

## Progression of Microvascular and Macrovascular Complications in Bangladeshi Type 2 Diabetic Patients: A Prospective Study

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### Abstract

**Background:** Type 2 diabetes mellitus (T2DM) poses a significant public health challenge globally, with a particularly pronounced impact in countries like Bangladesh. This study aims to evaluate the outcomes in Bangladeshi T2DM subjects to gain insights into the deterioration or improvement of with respect to major macro and microvascular complications by examining for relevant clinical parameters over time.

**Methods:** This prospective observational study was conducted at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Bangladesh Medical University (BMU), and National Institute of Kidney Diseases and Urology (NIKDU Dhaka Bangladesh. A total of 800 T2DM patients (400 males, 400 females) were enrolled. Patients were evaluated at baseline and at 6- and 12-month follow-up visits through clinical assessment, physical examination and laboratory investigations including- hemoglobin (Hb), glycated hemoglobin (HbA1c), serum creatinine, serum lipid profile, urine albumin creatinine ratio (ACR), electrocardiography (ECG), echocardiography and renal ultrasonography.

**Results:** The frequencies of microvascular complications like retinopathy and neuropathy among both males and females showed a steady rise over the study period. Also, a progressive increase in macrovascular complications over time in both male and female participants observed. The incidence of hypertension was 82%. The study demonstrated a significant improvement in blood pressure control over the follow-up period ( $p < 0.05$ ), while cardiac status ejection fraction showed a slight declining trend ( $p > 0.05$ ). Glycemic and lipid control were not improved significantly ( $p > 0.05$ ) and females had worse control over their blood glucose levels. Significant improvement in hemoglobin (Hb) levels was found among both male and female participants ( $p < 0.05$ ). Overall, the findings suggest a trend toward progressive renal dysfunction and increasing proteinuria during follow-up, more pronounced in female participants. The findings indicate an initial deterioration in renal function after anti-proteinuria drugs initiation followed by partial improvement after drug withdrawal.

**Conclusion:** This study indicates that, both microvascular and macrovascular complications increased progressively over time in T2DM. Although significant improvement in blood pressure control and hemoglobin levels was observed, glycemic and lipid control remained suboptimal, particularly among female patients. Progressive renal dysfunction and worsening proteinuria was found during follow-up, more in female participants. Renal function initially declined after anti-proteinuria therapy, with partial recovery following drug withdrawal. These findings emphasize the need for long-term monitoring and improved management for T2DM.

**Keywords:** Type 2 Diabetes Mellitus (T2DM), Glycemic and Lipid Control, Microvascular and Macrovascular Complications, Proteinuria, Renal Dysfunction

**How to cite this article:** Faroque MO, Hossain RM, Hadiuzzaman K, Iqbal S, Jahan F, Hasan GMS, Islam RN, Karim MM, Rahman AKMS. Progression of microvascular and macrovascular complications in Bangladeshi type 2 diabetic patients: a prospective study. *Int J Drug Deliv Technol.* 2026;16(79s): 362-374. DOI: 10.25258/ijddt.16.79s.39

## 1. Introduction

Type 2 diabetes mellitus (T2DM) has emerged as one of the most alarming global public health challenges of the 21st century, affecting millions of individuals worldwide. According to the International Diabetes Federation (IDF), approximately 537 million adults are currently living with T2DM, and this number is projected to rise substantially in the coming decades, particularly in low- and middle-income countries [1]. Countries like Bangladesh are experiencing a rapid epidemiological transition, where urbanization, lifestyle modification, and population aging have contributed significantly to the increasing prevalence of T2DM [2, 3]. In Bangladesh, the prevalence of T2DM has shown a consistent upward trend over the recent decades [3, 4]. Factors such as rapid urban expansion, reduced physical activity, increased consumption of processed and high-calorie foods, and genetic susceptibility have collectively contributed to this rise. Moreover, limited awareness, delayed diagnosis, and suboptimal glycemic control further exacerbate the burden of T2DM and its complications in this setting [2]. The clinical significance of T2DM lies not only in persistent hyperglycemia but also in its long-term consequences, which are broadly categorized into macrovascular and microvascular complications. Macrovascular complications including- coronary artery disease (CAD), cerebrovascular disease (CVD), and peripheral arterial disease (PAD) are the leading causes of morbidity and mortality among diabetic patients [5]. These macrovascular complications arise primarily due to accelerated atherosclerosis and endothelial dysfunction and are frequently aggravated by coexisting cardiovascular risk factors- such as hypertension, dyslipidemia, and obesity [6, 7]. On the other hand, microvascular complications, including diabetic retinopathy, nephropathy, and neuropathy, result from chronic hyperglycemia induced damage to small blood vessels [8]. Diabetic retinopathy remains a leading cause of preventable blindness, while diabetic nephropathy is a major contributor to chronic

