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Molecular characterization of hepatitis B virus among patients co-infected with hepatitis D virus

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Abstract
Background: Hepatitis B virus and Hepatitis D virus coinfection arises from a unique virological interaction wherein HDV depends on hepatitis B surface antigen (HBsAg) for its replication and transmission. The global prevalence of HDV may vary based on the geographical location. Approximately 300 million people in the world are chronically infected with HBV, placing them at risk of acquiring HDV. Coinfection with HDV accelerates the progression of liver disease often leading to cirrhosis, severe hepatitis and hepatocellular carcinoma. Molecular assays targeting HBV S gene and polymerase gene help in identifying genotype specific variations and associated resistance mutations, which are crucial for guiding effective antiviral therapy.
Objective: This study was aimed to determine the prevalence of Hepatitis D infection among Hepatitis B positive cases and the genotyping of Heptitis B virus in samples co-infected with Hepatitis D virus.
Materials and Methods: This was a Descriptive cross-sectional study conducted over 6 months (April 2024-September 2024) at Government Stanley Medical College and Hospital, Chennai. Consecutive, non -repetitive HBsAg positive (Sandwich ELISA) blood samples of 118 patients were subjected to detection of HDV antibodies (Competitive ELISA) was done.
Results: A total of 118 samples that tested positive for hepatitis B surface antigen (HBsAg), all were negative for hepatitis D virus antibodies, indicating that HDV coinfection was not evident in this subgroup.
Conclusion: The low prevalence of HDV among HBV infected individuals in the study population may be due to the miss matched genotype combinations of HBV and HDV and less efficient HDV replication among HBV genotype D and HDV genotype 1 which are prevalent in India. Considering the increased risk of hepatocellular carcinoma up to threefold and two fold mortality among HDV confected individuals, continued surveillance and targeted HDV testing may be necessary among all the HBV positive individuals.

Keywords: HBsAg, hepatitis b virus, hepatitis d virus, ELISA, coinfection, hepatocellular carcinoma

Introduction
Viral hepatitis results from inflammation of the liver and is caused by infection by hepatotropic viruses, primarily Hepatitis A, B, C, D and E viruses [1]. WHO estimates about 254 million people are living with chronic hepatitis B virus infection in 2022 with 1.2 million new infections each year and 1.1 million deaths mostly from cirrhosis and hepatocellular carcinoma(primary liver cancer) and will continue to rise to a peak of 1.14 million deaths by 2034 without effective intervention [2].
Hepatitis B was recognized as a disease since ancient times. Genetic studies have found HBV DNA in humans dating back to 7,000-10,000 years, confirming its long-standing presence in human population and even non-human primates. Early outbreaks in 1883 (1880s-1940s) of “serum hepatitis” occurred after smallpox vaccinations administered via human lymph in Bremen, Germany. During World War II, up to 330,000 American soldiers were infected through contaminated yellow-fever vaccines. In 1965, Baruch Blumberg identified an antigen in blood samples, later called the “Australia antigen” in transfused patients and received Nobel Prize in 1976. Soon Blumberg linked the antigen to viral hepatitis while transmission studies confirmed it as a disease, caused by virus, later this was recognized to be the Hepatitis B surface antigen (HBsAg). Electron microscopy by David Dane revealed the complete HBV particle, known as the Dane particle. Detection of HBsAg a for the first time allowed screening of in apparently infected blood donors for a dangerous pathogen. Blood banks in the UK (1972) and the US (1971) began screening for HBsAg, drastically reducing transfusion-related hepatitis [3].

In 1971, Saul Krugman conducted early vaccine experiments, a significant step towards immunization by using inactivated HBsAg from plasma. In the year 1975-81**,** Maurice Hilleman and collaborators at Merck developed the first plasma-derived vaccine ("Heptavax"), which showed high efficacy (~95%) in preventing HBV infections and FDA approved the vaccine in 1981. FDA approved the first yeast-derived recombinant vaccine (DNA-based), replacing plasma-derived version in 1986. In 1992, WHO endorsed universal childhood HBV vaccination worldwide? The need to diagnose clinically silent HBV infections was a strong driving force in the development of modern virology [3].

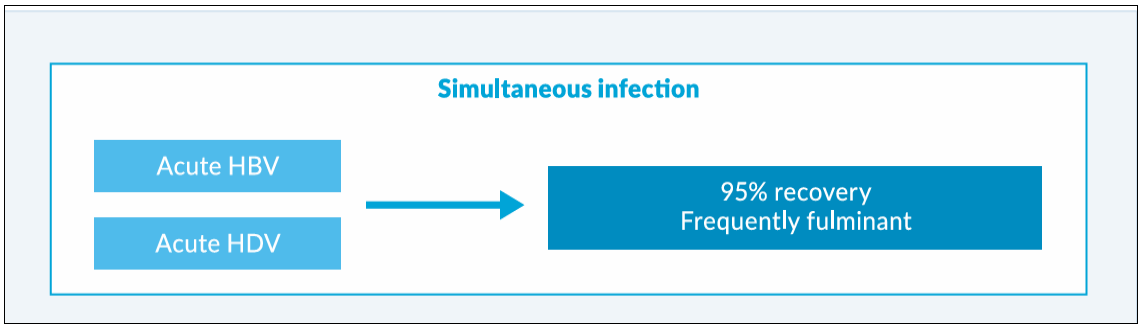
Mario Rizetto identified the hepatitis delta virus (HDV) in 1977. HDV is a satellite RNA virus that depends on HBV for propagation. HDV belongs to the genus Deltavirus and family Deltaviridae. It uses the HBsAg as a viral envelope and shares the same hepatocyte receptor for viral entry. HBV co-infection with HDV is the most severe form of viral hepatitis. Since it is a defective RNA virus HDV can only be transmitted in the presence of a concomitant HBV infection, by coinfection or superinfection. While both of these viruses are transferred parenterally, HDV spreads horizontally in areas where it is hyperendemic [3].

The Hepatitis D virion is approximately 36 nm in size, containing HDV RNA and delta antigen. HDV RNA is single-stranded, highly base-paired and circular containing close to 1700 nucleotides. It is coated with the envelope protein derived from the pre-S and S antigens of HBV [28]. Two HDAgs exist, the small HDAg (24 kD) is 155 amino acids long and the large HDAg (27 kD) is 214 amino acids long. A single nucleotide change (A-G) in the small HDAg sequence leads to the synthesis of the large HDAg[5].The small HDAg accelerates genome synthesis, while the large HDAg that inhibits HDV RNA synthesis is necessary for virion morphogenesis. Replication of HDV RNA occurs through a 'double rolling circle' model in which the genomic strand is replicated by a host RNA polymerase to yield a multimeric linear structure. Genetic analysis has revealed the presence of at least eight HDV genotypes.

