Review Article

A review of hepatitis viral infections in Pakistan

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Abstract

A review of published literature on viral hepatitis infections in Pakistan is presented. A total of 220 abstracts available in the Pakmedinet and Medline have been searched. All relevant articles were reviewed to determine the prevalence of hepatitis viral infections in Pakistan. Two hundred and three (203) relevant articles/abstracts including twenty nine supporting references are included in this review. Of the articles on prevalence of hepatitis infection, seven were related to Hepatitis A, fifteen to Hepatitis E while the remaining articles were on frequency of hepatitis B and C in different disease and healthy population groups. These included eight studies on healthy children, three on vertical transmission, nineteen on pregnant women, fifteen on healthy individuals, six on army recruits, thirty one on blood donors, thirteen on health care workers, five on unsafe injections, seventeen on high risk groups, five on patients with provisional diagnosis of hepatitis, thirty three on patients with chronic liver disease, four on genotypes of HBV and five on genotypes of HCV. This review highlights the lack of community-based epidemiological work as the number of subjects studied were predominantly patients, high risk groups and healthy blood donors.

High level of Hepatitis A seroconversion was found in children and this viral infection accounts for almost 50%-60% of all cases of acute viral hepatitis in children in Pakistan. Hepatitis E is endemic in the country affecting mostly the adult population and epidemic situations have been reported from many parts of the country.

The mean results of HBsAg and Anti-HCV prevalence on the basis of data aggregated from several studies was calculated which shows 2.3% and 2.5% prevalence of HBsAg and Anti-HCV in children, 2.5% and 5.2% among pregnant women, 2.6% and 5.3% in general population, 3.5% and 3.1% in army recruits, 2.4% and 3.6% in blood donors, 6.0% and 5.4% in health care workers, 13.0% and 10.3% in high risk groups, 12.3% and 12.0% in patients with provisional diagnosis of hepatitis and 25.7% and 54% in patients with chronic liver disease respectively.

This review has illustrated the high endemicity of hepatitis viral infections in Pakistan where hepatitis B and C potentially account for a serious burden of the disease. This review has triggered the launching of a network intervention for the control of hepatitis viral infectious.

This review was used as the basis for the launch of hepatitis programme, but putting it into a formal review took time and the hepatitis program was initiated.

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Introduction

Viral hepatitis is a serious global public health problem. At present, six distinct types of hepatitis virus have been identified and called as hepatitis A, B, C, D, E and G viruses. For Hepatitis A virus (HAV) and Hepatitis E virus (HEV), the primary source of infection is the faeces with fecal-oral route being the most predominant mode of transmission. Hepatitis B virus (HBV), Hepatitis C virus (HCV), and Hepatitis D virus (HDV) are blood borne viruses and are primarily transmitted through a breach in the skin (percutaneous) or mucosa (mucosal). All hepatitis viral infections are acute but hepatitis B, C and Delta can also result in chronic infections.

Acute viral Hepatitis A is a common infection among children in Pakistan and accounts for 50-60% of all cases of acute viral hepatitis in children. Almost 96% of the population is exposed to HAV by the age of 5 years and 98-100% at adulthood.[1-3]

Size and this is a review and what ever published data is available is compiled here so the question of small sample does not arise. The method of diagnosis, sample site of data is given in the tables.

Hepatitis E is a disease of mild to moderate severity (mortality rate of 0.4 - 4.0%) except in pregnancy, where the mortality rate may reach 20% in last trimester of pregnancy especially during epidemics.[4] HEV is a major cause of acute viral hepatitis (AVH) in Pakistan particularly in adults from lower socioeconomic groups. Hepatitis E virus typically spreads by faecal contamination of water. The infection is endemic in developing countries and turns into mini epidemics in grave situations. Hepatitis E is endemic in Pakistan[5] and occurs mostly during summers, rains and floods. Major epidemic outbreaks occur in areas where drinking water gets contaminated with sewage and where people have a communal living and drinking water from a

common contaminated source.

Hepatitis B (HBV) and C (HCV) viral infections are transmitted through blood and body secretions which penetrate the human body through a breach in the skin, mucosa or vein. Both the viruses cause acute hepatitis which clears within 6 months in 80% cases of HBV and 20% cases of HCV. In 20% HBV and 80% HCV cases the virus becomes chronic and may progress to chronic liver disease.

The consequences of HBV infection depend on the age of its acquisition. There is an over 90% risk of a new born to get infected and become a long term carrier of HBV. This risk drops from about 90% in the first six months of life, to about 25% by the age of five years, and to 10% by the age of 15 years. It is unusual (2%- 5%) for adults who are infected later in life to become chronic carriers.[6]

The most common routes of transmission of HCV in developed countries include intravenous drug use, blood transfusions, haemodialysis, needle-stick injuries, tattooing, sexual intercourse and peri-natal infections. In developing countries, therapeutic injections from reused needles and syringes and improper sterilization of invasive medical devices is the major vehicle for transmission of blood borne organisms including hepatitis B virus (HBV), HCV and HIV.[7] Overuse and unsafe injection practices cause an estimated 8 to 16 million Hepatitis B virus infections, 2 to 5 million Hepatitis C virus infections and 80,000 to 160,000 HIV infections globally.[8] These infections lead to a high burden of chronic disease, disability and death.

