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EVALUATION OF LIVER FUNCTION TESTS AS BIOMARKERS IN PUBLIC HEALTH MANAGEMENT OF CHRONIC HEPATITIS B PATIENTS

Original Research

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Acknowledgement: The authors express gratitude to the Pakistan Institute of Medical Sciences for facilitating this research.

Conflict of Interest: None

Grant Support & Financial Support: None

ABSTRACT

Background: Chronic Hepatitis B (CHB) remains a major global health burden, contributing to significant morbidity and mortality, particularly in regions with limited access to advanced diagnostic tools. Liver function tests (LFTs), including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), albumin, and total bilirubin, are essential for assessing liver health. Identifying their role in predicting disease progression and guiding treatment strategies is crucial for optimizing CHB management in public health settings.

Objective: This study aimed to evaluate the utility of LFTs and fibrosis markers as biomarkers for disease monitoring, progression prediction, and treatment decision-making in CHB patients.

Methods: A prospective cohort study was conducted at the Pakistan Institute of Medical Sciences, Islamabad, from January 2022 to December 2023. A total of 208 CHB patients (HBsAg positive for ≥6 months) were enrolled. LFTs, including ALT, AST, ALP, albumin, and total bilirubin, were assessed at baseline and every three months over 24 months. Fibrosis indices (AST-to-Platelet Ratio Index [APRI] and Fibrosis-4 [FIB-4] score) were calculated using standard formulas. Statistical analysis included multivariate logistic regression, Pearson correlation, t-tests, and chi-square tests to evaluate associations between LFTs, fibrosis markers, and disease progression.

Results: The mean age of participants was 45.6 ± 11.2 years, with 57.69% males and 42.31% females. ALT increased from 81.3 ± 35.5 U/L at baseline to 95.1 ± 44.6 U/L at 24 months, while AST rose from 75.2 ± 31.7 U/L to 87.2 ± 41.4 U/L. ALP increased from 140.5 ± 61.2 U/L to 160.9 ± 72.5 U/L. Total bilirubin levels rose from 1.1 ± 0.4 mg/dL to 1.5 ± 0.6 mg/dL, while albumin decreased from 3.9 ± 0.7 g/dL to 3.5 ± 0.8 g/dL. The APRI score increased from 0.91 ± 0.45 to 1.02 ± 0.56, and the FIB-4 score from 2.57 ± 1.09 to 2.78 ± 1.21. Multivariate logistic regression showed ALT (OR: 1.05, $p<0.001$), AST (OR: 1.04, $p<0.001$), ALP (OR: 1.02, $p=0.012$), and total bilirubin (OR: 1.43, $p=0.002$) as significant predictors of disease progression, while albumin had a protective effect (OR: 0.54, $p<0.001$).

Conclusion: LFTs, particularly ALT, AST, ALP, total bilirubin, and albumin, alongside fibrosis markers APRI and FIB-4, serve as reliable indicators of CHB progression. Integrating these biomarkers into public health strategies may enhance disease surveillance, facilitate early interventions, and improve clinical management.

Keywords: Alanine Aminotransferase, Aspartate Aminotransferase, Biomarkers, Chronic Hepatitis B, Disease Progression, Fibrosis Markers, Liver Function Tests.

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INTRODUCTION

Chronic hepatitis B (CHB) remains a significant global health challenge, affecting approximately 296 million individuals and contributing substantially to morbidity and mortality worldwide (1). The disease is a major cause of liver-related complications, including cirrhosis and hepatocellular carcinoma (HCC), particularly in regions such as East Asia and sub-Saharan Africa, where perinatal and early childhood transmission are prevalent (2,3). Despite advancements in antiviral therapy and the widespread implementation of vaccination programs, CHB continues to pose a substantial public health burden, necessitating effective monitoring and management strategies to mitigate disease progression and associated complications (4). Liver function tests (LFTs) serve as fundamental biochemical markers in evaluating hepatic health, particularly in individuals with CHB. These tests, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, albumin, and alkaline phosphatase (ALP), provide valuable insights into hepatic inflammation, fibrosis, and synthetic function (5). Elevated ALT and AST levels are indicative of hepatocellular injury, while hypoalbuminemia reflects impaired liver synthetic capacity, which may signify advanced disease (6,7). Additionally, non-invasive fibrosis markers such as the AST-to-Platelet Ratio Index (APRI) and Fibrosis-4 (FIB-4) score are increasingly utilized in clinical practice for assessing liver fibrosis without the need for invasive procedures like biopsy (8). These tests not only aid in evaluating disease severity but also guide therapeutic decision-making and prognosis in CHB patients.