Table1: HBV and HDV genotypes

Region	HDV Genotype	HBV Genotype
Europe	1	D/A
Brazil	1/3	F/A/D
China, Taiwan, Japan	1/2/4	B/C
Turkey, Iran, Pakistan, India	1	D
Western Pacific	1/2	B/C/D
Africa	1, 5-8	D/A/E

HDV infection can take two different forms-Coinfection and Super infection. Coinfection occurs when an acute HBV infection coexists with acute hepatitis B, and most patients recover from both viruses in six months. Patients with chronic hepatitis B may have superinfection with HDV, which might mimic chronic hepatitis B with acute exacerbation [4]. When compared to HBV monoinfection, dual HBV-HDV infection doubles mortality and speeds up the development of cirrhosis and hepatocellular cancer [9]. People with coinfection have increased risk of severe acute hepatitis and acute liver failure [21]. Acute hepatitis resembling acute hepatitis B is caused by HBV/HDV coinfection and is often more severe than acute hepatitis B. It also increases the risk of acute liver failure [10].



The HDV envelope contains HBsAg of HBV. Three HBsAg species co-exist based on the different amino terminal and a common carboxyl-terminus.Based on the size they are classified as Large (L), Medium (M) and Small (S). HDV nucleocapsids assembled only by HBsAg-S alone are not infectious. Only when these particles are associated even with small amount of HBsAg-L forms are infectious. HBsAg-M form are not essential for assembly or infectivity. Relatively HBsAg-M and HBsAg-L has a unique amino-terminal domain referred to as pre-S1, which is essential for the infectivity of both HBV and HDV. HBV and HDV share similar mechanism of attachment and entry, but still the nature of the host receptor is unknown [3]. HDV viremia is not directly associated with the stage of liver disease in HDV genotype 1 infection while in HDV genotype 3 infection higher viral loads were observed in patients with cirrhosis. In the human HBV receptor (sodium taurocholate co-transporting polypeptide (NTCP)) HDV infection provokes a marked and broad induction of interferon stimulated genes and cytokines which were more pronounced than in HBV monoinfection and May directly contribute to the more severe inflammation in patients with HDV [10]. Cellular immune responses against the HDV have been described, suggesting that the quantity and quality of T cell responses may be associated with some control of the infection. A molecular explanation for the suppression of HBV replication by HDV has been suggested via the HDV proteins p24 and p27 repressing HBV enhancers. In

addition, induction of a type-I interferon response by HDV may contribute to HBV repression. This hypothesis is supported by the induction of interferon stimulated genes in HBV cells which were superinfected with HDV which led to a decrease of HBV replication markers [9]. HBV/HDV coinfection has been identified as a main factor for the development of HCC in most studies, with a 3-fold increased risk compared to HBV infection [10].

Anti-HDV prevalence was higher in people who inject drugs (PWID) and in haemodialysis recipients. Among HBsAg-positive people, the nation with highest anti-HDV prevalence (36.9%) was Mongolia; prevalence rates >10% were also estimated from the Republic of Moldova and countries in Western and Middle Africa [4].In the general population, the globally estimated anti-HDV prevalence among HBsAg-positive people was 4.5% and in overall general population without HBV infection it was 0.16%, with the regional estimates for HBsAg-positive people ranging from 3.0% in Europe to 6.0% in Africa[4].The prevalence of HDV infection in India was around 44% in 1992 and now there is a declining trend up to 2.1% in 2021[23]. There are eight known HDV genotypes, seven of which share a genomic sequence that is more than 90% identical. Genotype 1 being the most prevalent globally.Other genotypes, genotype 2 in Asia, genotype 3 in South America, genotype 4 in eastern Asia, genotype 5 in western Africa and genotypes 6 to 8 in central Africa [21]. HBV-genotype-dependent viral replication interference between HBV and HDV is more noticeable in patients infected with HBV-genotype A than with HBV-D or E [29].

Materials and Methods

This is a descriptive cross sectional study conducted for a period of 6 months (April 2024 to September 2024) at the Department of Microbiology, at Government Stanley Medical College in Chennai, Tamilnadu. The inclusion criteria comprises the serum samples which were tested positive for Hepatitis B virus, received from various clinical departments and from all age groups at the virology section.The improperly labelled/leaky containers, repeat samples from same positive patient, known Hepatitis B positive patients, HBV patients on treatment, coexisting other infections like Hepatitis C virus, HIV, Autoimmune Hepatitis A & E were excluded from testing.Ethical clearance was obtained from the College Ethical committee before the commencement of the study.

A total of 118 HBsAg positive samples from patients were included in the study. A detailed history including the presenting illness, blood transfusion, previous surgeries, hemodialysis, organ transplant, sexual promiscuity, tattooing and intra-venous drug abuse (IVDA) were taken. Parameters of Liver function test was evaluated for the study population. HBV viral DNA quantification was done for all the study population by Quantitative RT PCR (q PCR). Anti-HDV Ab analysis was done using ELISA (HDV Ab, Dia. Pro kit) and the Anti HDV Antibody positive samples were subjected for molecular characterisation.

Results

Out of 118 HBsAg positive samples, majority 44 (37.28%) were from the age group of 41-50 years and 69 (58.47%) of HBsAg positive were male patients. Maximum number of patients were from the department of Gastroenterology 24(20.33%). Most 96 (81.35%) of the patients were diabetics followed by others like alcohol consumption 65(55.08%), smoking, hypertension. The most common risk factor was found to be blood transfusion 48(40.67%) followed by Tattooing and other body piercing in 24(20.33%), and least in health care workers 1(0.84%). Majority of patients presented with fatigue, fever, jaundice, abdominal distension, abdominal pain and vomiting. All the HBV positive patients showed elevated liver parameters.Among the 118(100%) study population, all showed detectable and quantifiable HBV DNA viral load. Out of which 106(89.83%) of HBsAg positive patients showed viral load in the range of 100 000 - 1000 000 ^{IU}/ml. None of the HBV positive sample showed positivity for Anti-HDV antibody test by ELISA, indicating nil coinfection among the HBV positive study group.

Results

Table 2: Age Wise Distribution of HBV Positive Samples (n=118).

