

Horizontal transmission of hepatitis B virus in children with chronic hepatitis B

Tumay Doganci, Gulnar Uysal, Tayfun Kir, Arzu Bakirtas, Necdet Kuyucu, Levent Doganci

Tumay Doganci, Department of Pediatric Gastroenterology, SSK Ankara Children's Hospital, 06018 Ankara, Turkey

Gulnar Uysal, Department of Pediatric Infectious Disease, SSK Ankara Children's Hospital, 06018 Ankara, Turkey

Tayfun Kir, Department of Public Health, Gulhane Military Medical Academy, 06018 Ankara, Turkey

Arzu Bakirtas, Department of Pediatrics, Dr. Sami Ulus Children's Hospital, 06018 Ankara, Turkey

Necdet Kuyucu, Department of Pediatric Infectious Disease, Dr. Sami Ulus Children's Hospital, 06018 Ankara, Turkey

Levent Doganci, Clinical Microbiology, Gulhane Military Medical Academy, 06018 Ankara, Turkey

Correspondence to: Dr. Levent Doganci, GATA Klinik Mikrobiyoloji 06018 Ankara, Turkey. levdog@gata.edu.tr

Telephone: +90-312-3043401 **Fax:** +90-312-3043402

Received: 2004-02-07 **Accepted:** 2004-05-13

Abstract

AIM: To determine the possible routes of intrafamilial transmission pattern in pediatric cases of chronic hepatitis B virus (HBV) infection.

METHODS: In this descriptive retrospective study, 302 children with chronic HBV infection from 251 families and their parents attending the Social Security Children's Hospital and Doctor Sami Ulus Children's Hospital in Ankara between December 1998 and May 2000, were enrolled in. Screenings and diagnosis of chronic HBV infections were established according to the Consensus 2000.

RESULTS: In the studied 302 children with chronic HBV infection, mothers of 38% and fathers of 23% were HBsAg positive. The HBsAg positivity in at least two siblings of the same family was 61% when both parents were HBsAg positive.

CONCLUSION: It is well known that horizontal transmission is quite common in countries where *Hepatitis B Virus* is moderately endemic. To our best knowledge, this is the largest series observed regarding the horizontal transmission in pediatric chronic HBV infection in Turkey. It is necessary to expand the preventive programs to target not only the newborn period but also all stages of childhood.

© 2005 The WJG Press and Elsevier Inc. All rights reserved.

Key words: Chronic hepatitis B; Horizontal transmission

Doganci T, Uysal G, Kir T, Bakirtas A, Kuyucu N, Doganci L. Horizontal transmission of hepatitis B virus in children with chronic hepatitis B. *World J Gastroenterol* 2005; 11(3): 418-420
<http://www.wjgnet.com/1007-9327/11/418.asp>

INTRODUCTION

In Turkey, hepatitis B surface antigen (HBsAg) positivity is

less than 10% and this result places our country within the moderately endemic regions^[1]. It is well known that the horizontal transmission is quite common in these regions. The majority of HBVs are acquired during childhood and in early adulthood in most of the Mediterranean countries, and HBV seroprevalence in late childhood is close to the rate in adults. On the other hand, higher rates of HBV infection have been reported from the east and southeast Turkey, where the families are highly populated. It has been well known that horizontal transmission by non-sexual close contact is very common for acute HBV infection in countries with moderate HBV endemic besides vertical, sexual and parenteral transmission^[2]. It has been accepted that transmission between family members (from father to children or between sisters and brothers) may occur in communities with poor socioeconomic and hygienic conditions, and with longer periods of interaction^[3]. Transmission patterns are thought to be the most important features for targeting mass vaccination campaigns in HBV endemic countries. Thus, in this study the impact of horizontal transmission of HBV infection was retrospectively investigated by analysis of risk factors and family screenings of children diagnosed with chronic hepatitis B infection.

MATERIALS AND METHODS

In this descriptive study, a total of 302 children with chronic HBV infection and their parents from two tertiary referral hospitals for sick children in Ankara, Turkey, were screened in 1998-2000^[4]. In this period, all cases from these two centers were included in the study. Two hundred and seventeen cases were from Social Security Children's Training Hospital, Ankara, Turkey and 85 cases were from Doctor Sami Ulus Children's State Hospital.

