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Unraveling Demographic Patterns in Hepatitis B Clinical and Laboratory Profiles: Insights From a Ghanaian Cohort: A Retrospective Study

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ABSTRACT

Background and Aims: The influence of age and gender on the manifestations of Hepatitis B (HB) disease is underexplored and yields varied findings. This study assessed the impact of age and gender on HB disease manifestations in a Ghanaian population.

Methods: This retrospective study evaluated 569 patients at Tamale Teaching Hospital. Disease manifestations were compared separately between male and female patients across different age groups and among four distinct age groups within male and female patients.

Results: It revealed a male-to-female ratio of 5.1:1, with significant differences observed among age categories. HBsAg was significantly more prevalent in adult males ($p < 0.05$), while polydipsia showed equal prevalence between genders ($p < 0.05$). Female adults exhibited higher rates of constipation and palpitation compared to males ($p < 0.05$). In older patients, females had higher ALT and HBeAg prevalence than males ($p < 0.05$). Disease manifestation did not significantly differ by gender among children and younger patients ($p > 0.05$). Among males, viral load differed significantly across age groups and correlated positively with age ($p < 0.05$). Females showed positive correlations of jaundice, HBeAg, low globulin, and high AST with age ($p < 0.05$), but nausea was negatively correlated ($p < 0.05$).

Conclusion: This study highlights unique clinical and laboratory features in reproductive-aged female HB patients.

1 | Introduction

Hepatitis B (HB) is considerably a life-threatening infection triggered by hepatitis B virus (HBV), a double-stranded DNA that belongs to the hepadnaviridae group that affects the liver and may cause acute and chronic disease phases. The virus is spread by contact to fluids from the human body or blood that is infected [1]. HBV transmission occurs vertically through infected mother to child, sexually, and through sharp wounds [2–4]. In the case of adults, they get the viruses through contact with blood that is infected or fluids from the human body, insecure injections, and sexual intercourse [5–10]. More than the one-third population of the world is infected with HBV, with > 350 million as chronic carriers [11], causing chronic liver diseases. Above 686,000 people die yearly as a result of complications of HB, as well as cirrhosis and hepatocellular carcinoma (HCC) [12]. Tumor is most prevalently caused by chronic HB infection and it is represented by 55% of worldwide cases and 89% of HBV infection in prevalent countries [13, 14]. In high-prevalence countries, HB is mostly contracted through child delivery or during the early stage of child

development [15]. Generally, almost half of the worldwide population stays in regions that have higher HB endemicity [16]. The progression of infection for chronic HBV happens in almost 90% of perinatal infected persons, with 30% early childhood infection and 6% after age 5 [17]. HBV chronically infected adults have 15%–25% peril of premature death due to HBV-associated cirrhosis, HCC, and acute fulminant liver failure [17]. Additionally, almost 10% of liver transplant surgeries that are currently performed are mainly triggered by HBV [14]. To quantify the burden of HBV in Africa is very challenging because of improper record keeping and substandard reporting. It is, however, estimated that the adult population of ~70%–95% shows proof of exposure to HBV carriers. Also, HBsAg seroprevalence is estimated to be around 6%–20% [18, 19]. Sub-Saharan Africa is known to have one of the utmost HBV-associated liver cancer rates globally [20]. HBV-associated liver cancer exists as the first and third most common cancer in males and females, respectively, in the African continent [21, 22]. It is alarming to note that the average age of HBV associated with HCC progression in Africa (mean age is 33) is considerably lower than the other developed countries such as Western Europe (mean age is 60 years). This implies that HBV-associated HCC destroys the most productive and reproductive stages of patients [23]. HB thus characterizes a serious threat to health and development as well as the economy of the African region.

In Ghana, HB is indicated as an important public health concern and needs maximum devotion and consideration [24, 25]. Ghana is considered to be part of the global countries with a high prevalence of chronic HBV carrier (from 8% upwards) [23, 26]. Sweitzer and colleagues, in assessing the worldwide menace of HB in 2013, placed the prevalence rate of chronic HBV carrier in Ghana at 12.92% [27]. The prevalence rate was obtained from the investigation of 12 articles. Some studies have pegged the prevalence of HB in Ghana to be ~10%–15% [28, 29]. Other studies have also assessed the HB prevalence rate of blood donors to be 6.7%–11% [30, 31], pregnant women to be 6.4% [32], and children also to be 15.6% in the total population [33]. A study conducted among blood donors with a sample size of 3402 showed a total seroprevalence of HBsAg of 9.6% [31].

