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Relationship Between HBV-Markers Prevalence and Promotive Factors among Human Urban Population of Bahawalpur District, Pakistan: A Cross-Sectional Study

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Abstract: Hepatitis B virus infection has become a major health problem world over. The present study was designed to investigate the prevalence of HBV-markers in relation to promotive factors among human urban population of Bahawalpur-district, Pakistan. Randomly selected population (both sex, 10-70 years) of Bahawalpur (n = 1464) divided into 3 age groups; young (10≥20 years), mature (20≥50 years) and old (>50 years) was tested for blood groups. HBsAg and/or Anti-HBc positive participants were interviewed regarding past and present life style to determine promotive factors. Over all HBV-markers prevalence was observed 12.57%. Maximum infection was 13.79% (95% CI: 11.09 to 17.03, p>0.01) in old group compared with mature and young groups. HBV-markers positivity was statistically not associated with sex, ABO blood groups and Rh-factors. An inverse relationship (p>0.01) was observed between prevalence of HBV-markers and socioeconomic level of under trial population. Significantly (p>0.01) high seroprevalence was found in individuals with high rate of crowding (>4/room), stored water users, regular parlor/barber's shop visitors, those who were living/working with HBV infected people (s), surgically operated/blood transfused participants, dental clinic visitors and due to non-sterile pricking. HBV-infection is spreading rapidly among population of Bahawalpur district, Pakistan linking with deprived socioeconomic conditions, poor sanitation, non-sterile pricking, unprotected surgery/blood transfusion, parlor/barber's shops, dentist's clinics and HBV infected/carriers.

Key words: Hepatitis B, socioeconomic condition, blood transfusion, viral hepatic infection, HBsAg, anti-HBc

INTRODUCTION

Worldwide, about 400 million people have chronic Hepatitis B Virus (HBV) infection, putting viral Hepatitis-B amongst the world's leading infectious disease health problems (Lee, 1997; Zuckerman and Zuckerman, 2000; Alter, 2003; Jury, 2003). It is a major health problem in many countries of the world, especially those in Asia, the Middle East and Africa (Lee, 1997; Andre, 2000). The average prevalence of chronic HBV infection worldwide is still estimated at 6.6% (2.8% in developed countries and 7.6% in developing countries) (Chen *et al*., 2000). HBV infection has an acute case fatality rate of 0.5-1.0%, while 2-10% of cases end up in chronic infection after 5 years. Premature mortality from chronic liver disease occurs in 15-25% of chronically infected persons, highlighting the importance of this global health concern (Lopalco *et al*., 2001).

Hepatitis-B has no seasonal distribution. The reported prevalence of carrier in different population varies widely from 0.1% in the advanced countries to 20% in the developing nations. The carrier rate is higher in the tropical than in the temperate regions. In South East Asia, roughly 14-16 million people are infected with hepatitis B virus every year. Prevalence of hepatitis B varies from country to country and depends upon a complex interplay of behavioral, environmental and host factors. In general, it is lowest in countries or area with high standards of living like Australia, North America, North Europe and highest in countries or areas where socio economic level is lower like China, South East Asia, South America (Behal *et al*., 2008).

The virus causes acute hepatitis of varying severity (Lee, 1997) and persists in 95% of children and 2-10% of adult patients (Bowyer and Sim, 2000; Joseph *et al*., 2006) leading to chronic liver disease, cirrhosis, hepatocellular carcinoma (Abe *et al*., 2000) and even fulminant hepatitis (Mahoney, 1999; Kremsdorf *et al*., 2006).

Therefore, HBV is an attractive candidate for public health measures aiming at prevention, early diagnosis and treatment. In this context, not only information on the general population but also on selected segment of populations with a potentially higher risk is important (Russmann *et al*., 2007).

Unfortunately, Hepatitis-B carrier rate in Pakistan has been alarmingly high i.e. approximately 10%. Both the acute and chronic hepatitis B virus infections cause major health problems (CDC, 2006).

