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Serum Alpha-Fetoprotein and Its Association with Glycemic Control, Liver Enzymes, and Renal Function among Adult Patients: A Cross-Sectional Study

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Abstract

Background: Serum alpha-fetoprotein (AFP) is widely used as a tumor marker, particularly in hepatocellular carcinoma; however, its levels may be influenced by non-malignant metabolic and biochemical factors. The relationship between AFP and glycemic status, liver enzymes, and renal function remains incompletely understood.

Objective: This study aimed to evaluate the association between serum AFP levels and glycemic control, liver enzymes, and renal function among adult patients.

Methods: This analytical cross-sectional study was conducted among 200 adult patients (130 males, 70 females) from January to December 2024 at a tertiary-level cancer hospital. Biochemical parameters including fasting blood glucose, liver enzymes, renal function markers, lipid profile, and hematological indices were analyzed. AFP levels were measured using immunoassay techniques. Data were expressed as mean ± standard deviation, and correlation analysis was performed to assess associations between AFP and other variables. A p-value <0.05 was considered statistically significant.

Results: The mean AFP level was 18.72 ± 96.45 ng/mL, showing a highly skewed distribution. Significant positive correlations were observed between AFP and fasting blood glucose ($r = 0.28$, $p = 0.002$), ALT ($r = 0.32$, $p < 0.001$), AST ($r = 0.25$, $p = 0.004$), creatinine ($r = 0.19$, $p = 0.021$), and urea ($r = 0.22$, $p = 0.011$). Abnormal AFP levels were more frequent among females (38.6%) compared to males (22.3%), while renal abnormalities were more prevalent in males.

Conclusion: Serum AFP levels are significantly associated with metabolic, hepatic, and renal parameters. These findings suggest that AFP elevation may reflect underlying metabolic and organ dysfunction rather than malignancy alone, highlighting the need for cautious clinical interpretation.

Keywords: Alpha-fetoprotein; Glycemic status; Liver enzymes; Renal function; Cross-sectional study.

Introduction

Glycemic dysregulation, encompassing prediabetes and diabetes mellitus, has emerged as a major global public health challenge, with a rapidly increasing burden in low- and middle-income countries [1]. Chronic hyperglycemia is associated with a spectrum of metabolic disturbances,

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including oxidative stress, low-grade inflammation, insulin resistance, and altered lipid and protein metabolism. These pathophysiological mechanisms contribute not only to classical complications such as cardiovascular, hepatic, and renal dysfunction but also influence routine biochemical parameters widely used in clinical practice [2]. Alpha-fetoprotein (AFP) is a glycoprotein predominantly produced during fetal development and is widely utilized as a tumor marker, particularly in the diagnosis and monitoring of hepatocellular carcinoma [3]. However, elevated AFP levels are not specific to malignancy and may be observed in various benign conditions, including chronic liver disease, hepatic regeneration, viral hepatitis, and metabolic disorders. In recent years, increasing evidence suggests that metabolic abnormalities, especially those associated with impaired glycemic control, may independently alter AFP levels, thereby complicate its clinical interpretation and potentially lead to diagnostic uncertainty [4]. Liver enzymes, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP), serve as essential indicators of hepatic function and are frequently altered in individuals with diabetes and metabolic syndrome [5]. Similarly, renal function markers such as serum creatinine and blood urea are affected by prolonged hyperglycemia and microvascular damage, reflecting underlying renal impairment [6]. The interplay between glycemic status, hepatic dysfunction, and renal impairment may collectively influence circulating biomarker levels, including AFP. Despite these biological plausibilities, the combined relationship between AFP and key metabolic parameters remains insufficiently explored in clinical settings [7]. In Bangladesh, the prevalence of diabetes and metabolic syndrome has been rising steadily over the past decade, posing a significant burden on the healthcare system. Concurrently, liver-related disorders, including viral hepatitis and non-alcoholic fatty liver disease, are also highly prevalent [8]. In such a context, the interpretation of AFP levels becomes particularly challenging, as both metabolic and hepatic factors may contribute to its elevation even in the absence of malignancy. However, there is a lack of comprehensive studies from Bangladesh evaluating the association of AFP with glycemic control, liver enzymes, and renal function in adult patients [9]. Furthermore, clinical and lifestyle factors such as hepatitis B and C infection, alcohol consumption, and history of chronic liver disease may act as important confounders influencing AFP levels. Understanding the combined impact of these variables is essential for improving the clinical utility and interpretation of AFP in routine practice. Therefore, the present study aimed to evaluate the association between serum alpha-fetoprotein levels and glycemic control, liver enzymes, and renal function among adult patients in a tertiary-level hospital setting in Bangladesh.