This review shall serve as a valuable technical resource article for policy makers, planners and health professionals with the objective to generate sufficient evidence for policy and programmatic action. The analysis of the currently available literature will also help in reorganizing the endemicity level of these hepatitis viral infections and thus enable future national control interventions.

Methods

Pakmedinet and MEDLINE search was undertaken using the key words "Hepatitis, Hepatitis A, B, C, D and E prevalence, epidemiology, transmission, and carrier". All studies pertaining to prevalence of infections conducted in Pakistan were included in this review. A manual search was also carried out on many indexed Pakistani journals. In most instances full articles were reviewed but in cases where full article could not be traced, the abstract was used. The 95% confidence intervals for the prevalence studies were calculated by using the prevalence reported and the sample size of the study.

All studies where less sensitive methods like CIEP or chromatography was used for testing were excluded from the analysis and only studies using assays like ELISA, EIA, MEIA were included, as these assays are more sensitive and specific.

Results

A total of 220 abstracts were reviewed and of these only 208 articles were finally included in this review to determine the prevalence of hepatitis A to E viral infections in Pakistan.

Very few community based studies on the prevalence of Hepatitis viral infections are available in Pakistan. However, most published studies are hospital or clinics based and therefore show a variation in the reported frequencies/prevalence. Overall, the data suggests that these infections are endemic in Pakistan. The reported prevalence figures in the general population, blood donors and among pregnant women have placed Pakistan among the countries with intermediate endemicity.

The results of the meta analysis of the present review have been tabulated separately for waterborne infections and blood borne infections and the group-wise results are given below:

Hepatitis A and E

Hepatitis A infection:

Almost all studies on hepatitis A showed high prevalence of Hepatitis A (HAV) infection in children especially those who were admitted in hospitals with acute hepatitis. Most of the children were exposed to the virus during early life and remain immune for life as seen by the presence of IgG antibodies in adults in these studies (Table-1).

Table-1: Hepatitis A infection.

Ref.	Place and study site	Year	Test used	Subject	Number	% Anti HAV
9	Karachi	2000	ELISA	Healthy Children	98	82
10	Combined Military Hospital, Peshawar.	2000	ELISA*	Children with sub clinical hepatitis	88	93.2
11	RMC Rawalpindi	1998	EIA	Healthy adult population	166	92.0 IgG
12	Tertiary Care Hospital, Lahore	1996	EIA	Adult patients with acute viral hepatitis	53	4.0 IgM
13	Lahore	1995	EIA	Pediatric patients (<12 years)	25	52 IgM
14	Karachi	1988	RIA	Healthy Adults	233	96.6 IgG
15	Karachi	2002-04	EIA	Low socio economic urban communities	380	100

Table-2: Hepatitis E infection.

Ref.	Place and study site	Year	Test used	Subject	Number	% Anti HEV
16	KTH & LRH Peshawar	2002	ELISA	Hospitalized jaundiced patients	21/148	14.2
17	Allama Iqbal MC Lahore	2001	ELISA	Hospitalized jaundiced patients	100	7.0
18	Allama Iqbal MC Lahore	2001	ELISA	Hospitalized jaundiced patients	100	22.0
19.	JPMC, Civil and Liyari Hospital Karachi	2000	EIA	Pregnant women with jaundice	65	57.0
09	Karachi	2000	ELISA	Healthy Children	98	18.3
20	JPMC Karachi	1999	ELISA	Healthy Children	98	19.4
				Health adults	100	16.0
21	PAF Bases Karachi	1998	EIA	Outbreak of acute hepatitis	204	Confirmed
22	G-10 Islamabad	1994	EIA	Outbreak of HEV in general public	3827	10.0 AR
23	Garrisons Lahore	1994	EIA	Outbreak of HEV in Army people	283	Confirmed
24	Karachi	1994	EIA	Pregnant women with acute viral hepatitis	53	61.0
25	Military Unit Abbottabad	1988	EIA	Outbreak of Hepatitis E in Military Unit	109	95.0
26	College Campus Sargodha	1987	EIA	Students	133	20% AR
15	Karachi	2002-04	EIA	Low socio economic urban communities	380	1.4%
27	Holy Family Hospital Rawalpindi	2005	EIA	Non pregnant females with acute hepatitis	24	All IgM +ve (8 33% died)
28.	Aga Khan Hospital Karachi	1996	ELISA	Fulminant hepatic failure in pregnancy	12	6/9 (66.6) 16% maternal death and 50% fetal death

Hepatitis E infection:

Most studies on hepatitis E infection (Table-2) were a part of the clinical work of acute hepatitis in patients who were admitted with jaundice. Four studies have reported mini epidemic outbreaks due to faecal contamination of water. Total HEV was checked in most studies while in few HEV IgM antibodies which are specific of acute infection were tested. Two studies on pregnant cases with jaundice showed HEV positivity of 57-61% while a 3rd study in non pregnant females showed mortality in 33% of the cases who went into fulminant hepatic failure.

Hepatitis B and C:

Hepatitis B and C infections cause significant morbidity and mortality in Pakistan. Many studies have been reported from medical screening camps, hospitals and clinics in different groups of individuals to see the magnitude of the problem. Prevalence of HBV and HCV infection in various groups is presented below:

Children:

Studies on HBs Ag and Anti-HCV in healthy children showed a prevalence of HBs Ag between 1.9%-3.6% and for Anti-HCV between 0.4%-4% (Table-3).

