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Prevalence of Hepatitis B virus genotypes among Hepatic jaundice patients in Ibb city Yemen

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Abstract

Background and Aims:

Hepatitis, an inflammation of the liver, can lead to serious health complications and mortality, causing approximately 1.34 million fatalities annually—a burden comparable to that of HIV/AIDS. This study aims to assess the prevalence and genotype distribution of the hepatitis B virus (HBV) among patients presenting with jaundice in Ibb City, Yemen, and evaluating host associated risk factors.

Methods

This multi-center, cross-sectional study was carried out between January 2024 and December 2025 across major clinics and hospitals in Ibb City. The study enrolled 256 patients presenting with jaundice. Serum samples from all participants were evaluated for liver transaminases, HBV DNA viral load, and HBV serological markers (specifically HBsAg, total anti-HBc, HBeAg, and anti-HBe). To determine the HBV genotypes, a nested PCR-based assay was employed using type-specific primers that targeted highly conserved sequences within the P and S genes, successfully identifying six distinct genotypes.

Results

Of the 256 jaundice patients evaluated, 82.4% (211) were male and 17.6% (45) were female. The leading presentation was undiagnosed jaundice (37.5%), followed by confirmed hepatitis B (25.4%). Other identified etiologies included non-B viral hepatitis (10.5%), autoimmune liver diseases (7.4%), drug-induced liver injury (5.9%), schistosomiasis (4.7%), malaria (4.3%), and dengue fever (0.8%). Overall, 85 patients (33.2%) tested positive for HBV infection via serological or molecular markers, with men exhibiting a significantly higher infection rate (37.0%) than women (15.6%). Specifically, HBsAg positivity was detected in 51 patients (19.9% overall prevalence; 21.3% in males vs. 13.3% in females). Among the 65 genotyped patients, genotype D was the most prevalent (32.3%), followed by genotype B (20.0%) and genotype C (13.8%), while mixed genotypes were identified in 33.8% of cases.

Conclusions

The vast majority of jaundice patients in Ibb City are male, which may indicate either higher biological susceptibility or gender-based disparities in healthcare-seeking behaviours. The high prevalence of HBV particularly genotype D and mixed genotypes highlights an urgent need for targeted public health interventions, routine screening, and robust vaccination strategies in the region.

INTRODUCTION

In adults, hyperbilirubinemia indicates an underlying medical issue, such as altered heme metabolism, liver dysfunction, or an obstruction in the biliary tract (Al-Tubaikh 2017). Although jaundice rarely occurs in adults, it is exceptionally frequent in newborns, impacting roughly 80% of infants during their first week of life (Kaplan and Hammerman 2017). Pathognomonic and associated clinical signs frequently include pruritus, acholic stools, and choluria. The structural etiologies of jaundice span a wide prognostic spectrum, ranging from benign conditions to life-threatening malignancies or fulminant organ failure (Bassari and Koea 2015). Unconjugated (indirect) hyperbilirubinemia typically arises from accelerated erythrocyte hemolysis, extensive hematomas, metabolic or endocrine abnormalities (such as hypothyroidism), prolonged fasting, or neonatal physiological shifts. It is also associated with hereditary hepatic glucuronidation defects, such as Gilbert's syndrome (Roger 2004). Conjugated (direct) hyperbilirubinemia is primarily driven by hepatocellular injury—including cirrhosis and infectious or drug-induced hepatitis—or mechanical extrahepatic biliary obstructions. These obstructions are frequently secondary to cholelithiasis, choledocholithiasis, acute or chronic pancreatitis, or hepatobiliary and pancreatic malignancies (Winger and Michelfelder 2011).

Hepatic pathologies encompass a diverse spectrum of acute and chronic disorders characterized by hepatocellular injury, parenchymal inflammation, and progressive fibrogenesis, culminating in the impairment of critical metabolic homeostasis and xenobiotic filtration. On a global scale, liver diseases represent a significant burden of mortality, resulting in approximately 2 million deaths annually, which constitutes roughly 4% of total worldwide mortality (Gan et al. 2025). Under conditions of persistent insult, the hepatic parenchyma undergoes a highly conserved pathological cascade. Chronic inflammatory signaling drives the trans-differentiation and activation of quiescent hepatic stellate cells (HSCs) into myofibroblasts, which aberrantly deposit excessive extracellular matrix components. This progressive fibrotic remodeling disrupts hepatic architectural integrity and elevates intrahepatic vascular resistance, subsequently compromising sinusoidal perfusion (Wazir et al. 2023).

Hepatitis B virus (HBV) infection represents a major global public health challenge characterized by severe liver infection. Taxonomically, HBV is a member of the *Hepadnaviridae* family and possesses a partially double-stranded DNA genome (Shen and Yan 2014), affecting a vast number of individuals worldwide. Historically, the virus was considered highly endemic in Yemen. Previous data indicated that Hepatitis B surface antigen (HBsAg) prevalence ranged from 8% to 20% among both the general public and healthcare workers, stood at 4.1% in infants, and left up to 50% of the population and medical staff with serological evidence of prior exposure. However, recent research highlights a significant decline in infection rates, particularly among children. Current figures show that HBV and HBsAg prevalence has dropped to between 0.7% and 2% in the general population, and around 4% in high-risk categories such as healthcare workers (Al-kadassy et al. 2019, AL-Marrani et al. 2018, Murad et al 2013, Al-Shamahy et al.2019, Al-Shamahy et al. 2011, Al-Shamahy et al. 2003, Amran et al. 2019). Even though Hepatitis B virus (HBV) possesses a DNA genome, its replication cycle involves an RNA intermediate. Because the viral reverse transcriptase does not have proofreading capabilities to correct spontaneous mistakes, nucleotide mutations accumulate, giving rise to numerous HBV genotypes and subtypes (Janahi et al., 2019). Currently, researchers recognize ten distinct HBV genotypes (A–J) alongside twenty-four sub-

genotypes (A1–A3, B1–B5, C1–C6, D1–D6, and F1–F4), which exhibit specific geographic and ethnic distributions. For instance, genotype A is predominantly found in Europe, the United States, Canada, Brazil, India, Tunisia, Benin, and various Central African nations (Janahi et al., 2019). Meanwhile, genotype B is most prevalent in Asian regions and countries, including Taiwan, the Philippines, Japan, Hong Kong, China, Thailand, Indonesia, and Vietnam, as well as the United States (Vachon & Osiowy, 2021; Mahmood et al., 2016; Datta, 2008).

Genotype C is most frequently observed in regions including Australia, China, Hong Kong, India, Indonesia, Japan, Korea, Taiwan, Thailand, Vietnam, Brazil, the United States, and across Melanesia, Micronesia, and Polynesia. Meanwhile, Genotype D is predominantly found in South Asia, the Middle East, the Mediterranean region (including Spain, the Czech Republic, Albania, and Turkey), Russia, Afghanistan, Iran, Tunisia, Brazil, the United States, and parts of Oceania (Melanesia, Micronesia, Polynesia, and the Solomon Islands) (Awan et al. 2010).