Materials and Methods

Study Design and Setting

This analytical cross-sectional study was conducted among adult patients attending a tertiary-level cancer hospital in Bangladesh. The study was carried out over a one-year period from January 2024 to December 2024. The objective was to evaluate the association between serum alpha-fetoprotein (AFP) levels and selected metabolic, hepatic, and renal parameters in a real-world clinical setting.

Study Population and Sample Size

A total of 200 adult participants aged ≥18 years were consecutively enrolled during the study period, including 130 males and 70 females. Participants were included if complete biochemical and clinical data were available. Patients with missing laboratory values, known malignancy (other than suspected hepatocellular conditions under evaluation), pregnancy, or incomplete medical records were excluded to ensure data consistency and analytical reliability. Sampling Technique A non-probability consecutive sampling method was applied, where all eligible patients presenting during the study period were included until the desired sample size was achieved.

Data Collection and Clinical Assessment

Demographic and clinical data, including age, sex, hepatitis B and hepatitis C status, alcohol consumption history, and presence of chronic liver disease, were collected using a structured and pre-tested data collection form. All data were anonymized prior to analysis to maintain confidentiality.

Blood Sample Collection

Venous blood samples were collected from all participants after an overnight fasting period of 8–12 hours following standard aseptic techniques. Samples were processed promptly, and serum was separated by centrifugation and analyzed according to standard laboratory procedures.

Laboratory Analysis

Biochemical parameters were measured using fully automated clinical chemistry analyzers in accordance with manufacturer-recommended protocols and internal quality control procedures. The analyzed parameters included fasting blood glucose (FBS), liver enzymes [alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP)], serum bilirubin, lipid profile [total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides], renal function markers (serum creatinine and blood urea), and hematological parameters (hemoglobin and platelet count). Serum alpha-fetoprotein (AFP) levels were measured using standardized immunoassay techniques (e.g., chemiluminescent microparticle immunoassay). All

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laboratory results were interpreted based on established reference ranges routinely used in clinical practice. Internal quality control (IQC) procedures were maintained daily, and external quality assurance standards were followed where applicable.

Variable Definition

Serum AFP was considered the primary dependent (outcome) variable. Independent variables included glycemic control (fasting blood glucose), liver function parameters, renal function markers, lipid profile, hematological parameters, and clinical risk factors such as hepatitis B and C infection, alcohol consumption, and chronic liver disease history. For analytical purposes, selected variables were also categorized based on standard clinical reference ranges (e.g., normal vs elevated AFP levels) to assess abnormality frequencies.

Statistical Analysis

Data was analyzed using SPSS. Continuous variables were expressed as mean ± SD or median (IQR), and categorical variables as frequencies and percentages. Normality was assessed using the Shapiro–Wilk test. Group comparisons were performed using independent t-test or Mann–Whitney U test, and categorical variables were analyzed using the chi-square test. Correlation was assessed using Pearson or Spearman methods, and multivariable linear regression was applied to identify independent predictors of AFP. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Confidentiality of patient information was strictly maintained throughout the research process.

Results

Baseline Demographic and Biochemical Characteristics

A total of 200 adult participants were included in the study, comprising 130 males (65%) and 70 females (35%). The overall mean age was 52.36 ± 14.28 years, with no statistically significant difference between males and females (p = 0.412). The baseline demographic, biochemical, and hematological characteristics of the study population are presented in Table 1. The baseline characteristics indicate that most biochemical parameters were comparable between male and female participants. However, fasting blood glucose, ALT, triglycerides, and hemoglobin showed statistically significant differences. Male participants exhibited higher fasting glucose levels, while females had higher ALT and triglyceride levels and lower hemoglobin concentrations.

Table 1: Baseline Demographic, Biochemical, and Hematological Characteristics of the Study Population.

