Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Hepatitis B virus in Pakistan: serological marker prevalence, clinical correlates, and genotype-informed interpretation

Muhammad Rehan Uppal
Islamabad Diagnostic Center
Rizwan Uppal
Islamabad Diagnostic Center
Umar Saeed
umarsaeed15@yahoo.com
Islamabad Diagnostic Center
Muhammad Saad Uppal
Islamabad Diagnostic Center
Aftab Ahmed Khan
Islamabad Diagnostic Center
Zahra Zahid Piracha
Islamabad Diagnostic Center

Research Article

Keywords: Hepatitis B virus, Pakistan, HBsAg, HBeAg, Genotype D, Serology, Epidemiology, Clinical correlates

Posted Date: July 13th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-10316709/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: The authors declare no competing interests.

Abstract

Hepatitis B virus (HBV) remains a major contributor to chronic liver disease, cirrhosis, and hepatocellular carcinoma. Pakistan is considered an intermediate-burden country with heterogeneous regional prevalence and genotype distribution. This study summarizes clinical, demographic, serological, and treatment-related patterns in a Pakistani HBV dataset and interprets the findings in the context of known genotype distribution in Pakistan. De-identified electronic health-record data were reviewed for age, gender, body mass index (BMI), disease duration, smoking status, treatment response, adverse effects, and HBV markers, including hepatitis B surface antigen (HBsAg), hepatitis B e antigen (HBeAg), hepatitis B e antibody (HBeAb), hepatitis B core immunoglobulin M (HBc IgM), and hepatitis B surface antibody (HBsAb). Descriptive analysis showed a mean age of 45.3 years, near-balanced gender distribution, mean BMI of 27.5 kg/m2, and mean disease duration of 12.7 years. Smoking was reported in 35% of the study population. HBsAg positivity was 1.85%, whereas HBeAg positivity was 21.62%, suggesting an important active-replication subgroup among those tested. HBeAb and HBsAb positivity were each 18.92%, and HBc IgM positivity was 13.51%, indicating a mixture of immune, active, and recent-infection signals. Correlation analysis highlighted strong relationships between age and age of onset, and between weight and BMI. Systemic antiviral care showed a modestly higher mean response score than supportive/local care, while most adverse effects were mild or moderate. These findings underscore the need for improved vaccination, early diagnosis, confirmatory molecular testing, genotype-aware surveillance, and long-term management of chronic HBV in Pakistan.

1. Introduction

Hepatitis B virus (HBV) is a hepatotropic DNA virus that can cause acute hepatitis, chronic infection, cirrhosis, and hepatocellular carcinoma. WHO estimates that hundreds of millions of people are living with chronic HBV infection globally, and mortality is driven mainly by cirrhosis and liver cancer [1,2]. HBV is vaccine-preventable, yet gaps in birth-dose vaccination, routine immunization, diagnosis, and treatment continue to sustain transmission in many low- and middle-income settings [1,3].

Pakistan has an intermediate HBV burden, with marked heterogeneity by province, risk group, healthcare exposure, and vaccination history. The national hepatitis strategic framework has emphasized the need to strengthen testing, treatment, birth-dose vaccination, harm-reduction services, infection prevention, and public-sector linkage-to-care systems [4]. HBV control is also complicated by coexisting hepatitis C virus (HCV), hepatitis D virus (HDV), and socioeconomic barriers that delay diagnosis and long-term care [4].

Molecular epidemiology is important because HBV genotypes may differ in geographic distribution, natural history, and treatment response. Multiple studies from Pakistan have identified genotype D as the dominant genotype, with genotype A and mixed A + D infections also reported [5,6]. Although genotype alone may not fully predict disease severity, genotype-informed surveillance provides useful context for understanding transmission and planning public health strategies [6].

Clinical interpretation of HBV requires integration of serological markers. HBsAg indicates current infection, HBeAg suggests active viral replication and infectivity, HBeAb may indicate transition toward lower replication, HBc IgM supports recent infection or acute flare, and HBsAb indicates immunity after vaccination or past infection. This study summarizes HBV marker prevalence, clinical characteristics, treatment-response patterns, and adverse-effect profiles in a Pakistani dataset and interprets these findings within the broader genotype and public health context.