Incorporating LFTs as standardized biomarkers in public health initiatives could enhance early detection, facilitate disease monitoring, and optimize healthcare resource allocation, particularly in low-resource settings where access to advanced diagnostic modalities such as elastography and liver biopsy is limited (9,10). Given that CHB often remains asymptomatic in its early stages, routine LFT screening could enable the identification of at-risk individuals and assist in stratifying patients based on disease severity, allowing for timely intervention and improved patient outcomes (11). Furthermore, the cost-effectiveness of LFTs makes them a practical tool for large-scale screening and disease surveillance programs, reinforcing their potential role in strengthening CHB management strategies at a public health level (12). Despite their widespread clinical use, the role of LFTs as standardized biomarkers in public health management remains inadequately explored. There is limited understanding of their predictive accuracy in monitoring disease progression across diverse populations, as well as their integration into large-scale screening programs and their subsequent impact on health policies. Addressing these knowledge gaps could enhance the utilization of LFTs in CHB management, ultimately contributing to improved patient outcomes and more effective disease control measures. Therefore, this study aims to evaluate the utility of LFTs as biomarkers in the public health management of CHB by assessing their effectiveness in disease monitoring, progression prediction, and treatment decision-making.

METHODS

This study employed a prospective cohort design to evaluate the utility of liver function tests (LFTs) as biomarkers in the public health management of chronic hepatitis B (CHB) patients. The research was conducted at the Pakistan Institute of Medical Sciences, Islamabad, over a two-year period from January 2022 to December 2023. Adult patients aged 18 years and older with a confirmed diagnosis of CHB, defined by the presence of hepatitis B surface antigen (HBsAg) for at least six months, were enrolled. Inclusion criteria required participants to have baseline LFT results, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, and albumin, and to provide informed consent. To ensure uniformity in the study population and minimize confounding factors, exclusion criteria included patients with pre-existing cirrhosis or hepatocellular carcinoma at the time of recruitment, those with incomplete clinical records, those who withdrew from the study, and individuals who had initiated antiviral therapy within the last six months before enrollment. This criterion was applied to focus on either treatment-naïve patients or those who had been on stable antiviral therapy for at least six months, ensuring a more consistent evaluation of LFT trends (13). Participants were recruited using a convenience sampling technique, with a total of 208 CHB patients included based on availability during the study period. While this sampling approach allowed for efficient data collection, its potential limitations in generalizability will be acknowledged in the study's limitations section. Data were collected prospectively using a structured data collection form, recording demographic and clinical information such as age, gender, medical history, and comorbid conditions. LFTs were assessed at baseline and subsequently every three months throughout the two-year follow-up period. In addition to routine LFT assessments, non-invasive

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fibrosis scores, including the Fibrosis-4 (FIB-4) and AST-to-Platelet Ratio Index (APRI), were calculated to evaluate hepatic fibrosis. Patient adherence to treatment, therapeutic interventions, and disease progression were systematically documented (14).

Statistical analysis was performed using SPSS version 25. Descriptive statistics, including means, standard deviations, frequencies, and percentages, were used to summarize demographic and clinical characteristics. Pearson's correlation test was applied to assess the relationship between LFT parameters and disease progression, as indicated by alterations in LFT values and clinical outcomes. Continuous variables were compared across patient subgroups using independent t-tests, while categorical variables were analyzed using chi-square tests. A multivariate logistic regression model was utilized to identify predictors of disease progression based on LFT data, with statistical significance set at $p<0.05$ (12). Ethical approval was obtained from the Institutional Review Board (IRB) of the Pakistan Institute of Medical Sciences, Islamabad. Written informed consent was obtained from all participants before enrollment, ensuring voluntary participation and adherence to ethical standards. The study complied with the principles outlined in the Declaration of Helsinki, maintaining patient confidentiality and safeguarding participants' rights throughout the research period.

