Original Article

DOI: 10.7860/JCDR/2021/48444.15079

Seroprevalence of Hepatitis B Virus Infection among the Tribal Population of Attapady, Kerala, India

Microbiology Section

IRENE JOSE MANJIYIL[1], KAVITHA PAUL KONIKKARA[2]

ABSTRACT

Introduction: Hepatitis B Virus (HBV) infection remains a significant global health concern that may cause acute or chronic hepatitis. Chronically infected patients are at risk for cirrhosis and hepatocellular carcinoma. The disease causes a problem in the tribal communities. There are lack of studies on the prevalence of HBV among the tribal population.

Aim: To assess the seroprevalence of HBV infection among the tribal population of Attapady, Kerala.

Materials and Methods: This was a community based cross-sectional study conducted on serum samples collected from 269 subjects among the tribal population of Attapady. Serum samples were tested for quantitative antibody to HBsAg (anti-HBs), Hepatitis B surface antigen (HBsAg) and Hepatitis B envelope antigen (HBeAg) Enzyme Linked Immunosorbent Assay (ELISA). Total hepatitis B core antibody (anti-HBc) and IgM antibody to hepatitis B core antigen (anti HBc IgM), frequencies were obtained using proportion and 95% Confidence Interval (CI).

Results: The seroprevalence of HBsAg was 10.4%. HBeAg was detected in 7.1% of HBsAg positive patients. A 21.2% had protective anti-HBs titre. Anti-HBe was detected in five patients. Anti-HBc total and anti-HBc IgM were positive for 26.7% and 2.6%, respectively. Anti-HBc IgM alone and isolated anti-HBc were detected in 1.5% and 5.9%, respectively. Anti-HBs and anti-HBc total both became positive in 8.6% cases.

Conclusion: The HBV infection poses a huge burden on tribal health. All HBsAg positive patients should be tested further to determine the stage of the disease. There is need to explore high HBV prevalence areas with studies on associated risk factors to bring out the ongoing transmission process and focus on preventive measures. HBV vaccination, antenatal screening, and health awareness should be given priority to tackle the burden.

Keywords: Enzyme linked immunosorbent assay, Hepatitis B surface antigen, Serology

INTRODUCTION

The HBV infection is a significant public health problem [1]. HBV, an enveloped DNA virus belongs to the family *Hepadnaviridae* [2]. It causes a spectrum of diseases ranging from self limiting hepatitis to acute fulminant hepatitis and chronic hepatitis that can lead to liver cirrhosis, hepatic failure and hepatocellular carcinoma [3].

The World Health Organistaion (WHO) has divided the world into three areas where the prevalence of chronic HBV infection is high (>8%), intermediate (2-8%), and low (<2%) [4]. According to the WHO, the Western Pacific Region and African Region have the highest prevalence of 6.2% and 6.1% of the adult population, respectively, while the American region has the lowest prevalence of 0.7% [5]. Nearly, 80-90% of infants were infected with HBV during the first year of life and 30-50% of children were infected with HBV before six years of age who of them developed chronic HBV infection [5]. The risk of chronicity in those infected as adults is <5% and 20-30% of them developed cirrhosis and/or liver cancer [5]. Although, acute HBV infection can be severe, serious consequences occur more in chronically infected persons. Eventhough, a large number of chronically infected patients remain symptomless, still they can transmit the infection to healthy ones [6].

Infection with HBV is mainly transmitted parenterally through infected blood and blood products [1]. Infection is also transmitted by both vertical and horizontal routes. Occupational transmission of HBV from infected patients to healthcare and public safety workers is also important [3,7].

The HBV infection create a large burden on tribal health. The tribal population of India, as per 2011 census, is 10.43 crores, constituting 8.6% of the total population [8]. Kerala is also home to many primitive tribes. As per 2011 census, scheduled tribe population in Kerala is 4.85 lacs, which accounts for 1.45% of the total population of the state [8]. The prevalence of HBV infection among the tribal communities is much higher worldwide (10-30%) [9]. This has been attributed to inbreeding, unhygienic living conditions, illiteracy, low immunisation rates, long close contact with HBV infected persons and some sociocultural practices like tattooing, ear/nose piercing [10].

