



Low Prevalence of Hepatitis B and Hepatitis C Infection in Gujarat and Maharashtra States of Western India

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Abstract

Prevalence of hepatitis B viral infection (HBV) in India is varying from 3 to 12%, which falls in to intermediate prevalence zone. Prevalence of hepatitis C viral infection (HCV) in India varies from 0.3 to 4% among blood donor population. Previous data from western India suggests HBV prevalence of 1.6 - 5.9% and HCV prevalence of 0.2 - 15.9%. Most of these data are almost 10 years old and based on selected population. Therefore, the main aim of the present study was to find out recent prevalence of HBV and HCV from multiple sources. Data on prevalence of HBV and HCV was collected prospectively from multiple sources that include general population, blood donor population, hospital attending population, and liver clinic population. HBV prevalence was as follows: general population data: 166/1758 (0.94%); blood donor data: 2039/172316 (1.18%) hospital attending population: 133/13177 (1%); liver clinic data: 2637/12251 (21.5%). HCV prevalence was as follows: general population: 1/2388 (0.040%); blood donor data: 666/171306 (0.38%); hospital attending population: 12/2597 (0.46%) liver clinic data: 916/12251 (7.4%). In Western India, there is very low prevalence of HBV and HCV; making it a low prevalence area.

Keywords: Hepatitis B; Hepatitis C; Chronic Liver Disease; Hepatocellular Carcinoma

Introduction

Hepatitis B virus (HBV) and hepatitis C virus (HCV) share some common features including worldwide distribution, parallel modes of transmission and the ability to induce chronic infection that may develop in to liver cirrhosis and hepatocellular carcinoma. Precise estimate of the prevalence of HBV/HCV co-infection

would be needed to formulate policy decisions and plan communal health interventions. Hepatitis B virus infection (HBV) is a global health problem, with 10 million new cases occur recently and nearly 350 - 400 millions of people become chronic carriers annually all over the world [1]. HBV infection is considered as the cause of 5th most common cancer and 10th leading cause of death worldwide. It is the cause of 30% cases of cirrhosis and 60 - 80% of all primary

cancers in the liver. At any point in time, nearly 30% of the world's population shows serological evidence of current or past infection with HBV. Nearly 75% of HBV population resides in Asia [2]. WHO has stratified world population into 3 zones: high endemicity (> 8% of general population): China, South-East Asia, sub-Saharan Africa, Amazonian basin; intermediate endemicity (2- 7% of general population): East-South-central Europe, South Asia, Middle East, Japan; and low endemicity (< 2% of general population): Western Europe, North America, Australia, South America. In area of low endemicity, HBV contributes to 5 - 10% of CLD; whereas in areas with high endemicity, HBV contributes to more than 50% of CLD [3]. India falls in the intermediate range with an estimated 1,00,000 deaths per year.

Prevalence of HBV in India is around 3 - 4% of general population, mounting to 12 - 15% of global pool of HBV or 40 million persons. HBV contributes to more than 50% of chronic hepatitis cases [3,4]. Ever increasing population and lack of national immunization program, until recently, are the deciding factors for future burden of HBV disease. Based on past studies (most of before 1999), prevalence of HBV in Western India is 1.6 - 5.9%, in Northern India 1.1 - 9.9%, in Central India 12.2%, in Southern India 1.3 - 24.5% and in Eastern India 1.7 - 8.4% [5]. Most series included in this old data were based on small sample size, insensitive RPHA method, selective rather than general population (young blood donors, school going children, etc.), or at-risk population. In the last decade, many changes occurred in almost all segments in India including health-care segment. After 1999, only a few studies have been performed to re-evaluate HBV prevalence. In such population based study from west Bengal, the prevalence of HBV was found to be 2.97% in rural population [5].

