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RESEARCH ARTICLE

Epidemiological and Molecular Characterization of Hepatitis B Virus in Pakistan: Prevalence, Genotypes, and Clinical Factors

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Abstract

Hepatitis B virus (HBV) remains a major public health challenge globally, with high prevalence rates in regions such as Pakistan. Despite significant advances, comprehensive studies on HBV prevalence, genotypes, and clinical correlates in Pakistan are limited. This study aims to analyze the prevalence, genotypic diversity, and clinical characteristics of HBV in Pakistan, with a focus on demographic factors, treatment responses, and adverse effects. Data were extracted from electronic health records and included age, gender, BMI, disease duration, smoking status, and HBV markers (HBsAg, HBeAg, HBeAb, HBcIgM, HBsAb). Statistical analyses were performed using SPSS, R, Python, and Excel, including descriptive statistics, correlation analysis, and comparative tests. The study population had a mean age of 45.3 years and a near-equal gender distribution. The overall prevalence of HBsAg was 1.85%, with 21.62% positive for HBeAg, indicating active infection. The mean BMI was 27.5, and the average disease duration was 12.7 years. Smoking prevalence was 35%. Systemic treatments showed slightly better responses compared to topical treatments. Adverse effects were predominantly mild (45%), with 15% experiencing severe effects. The findings reveal significant insights into the HBV epidemiology in Pakistan, including genotypic diversity and clinical factors. The results highlight the need for targeted public health interventions, improved vaccination strategies, and tailored treatment approaches to address the HBV burden effectively. Further research is needed to explore the regional variations in HBV genotypes and their impact on disease progression and treatment outcomes.

Keywords: Prevalence | Hepatitis B virus | Epidemiology| Genotypes | HBsAg | HBV markers

Significance

This study examines the prevalence, genotypic diversity, and clinical characteristics of Hepatitis B virus (HBV) in Pakistan, addressing gaps in understanding the disease. It highlights the need for targeted public health interventions and tailored treatments. The findings emphasize the importance of further research on regional variations in HBV genotypes and their impact on disease progression.

Introduction

Hepatitis B virus (HBV) remains a significant global health concern, particularly in regions like Asia and Africa, where the burden of the disease is substantial (1-3). Pakistan, in particular, reports some of the highest prevalence rates of HBV, with an estimated 3-5% of the population affected (4, 5). Genotype D is the most prevalent genotype in the country, posing challenges for effective disease management and control (5). Despite the high prevalence, comprehensive studies focusing on the various genotypes and their epidemiological implications in Pakistan are limited. This gap in research is critical, as understanding the genetic diversity of HBV is essential for developing targeted public health strategies. The global prevalence of HBV varies widely, with regions like Sub-Saharan Africa and East Asia reporting the highest rates, often exceeding 8% (6). In Pakistan, the situation is exacerbated by factors such as inadequate healthcare infrastructure, low vaccination coverage, and limited public awareness (7). Recent studies have highlighted the urgent need for mass vaccination and awareness programs to mitigate the spread of HBV and reduce the associated morbidity and mortality (8). Historical data suggest that HBV has been endemic in Pakistan for decades, with rural areas disproportionately affected due to poor healthcare access and lower socioeconomic conditions (10).

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Research from neighboring countries, including India and Iran, has shown that genotype distribution plays a crucial role in the clinical outcomes of HBV infections (11, 12). In Pakistan, genotype D's dominance is particularly concerning, as it is often associated with a higher risk of chronic liver disease and hepatocellular carcinoma (13, 14). However, recent findings indicate a heterogeneous distribution of HBV genotypes across different regions of Pakistan, with genotype A emerging as predominant in certain areas, such as Khyber Pakhtunkhwa (15). This diversity in genotypes underscores the need for region-specific studies to understand the implications for disease progression and treatment efficacy.

Moreover, the epidemiological landscape of HBV in Pakistan is shaped by various socio-demographic factors, including age, gender, and urban-rural disparities (16). For instance, older age groups and males are often more affected, possibly due to cumulative exposure risks and cultural practices that influence healthcare-seeking behavior (17). The rural-urban divide is particularly pronounced, with rural populations showing higher prevalence rates, possibly due to limited access to healthcare services and vaccination programs (18).

This study aims to provide a comprehensive analysis of the prevalence and molecular characterization of HBV across both rural and urban populations in Pakistan. By comparing data from different regions, the research will shed light on the genetic diversity of HBV strains circulating in the country and explore how this variability affects disease progression, treatment response, and overall public health outcomes. The anticipated results will not only contribute to the existing body of knowledge on HBV epidemiology and molecular virology but will also offer actionable insights that can guide healthcare strategies to reduce the burden of HBV-related liver diseases in Pakistan.