kidney disease (CKD) and end-stage renal disease (ESRD) globally [9]. Diabetic neuropathy, often underdiagnosed, significantly impairs quality of life through chronic pain, sensory loss, and increased risk of foot ulcers and amputations [10]. The burden of these complications is particularly profound in resource-limited settings like Bangladesh, where access to early screening and specialized care may be constrained. The coexistence of macrovascular and microvascular complications in patients with T2DM reflects the systemic nature of the disease and highlights the importance of comprehensive management strategies. Intensive glycemic control, along with aggressive management of cardiovascular risk factors, has been shown to reduce the risk and progression of these complications. Landmark studies such as the UK Prospective Diabetes Study and the Diabetes Control and Complications Trial have demonstrated the benefits of intensive glycemic control in reducing microvascular complications, while multifactorial interventions have been effective in lowering macrovascular risk [11, 12]. Despite these advances, there remains a paucity of comprehensive data evaluating the combined burden and progression of both macrovascular and microvascular complications among diabetic patients in Bangladesh. Most existing studies focus on individual complications rather than providing an integrated assessment of overall disease burden and therapeutic outcomes. Understanding the pattern, severity, and progression of these complications in the Bangladeshi population is essential for developing targeted interventions and optimizing patient management strategies. Therefore, the present study aims to evaluate the prevalence and clinical outcomes of macrovascular and microvascular complications among patients with T2DM in a Bangladeshi cohort. By examining relevant clinical parameters over time, this study seeks to provide insights into the progression, deterioration, or improvement of these complications, thereby contributing to evidence-based strategies for improving diabetes care in Bangladesh.

## 2. Methodology

This longitudinal observational study enrolled pre-diagnosed Type 2 diabetic subjects aged  $\geq 40$  years and reassessed them six monthly for one year. Participants were recruited from the Out Patient Departments (OPD) of Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Bangladesh Medical University (BMU), and National Institute of Kidney Diseases and Urology (NIKDU). All study patients were selected using computer-generated random numbers from an initial set of serial numbers for 1000 subjects. Exclusion criteria included Type 1 or other diabetes types, acute illness (e.g., multi-organ failure, disseminated malignancy), immunosuppressive therapy, or gross debilitation. According to previous studies, it was seen that 21.8% of the diabetic population have nephropathy [13], 55% are hypertensive [14], 7 to 75 % have diabetic neuropathy [15] and 36.3% have some form of diabetic retinopathy [16]. Using sample size calculations to ensure adequate statistical power (80%) at a 95% confidence level for this study, the number of cases needed to detect clinically relevant changes in the progressive microvascular complications (nephropathy and retinopathy) was estimated. A minimum detectable absolute difference (d) of 5% was chosen to capture minimal deterioration in these conditions. Accounting for at least an estimated 10% loss to follow-up (5% at each visit), a final sample size of 846 subjects (423 males, 423 females) was enrolled at baseline from the initial patient pool.

Patient evaluation involved an initial visit to collect clinical data, followed by two subsequent visits at six-month intervals to document findings obtained from retaking medical history and record physical examination data. Laboratory assessments performed in each visit included blood analyses for hemoglobin, glycated hemoglobin (HbA1c), serum creatinine, fasting lipid profile and urine albumin creatinine ratio (ACR) alongside an electrocardiogram (ECG) echocardiogram and ultrasonogram (USG) of the kidneys. The study received approval from the Institutional Review Board (Ethical Review Committee) of BIRDEM Hospital, and informed written consents were obtained from all study subjects or their legal guardians. The data collection team at each hospital included a research assistant and an aid nurse who had all received adequate training on the study methods.

### Statistical analysis of data

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 26, with quantitative data presented as mean with standard deviation ( $\pm$ SD) and qualitative data as frequency with corresponding percentages. Data were analyzed using

Repeated Measures ANOVA with Bonferroni correction for pairwise comparisons. Categorical variables (Prevalence of Complications) were analyzed using Cochran's Q test for trends across the three time points. A p value  $< 0.05$  was considered statistically significant

## 3. Results and Observations

Among total 846 T2DM cases enrolled at first visit, 16 cases were excluded as per exclusion criteria and 22 were gradually lost from follow up visits by the end of the study despite sincere efforts. 8 cases were omitted for missing data and finally 800 cases (400 males, 400 females) were available for analysis. We have analyzed the data and the results are presented below in Tables and Figures.