The evolution of serological markers following HBV infection is complex and depends largely on host immune response. Serodiagnosis of HBV infection involves testing a panel of HBV specific antigens- Hepatitis B surface antigen (HBsAg) and Hepatitis B envelope antigen (HBeAg) and antibodies- antibody to HBsAg (anti-HBs), antibody to HBeAg (anti-HBe) and antibody to HBcAg (anti-HBc IgM and IgG). At least one serological marker is present in all phases of infection. Only 9% of HBV infected persons have been diagnosed worldwide [11].

The HBsAg is the first serological marker to appear in acute HBV infection [2]. Routine screening for HBV infection is primarily based on the detection of serum HBsAg. It is the commonly done test for the diagnosis of acute HBV infection and carrier state [12,13]. Serological assays are commercially available for all HBV markers except for HBcAg. The presence or absence of a combination of these viral markers helps to know whether the patient has acute, resolving, chronic infection or whether the person is immune or susceptible to HBV infection.

To the best of our knowledge, there is no published data on the seroprevalence of HBV infection among the tribal population of Attapady, Palakkad district of Kerala, India. Most of the studies in the literature were focused to detect only the seroprevalence of HBsAg [1,3]. In this study, as an initial effort to know the burden of HBV infection, all the HBV serological markers were evaluated among the accessible tribal population of Attapady, Kerela, India.

MATERIALS AND METHODS

A community based, cross-sectional study was conducted for a period of one year from July 2016 to June 2017 in Government

Medical College, Thrissur, Kerala, India, after getting due approval from the Institutional Ethical Committee (IEC).

Sample size calculation: A HBsAg prevalence of 28.8% was reported among the tribal population of Agali and Pudur areas of Attapady following a Hepatitis B outbreak investigation conducted by a medical team from Government Medical College, Thrissur in June 2014. As per the formula, $n=4pq/l^2$, the minimum sample size for the present study was calculated as 228.

For this study, out of the 28 primary health subcentres in Attapady, six subcentres were selected by lottery method. Forty-five participants from each subcentre were selected by simple random sampling method. Medical camps were conducted at these subcentres with the help of the Health Service Department.

Inclusion and Exclusion criteria: All the available members in the household who gave informed consent were included in the study. Informed consent from their parent/guardian was taken in case of a minor subject. And those who cannot attend the medical camp due to physical disability were excluded. Blood samples were collected from 270 study subjects, one blood sample was lysed and so, the study was carried out with 269 participants.

Study Procedure

Approximately, 5 mL of the venous blood sample was collected from each participant under aseptic precautions. The samples were transported in the cold chain to Microbiology Laboratory, GMC Thrissur. Blood samples were centrifuged, sera separated and transferred into sterile vials and stored at -20^{0}C till the test was performed. All serum samples were tested for the detection of HBsAg, anti-HBc total and anti-HBc IgM. Quantitative anti-HBs was estimated for HBsAg negative samples. HBsAg positive sera were tested for HBeAg.

All viral markers were tested employing commercially available ELISA kits. HBsAg was detected using Meriscreen ELISA kits. Quantitative anti-HBs, anti-HBc total, anti-HBc IgM, HBeAg and anti-HBe were tested by ELISA kits manufactured by DIA-PRO Diagnostics Bioprobes Srl (Italy). Tests were performed as per the manufacturer's instructions. Detection of anti-HBs titre of ≥10 mIU/mL is considered a correlate of vaccine induced protection and adequate immunity [14]. Based on the presence or absence of the serological markers detected, participants who were susceptible or immune to infection, or in different stages of HBV infection was identified [Table/Fig-1] [4,15-18].