Clinical and laboratory manifestations of the HBV infection are influenced by age, sex, and host immunity status [34]. Clinical manifestations exist more frequently in adults than in children, who commonly have an asymptomatic acute course [35]. The clinical features of HB infection are nonspecific and are characterized by the furtive onset of dark urine, fever, arthralgia and arthritis, myalgia, anorexia, skin rashes, abdominal pain, headache, vomiting, malaise, and nausea [35]. A study revealed that the response rate of T-cell to HBsAg was decreased in pregnant women than in male adults as well as nonpregnant women [36]. Previous studies showed that the prevalence of HB with respect to HCC remained elevated in adults such that their increased serum viral load concentration increased the risks of cirrhosis and HCC [37, 38]. Generally, the possibility of the disease becoming chronic is dependent on the age of the patient and the strength of the immune system at the time of developing HB [39]. HB is chronic in 90% of infected newborns between the ages of 1 and 5, the probability of treatment is up to 50%, however, this probability reduces to 6%–10% in older children and adults [40, 41]. One of the most significant ways of preventing HB is through vaccination [39].

In Ghana, the prevalence of HB is high [23, 26] and requires greater public health attention [24, 25]. Presently, there are no studies done in the study area on the influence of demographic characteristics on the disease manifestations of HB. Therefore, in order to compare the effects of demographic features on clinical and laboratory characteristics, this study was conducted into age and gender influence on clinical and laboratory characteristics of HB in a Ghanaian population.

2 | Materials and Methods

2.1 | Study Design and Setting

This was a hospital-based cross-sectional study conducted at Tamale Teaching Hospital, Ghana. The study was designed to assess clinical and laboratory manifestations among patients diagnosed with HB. Data were collected from patients' medical records.

2.2 | Study Population and Eligibility Criteria

A total of 569 patients diagnosed with HBV were included in this study. Patients were eligible for inclusion if they had tested positive HBV based on standard diagnostic criteria outlined by the American Association for the Study of Liver Disease (AASLD) guidelines. Patients with coexisting liver diseases, such as hepatitis C and autoimmune hepatitis, or any other major medical conditions were excluded from the study.

2.3 | Data Collection Procedures

Demographic, clinical, and laboratory data were extracted from hospital records using a structured data collection form. A trained medical team, including gastroenterologists, reviewed patient records to confirm the accuracy of diagnoses and clinical findings. Disease manifestation data were classified into two categories: clinical manifestations and laboratory features.

2.4 | Clinical Manifestations

The following clinical symptoms and signs were recorded: jaundice, hepatomegaly (enlarged liver), variceal bleeding, abdominal pain, icterus, portal hypertension, anicteric hepatitis, constipation, dark stool, fatigue, nausea, fever, anorexia, itching, palpitations, polyuria, and polydipsia.

2.5 | Laboratory Manifestations

The laboratory parameters were evaluated using standardized diagnostic tests, including:

Liver function test (LFT): aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, albumin, and globulin levels. Renal function test (RFT): serum creatinine and blood urea nitrogen levels. Coagulation profile: prothrombin time (PT) and partial thromboplastin time (PTT). HB virology markers: hepatitis B surface antigen (HBsAg), hepatitis B

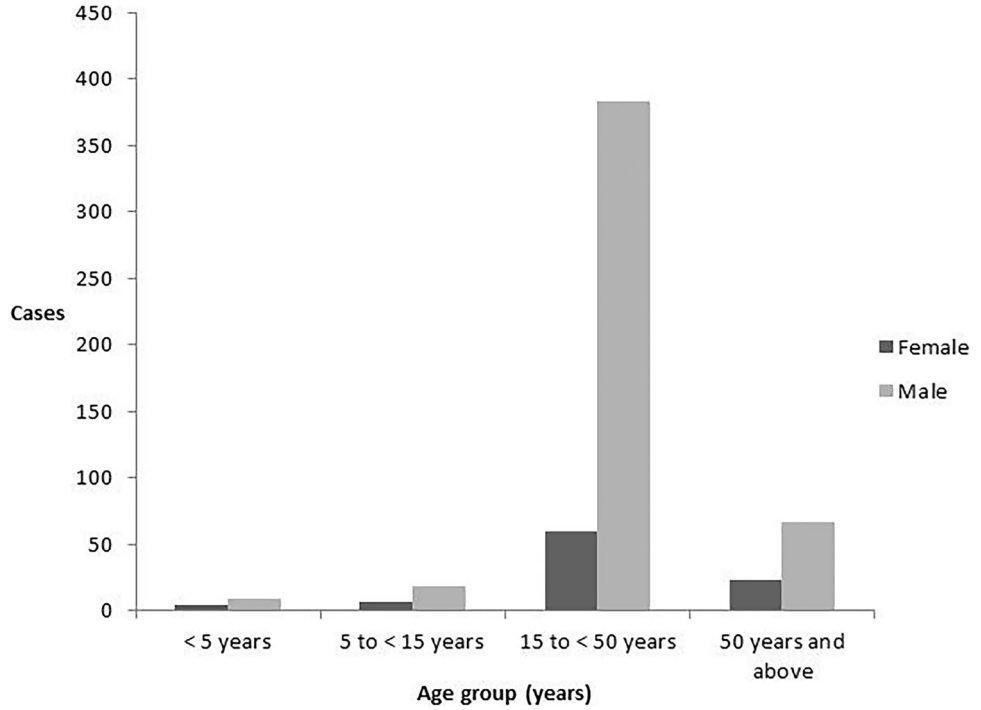

FIGURE 1 | Age distribution of hepatitis B patients at the onset by gender.