Risk factors, family screening results, ages, ALT values, HBeAg and HBV-DNA positivity were analyzed as descriptive variables.

RESULTS

The index cases of chronic HBV infection consisted of 103 girls and 199 boys from 251 families. Of the 251 families included in the study, 39 had two children, and 6 had three children who had chronic HBV infection. The age of the patients ranged between six months to 15 years (average 7.1 years). The patients who were younger than two years old constituted 7% of the cases, and 72% were older than five years (Table 1).

Table 1 Distribution of cases according to age groups

Age (yr)	n	%
6-23 mo	21	7.0
24 mo-5 yr	63	20.9
>5-10 yr	143	47.3
>10 yr	75	24.8
Total	302	100.0

Table 2 ALT values, HBeAg and HBV-DNA positivity of cases

	ALT (U/L) (n = 302)			HBeAg (n = 298) ¹		HBV-DNA (n = 156) ¹	
	<40	40-80	>80	Positive	Negative	Positive	Negative
n	135	89	78	205	93	125	31
%	44.7	29.5	25.8	68.8	31	80.4	19.6

¹Not all data available for these parameters.

Of the cases, 38% consulted us due to HBV infection in the family. HBsAg positivity was found in 40% either by chance or during preoperative laboratory evaluation, and in 22% of the cases during hospitalization for other reasons. Twenty-three percent of the cases had a history of chronic disease, surgical or dental manipulations, and blood transfusions as risk factors. While screening the family members of these patients, positive HBsAg was found in 38.1% of mothers, 23.1% of fathers and 10.9% of siblings. Both parents were HBsAg positive in 23 cases (7.6%). Four mothers and eight fathers in this group were under interferon treatment due to chronic hepatitis B infection. The parents of 95 (31.4%) children were antiHBs positive (Table 2). No risk factors could be identified in 7.3% of cases, but hepatitis B markers were not available in 54 (21.5%) mothers and 98 (39%) fathers. At least two siblings were HBsAg positive in 44% of families with HBsAg-positive mothers. This proportion fell down to 25% when only fathers were HBsAg positive, and increased to 61% when both parents were HBsAg positive.

There were 20 cases in 6-23 mo age group. In 12 of these cases only the mothers were HBsAg positive, whereas positive HBsAg was observed in only the fathers of two cases and in both parents of one case. Another case had a history of exchange transfusion in the newborn period.

Forty-four point seven percent (44.7%) of all cases had normal alanine transaminase value (ALT: <40 U/L), whereas 25.8% had high ALT value, (over 80 U/L). HBeAg was positive in 68.8% of 298 patients. HBV-DNA was observed in 156 cases and 125 of them (80.4%) had positive HBV-DNA either by polymerase chain reaction (PCR) or by fluid-hybridization methods. Anti-HBe antibody was positive in 8% of these 125 cases (Table 3).

Table 3 Some risk factors in the cases

Risk factors	n	%
Only mother HBsAg positive	92	30.5
Both parents HBsAg positive	23	7.6
Only father HBsAg positive	47	15.5
Only other siblings HBsAg positive	33	10.9
Mother and/or father antiHBs positive	95	31.4
Chronic disease	26	8.6
Surgical intervention	29	9.6
Dental manipulanon	11	3.6
Blood transfusion	4	1.3
No risk factors identified	22	7.3

DISCUSSION

Hepatitis B virus is a worldwide problem and leads to chronic hepatitis in 5-10% of infected adults. However, 90% of the infants born by HBsAg and HBeAg-positive mothers would develop chronic hepatitis and therefore childhood is the most risky period considering HBV infection^[5-9]. It is known that susceptibility to HBV infection increases by age and in males. In our study group we also found that HBV infection rate increased by age. In consistence with the relevant literature, 65% of our cases were males. In a previous study done in Turkey,

HBsAg positivity was 6.6% in the group younger than one year old and the highest rate was between the ages of 6-10. The results were statistically significant ($P<0.05$), as they showed that the primary school age could be stated as the most risky period for transmission of HBV infection at low socioeconomic levels. In countries where HBV endemic is low, the main route of transmission is parenteral; however, in countries like Turkey where HBV is moderately endemic, nonparenteral transmission becomes more prevalent^[10-17]. There were risk factors suggesting parenteral transmission in 23% of our cases, so it seems that nonparenteral transmission is more likely. In 6-23 mo age group in our study, 63% of mothers were HBsAg positive, indicating the vertical transmission in this age group. The importance of horizontal transmission as well as vertical transmission in the spread of HBV infection among family members especially in the endemic regions has been reported^[3,6,11,15-19]. It has been reported that transmission of HBV to younger children is easier from a HBeAg-positive family member and the use of same towels, tooth brushes, sharing chewing gums and candies among siblings were proposed to have a role in transmitting HBV^[18-20].

