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Analysis of Hematological Profiles in Hepatitis B Patients; Understanding the Interplay Between Viral Infections and Blood Parameters

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Abstract

Introduction: *Hepatitis B virus (HBV) infection is a worldwide health concern, associated with heightened risks of liver failure, hepatic dysregulation, and hepatocellular carcinoma. Despite progress in developed nations, underdeveloped regions face challenges like increased chronic hepatitis B frequency, limited access to prevention measures, and insufficient infection control. This study explores the hematological profiles of individuals with HBV to enhance diagnostic, prognostic, and treatment strategies.*

Methodology: *A cross-sectional study at Fauji Foundation Hospital analyzed 85 HBV-positive and 85 control individuals. Ethical approval was obtained, and HBV serological markers were assessed. Hematological parameters were measured using an automated analyzer, and NLR and PLR were calculated. Software for statistical analysis, SPSS version 26, was used.*

Results: *Statistical analysis unveiled significant differences in key hematological parameters between hepatitis B virus (HBV) positive individuals and the control group. HBV-infected subjects exhibited lower white blood cell counts (7.75 x 10^9/L vs. 8.878 x 10^9/L, p = 0.013) and platelet counts (228.38 x 10^9/L vs. 264.34 x 10^9/L, p = 0.007), indicating potential impacts on immune response and coagulation. Moreover, the HBV group demonstrated an elevated neutrophil-to-lymphocyte ratio (NLR) (2.27 vs. 1.74, p = 0.0002) and platelet-to-lymphocyte ratio (PLR) (104.3 vs. 115.4, p = 0.039), indicative of a pro-inflammatory state. Lymphocyte percentages were significantly lower in the HBV group (26.756% vs. 32.535%, p = 0.0003), suggesting compromised immune function.*

These findings highlight the hematological impact of HBV infection, emphasizing its potential clinical implications for diagnosis and treatment strategies.

Conclusion: *This study illuminates the complex interaction between hepatitis B virus (HBV) infection and hematological parameters. The observed deviations in key blood markers underscore the impact of HBV on immune function and coagulation. Reduced platelet and white blood cell counts suggest heightened susceptibility to complications. Alterations in the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) highlight a pro-inflammatory state, offering valuable insights for prognosis. These findings, while contributing to diagnostic advancements, underscore the importance of considering hematological parameters in the comprehensive management of HBV-infected individuals. Despite study limitations, including restricted hospital access and potential biases, the results provide a foundation for refining diagnostic and therapeutic strategies, advancing our understanding of HBV-related pathophysiology.*

Keywords: Blood Parameters, Hepatitis B, Hematological Profiles, Viral Infections.

Introduction

Hepatitis B virus infection (HBV) is a major tenet of illness and death all over the world. Liver failure, hepatic dysregulation, and hepatocellular carcinoma (HCC) are all heightened risks of chronic hepatitis B (CHB) disease. The risk of getting CHB varies with age of infection; it is lowest in adults and exceeds 90% in newborns whose mothers have hepatitis B antigen positivity. Given the increased frequency of CHB, restricted access to PEP

and the HBV vaccination, and disdain for traditional infection control techniques, it continues to be a major concern in under developing countries [1]. The disease spreads through contact with contaminated blood and semen. About thirty percent of people on the planet have serological evidence of an infection, either previous or present [2].

As stated by the WHO, in 2019, 1.5 million new cases of HBV infection were reported, bringing the total number of affected individuals to 296 million worldwide. While Western countries have an HBV infection prevalence of less than 1% of the entire population, the Middle East has a higher incidence of the disease. Recent studies and modeling have shown that the current prevalence of HBV in Saudi Arabia is 1.7%, and it ranges from 1.0% to 1.5% across the United Arab Emirates (UAE) [3]. Elevated blood ALT readings and liver histology suggest that around 50% of hepatitis B carriers in Singapore have chronic hepatitis, while approximately 10% have pre-existing mutant viral infections. On average, 20% of carriers suffer from cirrhosis. A significant number of HCC patients, up to 75%, test positive for HBsAg, and 45% of these patients still have the virus in their system [4].