e-antigen (HBeAg), and HBV DNA viral load via Polymerase Chain Reaction (PCR). Abdominal ultrasound (USG): to assess liver structure and pathology. Lipid profile: total cholesterol and triglyceride levels.

2.6 | Categorization of Patients

Patients were categorized into four age groups: Under 5 years, younger-onset (5 to < 15 years), adult-onset (15 to < 50 years), and older-onset (≥ 50 years). Hospitalization duration was defined as the time from hospital admission to discharge or death.

2.7 | Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 23. Descriptive statistics were applied to summarize demographic, clinical, and laboratory characteristics. Continuous variables were presented as means with standard deviations (mean ± SD) if normally distributed or medians with interquartile ranges (median [IQR]) otherwise. Categorical variables were expressed as frequencies and percentages. Comparisons of continuous variables were conducted using the Student's *t*-test for normally distributed data and the Mann–Whitney *U* test for nonnormally distributed data. χ^2 tests or Fisher's exact tests were applied to assess associations between categorical variables. Additionally, Spearman's correlation was used to explore relationships between continuous and categorical variables. Clinical and laboratory features were analyzed across gender and age groups, and subgroup analyses were performed to assess gender differences within each age category. A $p < 0.05$ was considered statistically significant as well as using the two-tailed test.

2.8 | Ethical Considerations

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from Tamale Teaching Hospital's Review Board, and permission for data collection was also granted by Tamale Teaching Hospital. All patients' data were anonymized to maintain confidentiality.

3 | Results

3.1 | Demographic Data

The study comprised 569 Ghanaian HB patients. Thirteen (13) patients, representing 2.3% were under the age of 5 years, 25 (4.4%) patients within the ages of 5 to < 15 years, 89 (15.6%) patients at 50 years and above, and the highest number of patients, aged 15 to < 50 years, accounted for 442 (77.7%). The majority of the patients were males (83.7%) and exactly 1 out of every 6 patients was a female. The male-to-female ratio was recorded as 5.1:1 and was statistically significant in all the age categories; in the category of adults was 6.5:1, in the category of young-onset was 2.6:1, in older patients was 2.9:1, and in childhood-onset patients was 2.3:1 ($p < 0.05$). In 383 out of 476 male patients (80.5%), the onset of the disease falls within 15 to < 50 years and also forms the peak concentration within the same age group. On the other hand, 59 female patients representing 63.4% out of 93 also had their peak concentration between 15 to < 50 years (Figure 1). The median age of the diseased patients was 35 (25, 43). Hospitalization duration was 6 (4, 10) days. No statistical significance was found in the median age of patients between males and females (35 (26, 43) vs. 32 (21, 48)) years, ($p > 0.05$). Again, the hospitalization duration for males (7 (4, 10)) did not significantly vary from the females'

TABLE 1 | Demographic characteristics of hepatitis B patients.

Variable	Frequency (%)	Gender (%)		*p*
		Female	Male	
Age (years)				0.004*
< 5	13 (2.3)			
5 to < 15	25 (4.4)			
15 to < 50	442 (77.7)			
50 and above	89 (15.6)			
Gender				
Female	93 (16.3)			
Male	476 (83.7)			
Age (median (IQR))	35 (25, 43)	32 (21, 48)	35 (26, 43)	0.234
Hospitalization duration (median (IQR))	6 (4, 10)	6 (4, 8)	7 (4, 10)	0.107

Abbreviation: IQR, interquartile range.
*A significant association ($p < 0.05$).

TABLE 2 | Clinical features in children, younger, adult, and older onset HB patients: comparison between female and male patients.

