. Alternatively, the HBsAg positive individual might have acquired the disease from outside and has already disseminated the disease to other family members in contacts.

We would like to investigate the extent and mode of disease transmission among the household contacts of HBV carriers as well as acutely infected individuals. This will reveal the importance of horizontal transmission compared to sexual and perinatal transmission of HBV in our society. Development of a vaccination strategy and selection of HBV markers during prevaccination screening of high risk families would also be possible by a serological study on such family members. This study is also targeted to develop awareness both among the physicians as well as the family members of patients with hepatitis B. Once we could know extent and predominant mode of disease transmission within the family members, we can propose a prevaccination screening strategy for high risk family. Selection of the HBV markers for prevaccination screening will depend on the rate of exposure (clinical or subclinical infection), rate of complete recovery with development of neutralizing antibody, and rate of infected acute or chronic carrier states within these families.

Materials and Methods

This cross sectional study population included 100 HBsAg positive patients randomly selected from the routine test service in the department of Immunology at BIRDEM hospital March 2009 to February 2010. All the family members of HBsAg positive patients were investigated for markers of HBV infection (HBsAg; hepatitis B e antigen: HBeAg; antibody to hepatitis B surface antigen: anti-HBs; antibody to hepatitis B core antigen: anti-HBc (both IgM and IgG) to find out the state of infection. Exposure to HBV was defined by the presence of anti-HBc, HBsAg, IgM anti-HBc and anti-HBs singly or in combination; carrier state defined by positive HBsAg and anti-HBc but negative for IgM anti-HBc; while immunity due to natural infection was defined by positive anti-HBc plus anti-HBs. Serological tests were performed by ELISA using commercially available kits following the instructions of the manufacturers. Ethical clearance was obtained from the ethical review committee of Diabetic Association of Bangladesh. Data were expressed in frequencies and mean \pm SD unless mentioned otherwise. Each person positive for HBsAg in a family was considered as a potential source of infection. Analysis about impact of relationship among persons in that family was done holding each HBsAg

positive person as index case in that circumstance. Comparison among different groups was done by Chi-square, Student's t-test or ANOVA. Relationship and predictive capability among the markers in the individuals at different state of infection were analyzed by Spearman's correlation and Logistic regression. P values ≤ 0.5 were considered as significant. Data were analyzed using SPSS version 16.

Results

Out of 100 families, 532 subjects were studied for various markers of HBV (Table I). Average number of subjects per family was 5 with a near equal sex distribution (male/female: 280/253). Mean (\pm SD) age was 25.98 ± 15.66 years ranging between 0.5-76 years. Some 506 (95%) were obligate family members (506/533), 161 (30.3%) had previous history of jaundice, 121 (22.7%) had history of surgery and 32 (60%) had history of blood transfusion. Vaccine against HBV was taken by 63 (11.9%) subjects.

Table I: Profile of the study subjects (n=532)

Character	Values
Number of families	100
Number of subjects studied	532
Average number of family members	5.0
Age (mean±SD; range) yrs	25.98 ± 15.66 (0.5-76.0)
Sex (male /female)	280 / 253
Obligate family members	506 (95%)
Family associates	27 (5%)
History of jaundice	161 (30.3%)
History of surgery	121 (22.7%)
History of blood transfusion	32 (6.0%)
History of vaccination for HBV	63 (11.9%)

A good number of subjects fell into active age group of 25-60 years (49.4%) followed by young adults (22.4%), children of school going age (20.7%), children of preschool age (4.3%), persons of retired age group (2.3%) and infants of age below 1 year (0.9%). Considering occupation of the

subjects, highest number was observed for students (35.9%) followed by house wife (21.1%), service holder (19.7%), businessmen (7.9%), healthcare personnel (1.9%). Some 0.8% of the study subjects were servants while 12.8% had no particular occupation.

Table II: Age and Occupational groups of the subjects

Age group (years)		Occupational group	
Ages	n (%)	Occupation	n (%)
< 1 year	5 (0.9)	Service	105 (19.7)
1 - 4 years	23 (4.3)	Business	42 (7.9)
5 - 14 years	110 (20.7)	Student	191 (35.9)
15 - 24 years	119 (22.4)	House wife	112 (21.1)
25 - 60 years	263 (49.4)	Servant	4 (0.8)
> 60 years	12 (2.3)	Health care personnel	10 (1.9)
		Others	68 (12.8)
Total	532 (100)	Total	532 (100)

(Within parentheses are percentages over column total)

HBV exposure: age groups, occupational groups and sex groups

Overall exposure to HBV was 58%. Exposure was comparably higher in the elderly group (83.3%) followed by active age group (67.7%), young adults (58.0%),

school going children (40.9%), infants of <1 year (40.0%) and 21.7% in preschool going age group. However, exposure rate was statistically different among these age groups ($\chi^2=39.4940$; $p=0.000$) (Table III).