Hepatitis viruses can be transmitted by means of acupuncture, tattooing and sharing razors. Nosocomial patient-to-patient transmission may occur by means of a contaminated colonoscope, via dialysis or during surgery, including organ transplantation (Yeung *et al*., 2001). The uncommon routes of transmission of hepatic viral infections, which affect <5% of the individuals at risk, include high-risk sexual activity and maternal-fetal transmission. Casual household contact and contact with the saliva of those infected are inefficient modes of transmission (Smith and Sterling, 2006). Hepatic viral infections like HBV have been found with shared routes of transmission, can cause serious morbidity and mortality globally (Smith and Sterling, 2006). Major routes of transmission for Hepatitis-B are more often associated with vertical transmission, sexual contact and both household and occupational contacts. Co-infection with HIV type 1 appears to increase the risk of both sexual and maternal-fetal transmission of HBV (Vincent *et al*., 2007).

In an earlier report, the prevalence of Hepatitis-B and C was determined in population of the urban area of Bahawalpur district (Zaman, 2006), while presently aimed to examine the prevalence of HBV infection in same segment of population in relation to promotive factors. No comparable studies were done recently and no previous studies have looked at the prevalence in relation to promotive factors in such a population.

MATERIALS AND METHODS

This was a population-based cross-sectional study which was carried out from February 01, 2007 to January 31, 2008. A 1464 peoples (both sex) of different age and professions of urban areas of Bahawalpur, Pakistan, selected by random sampling were screened out for Hepatitis-B markers and promoting factors.

Selection and division criteria: Selected sample of population of both sex, age; 10-70 years, without any previous diagnosis, was divided into 3 groups i.e. young (10≤20 years), mature (20≤50 years) and old (>50 years). The male and female of same age were grouped together. A willingness certificate for co-operation in carrying out the purpose of present study was obtained, singed by each individual/parents/guardians before his/her inclusion in the study (Tassaduqe *et al*., 2004).

Interview and blood collection: All of the participants were interviewed in person at enrollment. Information on socioeconomic characteristics, dietary habits, personal medical and surgical history, family history of major diseases and life style were obtained by using a structured questionnaire. A 3 mL blood sample was collected from each participant (Yang *et al*., 2008).

Evaluation of specimen: Blood samples were processed immediately following their collections by using commercially available kits (rapid chromatographic immunoassay from Acon Laboratories USA) to test serum samples for HbsAg and anti-HBc. Blood group of each participant was tested and categorized according to their respective blood groups in relation to promotive factors (Behal *et al*., 2008; Yang *et al*., 2008).

Statistical analysis: The data was analyzed statistically by using tests of proportions, Chi-square (χ^2) tests and confidence interval. A $p<0.05$ was considered statistically significant. A 95% confidence interval of the proportions of HBV-markers prevalence was determined as follows:

$$P \pm (\sqrt{pq/n}) \times Z_{d/2}$$

where:

P = Proportions of population found positive for HBsAg
q = 1-p
n = Total number of cases
z = Standard normal variate (1.96)
d = Degree of freedom

RESULTS

Prevalence of Hepatitis-B viral markers: A total of 1464 volunteers (328 young, 588 mature and 548 old of both sex) were screened out in the study. Over all prevalence of infection of Hepatitis B was 12.57% in tested population. The prevalence of HBsAg was found to be 6.35% and the prevalence of anti-HBc was found to be 11.95% (Fig. 1 and Table 1).

Age specific prevalence: HBV-markers seroprevalence increased with age, 10.34% (95% CI: 7.54-14.02) in young, 13.01% (95% CI: 10.51-16.00; $p>0.01$) in mature and 13.79% (95% CI: 11.09-17.03; $p>0.01$) in old groups (Table 1). The study showed maximum prevalence at 13.36% (95% CI: 9.64-18.21) in old female followed by 13.14% (95% CI: 9.61-17.69) in mature male groups and minimum prevalence at 10.63% (95% CI: 6.65-16.44) in young female group (Table 2).