Variable	Total (%)	All ages (%)		< 5 yrs (%)		5 to < 15 yrs (%)		15 to < 50 yrs (%)		50 yrs and above (%)	
		F	M	F	M	F	M	F	M	F	M
Abdominal pain	87.5	84.9	88.0	3.8	1.4	7.6	3.6	60.8	81.4	27.8	13.6
Jaundice	82.2	87.1	81.3	2.5	1.8	6.2	4.4	64.2	80.1	27.2	13.7
Fever	17.4	15.1	17.9	0.0	2.4	14.3	1.2	42.9	81.2	42.9	15.3
Nausea	10.9	9.7	11.1	33.3	3.8	22.2	3.8	33.3	79.2	11.1	13.2
Constipation	7.6	1.1	8.8*	0.0	2.4	0.0	2.4	100.0	85.7*	0.0	9.5
Variceal bleed	11.6	10.8	11.8	0.0	1.8	0.0	3.6	60.0	76.8	40.0	17.9
Icterus	10.5	5.4	11.6	0.0	1.8	0.0	3.6	40.0	78.2	60	16.4
Enlarge liver	14.4	11.8	14.9	9.1	1.4	0.0	1.4	63.6	78.9	27.3	18.3
Polyuria	7.2	7.5	7.1	14.3	5.9	28.6	5.9	42.9	67.6	14.3	20.6
Fatigue	5.8	7.5	5.5	0.0	3.8	0.0	3.8	85.7	69.2	14.3	23.1
Polydipsia	2.6	6.5	1.9*	0.0	11.1	0.0	0.0	66.7	66.7*	33.3	22.2
Palpitation	4.0	7.5	3.4	0.0	12.5	0.0	6.3	85.7	75.0*	14.3	6.3
Anicteric	2.6	2.2	2.7	0.0	7.7	0.0	7.7	50.0	69.2	50.0	15.4
Anorexia	3.7	4.3	3.6	0.0	5.9	0.0	0.0	75.0	82.4	25.0	11.8
Dark stool	5.4	8.6	4.8	12.5	0.0	0.0	8.7	75.0	87.0	12.5	4.3
Portal hypertension	3.2	3.2	3.2	0.0	26.7	1.0	0.0	33.3	53.3	33.3	20.0
Itching	3.7	1.1	4.2	0.0	5.0	0.0	0.0	0.0	85.0	100	10.0

Abbreviations: F, female; HB, hepatitis B; M, male; Yrs, years;
*Significant association ($p < 0.05$).

(6 (4, 8); $p > 0.05$). The details of the demographic features are recorded in Table 1.

3.2 | Disease Manifestations With Gender

In adults, males were significantly associated with constipation (100.0 vs. 85.7, $p < 0.05$), polydipsia (66.7 vs. 66.7, $p < 0.05$), and palpitation (85.7 vs. 75.0, $p < 0.01$) than the females. However, the frequencies of constipation (85.7%) and palpitation (75.0%) in male patients were less than that of the females. Other clinical characteristics, such as abdominal pain, jaundice, fever, nausea, variceal bleed, icterus, enlarge liver, polyuria, fatigue, anicteric, anorexia, dark stool, portal hypertension, and itching, recorded no significant differences between males and females. This study showed no significant difference in the clinical characteristics of the sex group for both young and older patients (Table 2).

TABLE 3 | Laboratory features in children, younger, adult, and older onset HB patients: comparison between female and male patients.

Variable	Total (%)	All ages (%)		< 5 yrs (%)		5 to < 15 yrs (%)		15 to < 50 yrs (%)		50 yrs and above (%)	
		F	M	F	M	F	M	F	M	F	M
AST	39.4	40.9	39.1	2.6	1.6	2.6	3.8	60.5	81.2	34.2	13.4
ALT	58.0	59.1	57.8	1.8	2.2	9.1	3.6	56.4	82.2	32.7	12.0*
Viral load	6.3	4.3	6.7	0.0	0.0	0.0	0.0	100.0	68.8	0.0	31.3
HBeAg	17.6	17.2	17.6	0.0	1.2	0.0	0.0	43.8	86.9	56.3	11.9*
HBsAg	13.7	19.4	12.6	5.6	5.0	5.6	3.3	72.2	78.3*	16.7	13.3
PT	85.1	84.9	85.1	5.1	2.0	8.9	3.7	62.0	81.5	24.1	12.8
PTT	85.1	84.9	85.1	5.1	2.0	8.9	3.7	62.0	81.5	24.1	12.8
Bilirubin	81.4	78.5	81.9	4.1	1.8	8.2	3.8	63.0	81.0	24.7	13.3
Albumin	80.3	77.4	80.9	4.2	1.8	8.3	3.9	62.5	81.0	25.0	13.2
Hemoglobin	26.7	25.8	26.9	8.3	1.6	4.2	3.9	70.8	77.3	16.7	17.2
Abdominal USG	17.0	15.1	17.4	7.1	1.2	7.1	2.4	57.1	77.1	28.6	19.3
Globulin	26.5	31.2	25.6	3.4	0.8	3.4	4.1	55.2	80.3	37.9	14.8
RFT	9.8	10.8	9.7	10.0	0.0	10.0	4.3	60.0	80.4	20.0	15.2
Total cholesterol	7.4	6.5	7.6	0.0	8.3	33.3	2.8	66.7	80.6	0.0	8.3
LFT	1.8	0.0	2.1	0.0	10.0	0.0	0.0	0.0	80.0	0.0	10.0

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; F, female; HB, hepatitis B; HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e-antigen; LFT, liver function test; M, male; PT, prothrombin time; PTT, partial thromboplastin time; RFT, renal function test; Yrs, years.
*Significant association ($p < 0.05$).