Parameter	Total (n=200)	Male (n=130)	Female (n=70)	p-value
Age (years)	52.36 ± 14.28	51.78 ± 13.92	53.42 ± 14.91	0.412
FBS (mg/dL)	148.2 ± 52.4	152.6 ± 54.3	140.5 ± 48.2	0.048*
ALT (U/L)	46.8 ± 35.6	44.1 ± 32.2	51.2 ± 41.3	0.041*
AST (U/L)	38.5 ± 28.4	36.7 ± 25.9	41.2 ± 32.1	0.221
ALP (U/L)	110.3 ± 62.5	105.4 ± 58.7	118.9 ± 69.2	0.136
Bilirubin (mg/dL)	0.92 ± 0.56	0.88 ± 0.49	0.99 ± 0.66	0.298
Creatinine (mg/dL)	1.21 ± 0.64	1.19 ± 0.59	1.25 ± 0.71	0.512
Urea (mg/dL)	46.7 ± 30.5	44.3 ± 27.8	50.9 ± 35.4	0.198
Hemoglobin (g/dL)	12.8 ± 1.9	13.4 ± 1.7	11.7 ± 1.8	<0.001*
Platelet (×10⁹/L)	242 ± 78	248 ± 74	231 ± 85	0.183
Cholesterol (mg/dL)	182.4 ± 49.6	178.1 ± 47.8	190.3 ± 52.1	0.087
LDL (mg/dL)	110.2 ± 36.7	107.5 ± 35.9	115.6 ± 38.1	0.144
HDL (mg/dL)	38.1 ± 9.4	37.5 ± 9.2	39.2 ± 9.8	0.265
Triglycerides (mg/dL)	196.5 ± 120.3	189.2 ± 115.4	210.8 ± 128.7	0.039*

*Statistically significant (p < 0.05)

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Serum AFP Levels

Serum alpha-fetoprotein (AFP) levels are presented in Table 2. AFP levels demonstrated a markedly skewed distribution with high variability across participants. Female participants showed slightly higher AFP levels compared to males.

Table 2: Distribution of Serum AFP Levels.

Parameter	Total	Male	Female
AFP (Mean ± SD)	18.72 ± 96.45	16.4 ± 82.3	22.9 ± 118.7
Median (IQR)	6.8 (3.2–14.5)	6.1 (3.0–12.8)	7.5 (3.5–16.9)
Min–Max	0.5–980	0.5–820	0.7–980

Abnormality Frequency Analysis

Table 3 presents the frequency of abnormal biochemical parameters and AFP levels. Abnormal AFP and liver enzyme levels were more frequent among female participants, whereas renal abnormalities were more prevalent among males.

Table 3: Frequency of Abnormal Parameters.

Parameter	Total (%)	Male (%)	Female (%)
AFP	28	22.3	38.6
ALT	20.5	18.5	24.2
AST	18	16.2	21.4
Creatinine	21.5	28.4	10.5
Urea	22.5	19.1	26.3

Correlation Analysis

The association between AFP and selected biochemical parameters is shown in Table 4. AFP showed statistically significant positive correlations with glycemic status, liver enzymes, and renal function markers, with the strongest association observed with ALT.

Table 4: Correlation of AFP with Biochemical Parameters.

Variable	r	p-value
FBS	0.28	0.002*
ALT	0.32	<0.001*
AST	0.25	0.004*
Creatinine	0.19	0.021*
Urea	0.22	0.011*

The scatter plot (Figure 1) demonstrates a positive linear relationship between serum AFP levels and fasting blood glucose. As glucose levels increase, AFP concentrations also tend to increase, indicating a potential association between glycemic dysregulation and AFP elevation.

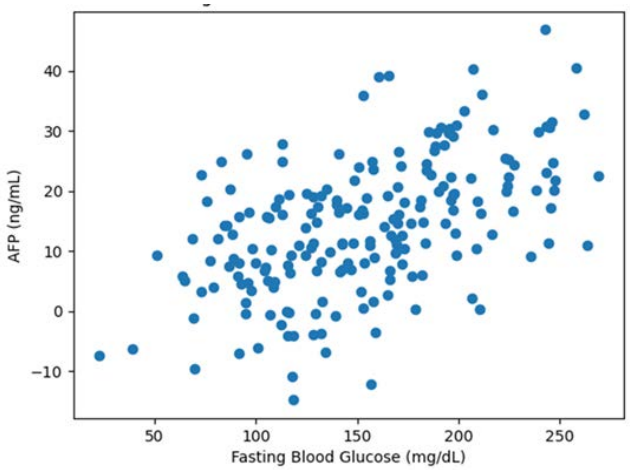

Figure 1: The Scatter Plot of AFP vs FBS.

The correlation heatmap (Figure 2) illustrates the interrelationships among AFP, glycemic parameters, liver enzymes, and renal markers. Liver enzymes (ALT and AST) show strong inter-correlation, while AFP demonstrates moderate positive correlations with fasting glucose and selected biochemical parameters.