RESULTS

The study analyzed 208 patients diagnosed with chronic hepatitis B (CHB), with a mean age of 45.6 ± 11.2 years. Among these, 57.69% were male (n=120) and 42.31% were female (n=88). A family history of CHB was reported in 63.46% of patients, while 45.7% had a documented family history of liver disorders. The mean disease duration was 8.6 ± 5.2 years. Comorbid conditions were prevalent, with hypertension in 35.10% (n=73), diabetes mellitus in 32.69% (n=68), and liver cirrhosis in 8.65% (n=18). Baseline liver function test (LFT) results showed mean ALT levels of 81.3 ± 35.5 U/L, AST levels of 75.2 ± 31.7 U/L, and ALP levels of 140.5 ± 61.2 U/L. Liver synthetic function was reflected by a mean albumin level of 3.9 ± 0.7 g/dL and total bilirubin levels of 1.1 ± 0.4 mg/dL. Fibrosis indices revealed an APRI score of 0.91 ± 0.45 and a FIB-4 score of 2.57 ± 1.09. Over the 24-month study period, progressive increases were observed in markers of liver injury. ALT levels rose from 81.3 ± 35.5 U/L at baseline to 95.1 ± 44.6 U/L at 24 months, while AST levels increased from 75.2 ± 31.7 U/L to 87.2 ± 41.4 U/L. ALP levels also showed an increasing trend, from 140.5 ± 61.2 U/L to 160.9 ± 72.5 U/L. Indicators of impaired liver function, such as total bilirubin, increased from 1.1 ± 0.4 mg/dL to 1.5 ± 0.6 mg/dL, while albumin levels declined from 3.9 ± 0.7 g/dL to 3.5 ± 0.8 g/dL. Fibrosis progression was evident, with the APRI score increasing from 0.91 ± 0.45 to 1.02 ± 0.56 and the FIB-4 score rising from 2.57 ± 1.09 to 2.78 ± 1.21.

Multivariate logistic regression analysis identified significant predictors of disease progression, with ALT (OR: 1.05, 95% CI: 1.03–1.07, $p<0.001$), AST (OR: 1.04, 95% CI: 1.02–1.06, $p<0.001$), ALP (OR: 1.02, 95% CI: 1.01–1.04, $p=0.012$), and total bilirubin (OR: 1.43, 95% CI: 1.16–1.77, $p=0.002$) showing strong associations with worsening liver function. Albumin demonstrated a protective effect, with lower levels correlating with disease severity (OR: 0.54, 95% CI: 0.43–0.68, $p<0.001$). Fibrosis markers APRI (OR: 1.58, 95% CI: 1.31–1.91, $p<0.001$) and FIB-4 (OR: 1.44, 95% CI: 1.20–1.74, $p<0.001$) were also significantly associated with disease progression. Further analysis revealed that patients with disease progression had higher rates of hospitalization (24.78% vs. 13.68%, $p=0.029$) and mortality (7.96% vs. 2.11%, $p=0.031$), despite similar rates of treatment initiation (95.58% vs. 92.63%, $p=0.55$) and adherence (94.69% vs. 95.79%, $p=0.74$). Pearson correlation analysis indicated strong positive associations between disease severity and ALT ($r=0.72$, $p<0.001$), AST ($r=0.68$, $p<0.001$), ALP ($r=0.53$, $p<0.01$), total bilirubin ($r=0.60$, $p<0.001$), APRI score ($r=0.77$, $p<0.001$), and FIB-4 score ($r=0.71$, $p<0.001$), while albumin exhibited a significant negative correlation ($r=-0.65$, $p<0.001$), supporting its role as a marker of hepatic function decline.

Chi-square analysis identified significant associations between disease progression and liver cirrhosis ($\chi^2=5.13$, $p=0.024$), diabetes mellitus ($\chi^2=7.25$, $p=0.007$), and hypertension ($\chi^2=4.12$, $p=0.042$), suggesting that these comorbidities may contribute to worsening liver function. No statistically significant correlations were found for gender ($\chi^2=1.42$, $p=0.23$) or family history of CHB ($\chi^2=3.20$, $p=0.073$). Comparative analysis using t-tests demonstrated significantly higher ALT (125.4 ± 45.2 vs. 61.3 ± 22.7, $p<0.001$), AST (120.2 ± 49.5 vs. 56.4 ± 18.1, $p<0.001$), ALP (160.9 ± 65.3 vs. 125.2 ± 50.1, $p<0.001$), and total bilirubin (1.3 ± 0.5 vs. 1.0 ± 0.3, $p<0.001$) levels in patients with disease progression compared to those without. Conversely, albumin levels were significantly lower in the progression group (3.6 ± 0.8 vs. 4.1 ± 0.6, $p<0.001$), reinforcing its role in indicating hepatic deterioration.