Age	Total samples	Percentage
1-10 Years	0	0
11-20 Years	1	0.84%
21-30 Years	8	6.77%
31-40 Years	33	27.96%
41-50 Years	44	37.28%
51-60 Years	18	15%
61-70 Years	9	7.66%
>70 Years	5	4.23%

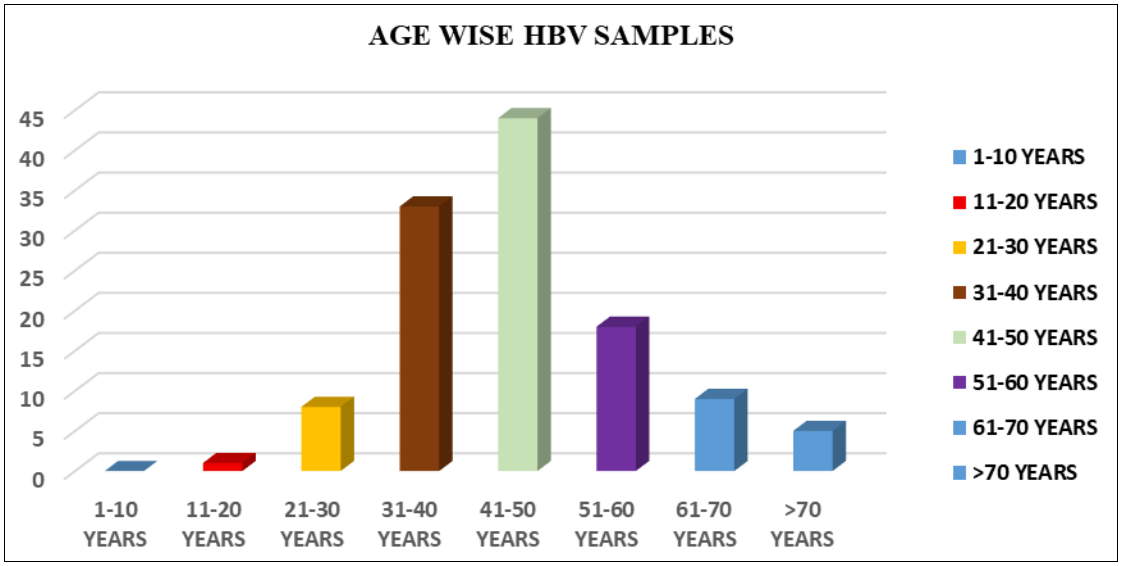


Chart 1: Age Wise Distribution of HBV Positive Samples **(N=**118).

Table 2: Gender Wise Distribution of HBV Positive Samples (N=118)

Gender	Numbers	Percentage
Male	69	58.47%
Female	49	41.52%

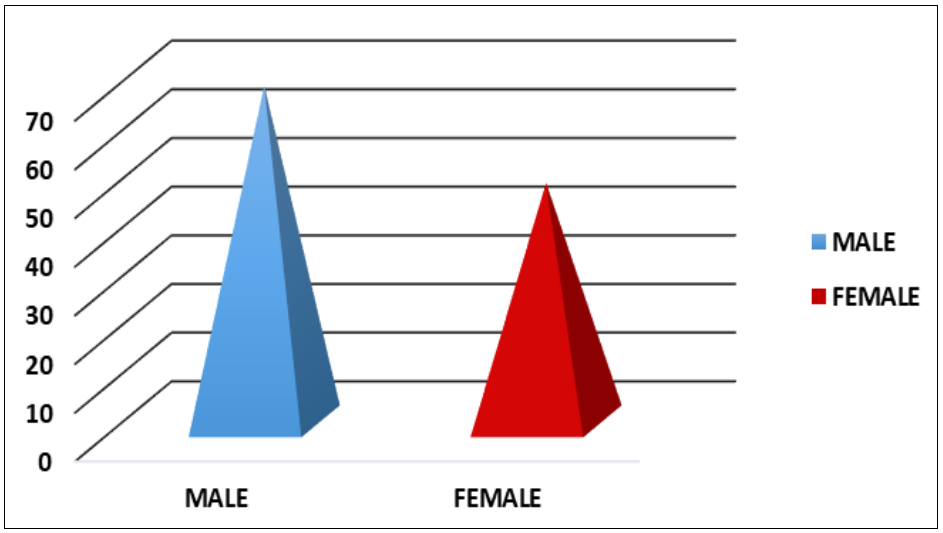


Chart 2: gender wise distribution of HBV positive samples (n=118)

Table 3: Ward Wise Distribution of HBV Positive Samples (N=118)

S.No	Ward	Numbers	Percentage
1.	Gastroenterology	24	20.33%
2.	Nephrology	22	18.64%
3.	General Surgery	17	14.4%
4.	General Medicine	14	11.86%
5.	Orthopaedics	11	9.32%
6.	ENT	8	6.77%
7.	TAEI/IMCU	7	5.93%
8.	Obstetrics and Gynaecology	4	3.38%
9.	Plastic Surgery	4	3.38%
10.	Vascular Surgery	2	1.69%
11.	Surgical Oncology	2	1.69%
12.	Cardiology	2	1.69%
13.	Respiratory Medicine	1	0.84%

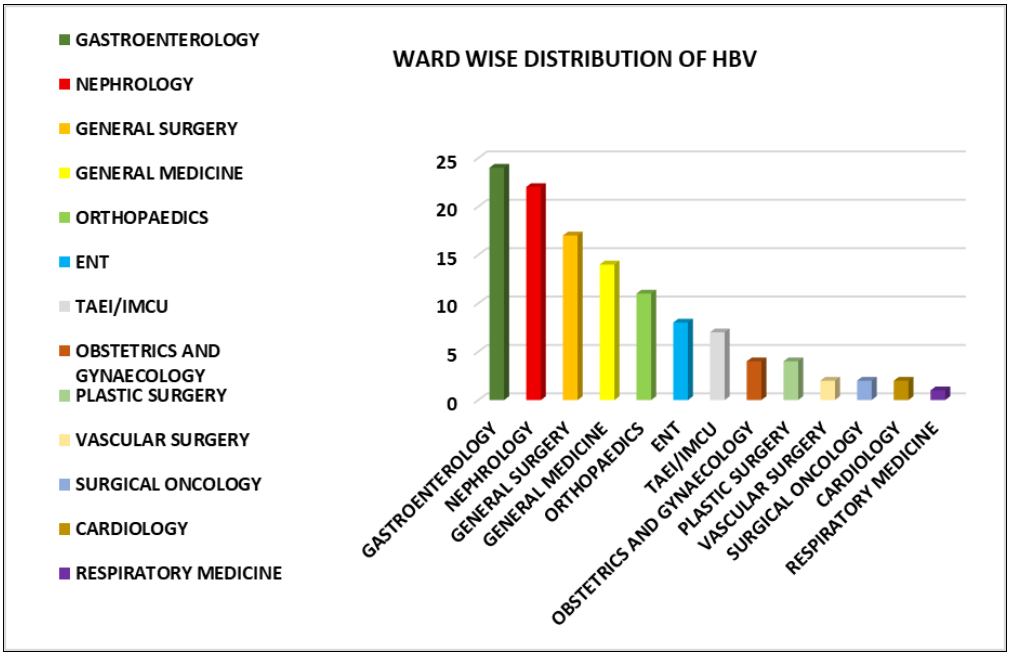


Chart 3: Ward Wise Distribution of HBV Positive Samples (n=118)

