Research Article

Iron Dysregulation in Hepatitis B Virus Infection: Association of Serum Ferritin and Iron Indices With Hepatic Injury And Fibrosis

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Abstract

Background: Sugar-sweetened beverages (SSBs) represent a significant source of added sugars in adolescent diets, potentially contributing to both obesity and dental caries. Understanding the interrelationships among these variables is essential for developing effective prevention strategies targeting adolescent health. Objective: This study aimed to investigate the relationship between sugar-sweetened beverage consumption, body mass index (BMI), and dental caries risk among adolescents, while exploring potential mediating and confounding factors. Methods: A cross-sectional study was conducted among 524 adolescents aged 12–17 years recruited from eight secondary schools. SSB consumption was assessed using a validated food frequency questionnaire. BMI was calculated from measured height and weight, with participants classified according to WHO age-specific criteria. Caries risk was evaluated using the DMFT index (Decayed, Missing, Filled Teeth) through clinical examination. Data analysis included descriptive statistics, correlation analysis, chi-square tests, ANOVA, and multivariate linear regression. Results: Mean SSB consumption was 4.8 ± 2.6 servings per week. Mean BMI was 22.4 ± 4.3 kg/m², with 28.6% classified as overweight/obese. Mean DMFT score was 3.2 ± 2.4. Significant positive correlations were observed between SSB consumption and BMI ($r=0.34$; $p<0.001$) and between SSB consumption and DMFT scores ($r=0.41$; $p<0.001$). High SSB consumers (≥7 servings/week) demonstrated significantly higher DMFT scores (4.6 ± 2.7) compared to low consumers (2.1 ± 1.8; $p<0.001$). Multivariate analysis confirmed SSB consumption as an independent predictor of both elevated BMI ($\beta=0.28$; $p<0.001$) and increased DMFT scores ($\beta=0.36$; $p<0.001$). Conclusion: Sugar-sweetened beverage consumption is significantly associated with both increased BMI and elevated caries risk in adolescents. Integrated public health interventions targeting SSB reduction may simultaneously address obesity and dental health concerns in this population.

Keywords: Sugar-sweetened beverages; dental caries; body mass index; adolescents; obesity; DMFT index.

1. Introduction

Hepatitis B virus (HBV) is a hepatotropic (meaning it affects the liver) noncytopathic (meaning it does not directly damage the cells) double-stranded DNA virus, and is a significant global health problem, transmitted mainly via percutaneous (through the skin) or mucosal (direct contact with mucous membranes) routes. HBV infection is highly endemic in sub-Saharan Africa, South-East Asia, and some parts of the Americas, with prevalence rates ranging from 8% to 20% of the population in India in 2022 alone being estimated to be nearly 29.8 million.

The liver is a key organ in controlling the systemic iron balance as a sensor and regulator of iron levels, with the production of key proteins including hepcidin, ferritin, and transferrin.7,8,9 Therefore, the liver injury or dysfunction will affect iron metabolism, and the pathological consequences may accelerate the progression of liver disease.10

Increased liver iron levels have been shown to cause hepatocellular necrosis, inflammation, fibrosis and carcinogenesis. In the setting of chronic HBV infection, chronic liver injury also affects both iron storage and mobilization from injured hepatocytes and Kupffer cells, and this results in measurable changes in serum iron indices, such as hyperferritinemia that reflects both liver injury and iron overload, and in alterations of transferrin saturation that reflects dysregulated iron utilization.11,12,13

There is now emerging evidence demonstrating a complex interplay between HBV infection and iron metabolism. This correlation is clinically and therapeutically relevant and informative. Serum iron indices have potential as easy, non-invasive markers for disease activity, severity and progression in HBV infected patients on one hand, and as potential markers of disease severity and response to treatment in those receiving antiviral treatment on the other. Targeted modulation of iron metabolism, however, may offer new adjunctive strategies in the treatment of HBV management. The present study was conducted with this objective in mind to see the correlation of serum iron profile and HBV

infection in this context. The study also investigates the relationship of HBV infection with serum iron markers such as serum iron, serum ferritin and total iron-binding capacity (TIBC) and to determine if these markers relate to the severity of liver injury. In addition, the study aims to evaluate the correlation between iron serum markers and the period of hepatitis B infection.

Materials and Methods

This observational study was a cross-sectional design that was conducted over 2 years in the Department of General Medicine at Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh, India from 2023–2025. This study included adult patients who visited the outpatient and inpatient wards of the Department of General Medicine, and were diagnosed with hepatitis B virus (HBV) infection, who met the predetermined eligibility criteria. Participants were sequentially recruited following informed consent for a written agreement.