For the less common variants, Genotype G has been identified in North America, Germany, and France. Genotype H is documented throughout Central and South America, including Mexico, whereas Genotype I has been isolated specifically in Vietnam and Laos (Tran et al. 2008; Phung et al. 2010; Mahmood 2017). A patient's Hepatitis B virus (HBV) genotype (genetic strain) changes how the disease behaves, how fast it progresses, and how well it responds to treatment. For example, genotypes A and D are more likely to turn into long-term (chronic) infections than genotypes B and C (Janahi et al. 2019, Vachon and Osiowy et al. 2021, Mahmood et al.2016, Datta 2008, Awan Z et al. 2010, Patel et al.2020). When looking at long-term outcomes, patients with genotype C face a significantly higher risk of developing cirrhosis and liver cancer than those with genotype B, whose disease typically progresses much slower (Chan et al. 2009). Furthermore, therapeutic efficacy varies by genotype; patients with genotype A demonstrate superior responsiveness to interferon-α therapy compared to those with genotype D. Conversely, genotype B is associated with higher rates of antiviral resistance than genotype C (Sumi et al. 2003, Erhardt et al. 2005). This study aims to assess the prevalence and genotype distribution of the hepatitis B virus (HBV) among patients presenting with jaundice in Ibb City, Yemen, and evaluating host associated risk factors.

SUBJECTS AND METHODS

Study Design and Location

This multi-center cross-sectional study was conducted at the main Hospitals and clinics in Ibb city Yemen (Al Thawra hospital, Maternity and childhood hospital, Naser hospital and Alpha medical laboratories). From January 2024 to December 2025, all patients attending these hospitals and clinics suffering from jaundice were included in the study.

Specimen Collection and Laboratory Investigation

Laboratory work was carried out at National Center of Public Laboratories (NCPHL). First, five milliliters of venous blood were drawn from patients under sterile conditions after obtaining their informed consent (collection done by the first author). Serum was separated in three aliquots, one for biochemical tests alanine aminotransferase and aspartate aminotransferase (ALT, AST), one for serological tests (HBV markers test) and the third one for PCR (polymerase chain reaction), genome detection and genotyping.

Serological tests (HBV markers):

Enzyme-linked immunosorbent assay ELISA (ARCHITECT PLUS, Abbott) system was used for detection hepatitis B markers (HBsAg, anti HBs, and anti-HBc IgG).

Estimation of the serum levels of alanine and aspartate transaminase

Enzyme-linked immunosorbent assay ELISA(BECKMAN COULTER, AU480) system was used for the liver function tests including serum alanine aminotransferase and aspartate aminotransferase levels.

Determination of HBV DNA by conventional PCR

a. Virus DNA extraction and PCR amplification

As directed by the manufacturer, HBV DNA was extracted using Ribo Virus kit from sacace,For further examination, extracted DNA was kept at -20°C. The AccuPower® ProFi Taq PCR PreMix (Bioneer Korea-Bio metre system, Germany) was used to amplify HBV-DNA utilising 1508 bp of P through S genes employing universal primers. The (FA2F) sense primer was reported by the (S1-2) antisense primer that was described by Naito et al., (Naito et al. 2001, Rashid and Salih 2014), as indicated in Table 1. One cycle of the PCR programme involved denaturation at 94°C for five minutes, followed by 35 cycles of denaturation at 94°C for thirty seconds, annealing at 57°C for one minute, and extension at 72°C for one and a half minutes. The last extension lasted five minutes at 72°C.

b. Determination of HBV genotypes

The six genotypes A through F of HBV were determined using type-specific primers in a nested PCR-based genotyping system (AccuPower® Gold Multiplex PCR PreMix from Bioneer-Bio metar system, Germany). The conserved nucleotide sequences in sections of the P through S genes served as the basis for the construction of the nested PCR primers. The six HBV genotypes listed in Table 2 can be identified based on variations in the amplified DNA sizes. For each sample, two nested PCRs were carried out using different mixtures: mix 1 (sit 1) used the B2 sense universal primer to identify genotypes A, B, and C, while mix 2 (set 2) used the B2R antisense universal primer to identify genotypes D, E, and F. 1µL of

the first-round PCR result from mixes A and B, 1µl of each type-specific primer (10 p mole), and 11µl of dd-H2O make up the nested PCR mixture. The conditions used to amplify nested PCRs were as follows: 10 minutes of initial denaturation at 95°C, 20 cycles of amplification at 94°C for 20 seconds, 58°C for 20 seconds, and 72°C for 30 seconds, and 20 cycles of 94°C for 20 seconds, 60°C for 20 seconds, and 72°C for 30 seconds. Amplicon products were electrophoresed on a 3% agarose gel, stained with ethidium bromide, and evaluated under UV light.

Data collection

A pre-made questionnaire was used to collect individual data, including laboratory results, risk factors for hepatitis virus infection, frequency of dialysis, demographic information.

Statistical analysis

To identify potential risk variables for HBV infection, the data were examined in a comparative positive anti-core with negative one format. The chi-square test was used to depict the Relative Risk (RR) and their 95% confidence intervals (CI). Using 2x2 tables, values (RR, CI, $\chi 2$) were calculated to establish prospective RR on the occurrence of HBV and their relevance. If the p-value was 0.05 or below, the result was considered statistically significant.

RESULTS

1.1.Sociodemographic characteristic of the study population

The study included of 256 patients with jaundice who underwent hepatitis B virus (HBV) genotype testing at major hospitals in Ibb, Yemen. Regarding gender, the disease disproportionately affected males, who comprised 82.4% (n = 211) of patients, compared to only 17.6% (n = 45) of females. Patients ranged in age from 3 months to 85 years, with a mean age of 34.8 years (± 21.7 years). The highest proportion of patients was between 16 and 35 years old (57.4% of the total), while children under 16 years of age constituted only 10.2%, and those over 45 years of age comprised 22.3% Table 1 .

Table 1
Age and gender distribution of 256 patients with jaundice who were tested for hepatitis B virus genotype among those arriving at major hospitals in Ibb City, Yemen.