Stages of HBV infection	HBsAg	HBeAg	Anti-HBc total	Anti-HBc IgM	Anti-HBe	Anti-HBs
Never infected, susceptible to infection [15]	-	-	-	-	-	-
Immune due to past infection [4,15,16]	-	-	+	-	-	+
Immune due to HBV vaccination [4,15,16]	-	-	-	-	-	+
Acute HBV infection [4,16]	+	+	+	+	-	-
HBsAg negative acute HBV infection in Window period [17]	-	-	-	+	-	-
Resolving HBV infection-early stage [16]	-	+/-	+/-	+/-	+/-	+/-
Resolving HBV infection-late stage [16]	-	-	+/-	-	+	+
HBeAg positive chronic HBV infection [16]	+	+	+	-	-	-
HBeAg negative chronic HBV infection [16]	+	-	+	-	+/-	-
Isolated anti-HBc [15,18]	-	-	+	-	-	-

[Table/Fig-1]: Hepatitis B virus serological markers in different stages of infection and convalescence.
+/- detected/not detected

STATISTICAL ANALYSIS

The data obtained was entered into Microsoft Excel and analysed using Statistical Package for the Social Sciences (SPSS) statistical software version 16.0. Frequencies were obtained using proportion and 95% Confidence Interval.

RESULTS

In this study, 269 participants between 1 and 75 years of age were included. Majority of them, (40.5%) belonged to the 21-30 years of age group. There were 185 (68.8%) females and 84 (31.2%) males. There were 153 females among the reproductive age group (15-49 years of age) which accounted for 56.9% of the participants. There were 36 antenatal women. (19.5% of women participants). The [Table/Fig-2] shows the age wise distribution of participants.

Age (in years)	No. of subjects n (%)	HBsAg positive n (%)	Serum HBeAg in HBsAg positive n (%)
0-10	31 (11.5)	1 (3.2)	1 (100)
11-20	33 (12.3)	0	0
21-30	109 (40.5)	16 (14.7)	1 (6.25)
31-40	54 (20.1)	6 (11.1)	0
41-50	24 (8.9)	2 (8.3)	0
51-60	14 (5.2)	2 (14.3)	0
61-70	3 (1.1)	1 (33.3)	0
71-75	1 (0.4)	0	0
Total	269	28 (10.4)	2 (7.14)

[Table/Fig-2]: Age wise prevalence of HBsAg and HBeAg.

All the 269 samples were tested for HBsAg. Serum HBsAg was detected in 28 participants. The seroprevalence of HBsAg in this study was found to be 10.4% (95% CI:7.42-13.4). The highest HBsAg seroprevalence was found to be among 21-30 years age group (14.7%), followed by those among 31-40 years of age (11.1%). Among the 185 females tested, HBsAg was positive for 21 females (11.4%). Among 153 females in the reproductive age group, 20 of them were HBsAg positive (13.1%). Only one, among 36 (2.8%) antenatal women was HBsAg positive. Out of 84 males tested, seven were HBsAg positive (8.3%). All HBsAg positive cases in the present study showed positivity to one/other serological markers of HBV.

The HBeAg detection was done for all (28) HBsAg positive patients. HBeAg was detected in two among 28 HBsAg positive patients (7.1%). One antenatal patient and a 10-year-old patient was HBeAg positive [Table/Fig-2].

[Table/Fig-3] shows the age wise prevalence of HBV antibodies- anti-HBs, anti-HBc total, Anti-HBc IgM. Quantitative estimation of anti-HBs was done for all HBsAg negative samples (n=241). Anti-HBs titre above 10 mIU/mL was considered to be protective. Out of the 241 subjects whose serum anti-HBs estimation was performed, 51 (21.2%) had a titre above 10 mIU/mL. Among the participants in the age group of 0-10 years, 56.7% had a protective anti-HBs level. Anti-HBs was the only serological marker detected in 22 subjects (9.1%). Anti-HBs level below 10 mIU/mL was detected in 190 subjects (78.8%). Anti-HBe could be done only for 13 patients who were HBeAg negative but, among them five cases were positive. Anti-HBc total and anti-HBc IgM were tested for all participants. Anti-HBc total was positive for 72 (26.7 %) and anti-HBc IgM was positive for seven cases (2.6%). Anti-HBc IgM alone was positive in four cases (1.5%). Anti-HBc total alone was positive for 16 (5.9%) cases. Anti-HBs and anti-HBc total both were positive in 23 (8.6%) cases while all the other markers tested were negative. In this study, 170 (63.2%) subjects were negative for all the HBV serological markers tested. The [Table/Fig-4] shows the different patterns of serological marker positivity detected in this study participants with possible interpretation.