Table 4: Comorbidities in Acute Hepatitis B Infection

S.No.	Etiological Factors	No.	%
1.	Diabetes Mellitus	96	81.35
2.	History of Alcohol Consumption	65	55.08
3.	Smoking	62	52.54
4.	Hypertension	58	49.15

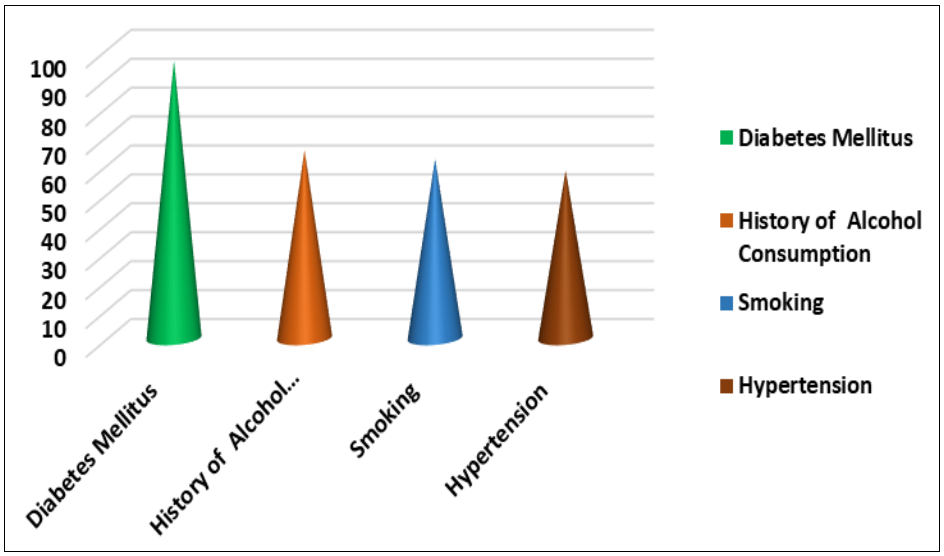


Chart 4: Comorbidities in Acute Hepatitis B Infection.

Table 5: Risk Factors in the Transmission of HBV (N=118).

S.No.	Factors	No.	%
1.	Blood Transfusion	48	40.67
2.	Tattooing and other body piercing	24	20.33
3.	History of Surgery	22	18.64
4.	Unknown	21	17.79
5.	Unprotected sex with multiple partners.	2	1.69
6.	Health care workers	1	0.84
7.	Incarceration	0	0
8.	History of sharing needles	0	0
9.	Male having sex with male	0	0
10.	Household contacts of HBV positive individuals	0	0

Table 6: Presentations of Symptoms among HBV Positive Individuals

S.No.	Symptoms	No. OF Patients	%
1.	Fatigue	102	86.44
2.	Fever	98	83.05
3.	Jaundice	71	60.16
4.	Abdominal Distension	57	48.30
5.	Abdominal Pain	52	44.06
6.	Pruritus	51	43.22
7.	Vomiting	37	31.35
8.	Loss of appetite	32	27.11
9.	Clay Coloured Stool	11	9.32

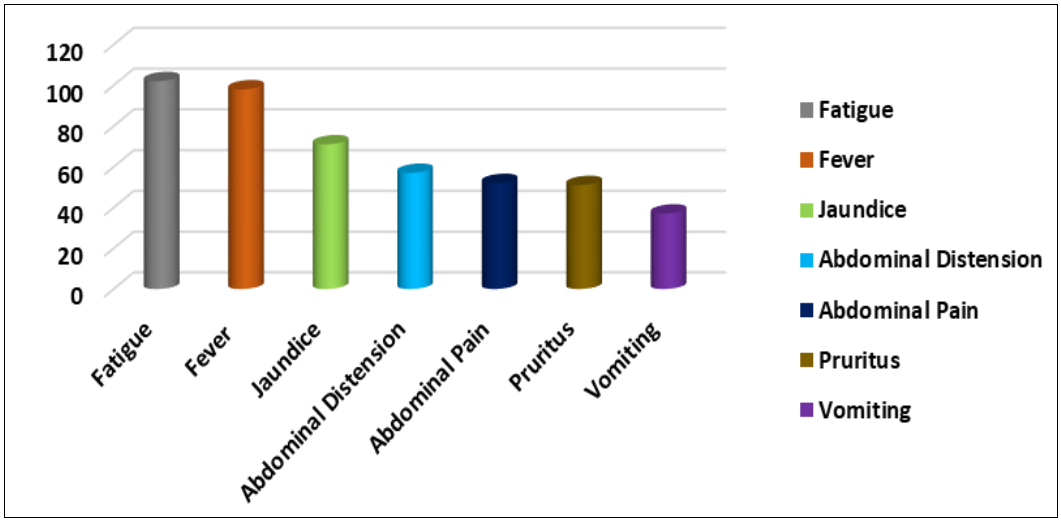


Chart 5: Presentations of Symptoms among HBV Positive Individuals.

Table 7: Laboratory Parameters among HBV Positive individuals (N=118).