Table 1: HBV-markers positivity in relation with sex, age, blood groups and Rh-factors among human urban population of Bahawalpur-Pakistan

Variables	Population (n = 175)	HBsAg +ve (n = 93)	Anti-HBc +ve (n = 184) (12.57%)	HBV +ve markers[a] (12.57%)	95% CI	p-value
Age groups						
Young (10≤20)	348	11	36	36 (10.34)	7.54-14.02	
Mature (20≤50)	584	40	40	76 (13.01)	10.51-16.00	>0.01
Old (>50)	522	42	67	72 (13.79)	11.09-17.03	>0.01
Sex						
Male	743	48	91	95 (12.79)	10.57-15.39	
Female	721	45	84	89 (12.44)	10.13-14.95	<0.2
Blood group						
A	166	5	19	20 (12.50)	7.86-17.95	
B	528	35	59	67 (12.79)	10.10-15.81	<0.2
AB	329	23	46	41 (12.46)	9.29-16.50	<0.2
O	441	30	51	56 (12.70)	9.89-16.15	<0.2
Rhesus-factor						
Positive	1408	92	168	177 (12.57)	10.94-14.41	
Negative	56	1	7	7 (12.50)	5.88-23.93	<0.2

HBsAg, Hepatitis B surface Antigen; anti-HBc, anti-Hepatitis B core antigen; HBV, Hepatitis B Virus; +ve, positive; CI, Confidence Interval; [a] Positive for HBsAg, anti-HBc, or both

Table 2: HBV-markers prevalence in association with age and sex among human urban population of Bahawalpur-Pakistan

Group (age)	Sex (743) (721)	Population tested (n = 1464)	HBsAg +ve (n = 175)	Anti-HBc +ve (n = 93)	HBV-markers +ve[a] (n = 184) (12.57%)	95% CI	p-value
Young (10≤20)		328	11	36	36 (10.98)	8.00-14.85	
	Male	168	6	19	19 (11.31)	7.29-17.06	
	Female	160	5	17	17 (10.63)	6.65-16.44	<0.2
Mature (20≤50)		588	40	72	76 (12.93)	10.44-15.89	
	Male	274	18	34	36 (13.14)	9.61-17.69	
	Female	314	22	38	40 (12.74)	9.47-16.91	<0.2
Old (>50)		548	42	67	72 (13.14)*	10.55-16.24	
	Male	301	22	36	39 (12.96)	9.60-17.25	
	Female	247	20	31	33 (13.36)	9.64-18.21	<0.2

HBsAg, Hepatitis B surface antigen; anti-HBc, anti-Hepatitis B core antigen; HBV, Hepatitis B Virus; +ve, positive; CI, Confidence Interval; [a]Positive for HBsAg, anti-HBc, or both

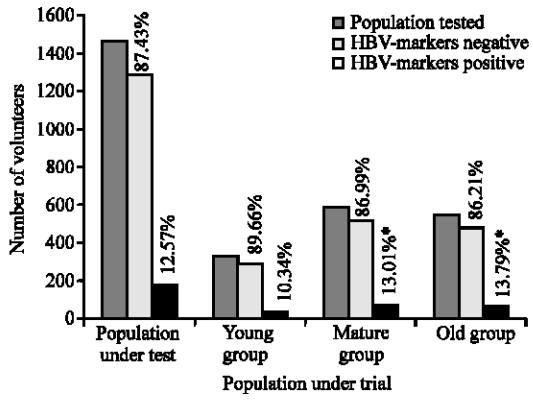

Fig. 1: HBV-markers seroprevalence in tested population

Gender specific prevalence: The prevalence of HBV-markers in male was 12.79% (95% CI: 10.57-15.39) compared to 12.44% (95% CI: 10.13+14.95) in female. The difference was found to be statistically insignificant (p<0.2) (Table 1 and 2).

Blood group specific prevalence: HBV-markers prevalence was higher in blood group B at 12.79% (95% CI: 10.10-15.81) and lowest in blood group AB at 12.46% (95% CI: 9.29-16.50). The difference though was statistically not significant (p<0.2). The prevalence was marginally high among the rhesus-positive groups 12.57% (95% CI: 10.94-14.41) than those with Rhesus-negative groups 12.50% (95% CI: 5.88-23.93) (Table 1).