Age in years	Anti-HBs*			Anti-HBc total			Anti-HBc IgM		
	No. tested (n)	No. above protective titre	%	No. tested (n)	No. positive (n)	%	No. tested (n)	No. positive (n)	%
0-10	30	17	56.7	31	1	3.2	31	0	0
11-20	33	4	12.1	33	4	12.1	33	1	3.0
21-30	93	13	13.9	109	31	28.4	109	5	4.6
31-40	48	6	12.5	54	17	31.5	54	1	1.8
41-50	22	3	13.6	24	7	29.1	24	0	0
51-60	12	6	50	14	9	64.2	14	0	0
61-70	2	1	50	3	2	66.67	3	0	0
71-75	1	1	100	1	1	100	1	0	0
Total	241	51	21.2	269	72	26.7	269	7	2.6

[Table/Fig-3]: Age wise prevalence of anti-HBs, anti-HBc total, anti-HBc IgM.
*anti-HBs was done for all HBsAg negative samples (n=241)

HBV antigens tested		HBV antibodies tested						
		Anti-HBc						
HBsAg	HBeAg	Anti-HBc total	Anti-HBc IgM	Anti-HBe	Anti-HBs	No.	%	Interpretation
-		-	-		-	170	63.2	Susceptible to HBV infection
-		+	-		+	23	8.6	Immune due to past infection
-		-	-		+	22	8.1	Immune due to HBV vaccination
+	-	+	+	-	-	1	0.4	Acute HBV infection/ acute exacerbation of chronic infection
-	-	-	+	-	-	4	1.5	HBsAg negative acute HBV infection in Window period
-		-	+		+	1	0.4	HBsAg negative acute HBV infection
-		+	+	+	+	1	0.4	Resolving HBV infection -early stage
-		+	-	+	+	4	1.5	Resolving HBV infection -late stage
+	+	+	-		-	2	0.7	HBeAg positive chronic HBV infection
+	-	+	-		-	25	9.3	HBeAg negative chronic HBV infection
-		+	-		-	16	5.9	Isolated anti-HBc
					Total	269		

[Table/Fig-4]: Different patterns of serological marker positivity of study participants with possible interpretation.

DISCUSSION

In this study, 269 participants between 1 and 75 years of age were included. There were 185 (68.8%) females and 84 (31.2%) males. This higher female participation in the present study could be explained by the fact that adult males were at their workplace during day time when we collected the blood samples. Similarly, in previous studies conducted tribal population with higher female gender composition has been explained as dual households are common among tribal groups and adult males go out for work during daytime [19-21].

Seroprevalence of HBsAg in this study was 10.4% (95% C.I: 7.42-13.4). Hence, according to the WHO classification, present study area has a high HBsAg prevalence [4]. The majority of HBsAg positive cases were between 21-30 years of age. The higher seropositivity after the second decade of life may be due to their greater exposure and social interactions. Gokale SK et al., and Trupti BN et al., have reported the highest incidence of HBsAg among 21-40 years of age and the lowest among 0-20 years of age [22,23]. In this study, only one HBsAg positive case was detected among 0-10 years of age. The lower prevalence of HBsAg seen in the younger age group in the present study could be due to the effect of Hepatitis B vaccination. The proportion of children under five years age with chronic HBV infection was estimated to be under 1% [5].

Seroprevalence of HBsAg among males and females was 8.3% and 11.4%, respectively. HBsAg was positive in 13.1% of females among the reproductive age group. A higher HBsAg prevalence (22.6%) in females was reported in the hilly tribes of Himachal Pradesh [19]. Even though the clearance is better in females, no sex predilection has been attributed to HBV infection [19]. Seroprevalence rate was reported higher in males in some studies [3,24].

Among 36 antenatal women tested in this study, only one was HBsAg positive (2.8%). This higher prevalence rate may be due to the less sample size of antenatal women studied. Data on recent HBsAg seroprevalence among antenatal women of tribal population of south India is restricted in the literature. HBsAg positivity among pregnant women of Nicobarese tribe of Andaman and Nicobar Islands was reported as 20.5% [9]. Studies conducted in different states of India among antenatal women of general population during 2011 to 2019 has revealed a decreasing trend in HBsAg seroprevalence rate towards the end of the decade [25-27].