S.No	Laboratory Parameters	No. of cases more than the upper limit	%
1.	Alanine Transferase (Alt)	118	100
2.	Aspartate Transferase (Ast)	118	100
3.	Total Bilirubin	116	98.30
4.	Direct Bilirubin	115	97.45

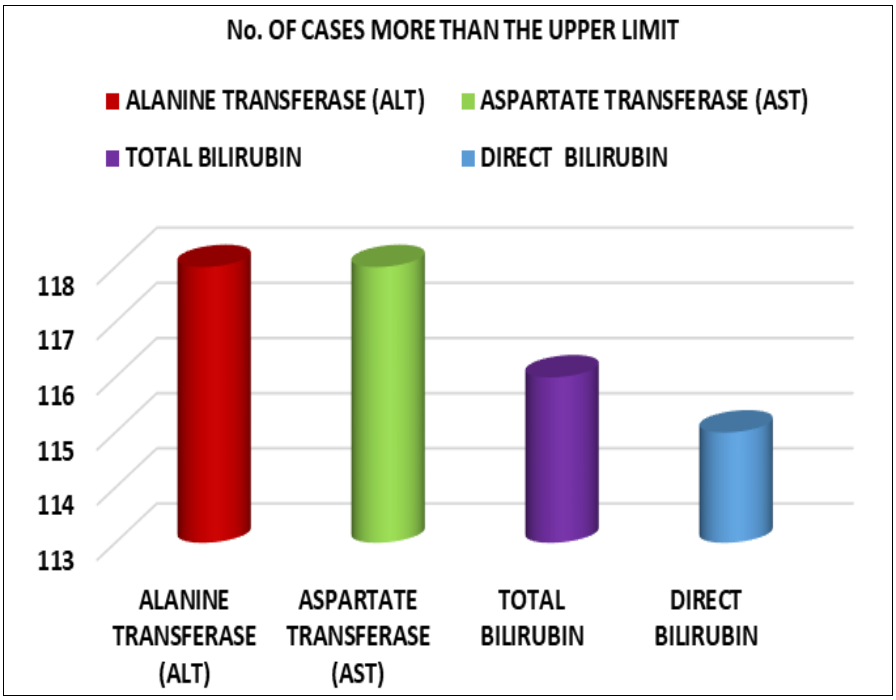


Chart 6: Laboratory Parameters among HBV Positive Individuals (N=118)

Table 8: HBV Viral Load Status among Hbsag Positive Samples (N=118).

HBV Dna	Number	Percentage
Detectable	118	100%
Not-Detectable	0	0

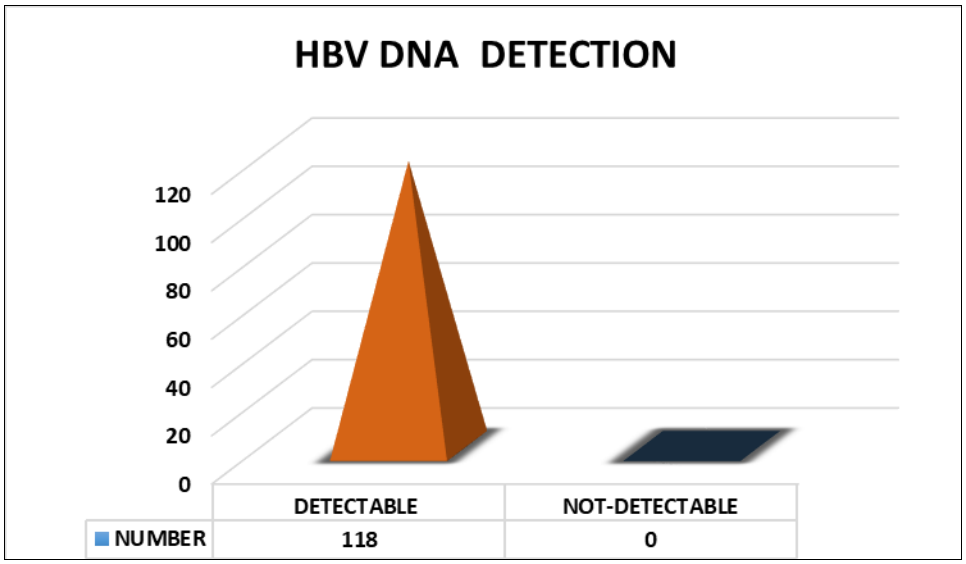


Chart 7: HBV Viral Load Status among HBSAG Positive Samples (n=118).

Table 9: Distribution of HBV Viral Load Results By Quantitative PCR among Hbsag Positive Samples (N=118).

HBV DNA Viral LOAD IU/ML	Number of Samples	%
< 100	0	0
100-1000	0	0
1000 -10 000	2	1.69
10 000 - 100 000	7	5.93
100 000 - 1000 000	106	89.83
> 1000 000	3	2.54

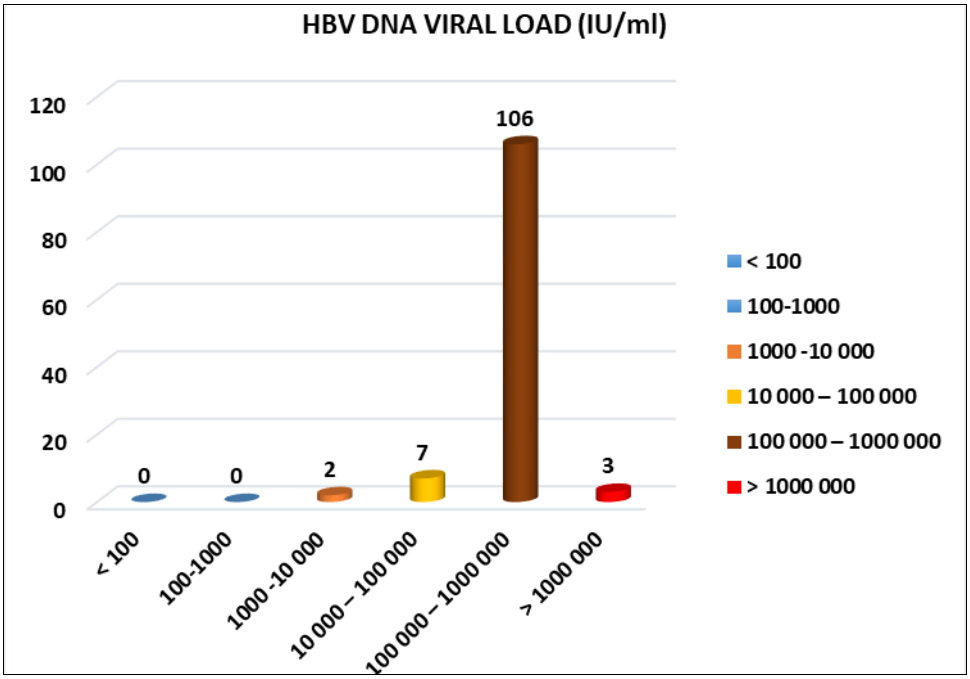


Chart 8: Distribution of HBV Viral Load Results By Quantitative PCR among Hbsag Positive Samples (N=118).