The data showed highest seroprevalence of HBV-markers in blood group AB 12.77% (95% CI: 9.53-16.90)and lowest in blood group A 12.03% (95% CI: 7.76-18.10) among Rh-positive groups. Among Rh-negative groups the highest seroprevalence was seen in blood group O 13.64% (95% CI: 3.90-34.18) and lowest in blood group B 11.11% (95% CI: 1.86-34.05) (Table 3).

Variable specific prevalence: The distribution of participants according to socioeconomic status; income and education, crowding (number of person living in a room), source of drinking water, visits of parlor/barber shop, presence of HBV-infected person (s) inside home/workplace, surgical history and/or blood transfusion, injection/pricking and visiting to dentist to HBV-markers is shown in Table 4.

Table 3: HBV-markers seroprevalence according-blood groups and Rh-factors among human urban population of Bahawalpur-Pakistan

Blood group (Rh-factor)	Population tested	HBsAg +ve (n = 93)	Anti-HBc +ve (n = 175)	HBV-markers +ve (n = 184, 12.57%)	95% CI[a]	p-value
A-positive	158	5	18	19 (12.03)	7.76-18.10	
A-negative	8	0	1	1 (12.50)	0.01-49.22	
B-positive	510	35	56	65 (12.75)	10.11-15.93	<0.2
B- negative	18	0	2	2 (11.11)	1.86-34.05	<0.2
Ab-positive	321	23	46	41 (12.77)	9.53-16.90	<0.2
Ab- negative	8	0	1	1 (12.50)	0.01-49.22	
O-positive	419	29	48	52 (12.41)	9.57-15.93	<0.2
O-negative	22	1	3	3 (13.64)	3.90-34.18	<0.2

HBsAg, Hepatitis B surface Antigen; anti-HBc, anti-Hepatitis B core antigen; HBV, Hepatitis B Virus; +ve, positive; CI, Confidence Interval; [a]:Positive for HBsAg, anti-HBc, or both

Table 4: HBV-markers seroprevalence according to selected variables among human urban population of Bahawalpur, Pakistan

Variables	Population tested (n = 1464)	HBsAg +ve (n = 93)	Anti-HBc +ve (n = 175)	HBV-markers +ve[a] (n = 184, 12.57%)	95% CI	p-value
Socioeconomic status						
Income						
High	318	3	9	9 (2.83)	1.42-5.37	
Moderate	653	46	93	96 (14.70)	11.76-17.14	>0.01
Lower	493	44	73	79 (16.02)	13.04-19.53	>0.01
Education						
High	207	4	6	6 (2.90)	1.19-6.32	
Middle	652	39	88	91 (13.96)	11.50-16.84	>0.01
Low	605	50	81	87 (14.38)	11.80-17.41	>0.01
Crowding (No. person/room)						
1-2	309	4	11	12 (3.88)	2.16-6.73	
3-4	813	58	105	110 (13.53)	11.34-16.06	>0.01
>4	342	31	59	62 (18.13)	14.39-22.57	>0.01
Source of drinking water						
Boiled/filtered	411	12	29	31 (7.54)	5.33-10.54	
Fresh	527	29	47	51 (9.68)	7.42-12.52	<0.2
Stored	526	52	99	102 (19.32)	16.17-22.91	>0.01
Regular use of parlor/barber shop						
No	326	19	21	25 (7.67)	5.21-11.12	
Yes	1138	74	154	159 (13.97)	12.07-16.11	>0.01
Presence of HBV-infected person (s) inside home/workplace						
No	499	21	32	35 (7.01)	5.06-9.62	
Yes	965	72	143	149 (15.44)	13.29-17.86	>0.01
Surgical history/blood transfusion						
No	1003	52	91	96 (9.57)	7.90-11.56	
Yes	461	41	84	88 (19.09)	15.75-22.94	>0.01
Injections/pricking						
Sterile	631	32	57	60 (9.51)	7.45-12.06	
Non-sterile	833	61	118	124 (14.89)	12.62-17.47	>0.01
Visit-dentist						
Never	453	27	36	38 (8.39)	6.15-11.33	
Yes	1011	66	139	146 (14.44)	12.40-16.75	>0.01

