

Outcome of screening of patients with hepatitis B virusinfection

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Abstract:

Background: Hepatitis B is a major health problem worldwide, with over two billion people with evidence of infection and more than 350 millions chronically infected. Chronic hepatitis B virus (CHB) infection is responsible for 60-80% of hepatocellular carcinomas, and it is the tenth leading cause of death worldwide. The household transmission of hepatitis B virus (HBV) is a major health problem. High incidence of HBV infection is observed within the household contacts of HBV carriers.

Transmission of HBV infection mainly occurs through parenteral and sexual exposure. Vertical transmission occurs from infected mother to her baby during the perinatal period. In addition, horizontal transmission among close contacts is well recognized as a mode of transmission of HBV infection.

Patients and Methods: This is a prospective study that included 63 patients with chronic HBV infection that follow up in HBV outpatient clinic in Qena university hospital “between January 2019 to June 2019”. All patients subjected to: full clinical evaluation, diagnostic modalities as: laboratory investigation and abdominal sonography.

Results: The whole number of screened members of all families are 300, while 77(25.66%) of all family members are infected.

Conclusion: The present study has clearly explored the role of the HBV intra-familial transmission and spread in upper Egypt. Three patterns of HBV transmission were determined in the current cohort infected with HBV genotype D; maternal and paternal, spousal, and between siblings.

Keywords: Intrafamilial, HBV, transmission, Vaccination, Immunization.

Introduction:

Hepatitis B is a major worldwide health problem, with over two billion people with evidence of infection and more than 350 millions chronically infected (*Miriam at el, 2003*). Chronic hepatitis B virus (CHB) infection is responsible for 60-80% of hepatocellular carcinomas, and it is the tenth

leading cause of death worldwide (*Lavanchy D at el, 2004*).

The household transmission of hepatitis B virus (HBV) is a major health problem. High incidence of HBV infection is observed within the household contacts of HBV carriers (*Sofian at el, 2016*).

Transmission of HBV infection mainly occurs through parenteral and sexual exposure. Vertical transmission occurs from infected mother to her baby during the perinatal period. In addition, horizontal transmission among close contacts is well recognized as a mode of transmission of HBV infection.

Patients and methods:

A Prospective study from the Outpatient clinic collecting the data from patients who live in families with chronic HBV infection (CHB) diagnosed by history and HBs Ag positivity.

The first member of the family with confirmed HBV infection will be assigned as the index patient. The rest of the family members will be screened by HBs Ag and PCR HBV DNA in HBs Ag positive individuals.

Study tools

All Index patients were subjected to:

1-Complete history taking, including history of vaccination, Immunization, and history of previous or current anti-HBV treatment was also evaluated.

2- Full Clinical Examination.

3- Laboratory Investigations: -

- Complete blood picture (CBC).
- Liver profile: alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, total bilirubin & direct bilirubin, prothrombin time and INR.
- Hepatitis B virus markers: Hepatitis B surface antigen (HBs Ag), Hepatitis B e-antigen (HBe Ag) and PCR HBV DNA.
- Abdominal Ultrasonography.

All family members were subjected to:

1-Complete history taking, including history of vaccination, Immunization, and history of previous or current anti-HBV treatment was also evaluated.

2- Full Clinical Examination.

3- Screening for HBV infection by HBs Ag for all family members.

4- In HBs Ag positive individuals:

-Liver Profile: alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, total bilirubin & direct bilirubin, prothrombin time and INR.

- Hepatitis B virus markers: Hepatitis B surface antigen (HBs Ag), Hepatitis B e-antigen (HBe Ag).

- PCR HBV DNA.

- Abdominal Ultrasonography.

Statistical Analysis

All patients had been analyzed using Statistical package for Social Sciences (SPSS).

Results:

Table 1.63 Index patients with chronic HBV infection with their Base line criteria.

Variable	Frequency	Percentage
Age (mean ± SD)	34.42 ± 9.316	
Sex of index case		
Male	33	52.3%
female	30	47.6%
Residence		
Urban	29	46%
rural	34	54%

The table shows:

- Mean age is 34.42 year.
- 33(52.3%) of index cases are males and 30(47.6%) are females.
- 34(54%) of them lives in rural areas while 29 (46%) lives in urban areas.

Table 2. The baseline criteria of the family members of index cases.

Variable		Frequency	Percentage
Relation to index case	brother or sister	31	49.2%
	Parents ,son or daughter	20	31.7%
	Husband or wife	12	19.1%
Sex of infected members	Male	36	57.14%
	Female	27	42.85%
PCR HBV DNA level	<2000	40	63.4%
	>2000	23	36.6%

This table shows:

- 49.2% of transmission of HBV infection is between siblings (brothers and sisters), 31.7% between parents and their of fsbrings and 19.1% between spouses (husbands and wives).
- There are 36(57.14%) infected males in the family members of index cases, while 27(42.85%) are females.

Table3. Medical data for the index cases.