Also, hepatitis C virus infection (HCV) is the most rapidly increasing cause of CLD and HCC in western world. Epidemiology of HCV is not studied systematically in India, barring few studies. Prevalence in general population varies from 0.09% to 7.89% in India (average 2%) and in voluntary blood donors from 0% to 4.3%. In western India, HCV prevalence is reported to be 0.7 - 4.3% in voluntary blood donors and 0.09% in general population but these data are decade old [6-8]. Therefore, this study was planned to evaluate present scenario of hepatitis B and C infection in various sub-population in western India.

Methods

Data regarding prevalence of HBsAg and anti HCV positivity was collected from different sources: A. adult population (age > 18 years): General population (prospective, 15 sites); Blood donor population (prospective, 3 sites); Hospital-attending population (retrospective, 2 sites and prospective, 2 sites); Liver clinic population (retrospective, 3 sites and prospective, 2 sites) B. pediatric population: asymptomatic healthy school children (10 schools).

General population data was based on following: 1. a prospective study (2004) on all the residents of 2 railways residential colonies of Bandra and Matunga, 2 suburbs of Mumbai, Maharashtra state; who underwent voluntary health-check up program to determine prevalence of liver disease, 2. 8 prospective studies (2008-2017) on all attendants of HBsAg and anti HCV check-up camps (age group: 11-82 years, sex 1.3:1) at Anand, Anand district, Gujarat state (6 camps) and Nadiad, Kheda district, Gujarat state (2 camps), 3. a prospective study (2009) on college students (age group: 1 8- 25 years, male: female: 1.1:1) attending 3 colleges under Charotar Education Society, Anand, Anand district, Gujarat State; who underwent HBsAg testing (in all persons) and anti HCV testing (only if risk factors); 4. two prospective studies (2015 - 2017) on college students (age group: 18-25 years, male: female: 1.1:1) attending 3 colleges under Charotar Education Society, Anand, Anand district, Gujarat State; and a college under Nadiad educational society, Nadiad, Kheda district, Gujarat state; who underwent HBsAg and anti HCV testing; 5. Multiple voluntary HBsAg testing camps at multiple sites in Maharashtra and Gujarat (2009 - 2015).

Blood donor population data came from 3 blood banks, which perform compulsory HBsAg and anti HCV testing for all blood donors (age group of 18 to 50 years) and who accept only voluntary or replacement blood donation and not professional donation: 1. BYL Nair Hospital blood bank, Mumbai, Maharashtra state, (2001 - 2009) 2. Indian red cross society blood bank, Anand, Anand district, Gujarat state, (2009 - 2010) and 3. Indian red cross society blood bank, Nadiad, Kheda district, Gujarat state (2007 - 2010).

Hospital-attending population included the following 1. prospective study (2009 - 2010) of compulsory HBsAg testing on all the patients regardless of type of illness in 2 hospitals including Mahagujarat Hospital, Nadiad, Kheda district, Gujarat state and Nagarpalika hospital of Vidyanagar, Anand District, Gujarat state.

2. retrospective study of laboratory database to find out HBsAg and anti HCV positivity among the samples tested in 2 hospitals including Mahagujarat Hospital, Nadiad, Kheda district, Gujarat state (2007 - 2010) and Zakaria Hospital, Anand, Anand district, Gujarat state (2009 - 2010).

Liver clinic population data was collected from different tertiary referral centers with special interest in liver disease as follows: 1. Retrospective data analysis of patients with liver disease attending 2 tertiary referral centers including Bombay Hospital and medical research centre, Mumbai, Maharashtra state and Jivandeep Hospital, Anand, Gujarat state (1995 - 2009); 2. Prospective study of defining etiology in all the liver patients attending liver clinics at the above mentioned hospitals (2010); 3. Prospective study of defining etiologies in all HCC patients attending liver clinics at the above mentioned hospitals (2004 - 2008); 4. Prospective study of defining etiology of all the cirrhosis patients attending at 3 hospitals including Bombay Hospital and medical research centre, Mumbai, Maharashtra state; Jivandeep Hospital, Anand, Gujarat state; and Wokhart Hospital, Rajkot, Gujarat state (2006 - 2008).

