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RESEARCH ARTICLE

Gender-Based Disparities in Glycemic Control and Bilirubin Metabolism in Type 2 Diabetes: A Multivariate Analysis from a Single-Center Study

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a rapidly increasing metabolic disorder worldwide, particularly in South Asia. Bangladesh faces a growing prevalence, with nearly one in ten adults affected. Beyond hyperglycemia, T2DM impacts renal, hepatic, lipid, and electrolyte metabolism. Sex-specific differences in biochemical profiles are increasingly recognized, but data from Bangladeshi populations remain limited. Objective: To evaluate biochemical profiles of adult patients with T2DM in Bangladesh, stratified by sex, and to explore interrelationships among laboratory indices using correlation and principal component analyses (PCA).

Methods: Routine biochemical parameters, including renal, hepatic, lipid, electrolyte, and glycemic markers, were analyzed in adult diabetic patients attending a single-center facility. Independent-sample *t* tests were used for group comparisons, Pearson's correlation assessed associations between variables, and PCA was applied to identify latent patterns and dimensionality reduction.

Results: Most biochemical parameters showed no significant sex differences. However, males had higher HbA1c (9.46 ± 1.76 vs. 8.86 ± 1.42; $p = 0.024$) and bilirubin levels (0.76 ± 0.21 vs. 0.61 ± 0.21 mg/dL; $p = 0.0005$). Strong correlations were observed between urea and creatinine ($r = 0.73$, $p < 0.001$), AST and ALT ($r = 0.64$, $p < 0.001$), and between fasting blood sugar and both random blood sugar ($r = 0.54$, $p < 0.01$) and HbA1c ($r = 0.52$, $p < 0.01$). Albumin inversely correlated with urea ($r = –0.39$, $p < 0.05$). In the lipid profile, cholesterol was strongly correlated with both HDL ($r = 0.75$, $p < 0.001$) and LDL ($r = 0.72$, $p < 0.001$). Electrolytes showed weak or nonsignificant associations. PCA revealed moderate dimensionality reduction, with PC1 and PC2 explaining 13.9% and 12.4% of variance, respectively. HbA1c, bilirubin, and creatinine contributed most to sex-based separation, whereas lipids and electrolytes had minimal influence.

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Conclusion: This study indicates that sex-specific differences in T2DM are primarily reflected in glycemic control and bilirubin metabolism, while most other biochemical indices remain comparable. Correlation and PCA findings emphasize the interconnected nature of renal, hepatic, and glycemic parameters, supporting their integrated evaluation in clinical management of diabetes.

Keywords: Type 2 diabetes, Glycemic control, Bilirubin metabolism, Biochemical markers, Principal component analysis

1. Introduction

Diabetes mellitus, particularly type 2 diabetes (T2D), is one of the fastest-growing non-communicable diseases and a leading cause of morbidity and mortality worldwide. The International Diabetes Federation (IDF) estimates that more than 500 million adults currently live with diabetes, a figure projected to rise to 783 million by 2045 if preventive strategies are not prioritized[1]. This rising prevalence is not only a clinical concern but also a significant socioeconomic burden, given the long-term complications associated with uncontrolled diabetes, including cardiovascular disease, nephropathy, retinopathy, and hepatic dysfunction[2].

South Asia, in particular, is disproportionately affected due to its rapid demographic transitions, urbanization, changes in dietary patterns, and sedentary lifestyle. India is recognized globally as the "diabetes capital of the world," and neighboring Bangladesh has also reported alarming increases in prevalence[3]. According to recent national surveys, approximately 9–10% of adults in Bangladesh have diabetes, with many remaining undiagnosed until complications arise. Furthermore, limited access to healthcare facilities, inadequate disease awareness, and poor long-term monitoring exacerbate the disease burden in this region[4].