Variable	Frequency	percenta
index cases received treatment	15	23.8%
DNA	<2000	31 49.2%
	>2000	32 50.8%
DNA (mean ± SD)		96538268 ± 2791767.9
No. of families having	1 member infected	49 77.7%
	More than 1 member infected	14 22.2%
No. of all family members	300	
No. of all infected members	77	25.66%

This table shows:

- 15(23.8%) of index cases are on treatment, while 48(76.2) not eligible for treatment.
- 31(49.2%) have their PCR HBV DNA level <2000 and 32(50.8%)> 2000 IU.
- 49(77.7%) families have only one member infected while 14(22.3%) families have more than one infected in the family.
- The number of all members infected in all families is 77(25.66%) of the total family members (300).

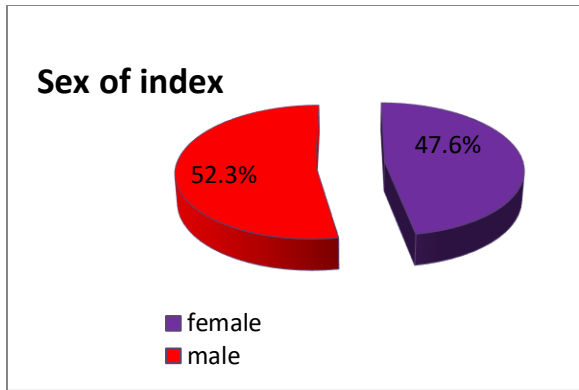


Figure 1. Sex of index case.

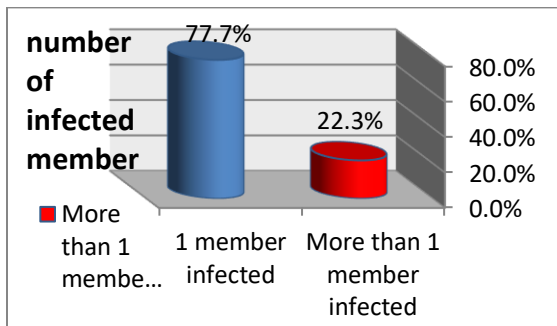


Figure 2. Number of infected members in family.

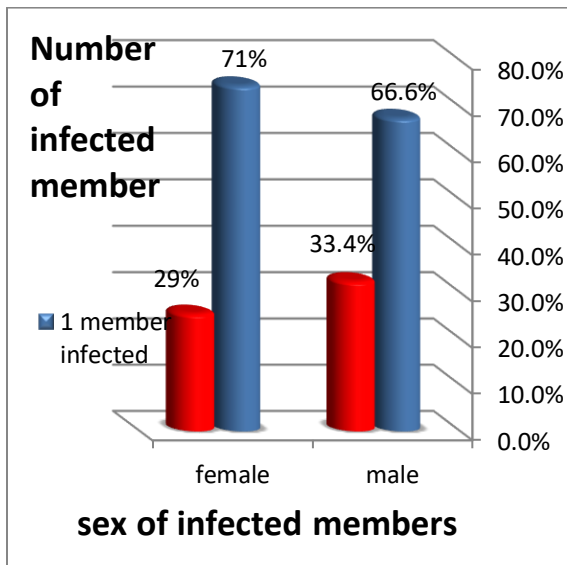


Figure 3. Number of infected members in family distribution according to sex of infected members.

Table 4. Patient characteristics distribution according to number of infected members in family.

Variable	No. of infected members		P-value
	1 member infected	More than 1 member infected	
Age (mean ± SD)	35.19± 9.495	31.63± 8.2	.078
Sex of index case	Male (79.4%)	7 (20.6%)	.156
	female (72.4%)	8 (27.6%)	
Sex of infected members	male (66.6%)	13 (33.4%)	.001*
	female (71%)	11 (29%)	

It shows:

- 27 of index cases with one member infected are males and 21 are females while in more than one member infected male number is 7 and female number is 8.
- Females are more than males in families with more than one member infected 27.6% while male percentage is 20.6%.

Table5. Medical data of the index cases distribution according to number of infected members in family.

Variable	No. of infected members		P-value
	1 member infected	More than 1 member infected	
Hb e Ag cases	+ve cases	3 (50%)	.012*
	-ve cases	46 (80%)	
DNA	<2000	25 (80.6%)	.298
	>2000	23 (71.8%)	
DNA (mean ± SD)	2303922.87± 9608038.9	4562464.67± 18539721.5	.391

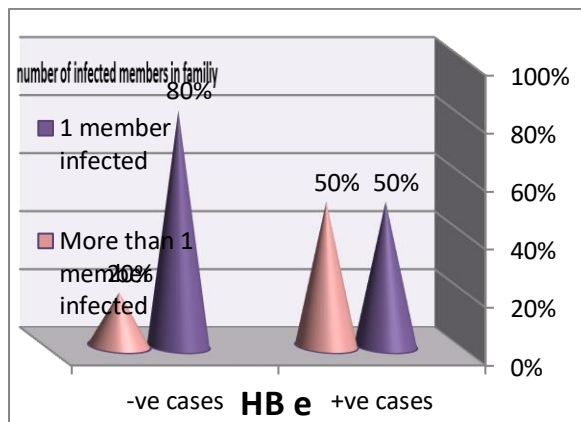


Figure4. Number of infected members in family distribution according to Hb e Ag.