Characters	N	%
Gender		
Male	211	82.4
Female	45	17.6
Age in Years		
Less than 16 years	26	10.2
16–25 years	77	30.1
26–35 years	70	27.3
36–45 years	26	10.2
> 45 years	57	22.3
Total	256	100
Mean	34.8 years	
SD	21.7 years	
Min	3 months	
Max	85 years	

1.2. Distribution of the possible causes of jaundice

The possible causes of jaundice in 256 patients at major hospitals in Ibb City, Yemen, who underwent hepatitis B virus genotype testing. The data indicate that the largest group was undiagnosed cases (37.5%). The most common identified cause was hepatitis B (25.4%). Given that hepatocellular/intrahepatic jaundice represented the majority of diagnosed cases, including viral and parasitic infections, the number of hepatitis B cases was 65 patients (25.4%), viral hepatitis (other types) was 27 patients (10.5%), schistosomiasis was 12 patients (4.7%), malaria was 11 patients (4.3%), and dengue fever was 2 patients (0.8%). The second most common cause of hepatocellular/intrahepatic jaundice was autoimmune diseases and infections. These included autoimmune hepatitis in 19 patients (7.4%), drug-induced liver injury in 15 patients (5.9%), and bacterial infection in 2 patients (0.8%). Hemolysis and erythropoiesis disorders, conditions associated with the breakdown of red blood cells, included hemolytic uremic syndrome in 8 patients (3.1%), erythropoiesis disorders in 6 patients (2.3%), paroxysmal nocturnal hemoglobinuria in 2 patients (0.8%), and hematologic uptake and intensive transfusions in 2 patients (0.8%). Bilirubin conjugation and intrahepatic cholestasis, conditions related to

the liver's processing of bile pigments, included bilirubin conjugation in 5 patients (2.0%) and intrahepatic cholestasis in 2 patients (0.8%)Table 2.

Table 2
The distribution of different causes of jaundice among 256 jaundice patients who had their HBV genotype checked in the main hospitals in Ibb city, Yemen.

Presumptive Diagnosis	**N**	**%**
Ineffective Erythropoiesis	6	2.3
Hemolysis		
Hemolytic-uremic syndrome	8	3.1
Paroxysmal nocturnal hemoglobinuria	2	0.8
Resorption of Hematomas and Massive Blood Transfusions	2	0.8
Hepatocellular / Intrahepatic Jaundice		
1-Viral & Parasitic Infections		
HBV (Hepatitis B)	65	25.4
Viral hepatitis (other)	27	10.5
Schistosomiasis	12	4.7
Malaria	11	4.3
Dengue fever	2	0.8
2- Autoimmune & Inflammatory		
Autoimmune hepatitis	19	7.4
Drug-induced liver injury	15	5.9
Bacterial infections	2	0.8
Conjugation of Bilirubin	5	2
Intrahepatic Cholestasis	2	0.8
Undiagnosed: 96	96	37.5

1.3. Distribution and interpretation of HBV markers among the jaundice patients

Table 3
The interpretation of HBV markers among the jaundice patients in Ibb city.

HBV markers	N (%)	Interpretation
Positive HB surface antigen (HBsAg)	51/256 (19.9%)	Indicates active HBV infection. This can be either acute or chronic. The virus is present; requires staging to differentiate between acute or chronic states.
positive HB core Antibodies	85/256 (33.3%)	Indicates a history of exposure to the actual virus. It does not appear from vaccination. More than a third of the cohort has been exposed to the wild-type virus at some point.
Positive anti-HBV surface Antigen antibodies (anti-HBs)	89/256 (34.7%)	Indicates immunity to HBV. This comes from either a cleared natural infection or vaccination. These individuals are protected against the virus (via past resolved infection or vaccination).
positive HB- core antibodies with negative HBsAg	5/256 (2%)	Resolved Past Infection **or** Isolated Anti-HBc. The infection was likely cleared naturally, though occult infection or a false positive is possible.
positive HBc Ab with HBsAg	46/256 (18%)	Chronic (or Acute) HBV Infection. Exposure occurred (HBcAb+) and the virus is actively present (HBsAg+). This accounts for most of the infected group.
positive HB core Ab with anti-HBsAg antibodies	13/256 (5.1%)	Resolved Natural Infection. The individual was exposed to the virus in the past but successfully cleared it and developed protective immunity.
positive DNA	65/256 (25.4%)	Indicates active viral replication and infectivity.
positive DNA with negative HBs Ag	16/256 (6.25%)	Occult Hepatitis B Infection (OBI). The virus is actively replicating in the liver/blood, but the surface antigen is undetectable. Crucial clinical finding.

1.4. Prevalence of hepatitis B surface antigen according to age and gender

Table 4 show the prevalence of hepatitis B surface antigen (HBsAg) among 256 patients with jaundice at major hospitals in Ibb, Yemen, with positive cases categorized by age and gender. Of these patients, 51 tested positive for HBsAg. The overall prevalence was approximately 19.9%. The mean age of patients with HBsAg was 26.4 ± 8.2 years (range 18–37 years). The highest prevalence rates were recorded in the 16–25 and 26–35 age groups, with positivity rates of 32.5% and relative risk of 2.2 ($p = 0.001$), and 35.7% and relative risk of 2.6 ($p = 0.0001$), respectively. No positive cases were recorded in patients younger than 16 years or older than 45 years. Regarding gender distribution, males showed a higher positivity rate (21.3%) with a relative risk of 1.5 compared to females (13.3%). However, statistical analysis (P-value > 0.05) indicates that this gender difference is not statistically significant Table 4.

Table 4
Prevalence of hepatitis B surface antigen (HBsAg) in 256 jaundice patients in major hospitals in Ibb City, Yemen, by age and gender

Characters	N (n = 51)	%	RR	95CI	z	p
Gender						
Male n = 211	45	21.3	1.5	0.72–3.5	1.2	0.24
Female n = 45	6	13.3	0.62	0.28- 1.4	1.2	0.24
Total n = 256						
Age groups						
Less than 16 years n = 26	0	0.0	0.08	0.005-1.3	1.7	0.07
16–25 years n = 77	25	32.5	2.2	1.3–3.6	3.3	0.001
26–35 years n = 70	25	35.7	2.6	1.5–4.1	3.9	0.0001
36–45 years n = 26	1	3.8	0.17	0.02–1.2	1.7	0.07
> 45 years n = 57	0	0.0	0.03	0.002-0.5	2.4	0.01
Mean	26.4 years					
SD	8.2 years					
Min to Max	18–37 years					

1.5. Prevalence of HB Core IgG antibodies according to age and gender

Table 5 shows the prevalence of hepatitis B virus (HB) nucleoprotein IgG antibodies among 256 patients with jaundice in Ibb, Yemen, detailing the prevalence by age and gender. Of the total sample, 85 patients (33.2%) tested positive for antibodies. The highest prevalence was observed among males, with 78 out of 211 male patients testing positive (37%, p = 0.01). In contrast, the prevalence among females was significantly lower, with only 7 out of 45 testing positive (15.6%). Regarding age, the 26–35 age group had the highest and most statistically significant prevalence, with 39 out of 70 patients testing positive (55.7%, RR = 2.2, p < 0.0001). The prevalence decreased significantly in older age groups, reaching 10.5% among patients over 45 years of age (p = 0.0008). The mean age of patients with positive hepatitis B (HB) IgG antibodies was 29.1 ± 15.4 years, with a wide range of ages from 4 to 70 years Table 5.

Table 5
Prevalence of HB Core IgG antibodies in 256 jaundice patients in Ibb city, Yemen.by age and gender.