Mother to infant transmission:

The contribution of perinatal transmission to the overall burden of disease is related to the prevalence of HBe Ag in the pregnant woman. If a mother is HBs Ag positive and HBe Ag positive there is over 90% chance that she will transmit the infection to her infants.[1]

Maternal to child transmission of HBsAg and HBeAg was done in 3 studies. Kazmi etal[35] screened 6225 mothers and found 249 HBs Ag positive. Out of 249 HBs Ag positive mothers 55 were HBeAg positive. In another study 50 infants born to HBsAg and HBeAg positive mothers were followed. The cord blood of these newborns was tested for HBeAg and the infants were followed for 18 months for the status of HBsAg. About 90% of HBeAg positive mothers transmitted HBV to their infants.

Aisha et al[36] conducted a study in 245 pregnant women and found 8 cases positive for HBs Ag, of whom one was positive for HBe Ag. Eight babies born to sero-positive mothers were tested for HBs Ag and HBe Ag and all were

Table-3: Prevalence of HBs Ag and Anti-HCV in healthy children.

Ref	Place and study site	Period	Test used	Number	% HBs Ag Positive (95% CI)	% Anti HCV Positive (95% CI)
29	Lahore (rural area)	2000	EIA*	171	…	0.58 (0.49 - 0.67)
30	Combined Military Hospital, Peshawar	2000	ELISA**	88	3.4 (3.00 - 3.80)	…
31	Children Hospital & Institute of Child Health, Lahore	1998	RPHA/ ELISA	392	2.0 (1.97 - 2.11)	…
32	PIMS & Model Schools Islamabad	1997	ELISA	664	3.6 (3.55 - 3.65)	…
33	Mayo & Aitcheson Hospital, Lahore	1995	EIA	538	3.3 (3.28 - 3.42)	4.0 (4.02 - 4.16)
34	Civil Hospital, Karachi	1994	EIA	236	3.0 (2.86 - 3.14)	0.40 (0.35 - 0.45)
15	Low Socio Urban Communities	2002-04	EIA	380	1.9	1.4
10	CMH, Peshawar	2000	ELISA	360	3.4	…

found negative for these markers.

Iqbal[33] screened 417 mothers and 538 children separately for HBs Ag and found 2.3% positive mothers and 3.3% positive children. Of these one mother and two children were HBe Ag positive.

Pregnant women:

Many studies are available on the status of HBs Ag and anti HCV in pregnant cases (Table-4). HBs Ag was generally reported with low frequency in private sector patients[39,41] and high in public sector patients.

Table-4: Prevalence of HBs Ag and Anti-HCV among pregnant women in Pakistan.

Ref	Place and study site	Period	Test used	Number	% HBs Ag+ Positive (95% CI)	% Anti HCV Positive (95% CI)
37	Shifa International Hospital, Islamabad	2001-2002	EIA	503		4.8 (4.72 - 4.88)
36	DMC and Sobhraj Maternity Home, Karachi	1999	ELISA	245	3.2 (3.12 - 3.40)	…
38	Ganga Ram Hospital, Lahore	Oct 2006 March 2007	ELISA	2439	2.2	7.3
39	Ziauddin Hospital, Karachi	1997-98	EIA	801	2.2 (2.16 - 2.24)	…
40	PNS Shifa Karachi	1997	RPHA	474	3.1	6.4
41	PMRc, JPMC, Karachi	1979	RPHA	45	9	…
42	JPMC Karachi	1989	RPHA	1000	4.0 (3.96 - 4.04)	…
43	LRH Peshawar	2001	EIA	352		5.1 (4.9 - 5.2)
44	Services Hospital, Lahore.	2002	ELISA	100	…	7
45	Lady Aitcheson Hospital, Lahore	2001	EIA	300	…	6.00 (5.84 - 6.16)
46	Ganga Ram Hospital, Lahore	2005	ICT	1000	1.8	…
34	NIH, Islamabad	1992	RPHA	6225	4.00 (3.99 - 4.01)	…
47	Shifa International Hospital, Islamabad	2001-02	ELISA	947	…	3.2
48	Jinnah Postgraduate Medical Centre, Karachi	2002	EIA	77	…	13.2
49	Shaikh Zayed Hospital, Rahim Yar Khan	2006	ELISA	450	12	18.2
50	Ghurki Trust Hopsital, Lahore	2005	ELISA	1569		6.8
51	LUMHS, Hyderabad	2003	ELISA	103	12.6	16.5
52	Ganga Ram Hospital, Lahore		ICT	1000	1.8	
53	Kharadar General Hospital, Karachi	2002-06	ICT	25482	1.6	

Table-5: Prevalence of HBs Ag and Anti-HCV in general population (Normal individuals).