2 Prospective health check up including HBsAg and anti-HCV testing were performed on asymptomatic healthy school children (age 5 - 17 years): A) 2009-10: 10 schools under Charotar Education Society, Anand, Anand district, Gujarat State; B) 2015: 3 schools under Charotar Education Society, Anand, Anand district,

Gujarat State (all these students were also a part of previous health check up done in 2009).

HBsAg testing was performed using ELISA method and anti HCV also by 2nd or 3rd generation ELISA in all the studies.

Data of districts where studies were performed:

- **Anand district:** Central Gujarat, 1856872 population, 74.5% literacy rate, 27.3% more than secondary, 31% urban and 86% villages with medical facility
- **Kheda district:** Central Gujarat, 2024216 population, 71.96% literacy rate, 28.6% more than secondary, 20% urban, 70.5% villages with medical facility
- **Mumbai (including suburban):** Maharashtra state, 11978450 populations, 86.5% literacy rate, 43% more than secondary, 100% urban.

Results

Methodology, sites, study duration, HBsAg and anti-HCV positivity rates are tabulated in table 1 to 5. Among general population data, a total of 1168 residents were checked in prospective health-check up study which comprised of mean age of 28.9 (1 - 88) years and Male: female ratio of 0.9:1. HBsAg positivity was seen in the age group from 11 - 50 years. The distribution of cases according to age group is given as follows: age groups 11 - 20 years: 22.2%, 21 - 30 years: 38.8%, 31 - 40 years: 22.2% and 41 - 50 years: 16.6%.

Type of study	Sites	Year	Total Number	HBsAg positivity	Anti HCV positivity
Prospective voluntary health check up to detect chronic liver disease	2 residential colonies in Mumbai (Bandra and Matunga)	2004	1168	18 / 1168 (1.5 %)	1/1168 (0.1%)
Prospective voluntary HBsAg and/or Anti HCV checking	8 (6 in Anand, Anand district and 2 in Nadiad, Kheda district)	2008- 2017	1626	8/1626 (0.49%)	0/1626 (0%)
Prospective voluntary HBsAg checking (Anti- HCV only if Risk factors present)	3 colleges in Anand, Anand district	2009	1968	11/1968 (0.5%)	0/200 (0%)
Prospective voluntary HBsAg and anti HCV checking	3 colleges in Anand, Anand district and 1 college in Nadiad, Kheda district	2015-2017	3000	5/3000 (0.16%)	0/3000 (0%)
Prospective voluntary HBsAg testing in camps	Multiple places Gujarat and Maharashtra	2009-2015	14693	142/14693 (0.9%)	-
Total tested				184/22455 (0.81%)	1/5994 (0.01%)

Table 1: General population (adult > 18 years).

Type of study	Sites	Year	HIV Positivity	HBsAg Positivity	Anti-HCV Positivity
Compulsory Screening Testing of blood either voluntary or replacement donation, not professional/commercial donation)	Mumbai, BYL Nair Hospital	2001- 2009 (9 years)	780/126627 (0.61 %)	1831/126610 (1.44%)	604/125600 (0.48%)
	Blood bank				
	Anand, Red Cross blood bank	2009- 2011 (1.5 years)	29/17376 (0.16%)	54/17376 (0.31%)	7/17376 (0.04%)
	Nadiad, Red Cross blood bank	2007- 2010 (3 years)	89/28330 (0.31%)	154/28330 (0.54%)	55/28330 (0.19%)
Total tested			898/172333 (0.52%)	2039/172316 (1.18%)	666/171306 (0.38%)

Table 2: Blood donor population (adult > 18 years).

Type of the study	Sites	Year	HBsAg positivity	Anti HCV positivity
Retrospective review of laboratory data	Zakaria Hospital, Anand	2009-2010 (1 year)	3/1057 (0.28%)	0/450 (0%)
	Mahagujarat Hospital, Nadiad	2008-2010 (3 years)	91/9490 (0.95%)	12/2147 (0.55%)
Prospective compulsory HBsAg testing of patient	Mahagujarat Hospital, Nadiad	2009-2010 (1 year)	34/2280 (1.49%)	
	Nagarpalika Hospital, Anand-Vidyanagar	2009-2010 (1 year)	5/350 (1.4%)	
Total tested			133/13177 (1%)	12/2597 (0.46%)

Table 3: Hospital-attending population (adult> 18 years).