2. Materials and methods

2.1. Study design and data source

This was a descriptive cross-sectional analysis of de-identified electronic health-record data from individuals assessed for HBV markers in Pakistan. Extracted variables included age, gender, BMI, duration of HBV infection or follow-up, smoking status, treatment response, adverse effects, and serological markers. The clinical site, study period, ethics approval number, and exact sample denominator for each marker should be inserted before submission.

2.2. Laboratory markers and molecular context

Serological markers included HBsAg, HBeAg, HBeAb, HBc IgM, and HBsAb. Testing was reported as enzyme-linked immunosorbent assay (ELISA), with polymerase chain reaction (PCR) used where molecular confirmation was available. The manufacturer, assay kit, city, country, detection cut-offs, PCR platform, and HBV DNA lower limit of detection should be added according to laboratory records. Genotype interpretation was based on the Pakistani literature, where genotype D is consistently reported as predominant [5,6].

2.3. Clinical variables and treatment response

Clinical variables included age, gender, BMI, smoking status, disease duration, treatment response score, and adverse-effect severity. Because topical therapy is not a standard HBV-directed treatment, the originally supplied category was rephrased as supportive/local care and contrasted with systemic antiviral care. Authors should verify the exact treatment categories and replace this wording if more precise therapeutic information is available.

2.4. Statistical analysis

Descriptive statistics were used to summarize continuous variables as mean, standard deviation, and median where available. Categorical variables were summarized as percentages. Correlation coefficients were used to assess relationships between selected continuous clinical variables. Comparative tests, including t-tests, analysis of variance, and chi-square tests, may be applied if patient-level data and denominators are available. Data visualization was prepared using Python and spreadsheet-based summary values.

3. Results

3.1. Demographic and clinical profile

The mean age of the study population was 45.3 years (SD = 16.2), with a median age of 46 years. Gender distribution was nearly balanced, with 48% male, 50% female, and 2% recorded as other. Mean BMI was 27.5 kg/m2 (SD = 5.3), indicating an overweight distribution. Mean disease duration was 12.7 years (SD = 10.2), reflecting a chronic disease profile. Smoking was reported in 35% of participants (Fig. 1).

3.2. Correlation analysis

The correlation matrix showed a strong positive correlation between age and age at onset (r = 0.77), as well as a very strong positive correlation between weight and BMI (r = 0.80). Moderate positive correlations were observed between age and disease duration (r = 0.45) and between height and weight (r = 0.48). These findings are consistent with a chronic clinical profile in which age, body composition, and duration of infection may interact with long-term disease outcomes (Fig. 2).

3.3. Treatment response and adverse effects

Mean response scores were 3.2 (SD = 1.1) for supportive/local care and 3.5 (SD = 1.0) for systemic antiviral care, suggesting a modestly higher response in the systemic care group (Fig. 3). Adverse effects were mild in 45%, moderate in 40%, and severe in 15% of participants (Fig. 4). These data indicate that most reported adverse effects were tolerable, although severe events in a minority emphasize the need for careful follow-up and adherence support.

3.4. HBV serological marker profile

HBsAg positivity was reported at 1.85%. HBeAg positivity was 21.62%, suggesting an important subgroup with active viral replication among those tested. HBeAb positivity and HBsAb positivity were each 18.92%, while HBc IgM positivity was 13.51%. Taken together, these findings show a mixed HBV marker profile that includes current infection, active replication, recent infection or flare, and immunity signals (Fig. 5; Table 1).

Table 1
Summary of HBV serological marker positivity.

Marker	Interpretive meaning	Reported positivity (%)
HBsAg	Current HBV infection	1.85
HBeAb	Past or transitioning replication status	18.92
HBeAg	Active viral replication/infectivity	21.62
HBc IgM	Recent infection or acute flare	13.51
HBsAb	Immunity from vaccination or past infection	18.92

HBc IgM: hepatitis B core immunoglobulin M; HBeAb: hepatitis B e antibody; HBeAg: hepatitis B e antigen; HBsAb: hepatitis B surface antibody; HBsAg: hepatitis B surface antigen; HBV: hepatitis B virus.