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Table 1: Demographic and Clinical Characteristics of CHB Patients (n=208)

Characteristic		Number of Patients (n;%)
Age	(Mean ± SD)	45.6 ± 11.2 years
Gender	Male	120 (57.69)
	Female	88 (42.31)
Comorbidities	Hypertension	73 (35.10)
	Diabetes Mellitus	68 (32.69)
	Liver Cirrhosis	18 (8.65)
	Family History of CHB	132 (63.46)
Medical History	Family History	95 (45.7)
Mean Duration of Disease (years)	(Mean ± SD)	8.6 ± 5.2

Table 2: Baseline Liver Function Test Results in CHB Patients

Liver Function Test Parameter	Mean ± SD
ALT (U/L)	81.3 ± 35.5
AST (U/L)	75.2 ± 31.7
ALP (U/L)	140.5 ± 61.2
Total Bilirubin (mg/dL)	1.1 ± 0.4
Albumin (g/dL)	3.9 ± 0.7
APRI Score	0.91 ± 0.45
FIB-4 Score	2.57 ± 1.09

Table 3: Disease Progression and Changes in LFT Parameters Over Time

LFT Parameter	Baseline	6 months	12 months	18 months	24 months
ALT (U/L)	81.3 ± 35.5	85.7 ± 38.2	89.6 ± 40.1	92.2 ± 42.3	95.1 ± 44.6
AST (U/L)	75.2 ± 31.7	79.1 ± 34.3	82.3 ± 36.2	84.9 ± 39.1	87.2 ± 41.4
ALP (U/L)	140.5 ± 61.2	145.2 ± 64.3	150.3 ± 68.4	155.8 ± 70.2	160.9 ± 72.5
Total Bilirubin (mg/dL)	1.1 ± 0.4	1.2 ± 0.4	1.3 ± 0.5	1.4 ± 0.5	1.5 ± 0.6
Albumin (g/dL)	3.9 ± 0.7	3.8 ± 0.7	3.7 ± 0.7	3.6 ± 0.7	3.5 ± 0.8
APRI Score	0.91 ± 0.45	0.93 ± 0.47	0.95 ± 0.49	0.98 ± 0.52	1.02 ± 0.56
FIB-4 Score	2.57 ± 1.09	2.63 ± 1.12	2.68 ± 1.15	2.72 ± 1.18	2.78 ± 1.21

Table 4: Predictors of Disease Progression Based on LFTs (Multivariate Logistic Regression)

Predictor Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
ALT (U/L)	1.05	1.03 - 1.07	<0.001
AST (U/L)	1.04	1.02 - 1.06	<0.001
ALP (U/L)	1.02	1.01 - 1.04	0.012
Total Bilirubin (mg/dL)	1.43	1.16 - 1.77	0.002
Albumin (g/dL)	0.54	0.43 - 0.68	<0.001
APRI Score	1.58	1.31 - 1.91	<0.001
FIB-4 Score	1.44	1.20 - 1.74	<0.001

Table 5: Impact of LFTs on Public Health Decision-Making and Patient Outcomes

Parameter	No Progression (n=95)	Progression (n=113)	p-value
Treatment Initiation	88 (92.63%)	108 (95.58%)	0.55
Adherence to Treatment	91 (95.79%)	107 (94.69%)	0.74
Hospitalization	13 (13.68%)	28 (24.78%)	0.029*
Mortality	2 (2.11%)	9 (7.96%)	0.031*

*P-value is significant

Table 6: Pearson Correlation Analysis Between Liver Function Test (LFT) Parameters and Disease Progression