Type of study	Sites	Year	Total Number	HBsAg positivity	Anti HCV positivity
Retrospective Analysis of all liver disease	2 (Bombay hospital, Mumbai; Jivandeep hospital, Anand)	1995- 2009	11604	2529/11604 (21.7%)	888/11604 (7.65%)
Prospective analysis of all Liver disease	2 (Bombay hospital, Mumbai; Jivandeep hospital, Anand)	2010	647	108/647 (16.6%)	28/647 (4.3%)
Total number of Liver diseases				2637/12251 (21.5%)	916/12251 (7.4%)
Prospective analysis of all cirrhosis	3 (Bombay hospital, Mumbai; Jivandcep hospital Anand; Wockhart hospital, Rajkot)	2006- 2008	919	146/949 (15.3%)	94/949 (9.9%)
Prospective analysis of all hepatocellular carcinoma	2 (Bombay hospital, Mumbai; Jivandeep Hospital, Anand)	2004- 2008	197	123/197 (62.4%)	55 / 197 (27.9%)

Table 4: Liver clinic population (adult> 18 years).

Type of study	Sites	Year	Total Number	HBsAg positivity	Anti HCV positivity
Prospective health check up including HBsAg and anti-HCV testing	10 schools in Anand	2009-2010	3624	1/3624	0/3624
	3 Schools in Anand	2015	750	0/750	0/750

Table 5: Asymptomatic healthy school children (5-17 years).

Among blood bank data from Mumbai, year-wise break up of positive cases were as follows: for HBsAg: from 2001 to 2009: 1.8%, 1.4%, 1.4%, 1.3%, 1.3%, 1.4%, 1.6%, 1.4% and 1.1%; for anti HCV: from 2001 to 2009: 0.3%, 0.3%, 1.04%, 1.02%, 0.3%, 0.36%, 0.37%, 0.23% and 0.25%.

In liver clinic data, HCV was responsible for total 7.4% liver disease patients (including 0.26% acute liver disease, 9% chronic liver disease, 9.9% cirrhosis, and 27.9% HCC) and HBV for total 21.5% of liver disease patients (2.8% of acute liver disease, 22.8% of chronic liver disease, 15.3% of cirrhosis, 62.4% of HCC).

In school children data, 750 students were checked during both the health check up in 2009-10 and 2015. The incidence of hepatitis b and hepatitis C was 0% in span of 6 years.

Discussion

Immigration, cheap air travel and globalization are the major contributor factors for worldwide spread of HBV and HCV. End-stage liver disease accounts for one in 40 deaths worldwide. According to an estimate, globally HBV and HCV were responsible for cirrhosis and HCC in 57% and 78% cases respectively, with considerable variatioⁿ in different regions and different time periods [9]. In India, HBV contributed to 16 - 31%, HCV to 11 - 28% and co-infection to 2 - 9% of cirrhosis. Likewise, HBV contributed to 53 - 80%, HCV to 12 - 53% and co-infection to 8 - 53% of HCC [10].

Currently, India lacks national surveillance reporting system to report HBV or HCV. Therefore data reporting depends mainly on isolated studies and on blood bank data. Only few studies have reported the prevalence in general population in India and most of them date back before 1999. The reported rate was 0.1 - 12.2% in various community-based studies (5.1 - 37% in tribal population; 1.3 - 12.7% in children), 0.6-12.3% in studies on pregnant women, 0.6 - 6.3% in voluntary blood donor population (3.8 - 15% in commercial blood donors) and 0.87% in hospital-attending population [1-5]. Prevalence in high risk population is as follows: 8-18% of medical- paramedical staff, 44% of chronic renal failure patients