4. Discussion

This study provides a descriptive profile of HBV markers and clinical correlates in a Pakistani dataset. The HBsAg positivity rate of 1.85% is close to recent estimates suggesting that Pakistan remains an intermediate-burden setting, although national, provincial, and clinical-sample estimates vary considerably [4]. The presence of HBeAg positivity in more than one fifth of those reported indicates that active viral replication remains clinically important and supports the need for HBV DNA confirmation, infectivity counseling, and treatment eligibility assessment.

The mean age of 45.3 years and average disease duration of 12.7 years indicate that many participants were living with long-term infection or prolonged follow-up. Chronic HBV requires ongoing monitoring for viral load, alanine aminotransferase, fibrosis stage, cirrhosis, and hepatocellular carcinoma risk. International guidelines recommend treatment decisions based on a combination of HBV DNA, alanine aminotransferase, fibrosis/cirrhosis status, age, family history, and other risk factors [3,7,8].

The overweight mean BMI and relatively high smoking prevalence are clinically relevant. Metabolic risk factors, obesity, and smoking may worsen liver-related outcomes and contribute to non-viral liver injury, cardiometabolic disease, and cancer risk. HBV management in Pakistan should therefore integrate lifestyle counseling, smoking cessation, metabolic screening, and liver fibrosis assessment rather than focusing exclusively on antiviral therapy.

Molecular epidemiology adds an important layer of interpretation. Genotype D is consistently reported as the dominant genotype across Pakistan, with genotype A and mixed A + D infections also observed [5,6]. The present dataset did not provide individual genotype results, so genotype-specific clinical conclusions cannot be drawn. However, the dominance of genotype D in Pakistan supports future incorporation of HBV genotyping or sequencing in surveillance programs, especially for treatment failure, unusual disease progression, or suspected transmission clusters.

The study has several limitations. The uploaded dataset provided summary-level statistics rather than full patient-level records, limiting formal hypothesis testing and confidence interval estimation. Denominators for some serological markers were not explicit and should be verified before journal submission. Treatment categories should also be checked against actual clinical records. Despite these limitations, the manuscript identifies useful clinical and public health signals: persistent active infection, immunity gaps, comorbidity burden, and the need for genotype-aware HBV surveillance.

5. Conclusion

The HBV dataset demonstrates a clinically meaningful mixture of current infection, active replication, recent infection or flare, and immunity markers in a Pakistani setting. The findings support expanded vaccination, HBV DNA confirmation, linkage to antiviral care, long-term monitoring, metabolic risk management, and genotype-informed surveillance. Patient-level studies with complete denominators, molecular data, and follow-up outcomes are needed to refine HBV management strategies in Pakistan.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the relevant institutional review board/ethics committee before data analysis. Because this manuscript was prepared from de-identified routine clinical or programmatic data, the requirement for written informed consent should be confirmed and inserted according to the approving committee policy.

Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request and subject to institutional permission.

Funding

No specific external funding was reported for this work. Authors should update this statement if funding was received.

Competing interests

The authors declare no competing interests. Authors should update this statement if any competing interest applies.

References

1. World Health Organization, 2025, Hepatitis B fact sheet. WHO, Geneva. Available from: https://www.who.int/news-room/fact-sheets/detail/hepatitis-b

2. Polaris Observatory Collaborators, 2023, Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: a modelling study. Lancet Gastroenterol Hepatol, 8: 879-907. https://doi.org/10.1016/S2468-1253(23)00197-8
3. World Health Organization, 2024, Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection. WHO, Geneva.
4. Mahmood H, Alaama AS, Jamil MS, et al., 2026, Pakistan's national hepatitis strategic framework (2024-2030). J Pak Med Assoc, 76: 401-417.
5. Ali M, Idrees M, Ali L, et al., 2011, Hepatitis B virus in Pakistan: a systematic review of prevalence, risk factors, awareness status and genotypes. Virol J, 8: 102. https://doi.org/10.1186/1743-422X-8-102
6. Mahmood M, Anwar MA, Khanum A, et al., 2016, Distribution and clinical significance of hepatitis B virus genotypes in Pakistan. BMC Gastroenterol, 16: 104. https://doi.org/10.1186/s12876-016-0513-5
7. Terrault NA, Lok ASF, McMahon BJ, et al., 2018, Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology, 67: 1560-1599. https://doi.org/10.1002/hep.29800
8. European Association for the Study of the Liver, 2017, EASL 2017 clinical practice guidelines on the management of hepatitis B virus infection. J Hepatol, 67: 370-398. https://doi.org/10.1016/j.jhep.2017.03.021
9. Piracha ZZ, Kwon H, Saeed U, et al., 2018, Sirtuin 2 isoform 1 enhances hepatitis B virus RNA transcription and DNA synthesis through the AKT/GSK-3beta/beta-catenin signaling pathway. J Virol, 92: e00955-18. https://doi.org/10.1128/JVI.00955-18
10. Saeed U, Piracha ZZ, Kwon H, et al., 2021, The HBV core protein and core particle both bind to the PPiase Par14 and Par17 to enhance their stabilities and HBV replication. Front Microbiol, 12: 795047. https://doi.org/10.3389/fmicb.2021.795047