Table 10: Distribution of HDV Positivity among HBV Positives by Elisa Method (N=118)

Infection	Number of Positive	Percentage
Hepatitis B Infection	118	100%
Hepatitis D Infection	NIL	NIL

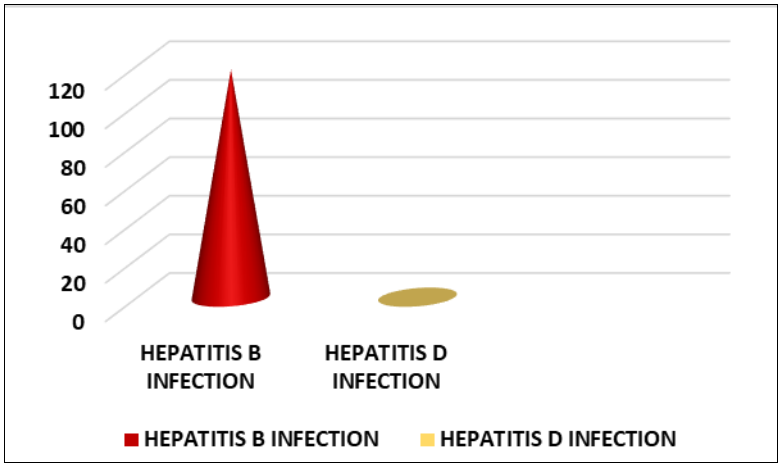


Chart 9: Distribution of HDV Positivity among HBV Positives by Elisa Method (N=118)

Discussion

Hepatitis D virus (HDV) is a defective RNA virus which requires Hepatitis B virus for its assembly, replication and transmission. This clinically worsens the condition of HBV infected individuals. Co-infection of HBV and HDV presents as severe acute hepatitis resembling HBV flare, leading to increased risk of acute liver failure. This also causes a biphasic peaks in aminotransferases (AST, ALT) serum levels, even weeks apart [8] and leads to chronicity in about 2-5% of cases[9,10].

HBV/HDV coinfection has been considered as a main factor for the development of cirrhosis and hepato cellular carcinoma in most studies, with a risk of 3-fold increase compared to HBV mono-infection [10, 11, 12]. The overall pooled effect showed that HBV/HDV coinfected patients were at risk of 2- fold increase in HCC compared to HBV mono- infected patients and a 6 - fold significant increase in the risk of HCC among HIV/HBV/HDV triple- infection patients, compared to HIV/HBV coinfected patients [14, 26.27], as suggested histological and clinical evidence of presence of higher levels of liver enzymes and a faster rate of developing cirrhosis [15, 26, 27].

This study was aimed to determine the prevalence of Hepatitis D coinfection among Hepatitis B positive cases in a tertiary care hospital and to determine the genotype for that corresponding Hepatitis B virus which showed coinfection with Hepatitis D virus.

A total of 118 HBsAg positive samples from patients were included in the study, highest number of 44(37.28%) of HBV positive samples[TABLE.1] belongs to the age group of 41-50 years followed by 33 (27.96%) in 31-40 years,18(15%) in 51-60 years,9 (7.66%) in 61-70 years,8 (6.77%) in 21-30 years,5(4.23%) among above 70 years and least 1(0.84%) from 11- 20 years of age group. These results were similar the study done by Wang *et al*.,[2024] which also showed the median age of HBV infection was 38(30-49)years of age group [19].The reason may be attributed to the behavioural and health care associated factors, tattooing, traditional scarification and blood transfusion.The high prevalence in the age group between 41-50 years may be attributed as they were born before the implementation of universal immunisation programme and more likely exposed to HBV during their childhood and adulthood without protection from vaccine [4].There are no HBV positive patients among the age group of less than 10 years which may be primarily attributed to the widespread introduction and implementation of Universal HBV vaccination programs especially birth dose vaccination, increased awareness in screening of pregnant women and school based catch-up vaccination for unvaccinated children[4].

Most of the HBV positive samples were received from male patients 69 (58.47%) and from females 49(41.52%)[TABLE.2].The reason for male preponderance may be attributed to the hormonal influence on viral replication, androgens enhance HBV replication by binding to androgen receptors whereas in females estrogen inhibits HBV transcription via estrogen receptors[6].Differences in immune response between male and females, higher rates of alcohol use and smoking among men, high risk professions in healthcare roles in certain regions[7]and low level of seroconversion rates post- HBV vaccination[4].

In the study most of the HBsAg positive patients [TABLE.3]were from Gastroenterology department 24 (20.33%) followed by Nephrology 22 (18.64%), General Surgery 17 (14.4%), General Medicine 14(11.86%), Orthopaedics 11 (9.32%), ENT 8(6.77%), TAEI/IMCU 7(5.93%) and between 1-4 (0.84% to 3.38%) from Obstetrics and Gynaecology, Plastic surgery, Cardiology, Respiratory medicine and Surgical oncology. Higher number of HBV positivity from Gasteroenterology may be attributed to the presence of symptoms like jaundice, hepatomegaly or cirrhosis, patients with abnormal liver function tests which are classical indications for referral from other departments to Gastroenterology department [8].

Among the comorbidities [TABLE.4] in the HBV positive patients, Diabetes mellitus was present in 96 (81.35%) followed by history of alcohol consumption in 65(55.08%),smoking in 62(52.54%),Hypertension in 58(49.15%).The risk factors [TABLE.5] for the transmission of HBV infection highly includes blood transfusion among 48(40.67%) followed by Tattooing and body piercing in 24 (20.33%), past history of surgery in 22(18.64%),unknown cause in 21(17.79%),unprotected sex with multiple sex partners in 2(1.69%),Health care worker 1(0.84%) was similar to the study done by Nikolopoulou *et al*.,[7].In the study there are no cases of transmission of HBV among incarcerated population, house hold contacts of HBV positive individuals, male having sex with male and from history of sharing needles. Two important factors affecting HBV prevalence are occupation (medical versus non-medical profession) and education. In general, knowledge and awareness of hepatitis B infection, the associated risks and the measures to prevent it, have been associated with a

lower HBV prevalence. This knowledge has been reported to be higher and more systematic among medical personnel, compared with non-medical personnel [7].Majority 102 (86.44%) of patients [TABLE.6] with HBV infection presented with fatiquability followed by low grade fever 98 (83.05%), jaundice 71(60.16%), abdominal distension, abdominal pain, loss of appetite and pruritus and clay coloured stool [9]. In coinfection there is Biphasic enzyme elevation will be present with two distinct peaks of ALT/AST can occur, first from HBV infection and a later surge from HDV infection. All the Liver parameters [TABLE.7] were elevated in all 118 (100%) HBV positive samples, indicating acute hepatitis status of patients [5, 25].