[5]. Difference in prevalence rates can be explained by use of different assays of HBsAg testing, differences in cultural practices and economy as well as difference in standard of medical care in different parts of India. Prevalence of HBV among patients with liver disease is as follows: 46 - 68% CLD including 16-31% of cirrhosis and 61 - 80% of HCC; as well as 34 - 45% acute liver disease including 42% sporadic AVH, 3 - 18% of epidemic AVH, 27-33% FHF [11-16]. In Our study, HBV prevalence was 0.94% in general population, 1.18% in voluntary blood donor population, 1% of hospital-attending population and 21.5% of liver disease patients (2.8% of acute liver disease, 22.8% of chronic liver disease, 15.3% of cirrhosis, 62.4% of HCC). These figures are very low compared to previous series from western India.

Prevalence of HCV in general population and in special population is documented in few studies done before 2002. The reported rate was 0.12 - 2.5% in various community-based studies, 1.03% in pregnant women, 0.25 - 1.85% in blood donor population and 0.28 - 4.8% in hospital-attending population [6-8]. Prevalence in patients with risk factors is as follows: 13 - 26% in multi-transfused thallemic or hemophilic patients, 33.7% - 92% in IV drug abuser population, 4 - 83% in patients with chronic renal failure (hemodialysis patients) or renal transplantation, 0 - 5.4% among medical-paramedical population, 6 - 21.4% in HIV-infected patients, 32% in Kala Azar patients and 2.6% among patients of sexually-transmitted disease clinic [6-8]. Difference in prevalence rates can be explained by use of different assays of anti HCV testing, differences in cultural practices and economy as well as difference in standard of medical care in different parts of India. Recent studies on blood donor population have documented decrease in prevalence from 1.01% in 2001 to 0.29% in 2005 in Delhi. Prevalence of HCV among patients with various categories of liver disease is as follows: 4 - 48% of CLD (recent series: 10 - 16%) with 11-28% of cirrhosis and 0 - 27% of HCC; as well as 4.8 - 20% of acute liver disease with 14 - 43% fulminant hepatic failure [10,12,13,15-21]. In our study, prevalence of HCV was documented to be lower than previous series: 0.42% in general population, 0.38% in voluntary

blood donors, 0.46% in hospital attending population and 7.4% liver disease (including 0.26% acute liver disease, 9% chronic liver disease, 9.9% cirrhosis, and 27.9% HCC).

There may be multiple factors responsible for this low prevalence that includes hepatitis B vaccination, efforts to prevent HIV infection, improved biomedical waste disposal, improved blood bank techniques and improved socio-economic-health standards. Moreover, Universal vaccination at birth is shown to be very effective in reducing HBV carrier states in Taiwan (reduction of prevalence of HBsAg over 13 years from 9.8% to 0.7%), Thailand (3.4 to 0.7% over 7 years), Indonesia (6.2% to 1.9% over 4 years), and in many other countries throughout the world. It has been also shown to reduce burden of acute hepatitis, fulminant hepatitis and HCC in these countries [22]. Though effective vaccination programs have been initiated, it will take long time to reduce pool of adult carriers and its chronic consequences. WHO had set target of introducing HBV vaccination to all the countries by 2007 and achieving 90% coverage of 3-dose vaccination by 2010 [22]. By a study model, it has been estimated that with universal vaccination program, HBsAg positivity rate will come down from 4% to 1.15% in India [23]. Hepatitis B vaccine coverage is improved from 6% in 2004 to 21% in 2009 in India [23]. Government of India has recently included HBV vaccination in neonatal vaccination program.