### Neuropathy and Retinopathy

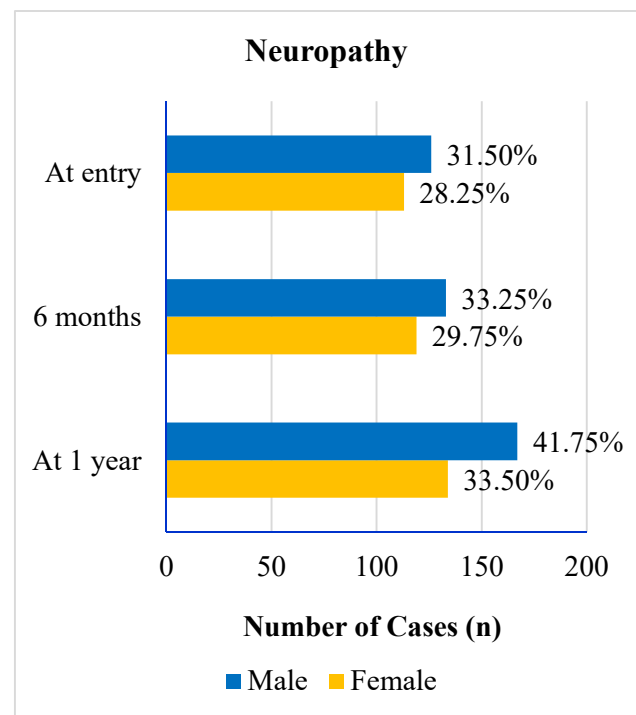
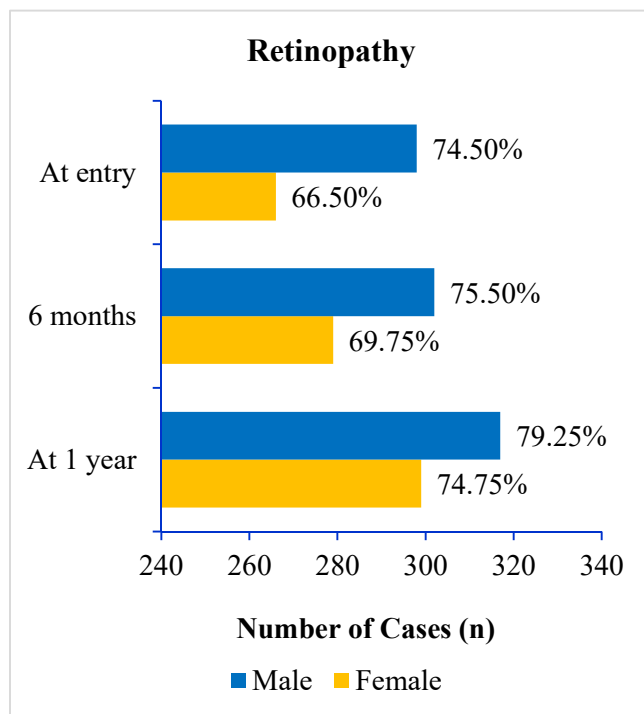
Neuropathy affected nearly a third of participants and retinopathy prevalence was over two thirds in females and around three quarters in males. The rising percentages for developing retinopathy attained significant p values (Table- 1).

**Table- 1: Six monthly frequency of cases of neuropathy and retinopathy**

| Neuropathy and retinopathy | At entry<br>n(%) | At 6 months<br>n(%) | After 1 year<br>n(%) | p value |
|----------------------------|------------------|---------------------|----------------------|---------|
| <b>Neuropathy</b>          |                  |                     |                      |         |
| Male (n=400)               | 126 (31.5%)      | 133 (33.25%)        | 167 (41.75%)         | 0.162   |
| Female (n=400)             | 113 (28.25%)     | 119 (29.75%)        | 134 (33.5%)          | 0.145   |
| <b>Retinopathy</b>         |                  |                     |                      |         |
| Male (n=400)               | 298 (74.5%)      | 302 (75.5%)         | 317 (79.25%)         | 0.032 * |
| Female (n=400)             | 266 (66.5%)      | 279 (69.75%)        | 299 (74.75%)         | 0.034 * |

Cochran's Q test was performed, \*Statistically significant at  $p < 0.05$

The frequencies for development of microvascular complications like retinopathy and neuropathy among both males and females showed a steady rise over the one year (figure- 1).



**Figure- 1: Frequency of cases of neuropathy and retinopathy**

#### Cardio-vascular comorbidities and blood pressure

The data indicate a progressive increase in macrovascular complications over time in both male and female participants. While the rise in ischemic heart disease (IHD) prevalence did not achieve statistical significance. Peripheral vascular disease (PVD) as evidenced by loss of pulsation at arteria dorsalis pedis and/or posterior tibial artery, with worsening atherosclerosis, was found to affect increasing cases over the year. PVD demonstrated a significant upward trend, highlighting its potential as an early and progressively worsening vascular complication in this cohort (Table- 2).