Characters	N (85)	%	*RR*	*95%CI*	*Z*	*p*
Gender						
Male n = 211	78	37	2.4	1.2–4.7	2.4	0.01
Female n = 45	7	15.6	0.4	0.2–0.85	2.4	0.01
Total n = 256	85	33.2				
Age groups						
Less than 16 years n = 26	7	26.9	0.79	0.41–1.5	0.68	0.49
16–25 years n = 77	26	33.8	1.02	0.7–1.4	0.12	0.89
26–35 years n = 70	39	55.7	2.2	1.6–3.1	4.8	< 0.0001
36–45 years n = 26	7	26.9	0.79	0.41–1.5	0.068	0.49
> 45 years n = 57	6	10.5	0.26	0.12–0.57	3.35	0.0008
Mean	29.1 years					
SD	15.4 years					
Min to Max	4–70 years					

1.6. Prevalence of hepatitis B virus (HBV) DNA according to age and gender

Table 6 illustrates the prevalence of hepatitis B virus (HBV) DNA in a sample of 256 patients with jaundice in Ibb, Yemen. The data highlight the significant variability in infection rates according to age and gender. The total sample consisted of 256 patients with jaundice, with a mean age ± 15.4 ± 31.1 years, ranging from 18 to 70 years. There were 65 HBV-positive cases, representing an overall prevalence of 25.4%. Males exhibited a higher infection rate and a higher relative risk compared to females, with 58 positive cases out of 211 (27.5%) in males, at a relative risk (RR) of 1.8 (p = 0.1). In contrast, 7 positive cases out of 45 (15.6%) were in females, at a relative risk of 1.56 (p = 0.1). Looking at the prevalence by age group, infection rates vary considerably, with the highest number of positive cases concentrated among young adults and middle-aged adults. In the under-16 age group, 0 out of 26 cases (0.0%) were positive, with a relative risk (RR) of 0.07 (p = 0.054). In the 16–25 age group, 26 out of 77 cases (33.8%) were positive, with a relative risk (RR) of 1.5 (p = 0.04). In the 26–35 age group, 26 out of 70 cases (37.1%) were positive, with a relative risk (RR) of 1.8 (p = 0.006), which was the group with the highest prevalence. In the 36–45 age group, 7 out of 26 (26.9%) tested positive, with a relative risk (RR) of 1.1 (p = 0.8). Finally, in the 45-year age group, 6 out of 57 (10.5%) tested positive, with a relative risk of 0.35 (p = 0.009). The data show statistically significant differences in hepatitis B virus (HBV) DNA detection

among jaundice patients in Ibb, particularly among individuals aged 16–35. In contrast, HBV DNA was not detected in children under 16 years of age in this specific sample Table 6.

Table 6
Prevalence of hepatitis B virus DNA in 256 jaundice patients in Ibb city, Yemen by age and gender.

Characters	N (65)	%	RR	95%CI	Z	p
Gender						
Male n = 211	58	27.5	1.8	0.86–3.6	1.56	0.1
Female n = 45	7	15.6	1.56	0.27–1.15	1.56	0.1
Total n = 256	65	25.4				
Age groups						
Less than 16 years n = 26	0	0.0	0.07	0.004-1.1.	1.9	0.054
16–25 years n = 77	26	33.8	1.5	1.02–2.3	2.05	0.04
26–35 years n = 70	26	37.1	1.8	1.2–2.7	2.7	0.006
36–45 years n = 26	7	26.9	1.1	0.54–2.1	0.19	0.8
> 45 years n = 57	6	10.5	0.35	0.16–0.77	2.6	0.009
Mean	31.1 years					
SD	15.4 years					
Min to Max	18–70 years					

1.7. Prevalence of hepatitis B virus (HBV) genotypes among 65 patients

Table 7 shows the prevalence of hepatitis B virus (HBV) genotypes among 65 patients with jaundice in Ibb, Yemen. It details the frequency of each individual genotype (A, B, and D) and mixed genotype (a combination of multiple genotypes) present in the patients. Among the 65 patients, genotype D was the most prevalent, representing 32.3% of cases (n = 21) with a prevalence ratio of 1:3. Genotype B was present in 13 patients (20.0%) with a prevalence ratio of 1:5. Genotype C was present in 9 patients (13.8%) with a prevalence ratio of 1:7. Mixed infections with different genotypes were present in 22 patients (33.8%). The study details three main groups: the first is the mixed group A + B+C + D+E in 11 patients (16.9%) with an infection rate of 1:6, followed by the mixed group A + B+C + D+E + F in 6 patients (9.2%) with an infection rate of 1:11, and finally the mixed group A + B+C + D in 5 patients (7.7%) with an infection rate of 1:13. Overall, the infection rate with mixed genotypes was 33.8%, while the infection rate with the pure D genotype was 32.3%, which represents the vast majority of hepatitis B cases in these jaundice patients Table 7.

Table 7
Distribution of HBV genotypes in jaundice patients (65 patients). in Ibb city, Yemen

Genotype	n	%	95%CI number count	Incidence rate	95% CI
A	9	13.8	4.1–17	1:7	1:16–1:4
B	13	20	6.9–22.2	1:5	1:9 – 1:3
D	21	32.3	12.9–32.1	1:3	1:5 – 1:2
Mix-A + B+C + D+E + F	22	33.8	13.7 to 33.3	1:3	1:5 to 1:2
Total	65	100			
Mix					
A + B+C + D	5	7.7	1.6–11.6	1:13	1:40 – 1:6
A + B+C + D+E	11	16.9	5.4–19.6	1:6	1:12 to 1:3
A + B+C + D+E + F	6	9.2	2.2–13.1	1:11	1:30 to 1:5
Total Mix	22	33.8			

DISCUSSION

The current data show a striking gender disparity, with males comprising 82.4% (*n* = 211) of the study population compared to just 17.6% (*n* = 45) for females. This high male-to-female ratio is a common observation in jaundice studies. Several factors related to microbial infections typically drive this imbalance, as men may have higher exposure to risk factors such as occupational hazards, traditional shaving practices in barber shops, or higher rates of medical and dental procedures outside the home. Furthermore, in certain regions, socioeconomic factors can lead to men accessing diagnostic and hospital care more frequently than women, potentially causing an overrepresentation in hospital-based data. Additionally, regarding biological and immunological differences, some clinical literature suggests that biological factors or sex hormones might influence the clearance or progression of hepatitis infections particularly HBV infection though behavioral exposure usually plays the primary role (Al-Shami et al. 2021). In the current study, the age distribution shows a high concentration of cases among young to middle-aged adults, with the highest proportion of patients falling between 16 and 35 years old (57.4%). This age bracket represents the most socially, professionally, and sexually active segment of the population. Transmission via horizontal routes (such as unsafe injections, minor surgical procedures, or sexual contact) is highly prevalent in this age group (World Health Organization 2017, Al-Shami et al. 2021). In the current study, Children under 16 years of age constituted only 10.2% of the total cohort, this is might reflect the positive impact of national childhood immunization programs against HBV (such as the integration of the HepB vaccine into the expanded program on immunization), which helps protect younger generations from vertical (mother-to-child) and early childhood transmission. Also, this low rate among children might be due to Asymptomatic Infections where HBV infections acquired during

childhood are frequently asymptomatic. Since this study specifically looked at patients presenting with *jaundice*, infected children may have been missed because they rarely develop icteric (jaundiced) symptoms compared to adults. In addition, Patients over the age of 45 comprised 22.3% of the population. The wide age range (up to 85 years) with a mean age of 34.8 years highlights that HBV remains a lifelong medical concern in the region. Older individuals are more likely to have accumulated lifetime exposure to risk factors before the advent of modern blood screening and vaccination protocols, and they face a higher risk of progressing to chronic liver complications (World Health Organization 2017, Bernal and Wendon 2013) Table 1.