Table III: Age Groups: Exposure vs. no Exposure to HBV Infection

Age group (years)	n	Exposed (%)	Not exposed (%)	χ^2	p
< 1 year	5	2 (40.0)	3 (60.0)		
1 - 4 years	23	5 (21.7)	18 (78.3)		
5 - 14 years	110	45 (40.9)	65 (59.1)	39.4940	0.000
15 - 24 years	119	69 (58.0)	50 (42.0)		
25 - 60 years	263	178 (67.7)	85 (32.3)		
> 60 years	12	10 (83.3)	2 (16.7)		
Total	532	309 (58.1)	223 (41.9)		

(Within parentheses are percentages over corresponding row totals)

As shown in Table IV, exposure to HBV among occupational groups was observed in 68.8% of house-wives, 66.7% of service holders, 64.3% of business persons, 60.0% of health care personnel, 48.2% of the students and about 53.0% of the persons having no particular occupation. However, among servants the rate of exposure was only 25% (1/4).

Table IV: Occupational risk for HBV infection

Occupational group	N (532)	HBVexposed	HBVnot exposed	χ^2	p
Service	105	70 (66.7)	35 (33.7)		
Business	42	27 (64.3)	15 (35.7)		
Student	191	92 (48.2)	99 (51.8)		
House wife	112	77 (68.8)	35 (31.2)	19.340	0.004
Servant	4	1 (25.0)	3 (75.0)		
Heath care personnel	10	6 (60.0)	4 (40.0)		
Others	68	36 (52.9)	32 (47.1)		
Total	532	309 (58.1)	223 (41.9)		

(Within parentheses are percentages over corresponding row totals, n = number of population)

Among the HBV exposed persons, on the basis of serological markers, 30 (5.6%) had acute infection, 110 (20.6%) had chronic infection. Of them 3.2% and 5.8% were in infective state respectively, 115 (21.6%)

were found to be recovered after exposure to HBV and 35 (10.0%) showed some infrequent serology [e.g.HBsAg only: 12 (2.3%); anti-HBc only: 41 (7.7%)] (Table V).

Table V: State of HBV infection among the exposed subjects (n=308)

State of infection	n	%
<i>Acute infection</i>	30	5.6
Infective state	17	3.2
Non-infective state	13	2.4
<i>Chronic infection</i>	110	20.6
Infective	31	5.8
Non-Infective	79	14.8
<i>Exposed but recovered</i>	115	21.6
<i>Infrequent serology</i>	53	10.0
HBsAg only	12	2.3
Anti-HBc only	41	7.7
Total	308	100

(* 1 subject was not tested for all markers, so excluded from calculation)

Among HBV exposed subjects, 37.0% had history of previous jaundice (p=0.000), 23.7% had history of surgery (p=0.272) and 8.1% had history of blood transfusion

(p=0.012) in comparison to 20.6%, 21.1% and 3.1% negative for HBV markers respectively (Table VI).

Table VI: HBV Exposure (n=308) and risk factors

Risk factors	Exposed	Not exposed	χ^2	p
	(n = 308)	(n = 223)		
History of jaundice (n=160)	114 (37.0)	46 (20.6)	16.698	0.000
History of surgery (n=120)	73 (23.7)	47 (21.1)	0.510	0.272
History of blood transfusion (n=32)	25 (8.1)	7 (3.1)	5.660	0.012

(Within parentheses are percentages over column total)

Discussion

Bangladesh is an intermediate endemic area (>2% but <7% chronic carrier) for HBV infection having a chronic carrier rate of about 4%.¹⁻⁸ Usually the carriers do not donate blood and reuse of syringes is not practiced for injection purposes. Sexual promiscuity is also not common and intravenous drug abuse also not high. All these information suggest perinatal and horizontal transmission may be the predominant modes of the disease spread. A family clustering tendency of HBV infection may be possible.

The present study investigated the markers of HBV infection in 100 families. Subjects were included on the basis of a single person positive for HBsAg and subsequently other members of the family were tested for the markers of HBV. Thus, holding 100 persons as index cases, 532 subjects were encompassed, of which 309 persons were observed positive for HBV markers. Therefore, it is clear that unless the family members would have been tested for the markers, at least 309 cases would probably remain unknown about their HBV exposure and likely that they could perpetuate the disease in some cases into other close mates and family members.