Though, the HBV prevalence is intermediate in India, it is reported very high among some isolated tribes [Table/Fig-5] [9,10,19-21,28-32]. In this study, 170 subjects (63.2%) were negative for all the markers tested and might have never infected with HBV and hence, identified as susceptible population.

Author	Year of study	Tribe	Location	Sample size	HBsAg seroprevalence (%)
Shyamala R et al., [21]	2016	Kurichiya	Kerala	240	Nil
Kalaivani V et al., [28]	2001	Kolli hilly area	Tamil Nadu	161	1.86
Reddy PH and Tedder RS, [29]	1995	Baiga	Madhya Pradesh	91	4.4
Dinesh R and Ramalakshmi S, [30]	2017	Irula	Tamil Nadu	372	5.1
Chandra M et al., [31]	2003	Lambada	Andhra Pradesh	890	5.2
Biswas D et al., [20]	2007	Idu Mishmi	Arunachal Pradesh	438	21.2
Barall D et al., [19]	2018	Spiti	Himachal Pradesh	1110	21.9
Murhekar MV et al., [10]	2008	Andamanese	Andaman and Nicobar islands	27	3.7
		Nicobarese		1144	23.3
		Onges		58	31
		Shompen		37	37.8
		Jarawa		64	65.6
Murhekar MV et al., [9]	2002	Nicobarese	Andaman and Nicobar islands	887	22.2
Batham A et al., [32]	2009	Tribal population	India		11.8
Present study	2017	Attapady tribal population	Kerala	269	10.4

[Table/Fig-5]: Review of literature-seroprevalence of HBsAg positivity in different tribal populations of India.

Quantitative estimation of anti-HBs was done for all HBsAg negative samples. A protective anti-HBs titre above 10 mIU/mL was detected in 51 subjects (21.2%) and 56.7% of them belonged to 0-10 years of age. Anti-HBs is the only serological marker detected in persons who acquire immunity solely due to hepatitis B vaccination [2]. Anti-HBs was detected as the only marker in 22 of the participants (9.1%). Anti-HBs titre below 10 mIU/mL was detected in 190 subjects (78.6%) who had no or inadequate immunity. Among the Nicobarese tribe of Andaman and Nicobar Islands, anti-HBs prevalence reported among those in 35-45 years of age and among children below five years of age was 38.1% and 4.3%, respectively [9]. Among the Idu Mishmi tribe of northeast India, 57.3% of those in the 6-15 years age group had adequate anti-HBs titre [20].

The HBeAg indicates a high infectivity and its seroconversion to anti-HBe indicates a low risk of disease progression [33]. HBeAg and anti-HBe testing should be done only when initial HBV screening turns positive [33]. Among the 28 HBsAg positive patients tested for HBeAg, two were HBeAg positive (7.14%). These two patients were positive for HBsAg, HBeAg, and anti-HBc total and considered as HBeAg positive chronic HBV infection. Also, 25 patients (9.3%) were detected to have HBeAg negative chronic HBV infection. Among 13 samples tested, anti-HBe antibodies were detected in five samples.

Though, HBcAg cannot be detected in the serum, anti-HBc is the earliest antibody to develop following acute HBV infection, appearing as anti-HBc IgM. Anti-HBc IgM alone may be detected in early convalescence or window period, when HBsAg has disappeared and anti-HBs not yet appeared [17]. IgM anti-HBc usually denotes acute infection [2]. However, it may be detected in low levels during reactivation of chronic hepatitis as well [15].

In present study, anti-HBc IgM was positive in seven of the patients (2.6%) and majority of them belonged to 21-30 years of age. We detected four cases (1.5%) positive for anti-HBc IgM alone and not to any other markers tested and might be in early convalescence or window period. Testing for anti-HBc IgM is important in the diagnosis of HBV infection in the window period in places where HBV DNA testing is not feasible [17].