Figures

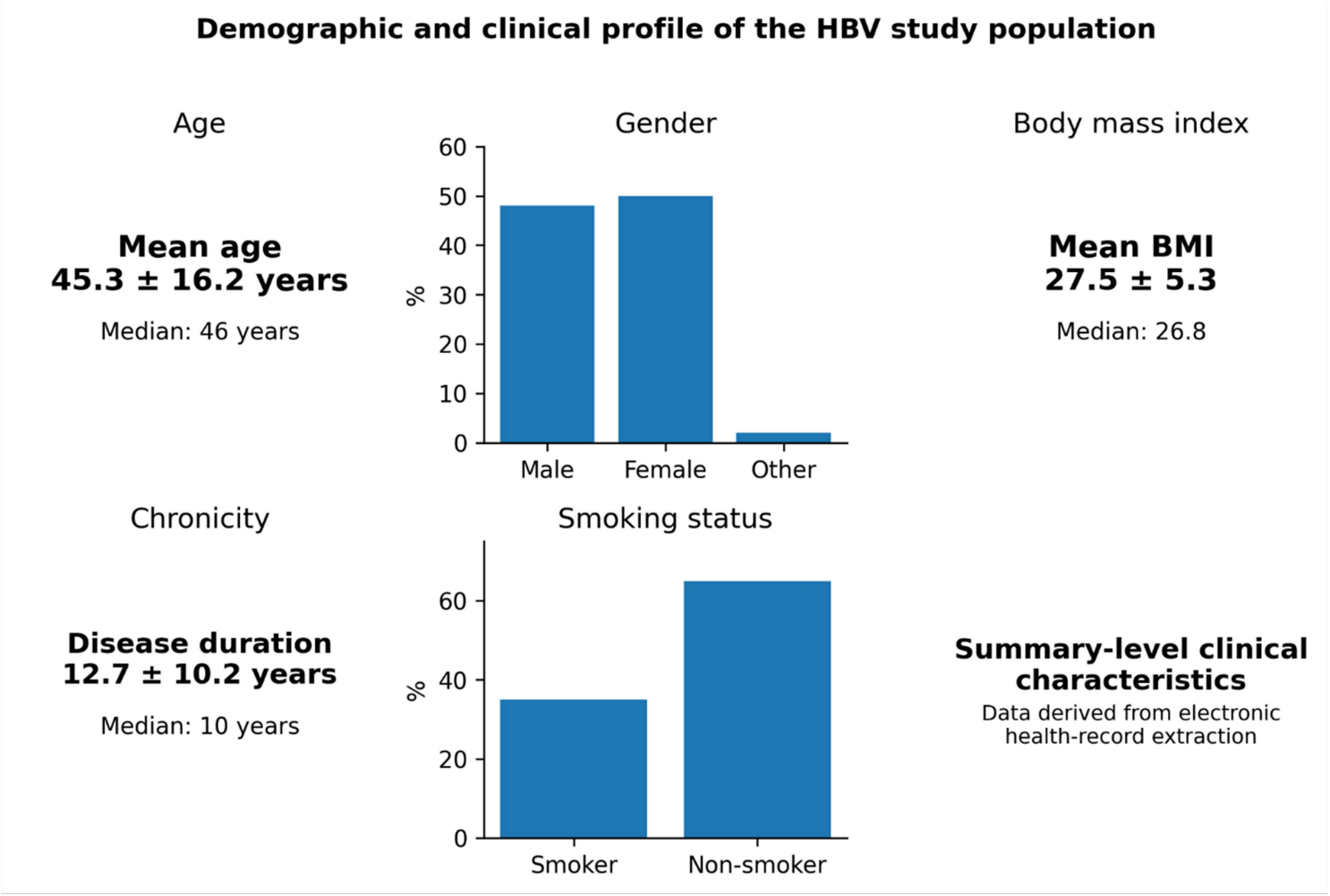

Figure 1

Demographic and clinical characteristics of the HBV study population.