**Table- 2: Six monthly frequency of cases of ischemic heart disease (IHD) and peripheral vascular disease (PVD) (N= 800)**

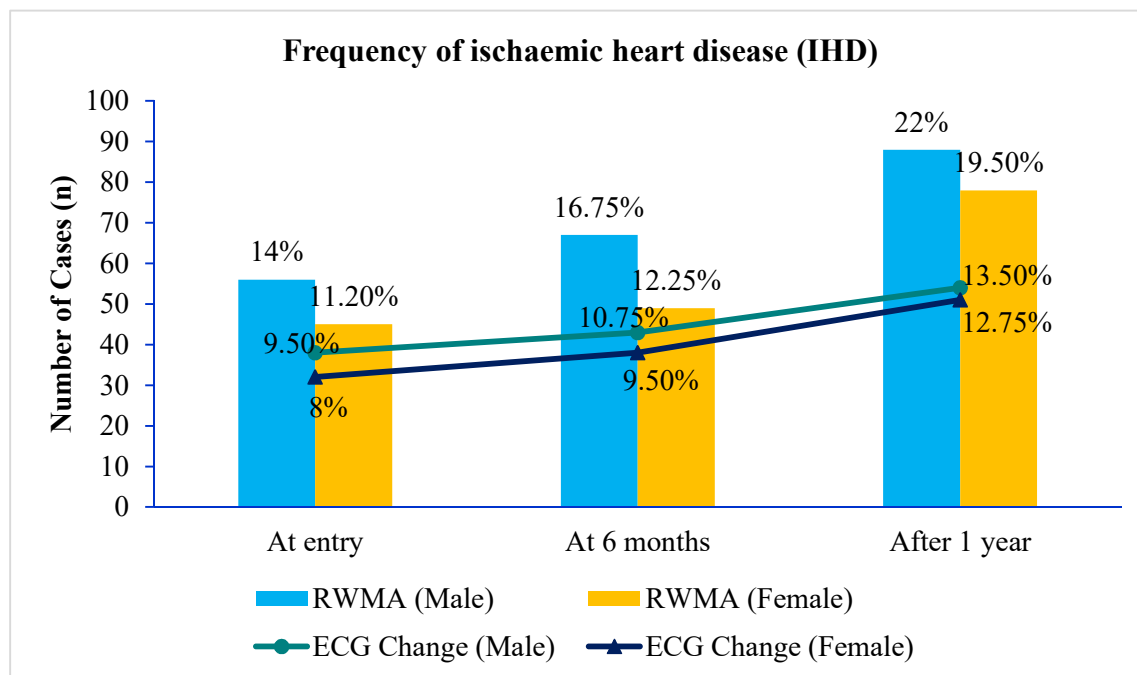
| Complications                                 | Sex             | At entry n (%) | At 6 months n (%) | After 1 year n (%) | p-value |
|-----------------------------------------------|-----------------|----------------|-------------------|--------------------|---------|
| IHD diagnosed clinically and confirmed by ECG | Male (n= 400)   | 38 (9.50)      | 43 (10.75)        | 54 (13.50)         | 0.063   |
|                                               | Female (n= 400) | 32 (8.00)      | 38 (9.50)         | 51 (12.75)         | 0.067   |

|                                                          |                 |            |            |            |        |
|----------------------------------------------------------|-----------------|------------|------------|------------|--------|
| IHD diagnosed clinically and confirmed by echocardiogram | Male (n= 400)   | 56 (14.00) | 67 (16.75) | 88 (22.00) | 0.085  |
|                                                          | Female (n= 400) | 45 (11.25) | 49 (12.25) | 78 (19.50) | 0.079  |
| PVD diagnosed clinically                                 | Male (n= 400)   | 68 (17.00) | 71 (17.75) | 74 (18.50) | 0.023* |
|                                                          | Female (n= 400) | 61 (15.25) | 68 (17.00) | 69 (17.25) | 0.037* |

IHD= Ischemic Heart Disease, PVD= Peripheral Vascular Disease, Cochran's Q test was performed,

\*Statistically significant at  $p < 0.05$

Frequency of patients having cardiac symptoms with evidence of myocardial ischemia on electrocardiogram rose progressively over the year as did the frequency of echocardiogram findings, though none reached significance (Figure- 2).



RWMA= Regional Wall Motion Abnormality, ECG= Electrocardiogram

**Figure- 2: Frequency of cases with ischemic heart disease (IHD)**

#### Status of blood pressure (BP) and cardiac function

The study demonstrated a gradual improvement in blood pressure control over the follow-up period. Mean systolic blood pressure decreased from  $167 \pm 32$  mmHg at baseline to  $139 \pm 19$  mmHg after one year, while mean diastolic blood pressure decreased from  $92 \pm 12$  mmHg to  $80 \pm 15$  mmHg. These reductions were statistically significant ( $p=0.001$  and  $p=0.026$ , respectively), indicating improved blood pressure management during follow-up. In contrast, ejection fraction (EF) showed a slight declining trend in both males and females over one year; however, these changes were not statistically significant (male:  $p=0.072$ ; female:  $p=0.081$ ). This suggests that overall cardiac systolic function remained relatively stable throughout the study period (Table- 3).