In older HB patients, significantly high ALT levels were recorded in 13.4.0% of male patients, much less than the 34.2% in females ($p < 0.05$). Also, HBeAg was significant in 11.9% of male patients and 56.3% of female patients ($p < 0.05$). No statistically significant difference was established in the other laboratory features (high AST, viral load, HBsAg, PT, PTT, high bilirubin, low albumin, low hemoglobin, abdominal USG, low globulin, RFT, total cholesterol, and LFT) between the sex groups. In the adult category, no significant differences were recorded in virtually all the laboratory features among gender, with the exception of HBsAg which was significantly expressed more in males than in females (72.2 vs. 78.3%, $p < 0.05$). No significant differences were observed in the laboratory features among the sex groups for younger patients (Table 3).

Disease expressions with age in female patients, the prevalence of jaundice, nausea, high AST, HBeAg, and low globulin were significantly different among the age groups of the patients ($p < 0.05$), and upon further analysis using Spearman's rank correlation, jaundice ($r_s = 0.243$), high AST ($r_s = 0.223$), HBeAg ($r_s = 0.339$), and low globulin ($r_s = 0.208$) were found to have positively correlated with age groups (all $p < 0.05$) whereas, nausea correlated negatively with the age groups ($r_s = -0.309$, $p < 0.05$). There was no statistical significance in the other laboratory or clinical characteristics among the age categories ($p > 0.05$) (Table 4).

In male patients, the prevalence of almost all the laboratory and clinical characteristics were not statistically significant among the age categories (all $p > 0.05$) with the exception of viral load characteristic that showed a significant prevalence among the age groups ($p < 0.05$). Spearman's rank correlation analysis indicated a positive correlation between viral load and age groups ($r_s = 0.339$, $p < 0.05$) (Table 5).

3.3 | Relationship Between Laboratory Markers and Clinical Manifestations

This study investigated the relationship between HB biochemical markers and clinical manifestations, providing important new information about the severity extent and progression of the disease (Table 6). Abdominal pain ($\chi^2 = 71.396$, $p < 0.001$) and jaundice ($\chi^2 = 20.801$, $p < 0.001$) had a significant association with liver function markers, such as LFT, ALT, AST, and bilirubin, which indicated inflammation and hepatic dysfunction. Jaundice ($\chi^2 = 23.316$, $p < 0.001$) and abdominal pain ($\chi^2 = 14.636$, $p < 0.001$) were associated with HBeAg positive, indicating the effect of active viral replication on hepatocyte injury. The association between fever and HBsAg ($\chi^2 = 4.464$, $p = 0.035$) suggested immunological activation.

Abdominal pain ($\chi^2 = 19.453$, $p < 0.001$) was strongly associated with coagulation abnormalities, particularly prolonged PT and PTT, indicating the significance of impaired hepatic synthesis in complications of bleeding. Jaundice ($\chi^2 = 17.406$, $p < 0.001$) and abdominal pain ($\chi^2 = 22.978$, $p < 0.001$) had a significant association with low albumin, suggesting hepatic synthetic failure. Abdominal pain was associated with low hemoglobin levels ($\chi^2 = 11.903$, $p = 0.001$), which might indicate anemia or

TABLE 4 | Cumulative disease manifestations in female patients with HB: comparison among children, younger, adult, and older onset patients.