Inclusion Criteria

Patients were eligible for inclusion if they met all of the following criteria:

1. Age should be 18 and 70 years, irrespective of sex.
2. Seropositive for hepatitis B surface antigen (HBsAg), either asymptomatic or symptomatic.
3. HBV-positive patients presenting with clinical features suggestive of hepatitis.
4. Willingness to participate and provide written informed consent

Exclusion Criteria

Patients were excluded if they had any of the following conditions:

1. Other chronic liver diseases, including decompensated chronic liver disease (DCLD), Wilson's disease, autoimmune hepatitis, hemochromatosis, or alcoholic/toxic hepatitis.
2. Hepatocellular carcinoma or any other malignancy.
3. Hematological disorders or non-viral chronic liver diseases.
4. Prior treatment for HBV or hepatitis C virus (HCV) infection.
5. Drug-induced hepatitis, autoimmune hepatitis, hemolytic anemia, or infiltrative liver disorders.
6. Chronic systemic illnesses such as congestive heart failure (CHF) or chronic kidney disease (CKD).
7. Pregnant women or females with abnormal uterine bleeding (AUB).
8. Ongoing therapy with steroids, pegylated interferon, or nucleos(t)ide analogues.
9. Homozygous or compound heterozygous mutations in the HFE gene associated with hereditary hemochromatosis.
10. Coinfection with hepatitis C virus, hepatitis D virus, hepatitis G virus, or human immunodeficiency virus (HIV).
11. History of significant alcohol consumption (>60 g/day).
12. Biochemical or histological evidence of alcoholic liver disease.
13. History of large-volume blood transfusion (>6 units).

Methods:

Demographic details such as age, sex, height, weight, and BMI of the patients were recorded. HBV infection was diagnosed by enzyme-linked immunosorbent assay (ELISA). After informed consent, five ml of venous blood samples were collected from all participants. Hematological tests, including hemoglobin, total leukocyte count, and differential leukocyte count, were performed using automated analyzers. Coagulation tests, such as prothrombin time and international normalized ratio, were conducted on plasma samples. Biochemical analysis included random blood sugar measurement and liver function tests, which assessed parameters such as serum bilirubin, liver enzymes, and protein levels. Imaging of the abdomen was carried out via ultrasound. The iron profile was assessed by measuring serum iron, ferritin, total iron-binding capacity, and transferrin saturation. Microscopic examination of peripheral blood smears was conducted to detect malaria parasites, if any. Serology tests for dengue IgM/IgG antibodies were performed using ELISA or rapid tests. After collection, the samples were allowed to clot for half an hour. Following that, the samples were centrifuged, and serum was collected and analyzed. Serum iron, transferrin, total iron-binding capacity, and ALT were measured with an automatic clinical chemistry analyzer (DIRUI CST 240). Ferritin was measured using the immunoassay system (TOSOH AIA1800). Quantification of HBV DNA was performed using a standardized real-time polymerase chain reaction (PCR) assay. Interpretation of viral load was carried out according to the assay detection limits as follows: values below 55 IU/mL were considered HBV DNA not detected or below the limit of detection; values

between 55 IU/mL and 9.6×10^1 IU/mL were interpreted as HBV DNA detected but below the quantifiable range of the assay; values between 9.6×10^1 IU/mL and 9.6×10^8 IU/mL were considered HBV DNA detected within the quantifiable range; and values above 9.6×10^8 IU/mL were interpreted as HBV DNA detected above the linear range of the assay.

Acute Hepatitis B: Acute hepatitis B referred to a newly acquired infection with hepatitis B virus in which the illness typically lasts less than 6 months. During this phase, patients may be
asymptomatic or present with features such as fever, malaise, anorexia, jaundice, and elevated liver enzymes. In most immunocompetent adults, the virus is cleared spontaneously within this period, and the infection resolves without long-term sequelae.

Chronic Hepatitis B: Chronic hepatitis B was defined as persistence of HBV infection for more than 6 months, usually indicated by continued presence of hepatitis B surface antigen (HBsAg) in serum.

- SGOT (AST) values were categorized as normal (≤40 U/L), mildly to moderately elevated (1–3 × ULN; 41–120 U/L), and markedly elevated (>3 × ULN; >120 U/L).
- SGPT (ALT) levels were categorized based on the upper limit of normal (ULN) of 55 IU/L, and classified as normal (≤55 IU/L), mildly to moderately elevated (1–3 × ULN; 56–165 IU/L), and markedly elevated (>3 × ULN; >165 IU/L).
- Serum ferritin levels were interpreted with a ULN of 300 ng/mL, and categorized as normal (≤300 ng/mL), elevated (1–3 × ULN; 300–900 ng/mL), and severely elevated (>900 ng/mL).
- Serum iron levels were classified as normal (60–170 µg/dL), elevated (>170 µg/dL), or deficient (<60 µg/dL).
- TIBC was categorized as normal (250–450 µg/dL), elevated (451–600 µg/dL), or reduced (<250 µg/dL).
- Transferrin saturation (TSAT) was calculated as the ratio of serum iron to TIBC multiplied by 100 and categorized as normal (20–50%), iron overload (>50%), or deficient (<20%).
- ALP values were interpreted using a ULN of 147 IU/L, with values > 147 IU/L considered elevated.
- The APRI score was calculated using the standard formula (AST/ULN) ÷ platelet count (109/L) × 100 (AST/ULN) ÷ platelet count (10^9/L) × 100(AST/ULN) ÷ platelet count(109/L) × 100, and values >1 were considered indicative of significant hepatic fibrosis.
- Anemia was defined as a reduction in hemoglobin concentration below WHO-recommended cut-off values, i.e. <13 g/dL in adult males, <12 g/dL in non-pregnant adult females.