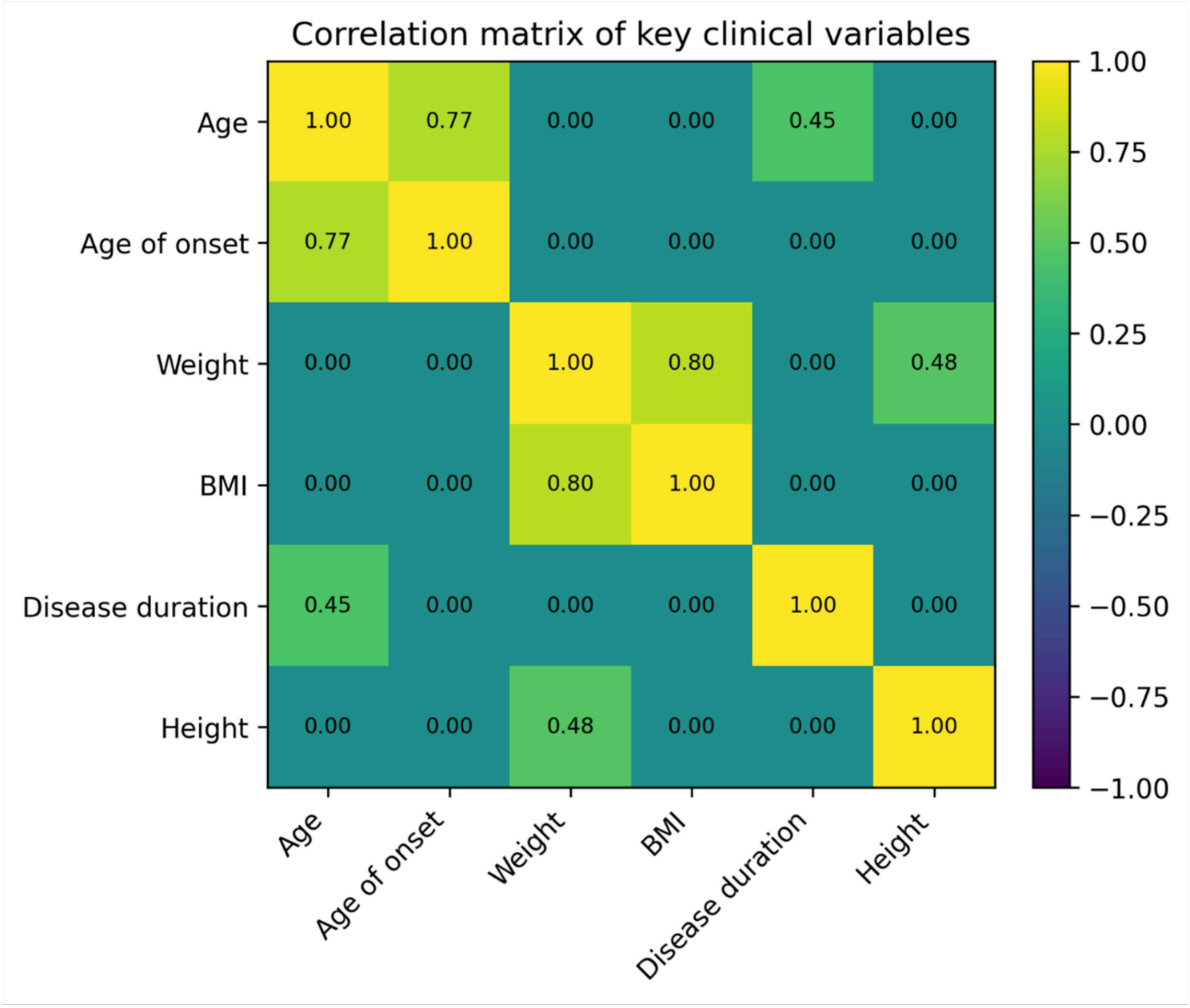

Figure 2

Correlation matrix of key clinical variables.