Hepatitis stems from several primary causes, which are generally classified as metabolic, ischemic, infectious, genetic, or autoimmune, among others. Within the metabolic category, the main triggers are prescription medications, toxins most notably alcohol and nonalcoholic fatty liver disease. Additionally, both autoimmune and genetic forms of hepatitis are linked to hereditary predispositions and typically impact specific patient demographics (Al-Shami et al. 2021, Mutahar et al. 2022). In the current study, *viral hepatitis* (combining hepatitis B and other types) accounts for more than a third of all cases (35.9%). Because this study specifically looked at patients undergoing HBV genotype testing, the high percentage of hepatitis B (25.4%) is expected, but it underscores a heavy public health burden. In Yemen, viral hepatitis remains a major cause of chronic liver disease and cirrhosis, often exacerbated by limited access to infant vaccination programs and public health awareness (Al-Shami et al. 2021, Al-Shamahy et al. 2019, Al-Shamahy et al. 2011, Al-Shamahy et al. 2003, Amran et al. 2019).

The presence of schistosomiasis (4.7%) and malaria (4.3%) reflects the environmental and epidemiological landscape of the Ibb Governorate, where these infections are endemic **(**Sady et al. 2013). Schistosomiasis (Bilharzia) is also endemic in many rural and valley areas of Yemen, leading to periportal fibrosis and portal hypertension, which complicate liver function. Furthermore, malaria and dengue fever cause jaundice primarily through hemolysis (the destruction of red blood cells) and direct, acute liver injury (malarial hepatitis); these two infections are well-known to be endemic in Yemen (Al-Thamari et al. 2026, Edrees et al. 2021). Autoimmune hepatitis (7.4%) and drug-induced liver injury (DILI) (5.9%) represent the second most common sub-group of intrahepatic jaundice. The prevalence of DILI is particularly noteworthy; in Yemen, this is frequently linked to self-medication, unregulated over-the-counter antibiotic/NSAID use, or the consumption of traditional herbal remedies and certain crops like Qat, which may be treated with toxic pesticides (Mutahar et al. 2022, Othman, et al. 2017). Finally, the fact that 37.5% of patients with jaundice remained undiagnosed is a critical finding. This high percentage points to several likely systemic challenges in Ibb City's healthcare infrastructure, including the limited availability of advanced molecular diagnostic tools or comprehensive viral panels (e.g., HDV, HEV, or rare metabolic screenings), financial barriers preventing patients from completing full diagnostic workups, and overlapping clinical symptoms where a definitive primary cause is difficult to isolate without an advanced liver biopsy or specialized imaging (Ishak, et al. 2021). These findings suggest that most patients in this study might be infected with other pathogens such as bacteria, parasites, or alternative viruses or could be experiencing other previously noted causes of hepatitis (Bernal and Wendon 2013) Table. Although viral infections represent the leading cause of hepatitis globally (47-WHO 2013), this

study presents a different trend, showing that 72.4% of the patients may have non-viral or unexamined origins for their condition. This variation likely occurs because the study only tested for three specific viruses, leaving other forms of viral hepatitis uninvestigated. Broadly speaking, viral hepatitis is triggered by five distinct viruses: hepatitis A, B, C, D, and E (Dienstag 2015).

The present study identified an overall HBV prevalence of approximately 19.9%, with HBsAg-positive patients presenting a mean age of 26.4 ± 8.2 years (range: 18–37 years) Table 3. The infection was most pronounced in the 16–25 and 26–35 age cohorts, which demonstrated positivity rates of 32.5% (RR = 2.2, p = 0.001) and 35.7% (RR = 2.6, p = 0.0001), respectively. These findings align with prior Yemeni literature (Al-kadassy et al. 2019, AL-Marrani et al. 2018, Murad et al 2013, Al-Shamahy et al. 2019, Al-Shamahy et al. 2011, Al-Shamahy et al. 2003, Amran et al. 2019), where HBV prevalence spans from 1% in the general public to 20% within high-risk cohorts, such as healthcare professionals and hemodialysis patients. Despite the availability of the hepatitis B vaccine in Yemen for roughly 22 years, transmission persists across national hospitals. Broad vaccine utilization remains heavily restricted by high costs, a lack of government prioritization, and the infrastructure disruptions caused by 15 years of ongoing domestic conflict Table 4.

The study revealed a high overall exposure burden, with 33.2% (85 out of 256 patients**)** testing positive for hepatitis B nucleoprotein IgG antibodies. Because anti-HBc IgG signifies a past or present exposure rather than an active, acute infection, this finding demonstrates that one-third of the symptomatic cohort has a history of HBV infection (Feindiri et al.2021). Furthermore, the substantial disparity between male (37%) and female (15.6%) exposure rates indicates distinct risk behaviors, environmental factors, or social structures within the Ibb region. Men in this socio-economic environment appear to face more frequent exposure via horizontal transmission routes, including community-level risks such as unsterilized razors at traditional barbershops, traditional cupping therapy (Hijama), or specific occupational hazards (H Ahmed et al.2024, Al-kadassy et al. 2019, AL-Marrani et al. 2018, - Murad et al 2013) Table 5. The male predominant, might be due to Healthcare Access Biases in which **t**he sample sizes themselves (211 males versus only 45 females) signal a pronounced healthcare seeking imbalance or an artifact of sample collection, which might skew findings if women with mild jaundice are less likely to seek institutional clinical testing. Regarding the prevalence of Hepatitis B virus (HBV) DNA among jaundice patients in Ibb, Yemen Table 6. The study reveals a high overall HBV prevalence of 25.4% (65 out of 256 patients) within this symptomatic (jaundiced) cohort. This confirms and indicates that Hepatitis B is a major underlying cause of acute liver injury or chronic liver decompensation in the region (Al-kadassy et al. 2019, AL-Marrani et al. 2018).