The data was collected using a predesigned template (proforma attached). The collected data variables obtained were compiled by using an excel spreadsheet. Baseline patient characteristics are presented with frequencies for categorical variables and either means with standard deviations for continuous variables. Upon appropriate data filtration, the dataset was analyzed using Graphpad Prism (Vs. 10.2.0). Quantitative variables between groups were compared using Student's t-test and One-way Analysis of Variance (ANOVA) for parametric data. For categorical data, Chi-square (χ^2) test was used. Correlation between serum ferritin and other lab markers was performed using Pearson correlation analysis. P-value of < 0.05 was considered statistically significant.

Informed consent process was initiated prior to the individual agreeing to participate in the study and continuing throughout the individual's study participation. The study was approved by the Institutional ethics committee.

Results:

A total of 78 patients with hepatitis B virus (HBV) infection were included in the analysis. The study population was predominantly male, with 58 patients (74.4%), while females constituted 20 patients (25.6%). The mean age was 50.3 ± 13.7 years, reflecting a predominantly middle-aged population. The largest proportion of patients belonged to the 40–59-year age group (n = 35; 44.9%), followed by those aged ≥60 years (n = 23; 29.5%) and 18–39 years (n = 20; 25.6%). Based on BMI categorization, 35 patients (44.9%) had normal BMI, 34 (43.6%) were overweight, and 9 (11.5%) were obese. With respect to clinical presentation, fever was the most common symptom, reported in 64 patients (82.1%), followed by pallor in 52 patients (66.7%). Vomiting and abdominal pain were observed in 38 (48.7%) and 20 (25.6%) patients, respectively, while icterus was documented in 27 patients (34.6%). Loss of appetite was reported by 16 patients (20.5%), and 14 patients (17.9%) were asymptomatic at presentation. 22 patients (28.2%) were diagnosed with acute HBV infection, whereas the majority, 56 patients (71.8%), had chronic HBV infection.

Hematological evaluation revealed a high prevalence of anemia. The mean hemoglobin level was 9.8 ± 2.3 g/dL, and the mean red blood cell (RBC) count was 3.4 ± 1.0 × 10^6/µL. Red cell indices were normal with mean corpuscular volume (MCV) (88.4 ± 8.6 fL) and mean corpuscular haemoglobin concentration (MCHC) (32.2 ± 3.2 g/dL) indicating normocytic normochromic anemia. The mean number of total leukocytes was 10322.

A mild inflammatory response of ± 3,906 cells/µL. The average platelet count was 178.1 Within lower normal limits: ± 32.0 × 10^9/L. Overall 52 patients (66.7%) were anemic, 21 patients (26.9% of total) had iron deficiency anemia while only 5 patients (6.4%) had normal hemoglobin levels (Table 1).

Renal function parameters revealed slightly elevated means of blood urea (39.1 ± 27.5 mg/dL) and serum creatinine (1.3 ± 0.7 mg/dL) indicating early renal impairment in a subset of patients. Marked hyper bilirubinemia was detected in the liver function tests (LFT) with a mean total bilirubin of 7.2 ± 6.4 mg/dL and direct bilirubin of 4.2 ± 3.9 mg/dL.

Hypoproteinemia (5.8±1.1mg/dL) and hypoalbuminemia (2.9 ± 0.6 g/dL), along with a reduced albumin-to-globulin (A/G) ratio (1.0 ± 0.3), reflected compromised hepatic synthetic function. Elevated alkaline phosphatase (165.0)
The levels of (2) aspartate aminotransferase (SGOT) (87.4 ± 8.4 U/L), and (3) alanine aminotransferase (SGPT) (116.9 ± 64.1 U/L) were signs of active hepatic injury with a mixed hepatocellular–cholestatic pattern. Coagulation parameters were also abnormal, with a prolonged prothrombin time (19.7 ± 4.1 seconds) and elevated international normalized ratio (INR) (1.37 ± 0.6), which is indicative of impaired hepatic synthesis of clotting factors.