Ref	Place	Year	Test used	Number	% HBs Ag Positive (95% CI)	% Anti HCV Positive (95% CI)
54	Abbasi Shaheed Hospital, Karachi	2000	EIA	200	3.0 (2.86 - 3.14)	…
55	Karachi	1979	CIEP	1200	3.6%	…
56	Institute of H&M, Lahore	1999	EIA	346		5.78
57	Ganga Ram Hospital, Lahore	1999	Lattix	220		5.9
58	Hafizabad	1993	ELISA	309	4.3(4.17 - 4.43)	6.5 (6.34 - 6.66)
59	PIMS and FGSH Islamabad	1998	EIA	100		4.0 (3.62 - 4.38)
60	Islamabad (Shifa Int)	1998- June 2004	Rapid/ EIA	47,538	2.5 (2.56 - 2.56)	5.3 (5.31 - 5.31)
61	Tertiary Care Hospitals in Islamabad	1996	ELISA	664	3.6 (3.55 - 3.65)	…
62	NWFP	2006			2.2	3.1
63	Screening Camp, Lahore	2003	ICT	757	2.6	13.5
64	Tharparkar	2005-06	ICT	612	11.9	
65	Combined Military Hospital, Sargodha	2006	ELISA	2038	5.8	3.0
66	Peshawar.	2003	ICT	11372	4.3	
67	Combined Military Hospital, Bahawalpur	2005	ELISA	1821	5.9	2.5
68	Lahore Medical & Dental College, Lahore			524	1.1	2.1

Table-6: Prevalence of HBs Ag and Anti-HCV in new recruits.

Ref	Place	Year	Test used	Subject	Number	% HBs Ag Positive (95% CI)	% Anti HCV Positive (95% CI)
69	Karachi	2000-02	EIA	Healthy Naval recruits	966	3.2 (2.10-4.30)	2.2 (1.30-3.10)
70	Rawalpindi	2002	ELISA	Young army recruits	5371	3.5 (3.52-3.54)	3.2 (3.28-3.30)
71	AFIT, Rawalpindi	2005-06	ELISA	Healthy Recruits		2.8	3.4
72	Combined Military Hospital	2001-02	EIA	Healthy recruits	4552		4
73	Combined Military Hospital, Khuzdar	2004	ELISA	Healthy recruits	665	3	3.3
74	Combined Military Hospital, Hyderabad	2007	ELISA	Healthy recruits	2835	7.3	5.2

General population:

Although there are no population studies on the prevalence of HBV and HCV infections in the country but the summation of available data on various healthy groups like voluntary blood donors, pregnant women, recruits and healthy individuals provide the infection status in the country (Tables-5,6,7). The HBV prevalence in general population ranged from 1.1-11.9% and the figures for HCV ranged from 2-13.5%

Special groups:

Recruits:

The healthy individuals who were screened prior to their induction in the armed forces showed HBsAg range from 3- 7.3% and HCV from 2.2- 5.2% (Table-7).

Blood donors:

75 and 76 new references to be added.

In Pakistan over 1.5 million pints of blood are collected each year.[77] The main source of blood (65%) was replacement donors[78] with another 10% from professional/paid donors. Only 25% donations came from volunteer non-remunerated blood donors.[79] Most of the replacement donors are patient's relatives or friends.

The blood screening data showed higher prevalence of Anti-HCV as compared to HBs Ag in all years.

High risk groups:

Significant HBV and HCV transmission occurs in selected high risk groups including health care workers, injecting drug users and patients receiving blood products.

Table-8 shows the data of 13 studies in health care workers. The prevalence of HBsAg in this group ranged from 2.4-20%. Highest prevalence was seen in dentists (17%) and sweepers (20%). The anti-HCV prevalence ranged from4-10% with highest positivity of HCV (10%) in health care workers who reported needle stick injuries while working.

Table-7: Prevalence of HBs Ag and Anti-HCV among voluntary blood donors in Pakistan.