According to a study in 2019, the mean hemoglobin concentration in patients who tested positive for hepatitis B infection was 11.2 g/dl, while in healthy individuals it was 13.6 g/dl. Patients who tested positive for hepatitis B had a higher neutrophil count (51.810.2%) than healthy individuals (48.310.3%). Conversely, patients with hepatitis B had a higher lymphocyte count (45.310.6%) than control participants (44.410.3%) [5]. Another study also found a significant reduction in lymphocytes, indicating that the chronic phase of HBV infection may be reducing the immune response. This behavior is indicative of an immune evasion strategy that allows the infection to persist [6]. According to Fasola et al., out of the total patients, 12 (24%) had anemia, and the mean WBC count was 8.1+11.4 x 109/mm3. Among the patients, 8 (16%) had abnormal WBC counts, and 2 (4%) had leucopenia. In addition, six (12%) individuals had neutrophilic and lymphocytic leukocytosis. None of the patients had thrombocytopenia. However, in one-third of the patients, the coagulation profile was found to be abnormal [7].

This study is being carried out to see the response of various blood indices in response to viral infections. It aims to analyze the hematological profiles of individuals with hepatitis B and understand the interplay between viral infections and blood parameters in order to aid in developing more efficient diagnostic, prognostic, and treatment approaches.

Materials and Methods

This cross-sectional study was carried through at the Haematology Section at Fauji Foundation Hospital (FFH) in Islamabad. Proper ethical approval was obtained from the Institutional Ethical Review Committee. All seropositive HBV samples delivered in the lab during the interval of the study (Jan. 2022–Dec. 2022) were accommodated in the study. Every identical sample was eliminated from the research. To compare the hematological parameters of HBV seropositive persons (n = 85) with those of controls (n = 85), blood bank donors were enlisted.

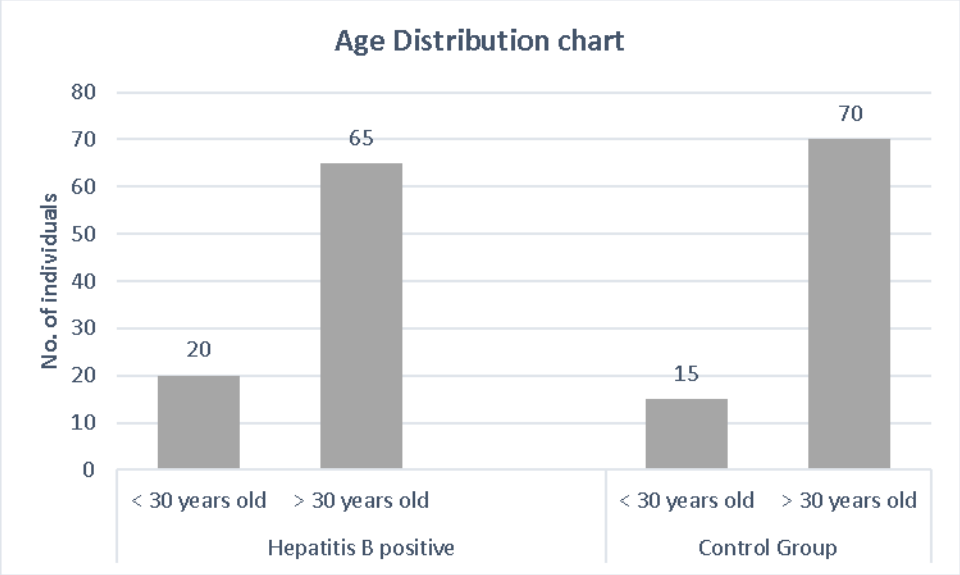
The selection of the control group involved recruiting discretionary blood donors at the blood bank. These donors underwent a comprehensive screening process, including a comprehensive clinical history, a clinical examination, and adherence to the same inclusion standard as the study group. Exclusion criteria encompassed subjects with a known history of HBV infection, other health morbids, recent blood transfusions, or critical surgery within the preceding six months.

