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PREVALENCE OF HEPATITIS B VIRUS AND GENOTYPES IN THE REGION OF KHYBER PAKHTUNKHWA PAKISTAN

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Abstract About 3% of Pakistani population is the carrier of hepatitis B virus, and infection is growing at a steady rate. The current study reviews the situation of HBV in the KP population. Approximately 85 studies related to the prevalence of HBV and its genotypes in this region were searched using various databases. The mean and standard deviation based on collected data indicates an HBV prevalence of 110.09%±3.71 in general population, $2.51\% \pm 0.01$ in healthy blood donors, $1.74\% \pm 0.01$ in health care workers, $3.40\% \pm 0.00$ in healthy children, $1.27\% \pm 0.00$ in pregnant women, 22.40% in drug abusers. The percent prevalence of infection is $5.98\% \pm 0.02$ in multi-transfused people, $26.61\% \pm 0.12$ in patients with liver disease, and $4.11\% \pm 0.02$ in patients with dental treatment and ophthalmic, respectively. Genotype D is the most prevalent genotype, with a value of 41.77%. The area must be vaccinated, and more preventive care and immunization services should be provided.

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Keywords: Hepatitis B virus; Prevalence; genotype D; liver disease; Khyber Pakhtunkhwa

Introduction

Hepatitis B caused by the hepatitis B virus (HBV), which is a DNA virus identified in 1947 (Blumberg et al., 1967), have great mobility and mortality rate (Manzoor et al., 2009; Rizzetto et al., 1980). It is a severe health-related issue in both developed and developing countries (Rizzetto et al., 1980). About two billion people were infected by this virus and 400 million are carriers of infection worldwide (Manzoor et al., 2009; Marín et al., 2012; Zhu and Dong, 2009). About 1 to 2 million people die due to HBV induced diseases like fibrosis, Chronic hepatitis cirrhosis, and HCC (hepatocellular carcinoma) every year (Khan et al., 2011a; Mahoney, 1999). Chronic liver disease was developed in 10% of patients, 20% become cirrhotic, and 80% remain as a carrier of hepatitis B surface antigen (HBs Ag) (Al Ghamdi and Safi, 2015). According to WHO (2010), HBV prevalence is the most common in China; how much? Followed by India with 0.04 billion and Indonesia with 12 million infected people.

In Pakistan, the Hepatitis B infection is growing at a fast rate. There were 7-9 million people infected, and 3% chronic HBV carriers were noticed in Pakistan (Khan et al., 2011b; Noorali et al., 2008; Workowski and Bolan, 2015). In KP in 2008, about 0.6 million

people had hepatitis B infection (Ahmed et al., 2016). About 67.5% of Pakistani population live in rural areas with poor economic status (Akbar et al., 1997), unavailability of proper health services, lack of awareness, and poor financial conditions; as a result, the infection is increasing day by day. (Bukhari, 1999; Kane et al., 1999). The infection is transmitted via blood and body secretions. The virus penetrates through a crack in the skin, mucous membrane, or vein (Agboatwalla et al., 1994; Bosan et al., 2010) and remains alive for many days on dehydrated surfaces, needles, syringes etc. (Hakim et al., 2008). It is also transmitted from an infected mother to her child at the time of birth (Fairley and Read, 2012). It is considered a major health problem due to its worldwide prevalence.

There are limited studies that have been conducted on the prevalence of HBV in this region; therefore, this review revealed the prevalence of Hepatitis B in KP population.

Literature Survey

Published data were searched in Google Scholar, PubMed, Directory Of Open Access Journals (DOAJ) and Springer link by using the keywords Global prevalence of HBV, Prevalence of HBV in Pakistan, prevalence of hepatitis B in KP Pakistan, hepatitis B



in blood donors, HBV in general population, hepatitis B in Pakistani healthcare workers, hepatitis B in surgical patients, HBV epidemiology in Pakistan, hepatitis B virus infection in pregnant women, HBV in children, prevalence of HBV genotype in KP Pakistan.

Analysis

Published information representing the prevalence of hepatitis B in various populations is listed in tables. The percent prevalence in various categories is presented in mean \pm standard deviation.

Using the following formula the mean prevalence of each population group was determined.

 $\mu = (\Sigma x i)/N$. The standard deviation (SD) of various population groups was determined by using the following formula

$$\sigma = \sqrt{\frac{1}{N} \sum_{i=0}^{N} (x - \mu)^2}$$

Where "x" is the percent HBV prevalence reported in each study and "N" is the total number of studies in the population groups.

Prevalence of hepatitis B in different population groups

General Population

About 10% of Pakistani general population have hepatitis B infection (<u>Malik et al., 1988; Yusuf, 1996</u>). Nineteen studies were conducted on the prevalence of HBV in the general population in various regions of KP with a mean prevalence of 110.09% \pm 3.71 (<u>Abbas et al., 2006</u>; <u>Ullah et al.,</u> 2017).