Parameter	< 5 yrs (%)	5 to < 15 yrs (%)	15 to < 50 yrs (%)	50 yrs and above (%)	r_s value
Abdominal pain	3.8	7.6	60.8	27.8	NS
Jaundice	2.5	6.5	64.2	27.2	0.243*
Fever	0.0	14.3	42.9	42.9	NS
Nausea	33.3	22.2	33.3	11.1	−0.309*
Constipation	0.0	0.0	100.0	0.0	NS
Variceal bleeding	0.0	0.0	60.0	40.0	NS
Icterics	0.0	0.0	40.0	60.0	NS
Enlarge liver	9.1	0.0	63.6	27.3	NS
Polyuria	14.3	28.6	42.9	14.3	NS
Fatigue	0.0	0.0	85.7	14.3	NS
Polydipsia	0.0	0.0	66.7	33.3	NS
Palpitation	0.0	0.0	85.7	14.3	NS
Anicteric	0.0	0.0	50.0	50.0	NS
Anorexia	0.0	0.0	75.0	25.0	NS
Dark stool	12.5	0.0	75.0	12.5	NS
Portal hypertension	0.0	33.3	33.3	33.3	NS
Itching	0.0	0.0	0.0	100.0	NS
AST	2.6	2.6	60.5	34.2	0.223*
ALT	1.8	9.1	56.4	32.7	NS
Viral load	0.0	0.0	100	0.0	NS
HBeAg	0.0	0.0	43.8	56.3	0.339*
HBsAg	5.6	5.6	72.2	16.7	NS
PT	5.1	8.9	62.0	24.1	NS
PTT	5.1	8.9	62.0	24.1	NS
Bilirubin	4.1	8.2	63.0	24.7	NS
Albumin	4.2	8.3	62.5	25.0	NS
Hemoglobin	8.3	4.2	70.8	16.7	NS
Abdominal USG	7.1	7.1	57.1	28.6	NS
Globulin	3.4	3.4	55.2	37.9	0.208*
RFT	10.0	10.0	60.0	20.0	NS
Total cholesterol	0.0	33.3	66.7	0.0	NS

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; HB, hepatitis; r_s, correlation coefficient; HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e-antigen; LFT, liver function test; NS, not significant; PTT, partial thromboplastin time. RFT, renal function test.
*Significant association ($p < 0.05$).

gastrointestinal bleeding. Metabolic disruptions were apparent, as total cholesterol was associated with fever ($\chi^2 = 3.939$, $p = 0.047$), which is consistent with documented changes in lipid metabolism in chronic liver disease.

4 | Discussion

This study broadly looked at the influence of gender and age on the disease manifestations. Though some previous studies [42, 43] have associated the prevalence of paraclinical features between different age groups or gender, age as a confounding variable was not controlled and may possibly influence the findings when the result is affected by gender or age. In order to exclude the influence of confounding variables, age was grouped into four categories. Data were matched independently between males and females for each age category and among the age categories in males and females. No statistical significance was found in the median age of patients between males and females. The age 15 to < 50 years recorded the maximum incidence for both male and female patients, similar to the result of Du and colleagues which established that the age distribution of HB patients was mainly concentrated in 20–40 years old [44].

Some studies have varied findings with respect to gender or age variations in the laboratory and clinical expressions of HB [43, 45–47]. This study analyzed the relationship of gender with age groups on disease manifestations. Except for HBsAg which was

TABLE 5 | Cumulative disease manifestations in male patients with HB: comparison among children, younger, adult, and older onset patients.

Parameter	< 5 yrs (%)	5 to < 15 yrs (%)	15 to < 50 yrs (%)	50 yrs and above (%)	r_s value
Abdominal pain	1.4	3.6	81.4	13.6	NS
Jaundice	1.8	4.4	80.1	13.7	NS
Fever	2.4	1.2	81.2	15.3	NS
Nausea	3.8	3.8	79.2	13.2	NS
Constipation	2.4	2.4	85.7	9.5	NS
Variceal bleed	1.8	3.6	76.8	17.9	NS
Icterus	1.8	3.6	78.2	16.4	NS
Enlarge liver	1.4	1.4	78.9	18.3	NS
Polyuria	5.9	5.9	67.6	20.6	NS
Fatigue	3.8	3.8	69.2	23.1	NS
Polydipsia	11.1	0.0	66.7	22.2	NS
Palpitation	12.5	6.3	75.0	6.3	NS
Anicteric	7.7	7.7	69.2	15.4	NS
Anorexia	5.9	0.0	82.4	11.8	NS
Dark stool	0.0	8.7	87.0	4.3	NS
Portal hypertension	26.7	0.0	53.3	20.0	NS
Itching	5.0	0.0	85.0	10.0	NS
AST	1.6	3.8	81.2	13.4	NS
ALT	2.2	3.6	82.2	12.0	NS
Viral load	0.0	0.0	68.8	31.3	0.143*
HBeAg	1.2	0.0	86.9	11.9	NS
HBsAg	5.0	3.3	78.3	13.3	NS
PT	2.0	3.7	81.5	12.8	NS
PTT	2.0	3.7	81.5	12.8	NS
Bilirubin	1.8	3.8	81.0	13.3	NS
Albumin	1.8	3.9	81.0	13.2	NS
Hemoglobin	1.6	3.9	77.3	17.2	NS
Abdominal USG	1.2	2.4	77.1	19.3	NS
Globulin	0.8	4.1	80.3	14.8	NS
RFT	0.0	4.3	80.4	15.2	NS
Total cholesterol	8.3	2.8	80.6	8.3	NS
LFT	10.0	0.0	80.0	10.0	NS