Among 269 subjects, one (0.4%) particular case positive for HBsAg, anti HBcIgM and anti-HBc total antibodies and negative for HBeAg was detected. This patient might be having an acute HBV infection or acute exacerbation of chronic infection [15]. Also,one (0.4%) HBsAg negative case with serological evidence of anti-HBc IgM and anti-HBs was detected and was considered as HBsAg negative acute HBV infection. Anti-HBc IgM in patients with HBsAg negative hepatitis with or without anti-HBs indicates acute HBV infection [34].

The serological test of choice for establishing past HBV infection is anti-HBc antibody [18]. In this study, 72 cases (26.7%) were positive for anti-HBc total antibodies and majority of them belonged to 21-30 years of age. This anti-HBc prevalence of 26.7% among apparently healthy persons at a community level suggested pockets of high HBV transmission in this study area. The persistence of infection in the older age groups may be due to the fact that they might have acquired infection early in life as they had no access to HBV vaccination at that time. Anti-HBc antibodies were detected in 78% of those among 25-34 years of age in the Nicobarese tribe of Andaman and Nicobar Islands [9]. A hyperendemic focus of HBV infection with a high anti-HBc prevalence (95.9%) among 6-15 years of age group was reported from an isolated tribe in northeast India [20]. In this study, among the participants, 23 (8.6%) were found to be positive for both anti-HBc total and anti-HBs and were immune due to resolved past HBV infection.

In present study, 16 cases (5.9%) of isolated anti-HBc which were negative for HBsAg and anti-HBs but positive for anti-HBc. Isolated anti- HBc is defined as the presence of IgG anti-HBc in the absence of detectable HBsAg and anti-HBs [18]. The quantitative anti-HBs titre of all these patients detected was very low and ranged from 0.0 to 5.4 mIU/mL. We could rule out the possibility of a resolving acute HBV infection as these 16 samples were negative for anti-HBc IgM. Another possibility considered particularly in an HBV endemic population was a distant resolved HBV infection with waning or undetectable anti-HBs titre. Thirdly, some patients with isolated anti-HBc may have Occult HBV Infection (OBI) with undetectable HBsAg levels, but the presence of HBV DNA in the liver and may be at risk of liver cirrhosis or hepatocellular carcinoma [18]. Being the strongest predictor of progression to cirrhosis and hepatocellular carcinoma, HBV DNA should be tested to find out OBI [12]. Hepatitis B screening without inclusion of anti-HBc antibodies can potentially miss a significant number of OBI cases and/or a history of past infection in the endemic population. Another possibility of a false positive result, especially in people with a low risk of past HBV infection should be kept in mind [15,35]. We also considered the possibility of passive transfer of maternal anti-HBc in children below three years, but none of them were among this age group [35].

In the present study, the seroprevalence of HBsAg was found to be highest among 21-30 years of age. HBeAg was detected in 7.1% of HBsAg positive patients. Protective anti-HBs titre was detected in majority among 0-10 years of age. Anti-HBc total and anti-HBc IgM were positive for 26.7% and 2.6%, respectively. Anti-HBe was detected in five patients. This HBV prevalence suggested pockets of high HBV transmission in this tribal area.

Limitation(s)

Authors could not study the risk factors associated with HBV infection among the study subjects. Also, HBV DNA tests could not perform on the participants or screen for sequelae of HBV infection, primarily hepatocellular carcinoma due to financial limitation.

CONCLUSION(S)

The findings strengthened the need to explore such areas of high HBV prevalence within Kerela. Unless persons are tested and diagnosed, such unseen pockets of transmission will remain active. Hepatitis B screening programs mainly test for HBsAg only. This study shows the need to include other HBV serological markers especially anti-HBc and anti-HBc IgM. All HBsAg positive patients should be tested further to determine the disease stage and screen for sequelae, primarily hepatocellular carcinoma. The data shows that HBV vaccination reduces the chances of childhood infection and thereby chronic infection.Vaccination may be considered for the susceptible population of this study. Efficient HBV vaccination, antenatal screening and awareness about infection and lifestyle modifications, especially among such high-risk populations should be given prime concern for disease control. Studies with detailed workup on the risk factors associated with HBV infection among high risk communities is essential to bring out the ongoing transmission and focus on preventive measures.

Acknowledgement

Sincere thanks to the people of Attapady who participated in the study and the staff of the Health Service Department, Government of Kerala.