In the studied population (n = 78), there was a predominance of elevated levels of SGPT. Mild elevation (1–3× upper limit of normal [ULN]) was observed in 66.7% (n = 52), while 20.5% (n = 16) demonstrated marked elevation (>3× ULN). Normal SGPT values were noted in 12.8% (n = 10). 56.4% (n = 44) had normal levels of ALP in the serum; 43.6% (n = 34) had elevated serum ALP levels, suggesting possible cholestatic or mixed hepatic involvement. Elevated ferritin levels were present in 75.6% (n = 59), with 52.6% (n = 41) showing mild elevation (1–3× ULN) and 23.0% (n = 18) demonstrating marked elevation (>3× ULN). In 24.4% (n = 19) the ferritin levels were normal.

The mean serum ferritin level was elevated (561.7 ± 326.3 ng/mL) in the iron profile analysis, and the mean serum iron level (115.8 ± 61.3 µg/dL) and transferrin saturation (34.0 ± 18.6%) levels were relatively preserved. Regarding iron indices, serum iron levels were normal in 48.7% (n = 38), elevated in 24.4% (n = 19), and reduced in 26.9% (n = 21). Total iron-binding capacity (TIBC) was within normal limits in 62.8% (n = 49), elevated in 14.1% (n = 11), and decreased in 23.1% (n = 18). Transferrin saturation (TSAT) was normal in 46.1% (n = 36), elevated in 24.4% (n = 19), and reduced in 29.5% (n = 23). HBV DNA quantification demonstrated very low-level viremia (55–9.6 × 10^1 IU/mL) in 37.2% (n = 29), quantifiable viral replication (9.6 × 10^1–9.6 × 10^8 IU/mL) in 26.9% (n = 21), and very high viral loads (>9.6 × 10^8 IU/mL) in 20.5% (n = 16). Undetectable HBV DNA was observed in 15.4% (n = 12).

Stratification by transaminase severity demonstrated a consistent stepwise pattern of biochemical deterioration (Table 2). Increasing SGOT categories were associated with progressive elevations in SGPT (47.7 ± 19.1 U/L in normal vs. 217.6 ± 55.0 U/L in >3×ULN; P < 0.001) and ALP (110.8 ± 33.1 vs. 245.2 ± 68.1 U/L; P < 0.001). The level of serum ferritin was significantly increased as a function of the severity of SGOT (880.1 ± 397.0 ng/mL in the group with SGOT levels >3×ULN; P < 0.001). In contrast, serum iron declined significantly (147.8 ± 56.1 to 66.4 ± 47.7 µg/dL; P = 0.002), accompanied by a modest but significant rise in TIBC (P = 0.0286). There was a downward trend in the transferrin saturation but this was not statistically significant (P = 0.065).

A reciprocal relationship was seen to be present when stratified by SGPT. There were significant increases of SGOT and ALP (both P < 0.001) and progressive rise in ferritin (P = 0.0019) as the SGPT categories increased. The serum iron concentration was significantly lower in each of the SGPT strata (P = 0.004) but the difference in TIBC and transferrin saturation were not significant (Table 3).

Elevated ALP levels were strongly associated with higher levels of SGOT (P < 0.001) and SGPT (P < 0.001) as well as higher ferritin levels (P < 0.001) in patients. In particular, serum iron and serum transferrin saturation were significantly reduced in this group (P = 0.027 and P = 0.0375, respectively), while TIBC was not. It is suggested by these findings that the elevation of cholestatic enzymes is directly related to the injury to the liver and to the redistribution of iron in the liver associated with inflammation.

This relationship was confirmed by ferritin-stratified analysis. There were significant stepped increases in SGOT (P<0.001) and SGPT (P=0.0376) with an increase in ferritin categories, and there was a significant decrease in serum iron (P<0.001). However, TIBC was seen to vary markedly between the ferritin groups (P = 0.0115) while ALP and transferrin saturation did not reach statistical significance (Table 5).

Iron deficient patients had significantly the highest SGOT, SGPT, ALP and ferritin levels (P ≤ 0.033), indicating that iron deficient patients also had increased inflammatory and hepatocellular activity. The iron categories were associated with different transferrin saturation (P = 0.004), with the lowest in patients with iron deficiency. The differences in TIBC were statistically significant (P < 0.001), but were small (Table 6).

Patients with APRI > 1 had significantly higher levels of SGOT, SGPT, ALP, ferritin and lower levels of transferrin saturation (all P ≤ 0.047) and thus elevated inflammatory hyperferritinemia and altered iron distribution were associated with advanced fibrosis (Table 7).

Comparison between acute and chronic HBV revealed no statistically significant differences in transaminases, ALP, ferritin, serum iron, TIBC, or transferrin saturation (all P > 0.19), suggesting comparable biochemical and iron profiles across disease phases in this cohort (Table 8).

