Case Report

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Familial transmission of hepatitis B: an interesting case report

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ABSTRACT

Hepatitis-B is a health problem of global importance. India falls in the low intermediate endemicity zone (prevalence rate 2-4%) for hepatitis-B virus infection. Intrafamilial transmission of HBV has an important role in maintaining endemicity in our country. Here we report an interesting case of intrafamilial clustering of HBV infection from western India. Out of 14 family members, 12 members (85.7%) were hepatitis-B infected (overt or occult). This report highlights that vertical transmission of hepatitis-B is also an important route of hepatitis-B transmission. Screening of family members and contacts of HBsAg positive individuals with both HBsAg and Anti-HBc is required for timely active immunization and adaptation of hygienic precautions to prevent the chain of transmission of hepatitis B.

Keywords: Hepatitis-B surface antigen, Chronic hepatitis-B, Hepatocellular carcinoma

INTRODUCTION

Hepatitis-B is a major health problem in the world with over 2 billion people with evidence of infection and more than 350 million chronically infected. According to a recent WHO report in the south east Asia region 2% of the general population is infected with hepatitis-B infection.1 India falls in the intermediate endemicity zone (prevalence in India 2-4 percentage) for hepatitis-B virus infection.2 Hepatitis-B prevalence is highest among thalassemia, chronic kidney disease (CKD), and chronic chemotherapy patients. The manifestation of hepatitis-B infection occurs in 3 different ways such as acute, chronic, and occult infection. Chronic hepatitis-B infection is responsible for 50% of cases of chronic hepatitis, 35-60% of cases of liver cirrhosis, and 60-80% cases of hepatocellular carcinoma (HCC).³

The age of acquisition of HBV is an important determinant of outcome; the earlier the age, the higher the risk of chronicity (e.g., >90% in new-borns (vertical transmission), 30% in children aged 2-5 years and <5% in adults)).² Occult hepatitis-B infection is generally characterized by the presence of total hepatitis B core antibody (HBc) and undetected surface antigen (HBsAg) in the serum. Among Indians, the most predominant mode of HBV transmission is the horizontal transmission (about 75%).4 However vertical transmission (mother to child) is also responsible for a significant number of transmissions (less than 30%).4 Despite the use of active and passive immunization, <10% of the neonates still acquire the HBV infection.⁵ The intrafamilial transmission of Hepatitis-B infection in members of the index positive cases ranges from 11 to 57 %.6-8 In this study, we report an interesting case of intrafamilial HBV transmission.

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CASE REPORT

Index case

A 29 years female was referred after being detected as HBsAg positive during routine health check-up for further evaluation and management to gastroenterology OPD. She was asymptomatic at the time of presentation with no history of jaundice in past or other risk factors (example: IV drug abuse, high-risk sexual behaviour). On laboratory and biochemical evaluation her hemoglobin was 12.5 gm/dl, total leukocyte counts 11200/uL, platelets 258000/uL, serum glutamic oxaloacetic transaminase (SGOT) 83 U/L and serum glutamic pyruvic transaminase (SGPT) 83 U/L, alkaline phosphatase levels were 138 U/L (ref value 110-310), HBV DNA level was 6.44 x 1010 IU/ml and HBeAg was reactive. Her, Alphafetoprotein (AFP) levels were 2.266 ng/ml. Her Ultrasonography of the abdomen was normal. She was started on Tab Tenofovir 300 mg once a day from January 2020.

She had 3 siblings (2 sisters and 1 brother). None of the family member except father gave any history of jaundice, blood transfusion, high-risk sexual behaviour, or hepatitis-B vaccination previously. They belonged to poor socio-economic status and were living in overcrowded conditions along with the sharing of items such as utensils, towels, shaving blades, etc. The laboratory investigations of all family members are mentioned in Table 1 and 2.

Her father expired due to HBV related hepatocellular carcinoma (HCC) 13 years ago, however his clinical details were not available. Her mother (aged 47 years) was HBsAg negative but anti-HBc reactive and she was asymptomatic at the time of evaluation. Her liver enzymes were within normal limits.