Five-milliliter whole blood specimens were gathered from all subjects and divided into two portions, with one component transferred to an ethylenediamine tetraacetic acid (EDTA) tube and the other left undisturbed in a plain tube for 30–60 minutes. After centrifugation, serum was extracted and promptly stored at the temperature of -20°C until analysis. Evaluation of HBV serological markers employed the ARCHITECT immunoassay system following the manufacturer's guidelines. The HBsAg ULTRA kit (Bio-Rad, Marnes-la-Coquette, France) detected HBsAg, while anti-hepatitis B core antibodies were identified using the anti-HBc PLUS kit (Bio-Rad, Marnes-la-Coquette, France). Anti-hepatitis B surface antibodies were tested in all anti-HBc-positive samples with the anti-HBs kit (Bio-Rad, Marnes-la-Coquette, France). Positive samples from the initial screening underwent retesting for result confirmation.

For both the control and HBV-positive groups, hematological studies and full blood counts were conducted by an automated hematology analyzer. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were subsequently determined. Data analysis utilized SPSS version 26, employing the Student t test for group comparisons, with statistical significance designate at p values < 0.05.

Results

A total of one hundred and seventy (170) individuals participated in this study. This cross-sectional study consists of eighty-five (85) confirmed hepatitis B positive subjects as a study group, whereas the control group consists of eighty-five (85) hepatitis B negative patients. Individuals who tested positive for HBV and the control group were divided into two age groups: those who were 30 years of age or younger. Twenty of the 85 HBV-positive people were younger than 30, and 65 of the people were older than 30. Within the control group, fifteen individuals were under thirty years of age, and seventy-one were over thirty.



The analysis of hematological parameters investigated the implications of Hepatitis B virus (HBV) infection on key blood markers relative to a control group. We observed significant variations in white blood cell (WBC) and platelet counts, suggesting potential impacts on immune response and coagulation.

Neutrophil percentages exhibited a trend towards increase in the HBV group, while lymphocyte percentages significantly declined. Mean Corpuscular Volume (MCV) remained consistent between the batches. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were notably higher in the HBV-infected cohort. These findings highlight the significant influence of HBV infection on hematological parameters, necessitating further investigation into their clinical implications.

Parameter/ Unit	Control	HBV	P value
WBCs (x109/L)	8.878±2.14	7.75±3.53	0.013
Platelets (x109/L)	264.34±73.68	228.38±96.91	0.007
Neutrophils (%)	56.68±10.98	60.74±13.624	0.0346
Lymphocytes (%)	32.535±9.22	26.756±10.99	0.0003
MCV (fL)	82.72±9.39	82.29±11.99	0.796
PLR	115.4±3.53	104.3±8.49	0.039
NLR	1.74±1.01	2.27±1.04	0.0002

WBC: total white blood cell count, NLR: neutrophil to lymphocyte ratio, and PLR: platelet to lymphocyte ratio are values that are displayed as Mean ± SD.

Table 1: Comparative Analysis of Hematological Parameters between Control Group and HBV Seropositive Individuals

Discussion

Hepatitis B virus (HBV) infection is a worldwide public health problem, particularly in the Asian continent and sub-Saharan Africa. It is responsible for causing chronic liver disease in more than 75% of cases [8]. A lower WBC count in individuals with HBV infection is likely due to several factors, including the virus attacking and destroying immune cells and the body's immune reaction to the virus. A compromised immune system can make subjects with HBV infections more prone to other diseases and illnesses [9]. The results of the current study have shown that individuals with HBV infection have a lower WBC count (7.75 x 109/L) compared to the control group (8.878 x 109/L). This finding is statistically significant, by a p-value of 0.013. The results of the current study were consistent with another study, according to which HBV patients showed significant deviations ($p<0.05$) in contrast to healthy groups and other patients [10].