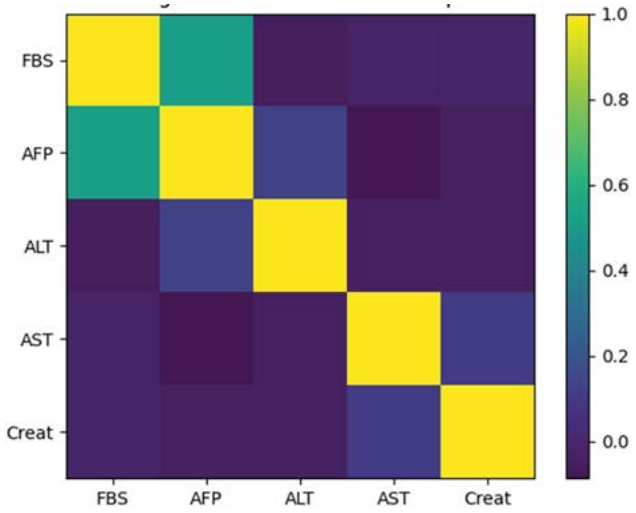

Figure 2: Correlation Heatmap.

Illustrates the distribution (Figure 3) of serum AFP levels between male and female participants. Female participants demonstrated relatively higher median AFP levels with greater variability compared to males, indicating possible sex-based differences in AFP expression.

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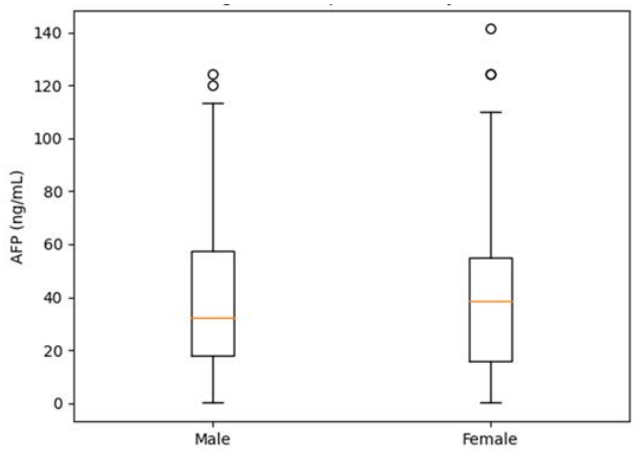

Figure 3: Boxplot of AFP by Gender

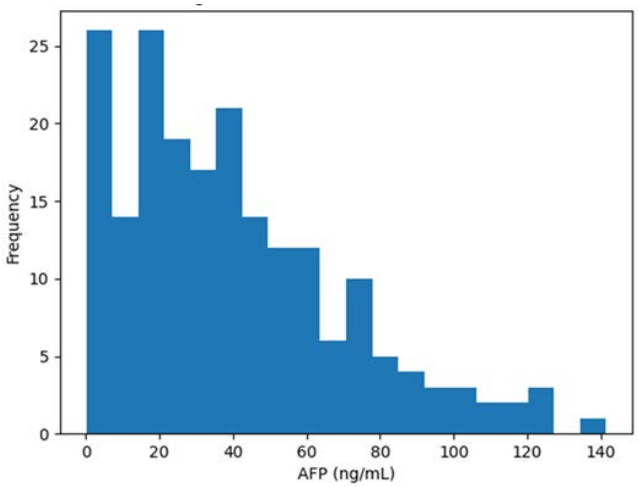

Figure 4: Distribution of AFP levels

Shows the distribution (Figure 4) of serum AFP levels in the study population. The distribution is right-skewed, with most participants having low AFP levels and a small proportion exhibiting markedly elevated values.