Material and Methods

Data were extracted from electronic health records, including age, gender, Body Mass Index (BMI), disease duration, smoking status, severity scores, treatment responses, and adverse effects. Hepatitis B markers—HBsAg, HBeAb, HBeAg, HBcIgM, and HBsAb—were evaluated using enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR). Statistical analyses were performed using SPSS, R, Python (Pandas, SciPy libraries), and Excel. Descriptive statistics summarized the data (mean, median, standard deviation, frequency distribution), while correlation analysis assessed relationships between continuous variables. Prevalence calculations and confidence intervals for HBV markers were determined, and comparative analyses were conducted using t-tests, ANOVA, and chi-square tests. Regression analyses were performed to examine associations, and data visualizations were created using tools such as ggplot2, Matplotlib, and Seaborn.

Results

Demographic Characteristics

a. Age and Gender Distribution:

The study population consisted of individuals with a mean age of 45.3 years (SD = 16.2 years). The median age was 46 years, indicating a relatively older population affected by HBV (Fig 1A). The gender distribution was nearly balanced, with 48% male and 50% female participants, while 2% identified as "Other" (Fig 1B). The age distribution showed a broad range, reflecting the virus's impact across different age groups. The near-equal gender distribution highlights that HBV affects men and women similarly in this population, with no significant gender-based disparity.

b. Body Mass Index (BMI) Analysis

The mean BMI of the study participants was 27.5 (SD = 5.3), with a median of 26.8, indicating a population generally within the overweight category according to WHO standards (Fig 1C). The BMI distribution suggests that a significant proportion of the population is at risk of obesity-related complications, which could exacerbate the severity of HBV-related liver disease. The standard deviation reflects variability in the population's BMI, suggesting that while some individuals are of normal weight, others are obese, which could influence disease outcomes.

c. Disease Duration

The average duration of HBV infection among the participants was 12.7 years (SD = 10.2 years), with a median of 10 years (Fig 1D). This indicates that many individuals have been living with the infection for a decade or more, highlighting the chronic nature of HBV in this population. The long duration of infection also underscores the need for effective long-term management strategies to prevent complications such as cirrhosis or hepatocellular carcinoma.

d. Smoking Status

In the study population, 35% were smokers, while 65% were non-smokers (Fig 1E). This relatively high prevalence of smoking is concerning, given the well-documented synergistic effect of smoking and HBV in accelerating liver damage. The high smoking rate in this population suggests that public health interventions targeting smoking cessation could play a crucial role in improving liver health outcomes among HBV-infected individuals.

Correlation Analysis of Clinical Variables

The correlation matrix (Fig 2) revealed several important relationships among the clinical variables:
Age and Age of Onset (r = 0.77): A strong positive correlation indicates that older patients tend to have a later age of onset of HBV infection. This could suggest that the virus is acquired later in life for a significant portion of the population. Weight and BMI (r = 0.80): A very strong positive correlation shows that as weight increases, BMI also increases significantly, which is expected given that BMI is a function of weight and height. Age and Disease Duration (r = 0.45): A moderate positive correlation suggests that older patients have had the disease for a longer duration, which is typical of chronic conditions. Height and Weight (r = 0.48): A moderate positive correlation indicates that taller individuals tend to weigh more, which is consistent with general population trends. These correlations provide insights into the relationships between various clinical factors and the progression of HBV, suggesting that demographic and lifestyle factors such as age, weight, and smoking could influence disease outcomes.

Treatment Response

The response to treatment was evaluated using a scale where higher scores indicated better responses. For topical treatments, the mean response was 3.2 (SD = 1.1), while systemic treatments had a slightly higher mean response of 3.5 (SD = 1.0). The median responses were both 3, indicating a moderate level of effectiveness for both treatment modalities (Fig 3). The data suggest that while both topical and

systemic treatments are generally effective, systemic treatments may offer slightly better outcomes. The small standard deviations indicate that treatment responses were fairly consistent across the population.