The platelet count is an essential component in determining the functioning of the liver, especially in individuals who have a hepatitis B virus (HBV) disease [11]. The platelet count among the control group (264.34 x 10^9/L) is higher than in the HBV group (228.38 x 10^9/L). This indicates that individuals with HBV infections have a lower platelet count in contrast to the control group, and this deviation is statistically significant (p-value = 0.009). This deviation implies that individuals with HBV disease are more prone to develop thrombocytopenia, a condition characterized by a low platelet count, than those without the infection [11]. Thrombocytopenia can lead to bleeding issues, which can be severe in individuals with chronic HBV infection and require immediate medical attention [12]. Platelets are responsible for blood clotting, which prevents the loss of blood from an injury or wound. With a low platelet count, individuals may experience prolonged bleeding and may have difficulty stopping bleeding, which can lead to more severe complications [13].

According to a study by Liu et al., the role of the inbuilt immune system, specifically neutrophils, in acute and chronic viral hepatitis infection is not yet fully analyzed due to inadequate liver biopsy samples. In people with chronic HBV infection, the innate immune response seems to be severely compromised, regardless of HBV replication, as multiple innate immunity-related genes are repressed based on intrahepatic gene expression patterns [14]. The findings of the current study showed that the neutrophil percentage in the HBV group was somewhat higher (60.74%) than in the control group (56.68%). However, the p-value (0.051) suggests that this difference is not statistically significant at the conventional significance level of 0.05. The observed greater proportion of neutrophils in the HBV group suggests a possible association between an altered neutrophil count and HBV infection. This result is consistent with other studies that suggested viral infections, such as HBV, might affect the makeup of immune cells (neutrophils) in the blood [15].

Our study shows that there is a significant deviation in the lymphocyte percentages among the HBV group (26.756%) and the control group (32.535%). The p-value of 0.001 indicates a high level of statistical significance. The lymphocyte percentages in people infected with HBV were significantly lower. This could indicate that the immune system is not functioning properly, as lymphocytes are essential for the immune response. This finding is consistent with other studies that show how chronic viral infections like HBV can cause changes in immune cells, including lymphocytes [16]. The strong statistical significance of the results highlights their reliability and provides support for the association between HBV infection and lower lymphocyte numbers. HBV can cause liver dysfunction by directly affecting the lymphocytes, which are essential for immunological control. Liver disease can alter the composition of immune cells in the bloodstream [17]. As a result of HBV's substantial impact on hematological parameters, healthcare systems must prioritize early detection and increased monitoring. To quickly detect HBV infections and closely monitor their effects on blood parameters, especially in high-risk populations, this means promoting more regular blood testing and putting improved serological screenings into place [18]. Another study has shown that persistent HBV infection leads to changes in lymphocyte numbers. Individuals with chronic HBV infection have significantly lower lymphocyte counts compared to healthy controls, according to a study by Li et al. in 2021. Patients with HBV-ACLF had a substantially lower lymphocyte percentage and circulating lymphocyte count [19]. The study outcome that there is no significant difference between the average volume of red blood cells in the HBV and control groups (p-value = 0.716). This means that HBV infection does not have a major effect on the size of red blood cells as measured by MCV. MCV is an important criterion for measuring red blood cell size, and the fact that it remains stable during HBV infection is significant for therapeutic purposes [20]. These findings have important implications for therapy as they confirm that HBV infection does not significantly alter MCV, which is a crucial hematological measure. This parameter measures the average volume of red blood cells and appears to be unaffected by HBV infection in this study.

The study findings revealed a significant deviation in NLR among the two groups - the HBV batch and the control batch. The NLR of the HBV batch was significantly greater (3.23) than that of the control batch (1.98), with a p-value of 0.001, indicating the statistical significance of the observation. The NLR biomarker is a cost-effective and easily accessible tool that shows the balance between two components of the immune process: acute and chronic inflammation, and adaptive immunity. Although there are no factual cut-off levels yet, changes in NLR levels over time can indicate immune system dysfunction [20]. An increased NLR in the HBV group is a sign of potential inflammation. The NLR represents the balance between lymphocytes (that are vital components of the adaptive immune system) and neutrophils (that are the initial responders to infection and inflammation) and serves as a sensitive measure of systemic inflammation. The significant difference in NLR between the two groups clearly suggests that those with HBV infection are more susceptible to heightened inflammation, which could result in severe health complications. These outcomes are accordant with a study conducted by Gong et al. (2018), which stated that severe liver disease in HBV patients leads to markedly