REFERENCES

[1] Puri P. Tackling the Hepatitis B disease burden in India. J Clin Exp Hepatol. 2014;4(4):312-19.
[2] Song JE, Kim DY. Diagnosis of Hepatitis B. Ann Transl Med. 2016;4(18):338-43.
[3] Quadri SA, Dadapeer HJ, Arifulla KM, Khan N. Prevalence of Hepatitis B Surface antigen in hospital based population in Bijapur, Karnataka. Al Ameen J Med Sci. 2013;6(2):180-82.
[4] World Health Organization.(2002). Hepatitis B. Geneva, Switzerland: World Health Organization. https://apps.who.int/iris/handle/10665/67746.
[5] World Health Organisation: Hepatitis B. WHO fact sheet. Available from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b.
[6] Sood S. Serological evaluation of Hepatitis B virus in out patient department patients of a private hospital in North West India. National J of Community Medicine. 2013;4(3):485-88.

[7] Patil SR, Ghorpade MV, Patil SS, Pawar SK, Mohite ST. Seroprevalence of Hepatitis-B surface antigen among the patients reporting at tertiary care Hospital from India. Bangladesh Journal of Medical Science. 2016;15(3):455-59.
[8] Statistical Profile of Scheduled Tribes in India 2013. Available from: https://ruralindiaonline.org/en/library/resource/statistical-profile-of-scheduled-tribes-in-india-2013/.
[9] Murhekar MV, Murhekar KM, Arankalle VA, Sehgal SC. Epidemiology of hepatitis B infection among the Nicobarese-a Mongoloid tribe of the Andaman and Nicobar Islands, India. Epidemiol Infect. 2002;128(3):465-71.
[10] Murhekar MV, Murhekar KM, Sehgal SC. Epidemiology of hepatitis B virus infection among the tribes of Andaman and Nicobar Islands, India. Trans R Soc Trop Med Hyg. 2008;102(8):729-34.
[11] WHO | Global hepatitis report, 2017 WHO. World Health Organization; Available from: http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/.
[12] Datta S, Chatterjee S, Veer V. Recent advances in molecular diagnostics of hepatitis B virus. World J Gastroenterol. 2014;20(40):14615-25.
[13] Naqshbandi I, Qadri SYA, Yasmeen N, Bashir N. Seroprevalence and risk factors of hepatitis b virus infection among general population of Srinagar, Kashmir. Int. J of Contem Med Res. 2016;3(4):1050-54.
[14] A Comprehensive Immunisation Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunisation Practices (ACIP) Part 1: Immunisation of Infants, Children, and Adolescents. Available from: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5416a1.htm.
[15] Mast EE, Weinbaum CM, Fiore AE, Alter MJ, Bell BP, Finelli L, et al. A comprehensive immunisation strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunisation Practices (ACIP) Part II: Immunisation of adults. MMWR Recomm Rep. 2006;55(RR-16):01-33.
[16] Hepatitis B: issues in laboratory diagnosis and vaccination- Australian Prescriber. Available from: https://www.nps.org.au/australian-prescriber/articles/hepatitis-b-issues-in-laboratory-diagnosis-and-vaccination.
[17] Japhet MO, Adesina OA, Donbraye E, Adewumi MO. Hepatitis B Core IgM antibody (anti-HBcIgM) among hepatitis B Surface antigen (HBsAg) negative blood donors in Nigeria. Virology Journal. 2011;8(1):513.
[18] Hyun CS, Lee S, Ventura WR. The prevalence and significance of isolated hepatitis B core antibody (anti-HBc) in endemic population. BMC Research Notes. 2019;12(1):251.
[19] Barall D, Gupta A, Sharma B, Mazta SR, Singh S. Prevalence of chronic hepatitis B infection among residents of hilly tribal district in northern India. Int J Community Med Public Health. 2018;5(7):2989-96.
[20] Biswas D, Borkakoty BJ, Mahanta J, Jampa L, Deouri LC. Hyperendemic foci of Hepatitis B infection in Arunachal Pradesh, India. J Assoc Physicians India. 2007;55:701-04.