HBV DNA viral load showed a significant positive correlation with SGPT (r = 0.261, 95% CI: 0.04096 to 0.4571; P = 0.021) and ALP (r = 0.287, 95% CI: 0.06929 to 0.4793; P = 0.011). No significant correlation was observed with SGOT (r = 0.072; P = 0.218), serum ferritin (r = 0.087; P = 0.451), serum iron (r = −0.045; P = 0.698), TSAT (r = 0.131; P = 0.251), or APRI (r = 0.210; P = 0.064), although APRI showed a borderline trend toward positive association (Table 9).

A significant negative correlation was observed between duration of HBV infection and SGPT (r = −0.248, 95% CI: −0.4461 to −0.02718; P = 0.028). No significant correlations were found with PT (r = −0.072; P = 0.529), INR (r = −0.134; P = 0.243), SGOT (r = −0.107; P = 0.349), ALP (r = −0.001; P = 0.992), serum ferritin (r = −0.173; P = 0.129), serum iron (r = 0.042; P = 0.718), TIBC (r = −0.106; P = 0.354), TSAT (r = 0.081; P = 0.483), HBV DNA viral load (r =−0.059; P = 0.609), or APRI (r = −0.169; P = 0.139) (Table 10).

Serum ferritin showed a moderate significant positive correlation with SGOT (r = 0.542; 95% CI: 0.3633–0.6823) and SGPT (r = 0.581; 95% CI: 0.4117–0.7115). A weak but significant positive correlation was also observed with ALP (r = 0.310; 95% CI: 0.0936–0.4979). Serum ferritin demonstrated a significant negative correlation with serum iron (r = −0.452; 95% CI: −0.6130 to −0.2553) and transferrin saturation (r = −0.358; 95% CI: −0.5375 to −0.1470). No significant correlation was observed between serum ferritin and TIBC (r = −0.042; 95% CI:−0.2624 to 0.1819). Also, a weak negative correlation was observed between serum ferritin and platelet (r= -0.053) and with albumin (r= -0.214). However, a moderate positive correlation was observed between serum ferritin and APRI (r = 0.591; 95% CI: 0.4241–0.7189) (Table 11).

Discussion

The present study evaluated the association between HBV infection and alterations in serum iron profile in relation to liver injury and disease severity. The findings demonstrate that HBV infection is associated with significant disturbances in iron metabolism, which correlate closely with biochemical markers of hepatocellular injury, cholestasis, and fibrosis. A male predominance was observed, with males constituting 74.4% of the study population and females 25.6%. This finding aligns with previous studies reporting a higher prevalence of hepatitis B virus infection among males. The predominance of males may be related to greater exposure to risk factors such as occupational hazards, high-risk behaviours, and biological factors including the modulatory effects of sex hormones on immune response and viral replication, may also contribute to differences in susceptibility and disease progression. Similar results have been found in other previous studies. Liu M et al.14 reported that 71.2% of their study participants were male and 28.8% female. Likewise, the male predominance was reported by Janahi EM et al.15 with 58.5% males and 41.5% females. In addition, majority of our patients were between 40–59 years of age (44.9%) with the age group ≥60 years (29.5%) and age group 18–39 years (25.6%). In the current study, middle aged and elderly people were more likely to have hepatitis B virus infection as indicated. These figures may be explained by the nature of HBV infection which is often latent for a long time and therefore is diagnosed late, thus skewing the higher proportion of older age

groups. The laboratory data confirmed that the patients in this study with HBV infection had hematological abnormalities, liver dysfunction, coagulopathy, and active viral replication, which are typical of chronic hepatitis B infection.

A rise in transaminases was correlated with the progressive changes of liver enzymes and iron parameters, corresponding to the progressive impairment of liver function in HBV infection. SGPT and ALP showed significant rise across all the SGOT strata ($P < 0.001$) which is indicative of concordant hepatocellular injury together with progression of cholestatic involvement. The same trend was seen in all the SGPT categories. The severity of SGOT and SGPT was positively correlated with the level of serum ferritin with a consistently significant stepwise increase for each stage of severity ($P \leq 0.0019$). However, serum iron decreased significantly in all transaminase categories ($P \leq 0.004$), suggesting that when hepatic injury is more severe, there is less iron available in circulation. There was a slight increase in TIBC as severity of the SGOT increased but no consistent relationship to SGPT. Transferrin saturation decreased significantly in all the SGOT groups, but was not statistically significant. Coexistence of high ferritin concentration and low serum iron concentration can be explained as iron sequestration not necessarily as iron overload. This is a biologically plausible model according to the hepcidin-mediated iron redistribution during chronic hepatic inflammation (Table 12).