The pathophysiology of T2D extends far beyond impaired glucose metabolism. Hyperglycemia contributes to oxidative stress, systemic inflammation, and endothelial dysfunction, which in turn disrupt biochemical homeostasis in multiple organ systems[5]. Renal function markers, hepatic enzymes, lipid profiles, and electrolyte levels provide valuable information on the metabolic derangements and end-organ involvement associated with diabetes[6]. Importantly, sex-related variations in these biochemical parameters are increasingly recognized as clinically relevant. Biological differences, including hormonal influences, fat distribution, and genetic predispositions, interact with sociocultural factors such as healthcare-seeking behavior, diet, and physical activity, leading to distinct metabolic profiles in men and women with diabetes[7,8].

Advanced statistical tools are increasingly being employed to unravel the complexity of these biochemical interactions. Multivariate statistical methods, particularly correlation analysis and principal component analysis (PCA), are powerful for identifying latent structures within complex datasets[9,10]. These approaches enable the simultaneous evaluation of multiple interrelated variables, providing insights into metabolic clusters and underlying physiological patterns that may not be evident from univariate analysis. Although such methods have been widely applied in large-scale global studies, research focusing on sex-based disparities in biochemical indices among diabetic patients in Bangladesh remains scarce[11]. To assess gender-specific variations in biochemical profiles of patients with type 2 diabetes in Bangladesh and to explore interrelationships among glycemic, hepatic, renal, lipid, and electrolyte parameters using correlation and principal component analyses.

2. Materials and methods

2.1. Study design and setting

This cross-sectional study was conducted at a specialized diabetic hospital in Dhaka, Bangladesh, over a three-month period from July to September 2024. The purpose of the study was to investigate gender-based differences and interrelationships among biochemical parameters in patients with type 2 diabetes mellitus.

2.2. Study population and data collection

A total of 109 diabetic patients were included in the analysis. Data were obtained from patient medical records after anonymization to ensure confidentiality. The dataset comprised demographic information such as age, gender, and marital status, along with a comprehensive panel of biochemical parameters. These parameters included glycemic markers (Fasting Blood Sugar [FBS], Random Blood Sugar [RBS], HbA1c (%), and 2-hour After Breakfast Blood Glucose [ABF]); renal function markers (urea and creatinine); liver function markers (albumin, bilirubin, Alanine Aminotransferase [ALT], Aspartate Aminotransferase [AST], and Alkaline Phosphatase [ALP]); lipid profile (total cholesterol, High-Density Lipoprotein [HDL], Low-Density Lipoprotein [LDL], and triglycerides); and electrolytes and minerals (sodium, potassium, chloride, magnesium, and calcium)[12]. All data were carefully cleaned prior to analysis, and patients with missing values or non-finite entries were excluded.

2.3. Inclusion and exclusion criteria

Eligible participants were adults aged 20 years and above who were diagnosed with type 2 diabetes mellitus based on hospital records and who attended the diabetic hospital during the study period. Patients with type 1 diabetes mellitus or gestational diabetes, those with incomplete demographic or biochemical data, and individuals with chronic comorbid conditions that could significantly influence biochemical results, such as advanced chronic liver disease, renal failure requiring dialysis, or active malignancy, were excluded.

2.4. Demographic information

Demographic variables included age and gender. Age was categorized into seven groups: 20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and 80–89 years. Among the 109 participants, 87 were male (79.81%) and 22 were female (20.18%). This demographic categorization was used to capture variations in biochemical parameters across different age and gender groups.

2.5. Statistical analysis

All analyses were conducted using R (RStudio version 2024.12.0). Biochemical parameters were compared between male and female patients using independent-sample t-tests, with statistical significance defined as $p < 0.05$. Correlation among biochemical markers was examined using Pearson's correlation analysis, and results were visualized with the corrplot package. Strong correlations ($|r| \geq 0.5$, $p < 0.05$) were further illustrated with scatter plots and regression lines. Principal Component Analysis (PCA) was applied after scaling and centering the data to standardize variables, and results were displayed using scree plots and biplots generated with ggplot2.