One of the means of HBV infection transmission is through infected blood, so it must be screened before transfusion. (Olokoba et al., 2009). 10 findings associated with healthy blood donors showed a percentage prevalence of 2.51±0.01 (Ahmad et al., 2004; Ahmad et al., 2017). 3 studies (Attaullah et al., 2011; Zuhaib Khan et al., 2016) indicated a prevalence of 1.74% ±0.01 in healthcare workers. In 2 different findings, the prevalence of $3.40\% \pm 0.00$ in healthy children (Malik et al., 2004) were reported. Insufficient data is available to show the HBV infection in pregnant women (Batool and Bano, 2008). Up to date, only two studies showing the prevalence of infection in pregnant women in KP are presented, indicating a percent prevalence of $1.27\% \pm$ 0.001 (Ahmad, 2016; Khan et al., 2009). In addition, only a single study is conducted showing the spread of disease in drug users, with a prevalence of 22.40% (Alam et al., 2007). However, about 4 to 4.8 million drug users are present in Pakistani population (Hussain, 2008).

Table 1. Prevalence of HBV in general population, healthy blood donors, healthy children, pregnant women
and drug abusers

Population	Region	Year	Method	Sample	HBV%	Male%	Female%	Reference
Туре	0			•				
General Population	Peshawar	2003	ICT	11372	4.30			23
•	NWFP	2007		17359	2.28			24
	NWFP	2007	ELISA & PCR	156	28			25
	Abbottabad	2009	ICT & ELISA	500	3			26
	Jamrud	2009	ELISA	4180	17.25	16.74	17.70	27
	Bannu	2010	ELISA	25944	1.93			28
	KP	2012	ICT	1439	49.55			29
	Malakand	2012	ICT	213	14.53			30
	Bannu	2012	ICT	200	13.50			29
	DI Khan	2012	ICT	200	14.63			29
	Kohat	2012	ICT	200	13.67			29
	Mardan	2012	ICT	200	13.35			29
	Karak	2014	ELISA,ICT	800	61.75	65.78	57.92	30
	Mardan	2014	ICT & RT-PCR	274	34.80	59.60	40.40	31
	KP	2016	ICT & ELISA	133193	2.03			32
	Charsadda	2016		100	29			33
	Havalian	2017	ICT & ELISA	287	6.39	3.84	2.55	34
	Mardan	2017	ICT	790	52.40	52.80	51.70	35
	Peshawar	2017	ICT,ELIA,RT PCR	300	21.67	20.80	22.20	36
Healthy Blood Donars								
	КР	2002- 2003	MEIA,IMX	4000	1.95	1.92	6.30	39

	Northern areas	2007	ICT	8949	3.66		 40
	Parachinar	2008	ICT	10343	2.71		 41
	Kurram Agency	2009	ICT	1300	5.07		 42
	Peshawar	2010	ELISA	32042	1.97	1.97	 43
	FATA,NWFP	2010	ICT,ELISA,RT- PCR	7148	1.85		 44
	Peshawar	2011	Abbott AxSym	3915	2.07		 45
	Peshawar	2014	ELISA	15842	1.80	1.80	 46
	Charsadda	2017	ICT & ELISA	460	2.60	2.60	 47
	Peshawar	2017	ELISA	3679	1.40		 48
Health Care workers							
	Abbottabad	2008	ELISA	125	2.40		 49
	Peshawar	2011	ICT	824	2.18		 50
	Malakand	2016	ICT,ELISA	626	0.64		 51
Healthy Children							
	Peshawar	2000	ELISA	360	3.40		 52
	Peshawar	2000	ELISA	88	3.40		 53
Pregnant women							
	Swat	2009	ICT	5607	1.37		 54
	Peshawar	2016	ICT	10288	1.16		 55
Drug Abusers							
	KP	2007		250	22.40		 57

ELISA: Enzyme-linked immunosorbent assay; ICT: Immuno-chromatographic Test, MEIA: Micro particle Enzyme Immunoassay; RT-PCR: Real time Polymerase chain reaction.

Multi-transfused population

Thalassemic and hemophilic patients' need blood transfusions continuously. Multi-transfused patients are more at risk to blood-borne infections (Waheed et

<u>al., 2009</u>). In four different studies, the percent prevalence was reported to be $5.98\% \pm 0.02$ in multi-transfused patients (<u>Hussain et al., 2003</u>; <u>Mohammad et al., 2003</u>).

Table 2.	Prevalence in I	Multi-transfuse	d patients

Region	Year	Subject	Method	Sample	HBV%	Reference
Peshawar	1999-2001	Thalasemics	ELISA	80	7.50	57
Peshawar	2000-2001	Hemophilic	ELISA	40	5.00	58
Peshawar	2000-2001	Thalassemia major	ELISA	250	8.40	59
Peshawar	2015-2016	Hemophilic	CMIA	396	3	60

ELISA: Enzyme linked immunosorbant assay; CMIA: Chemiluminescent immunoassay.Patients with liver diseaseand chronic hepatitis B were the major liver diseasesDifferent geographic locations have different patterns
of liver disease due to differences in environmental
factors, eating habits, socioeconomic habits, and other
reasons (Burki and Orakzai, 2001). Liver cirrhosisCMIA: Chemiluminescent immunoassay.
and chronic hepatitis B were the major liver diseases
(Burki and Orakzai, 2001; Hamzullah, 2006). Nine
different studies discovered a 26.61% ± 0.12
prevalence rate in patients suffering from liver
diseases (Iqbal, 2002; Khan et al., 2009).