elevated NLR levels. Moreover, NLR is an independent predictor of mortality in those with HBV infection [20]. Modern studies have revealed that a higher NLR is linked to a poorer prognosis in various cancers, such as advanced HCC (hepatocellular carcinoma) due to HBV. Conversely, a lower NLR in individuals with persistent HBV infection is indicative of a reduced risk and a better prognosis for HCC [21]. Another study conducted reveals that a higher NLR was associated with an increased severity of HBV-decompensated cirrhosis in hospitalized patients [22].

The results of our study reveal a significant difference in PLR (platelet-to-lymphocyte ratio) between the control batch and those with HBV infection. The HBV group had a much higher PLR (10.82) than the control group (8.74), and the p-value of 0.041 highlights the statistical importance of this finding. It is worth noting that a higher PLR in the HBV group could indicate inflammation. PLR is a marker of systemic inflammation and shows the balance between platelets and lymphocytes [23]. The results of this study suggest that people with HBV infection have increased inflammation due to the significant difference in PLR between the two groups. A study done by Li et al. showed that in patients with hepatitis B virus (HBV) disease, high PLR values are associated with poor overall survival [24].

Another study's data shows a strong association between an increase in PLR and systemic inflammation [25]. Elevated levels of platelet-to-lymphocyte ratios (PLR) were found to be associated with higher levels of blood HbeAg, which is a viral marker, in individuals with active Hepatitis B (HBV) infections. Moreover, a greater neutrophil-to-lymphocyte ratio (NLR) has been linked to higher levels of HbeAg in individuals with advanced HBV illness. These ratios could potentially be used as markers to determine the extent and activity of HBV infection in different patient populations [26]. The results of the study highlight the possible advantages of focusing HBV treatment on reducing the inflammatory response. The creation of drugs that target immune response modulation, namely high levels of NLR and PLR, may be a potential approach to controlling the course of the disease and lowering related consequences. These therapeutic approaches have the potential to improve patient outcomes and the way HBV infections are managed generally [27]. The study's findings highlight the pressing need for intensified public health initiatives to combat the substantial health impact of HBV, particularly in underprivileged areas. Emphasizing vaccination and preventive measures through targeted public health campaigns can play a pivotal role in raising awareness about HBV transmission and prevention methods. Additionally, efforts to enhance accessibility to vaccination in regions with elevated prevalence rates are crucial for mitigating the disease burden and safeguarding public health.

Conclusion

In conclusion, the hematological parameters and immunological response of afflicted patients are significantly impacted by hepatitis B virus (HBV) infection. The outcomes of the study show that people with HBV infection have reduced platelet and white blood cell counts, which may pose health hazards to them such as increased bleeding and susceptibility to infections. The study also reveals a shift in the proportions of immune cell groups, with notably lower lymphocyte percentages and greater neutrophil percentages in the HBV group, indicating immune system failure. The research also shows that the platelet-to-lymphocyte ratio (PLR) and the neutrophil-to-lymphocyte ratio (NLR)) can be handy indicators for determining the prognosis and level of inflammation in people infected with HBV. These findings highlight the complex interplay between hematological parameters and HBV infection, underscoring the need for comprehending and addressing these factors in the context of hepatitis B illness. The study highlights the value of improved HBV surveillance and early detection techniques and raises the possibility of therapeutic benefit when addressing the inflammatory response. Additionally, given the substantial health burden of HBV, more public health initiatives are needed, especially in developing nations. These initiatives should include vaccine programs and prevention education.

Limitations

Our research may be subjected to some limitations. Access to this hospital is restricted to hospital staff, retired military members, and their families. As a result, patients are more likely to be women than men. The study will be biased because there are more females and kids than men participating. There can be variations in the findings due to the limited sample size.

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