3. Results

A total of 109 patients with type 2 diabetes mellitus were included in this study, comprising 87 males (79.8%) and 22 females (20.2%). The age distribution showed that the largest proportion of participants was

in the 50–59 year group (32.1%), followed by 60–69 years (27.5%) and 40–49 years (13.8%). Very few were aged ≥80 years (3.7%) or <30 years (1.8%). Men predominated in all age groups, while the proportion of women ranged between 9% and 36%, with their highest representation in the 50–59 year group (36.4%). Almost all participants were married, except for two unmarried individuals (1.8%) in the 20–29 year group (Table 1).

Table 1. Demographic characteristics of Diabetics patients (n=109)

Age group	Total (n=109)	Male (n=87)	Female(n=22)	Married	Unmarried
20-29	02 (1.83%)	01 (1.15%)	01 (4.54%)	0	2 (1.83%)
30-39	07 (6.42%)	05 (5.75%)	02 (9.09%)	07 (6.422%)	0
40-49	15 (13.76%)	13 (14.94%)	02 (9.09%)	15 (13.76%)	0
50-59	35 (32.11%)	27 (31.03%)	08 (36.36%)	35 (32.11%)	0
60-69	30 (27.52%)	25 (28.73%)	05 (22.72%)	31 (28.44%)	0
70-79	15 (13.76%)	11 (12.64%)	04 (18.18%)	15 (13.76%)	0
80-89	04 (3.66%)	04 (4.59%)	0	04 (3.66%)	0

The laboratory parameters of diabetic patients stratified by sex. Most biochemical variables did not differ significantly between male and female patients. However, significant differences were observed for two parameters. Males exhibited higher HbA1c levels (9.46 ± 1.76) compared to females (8.86 ± 1.42; $p = 0.024$) and elevated bilirubin concentrations (0.76 ± 0.21 vs. 0.61 ± 0.21 mg/dL; $p = 0.0005$). Other indices, including renal markers (creatinine, urea), hepatic enzymes (ALT, AST, ALP), lipid profile (cholesterol, HDL, LDL, triglycerides), and electrolytes (Na, K, Cl), did not show statistically significant sex-based differences ($p > 0.05$). Comparison of male and female patients (Table 2) showed that most laboratory indices were not significantly different between sexes. However, HbA1c was significantly higher in males (9.46 ± 1.76 vs. 8.86 ± 1.42; $p = 0.024$), as was bilirubin (0.76 ± 0.21 vs. 0.61 ± 0.21 mg/dL; $p = 0.0005$). Other variables, including renal indices, lipid profile, and liver enzymes, showed no significant sex-related variation.

Table 2. Laboratory Parameters from diabatics patients (n=109)

Parameter	Female (Mean ± SD)	Male (Mean ± SD)	P value
Age	56.5 ± 12.42	57.66 ±12.49	0.634175
RBS (mmol/L)	16.83 ± 4.57	17.91± 3.55	0.322778
FBS (mmol/L)	8.66 ± 1.48	9.19 ± 2.08	0.184213
2 Hour ABF (mmol/L)	10.52 ± 2.50	9.94 ± 2.38	0.18421
HbA 1c (%)	8.86 ± 1.42	9.46± 1.76	0.02413
Creatinine (mg/dl)	1.02 ±0.32	1.19± 0.66	0.06945
Urea (mg/dl)	32.72 ± 13.70	39.35± 23.13	0.09376
Bilirubin (mg/dL)	0.61 ± 0.21	0.76 ± 0.206	0.00505

Parameter	Female (Mean ± SD)	Male (Mean ± SD)	P value
ALT (U/L)	37.41 ± 30.63	37.50 ± 14.18	0.98887
AST (U/L)	38.82± 54.55	23.33 ± 8.11	0.20860
ALP(U/L)	85.64 ± 33.15	93.28± 32.09	0.34688
Cholesterol(mg/dL)	158.60 ± 33.66	149.83 ± 43.32	0.31941
HDL (mg/dL)	32.77± 7.627	32.51 ± 7.62	0.89133
LDL (mg/dL)	92.41 ± 27.55	86.56 ± 32.10	0.40719
Triglycerides (mg/dL)	152.95± 43.32	190.29± 142.60	0.04043
Sodium (mmol/L)	139.18± 3.27	137.74 ± 4.41	0.10268
Potassium (mmol/L)	3.95± 0.44	4.06 ± 0.47	0.31824
Choloride (mmol/L	103 ± 5.13	102.62± 5.69	0.76837
Albumin (gm/L)	34.55± 3.30	34.52 ± 3.67	0.97277
Magnesium (mmol/L)	0.77± 0.072	0.75 ± 0.076	0.43116
Calcium (mmol/L)	2.22 ± 0.099	2.21 ± 0.11	0.77244