HBsAg, Hepatitis B surface Antigen; anti-HBc, anti-Hepatitis B core antigen; HBV, Hepatitis B Virus; +ve, positive; CI, Confidence Interval; [a]:Positive for HBsAg, anti-HBc, or both; High income mean = one million; moderate income mean = 1/20 million; low income mean less than 1/20 million rupees per annum; Higher education means university or higher; Middle education means less than university level or high school; Lowe education means no school

DISCUSSION

Hepatitis B virus infection is widespread in Pakistan and has led to a higher incidence of acute and chronic liver diseases in the region (Alam *et al*., 2007). The prevalence of HBV infection in relation to promotive factors was therefore, investigated in a randomly selected sample of urban population of Bahawalpur district of Pakistan in the present study. A total of 1464 individuals were tested for the presence of infection, out of which 184 were infected (Fig. 1). The study exhibited an overall 12.57% HBV-markers prevalence (Fig. 1). This figure is higher than the prevalence of infection detected earlier (Zaman, 2006), 2.9% prevalence of HBV carriers among local population of Bahawalpur was reported by Khichi and Channar (2000). A 7.8% HBV infection with male to female ratio of 7:1 showed by Hussain and Ahmad (1998). A 2.06% blood donors were found HBsAg positive in Faisalabad, 3.3% in Northern Pakistan (Khattak *et al*., 2002). HBV prevalence rate of 2% was found in male volunteer blood donors at Karachi. HBV prevalence documented from Lahore was 2.04% (Alam *et al*., 2007). The frequency of Hepatitis B antigen and antibody in healthy subjects and patients with liver disease was 2.9%

and 35%, respectively, while 33% patients with acute viral hepatitis, 20% with cirrhosis and 10% with Hepatocellular Carcinoma (HCC) determined HbsAg positive by Zuberi *et al.* (1978). Tong *et al.* (1996) reported 55% of chronic liver disease and hepatocellular carcinoma patients positive for HBsAg. 3.4% seroprevalence of HBsAg in male sex workers at Karachi was found by Baqi *et al.* (1999). Alam *et al.* (2007) showed 52 (4%) individuals HBsAg positive with mean age 23.5±3.7 years while 9.30, 33.47 and 12% individuals had HBeAg, antibodies for HBsAg and antibodies for HBcAg, respectively.

The finding is also comparable with the studies that have been conducted in other countries like Saudi Arabia (19.7 %) (Al-Faleh *et al.*, 1992).

The analysis of data indicated a maximum prevalence of hepatitis B at 13.79% (95% CI: 11.09-17.03) in old group followed by mature (13.01, 95% CI: 10.51-16.00) and young groups (10.34, 95% CI: 7.54-14.02) (Table 1). The significant association of HBV-markers with older ages (Table 2) could be due to the greater number of years of potential exposure, a lack of adult HB vaccination programs and the lack of awareness of HBV infection in earlier decades which is in agreement with the CDC (2005). The drug abuse, high number of sexual partners, divorced or separated marital status and low educational level remained some other means (Moayyed *et al.*, 2002; McQuillan *et al.*, 2004).

HBV-markers prevalence difference between male (12.79, 95% CI: 10.57-15.39) and female (12.44, 95% CI: 10.13-14.95) was insignificant ($p<0.2$) (Table 1 and 2).

The data indicated no significant association between ABO blood group distribution and seroprevalence of HBV-markers (data not statistically significant, $p<0.2$) in accord with other studies (Table 1) (Farzadegan *et al.*, 1979; Emeribe and Ejezie, 1992; Behal *et al.*, 2008).