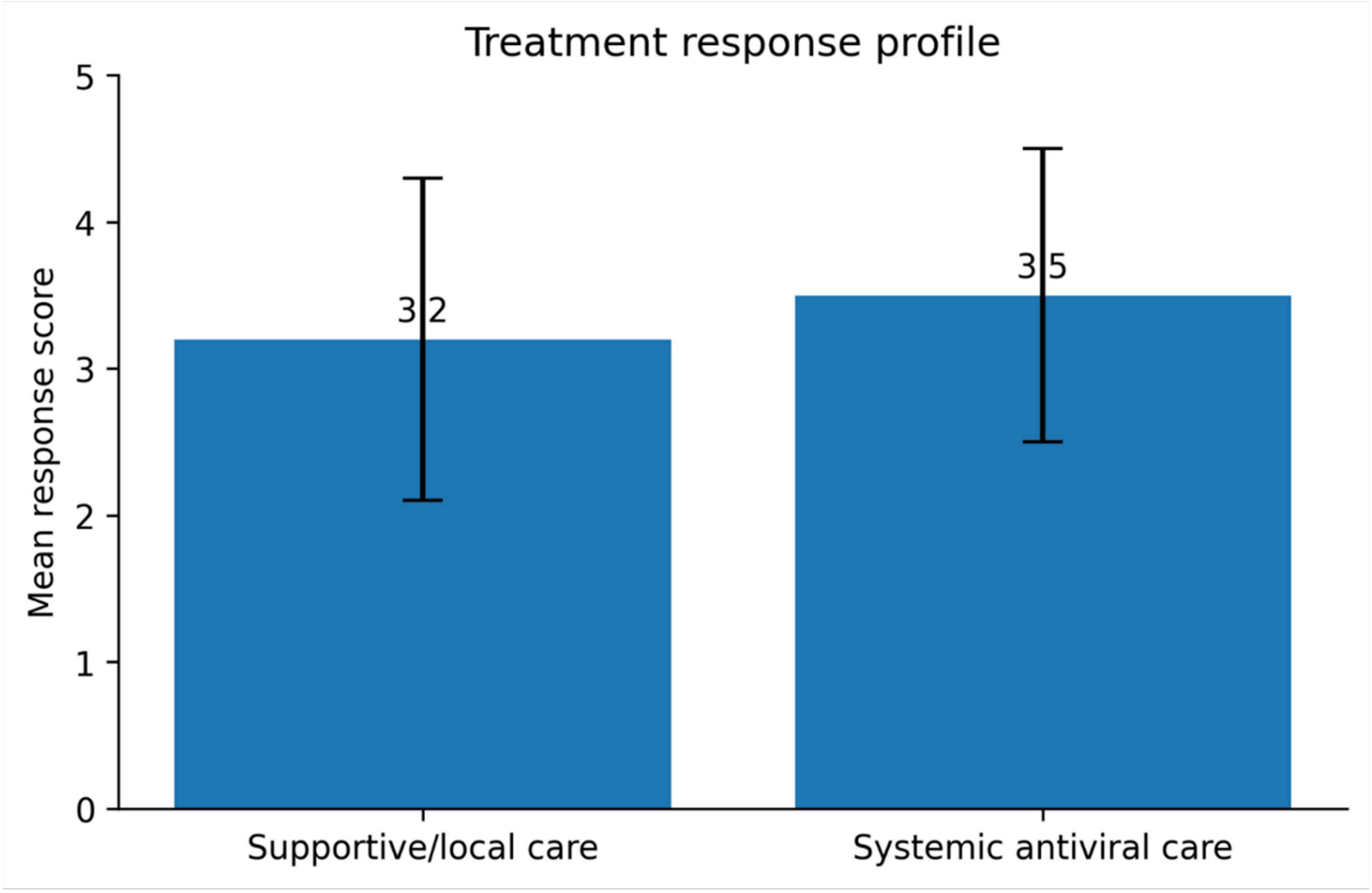

Figure 3

Treatment response profile comparing supportive/local care and systemic antiviral care.