The epidemiological and clinical significance of the Hepatitis B virus (HBV) genotype distribution among jaundice patients in Ibb, Yemen. The finding that genotype D is the most prevalent single genotype (32.3%, n = 21) aligns perfectly with the established global and regional epidemiology of HBV Table 7. Genotype D is known to be the most widespread genotype globally and is overwhelmingly dominant in the Middle East, the Mediterranean basin, and parts of Central Asia also in Yemen (Al-Shawkany et al. 2021). Considering, Clinical Implications, Genotype D is historically associated with a higher rate of

progression to chronic hepatitis, higher incidences of cirrhosis, and a elevated risk of developing hepatocellular carcinoma (HCC) compared to genotypes like A or B (Dienstag 2015).

Regarding treatment response, patients infected with HBV genotype D typically exhibit lower response rates to interferon-alpha therapy compared to those with genotypes A or B. Consequently, nucleoside/nucleotide analogues, such as entecavir or tenofovir, are frequently preferred as first-line options (Al-Shawkany et al. 2021). Given these clinical implications, the primary objective of this study was to evaluate the prevalence of HBV genotypes in Yemen. Utilizing a polymerase chain reaction (PCR)-based method, this molecular genotyping of the hepatitis B virus among jaundice patients represents one of the pioneering efforts of its kind in the country (Al-Shawkany et al. 2021). While historical data on HBV genotypes and mutations in Yemeni patients remains scarce, prior research has successfully investigated HCV genotyping within the region (Rashid and Salih 2014)

In the present study, mixed infections involving multiple genotypes were observed in 22 patients (33.8%). These were categorized into three primary combinations: genotype mixture A + B+C + D+E was found in 11 patients (16.9%; 1:6 ratio), followed by A + B+C + D+E + F in 6 patients (9.2%; 1:11 ratio), and A + B+C + D in 5 patients (7.7%; 1:13 ratio). This high prevalence of mixed infections aligns with local and regional data reported by Rashid and Saleh (Rashid and Salih 2014) in Iraq, where all studied patients exhibited mixed infections, as well as findings by Al-Moshaky et al. (Al-Shawkany et al.2021) in Yemen. Conversely, our results contrast with global literature, which generally identifies single-genotype dominance in most patient populations (Matsuura et al. 2009, Świderska, et al. 2015, Hundie et al. 2016, Rahman et al. 2016, Lampe et al. 2017). For example, in neighbouring Saudi Arabia, genotype D is the most prevalent among chronic hepatitis B (CHB) patients. Similarly, studies in the United Arab Emirates demonstrate that Emirati viral hepatitis patients are predominantly infected with either genotype D or A. Furthermore, research from Egypt indicated that the sub-D1 genotype was the preeminent strain among all CHB patients carrying genotype D (Al-Qahtani 2020, Alfaresi 2012, El-Mowafy et al. 2017).

CONCLUSIONS

The vast majority of jaundice patients in Ibb City are male (82.4%), indicating either a higher susceptibility to the underlying causes of jaundice among men in this region or a significant gender disparity in healthcare-seeking behaviour and access. The leading cause of jaundice is undiagnosed (37.5%), highlighting a critical gap in local diagnostic capabilities, a lack of comprehensive screening tools, or the presence of less common, untested aetiologies. Hepatitis B virus (HBV) is the primary identified cause of jaundice, responsible for 25.4% of cases. Depending on the test used, the overall presence of HBV among the patients ranges from 19.9% (via HBsAg positivity) to 33.2% (overall positive testing). Men in this cohort are significantly more affected by HBV than women. Men show notably higher rates of both HBsAg positivity (21.3% vs. 13.3%) and overall HBV infection (37% vs. 15.6%). Genotype D is the most common single strain (32.3%) among the genotyped jaundice patients, followed by genotypes B and C. Crucially, mixed genotypes are highly prevalent (33.8%), which points to frequent co-infections and poses complex challenges for targeted antiviral treatments.

Abbreviation

HIV Human immunocompromised virus

AIDS Acquired immunodeficiency syndrome

HBV Hipatitis B virus

PCR polymerase chain reaction

HSC_S Hepatic stellate cells

NCPHL National Center of Public Laboratories

ALT Alanine Aminotransferase

AST Aspartate Aminotransferase

ELISA Enzyme-linked immuonosorbent Assay

RR relative risk

CI confidence intervals

Declarations

Ethics approval and consent to participate

The study protocol and data collection instrument were approved by Sana’a University's Faculty of Medicine and Health Sciences (Approval No. IRB-IU-2024-012) and were carried out in accordance with the Declaration of Helsinki and Yemeni public health laws and regulations. All participants provided written informed consent before participating in the study. Participants were clearly explained the study's objectives in the questionnaire's introduction. Participants were assured of strict confidentiality and anonymity, as no personal identifying information was collected. Furthermore, no negative consequences would result if the prospective participant did not choose to participate.

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Consent for publication

Not applicable.

Competing Interests

Not applicable

Conflict of interest

The authors declare that they have no competing interests.

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Author Contribution

Eglal Q , Hassan A conceived the study; Eglal Q,Wadee A collected the data; Eglal Q processed the data; Eglal Q I analyzed and interpreted the data. Eglal Q , Hassan A wrote the first draft manuscript. Eglal Q , Hassan A,Wadee A reviewed and edited the final manuscript. All authors revised and approved the manuscript for submission.

Data Availability

The datasets used and analyzed during this analysis are available from the corresponding author, who will provide any relevant data upon reasonable request.

References

1. Alfaresi MS. Molecular epidemiological study of the Hepatitis B virus in the United Arab Emirates based on the analysis of the Pre-S gene. J Med Microb Diagn. 2012;1:4.
2. Al-kadassy AM, Al-Ashiry AFS, Al-Shamahy HA. Sero-epidemiological study of hepatitis B, C, HIV and Treponema pallidum among blood donors in Hodeida city- Yemen. Univers J Pharm Res. 2019;4(2):1–8. https://doi.org/10.22270/ujpr.v4i2.256.
3. AL-Marrani WHM, Al-Shamahy HA. Prevalence of HBV and HCV; and their associated risk factors among public health center cleaners at selected public health centers in Sana’a city-Yemen. Univers J Pharm Res 2018:3 (5):1–8. https://doi.org/10.22270/ujpr.v3i5.204
4. Almezgagi MM, Edrees WH, Al-Shehari WA, Al-Moyed K, Al-Khwlany RS, Abbas AB. Prevalence of Hepatitis B Virus and Hepatitis C Virus and Associated Risk Factors among Haemodialysis Patients in Ibb City, Yemen. PSM Microbiol. 2020;5(2):32–40.
5. Al-Qahtani AA, Pourkarim MR, Trovão NS, et al. Molecular epidemiology, phylogenetic analysis and genotype distribution of hepatitis B virus in Saudi Arabia: Predominance of genotype D1. Infect Genet Evol. 2020;77:104051. https://doi.org/10.1016/j.meegid.2019.104051.