The correlation analysis revealed several important associations among biochemical and clinical parameters, many of which are biologically consistent. Pearson's correlation matrix was constructed to evaluate associations among biochemical parameters (Figure 1).

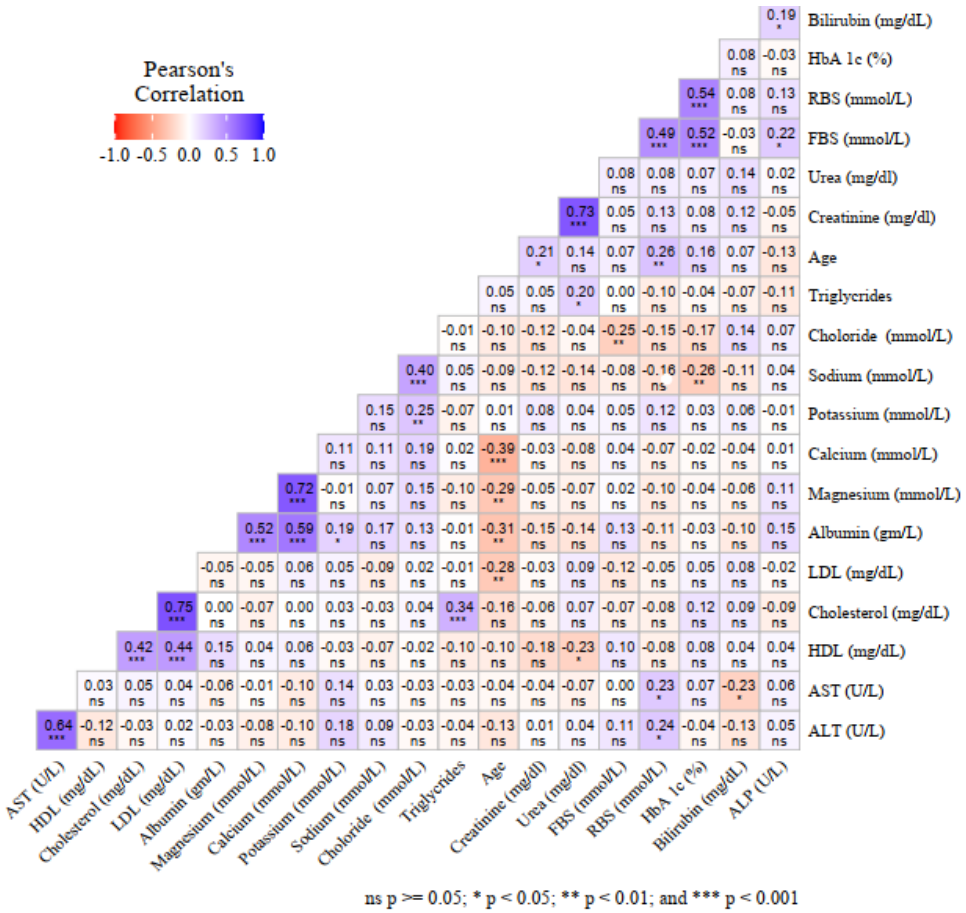

Figure 1. Pearson's correlation matrix among biochemical and clinical parameters. The heatmap represents correlation coefficients (r-value) between variables, with blue indication positive and red indicating negative correlations. The strength of correlation ranges from -1 to +1 as shown in color scale. Significance levels are denoted as ns=non-significant ($p \geq 0.05$), *p< 0.05, **p<0.01, ***p<0.001.