For all the HBV positive patients, quantitative detection of HBV viral load was done using Real time PCR (q PCR), which showed in all the 118 (100%) samples, HBV DNA was detectable and quantifiable [TABLE.8]. Majority 106 (89.83%) of HBV positive samples [TABLE 9] showed viral load of 100 000 to 1000 000 IU/ml, 7(5.93%) showed 10 000 to 100 000 IU//ml, 3 (2.54%) showed above 1000 000 and 2(1.69%) showed 1000 to 10 000 IU/ml.None of the samples had viral load in the range from 1 to 1000 IU/ml.The findings are similar to the study done by Jun zi et.,al in the range of 2 x 10^{3} to 2 x10^{4} IU/ml [31]. The results from the study showed majority of HBV positive samples showed high viremia levels> 20,000 IU/ml as per CDC guidelines) as in the early phase, determining the acute state and high viral replication status [25,30].

Detection of anti-HDV antibody [TABLE.10] was done among 118 HBV positive patients showed none of the patient turned to be positive indicating zero prevalance of HDV coinfection among the study cohort. These findings were consistent with the study done by krithiga *et al*., [23], SM Shrestha and Tusuda F with zero prevalence of co-infectionLal [19]. Another study conducted by Lal JS in India showed no coinfection with HDV [17]. The highest prevalence was observed from Mumbai 37.4% and in Ludhiana 33%. [17]. the low level of HDV infection was probably due to decline in the HDV transmission. This may be due the miss matched genotype combinations among HBV Genotype D and HDV Genotype 1, prevalent in India which lead to the less efficient HDV replication. HDV coinfection with HBV can be reduced by the improvement in socioeconomic status, increased awareness among people about parenteral route of transmission of viruses, health care development, improved screening for transmission based infections and more importantly, enhanced vaccination strategies, including mandatory birth dose of HBV vaccination [28].

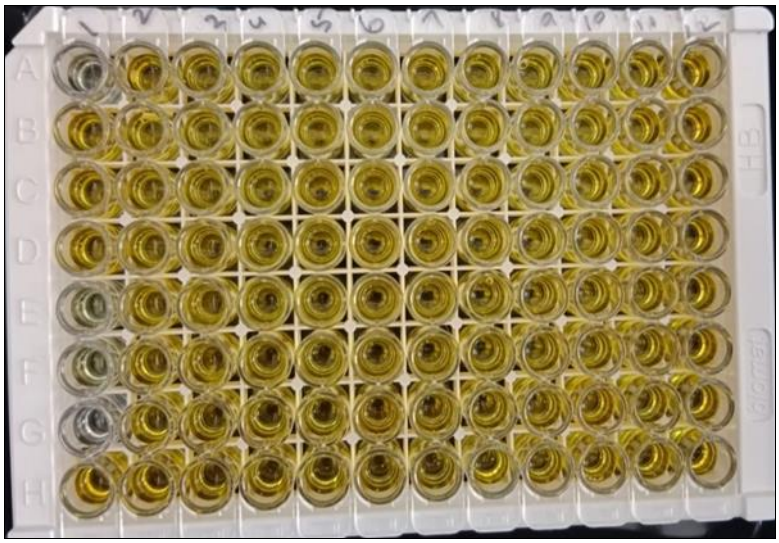


Fig 1: Hepatitis d Virus Anti-HDV Antibody elisa plate

Fig2: OD value of anti-HDV antibody ELISA.

Conclusion

In the current study, which included 118 HBsAg positive samples, the majority of cases had high levels of viremia, indicating active viral replication and a higher risk of hepatic inflammation and long-term liver damage. None demonstrated serological evidence of HDV coinfection as determined by the absence of anti-HDV antibodies, suggesting low or possibly declining prevalence of HDV among HBV infected individuals in the study population. This may be due the miss matched genotype combinations among HBV genotype D and HDV genotype 1, prevalent in India which lead to the less efficient HDV replication. The study highlights the ongoing burden of HBV monoinfection in the population and the necessity of routine virological monitoring and early antiviral treatment in indviduals with high viral loads. Considering the increased risk of hepatocellular carcinoma up to threefold and mortality up to two fold among HDV coinfected individuals, continued monitoring and targeted HDV testing may be necessary among all the HBV positive individuals. Continuous surveillance especially in high risk groups and regions previously endemic for HDV is essential to assess the potent demographic variability.