Ref	Place and study site	Year	Method used	Number tested	% HBs Ag Positive (95% CI)	% Anti HCV Positive (95% CI)
80	Shifa International Hospital, Islamabad	2002- 2003	AXSYM-MEIA	(Repl) 3187	2.5 (2.50 - 2.52)	5.1 (5.13 - 5.15)
				VBD 2430	0.8(0.75 - 0.89)	2.4 (2.34 - 2.58)
81	124 Blood Banks in the country	2000-2003	Rapid/EIA	1176284	2.3 (2.30 - 2.30)	…
82	Railway Hospital, Rawalpindi.	2001- 2002	*IACT	580	5.8 (5.78 - 5.94)	6.2 (6.13 - 6.29)
83	Blood Transfusion Services Punjab	2000-2001	Rapid/EIA	166183	…	4.1 (4.10 - 4.10)
84	Combined Military Hospital, Quetta	2000- 2001	ELISA	1500	…	1.8 (1.85 - 1.89)
85	Services Hospital, Lahore	2000-01	Rapid/EIA	5789	…	4.9 (4.96 - 4.98)
86	Abbasi Shaheed Hospital, Karachi	2000	ELISA	590	…	1.0 (0.97 - 1.03)
87	Abbasi Shaheed Hospital, Karachi	2000	ELISA	964	0.8 (0.78 - 0.82)	…
88	JPMC, Karachi	1999	Abbott Diagnostic Sys	612	2.2 (2.16 - 2.26)	0.5 (0.48 - 0.52)
89	CMH, Sialkot	1998- 2000	Rapid/EIA	(Army) 1867	…	3.2 (3.24 - 3.28)
				Civilian 1457	…	6.5 (6.49 - 6.55)
90	AIFP, Rawalpindi	1996-2000	EIA	103858	3.3 (3.30 - 3.30)	4.0 (4.00 - 4.00)
91	AKU Hospital Karachi/ Hyderabad.	1995-1996	Rapid/EIA	51257	2.3 (2.30 - 2.30)	1.1 (1.18 - 1.18)
92	PMRC/JPMC, Karachi	1974	CIEP	1111	3.4	
93	Rehman Medical Institute, Peshawar	2002-03	NEIA	4000	1.9	2.2
94	Shifa International Hospital, Islamabad	2002-03	NEIA	3430	2.5	5.1
95	Hayatabad Medical Complex, Peshawar	2003	ELISA		1.4	1.3
96	PNS Shifa, Karachi	2001-03	ELISA	302	1.4	2.8
97	Combined Military Hospital, Quetta	2000-01	ELISA	1635		1.8
98	Saidu Hospital, Swat	2003-05	ICT	41613	1.1	2.2
99	DHQ, Skardu			850	8.4	1.1
100	ISRA University Hyderabad	2004-05		3677	3.6	8.6
101	Jinnah Hospital, Lahore	2000-01	ELISA	890		6
102	Shaikh Zayed Hospital, Lahore	2005	ICT	18216	3.3	4.1
103	Jinnah Postgraduate Medical Centre, Karachi	2001-02		150		4.6
104	Bahawal Victoria Hospital, Bahawalpur	2005	EIA	27938	2.6	2.5
105	Fauji Foundation, Rawalpindi	2005		1428	2.4	2.5
106	Ghurki, Lahore	2004-06		7431	1.5	5.3
107	DHQ Skardu	2003-05	ICT	8949	3.6	1.3
108	Taluka Hospital, Sajawal Thatta	2004-05	ICT	310	5.8	1.3
109	Baqai Medical University, Karachi	2006	ICT	688	4.5	4.3
110	Blood Transfusion Centre, Multan			6000	3.3	0.2

Table-8: Prevalence of HBs Ag and Anti-HCV in health workers.

Ref	Place	Period	Test used	Subject	Number	% HBs Ag+ (95% CI)	% Anti HCV (95% CI)
111	DHQ Hospital, Rawalpindi	2002	ELISA	Health care naval workers	217	…	6.00 (5.79 – 6.21)
112	AFIP, Rawalpindi	1999	ELISA	randomly selected from 27 hospitals. - 155 Laboratory workers - 28 dental staff and - 48 operation theatre staff	231	7.7 (7.47 – 7.93)	…
113	Civil Hospital, Karachi	2001	ELISA	Health care workers	250	2.4 (2.28 – 2.52)	5.60 (5.42 – 5.78)
114	Karachi	1994	ELISA	- Doctors	145	7	
				- Dentists	41	17	
				- Paramedics &	20	5	…
				- Sweepers	35	20	
115	Karachi	1977	RIA	Health care workers	383	2.8	…
116	Karachi	1998	ELISA	Operation room personnel	114	7.5 (7.05 – 7.95)	4.00 (3.66 – 4.34)
117	CMC Hospital, Larkana	1996	ELISA	Doctors, medical students, paramedics, staff	304	9	
118	LMC Hospital Hyderabad	1995	ELISA	Doctors, medical students, paramedics, staff of the hospital	145	7	
119	Ganga Ram and FJMC Hospital, Lahore	1996	ELISA	Health care workers and medical students	1020	6.30 (6.25-6.35)	…
120	Ganga Ram Hospital, Lahore	1995	RPHA	Doctors, medical students, paramedics, staff of the hospital	1000	6.3	
121	AIMC and Sheikh Zayed Hospital, Lahore	1996	ELISA	Medical staff	95	5	4
122	DHQ, Rawalpindi	2002		Health care workers with needle stick injury	217	…	6%
123	Abbasi Shaheed Hospital, Karachi	1995-00		Health care workers with needle stick injury	612	42	10%

Trend of HBV & HCV infection in a community as per the use of injections:

Few studies have been published in Pakistan where the risk of unsafe injections for transmission of Hepatitis B and C infections has been highlighted (Table-9).

In a cross sectional study Khan et al[124] identified injections as the major risk factor for Hepatitis C infection in patients seeking health care in a peri-urban community in Karachi. Luby[125] found 16% HCV infection among households of HCV infected patients in Hafizabad. Khan et al[126] studied the risk factors for the transmission of HBV or HCV in patients with chronic liver disease and found therapeutic injections, surgery, blood transfusion and dental extraction as the major risk factors for both these diseases.

Trend of HBV & HCV infection in other high risk groups:

Many studies have been done on the high risk groups like injecting drug users, commercial sex workers, transvestites and patients receiving blood products. All these studies also revealed high prevalence of HBs Ag and Anti-HCV in these

Table-9: HBV & HCV infection in a community as per the use of injections.