The sister (aged 26 years) of the index case was anti-HBc reactive and HBV DNA level was undetectable was asymptomatic at the time of evaluation. Her liver enzymes were within normal limits. The brother (aged 22 years) was HBsAg negative, anti-HBc negative and was asymptomatic at the time of evaluation and his liver enzymes were within normal limits, he was advised active immunization. The youngest sister (aged 15 years) was HBsAg negative but anti-HBc reactive and HBV DNA level was undetectable and she was asymptomatic at the time of evaluation. Her liver enzymes were within normal limits. The husband (aged 34 years) was HBsAg negative but anti-HBc reactive and HBV DNA level was undetectable and he was asymptomatic at the time of evaluation. His liver enzymes were within normal limits.

The index positive woman was married for the last 14 years and she was having 4 children (3 sons and 1 daughter). Among the 4 children's 1st delivery was an institutional delivery and rest 3 deliveries were at home. She was not tested for hepatitis B during routine

pregnancy check-up. Familial pedigree clustering of HBV infection was shown in Figure 1.

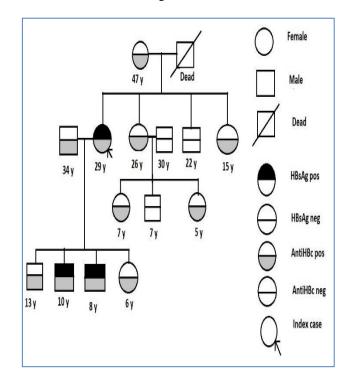


Figure 1: Familial pedigree showing clustering of HBV infection.

Her elder son was 13 years old and had been tested negative for hepatitis-B surface antigen (HBsAg) however positive for Anti-HBc (occult infection), surprisingly his HBV DNA viral load was very high (log 10.1 IU/ml) his liver enzymes were within normal limits. The other two sons (10 y, 8 y) were positive for both the tests (HBsAg, Anti-HBc) presenting an overt hepatitis-B infection and HBV DNA levels were approximately log 9 IU/ml and their liver enzymes were within normal limits. Among them, an 8 years old son was HBeAg positive and the other son (10 years old) was negative for HBeAg.

One daughter (4 years) also had occult hepatitis-B infection (HBsAg negative and anti-HBc positive), however, having comparatively low HBV DNA levels (log 2.47 IU/ml) and her HBeAg status were negative and her liver enzymes were within normal limits. Her brother in law (husband of her younger sister, 30 years old) was HBsAg non-reactive, anti-HBc reactive and liver enzymes were within normal limits. His parents were checked and were negative for HBsAg and anti-HBc.

Elder daughter (7 years age) of her sister was HBsAg nonreactive, anti-HBc reactive and liver enzymes were within normal limits. Son (7 years age) of her sister HBsAg non-reactive, anti-HBc nonreactive, liver enzymes were within normal limits and he was immunized. Younger daughter (5 years of age) of her sister was HBsAg nonreactive, anti-HBc reactive and liver enzymes were within normal limits.

Table 1: Clinical details of the family cases.

ID	Relationship to index case	Age (in years)	Sex	HBsAg	Anti-HBc	Anti-HBS
Index 01	Index case	29	F	R	R	-
F01/01	Mother	47	F	NR	R	<10
F01/02	Sister	26	F	NR	R	>10
F01/03	Sister	15	F	NR	R	>10
F01/04	Brother	22	M	NR	NR	<10
F01/05	Husband	34	M	NR	R	>10
F01/06	Son	13	M	NR	R	<10
F01/07	Son	10	M	R	R	<10
F01/08	Son	8	M	R	R	<10
F01/09	Daughter	6	F	NR	R	<10
F01/10	Brother in law	30	M	NR	R	<10
F01/11	Niece	7	F	NR	R	>10
F01/12	Nephew	7	M	NR	NR	<10
F01/13	Niece	5	F	NR	R	<10

HBsAg: Hepatitis-B surface antigen, Anti-HBc: Anti hepatitis B core antibodies, R: Reactive, NR: non-reactive.