Slightly higher prevalence of HBV-markers in blood group B could be due to the fact that blood group B is more prevalent in the area under study (36.07%). The study also demonstrated no significant difference ($p<0.2$) in the HBV-markers positivity among Rh-positive group (12.57, 95% CI: 10.94-14.41) and Rh-negative group (12.50, 95% CI: 5.88-23.93). The slight variation observed may be accorded due to random chance variation (Table 3) (Behal *et al.*, 2008).

An inverse relationship was observed between prevalence of HBV-markers and the socioeconomic level of under trial population (Table 4). Finding is in consistent with other similar studies (Jafari *et al.*, 2006).

Socioeconomic status is a surrogate marker for the level of sanitary and hygienic practices and it is a major factor that directly correlates with viral hepatic infection. HBV-markers positive participants showed a significant relationship ($p>0.01$) among moderate-low income and/or education levelers compared with high levels of income and/or educated peoples in selected population (Table 4). Pakistan lies between middle to low income countries with over one-twelfth of labor force unemployed, where over one fifth of the population subsides in poverty and over half of the population is illiterate (Jafari *et al.*, 2006). It has been well documented that HBV infection is more prevalent in low socio-economic settings in majority of the world regions like Indonesia (Akbar *et al.*, 1997) and similarly in Pakistan (Alam *et al.*, 1997).

Crowding is an indirect measure of household hygiene and it has been reported to be an important risk factor for hepatic viral infection like HBV acquisition (Jacobs *et al.*, 2007). The findings demonstrated the direct relation of crowding with the spread of infection (Table 4). The boiled/filtered water users acquired infection for less ($p>0.01$) in comparison to the fresh and stored water users (Table 4). This finding is consistent with the studies that reported the water source being another important mean for spread of infection (Jacobs *et al.*, 2007).

The study indicated the parlor/barber shop; major source of viral particle acquisition and visitors of parlor/barber's shop got high rate of infection in comparison to non-visitors (data statistically significant $p>0.01$) (Table 4). The study showed surgical history/blood-transfusion; another source of HBV mode of transmission, 19.09% (95% CI; 15.75-22.94) of those who surgically operated and/or blood transfused were infected compared with 9.57% (95% CI; 7.90-11.56, $p>0.01$) of those were not ever operated/transfused (Mirza *et al.*, 2007). Furthermore, non-sterile pricking and/or injection with reused syringes presented high risk ($p>0.01$) of HBV infection. It has been noted previously that such practice is a risk factor for infection (Mirza *et al.*, 2007). Another major finding of the current study was the higher prevalence of infection among those who had any patient suffering from hepatitis-B in their home or at work places (15.44% compared with 7.01%, which had no HBV-infected person; $p>0.01$) (Russmann *et al.*, 2007). Additional risk factor for transmission of infection was found dentist clinic; among visitor, 14.44% (95% CI; 12.40-16.75) were infected in comparison with 8.39% (95% CI; 6.15-11.33) non-infected ($p>0.01$) (Table 4).

The living conditions or exposure to environmental factors, cultural practices, nutritional factors or sanitary circumstances are relevant factors in addition to percutaneous factors for increasing prevalence of hepatitis such as HBV. As several other studies have shown, poor socioeconomic conditions associated with

overcrowding and inadequate hygiene at home are important risk factors for infection (Mirza *et al*., 2007; Russmann *et al*., 2007). Indeed, in our study, a significant correlation was found between socioeconomic conditions, house over-crowding, non-sterile pricking, surgery/blood transfusion, use of parlor/barber's shop and dental procedure, confirming the previously reported data (Jacobs *et al*., 2007; Khaja *et al*., 2006; Quddus *et al*., 2006; Zaman, 2006). The findings of present study also confirmed the previous report (Zaman, 2006) and indicated further, a marked increase in the prevalence of infection in same segment of population within 2 years.

CONCLUSION

The prevalence of HBV markers among human urban population of Bahawalpur district, Pakistan is increasing day by day. Socioeconomic development, health education programs and adult HB immunization programs targeting high-risk groups should be initiated.

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