Ref	Place	Year	Subject	Test Used	No tested	% HBs Ag+ (95% CI)	% Anti HCV (95% CI)
124	Periurban Karachi	1995	Patients leaving the clinics in, Periurban community, Karachi	EIA	135	19 (18.43 - 19.57)	44 (43.28 - 44.72)
125	Hafizabad, Punjab	1994	Household members of patients with hepatitis C infection	ELISA	74	…	16.2 (15.22 - 17.18)
126	Public sector hepatology clinic	2008	Patients with chronic liver disease	ELISA	497	41.9	58.1
127	Karachi	2000-01	Acute HBV (IgM)	ELISA	67	Estimated population attributable risk (PAR) for therapeutic injections was 53%	
128	Karachi	2001	Injection Practices	--	1150	68% population received at least one injection	

Table-10: Prevalence of HBs Ag and Anti-HCV in other high risk groups.

Ref	Place and study site	Year	Test used	Subject	No tested	% HBs Ag + (95% CI)	% Anti HCV + (95% CI)
129	Karachi	1999-2000	ELISA	Drug addicts	57	22.8 (21.36-24.24)	…
				Hemodialysis pts	290	6.9 (6.73-7.07)	
130	Lahore	1997-98	ELISA	Female sex workers	103	11.65 (11.04-12.26)	…
131	Karachi	1998	ELISA	Transvestites (Hijra)	208	3.4 (3.23-3.57)	
132	Shifa Hospital, Islamabad	2002-03	ELISA	Hemodialysis pts	97	12.4 (11.73-13.07)	…
133	Ganga Ram Hospital, Lahore	2001-02	ELISA	Hemodialysis pts	190	…	24.7 (24.26-25.14)
134	KTH and Fatmid BT, Peshawar	2000-01	ELISA	Heamophilic children	40	5.0 (3.93-6.07)	25 (22.9-27.12)
135	KTH Peshawar	1999-2001	ELISA	Thallasemics children	80	7.5 (6.85-8.15)	36.2 (35.02-37.38)
136	JPMC Karachi	2002	EIA	Single transfused obstetric cases	38	…	13.2 (11.5-14.95)
				Multiple transfused obstetric cases	39	…	15.4 (13.59-17.21)
137	Hayatabad Medical Complex, Peshawar	2002-03	ELISA	Plastic Surgery pts	1382	…	3.04 (3.02-3.06)
138	Abbasi Shaheed	1998-99	EIA	Surgical patients	750	18.66 (18.56-18.76)	16.24 (16.15-
16.34)	Hospital, Karachi						
139	Khyber Teaching Hospital and Fatmid, Peshawar	2000-01	ELISA	Hemophiliac children	40	5	25
140	Khyber Teaching Hospital and Fatmid, Peshawar		ELISA	Thallasemics	80	7.5	36.2
141	Hemophilia Centre, Lahore	2002		Hemophilia	100	4	56
142	Khyber Teaching Hospital and Fatimed, Peshawar	2000-01	ELISA	Thalessemia major	250	8.4	56.8
143	PIMS, Islamabad	2002-03	ELISA	Thalessemia major	180		41.7
144	Shaikh Zayed Hospital, Lahore	2000-02	ELISA	Hemodialysis	122		19.7
145	Shifa International Hospital, Islamabad	2002-03	ELISA	Hemodialysis	97	12.4	

groups. HBs Ag infection was found in 12% of the commercial sex workers (women) in Lahore while it was only 3.4% among transvestites in Karachi who acknowledged commercial sex with men. The mean prevalence of HBV and HCV in these groups was 15.5% and 12.3% respectively (Table-10).

The prevalence of these infections in individuals receiving multiple blood transfusions was high. For thalaessemia, the HBV figures ranged between 7.5-8.4% while for HCV they were between 36-56%. Figures in haemophilia were similarly high. In dialysis population HBV figures were 12.4% and HCV 20%.

Patients with provisional diagnosis of hepatitis:

Studies in patients who were admitted with a provisional diagnosis of hepatitis (Table-11) showed a prevalence of HBs Ag ranging between 10% - 45% while only one study showed 12% HCV infection.

Chronic liver disease patients:

Many studies are reported on HBV/ HCV positivity in chronic liver disease cases (Table-12). The HBsAg positivity in patients with chronic liver disease ranged from 10-46.6% and for HCV from 40-86% which is more than twice of that seen with HBV. Two studies are available in children and both show high prevalence of HBV but low of HCV.

Genotypes and serotypes of HBV and HCV:

Variable results are seen on genotypes of HBV (Table-13). Majority of the studies from Sindh showed a high prevalence of genotype D while a study from Punjab showed high C.

Many studies on HCV serotypes have been carried out (Table-14) and all showed that in over 80% the cases, genotype 3 was detected, followed by genotype 1, 2 and 4.

Table-11: Prevalence of HBs Ag and HCV infection in patients with provisional diagnosis of hepatitis.

Ref	Place and study site	Year	Test used	No. tested	% HBs Ag + (95% CI)	% Anti HCV + (95% CI)
146	Lahore	1998	EIA	2285	10.2 (10.14-10.26)	…
17	Allama Iqbal Medical College, Lahore.	2001	ELISA	100	25.0 (24.15-25.85)	12.0 (11.36-12.64)
147	PNS Shifa Karachi	1998	EIA	1225	12.0 (11.95-12.05)	…
148	Karachi	1991	RIA	163	45%	…
149	Karachi	1979	CIEP	254	37.8%	…

Table-12: Prevalence of HBs Ag and Anti-HCV in patients with chronic liver disease.