[21] Shyamala R, Ismail IM, Bijapur GA, Shobith, Leeja LL. Null seroprevalence of HBsAg carrier state among Kurichia tribal community around Kannur, Kerala,India. Int J Res Ayurveda Pharm. 2016;7(4):101-05.
[22] Gokale SK, Sonth SB, Solabannavar SS. Seroprevalence of Hepatitis B virus among patients at a tertiary care centre in north Karnataka. Int J Curr Microbiol App Sci. 2017;6(9):755-57.
[23] Trupti BN, Sathish JV, Mita DW. Seroprevalence of Hepatitis b surface antigen (HBsAg) among patients attending a tertiary care hospital at Chamarajanagar, Karnataka, India. Int J Curr Microbiol App Sci. 2018;7(1):1279-84.
[24] Bula A, Gaddam SR. Seroprevalence of Hepatitis B surface antigen positive patients attending a tertiary care hospital in Srikakulam, Andhra Pradesh. Annals of Pathology and Laboratory Medicine. 2017;4(1):96-99.
[25] Sibia P, Mohi MK, Kumar A. Seroprevalence of Hepatitis B infection among pregnant women in one of the institute of northern India. J Clin Diagn Res. 2016;10(8):QC08-09.
[26] Sathiyakala R, Ushadevi G, Karthika J. Seroprevalence of Hepatitis B infection among pregnant women in South India. Int J Reprod Contracept Obstet Gynecol. 2017;6(1):249-51.
[27] Das R, Kumar S. Status of seroprevalence of Hepatitis B in pregnant females: A hospital-based study. Int J Reprod Contracept Obstet Gynecol. 2019;8(12):4858-61.
[28] Kalaivani V, Rajendran P, Thyagarajan SP, Rajesh PK, Hari R, Selvakumar C, et al. Seroprevalence of hepatitis B and C viruses and the associated risk factors in the Kolli hills tribal population of Tamil Nadu. Biomedicine. 2001;21:07-13.
[29] Reddy PH, Tedder RS. Hepatitis virus markers in the Baiga tribal population of Madhya Pradesh, India. Trans R Soc Trop Med Hyg. 1995;89(6):620.
[30] Dinesh R, Ramalakshmi S. Prevalence of Hepatitis B virus and associated risk factors in Irula tribal population. Asian J Pharm Clin Res. 2017;10(8):100-02.
[31] Chandra M, Khaja MN, Farees N, Poduri CD, Hussain MM, Habeeb M, et al. Prevalence, risk factors and genotype distribution of HCV and HBV infection in the tribal population: A community based study in South India. Trop Gastroenterol. 2003;24:193-95.
[32] Batham A, Gupta MA, Rastogi P, Garg S, Sreenivas V, Puliyel JM. Calculating prevalence of Hepatittis B in India: Using population weights to look for publication bias in conventional meta- analysis. Indian J Pediatr. 2009;76(12):1247-57.
[33] Screening for Viral Hepatitis During the Domestic Medical Examination of Newly Arrived Refugees|Immigrant and Refugee Health | CDC 2019. Available from: https://www.cdc.gov/immigrantrefugeehealth/guidelines/domestic/hepatitis-screening-guidelines.html.
[34] Kryger P, Aldershvile J, Mathiesen LR, Nielsen JO. Acute type B hepatitis among HBsAg negative patients detected by anti-HBc IgM. Hepatology. 1982;2(1):50-53.
[35] Practitioners TRAC of G. RACGP- Hepatitis B serology. Available from: https://www.racgp.org.au/afp/2012/april/hepatitis-b-serology/.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Microbiology, Government Medical College, Thrissur, Kerala, India.
2. Associate Professor, Department of Microbiology, Government Medical College, Thrissur, Kerala, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Kavitha Paul Konikkara,
Associate Professor, Department of Microbiology, Government Medical College, Thrissur, Kerala, India.
E-mail: kavithageejo@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 13, 2021
- Manual Googling: Mar 09, 2021
- iThenticate Software: Apr 19, 2021 (12%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jan 08, 2021**
Date of Peer Review: **Feb 03, 2021**
Date of Acceptance: **Mar 25, 2021**
Date of Publishing: **Jul 01, 2021**