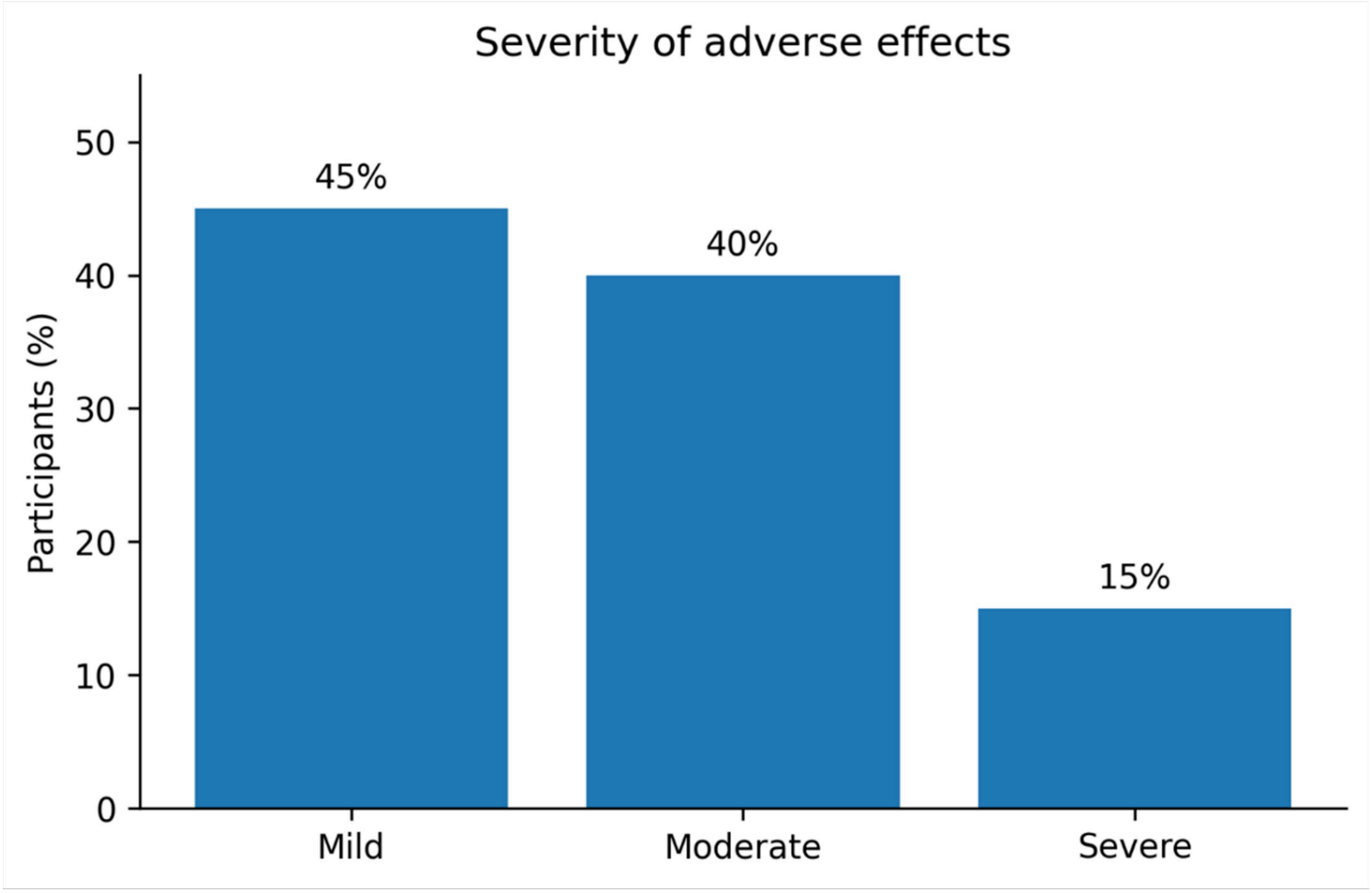

Figure 4

Severity distribution of treatment-associated adverse effects.