Ref	Place and study site	Year	Test used	No. tested	% HBs Ag+	% Anti HCV+
150	HMC, Peshawar	1998-99	ELISA	100	30.00	41.00
151	HMC & KTH Peshawar	1996-98	EIA	115	36.52	63.48
152	HMC & KTH Peshawar	1995-98	EIA	410	29.26	43.90
153	HMC & KTH Peshawar	1995-98	EIA	56	14.30	67.80
154	HMC, Peshawar	1998-99	EIA	100	30.00	41.00
155	District Teaching Hospital DI Khan	2002	IACT	60	46.67	13.30
156	Saidu Medical College, Swat, NWFP	2001	ELISA	55	32.00	59.00
157	Ayub Medical College, Abbottabad	2000-02	IACT	614	…	40.80
158	Ayub Medical College, Abbottabad.	2002	IACT	893	30.35	…
159	Karachi	2004	ELISA	55	24.00	…
160	AKU, Karachi	1994-98	ELISA	201	36.00	41.00
161	Karachi	1979		83	26.5	…
162	CMC Larkana Sindh	1997-2002	ELISA	564	…	51.00
				510	…	57.00
163	Mayo Hospital, Lahore	1998-2000	ELISA	100	23.00	55.00
164	Sheikh Zayed Hospital, Lahore.	1997	ELISA	94	23.00	…
165	Lahore	2001	EIA	50	30.00	45.00
166	Sheikh Zayed Hospital, Lahore.	1998	ELISA	30	20.00	76.60
167	Mayo Hospital, Lahore	1996-97	ELISA	50	24.00	52.00
168	FGSH, Islamabad	2000-2002	ELISA	108	13.90	79.60
169	Shifa International Hospital, Islamabad	1994-2000	ELISA	354	10.70	86.00
170	Holy Family Hospital, Rawalpindi.	2000	EIA	75	10.00	72.00
171	Rawalpindi Medical College, Rawalpindi.	2001	EIA	44	25.00	54.00
172	Rawalpindi Medical College, Rawalpindi	2001	EIA	30	10.00	86.60
173	Holy Family Hospital, Rawalpindi.	1998-99	EIA	120	25.00	58.00
174	Hazara	2000-02	ICT	893	33.3	
175	Military Hospital, Rawalpindi	2002-04	ELISA	650	28	70
176	Allied Hospital Faisalabad	2005	ELISA	100	20	66
177	DHQ DI Khan	2002	ICT	60	13	40
Children						
159	National Institute of Child Health, Karachi	2002	ELISA	55	24	00
178	Paediatric Unit, Civil Hospital, Karachi	2001-05	ELISA	92	23.4	8
Liver Cancer						
179	Karachi	1997	ELISA	54 (HCC Cases)	66	33
180	PMRC JPMC, Karachi	1969	RIA	366	60 (40% Delta positive)	-
181	Shifa International Hospital, Islamabad	2001-02	--	283 out of 8529 admissions	20.6% died from CLD	

Table-13: Genotypes of HBV.

Study	Samples	Genotype A	Genotype B	Genotype C	Genotype D	Mixed
182	107	21.4%	17.8%	41%	8%	7.1%
183	295				70%	
184	180				84%	16%
185	110	5	27		65	3

Genotypes are important to determine the treatment response and disease transmission epidemiology. Better response to interferon and short term treatment (6 months) is reported in hepatitis C patients infected with serotype 3 while for all other genotypes a longer duration of therapy is suggested.

Sexual transmission of HCV was checked in few studies to see inter spousal transmission of the disease (Table-15). Studies from Sindh[192,195] show a higher frequency of disease in the spouses while those from Punjab show a low frequency.[191,193,194]

Hepatitis Delta (HDV):

Delta virus is dependant on presence of HBsAg for its transmission and survival. It can infect as co infection where both viruses are transmitted at the same time resulting in high mortality because of fulminant hepatitis. Super infection occurs in an already known HBV carrier who is exposed to delta virus, thus resulting in chronic liver disease. Zuberi[196] reported 408 cases of chronic liver disease due to HBV infection of which 44% had delta super infection and 1.4% co infection. Riaz et al[197] from Karachi studied 531 cases of HDV at a hepatology unit of a public sector hospital using

Table-14: HCV serotypes.

Ref	186		187		188		189		190	
Study period	2000-2001		1999-2000		2000-2001				2000-2002	
No of HCV positive sera tested	215		50		255		55		125	
Results	No	%	No	%	%	%	%	%	No.	%
Serotype 1	18	8.4	6	12	12	12				6
Serotype 2	3	1.4	2	4	2.3	2.3	6	3.6		4.8
Serotype 3	171	79.5	25	50	77.6	77.6	48	87.2		69.6
Serotype 4	2	0.9	1	2	2.3	2.3				2.4
Serotype 5	0	0	0	0	0.4	0.4				00
Serotype 6	2	0.9	0	0	2.7	2.7				0.8
Mixed	19	8.8	2	4	2.3	2.3	1	9.1		00
Untypable	63	22.7	14	28	16.6	16.6			20	16.0

Table-15: HCV in spouses.