LFT Parameter	Disease Severity (based on LFT changes)	p-value
ALT (U/L)	0.72** (positive correlation)	<0.001
AST (U/L)	0.68** (positive correlation)	<0.001
ALP (U/L)	0.53** (positive correlation)	<0.01
Total Bilirubin (mg/dL)	0.60** (positive correlation)	<0.001
Albumin (g/dL)	-0.65** (negative correlation)	<0.001
APRI Score	0.77** (positive correlation)	<0.001
FIB-4 Score	0.71** (positive correlation)	<0.001

Table 6: Chi-Square Test Results for Associations Between Categorical Variables and Disease Progression

Categorical Variable	Disease Progression	Chi-Square Value	p-value
Gender (Male vs. Female)	No Progression: 63 (30.30%) Progression: 57 (27.40%)	1.42	0.23
Hypertension (Yes vs. No)	No Progression: 55 (26.44%) Progression: 70 (33.65%)	4.12	0.042*
Diabetes Mellitus (Yes vs. No)	No Progression: 49 (23.56%) Progression: 85 (40.87%)	7.25	0.007**
Liver Cirrhosis (Yes vs. No)	No Progression: 10 (4.81%) Progression: 8 (3.85%)	5.13	0.024*
Family History of CHB (Yes vs. No)	No Progression: 77 (37.02%) Progression: 55 (26.44%)	3.20	0.073

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Table 7: t-Test Comparison of Liver Function Test (LFT) Values Between Patient Groups Based on Disease Progression

LFT Parameter	No Progression (n=95)	Progression (n=113)	t-Statistic	p-value
ALT (U/L)	61.3 ± 22.70	125.4 ± 45.20	9.61	<0.001
AST (U/L)	56.4 ± 18.10	120.2 ± 49.50	8.72	<0.001
ALP (U/L)	125.2 ± 50.10	160.9 ± 65.30	5.21	<0.001
Total Bilirubin (mg/dL)	1.0 ± 0.30	1.3 ± 0.50	4.83	<0.001
Albumin (g/dL)	4.1 ± 0.60	3.6 ± 0.80	7.68	<0.001