In the present study, 95% of the subjects were obligate family members. Most of

them were of active age group or young adults. However, a good number also encompassed school going and preschool aged children. In regards to occupation, highest frequency was observed for students and housewives followed by service holders and business persons. Therefore, chance of frequent social contacts related to service and business as well as repeat contacts of usual nature in the family related to the house wives are likely possibilities for transmission of HBV if it happened so in this study. As a matter of fact, exposure rate was comparatively higher among the very elderly groups who are supposed to be staying most of their time in the household as well as in the active age group and young adults, many of whom should fall into the group of housewives and service or business persons. On the other hand, exposure in the younger age group ranged from 22 to 41 percent. Younger age group acquiring the disease usually have more chance of becoming chronic carrier and serve as major source of infection in the community. Moreover, morbidity and mortality becomes more concerned for younger age group because they have to live longer times in their lives than the elderly people. Therefore, a relatively lower rate of exposure in the younger age group is not safe in the sense that they are real people who perpetuates the disease in the

community and because of their longer time survival after being exposed to HBV, ultimately overwhelms the risk of transmission in the family and community. Similar results were also found in other studies elsewhere.¹⁵⁻¹⁷

This study revealed overall exposure rate was 58.1%. About 69% of the housewives were exposed. Housewives become a constant source of transmission in the family by various modes. On the other hand, exposure was also very higher ranging from 60 to 70 percent among the health care personnel, service holders and business persons. These groups of people are real source of horizontal transmission of the virus in the community. We have seen, 95 % of the subjects were obligate family members; it is more likely that transmission was more in the family atmosphere than by other environmental possibilities. A good number of students (48%) who are likely to be abide by in the family atmosphere or may be hostel living, were also found to be exposed to HBV indicating the possibility of transmission by close mates in the institutions or housewives (mother or such relatives of students) in the household, because of the possibility that these two types of persons are likely to be frequently in contact with the subjects of student age group.

On overall, there was a male preponderance for HBV exposure. But, it was interesting to observe that in the age group of 1 to 24 years there was a female preponderance for the exposure. This can be explained in a way that due to estrogen influence in these females, as has been observed by some other investigators, there was a female preponderance in these age groups. However, more important is the risk they bear for future transmission. Because, the younger females in the family becomes more carrier and during their child bearing ages they also transmit the infection vertically in addition to their constant risk of transmitting the infection in the household atmosphere by other modes. Therefore, this perpetuating phenomenon of the females becomes vicious unless broken by preventive measures for the younger aged members of the family. These results are similar to study carried out by Abdool Karim SS et al.¹⁸

Transmission of HBV does not follow any definitive rule. In our study, it was difficult to identify among the family members, who transmitted and who acquired the virus. But, as has been mentioned earlier, about 2/3rd of the exposed persons would not come into notice unless tested for the viral markers on being convinced and approached through the HBsAg positive index member of the family. Therefore, it is really alarming that

the rate of transmission of HBV is much more than it is assumed and in many instances the transmission is likely to be by some different way than the conventionally believed modes of transmission. Those alternative modes are likely to be some way of close or repeat contacts in the family atmosphere, broadly claimed as horizontal transmission.

In regards to the state of infection among the exposed subjects, 30 had acute infection of which 17 were in infective state; while 31 out of 110 of chronic infected persons were in the infective state. Thus, only 48 cases were holding infective state during the time of testing for the markers, and a few might have been in the window phase of acute infection. Therefore, most of the observed total 309 HBV exposed cases must have been exposed either earlier or by other means than the conventionally believed state and mode of transmission. These results were in concordance with other studies.¹⁹⁻²⁰

There is a strong possibility that persons positive for HBV markers may have the capability of transmitting the virus even in some state of infection which are not conventionally thought to be much important for transmission of the virus.

Of the risk factors, 37% of the subjects with previous history of jaundice, 24% of subjects with history of surgery, and 8% of subjects with history of blood transfusion

were positive for HBV markers. Similar results were also found in other studies.²¹⁻²²

None of these factors could explain the high rate of positivity among the subjects observed in the study. Risk factors should be emphasized; but, other modes and possibilities of HBV must be kept in mind for the possibility of HBV infection in the community as which is observed and vivid from the present study.

Conclusion

In this study findings indicate that there is higher rate of transmission of HBV among the family members in Bangladesh which can not be assessed by any particular predictor. Horizontal transmission due to repeated contacts among the family members may be one of the most important modes of transmission of HBV in a family and community in our country.

Contribution of the Authors

First author was the main researcher of this study. Second author helped in data collection and computer composing.

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