The strong positive correlation between urea and creatinine ($r = 0.73$, $p < 0.001$) reflects their shared role as renal function biomarkers. Similarly, the correlation between age and creatinine ($r = 0.28$, $p < 0.05$) may indicate the age-related decline in renal function, which has been widely reported in epidemiological studies. Liver enzyme analysis showed a strong correlation between AST and ALT ($r = 0.64$, $p < 0.001$), consistent with their co-release from hepatocytes during liver injury. Interestingly, albumin showed a negative correlation with urea ($r = –0.39$, $p < 0.05$). Regarding glycemic control, a strong correlation was observed between fasting blood sugar (FBS) and random blood sugar (RBS) ($r = 0.54$, $p < 0.01$), while HbA1c was moderately correlated with FBS ($r = 0.52$, $p < 0.01$). These associations reinforce the use of HbA1c as a reliable long-term marker of glycemic status and its relationship with short-term glucose fluctuations. In the lipid profile, cholesterol showed significant positive correlations with both HDL ($r = 0.75$, $p < 0.001$) and LDL ($r = 0.72$, $p < 0.001$). On the other hand, electrolytes (Na, K, Cl, Ca, Mg) demonstrated weak or nonsignificant correlations with most metabolic and hepatic parameters.

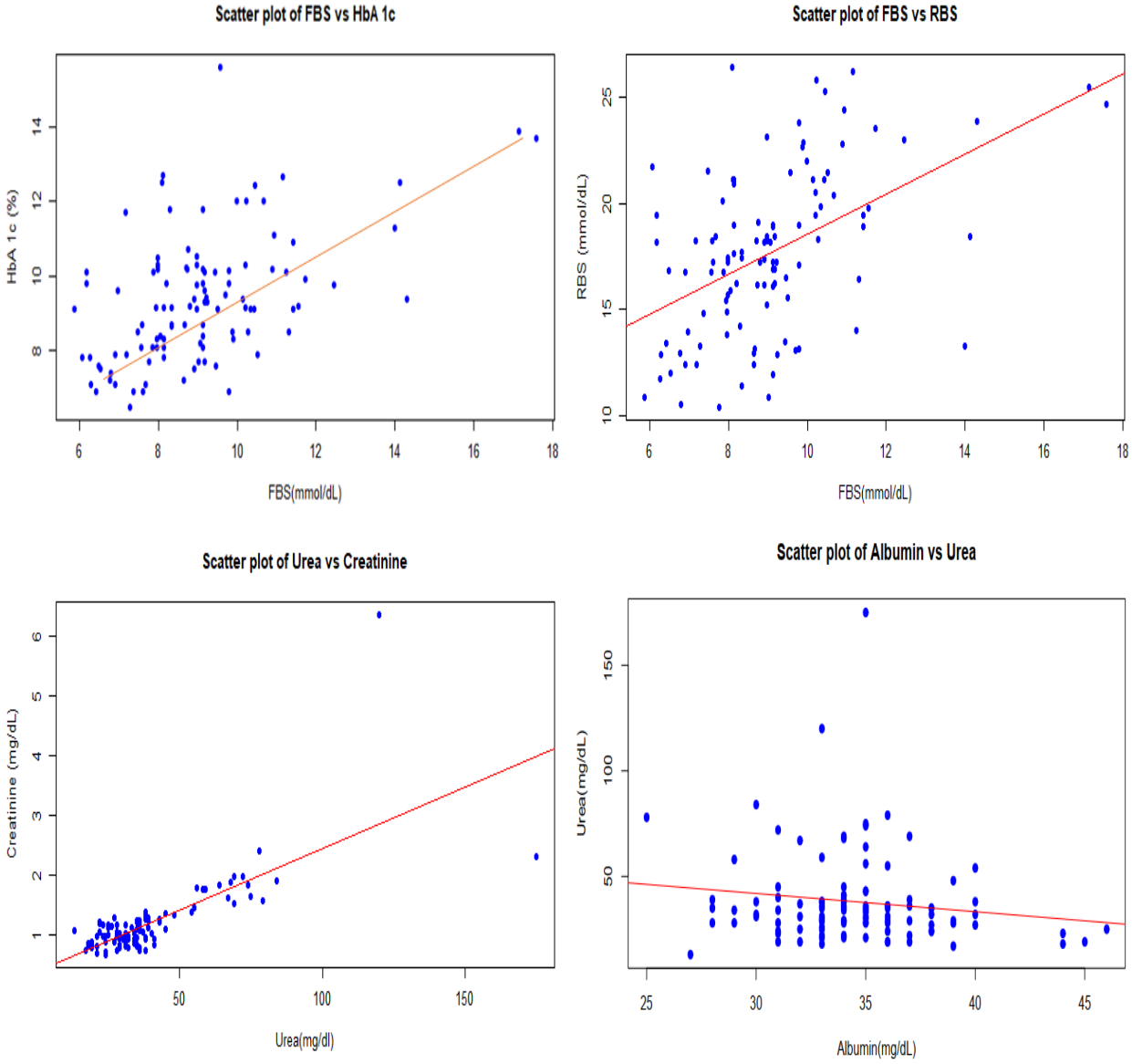

Figure 2. Scatter plot showing the relationship between two variables with a linear regression line indicating the trend a) Fasting Blood Sugar (FBS) and HbA1c (%), b) Fasting Blood Sugar (FBS) and Random Blood Sugar (RBS), c) Urea and Creatinine levels d) Albumin and Urea

Scatter plots with fitted regression lines (Figure 2) illustrate the pairwise relationships between selected biochemical variables. Fasting blood sugar (FBS) showed a clear positive association with HbA1c, indicating that higher FBS values corresponded to higher long-term glycemic status. FBS was also positively related to random blood sugar (RBS), reflecting consistency between fasting and casual glucose measurements. Urea and creatinine concentrations demonstrated a marked linear relationship, consistent with their shared dependence on renal function. Albumin and urea showed only a weak relationship, suggesting limited overlap between protein status and urea metabolism in this cohort.