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; HB, hepatitis; r_s, correlation coefficient; HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e-antigen; LFT, liver function test; NS, not significant; PTT, partial thromboplastin time. RFT, renal function test.
*Significant association ($p < 0.05$).

more likely present in adult-onset male patients, there was no statistical significance in the other laboratory characteristics between males and females in the adult category. However, when matched with males in the adult category, females were significantly related to the higher presence of constipation, palpitation, and equal presence of polydipsia. In older patients, females frequently presented high ALT and HBeAg than in males. In support of our findings, Barker and Murray [45] revealed that healthy male prison inmates aged 21–35 years were infected with HBsAg following parenteral contact to both diluted and undiluted icterogenic materials. The following contradicts earlier findings in this study that high ALT was significantly associated with female patients. In a study by Sali et al. [46], indications were that the mean levels of ALT were higher in males. In studies with regards to gender consideration, ALT was shown to be an independent risk factor for HB infection because high ALT levels had been reported more frequently in males [48, 49]. Ciftci et al. [50] also found out that ALT levels were significantly higher in male patients than in females.

We further analyzed the relationship of age with disease expressions in males and also in females. Our findings revealed that only viral load was significantly different among the age categories in males and correlated positively with age. Female

TABLE 6 | Relationship between laboratory markers and clinical manifestations.

Clinical features	Laboratory features	χ^2	*p*
Abdominal pain	HBeAg	14.636*	< 0.001
Abdominal pain	PT	19.453*	< 0.001
Abdominal pain	PTT	19.453*	< 0.001
Abdominal pain	High bilirubin	26.412*	< 0.001
Abdominal pain	Low albumin	22.978*	< 0.001
Abdominal pain	Low hemoglobin	11.903*	0.001
Abdominal pain	RFT	4.556*	0.033
Abdominal pain	LFT	71.396*	< 0.001
Jaundice	High ALT	7.816*	0.005
Jaundice	HBeAg	23.316*	< 0.001
Jaundice	HBsAg	10.494*	0.001
Jaundice	PT	13.443*	< 0.001
Jaundice	PTT	13.443*	< 0.001
Jaundice	High bilirubin	20.801*	< 0.001
Jaundice	Low albumin	17.406*	< 0.001
Jaundice	LFT	47.166*	< 0.001
Fever	High ALT	5.623*	0.018
Fever	HBsAg	4.464*	0.035
Fever	Total cholesterol	3.939*	0.047
Fever	LFT	48.324*	< 0.001

Abbreviations: AST, aspartate aminotransferase; ALT, alanine aminotransferase; HB, hepatitis; HBsAg, hepatitis B surface antigen; HBeAg, hepatitis B e-antigen; LFT, liver function test; PT, prothrombin time; PTT, partial thromboplastin time RFT, renal function test.
*Significant association.

patients recorded positive correlations of jaundice, HBeAg, low globulin, and high AST with age categories; however, nausea was negatively correlated with age. Our finding was in line with the finding of McMahon et al. [43] who found that HBsAg was significantly higher in the younger category than in older patients. However, there was a contradictory finding by Shao et al. [51] that the serum HBV DNA (viral load) levels do not correlate with age. The various clinical stages of chronic hepatitis B (CHB) are mainly determined by the levels of the HBV, ALT, and HBeAg. The immune-tolerant phase, immune-active phase, inactive carrier state, and HBeAg-negative CHB are among the phases. Comprehending these stages is essential for assessing the prognosis of the disease and directing suitable treatment measures [52, 53]. Some studies have highlighted the importance of gender and age in the development of CHB. The immune-tolerant phase, which is marked by strong HBV replication but little liver inflammation, is frequently seen in younger patients. Immune activation rises with age, increasing the risk of HCC, fibrosis, and possible liver injury. Males are more likely than females to develop fibrosis and HCC, indicating that gender differences are also important in the course of the disease. Hormonal variations, immunological reactions, and lifestyle factors like alcohol use and metabolic syndrome are probably responsible for this discrepancy. Again, similar studies highlight new approaches to managing CHB, such as risk stratification for HCC, antiviral medication considerations based on disease phase, and the need of early preventative measures like screening and vaccination [52, 53].

Traditional characteristics of the immune-tolerant phase of CHB include low levels of liver fibrosis and inflammation and strong HBV replication. Recent histological study, such as the results from Yoo et al. [54], contradicts this traditional wisdom by showing that even in patients with immune-tolerant CHB, underlying liver damage may be present despite normal ALT levels and few clinical signs. These findings imply that, particularly in younger patients, liver biopsy or noninvasive fibrosis assessment may be useful in improving disease categorization and directing clinical judgments. It is also important to observe how disease manifestation varies with age. The immune-tolerant phase, which frequently lasts for decades, is more common in children and adolescents with CHB. However, immunological activation tends to rise with age in adults, increasing the risk of HCC and the advancement of fibrosis. Significant concerns regarding the long-term effects of HBV replication and the necessity of early intervention techniques are brought up by the discovery of minor histological alterations even in patients who are thought to be immune-tolerant [54]. The differences in these studies might partly be accounted for by sociodemographic, environmental factors, and hereditary differences. Also, the absence of normalization in the selection of patients and variations in study design contributed partly to the discrepancies.