Table 2: Hepatitis-B viral load and HBeAg status of the children of index positive case.

Sample number	Sex	Age	HBsAg	Viral load (IU/ml) log value	HBeAg
Index case 01	F	29	Positive	6.64	Reactive
F01/06	M	13	Occult	10.109	Non-reactive
F01/07	M	10	Positive	9.64	Reactive
F01/08	M	08	Positive	9.915	Reactive
F01/09	F	06	Occult	2.47	Non-Reactive

HBsAg: Hepatitis-B surface antigen; HBeAg: Hepatitis-B e-antigen.

Table 3: SGOT and SGPT levels in index positive cases.

Date	SGOT	SGPT
19/12/2019	83	83
20/12/2019	80	77
11/01/2020	50	50
03/03/2020	34	32

SGOT: Serum glutamic oxaloacetic transaminase SGPT: Serum glutamic pyruvic transaminase.

DISCUSSION

The hepatitis B infection can be transmitted by either horizontally with (sexual transmission between spouses/partners and non-sexual transmission between family members (child-to-child or household personal contact)) with vertically (perinatal/during delivery from mother to child) among intrafamilial members. In India, chronic hepatitis B (CHB) is acquired predominantly by horizontal transmission in early childhood (mostly from family contacts). Horizontal spread during early childhood may account for about 75% of all HBV transmission in India and less than 30% is thought to result from perinatal vertical transmission. Vertical transmission is also an important route of hepatitis B infection however it has not been paid much attention.

In most of the previous studies, spouses were frequently anti-HBs positive while siblings or the parents were often HBsAg positive.⁹ A higher rate of HBsAg+ children (10.2%) was found in families in which the mother was positive for HBsAg compared with families where the father was positive for HBsAg (6.3%).¹⁰ Therefore it is suggested that the hepatitis B virus in such cases may be transmitted through intra-familial contact and the higher rate of carriers among siblings is associated with the early infancy infection and more efficient mother-to-child transmission compared to sexual transmission of HBV.¹¹

A previous study from eastern India by Chakravarty et al in 2004 (evaluated 215 HBV-infected cases and 722 members of their households), reported cases of 140 (19.4%) HBsAg positive individuals from 722 households of HBV infected patients, 272 (37.6%) were negative for HBsAg but positive for either anti-HBc or anti-HBs Prevalence for HBsAg was 28.81%. Among HBsAg-positive women in the childbearing age group 15.2% were found to be HBeAg positive, these results suggest that intrafamilial childhood horizontal transmission is important for HBV transmission in our community. In another Indian study from Kerala (376 index cases with 1115 family members) HBsAg positivity among family members were 14.53%, with positivity among mothers 11.3% and 4.7% among spouses.

The seroprevalence rate in other countries was 12.1% in Bosnia and Herzegovina, 12.2% in Egypt, 14.1% in South Korea, 16% in Australia, 21.1% in Brazil, 30.5% in Turkey and 33.5% in Spain, and 23.4% of the family members in Iran. ¹³⁻¹⁹

An earlier study by Thakur et al showed that forty-nine of 65 (75.4%) families of HBeAg positive and 63% families of HBeAg negative index patients had one or more family member exposed to HBV. Hepatitis-E antigen (HBeAg) positivity is associated with active hepatitis B virus replication as well as high infectivity.²⁰

The exact mechanism of intrafamilial spread of HBV infection is not determined. It may be transmitted through direct and indirect individual contacts and also some oral, mucosal or cutaneous contacts between family members. The sharing of personal items such as clothes, bath towels, eating and drinking utensils, toothbrushes, nail clippers, etc has been shown to be important factors related to intrafamilial clustering of infection in previous studies. In an investigation in Ghana, the reported prevalence of hepatitis-B was 20.9% and common use of towels, chewing gums, toothpastes, and making excoriations on the skin were among behaviours that were significantly associated to the prevalence of hepatitis-B in family members of patients.²¹ In a Brazilian survey, sharing toothpaste in family members was significantly related to the prevalence of hepatitis-B.⁶