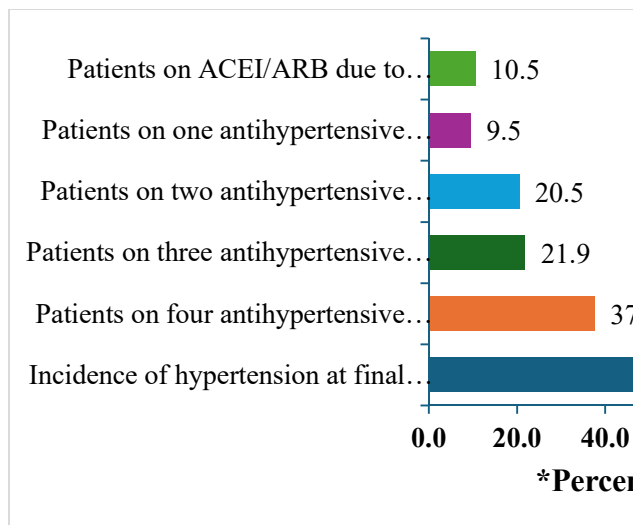
**Table- 3: Six monthly status of blood pressure (BP) and cardiac function**

| Variables             | At entry     | At 6 months  | After 1 year | p-value |
|-----------------------|--------------|--------------|--------------|---------|
| Blood pressure (mmHg) |              |              |              |         |
| Systolic BP           | $167 \pm 32$ | $153 \pm 26$ | $139 \pm 19$ | 0.001*  |

|                       |                  |                  |                  |        |
|-----------------------|------------------|------------------|------------------|--------|
| Diastolic BP          | $92 \pm 12$      | $85 \pm 11$      | $80 \pm 15$      | 0.026* |
| Ejection fraction (%) |                  |                  |                  |        |
| Male (%)              | $56.22 \pm 8.86$ | $55.21 \pm 7.74$ | $55.11 \pm 7.23$ | 0.072  |
| Female (%)            | $58.54 \pm 7.65$ | $57.66 \pm 7.13$ | $56.54 \pm 6.98$ | 0.081  |

BP= Blood Pressure, Repeated-measures ANOVA test was performed, \*Statistically significant at  $p < 0.05$

In our final follow up the incidence of hypertension was 82%. Of them 37.6% were on four drugs, 21.9% on three drugs, 20.5% on two and 9.5% on one anti-hypertensive drugs. However, 10.5 % ( $n=84$ ) were on angiotensin-converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB) due to proteinuria but they were not hypertensive (Figure-3).



\*Multiple response, ACEI= Angiotensin-Converting Enzyme Inhibitor, ARB= Angiotensin II Receptor Blocker

**Figure- 3: The incidence of hypertension and use of anti-hypertensive drugs**

#### Glycemic control (HbA1c) and lipid profile

The table shows a slight reduction in glycated hemoglobin (HbA1c) levels over the one-year follow-up period in both male and female participants; however, these changes were not statistically significant ( $p>0.05$ ). Female participants consistently had higher HbA1c values compared to males throughout the study period. Regarding the lipid profile, total cholesterol (TC), low density lipoprotein cholesterol (LDL) and triglyceride (TG) levels demonstrated a gradual decline over time, suggesting an improving lipid status, although these reductions did not reach statistical significance ( $p>0.05$ ). In contrast, high density lipoprotein cholesterol (HDL) levels decreased significantly during follow-up ( $p=0.042$ ), indicating worsening protective lipid status despite improvements in other lipid parameters (Table- 4).

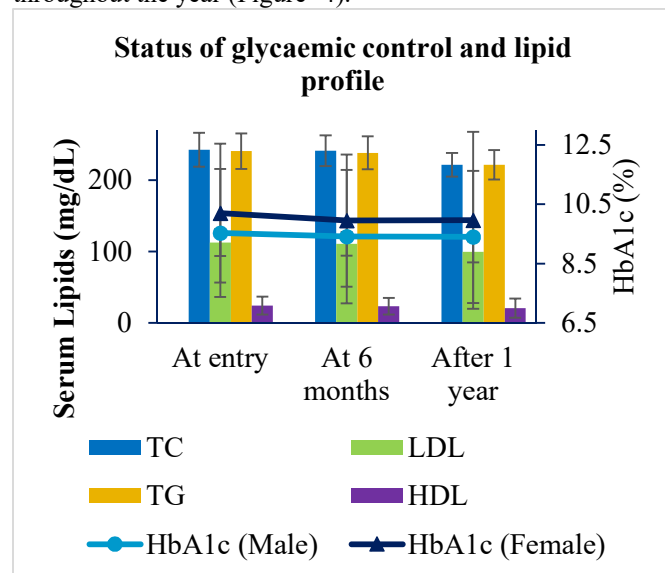
**Table- 4: Six monthly status of glycemic control (HbA1c) and serum lipids**

| HbA1c (%) and Lipid Profile (mg/dL) | At entry  | After 6 months | After 1 year | p value |
|-------------------------------------|-----------|----------------|--------------|---------|
| HbA1c (%)                           |           |                |              |         |
| Male                                | 9.53±2.16 | 9.41±2.25      | 9.40±2.23    | 0.098   |

| HbA1c (%) and Lipid Profile (mg/dL) | At entry    | After 6 months | After 1 year | p value |
|-------------------------------------|-------------|----------------|--------------|---------|
| Female                              | 10.2±2.34   | 9.95±2.23      | 9.96±2.98    | 0.096   |
| Lipid Profile (mg/dL)               |             |                |              |         |
| TC                                  | 242.45±23.6 | 241.12±21.6    | 221.54±16.7  | 0.052   |
| HDL                                 | 24.26±12.5  | 23.51±11.7     | 20.59±13.4   | 0.042*  |
| LDL                                 | 112.65±18.9 | 110.54±16.6    | 99.48±14.7   | 0.051   |
| TG                                  | 240.53±24.7 | 238.22±22.9    | 221.41±20.56 | 0.052   |