Ref	Place and study site	Year	No. tested	Spouse tested	% Anti HCV+
191	RMC, Rawalpindi	2002	68	23	5.1
192	JPMC, Karachi	2003-04	50	09	19
193	Federal Govt. Services Hospital, Islamabad	2000-02	23	01	4.3
194	Shifa International Hospital, Islamabad	2001-04	227	10	4.4
195	PMRC JPMC, Karachi	2003-04	153	58	38

EIA. Majority of their cases (68%) came from Northern Sindh, followed by Balochistan (17%) and death in most of these cases was due to complications of liver disease and failure. Mumtaz et al[198] studied 8721 patients with chronic HBV disease and found HDV antibody in 1444(16.6%) cases and HDV infected cases has milder liver disease when compared with non delta infected HBV cases.

Discussion

Pakistan has a high disease burden of hepatitis A to E, with maximum morbidity in hepatitis A and E and maximum mortality in hepatitis B, C and D. The aim of this review was to determine the extent of hepatitis problem in the country and to provide road map for the policy makers in the development of national strategy on the prevention and control of hepatitis. This review provides sufficient evidence of infection in different groups.

Hepatitis A accounts for 50-60% of all cases of acute viral hepatitis in children. This infection is uncommon in adults but those who get infected have a longer convalescence and prolonged morbidity. Most of the children are exposed to this virus during their early age and remain immune for rest of their life. Vaccine is available for its prevention but its use is recommended for travelers coming from low endemicity areas and during epidemics and natural disasters.[199] Two doses of hepatitis A vaccine are recommended which produce life long immunity

In Pakistan, Hepatitis E mainly affects the adult population. A number of mini epidemics have been reported in the country. Once infected recovery is a rule except in late trimester of pregnancy where a 30% maternal or foetal loss is reported especially during epidemics.[200] Hepatitis E like hepatitis A infection is endemic in Pakistan due to faecal contamination of drinking water. In urban areas, the main water supply line gets contaminated from the nearby leaking sewage pipe while in rural areas water from wells, streams, canals, rivers and ponds gets contaminated by direct disposal of sewage in these sites. The immunity of hepatitis E lasts for 8-10 years and is lost thereafter making the individual susceptible to re-infection. A vaccine trial was done in Nepal with good results,[201] but no vaccine is commercially available, therefore prevention of hepatitis E infection needs to be propagated.

Hepatitis B and C infections are blood borne and are transmitted through unscreened blood transfusions, inadequately sterilized invasive medical devices and re use of syringes.

Using WHO's criteria of endemicity of hepatitis B virus countries with a carrier rate of less than 3% fall in the low endemic region, those with rates between 3-5% fall in intermediate and those above 5% in high endemic region.[202] The previous review showed that the prevalence of hepatitis B in Pakistan is around 4% in general population.[196] With a sizable pool of delta positive cases in some parts of Sindh Punjab and Baluchistan,[196-98] and a low EPI coverage of hepatitis B vaccine in some districts[203] there is a high chance that this viral infection will continue to cause a major disease burden in our country. To contain the disease strategies have to be laid down to improve immunization coverage. Studies

on vertical transmission of HBeAg are scarce; and some published studies are not so much supportive to decide for introducing the birth dose hepatitis B vaccine. There is need to study the HBsAg status in vaccinated children and see if vaccination at 6 weeks should be continued or an extra dose should be given at day zero.

For HCV, the global figures are that about 3% of the world's population is suffering from this viral infection. In Pakistan the prevalence of HCV infection is around 5%.[196] Pakistan has the highest rate of therapeutic intramuscular injections per person per year.[124,127,128] Apart from the known risk factors of blood transfusion, reuse of syringes and improper sterilization of invasive medical devices; shaving by barbers is coming up as another source of spread of this disease. As no vaccine is available for its prevention therefore adherence to best clinical practices and standard operating procedures for sterilization and disposal of hospital waste must be practiced along with legislation against non compliant blood banks and hospitals.

Clinical significance of HBV and HCV serotypes is important to see the disease response to treatment and progression. Of the HBV serotypes, type A and D are associated with cirrhosis of the liver and type C with liver cancer. Studies from Sindh show higher frequency of genotype D,[183-85] while those from Punjab show more HBV genotype C[182] which is associated with the development of cirrhosis and HCC as well as lower response rate to interferon or nucleoside analogue therapy as compared to genotype B.[182]

In hepatitis C six serotypes have been identified.[1-6] Global studies have shown that serotype 3 is most easy to treat with a cure rate of around 80 percent.[204] In Pakistan serotype 3 is most common. Most studies show about 50-70% sustained viral response with interferon therapy for 6 months.[205-207]

There is no national data on the leading causes of admissions to hospitals in Pakistan and the contribution of liver disease to overall mortality. One study from Peshawar showed 23% of total admissions of gastroenterology in a year were made for liver diseases.[208] Khokhar et al[181] reviewed twelve months admission data to see the cause of deaths in 283 cases out of 8529 admissions. There were 160 deaths related to medical causes, including 33 (20.6%) deaths from chronic liver disease.

Keeping in view the high disease burden of viral hepatitis infections and severity of its complications from hepatitis to cirrhosis and cancer, the Prime Minister of Pakistan launched a hepatitis prevention and control programme in collaboration with the ministry of health, the provincial health departments, to reduce the disease prevalence and incidence.

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