Region	Year Method S		Sample (n)	HBV%	Reference
Peshawar	2005	ICT,ELISA,PCR	181	18.23	64
Peshawar	1998-1999	ELISA	100	30.00	65
Peshawar	1996-1998	EIA	115	36.52	66
Peshawar	1995-1998	EIA	410	29.26	67
Peshawar	1995-1998	EIA	56	14.30	68

Table 2 Duanalana	a in Dationta	Diagona
Table Y Prevalence	e in Patients	with Liver Disease
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Dera Ismail Khan	era Ismail Khan 2002		60	46.00	69
Swat	2001	ELISA	55	32.00	70
Hazara	2002	ICT	893	30.35	71
Swat	2006	ELISA	110	2.81	72

ELISA: Enzyme linked immunosorbant assay; PCR: polymerase chain reaction; ICT: Immuno-chromatographic Test

Patients with dental treatment and ophthalmic

Dentist and dental health care workers are more exposed to HBV infection. As the virus exists in blood and saliva, unsterilized apparatuses are a common means of HBV transmission (Bukhari, 1999). Patients are not screened before surgery, and contaminated

syringes and instruments are reused; therefore, the prevalence of HBV is higher in surgically hospitalized patients; as a result, the disease is easily transmitted from individual to individual (Masood et al., 2005). In KP, a single study was conducted on ophthalmic patients, and two studies on dental treatment indicated the percent prevalence as $4.11\% \pm 0.02$ (Haider et al., 2017; Khan et al., 2015).

Table 5. Prevalence in	patients with dental	treatment and o	phthalmic

Region	Subject	Method	Sample size	HBV%	Male%	Female%	Reference
Dera Ismail	Ophthalmic	ICT,ELISA	1130	3.18%			77
Khan	Patients						
Peshawar	Dental	ICT	1540	2.14%	2.50	1.90	78
	Treatment						
Mardan	Dental	ICT	400	7.00%	7.70	6.10	79
	Treatment						

ELISA: Enzyme linked immunosorbant assay; ICT: Immuno-chromatographic Test

Genotypes of HBV

The hepatitis B virus has 8 genotypes from A to H, while genotypes I and J have been identified recently. The geographic distribution of these genotypes varies (Mahboobi et al., 2013). Studies about the prevalence of HBV genotypes in Pakistan have disagreeing outcomes. Limited data shows the prevalence of HBV genotypes, most specific to certain cities (Mahmood et al., 2016). In 6 different works, the prevalence of

HBV in KP Population due to Genotype D is higher, with an overall prevalence rate of 41.77%, followed by Genotype A at 12.25%. The prevalence rate of genotypes B, C, F, untypable, and mixed was reported to be 6, 3, 1, 2, and 16.95%, respectively (<u>Alam and Naeem, 2007; Awan et al., 2010; Awan et al., 2012;</u> <u>Iqbal et al., 2015; Mahmood et al., 2016</u>). All genotypes with their prevalence are listed in table 6.

	Sample			Untype	Reference					
Region	size	Α	В	С	D	Е	F	Mixed		
KP(2007)	56	8.92%	0%	0%	62.50%	0%	0%	28.50%	0%	82
KP(2007)	28	0	10%	0%	15%	0%	0%			25
KP(2010)	36	16.60%	13.80%	38.80%	5.50%	0.00%	0.00%	9%	0.00%	83
KP(2012)	713	33.66%		2.10%	29.50%	0.00%	1.40%	10.52%	5.90%	84
KP(2015)	128	7.03%	2%	0.00%	71.09%	0.00%	0.00%	18.75%	2%	85
KP(2016)	99	7%	2%	3%	67%	0.00%	0%	18%	2%	86

Table 6. Prevalence of HBV genotypes in Khyber Pakhtunkhwa

Conclusion

This study reviewed the prevalence of the hepatitis B virus and its genotypes in various areas of Khyber *Pakhtunkhwa* Pakistan. The study concluded that the prevalence varies from region to region due to the lack of medical facility, unawareness, and poor clinical management. Therefore, areas with a more than 5% prevalence rate urgently need vaccination and proper Hepatitis awareness programs. There is a controversy about the prevalence of HBV genotypes in KP Populations. The published information related to prevalent genotypes gives conflicting results. The prevalence of HBV and its prevalent genotypes needs to be explored more.

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Declarations

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Competing interests

The authors declare that they have no competing interests.



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