Coinfections, alcohol consumption, and metabolic disorders are examples of confounding factors that significantly influence the course of HB and patient outcomes. For example, coinfections of HIV and hepatitis D can drastically change the natural course of HB, increasing the likelihood of complications including cirrhosis and HCC and accelerating the disease's progression. Alcohol use aggravates the consequences of HB by raising oxidative stress and encouraging fibrosis, which worsens liver damage. Furthermore, the growing significance of metabolic dysfunction-associated fatty liver disease (MAFLD) in relation to chronic HB has been brought to light by recent studies [55, 56]. Accordingly, MAFLD may interact with an HBV infection to affect liver fibrosis, the severity of the disease, and the responsiveness to treatment. Regardless of the HBV viral load, the metabolic changes linked to MAFLD, such as insulin resistance, dyslipidemia, and obesity, may accelerate the development of liver disease [55, 56]. Therefore, including metabolic parameters in the study might improve our comprehension of patient outcomes and direct more individualized treatment plans.

The clinical importance of indicators like HB core-related antigen (HBcrAg) in determining disease activity and prognosis has been highlighted by recent developments in HB research. In addition to more established indicators like HBsAg and HBeAg,

HBcrAg is becoming more widely acknowledged as a reliable indicator of viral replication and immunological response [57–59]. Due to the lack of data for HBcrAg, this study did not include an analysis of this marker. This limitation of lack of HBcrAg data would have allowed for a more thorough comprehension of the disease dynamics within the population under study. HBcrAg, for example, may have made it possible to stratify individuals according to disease stage and conduct a more thorough evaluation of viral activity. Again, the prognosis and course of the disease in HB patients are significantly influenced by liver fibrosis. Evaluation of fibrosis and clinical decision-making have been aided by noninvasive techniques such as APRI, FIB-4, and transient elastography [60, 61]. Our study's lack of fibrosis data, however, is a drawback that might have improved the findings' therapeutic applicability. Future studies should combine these approaches to offer a more thorough comprehension of the course of the disease and risk assessment in the management of HB. Some additional limitations were also revealed in this study: (1) Data collection was done in retrospect and might result in potential diagnostic bias. (2) There was a relatively limited sample size since some patients were excluded from this study due to insufficient data. (3) The study's generalizability may be limited by selection bias because it only included patients from one teaching hospital in northern Ghana. The sample may be biased toward more severe cases due to the hospital's function as a referral center, and regional variations in healthcare access, socioeconomic circumstances, and cultural customs might not accurately represent the larger Ghanaian HB population. The results shed important light on the disease in northern Ghana despite these drawbacks and emphasize the necessity of multicenter research to guarantee a more representative understanding across the country. We acknowledge that the dynamic evolution of chronic hepatitis B (CHB), especially the impact of age and gender on the course of the disease, would be better captured by a longitudinal study. Our next study will look at monitoring CHB patients over time and include serial assessments of liver function, viral load, and fibrosis progression in order to address this. This method will support more individualized illness treatment techniques and offer more solid data on demographic factors.

The study focused on the influence of age and gender on disease manifestations as well as relatively high sample size with 8-year span data which is necessary for both epidemiological reasons and for planning rational target treatment. To the best of our knowledge, this study is the first of its kind in Ghana that has reviewed the influence of age and gender on disease manifestation on HB patients.

5 | Conclusion

This study established that women HB patients at productive and reproductive ages possess unique clinical and laboratory features. This study is useful in the clinical management of females of the potential risk of HB and also for planning rational target treatment. It also gives a better understanding of possible implications for public health especially in female adults in the fight against HB. Further research studies are essential to endorse the findings and to expound the causal pathogenesis with respect to age.

Author Contributions

Napoleon Bellua Sam: conceptualization, methodology, formal analysis, supervision, writing – review and editing. **Saeed Folorunsho Majeed:** writing – original draft, formal analysis, methodology. **Adam Dramani:** writing – original draft, validation, formal analysis. All authors have read and approved the final version of the manuscript.

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Ethics Statement

The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from Tamale Teaching Hospital's Review Board, and permission for data collection was also granted by Tamale Teaching Hospital.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Transparency Statement

The lead author, Napoleon Bellua Sam, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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