HbA1c= Glycated Hemoglobin, TC= Total Cholesterol, HDL= High Density Lipoprotein Cholesterol, LDL= Low Density Lipoprotein Cholesterol, TG= Triglyceride, Repeated-measures ANOVA test was performed, \*Statistically significant at  $p<0.05$

Despite enrollment into this study and subjecting cases to close supervision, glycemic and lipid control on average, over the one year follow up period improved insignificantly. Females had worse control over their blood glucose levels than their male counterparts throughout the year (Figure- 4).



TC= Total Cholesterol, LDL= Low Density Lipoprotein Cholesterol, TG= Triglyceride, HDL= High Density Lipoprotein Cholesterol, HbA1c= Glycated Hemoglobin

**Figure- 4: Six monthly control of HbA1c and serum lipids**

#### Anemia and Nephropathy

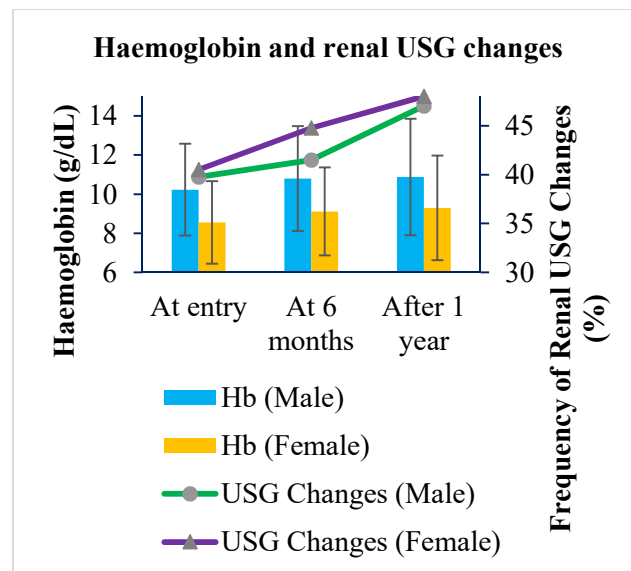
The data demonstrates a gradual improvement in hemoglobin (Hb) levels among both male and female participants over the one-year follow-up period. The increase was statistically significant in both sexes ( $p < 0.05$ ), indicating partial improvement in anemia status during follow-up. However, female participants continued to have lower hemoglobin levels compared to males throughout the study period. Renal parenchymal changes detected on ultrasonography (USG) showed a progressive increase in both male and female participants over time, suggesting worsening nephropathy. Although the rise was not statistically significant ( $p > 0.05$ ), the findings indicate a clinically important progression of renal involvement during the study period (Table- 5).

**Table- 5: Six monthly status of anemia and renal parenchymal changes on ultrasonography (USG)**

| Hemoglobin and Renal parenchymal changes on USG | At entry     | At 6 months  | After 1 year | p value |
|-------------------------------------------------|--------------|--------------|--------------|---------|
| Hemoglobin (g/dL)                               |              |              |              |         |
| Male                                            | 10.23±2.34   | 10.79±2.68   | 10.88±2.98   | 0.045*  |
| Female                                          | 8.56±2.11    | 9.12±2.24    | 9.3±2.67     | 0.047   |
| Renal parenchymal changes on USG                |              |              |              |         |
| Male, n (%)                                     | 159 (39.75%) | 166 (41.5%)  | 188 (47%)    | 0.055   |
| Female, n (%)                                   | 162 (40.5%)  | 179 (44.75%) | 192 (48%)    | 0.056   |

USG= Ultrasonogram, Repeated-measures ANOVA test was performed, \*Statistically significant at  $p < 0.05$

Blood hemoglobin (Hb) levels improved slightly on treatment for anemia (although no blood transfusions were given) despite deteriorating renal function in both males and females. Sonographic changes in the renal parenchyma inclusive of increased cortical echogenicity and/or loss of cortico-medullary differentiation were assessed by the same group of radiologists and found to be more frequent as time progressed (Figure- 5).