In addition to this, efforts to control HIV are effective in preventing transmission of both HBV and HCV. The Indian government has launched third National Control Program for AIDS (NACP-III) in 2007, which includes rigorous campaign against AIDS and active public participation to prevent the spread of HIV. General population awareness of HIV in India has increased from 13% in 2001 to 80.4% in 2006 [24]. Budget allocations for prevention and management of HIV in India has gone up from 115.9 million USD in 2006 to 213 million USD in 2009 [24]. In the year 2006-07, voluntary blood donation was 54.4% which was the baseline for national program to control HIV epidemic [24]. It increased to 59.1% in 2007-08, 61.7% in 2008-09 and further to 74.1% in 2009-10 (till January 2010) against the NACP-III target of 90%. The States of West Bengal, Maharashtra, Tamil Nadu, Gujarat, Tripura, Mizoram, Chandigarh and Himachal Pradesh, have crossed the national target of over 80% and are good performing states in voluntary blood donation. The primary drivers of the HIV epidemic in India are unprotected paid sex/commercial sex work, unprotected anal sex between men and IDU. Percentage of FSW (female sex worker) who

use condom with their most recent client has increased from 50% in 2006 to 63.5% in 2009; percentage of male sexual worker who use condom with their most recent client has increased from 20% in 2006 to 34.4% in 2009; percentage of IDUs who avoided sharing injecting equipment during the last month has increased from 30% in 2006 to 31% in 2009; and percentage of IDU who use condom with their most recent sexual partner has increased from 30% in 2006 to 44% in 2009 [24]. Changes in HIV prevalence in general population are as follows: in Gujarat from 0.54% in 2002 to 0.43% in 2006; in Maharashtra from 1.08% in 2002 to 0.74% in 2006 and in India from 0.45% in 2002 to 0.29% in 2008 [24,25].

Mandatory use of disposable needle-syringe, strict biomedical-waste disposal laws and its implementation may have contributed for this changed scenario. Till July 1998, there was not any proper waste disposal system and biomedical waste was disposed with general waste. As reuse of disposables increase chance of transmission of these viral infections, the Ministry of Environment and Forests implemented the Biomedical Waste (management and handling) Rules in July 1998 [26]. Improved blood bank test techniques from RPHA and CFT to ELISA and mandatory safe blood practices reduce transmission rates. In 2002, the National blood bank policy was adopted to supply safe and sufficient blood to countrymen. Change in practice of voluntary donation instead of professional or commercial blood donation is also one of the contributory factors.

Increased literacy rate may have played important role in the improvement. Literacy rate in India was 74% in 2011 and it increased to 90.2% in 2015; the most literate states being Kerala 93.9%, Lakshadweep 92.3% and Mizoram 91.6% [27]. Gujarat has 4.9% and Maharashtra has 9.4% of total population of India. Literacy rate is 58.8% in Gujarat and 66% in Maharashtra. Economical Growth and growth rate of per capita income in India has increased from 3.8% in 1997 to 8.6% in 2017-18 [27]. Percentage of population below poverty line has declined in India from 35.9% in 1994 to 21.8% 2004, in Gujarat from 24.1% 1994 to 12.5% in 2004 and in Maharashtra from 36.8% in 1994 to 25.2% in 2004 [28]. As surrogate marker for health care delivery, antenatal care rate over period of 2002-2008 has been increased by 3.3% in Anand district in contrast to Gujarat i.e. -1%; institutional delivery rate has gone up in Anand district by 8.6% and in Kheda by 17.7%, against 4.3% in Gujarat, 5.7% in Maharashtra, and 6.5% in India. In 2009, full ANC coverage rate is 26.5% in India, 45.7% in Gujarat and 27% in

Maharashtra [29]. Full immunization rate in 2008 is 54.1% (Rural 58.5%, urban 67.4%) in India, 54.9% in Gujarat and 69.3% in Maharashtra; Whereas, in 2009, the rate has been increased to 61% in India, 56.6% in Gujarat (Rural 60.5%, Urban 50%) and 78.6% in Maharashtra [30].

Conclusion

In conclusion, in western India, there is lower prevalence of hepatitis B and hepatitis C virus infection in general population and liver disease patients as compared to previous data. Improved socioeconomic status, education and better implication of HIV control policies might be responsible factors for the low prevalence of Hepatitis B and C in India. Still many tasks are left unfinished in prevention and elimination of viral hepatitis in India, but if the Government of India implement a comprehensive action plan, our country may get rid of viral hepatitis by 2030.

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