Conflict of Interest

Not available

Financial Support

Not available

References

1. Jefferies M, Rauff B, Rashid H, Lam T, Rafiq S. Update on global epidemiology of viral hepatitis and preventive strategies. World J Clin Cases. 2018 Nov 6;6(13):589-599. DOI:10.12998/wjcc.v6.i13.589. PMID:30430114.
2. World Health Organization. Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection. Geneva: World Health Organization; 2024 Mar 29. 272 p. ISBN:9789240090903.
3. Howley PM, Knipe DM, Whelan SPJ, editors. Fields Virology: Emerging Viruses. 7th ed. Philadelphia (PA): Lippincott Williams & Wilkins; 2020 Apr 17. 1256 p. ISBN:9781975112547.
4. Stockdale AJ, Kreuels B, Henrion MYR, Giorgi E, Kyomuhangi I, de Martel C, *et al*. The global prevalence of hepatitis D virus infection: systematic review and meta-analysis. J Hepatol. 2020 Jun;73(3):523-532. DOI:10.1016/j.jhep.2020.04.008. PMCID: PMC7438974.
5. Bennett JE, Dolin R, Blaser MJ, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 9th ed. Philadelphia: Elsevier; 2020.
6. Cooper KM, Delk M, Devuni D, Sarkar M. Sex differences in chronic liver disease and benign liver lesions. JHEP Rep. 2023 Aug 1;5(11):100870.
7. Nikolopoulou GB, Tzoutzas I, Tsakris A, Maltezou HC. Hepatitis B in healthcare personnel: An update on the global landscape. Viruses. 2023 Dec 18;15(12):2454. DOI:10.3390/v15122454. PMCID: PMC10748141.
8. Sandmann L, Wedemeyer H, Cornberg M. Hepatitis D - diagnosis and treatment. In: Wedemeyer H, Mauss S, Berg T, Keitel V, Rockstroh J, Sarrazin C, editors. Hepatology - a clinical textbook. 11th ed. 2024-2025. Chapter 4.
9. Reddy K, Patrick C, Liaquat H, Rodriquez E, Stocker A, Cave B, *et al*. Differences in referral access to care between gastrointestinal subspecialty patients: barriers and opportunities. J Gastrointest Oncol. 2018;9(6):1128-1138. PMCID: PMC6071906. PMID:30283855.
10. Sagnelli C, Sagnelli E, Russo A, Pisaturo M, Occhiello L, Coppola N. HBV/HDV co-infection: Epidemiological and clinical changes, recent knowledge and future challenges. Life (Basel). 2021 Feb 22;11(2):169. DOI:10.3390/life11020169.
11. Rizzetto M, Durazzo M. Hepatitis delta virus (HDV) infections. J Hepatol. 1991;13(Suppl 4):S116-S118. DOI:10.1016/0168-8278(91)90040-I.
12. Romeo R, Del Ninno E, Rumi M, Russo A, Sangiovanni A, De Franchis R, *et al*. A 28-year study of the course of hepatitis Δ infection: a risk factor for cirrhosis and hepatocellular carcinoma. Gastroenterology. 2009;136(4):1629-1638. DOI:10.1053/j.gastro.2009.01.052.
13. Cross TJ, Rizzi P, Horner M, Jolly A, Hussain MJ, Smith HM, *et al*. The increasing prevalence of hepatitis delta virus (HDV) infection in South London. J Med Virol. 2007;80(2):277-282. DOI:10.1002/jmv.21078.
14. Niro GA, Smedile A, Ippolito AM, Ciancio A, Fontana R, Olivero A, *et al*. Outcome of chronic delta hepatitis in Italy: a long-term cohort study. J Hepatol. 2010 Nov;53(5):834-840. DOI:10.1016/j.jhep.2010.06.008.
15. Palom A, Rodríguez Tajes S, Navascués CA, García Samaniego J, Riveiro Barciela M, Lens S, *et al*. Long-term clinical outcomes in patients with chronic hepatitis delta: the role of persistent viraemia. Aliment Pharmacol Ther. 2019 Jul;51(2):158-166. DOI:10.1111/apt.15520.
16. Kamal H, Fornes R, Simin J, Stål P, Duberg AS, Brusselaers N, Aleman S. Risk of hepatocellular carcinoma in hepatitis B and D virus co-infected patients: a systematic review and meta-analysis of longitudinal studies. J Viral Hepat. 2021 Oct;28(10):1431-1442. DOI:10.1111/jvh.13577.
17. Shah R, Ghimire H; JNMA Team. Prevalence of hepatitis D among patients with hepatitis B viral infection attending a tertiary care centre of Nepal. J Nepal Med Assoc. 2017 Oct-Dec;56(208):417-420. DOI:10.31729/jnma.3378.
18. Banker DD, Desai P, Brawner TA, Decker RH. Hepatitis delta virus infection in Bombay. Trans R Soc Trop Med Hyg. 1992 Jul;86(4):424-425. PMID:.
19. Shrestha S, Tsuda F. Hepatitis delta virus infection in Nepal. Trop Gastroenterol. 1991;12(4):185-187. PMID: Jat SL, Gupta N, Kumar T, Mishra S, S A, Yadav V, *et al*. Prevalence of hepatitis D virus infection among hepatitis B virus infected individuals in India. Indian J Gastroenterol. 2015 Mar;34(2):164-168. PMID:
20. World Health Organization. Global hepatitis report 2024: action for access in low- and middle-income countries. Geneva: WHO; 2024 Apr 9.
21. Wang Y, Shen G, Lu R, Wang H, Cai W, Zhang F, *et al*. The prevalence of HDV among HBsAg-positive populations with and without HIV-1 in China. J Viral Hepat. In press 2024.

22. Ramachandran K, Agarwal R, Sharma MK, Bhatia V, Gupta N. Prevalence of hepatitis delta virus infection among hepatitis B virus infected and exposed patients. J Glob Infect Dis. 2020 Oct-Dec;12(4):197-201. DOI:10.4103/jgid.jgid_137_19.
23. Botelho Souza LF, Vasconcelos MPA, Dos Santos AO, Villalobos Salcedo JM, Vieira DS. Hepatitis delta: virological and clinical aspects. Virol J. 2017 Sep 13;14(1):177. DOI:10.1186/s12985-017-0845-y.
24. Wu C-C, Chuang W-K, Yeh C-T, Chen Y-T, Liu C-J, Su C-W, *et al*. Role of hepatitis D virus in persistent alanine aminotransferase abnormality among chronic hepatitis B patients treated with nucleotide/nucleoside analogues. J Formos Med Assoc. 2021 Jan;120(1 Pt 2):303-310. DOI:10.1016/j.jfma.2020.10.002. PMID:33109431.
25. Balt AAS, Ignat MD, Eloise BR, Debita M. HBV, HCV, and HDV triple infection—a therapeutic challenge. Future Virol. 2025 Feb;20(1):45-60. [In press].
26. Yen DW, Soriano V, Barreiro P, Sherman KE. Triple threat: HDV, HBV, HIV coinfection. Clin Liver Dis. 2023 Nov;27(4):955-972. DOI:10.1016/j.cld.2023.05.010. PMID:37778779.
27. Verma R, Khanna P, Prinja S, Rajput M, Chawla S, Bairwa M. Hepatitis B vaccine in national immunization schedule: a preventive step in India. Hum Vaccin Immunother. 2011 Dec;7(12):17878. DOI:10.4161/hv.7.12.17878. PMID:22134433.
28. Madejón A, Romero M, Hernández Á, García-Sánchez A, Sánchez-Carrillo M, Olveira A, García-Samaniego J. Hepatitis B and D viruses replication interference: Influence of hepatitis B genotype. World J Gastroenterol. 2016 Mar 22;22(11):3165-3174. DOI:10.3748/wjg.v22.i11.3165. PMID:27003993.
29. Gish RG, Yi DH, Kane S, Clark M, Mangahas M, Baqai S, *et al*. Coinfection with hepatitis B and D: epidemiology, prevalence and disease in patients in Northern California. J Gastroenterol Hepatol. 2013 Sep;28(9):1521-1525. DOI:10.1111/jgh.12217. PMID:23574043.
30. Jun Z, Li YH, Wang XM, Xu HQ, Liu WH, Cui JY, *et al*. Hepatitis D virus dual infection among Chinese hepatitis B patients related to hepatitis B surface antigen, hepatitis B virus DNA and age. World J Gastroenterol. 2023 Oct 14;29(38):5395-5405. DOI:10.3748/wjg.v29.i38.5395. PMID:37900584.

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