According to Kim et al, the offspring of carriers showed a significantly higher risk of HBV infection (relative risk; 6.6). Sharing of towels, handkerchiefs, and vessels were found to be associated with an increased risk of HBV infection via intrafamilial transmission (relative risk 11.5 for towel and handkerchief, 12.1 for drinking vessels).¹⁵

In an Indian study, the most prevalent household contacts of patients with hepatitis-B were related to sharing common eating materials and sharing dress and towels, shaving material and also the history of dentistry procedures and surgery were the risk factors which were associated to the prevalence of hepatitis-B among family members.⁸

In the present case study from western India, it was observed that the major route of transmission is vertical (mother to child). This report presents a very interesting case study of intrafamilial hepatitis-B transmission. In this family, a young woman was incidentally detected as hepatitis-B positive. Upon screening all the family members, it was observed that only 2 of her family members (sister and brother) were negative for hepatitis-B infection. Out of 14 family members, 12 members (85.7%) were infected (overt or occult) hepatitis-B infection. In this report, the index positive woman was found to be HBeAg positive and could be the source of infection to her husband and children. The index positive woman might have acquired the infection from her father as he expired 13 years ago due to hepatocellular

carcinoma. Her mother was also found to be having an occult infection. Over the years, the mother has not shown any symptoms and became an asymptomatic chronic carrier. Another interesting finding of this report was the index positive woman's elder son (13 years) was found to have occult hepatitis-B infection. Occult hepatitis-B is generally characterized by a very low or undetectable viral load. Surprisingly son was having a very high viral load (log 10) with normal liver function test (Inactive carrier state or HBeAg negative chronic infection). Two of her other sons (10 years) were having overt hepatitis-B infection with a high viral load associated with HBeAg positivity with normal liver function test (Immune tolerant phase or HBeAg positive chronic infection). The daughter of index positive woman (4 years) was having occult hepatitis-B infection but having low viral load (log 2) (Inactive carrier state or HBeAg negative chronic infection). In this study, it was observed that 3 of the family members were HBeAg positive (21.4%). Over the years the young woman was unaware of her status and was incidentally detected as. These findings emphasized that family screening in all the families of hepatitis B positive index case is very important as both the route of hepatitis-B transmission (horizontal and vertical) are important. In this case, the index positive case is the most likely source to transfer this infection to her husband (horizontal route), son, and daughter (by vertical route) and horizontal transmission from her sister to brother in law. In India, the hepatitis-B vaccine is given at birth that will only cause anti HBs positivity, now when anti-HBc is positive it is suggestive of hepatitis-B infection via horizontal transmission.

Horizontal transmission of hepatitis-B in intra-familial members is extensively studied. However, vertical transmission of hepatitis-B has not been paid much attention among intrafamilial members. This report highlights that some of the family members acquired hepatitis-B infection overt or occult while a few of them did not acquire any. The probable reason for this may be that host immune factors are involved in either transmission or protection of the infection. The results of a recent study showed that maternal immune responses play a major role in the transmission of HBV to newborns. Decreased T follicular helper (TFH)-cell and plasma B-cell frequencies and low serum IL-21 levels were found to be associated with the vertical transmission of HBV to newborns. These features are indicative of low protective maternal immunity.²²

CONCLUSION

In conclusion, the present report showed that familial transmission of hepatitis-B infection is very common as in this case as almost all the family members were either having overt or occult hepatitis-B infection. This report also highlights that vertical transmission is also an important route of transmission. Screening of family members and contacts of HBsAg positive individuals with both HBsAg and anti-HBc for timely active

immunization and adaptation of hygienic precautions and health education to prevent the chain of transmission of hepatitis B. Whether those individuals with Anti-HBc positivity low anti-HBs titer should receive active immunization in low intermediate prevalence zone like us remains a matter of debate.

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