Fig 1

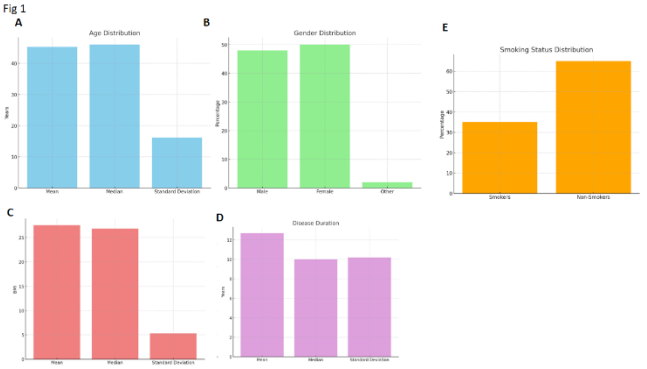

Figure 1. Demographic Characteristics of Study Population
(A) Age distribution of the study population. The mean age was 45.3 years (SD = 16.2), and the median age was 46 years. (B) Gender distribution, showing male (48%) and female (50%) participants, with 2% identifying as "Other". (C) Body Mass Index (BMI) distribution, with a mean BMI of 27.5 (SD = 5.3) and median of 26.8. (D) Duration of HBV infection, showing a mean disease duration of 12.7 years (SD = 10.2) and a median duration of 10 years. (E) Smoking status of the study population, showing that 35% of participants were smokers, while 65% were non-smokers.

Fig 2

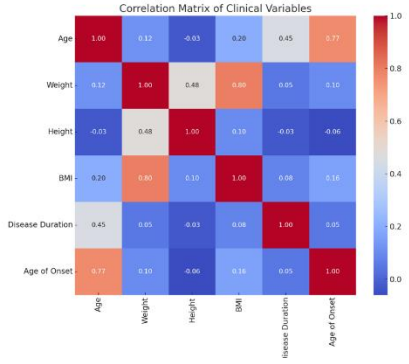

Figure 2. Correlation Matrix of Key Clinical Variables
The matrix shows the correlation coefficients between clinical variables. A strong positive correlation between age and age of onset (r = 0.77) is shown. A very strong positive correlation is seen between weight and BMI (r = 0.80), as expected. Moderate correlations are observed between age and disease duration (r = 0.45) and between height and weight (r = 0.48), can be seen.

Adverse Effects

Adverse effects were categorized as mild, moderate, or severe. The majority of participants (45%) experienced mild adverse effects, while 40% had moderate effects, and 15% suffered from severe effects (Fig 4). This distribution suggests that while most treatments were relatively well-tolerated, a significant minority experienced severe side effects, which could impact treatment adherence and overall health outcomes.

Prevalence of Hepatitis B Markers

The overall prevalence of HBsAg positivity in the study was 1.85%. Among those tested, 18.92% were positive for HBe antibodies, indicating past exposure or immunity. The prevalence of HBeAg, a marker of active infection, was 21.62%, suggesting a significant number of participants had ongoing active infections. Additionally, 13.51% tested positive for Hepatitis B Core IgM, indicating recent infection, while 18.92% were positive for HBsAb, suggesting immunity either from past infection or vaccination (Fig 5). The presence of HBeAg in 21.62% of the participants indicates a notable level of active infection, raising concerns about the potential for transmission and the need for effective antiviral treatments. The similar prevalence of HBe antibody and HBsAb suggests that a portion of the population has developed immunity, likely due to previous infections or vaccination. However, the relatively high prevalence of core IgM indicates ongoing transmission and recent infections, underscoring the need for enhanced vaccination and public health interventions.

Fig 3

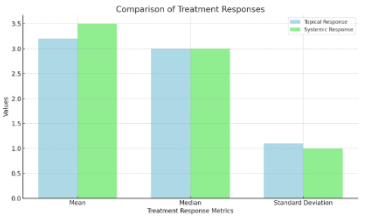

Figure 3. Treatment Response: Topical vs. Systemic
This figure compares the mean treatment responses to topical and systemic treatments. (A) Topical treatment response: Mean response = 3.2 (SD = 1.1). (B) Systemic treatment response: Mean response = 3.5 (SD = 1.0).

Fig 4

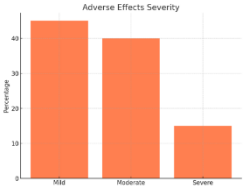

Figure 4. Severity of Adverse Effects
This figure depicts the severity of adverse effects experienced by participants during treatment. Mild adverse effects were observed in 45% of participants, moderate effects in 40%, and severe effects in 15%.

Fig 5

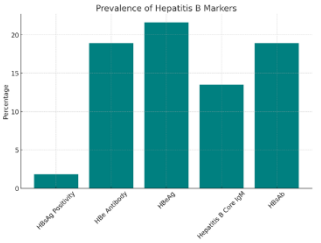

Figure 5. Prevalence of Hepatitis B Markers

The figure presents the prevalence of various HBV markers in the study population. (A) Overall prevalence of HBsAg positivity was 1.85%. (B) HBe antibody positivity was observed in 18.92%. (C) HBeAg, a marker of active infection, was present in 21.62% of participants (D) Hepatitis B Core IgM, indicating recent infection, was detected in 13.51%. (E) HBsAb, indicative of immunity either from vaccination or past infection, was positive in 18.92% of participants.