A tendency to be associated with liver injury was further confirmed by stratification by ferritin. SGOT and SGPT increased significantly with increasing ferritin categories ($P < 0.001$ and $P = 0.0376$, respectively) and ALP a non-significant increase. The amount of serum iron and TIBC varied significantly with ferritin ($P < 0.001$ and $P < 0.05$, respectively). The profile of hyperferritinemia and lower ferritin saturation is highly suggestive that ferritin is mostly an inflammatory marker in HBV in the context of lower iron level than usual, not a marker of systemic iron excess.
All P values < 0.05).Transaminase and ALP levels were the highest in patients with low serum iron (all $P < 0.05$).

This is seen as a greater degree of hepatocellular and cholestatic injury ($p < 0.033$). Of particular interest was the significantly higher ferritin levels in the iron-deficient group ($P < 0.001$), which support the concept of a paradoxical increase in ferritin in the iron-deficient group, typical of functional iron deficiency. Differences in transferrin saturation were significantly lower in these patients ($P = 0.004$), but differences in TIBC were not large. This study confirms the notion that inflammation is the cause of the disease.

In HBV infection, there is the phenomenon of driven iron sequestration, in which there is an increase in ferritin stores, but iron is not available for systemic use. The presence of higher APRI scores (>1) associated with significant fibrosis was associated with higher transaminases, ALP and ferritin (all $P < 0.001$) and lower serum iron and ferritin saturation. TIBC had a slight, but positive, increase. This suggests there is a progression of iron dysregulations with advancing fibrosis and inflammatory burden. The positive association of ferritin with APRI also adds to the evidence that it is linked to fibrosis severity, but not to liver necroinflammation per se.

Ferritin exhibited moderate positive correlation with SGOT ($r = 0.542$) and SGPT ($r = 0.581$) and less correlation with ALP. There were, however, significant inverse correlations with serum iron and transferrin saturation. Hyperferritinemia was strongly correlated with APRI ($r = 0.591$) indicating a relationship between hyperferritinemia and progression of fibrosis. In general, the associations suggest that high levels of ferritin are associated with inflammatory activity and fibrosis, not necessarily with iron overload. Modest positive correlation with HBV DNA levels with SGPT and ALP but not with SGOT and iron parameters. Iron indices were not significantly correlate with viral load and may be more associated with inflammatory and fibrotic mechanisms as compared to viral replication in HBV.

Limitations:

The present study has certain limitations which should be kept in mind while interpreting the findings. The sample size and limited number of centers is small and may have restricted applicability to other populations. Second, some investigations may be influenced by other factors that may be related to iron metabolism such as dietary iron intake, genetic predisposition and any coexisting metabolic condition, which should be taken into consideration. Lastly, the study did not assess the long-term effect of iron abnormalities on disease outcomes or treatment. The study, however, still has some drawbacks, but valuable information is provided regarding the possible links between HBV infection, liver damage and iron metabolism.

Conclusion:

This study confirms that the level of serum ferritin does not necessarily reflect iron overload, but is rather more of a marker of inflammation in individuals with hepatitis B. Increased ferritin levels correlated with increased transaminases and ALP as well as greater fibrosis severity (as measured by APRI), suggesting that this marker is a surrogate for ongoing hepatocellular damage and systemic inflammatory activation. Ferritin is an acute-phase reactant, which seems to be a marker of hepatocyte injury associated with inflammation in HBV infection. It has the greatest clinical value when used along with liver Function tests and complete iron profile, especially to differentiate inflammatory hyperferritinemia from states of true iron overload.

The levels of serum iron, by contrast, were all significantly inversely correlated with disease severity, with iron levels decreasing as transaminase increased, as ferritin category increased, as ALP increased, and as fibrosis increased. Hepatic injury is greater in patients who have reduced transferrin saturation, which further supports functional iron deficiency. TIBC had variable changes, but the trend indicates that the iron is being sequestered in an inflammatory manner, not stored systemically, possibly due to the role of hepcidin in the regulation of iron during chronic HBV infection. Concluding, HBV infection is accompanied by remarkable changes in iron metabolism that include increased ferritin and decreased bioavailable iron corresponding to the level of liver injury. Iron profile parameters particularly ferritin, serum iron, and transferrin saturation may serve as adjunct biomarkers for disease activity and fibrosis assessment in hepatitis B. Longitudinal studies are required to clarify mechanistic pathways and determine the prognostic and therapeutic implications of iron dysregulation in chronic HBV infection.

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Table 1: Baseline demographics, clinical characteristics and lab evaluation.