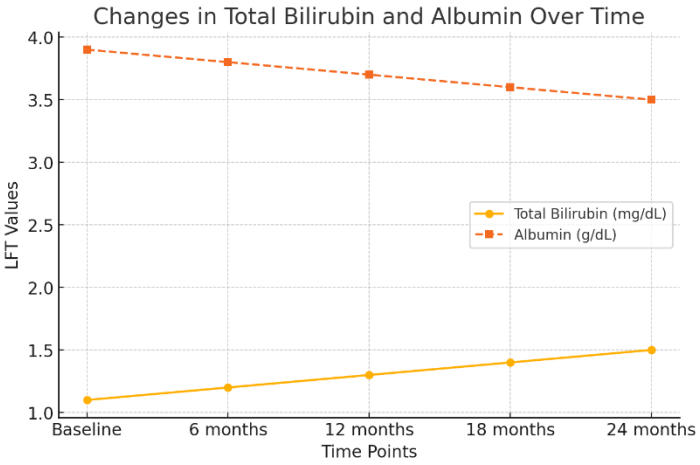

Figure 2 Changes in Total Bilirubin and Albumin Over Time

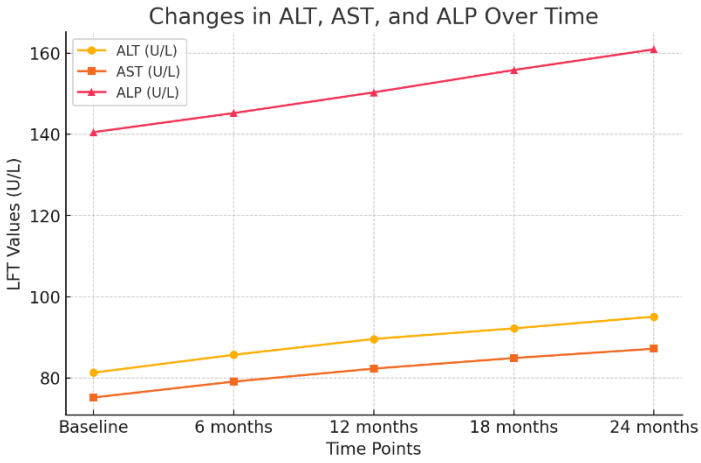

Figure 1 Changes in ALT, AST, and ALP Over Time

DISCUSSION

This study evaluated the utility of liver function tests (LFTs) in monitoring disease progression and guiding public health strategies for chronic hepatitis B (CHB) patients. Findings demonstrated that LFTs played a significant role in assessing liver injury, fibrosis progression, and predicting clinical outcomes. The observed trend of increasing alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) levels over 24 months was consistent with previously reported associations between elevated LFT markers and hepatic deterioration in chronic viral hepatitis. Elevated ALT and AST levels were strongly linked to liver inflammation and fibrosis, which aligns with prior research highlighting their diagnostic and prognostic value in CHB management (15). The progressive decline in albumin levels alongside an increase in total bilirubin further supported the indication of worsening hepatic synthetic function. The observed reduction in albumin levels from baseline to 24 months corresponded with findings from earlier studies where hypoalbuminemia was associated with advanced liver disease and reduced hepatic reserve. Similarly, the rise in total bilirubin levels reflected declining liver excretory function, a finding that has been widely documented in CHB disease progression. These biochemical alterations collectively reinforce the role of LFTs as reliable indicators of hepatic function impairment (16).

The predictive utility of LFTs was further substantiated by multivariate logistic regression analysis, which identified ALT, AST, ALP, and total bilirubin as significant predictors of disease progression, while albumin exhibited a protective effect. Fibrosis indices, including APRI and FIB-4 scores, showed a steady increase over time, reinforcing their relevance as non-invasive markers of hepatic fibrosis. The strong correlation between LFT abnormalities and worsening disease severity was consistent with previous findings demonstrating their predictive capability for CHB-related complications (17). The impact of disease progression on patient outcomes was evident, as individuals with worsening LFT parameters exhibited higher hospitalization and mortality rates compared to those with stable liver function. These findings highlighted the potential role of routine LFT monitoring in identifying high-risk patients early, thereby

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facilitating timely clinical intervention and improving long-term outcomes. Evidence from previous studies has emphasized the importance of integrating LFT assessments into routine CHB management to optimize public health strategies and resource allocation (18).

This study was strengthened by its prospective design and comprehensive evaluation of multiple LFT parameters, which allowed for a detailed assessment of their trends over a prolonged period. The inclusion of non-invasive fibrosis scores further enhanced the robustness of the analysis. However, certain limitations need to be considered. The single-center design may limit the generalizability of findings to broader populations with varying demographic and geographic characteristics. Although the sample size was sufficient for statistical analysis, the use of convenience sampling introduced potential selection bias. Additionally, the absence of a control group restricted direct comparisons with non-CHB individuals or those receiving different therapeutic interventions. The lack of liver biopsy data also prevented direct histological validation of fibrosis progression, necessitating reliance on APRI and FIB-4 scores as surrogate markers. Furthermore, the influence of antiviral therapy on LFT trends was not accounted for, which could have impacted biochemical parameters over time (19,20). Future research should focus on multicenter studies with larger, more diverse cohorts to enhance the external validity of findings. Incorporating liver biopsy data or elastography assessments alongside LFTs would provide a more comprehensive evaluation of hepatic fibrosis progression. Further exploration of the interplay between antiviral therapy and LFT trends could yield valuable insights into treatment efficacy and disease monitoring. Expanding research into the cost-effectiveness of routine LFT screening in public health settings could also inform policy decisions regarding large-scale CHB management programs (21,22).

CONCLUSION

This study underscores the significance of liver function tests as valuable biomarkers for monitoring, diagnosing, and managing chronic hepatitis B. The findings highlight the strong predictive value of elevated liver enzymes, increased bilirubin levels, declining albumin, and fibrosis markers in assessing disease progression. These biomarkers serve as practical and cost-effective tools, particularly in resource-limited settings, facilitating early intervention and improving patient management. The integration of LFTs into public health strategies holds promise for enhancing disease surveillance, guiding timely treatment decisions, and optimizing healthcare resources. Further research is essential to establish standardized protocols for their broader implementation in diverse populations, ensuring more effective disease control and improved patient outcomes.

AUTHOR CONTRIBUTIONS

Author	Contribution
Tahrim Zafar	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Urooj Liaqat	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Zeeshan Asghar*	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Sohail Munawar	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Mazalfa Tariq	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Umm E Habiba	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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