Hb= hemoglobin, USG= Ultrasonogram

**Figure- 5: Six monthly status of anemia and frequency of renal parenchymal USG changes**

In this study a progressive worsening of renal function was observed over the one-year follow-up period. Serum creatinine levels increased in both males and females, with a statistically significant rise observed in females ( $p = 0.034$ ) and a non-significant increase in males ( $p = 0.087$ ), indicating advancing renal impairment over time. Similarly, urine albumin creatinine ratio (ACR) demonstrated a gradual increase in both sexes, reflecting worsening proteinuria; however, these changes were not significant ( $p > 0.05$ ) (Table- 6).

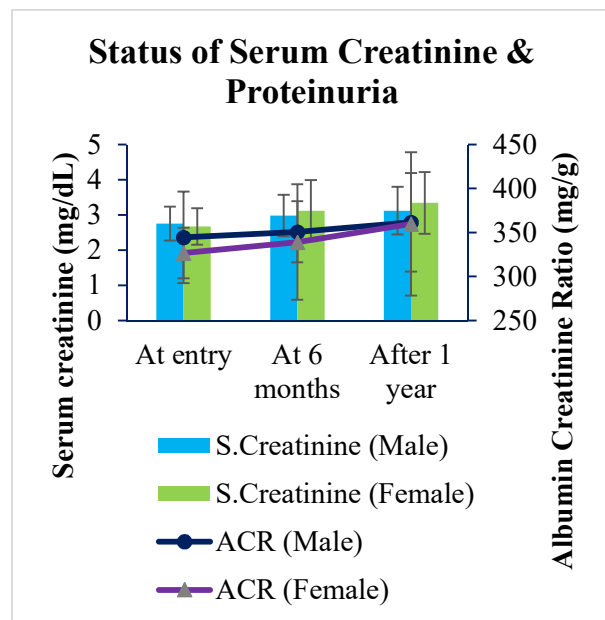
**Table- 6: Six monthly status of renal function and proteinuria (ACR)**

| Renal function and proteinuria | At entry     | At 6 months  | After 1 year | p value |
|--------------------------------|--------------|--------------|--------------|---------|
| Serum creatinine (mg/dL)       |              |              |              |         |
| Male                           | 2.75±0.48    | 2.98±0.59    | 3.12±0.68    | 0.087   |
| Female                         | 2.67±0.52    | 3.12±0.87    | 3.34±0.88    | 0.034*  |
| Urine ACR (mg/g)               |              |              |              |         |
| Male                           | 344.45±52.11 | 350.65±34.76 | 361.54±55.98 | 0.092   |
| Female                         | 326.65±28.67 | 329.07±65.67 | 335.68±81.54 | 0.119   |

ACR= Albumin Creatinine Ratio, Repeated-measures ANOVA test was performed, \*Statistically significant at  $p < 0.05$

The participants overall had deteriorating proteinuria over time though not statistically significant (possibly because of treatment). However, rising serum

creatinine over the year did attain significance for females (Figure- 6).



ACR= Albumin Creatinine Ratio

**Figure- 6: Six monthly status of serum creatinine and urine ACR**

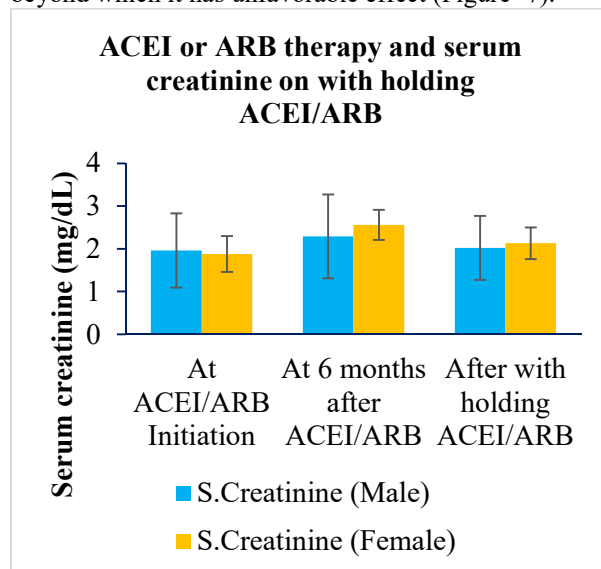
The incidence of nephropathy (presence of albuminuria and/or raised serum creatinine) was approximately 72%. At entry roughly 45% patients were not on ACEI or ARB even when there was a clear indication of these agents to be used, and were thus administered these agents as part of standard treatment. It was found that serum creatinine levels increased after 6 months of ACEI/ARB therapy in both male and female patients, indicating a transient decline in renal function following initiation of treatment. This rise was statistically significant in both sexes (male  $p=0.042$ , female  $p=0.041$ ). After discontinuation of this therapy (ACEI/ARB), serum creatinine levels showed a partial reduction compared to the 6-month values, suggesting some degree of renal function recovery, although levels remained slightly higher than baseline. Overall, the findings indicate an initial deterioration in renal function after ACEI/ARB initiation followed by partial improvement after drug withdrawal (Table- 7).