Parameter		N	%
Gender	Male	58	74.4
	Female	20	25.6
Age Group	18 - 39 years	20	25.6
	40 - 59 years	35	44.9
	≥ 60 years	23	29.5
BMI	Normal	35	44.9
	Overweight	34	43.6
	Obese	9	11.5
Signs & Symptoms	Abdominal pain	20	25.6
	Fever	64	82.1
	Pallor	52	66.7
	Icterus	27	34.6
	Vomiting	38	48.7
	Loss of appetite	16	20.5
	Asymptomatic	14	17.9
Anaemic status	Anaemia	52	66.7
	Iron deficiency anaemia	21	26.9
	Normal	5	6.4
Hepatitis B	Acute HBV	22	28.2

	Chronic HBV	46	71.8
SGOT	Normal	6	7.7
	1 - 3 ULN	58	74.4
	> 3 ULN	14	17.9
SGPT	Normal	10	12.8

Table 2: Mean ± SD of lab parameters across SGOT categories.

Parameter	**SGOT**			**Significance**
	Normal	1 - 3 ULN	> 3 ULN	
SGPT (U/L)	47.7 ± 19.1	99.7 ± 39.2	217.6 ± 55.0	P < 0.001
ALP (U/L)	110.8 ± 33.1	152.3 ± 83.6	245.2 ± 68.1	P < 0.001
Ferritin (ng/mL)	235.0 ± 121.9	518.6 ± 261.7	880.1 ± 397.0	P < 0.001
S. Iron (µg/dL)	147.8 ± 56.1	126.5 ± 62.6	66.4 ± 47.7	P = 0.0024
TIBC (µg/dL)	329.7 ± 93.5	328.9 ± 88.7	391.9 ± 92.1	P = 0.0286
TSAT (%)	46.2 ± 15.3	41.8 ± 26.7	16.7 ± 10.2	P = 0.0650

Table 3: Mean ± SD of lab parameters across SGPT categories.

Parameter	**SGPT**			**Significance**
	Normal	1 - 3 ULN	> 3 ULN	
SGOT (U/L)	42.7 ± 15.1	79.9 ± 27.3	138.6 ± 47.8	P < 0.001

ALP (U/L)	108.8 ± 38.6	149.9 ± 82.5	249.5 ± 68.2	P < 0.001
Ferritin (ng/mL)	346.5 ± 132.0	535.7 ± 277.4	780.4 ± 436.1	P = 0.0019
S. Iron (µg/dL)	158.7 ± 65.1	121.6 ± 61.9	77.8 ± 50.6	P = 0.004
TIBC (µg/dL)	306.6 ± 83.8	338.8 ± 92.5	368.0 ± 88.5	P = 0.2265
TSAT (%)	32.6 ± 15.3	39.5 ± 13.2	42.1 ± 11.0	P = 0.199

Table 4: Mean ± SD of lab parameters across ALP categories.

Parameter	**ALP**		**Significance**
	Normal	Elevated	
SGOT (U/L)	64.7 ± 22.9	116.4 ± 44.6	P < 0.001
SGPT (U/L)	77.3 ± 26.4	168.0 ± 62.6	P < 0.001
Ferritin (ng/mL)	449.0 ± 222.7	707.4 ± 380.7	P < 0.001
S. Iron (µg/dL)	132.3 ± 62.2	99.3 ± 62.5	P = 0.027
TIBC (µg/dL)	334.2 ± 93.5	348.1 ± 90.3	P = 0.5087
TSAT (%)	42.8 ± 26.2	30.9 ± 23.6	P = 0.0375

Table 5: Mean ± SD of lab parameters across ferritin levels.

Parameter	**S. Ferritin**	**Significance**

	Normal	1 - 3 ULN	> 3 ULN	
SGOT (U/L)	63.6 ± 27.3	76.3 ± 26.8	126.3 ± 54.2	P < 0.001
SGPT (U/L)	86.3 ± 34.4	104.6 ± 66.8	176.7 ± 65.5	P = 0.0376
ALP (U/L)	150.4 ± 81.8	165.9 ± 88.5	197.5 ± 94.5	P = 0.0664
S. Iron (µg/dL)	137.6 ± 50.8	121.8 ± 60.9	63.1 ± 54.9	P < 0.001
TIBC (µg/dL)	348.0 ± 98.7	326.9 ± 85.4	339.7 ± 102.7	P = 0.0115
TSAT (%)	43.5 ± 24.0	32.6 ± 14.9	22.3 ± 20.1	P = 0.1626

Table 6: Mean ± SD of lab parameters across serum iron levels.