Discussion:

The investigation of the intra-familial transmission in a particular region usually reveals valuable information about the routes of HBV spread in general and may help in exploring the HBV spread problem and local peculiarities. This study was conducted to explore the intra-familial spread of HBV infection (*Alizadeh et al, 2005*).

Clustering of the HBV infection within the families has been described in nearby countries located within the same zone of

the HBV endemicity but with different incidences; 30% in Turkey, 15.8% in Greece, and 11.9% in Iran (*Alizadeh et al, 2005*). An important risk factor was found to be implicated in acquiring the infection among the family was the presence of female infected with HBV.

Similarly, *Salkic et al. (2007)* reported the same observation in his study from Bosnia. However, in Taiwan no significant difference was found in the HBs Ag positivity among the offspring of the two groups, suggesting the importance of the paternal as well as the maternal transmission for the HBV intra-familial spread in Taiwan (*Lin et al, 2005*).

This was different from the transmission pattern characteristics of genotype D in Uzbekistan where the horizontal transmission was the predominant route of infection with HBV genotype D within a family (*Avazova et al, 2008*).

However, in our study there are three different patterns of HBV genotype D transmission within the families in Egypt; maternal and paternal transmission, spousal transmission and sibling transmission.

A recent study has shown a different data through exploring that both genotypes B and C can be transmitted by maternal and horizontal routes (*Wen et al, 2011*).

Whether different HBV genotypes have different transmission routes remains a question, which needs further global studies to clarify this interesting and important issue. In an attempt to evaluate the influence of the universal vaccination on the intra-familial HBV infection, it was surprising to find a high prevalence rate of HBs Ag among the vaccinated members with no significant difference when compared to the unvaccinated group. In an agreement with

the present data, *El Sherbini et al. (2006)*, reported the unchangeable prevalence of HBsAg among the vaccinated school children across a decade despite the significant decrease of the anti-HBc rate.

The possible explanation for this vaccine failure is the acquiring of the HBV infection in the lag period between the birth and the time of receiving the first HBV vaccine dose at the age of 2 months. Supporting our explanation is the recent data coming from Taiwan where a different HBV infection prophylactic strategy is applied by administering the first dose of the HBV vaccine at birth with the administration of the hepatitis B immunoglobulin to the infants born to the HBe Ag positive mother within 24 hr after birth.

The recent study has clearly demonstrated that the current HBV prophylactic strategy in Taiwan was capable of reducing the intra-familial HBV transmission and reducing the overall HBs Ag positive rate among the infants (*Mu et al, 2011*).

In Japan, the extension of the active and passive immunization to the babies born to HBeAg negative mother had greatly reduced the HBsAg prevalence to 0.2% of blood donors younger than 19 years old (*Noto et al, 2003*).

In our study, 27.1 % of female carriers had more than one member infected in their families and about 43.9 % of families with more than one infected members had the infection through their parents so we recommend a prophylactic policy that provide the first dose of the HBV vaccine at birth together with screening for HBV infection markers prenatally and administration of the HBIG to the infants born from HBe Ag-positive mothers.

The documented role of the HBV spousal transmission was clearly detected in our study, there are 22.4% of 125 families was between spouses and this coincides with the recent data conducted in Egypt that the first sexual contact with an infected spouse was a significant risk factor for infection with HBV among females (*Paez et al, 2009*).so we recommend that the premarital screening for HBV in Egypt is mandatory.

Despite being a tedious and labor-intensive method, sequencing of the viral genomes isolated from different individuals, with the subsequent homology comparison and the phylogenetic analysis remains the golden approach for demonstrating the HBV transmission in a given population (*Tajiri et al, 2007*).

The full length HBV sequence analysis is the gold standard for this purpose but remains a cost approach.

Highly variable HBV genomic region is recommended by some investigators to study the transmission event. Variability of the genomic region is affected by several factors one of which is the clinical characteristics of the studied cohort (*Wu et al, 2005*).The high S gene variability is documented among the chronic hepatitis B carriers and their families, thus investigating the genotype, subgenotype, subtypes, and mutations by the sequence analysis of the S gene with further analysis by testing the constructed phylogenetic tree with the bootstrap resampling maximum-likelihood test, may provide enough confidence to prove the transmission event in the case of chronic HBV carriers (*Thakur et al, 2003*).

Conclusion:

In conclusion, the present study has clearly explored the role of the HBV intra-familial transmission and spread in upper Egypt. Three patterns of HBV transmission were

determined in the current cohort infected with HBV genotype D; maternal and paternal, spousal, and between siblings.

The present study recommends the prophylactic policy against the HBV infection in Egypt by including the first dose of HBV vaccine at birth, screening of pregnant women for HBs Ag and the administration of HBIG to the infants born from HBe Ag positive mothers within 24 hr after birth, and recommend the premarital screening for HBV.

Further studies are needed globally to determine the transmission patterns of different HBV genotypes and locally in different districts in Egypt to explore the impact of familial transmission in HBV infection in Egypt.

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