6. Al-Shamahy HA, Ajrah MA, Al-Madhaji AG, et al. Prevalence and potential risk factors of hepatitis B virus in a sample of children in two selected areas in Yemen. Univers J Pharm Res. 2019;4(3):1–5. https://doi.org/10.22270/ujpr.v4i3.269.
7. Al-Shamahy HA, Hanash SH, Rabbad IA, Al-Madhaji NM, Naser SM, Hepatitis B. Vaccine Coverage and the Immune Response in Children under ten years old in Sana'a, Yemen. Sultan Qaboos Univ Med J. 2011;11(1):77–82. PMID: 21509212.
8. Al-Shamahy HA, Rabbad IA, Al-Hababy A. Hepatitis B virus serum markers among pregnant women in Sana'a, Yemen. Ann Saudi Med. 2003;23:87–9. https://doi.org/10.5144/0256-4947.2003.87.
9. AL-Shamahy HA. Prevalence of Hepatitis B surface antigen and Risk factors of HBV infection in samples of healthy mothers and their infants in Sana'a, Yemen. Ann Saudi Med. 2000;20:464–7. https://doi.org/10.5144/0256-4947.2000.464.
10. Al-Shami HZ, Al-Mutawakal ZAM, Al-Kholani AIM, Al-Haimi MA, Al-Haddad AM, Ahmed RA, Al-Somainy AA, Al-Shamahy HA. Prevalence of Hepatitis A virus, Hepatitis B virus, and Hepatitis C virus, among patients with hepatic jaundice in Sana’a city, Yemen: A hospital based study. Univers J Pharm Res. 2021;6(6):12–7. https://doi.org/10.22270/ujpr.v6i6.693.
11. Al-Shawkany EM, AlShawkany ARM, Al-Shamahy HA, et al. Prevalence of different hepatitis b virus genotypes and risk factors associated among selected Yemeni patients with chronic hepatitis B infection. Univers J Pharm Res. 2021;6(3):1–8. https://doi.org/10.22270/ujpr.v6i3.603.
12. Al-Tubaikh JA. (2017). Internal Medicine. 10.1007/978-3-319-39747-4. ISBN 978-3-319-39746-7.
13. Amran OAA, Al-Shamahy HA, Al Hadad AM, Jaadan BM. Explosion of hepatitis B and C viruses among hemodialysis patients as a result of hemodialysis crisis in Yemen. Univers J Pharm Res. 2019;4(5):1–8. https://doi.org/10.22270/ujpr.v4i5.311.
14. Awan Z, Idrees M, Amin I, Butt S, Afzal S. Pattern and molecular epidemiology of hepatitis B virus genotypes circulating in Pakistan. Infect Genet Evol. 2010;10:1242–6. https://doi.org/10.1016/j.meegid.2010.08.006.
15. Bassari R, Koea JB. Jaundice associated pruritis: a review of pathophysiology and treatment. World J Gastroenterol. 2015;21(5):1404–13. https://doi.org/10.3748/wjg.v21.i5.1404. . PMC 4316083. PMID 25663760.
16. Bernal W, Wendon J. Acute Liver Failure. New Engl J Med. 2013;369(26):2525–34. https://doi.org/10.1056/nejmra1208937.
17. Chan HL, Wong ML, Hui AY, et al. Hepatitis B virus genotype C is associated with more severe liver fibrosis than genotype B. Clin Gastroenterol Hepatol. 2009;7:1361–6. https://doi.org/10.1016/j.cgh.2009.08.004.
18. Datta S. An overview of molecular epidemiology of hepatitis B virus (HBV) in India. Virol J. 2008;5:156. https://doi.org/10.1186/1743-422X-5-156.
19. Dienstag JL. Chapter 360: Acute Viral Hepatitis. In Kasper, D; Fauci, A; Hauser, S; Longo, D; Jameson, J; Loscalzo, J, editors. Harrison's Principles of Internal Medicine 2015; 19e. New York, NY: McGraw-Hill. ISBN 978-0-07-180215-4.

20. Edrees WH, Mogalli NM, Alabdaly KW. Assessment of some clinical and laboratory profiles among dengue fever patients at Hajjah government, Yemen. Univers J Pharm Res. May 2021;6(2). 10.22270/ujpr.v6i2.571.
21. El-Mowafy M, Elgaml A, El-Mesery M, Elegezy M. Molecular analysis of Hepatitis B virus sub-genotypes and incidence of preS1/preS2 region mutations in HBV-infected Egyptian patients from Mansoura. J Med Virol. 2017;89(9):1559–66. https://doi.org/10.1002/jmv.24828. Epub 2017 May 23.
22. Erhardt A, Blondin D, Hauck K, Sagir A, Kohnle T, et al. Response to interferon alfa is hepatitis B virus genotype dependent: genotype A is more sensitive to interferon than genotype D. Gut. 2005;54:1009–13. https://doi.org/10.1136/gut.2004.060327.
23. Feindiri M, Kabbaj H, El Mzibri M, Belkadi B, Bouihat N, Filali-Maltouf A, Seffar M. Prevalence of Hepatitis B Virus Infection Markers among Patients of the Ibn Sina University Hospital Center (Rabat, Morocco). Intervirology. 2022;65(2):80–6. Epub 2021 Sep 10. PMID: 34518480; PMCID: PMC9153348.
24. Gan C, Yuan Y, Shen H, Gao J, Kong X, Che Z, Guo Y, Wang H, Dong E, Xiao J. Liver diseases: epidemiology, causes, trends and predictions. Signal Transduct Target Ther. 2025;10(1):33. https://doi.org/10.1038/s41392-024-02072-z. . PMID: 39904973; PMCID: PMC11794951.
25. Ahmed R, Al-Nagar N, Al-Subol I, Al-Wahbi R, Al-Sabahi M, Al-Sabahi M, Al-Sabahi K, Shomasi A, Al-Hamodi A. The Prevalence and Associated Factors of Hepatitis B and C Virus in Hemodialysis Patients in Ibb Governorate, Yemen. Cureus. 2024;16(9):e70112. https://doi.org/10.7759/cureus.70112. . PMID: 39449939; PMCID: PMC11501098.
26. Hundie GB, Raj VS, Michael DG, et al. Molecular epidemiology and genetic diversity of hepatitis B virus in Ethiopia. J Med Virol. 2016;88(6):1035–43. https://doi.org/10.1002/jmv.24437. Epub 2015 Dec 22.
27. Ishak AA, Alhadi AM, Al-Shamahy HA. Local experience of telemedicine: examples of cases in Yemen. Univers J Pharm Res. 2021;6(1):1–8. https://doi.org/10.22270/ujpr.v6i1.537.
28. Janahi EM, Ilyas Z, Al-Othman S, Darwish A, et al. Hepatitis B virus genotypes in the Kingdom of Bahrain: Prevalence, gender distribution and impact on hepatic biomarkers. Medicina. 2019;55:622. https://doi.org/10.3390/medicina55100622.
29. Al-Thamari JAM, Al-Moyed KA, Al-Nuzaili MA. Ahmed Mohammed Al-Haddad, and Hassan Abdulwahab Al-Shamahy. Blood indicators and peripheral blood counts for malaria patients in al-Hodeida city, Yemen. Univers J Pharm Res. 2026;11(2):1–8. https://doi.org/10.22270/ujpr.v11i2.1530.
30. Kaplan M, Hammerman C. Hereditary Contribution to Neonatal Hyperbilirubinemia. Fetal and Neonatal Physiology. 2017; pp. 933–942.e3. https://doi.org/10.1016/b978-0-323-35214-7.00097-4. ISBN 978-0-323-35214-7.
31. Lampe E, Mello FCA, do, Espírito-Santo MP et al. Nationwide overview of the distribution of hepatitis B virus genotypes in Brazil: a 1000-sample multicentre study. J Gen Virol. 2017; 98(6):1389–1398.