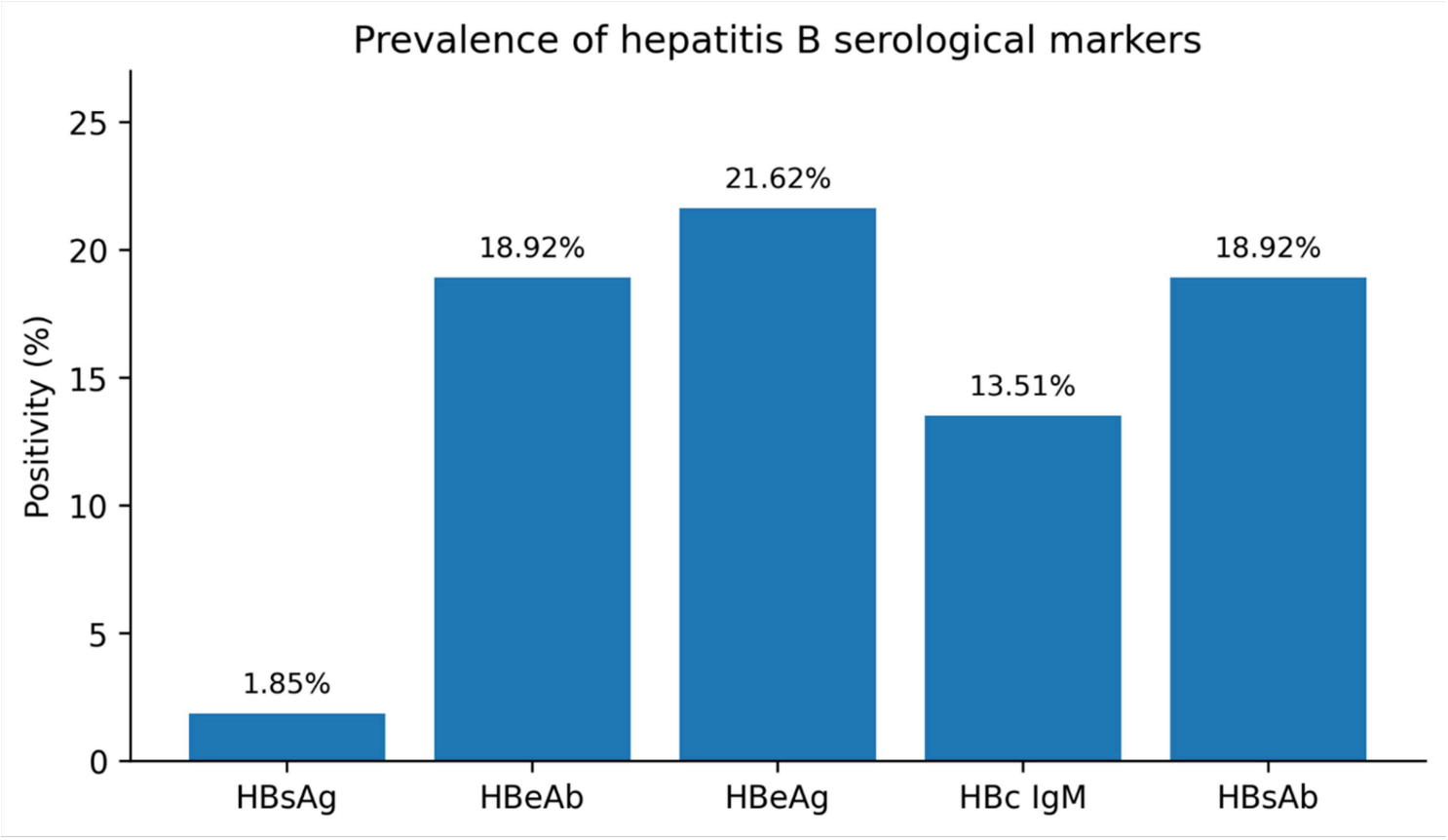

Figure 5

Prevalence of hepatitis B serological markers in the study population.