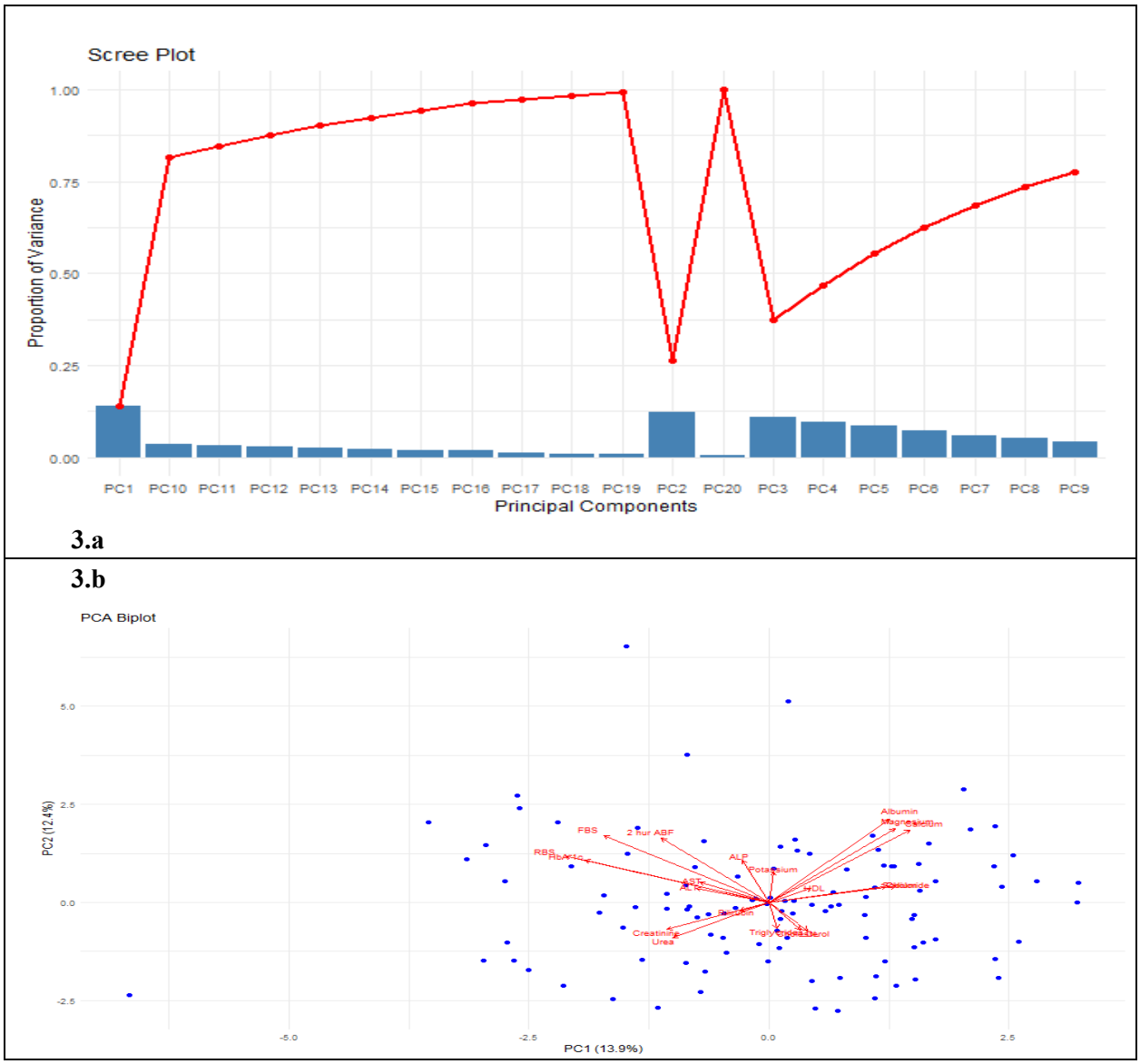

Figure 3. (a) Scree plot showing that PC1 (13.9%) and PC2 (12.4%) explain most variance. (b) PCA biplot of 20 standardized biochemical parameters. Albumin, magnesium, and chloride load mainly on PC1, while liver enzymes and glucose-related variables align with PC2. The clustering of points around the origin suggests moderate correlations among variables and no marked separation between individuals.

All 20 biochemical variables were subjected to PCA after standardization. A scree plot (Figure 3.a) showed the proportion of variance explained by each principal component. The first two components (PC1 = 13.9%, PC2 = 12.4%) accounted for the highest proportion of variance, while subsequent components contributed progressively less after PC2. The PCA biplot (Figure 3.b) visualized the distribution of samples and the contribution of variables. Albumin, magnesium, and chloride had high loadings on PC1, while liver

enzymes (ALT, AST, ALP) and glucose-related measures (RBS, FBS, 2-hour ABF) were mainly associated with PC2. The majority of points were clustered near the origin, indicating moderate correlations between variables and limited separation among individuals.

4. Discussions

The higher HbA1c values in males observed in this study may reflect relatively poorer glycemic control among men, consistent with previous research reporting that males often present with higher fasting glucose levels and reduced adherence to dietary and lifestyle interventions compared with females. Other studies have also documented sex-related variations in glycemic control, with men frequently demonstrating greater insulin resistance and more rapid β-cell decline, which may explain the elevated HbA1c levels. Conversely, some research has found no sex-based differences in HbA1c, suggesting that variations across populations may be influenced by cultural, behavioral, and genetic factors[13].

Increased bilirubin levels in males align with evidence that bilirubin metabolism differs between sexes, partly due to hormonal and enzymatic regulation. Bilirubin has been recognized as a potent endogenous antioxidant, and higher concentrations in males may provide some cardiovascular protection. However, other studies have reported inconsistent findings, with some noting no sex-related differences. These discrepancies may be attributed to variations in sample size, population characteristics, and analytical methods across studies[14].

The correlation analysis confirmed several biologically plausible associations. The strong positive correlation between urea and creatinine reflects their shared role as indicators of renal clearance, a finding consistently reported across clinical and epidemiological studies. The association between age and creatinine further supports age-related declines in renal function, a common observation in diabetic cohorts. Similarly, the strong correlation between ALT and AST is in line with their role as markers of hepatocellular injury[15].