Discussion

The present cross-sectional study evaluated the association between serum alpha-fetoprotein (AFP) levels and glycemic status, liver enzymes, and renal function among adult patients. The findings demonstrate that AFP levels are significantly associated with metabolic and biochemical parameters, even in the absence of overt malignancy, highlighting the importance of careful clinical interpretation. In this study, the overall mean age of participants was 52.36 ± 14.28 years, with no significant age difference between males and females ($p = 0.412$), indicating a well-balanced study population. However, several biochemical parameters showed significant gender-based differences. Male participants exhibited higher fasting blood glucose levels (152.6 ± 54.3 mg/dL vs 140.5 ± 48.2 mg/dL, $p = 0.048$), while females had significantly higher ALT levels (51.2 ± 41.3 U/L vs 44.1 ± 32.2 U/L, $p = 0.041$) and triglycerides (210.8 ± 128.7 mg/dL vs 189.2 ± 115.4 mg/dL, $p = 0.039$). Additionally, hemoglobin levels were significantly lower in females (11.7 ± 1.8 g/dL vs 13.4 ± 1.7 g/dL, $p < 0.001$). These findings suggest that female participants may have a relatively higher metabolic and hepatic burden, while males exhibit poorer glycemic control [10]. Serum AFP levels in this study demonstrated marked variability, with a mean of 18.72 ± 96.45 ng/mL and a median of 6.8 ng/mL (IQR: 3.2–14.5), indicating a highly skewed distribution. Female participants showed slightly higher AFP levels compared to males, consistent with the observed higher frequency of abnormal AFP among females (38.6% vs 22.3%). This suggests that AFP elevation may be influenced by underlying metabolic or hepatic factors rather than malignancy alone [11]. The frequency analysis further supports these observations. Abnormal AFP levels were present in 28.0% of the total population, with a notably higher proportion in females. Similarly, liver enzyme abnormalities (ALT: 24.2% in females vs 18.5% in males; AST: 21.4% vs 16.2%) were more prevalent among females, whereas renal dysfunction, particularly elevated creatinine, was more common in males (28.4% vs 10.5%). These findings indicate a differential pattern of metabolic and organ-specific involvement between genders, which may contribute to variations in AFP levels [12]. Correlation analysis revealed significant positive associations between AFP and key biochemical parameters. AFP showed a moderate positive correlation with fasting blood glucose ($r = 0.28$, $p = 0.002$), suggesting that hyperglycemia may influence AFP levels. Stronger associations were observed with liver enzymes, particularly ALT ($r = 0.32$, $p < 0.001$) and AST ($r = 0.25$, $p = 0.004$), indicating that hepatic dysfunction plays a crucial role in AFP variability. Additionally, AFP was positively correlated with renal function markers, including creatinine ($r = 0.19$, $p = 0.021$) and urea ($r = 0.22$, $p = 0.011$), suggesting that renal impairment may also contribute to altered AFP clearance or metabolism [13].

The graphical analyses further reinforce these findings. The scatter plot demonstrated a clear positive relationship between AFP and fasting blood glucose, while the correlation heatmap highlighted clustering among liver enzymes and their association with AFP. The boxplot analysis indicated higher median AFP levels and greater variability among females, and the histogram confirmed a right-skewed distribution, emphasizing the presence of outliers and non-normal distribution of AFP values [14]. Overall, the findings of this study suggest that serum AFP is influenced by multiple non-malignant factors, including glycemic status, hepatic function, and renal function. The observed associations indicate that metabolic dysregulation, particularly hyperglycemia and liver

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enzyme elevation, may contribute to increased AFP levels. This has important clinical implications, as mild to moderate AFP elevation in patients with metabolic disorders may not necessarily indicate malignancy and should be interpreted cautiously [15].

Furthermore, the gender-based differences observed in this study highlight the need for sex-specific consideration when evaluating biochemical and tumor marker profiles. The higher frequency of abnormal AFP and liver enzymes among females suggests a potential interaction between metabolic and hormonal factors, while the higher prevalence of renal abnormalities in males indicates differing physiological responses.

Conclusion

Serum alpha-fetoprotein (AFP) levels were significantly associated with glycemic status, liver enzymes, and renal function, showing moderate positive correlations with fasting glucose, ALT, AST, creatinine, and urea. AFP demonstrated marked variability and a skewed distribution, with higher abnormality rates among females, while renal dysfunction was more common in males.

These findings indicate that AFP elevation may reflect underlying metabolic, hepatic, and renal disturbances rather than malignancy alone. Therefore, AFP should be interpreted cautiously, considering associated biochemical parameters to improve its clinical relevance**.**

Limitations of the Study

This study has several limitations that should be considered when interpreting the findings. First, the cross-sectional design precludes the establishment of causal relationships between AFP levels and the studied biochemical parameters. Second, the study was conducted in a single tertiary-level hospital, which may limit the generalizability of the findings to broader populations. Additionally, potential confounding factors such as medication use, dietary habits, inflammatory markers, and body mass index were not included in the analysis, which may have influenced AFP levels. The absence of longitudinal follow-up data also limits the ability to assess temporal changes in AFP and their clinical implications. Despite these limitations, the study provides valuable insights into the relationship between AFP and metabolic, hepatic, and renal parameters, highlighting the need for comprehensive evaluation in clinical interpretation.

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