Among the screened family members, 38% of mothers, 23% of fathers and 10.9% of siblings were HBsAg positive and 31% of parents were anti-HBs positive; results suggested a clear intrafamilial spread of HBV infection. Since HBV markers of 21.5% of mothers and 39% of fathers were not known, horizontal transmission was more frequent than parenteral and vertical transmission in our cases. In the medical literature, many studies showed that HBV infection rate was high in the families of chronic hepatitis B cases than in normal population. In one study performed in our country, hepatitis B screening was performed in families of HBsAg-positive pregnant women. The study carried out with pregnant women as a designated index case in a family, and the results also indicated the importance of horizontal transmission in these families^[21]. Similar results were achieved in another well-designed study from the eastern Anatolian region of Turkey, which revealed that mothers did not have an important role in the acquisition of HBV infection in our country^[2]. Intrafamilial clustering of HBV infection was well documented either in convalescent phase or in persistence form, in two-thirds of the family members of asymptomatic HBsAg carriers from a developed country where HBV has a very low prevalence^[13]. In our study, at least two siblings were HBsAg positive in 44% and 25% of families where only either mothers or fathers were HBsAg positive. An increase to 61% when both parents were HBsAg positive indicated the increased risk for the family, and underlined the role of the fathers in transmission of HBV to children. Similar results were also reported in 10 Saudi families^[6] as well as in parallel studies carried out in our country expressing same phenomena in Turkish families^[2,22,23].

Thirty-eight percent of our chronic cases were identified as a result of family screening procedure. This high rate signifies the importance of family screenings and immunization programmes. Serological markers of 21.5% of the mothers and 39% of the fathers were not known due to lack of any interest about HBV infection in these parents, arising from poor education.

In conclusion, considering low socio-cultural level and poor hygienic conditions of our infected populations, we think that studies on school age children should be continued vigorously and expanded immunization programs should comprise not only the newborns but also the teenagers^[24,25].