Glycemic parameters clustered together in the correlation matrix, with FBS strongly associated with RBS and moderately with HbA1c. This supports the use of HbA1c as a long-term glycemic marker that integrates both fasting and postprandial glucose fluctuations. Previous research has demonstrated similar relationships, reinforcing the clinical utility of HbA1c for long-term monitoring, even though short-term glucose variability may not always be fully captured. The inverse correlation between albumin and urea observed in this study suggests a possible link between impaired protein synthesis and renal dysfunction. Comparable findings have been reported in research investigating the interplay of liver and kidney function in metabolic disease[16,17]

In the lipid profile, cholesterol correlated strongly with both HDL and LDL, reflecting the interdependence of lipid fractions. This observation supports the view that total cholesterol should be interpreted alongside its subcomponents when assessing cardiovascular risk in diabetic patients. Previous studies have reported similar patterns, though some have also emphasized the importance of triglyceride-rich lipoproteins, which in this study were significantly higher in males. The sex-based difference in triglyceride levels has been noted in other populations and may relate to differences in visceral fat distribution and hormonal influences on lipid metabolism[18].

Electrolytes showed weak or nonsignificant correlations with other parameters, suggesting that their regulation remains relatively independent of hepatic and renal function in stable diabetic patients. Other studies have similarly reported minimal associations between electrolytes and metabolic markers, though disturbances may become more pronounced in advanced or complicated diabetes[19,20].

Principal Component Analysis provided additional insights by summarizing interrelationships among the 20 biochemical parameters. The first two components explained a substantial portion of variance, highlighting that much of the biochemical variation could be reduced to a few key dimensions. Electrolytes and nutritional markers such as albumin, magnesium, and chloride were aligned with PC1, whereas liver enzymes and glycemic indicators contributed predominantly to PC2. This pattern suggests that electrolyte/nutritional status and glucose/hepatic metabolism represent distinct but complementary dimensions of metabolic regulation in diabetes. Previous multivariate studies of diabetic populations have demonstrated similar clustering, indicating that diabetes exerts systemic but compartmentalized effects on different physiological pathways[21].

Overall, these findings suggest that while type 2 diabetes exerts widespread effects on renal, hepatic, and metabolic pathways, sex-specific differences are relatively limited, being most apparent in glycemic control and bilirubin metabolism. The results reinforce the need for sex-sensitive approaches in diabetic monitoring, as well as the value of integrating multivariate statistical techniques to unravel complex biochemical interactions. Compared with other studies, the present findings are broadly consistent, though minor discrepancies highlight the influence of population heterogeneity, clinical characteristics, and healthcare practices.

5. Conclusion

This study highlighted gender-based disparities in biochemical parameters among patients with type 2 diabetes in Bangladesh, revealing that males exhibited higher HbA1c and bilirubin levels compared with females, while most other laboratory markers showed no significant sex-related variation. The correlation analysis confirmed established physiological linkages between renal, hepatic, and glycemic parameters, while PCA provided additional insights into the clustering of metabolic, hepatic, and electrolyte variables. These findings reinforce the systemic impact of diabetes on multiple organ systems and suggest that male patients may be at greater risk of poor glycemic control and altered bilirubin metabolism. Incorporating multivariate statistical techniques into routine laboratory data interpretation can improve the identification of at-risk groups and guide more tailored clinical management strategies.

6. Limitations of the Study

- The study was conducted at a single center, which may limit the generalizability of findings to broader populations.
- The cross-sectional design precludes causal inference regarding sex differences and biochemical interrelationships.
- Lifestyle, dietary, medication adherence, and socioeconomic factors, which may influence laboratory outcomes, were not assessed.
- The relatively small sample size may have reduced the power to detect subtle differences in certain parameters.
- Lack of longitudinal follow-up restricted the ability to examine changes over time or associations with complications of diabetes.

Conflict of interest

The authors declare no conflict of interest

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