Parameter	**S. Iron**			**Significance**
	Normal	Elevated	Deficiency	
SGOT (U/L)	79.0 ± 30.2	66.7 ± 27.4	120.6 ± 53.9	P < 0.001
SGPT (U/L)	98.9 ± 51.3	89.1 ± 54.4	166.4 ± 69.1	P < 0.001
ALP (U/L)	163.6 ± 86.0	128.8 ± 67.6	200.3 ± 95.1	P = 0.033
Ferritin (ng/mL)	456.1 ± 234.5	431.5 ± 199.8	870.5 ± 367.0	P < 0.001
TIBC (µg/dL)	345.9 ± 91.5	330.4 ± 96.0	338.8 ± 92.1	P < 0.001
TSAT (%)	35.8 ± 13.7	68.7 ± 25.9	12.8 ± 4.0	P = 0.004

Table 7: Mean ± SD of lab parameters with respect to APRI scoring.

Parameter	APRI ≤ 1	APRI > 1	Significance
SGOT (U/L)	54.3 ± 71.2	107.8 ± 40.6	P < 0.001
SGPT (U/L)	70.1 ± 29.6	145. ± 63.5	P < 0.001
ALP (U/L)	108.8 ± 35.4	200.2 ± 92.1	P < 0.001
Ferritin (ng/mL)	422.7 ± 199.3	648.5 ± 360.3	P < 0.001
S. Iron (µg/dL)	143.9 ± 65.3	100.8 ± 57.9	P = 0.0045
TIBC (µg/dL)	315.4 ± 78.2	355.8 ± 96.9	P = 0.0474
TSAT (%)	49.9 ± 29.2	30.0 ± 19.8	P = 0.0021

Table 8: Mean ± SD of lab parameters with respect to Acute and Chronic HBV.

Parameter	HBV		Significance
	Acute HBV	Chronic HBV	
SGOT (U/L)	91.4 ± 43.6	85.5 ± 42.4	P = 0.5965
SGPT (U/L)	115.7 ± 62.3	117.3 ± 65.4	P = 0.9240
ALP	149.5 ± 93.2	171.2 ± 85.1	P = 0.3436
Ferritin (ng/mL)	641.2 ± 304.9	530.4 ± 331.7	P = 0.1908

S. Iron (µg/dL)	123.6 ± 70.8	112.7 ± 57.5	P = 0.5003
TIBC (µg/dL)	361.9 ± 87.5	336.0 ± 91.4	P = 0.52719
TSAT (%)	35.4 ± 21.0	35.1 ± 18.5	P = 0.9524

Table 9: Correlation between HBV DNA viral load and other parameters.

Parameter	Correlation coefficient	95%CI	P value
SGOT	r = 0.072	-0.08419 to 0.3525	P = 0.218
SGPT	r = 0.261	0.04096 to 0.4571	P = 0.021
ALP	r = 0.287	0.06929 to 0.4793	P = 0.011
S. Ferritin	r = 0.087	0.1386 to 0.3033	P = 0.451
S. Iron	r = -0.045	-0.2645 to 0.1797	P = 0.698
TSAT	r = 0.131	-0.09381 to 0.3439	P = 0.251
APRI	r = 0.210	-0.01272 to 0.4136	P = 0.064

Table 10: Correlation between duration of HBV and other parameters.

Parameter	Correlation coefficient	95%CI	P value
PT	-0.072	-0.2903 to 0.1526	P = 0.529
INR	-0.134	-0.3459 to 0.09163	P = 0.243
SGOT	-0.107	-0.3222 to 0.1180	P = 0.349
SGPT	-0.248	-0.4461 to -0.02718	P = 0.028
ALP	-0.001	-0.2236 to 0.2215	P = 0.992
Ferritin	-0.173	-0.3812 to 0.05110	P = 0.129
S. Iron	0.042	-0.1827 to 0.2617	P = 0.718

TIBC	-0.106	-0.3213 to 0.1190	P = 0.354
TSAT	0.081	-0.1445 to 0.2978	P = 0.483
DNA Load	-0.059	-0.2777 to 0.1659	P = 0.609
APRI	-0.169	-0.3775 to 0.05543	P = 0.139

Table 11: Correlation between serum ferritin and other parameters.

Parameter	Correlation coefficient	95%CI	P value
Platelet	r = -0.053	-0.2722 to 0.1717	P = 0.646
Albumin	r = -0.214	-0.4172 to 0.008326	P = 0.022
Globulin	r = 0.046	-0.1788 to 0.2654	P = 0.189
SGOT	r = 0.542	0.3633 to 0.6823	P = 0.146
SGPT	r = 0.581	0.4117 to 0.7115	P = 0.398
ALP	r = 0.310	0.09360 to 0.4979	P = 0.377
S. Iron	r = -0.452	-0.6130 to -0.2553	P = 0.005
TIBC	r = -0.042	-0.2624 to 0.1819	P = 0.011
TSAT	r = -0.358	-0.5375 to -0.1470	P = 0.568
APRI	r = 0.591	0.4241 to 0.7189	P = 0.0065
PT	r = 0.133	-0.09214 to 0.3454	P = 0.245
INR	r = 0.284	0.06515 to 0.4761	P = 0.012