REFERENCES

- 1 **Doganci L**, Haznedaroglu T. Prevalence of hepatitis A, B and C in Turkey. *Eur J Clin Microbiol Infect Dis* 1992; **11**: 661-662
- 2 **Erol S**, Ozkurt Z, Ertek M, Tasyaran MA. Intrafamilial transmission of hepatitis B virus in the eastern Anatolian region of Turkey. *Eur J Gastroenterol Hepatol* 2003; **15**: 345-349
- 3 **Craxi A**, Tine F, Vinci M, Almasio P, Camma C, Garofalo G, Pagliaro L. Transmission of hepatitis B and hepatitis delta viruses in the households of chronic hepatitis B surface antigen carriers: a regression analysis of indicators of risk. *Am J Epidemiol* 1991; **134**: 641-650
- 4 **Lok AS**, McMahon BJ. Chronic hepatitis B. *Hepatology* 2001; **34**: 1225-1241
- 5 **Vegnente A**, Iorio R, Guida S, Cimmino L. Chronicity rate of hepatitis B virus infection in the families of 60 hepatitis B surface antigen positive chronic carrier children: role of horizontal transmission. *Eur J Pediatr* 1992; **151**: 188-191
- 6 **Ramia S**. Intrafamilial clustering of hepatitis B virus (HBV) infection: study of 10 Saudi families. *Ann Trop Med Parasitol* 1990; **84**: 623-627
- 7 **Tan CC**, Guan R, Yap I, Tay HH, Kang JY. Horizontal or vertical transmission of hepatitis B virus? A serological survey in family members of hepatitis B carriers in Singapore. *Trans R Soc Trop Med Hyg* 1991; **85**: 656-659
- 8 **Abdool Karim SS**, Thejpal R, Coovadia HM. Household clustering and intra-household transmission patterns of hepatitis B virus infection in South Africa. *Int J Epidemiol* 1991; **20**: 495-503
- 9 **Kuru U**, Senli S, Turel L, Kuru N, Baskent A, Ulucakli O. Age-specific seroprevalence of hepatitis B virus infection. *Turk J Pediatr* 1995; **37**: 331-338
- 10 **Tong MJ**, Weiner JM, Ashcavai MW, Redeker AG, Comparini S, Vyas GN. A comparative study of hepatitis B viral markers in the family members of Asian and non-Asian patients with hepatitis B surface antigen-positive hepatocellular carcinoma and with chronic hepatitis B infection. *J Infect Dis* 1979; **140**: 506-512
- 11 **Hess G**, Born M, Dormeyer H, Zoller B, Arnold W, Knolle J. Hepatitis B virus markers among family contacts of asymptomatic HBsAg carriers. *Scand J Gastroenterol* 1979; **14**: 373-378
- 12 **Dormeyer HH**, Hess G, Born M, Schonborn H, Arnold W, Knolle J, Zoller B. Spread of hepatitis B virus infection among family contacts of asymptomatic HBsAg carriers (author's transl). *Klin Wochenschr* 1979; **57**: 1287-1294
- 13 **Sampliner RE**, Loevinger BL, Tabor E, Gerety RJ. Intrafamilial cluster of hepatitis B virus infection: study of a large family in the United States. *Am J Epidemiol* 1981; **113**: 50-54
- 14 **Kashiwagi S**, Hayashi J, Ikematsu H, Nomura H, Kajiyama W, Shingu T, Hayashida K, Kaji M. Transmission of hepatitis B virus among siblings. *Am J Epidemiol* 1984; **120**: 617-625
- 15 **Kashiwagi S**, Hayashi J, Nomura H, Ikematsu H, Kajiyama W. Large scale survey of hepatitis B virus infection in families. *Microbiol Immunol* 1985; **29**: 951-958
- 16 **Lok AS**, Lai CL, Wu PC, Wong VC, Yeoh EK, Lin HJ. Hepatitis B virus infection in Chinese families in Hong Kong. *Am J Epidemiol* 1987; **126**: 492-499
- 17 **Chang MH**. Chronic hepatitis virus infection in children. *J Gastroenterol Hepatol* 1998; **13**: 541-548
- 18 **Martinson FE**, Weigle KA, Royce RA, Weber DJ, Suchindran CM, Lemon SM. Risk factors for horizontal transmission of hepatitis B virus in a rural district in Ghana. *Am J Epidemiol* 1998; **147**: 478-487
- 19 **Bisharat N**, Elias M, Raz R, Flatau E. Familial pattern of infection with hepatitis B virus among immigrating Ethiopian Jews in Israel. *Eur J Epidemiol* 1998; **14**: 89-91
- 20 **Leichtner AM**, Leclair J, Goldmann DA, Schumacher RT, Gewolb IH, Katz AJ. Horizontal nonparenteral spread of hepatitis B among children. *Ann Intern Med* 1981; **94**: 346-349
- 21 **Kuru U**, Turan O, Kuru N, Saglam Z, Ceylan Y, Nurluoglu M, Agacfidan A. Prevalence of hepatitis B virus infection in pregnant Turkish women and their families. *Eur J Clin Microbiol Infect Dis* 1996; **15**: 248-251
- 22 **Kuyucu N**, Dokmen A, Yoney A, Tezic T. Seroprevalence of hepatitis B infection in Turkish children. *Infection* 1998; **26**: 317-318
- 23 **Cakaloglu Y**, Kaymakoglu S, Okten A, Besisik F, Badur S, Yalcyn S. Horizontal transmission of hepatitis B virus infection. *J Hepatol* 1992; **15**: 265-266
- 24 **Chang MH**. Hepatitis B: long term outcome and benefits from mass vaccination in children. *Acta Gastroenterol Belg* 1998; **61**: 210-213
- 25 **Doganci L**, Saracli MA, Guney C. A high anti-HBs response in Turkish students of nursing with inexpensive, multidose vial hepatitis B vaccine. *Am J Gastroenterol* 2000; **95**: 2137

Edited by Wang XL