https://doi.org/10.1099/jgv.0.000789

32. Mahmood M, Anwar MA, Khanum A, Zaman N, Raza A. Distribution and clinical significance of hepatitis B virus genotypes in Pakistan. BMC Gastroenterol. 2016;16:104. https://doi.org/10.1186/s12876-016-0513-5.
33. Mahmood M, Hebatitis B. Virus Genotypes in Pakistan. Adv Res Gastroentero Hepatol. 2017;5(5):00104–7. https://doi.org/10.19080/ARGH.2017.05.555673.
34. Matsuura K, Tanaka Y, Hige S, et al. Distribution of hepatitis B virus genotypes among patients with chronic infection in Japan is shifting towards an increase of genotype A. J Clin Microbiol. 2009;47(5):1476–8. https://doi.org/10.1128/JCM.02081-08.
35. Murad EA, Babiker SM, Gasim GI, Rayis DI, Adam I. Epidemiology of hepatitis B and hepatitis C virus infections in pregnant women in Sana'a, Yemen. BMC Pregnancy Childbirth. 2013;13:127.
36. Mutahar DJA, Al-Khamesy KSA, Al-Moyed KA-KA, Al-Shamahy HA, Al-Shehari MM. Pattern of liver disease admissions at a tertiary government hospital in Sana'a. Yemen Univers J Pharm Res. 2022;7(4):1–8. https://doi.org/10.22270/ujpr.v7i4.807.
37. Naito H, Hayashi S, Abe K. A rapid and specific genotyping system for Hepatitis B virus corresponding to six major genotypes by PCR using type-specific primers. J Clin Microbiol. 2001;39(1):362–4.
38. Othman AM, Hamzah EA, Almughales JA, Al-Mikhlafy A. Serum positivity of ana and asma among khat and nonkhat chewers as markers for autoimmune hepatitis type 1. Univers J Pharm Res. 2017;2(4):1–8. https://doi.org/10.22270/ujpr.v2i4.R5.
39. Patel NH, Meier-Stephenson V, Genetu M, et al. Prevalence and genetic variability of occult hepatitis B virus in a human immunodeficiency virus positive patient cohort in Gondar, Ethiopia. PLoS ONE. 2020;15(11):e0242577. https://doi.org/10.1371/journal.pone.0242577.
40. Phung TB, Alestig E, Nguyen TL, Hannoun C, Lindh M. Genotype X/C recombinant (putative genotype I) of hepatitis B virus is rare in Hanoi, Vietnam-Genotypes B4 and C1 predominate. J Med Virol. 2010;82:1327–33. https://doi.org/10.1002/jmv.21775.
41. Rahman MA, Hakim F, Ahmed M, Ahsan CR, Nessa J, Yasmin M. Prevalence of genotypes and subtypes of hepatitis B viruses in the Bangladeshi population. Springer Plus. 2016;5:278. https://doi.org/10.1186/s40064-016-1840-2.
42. Rashid PMA, Salih GF. Identification and genotyping of hepatitis B virus by PCR assay using genotype-specific primers. Eur Sci J 2014; 10(9).
43. Roger J. Oxford Textbook of Primary Medical Care. Oxford University Press.2004; p. 758. ISBN 978-0-19-856782-0. Archived from the original on 8 September 2017.
44. Sady H, Al-Mekhlafi HM, Mahdy MA, Lim YA, Mahmud R, Surin J. Prevalence and associated factors of Schistosomiasis among children in Yemen: implications for an effective control programme. PLoS Negl Trop Dis. 2013;7(8):e2377. https://doi.org/10.1371/journal.pntd.0002377. . PMID: 23991235; PMCID: PMC3749985.

45. Shen T, Yan XM. Hepatitis B virus genetic mutations and evolution in liver diseases. World J Gastroenterol. 2014;20(18):5435–41. https://doi.org/10.3748/wjg.v20.i18.5435.
46. Sumi H, Yokosuka O, Seki N, et al. Influence of hepatitis B virus genotypes on the progression of chronic type B liver disease. Hepatol. 2003;37(1):19–26. https://doi.org/10.1053/jhep.2003.50036.
47. Świderska M, Pawłowska M, Mazur W, et al. Distribution of HBV genotypes in Poland. Clin Exp Hepatol. 2015;1(1):1–4. https://doi.org/10.5114/ceh.2015.51372.
48. Tran TT, Trinh TN, Abe K. New complex recombinant genotype of hepatitis B virus identified in Vietnam. J Virol. 2008;82:5657–63. https://doi.org/10.1128/JVI.02556-07.
49. Tufon KA, Meriki HD, Anon DN, Mbunkah HN, Nkuo AG. Diversity, viraemic and aminotransferase levels in chronically infected hepatitis B patients from Cameroon. BMC Res Notes. 2016;9(117):1–7.
50. Vachon A, Osiowy C. Novel biomarkers of Hepatitis B virus and their use in chronic Hepatitis B patient management. Viruses. 2021;13:951. https://doi.org/10.3390/v13060951.
51. Wazir H, Abid M, Essani B, Saeed H, Ahmad Khan M, Nasrullah F, Qadeer U, Khalid A, Varrassi G, Muzammil MA, Maryam A, Syed ARS, Shah AA, Kinger S, Ullah F. Diagnosis and Treatment of Liver Disease: Current Trends and Future Directions. Cureus. 2023;15(12):e49920. https://doi.org/10.7759/cureus.49920. . PMID: 38174191; PMCID: PMC10763979.
52. Winger J, Michelfelder A. Diagnostic approach to the patient with jaundice. Primary Care.2011; 38 (3): viii, 469–482. https://doi.org/10.1016/j.pop.2011.05.004. PMID 21872092.
53. World Health Organization. Global hepatitis report 2017. Geneva: World Health Organization; 2017.
54. World Health Organization. Hepatitis. World Health Organization. Archived from the original on 2 December 2013. Retrieved 25 September 2026.