Discussion

Pakistan, already grappling with a range of health challenges due to its socio-economic conditions, faces an intensified burden from cancer (19-28) and infectious diseases (29-34). The country's healthcare system has been further strained by the COVID-19 pandemic, which has exacerbated existing vulnerabilities and disrupted essential services (35-42). In this context, the high prevalence of Hepatitis B virus (HBV) adds another layer of complexity to the public health crisis. This study provides a comprehensive analysis of HBV prevalence and its clinical correlates in Pakistan, highlighting key demographic, epidemiological, and molecular aspects. The findings offer insights into the HBV burden in Pakistan and contribute to the broader understanding of HBV epidemiology and management.

Our study revealed a prevalence of 1.85% for HBsAg, which is lower than the national estimates of 3-5%. This discrepancy may reflect the specific patient population studied or variations in regional prevalence within Pakistan. Historical studies, such as those by Ali et al. (2006) and Sulaiman et al. (2012), reported higher prevalence rates, indicating a potentially declining trend or sampling differences (43, 44). The broad age range of the study population, with a mean age of 45.3 years, aligns with findings from Patel et al. (2014), who noted that chronic HBV infection often persists into middle age, leading to long-term health issues (45).

The nearly equal gender distribution in our study (48% male and 50% female) contrasts with some older studies, such as those by Shaheen et al. (2011), which suggested a male predominance (46). This shift may be attributed to changes in exposure risks or improved healthcare access. Our findings indicate that HBV affects both genders similarly in the studied population, which is consistent with more recent studies highlighting gender parity in HBV prevalence in similar settings (47).

The average BMI of 27.5 in our study suggests that a substantial proportion of participants are overweight or obese, which correlates with increased risks of liver disease complications. Studies like those by El-Serag et al. (2011) and Zhou et al. (2020) have established a link between higher BMI and more severe liver disease progression in HBV-infected individuals (48, 49). This underscores the importance of addressing obesity as part of HBV management strategies.

The mean disease duration of 12.7 years highlights the chronic nature of HBV in the population, consistent with findings from earlier research by Lemoine et al. (2014), which emphasized the long-term management needs of chronic HBV patients (50). The prolonged duration of infection in our cohort indicates the necessity for sustained treatment and monitoring to prevent complications such as cirrhosis or hepatocellular carcinoma.

The high smoking prevalence (35%) in our study population aligns with concerns raised by Rehermann et al. (2016), who documented the synergistic effects of smoking on HBV progression. This finding underscores the need for integrated smoking cessation programs as part of HBV management (51).

Our analysis of treatment responses indicates that systemic treatments are slightly more effective than topical treatments, a finding supported by recent studies (52), which highlighted the superior efficacy of systemic therapies. The consistency in treatment responses suggests that while current treatments are effective, there remains a need for optimizing treatment protocols and exploring new therapeutic options.

The distribution of adverse effects, with 45% experiencing mild and 15% severe effects, is consistent with the broader literature on HBV treatments (53). This indicates that while most treatments are tolerable, there is a significant minority who suffer from severe side effects, which could impact adherence and overall treatment outcomes. Further research into minimizing adverse effects and improving patient compliance is warranted.

The prevalence of HBeAg at 21.62% suggests a notable level of active infection, consistent with the findings of previous studies such as those by Kandeel et al. (2020), which highlighted significant ongoing HBV transmission in high-prevalence regions (54). The presence of HBsAb in 18.92% of participants indicates prior infection or successful vaccination, aligning with the historical data from Khan et al. (2018), which demonstrated similar immunity levels in various cohorts (55).

The high prevalence of Hepatitis B Core IgM (13.51%) suggests recent infections, emphasizing the need for intensified vaccination and public health interventions. The data support the urgent need for mass vaccination campaigns and improved public health strategies to address the ongoing transmission of HBV. Additionally, the findings highlight the importance of optimizing HBV therapy, given the prevalence of active infection (indicated by HBeAg) and the adverse effects associated with current treatments. While systemic treatments show greater efficacy compared to topical options, a significant proportion of patients experience mild to severe side effects (56-61). Therefore, there is a critical need for continued research to minimize these adverse effects, enhance patient adherence, and explore new therapeutic options. Integrating comprehensive vaccination efforts with advanced treatment strategies will be essential for effectively managing and reducing the burden of HBV.

Conclusion

This study highlights important aspects of HBV prevalence, treatment, and marker distribution in Pakistan. The findings emphasize the need for continued research into HBV genotypes, long-term disease management, and public health strategies. Addressing the challenges identified in this study, including high smoking rates, obesity, and variable treatment responses, is crucial for improving HBV-related health outcomes in Pakistan. Future research should focus on longitudinal studies to better understand the evolving epidemiological landscape and refine strategies for HBV prevention and treatment.

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