**Table- 7: Status of renal function in patients with ACEI/ARB therapy and improvement on holding ACEI/ARB**

| Renal function           | After initiating ACEI or ARB | After 6 months | After discontinuing ACEI and ARB | p value |
|--------------------------|------------------------------|----------------|----------------------------------|---------|
| Serum creatinine (mg/dL) |                              |                |                                  |         |
| Male                     | 1.96±0.87                    | 2.29±0.98      | 2.02±0.75                        | 0.001*  |
| Female                   | 1.88±0.42                    | 2.56±0.35      | 2.13±0.37                        | 0.001*  |

ACEI= Angiotensin-Converting Enzyme Inhibitor, ARB= Angiotensin II Receptor Blocker, Repeated-measures ANOVA test was performed, \*Statistically significant at  $p<0.05$

A subset of 18% of patients who were on either ACEI or ARB upon enrollment had deteriorated in terms of renal function as detected at six months, but after discontinuing these agents' serum creatinine improved significantly (and transiently) in most of these cases. Patients on ACEI or ARB had rapid deterioration of renal function when serum creatinine was more than 2.5 mg/dL. This finding indicates that the use of these agents in diabetic nephropathy has beneficial effect only up to a certain serum level of serum creatinine beyond which it has unfavorable effect (Figure- 7).



ACEI= Angiotensin-Converting Enzyme Inhibitor, ARB= Angiotensin II Receptor Blocker

**Figure- 7: Serum creatinine in patients with improvement on with holding ACEI/ARB**

#### 4. Discussion

In this prospective cohort of 846 patients with type 2 diabetes mellitus (T2DM), 800 participants (400 males and 400 females) completed follow-up and were included in the final analysis after exclusion of cases due to missing data, loss to follow-up, and predefined criteria. The analysis demonstrated a progressive increase in microvascular complications over one year, particularly neuropathy and retinopathy, reflecting the ongoing burden of chronic hyperglycemia and vascular injury in diabetes.

Peripheral neuropathy showed a gradual increase in prevalence in both sexes over time (males: 31.5% to 41.75%; females: 28.25% to 33.5%), although this rise was not statistically significant. This trend is consistent with the known chronic and cumulative nature of diabetic neuropathy, which develops due to prolonged metabolic stress, oxidative injury, and microvascular dysfunction affecting peripheral nerves. Similar progression patterns have been reported in longitudinal studies highlighting that neuropathy increases with disease duration and poor glycemic control [17, 18]. In contrast, diabetic retinopathy showed a statistically significant increase in both males (74.5% to 79.25%,  $p=0.032$ ) and females (66.5% to 74.75%,  $p=0.034$ ). This finding is clinically important, as retinopathy is a sensitive marker of diabetic microvascular damage. The observed progression aligns with global evidence indicating that retinopathy prevalence increases with diabetes duration, poor glycemic control, and coexisting cardiovascular risk factors [19]. Furthermore, retinopathy is recognized as a dynamic microvascular process that may progress even over relatively short periods in high-risk patients [20].

The higher baseline prevalence of retinopathy compared to neuropathy may reflect delayed diagnosis and late presentation, which is common in resource-limited settings. According to the American Diabetes Association, microvascular complications may already be present at diagnosis in many patients with T2DM due to prolonged undetected hyperglycemia, underscoring the need for early screening and intervention [21]. The significant upward trend in retinopathy over one year further suggests ongoing microvascular deterioration despite follow-up care.

Overall, these findings indicate that microvascular complications are highly prevalent and progressively worsening in this Bangladeshi T2DM cohort. The differential pattern between neuropathy (non-significant increase) and retinopathy (significant increase) may reflect differences in detectability, diagnostic sensitivity, and temporal progression of microvascular injury. These results highlight the importance of early screening, strict glycemic control,

and multidisciplinary management to reduce long-term complications.

The present study demonstrated a gradual increase in macrovascular complications among the study participants over the follow-up period. Although the rise in ischemic heart disease (IHD) was not statistically significant, an increasing trend was evident, suggesting progressive cardiovascular involvement in patients with T2DM. Similar findings have been reported in previous studies, where prolonged duration of diabetes, poor glycemic control, dyslipidemia, and hypertension contributed to increased cardiovascular morbidity among diabetic populations [22, 23]. Peripheral vascular disease (PVD) showed a significant upward trend during the study period, indicating that peripheral vascular involvement starts early and progressively worsens over time in diabetic patients. Chronic hyperglycemia promotes endothelial dysfunction, accelerated atherosclerosis and impaired peripheral circulation, thereby increasing the risk of PVD [24]. Previous studies have also demonstrated that diabetic patients are at significantly higher risk of developing PVD and related complications, particularly in South Asian populations [25, 26]. The progressive increase in macrovascular complications observed in this study highlights the importance of regular cardiovascular assessment, strict glycemic control, and early risk-factor modification in patients with T2DM to reduce long-term vascular morbidity and mortality.

The current study demonstrated significant improvement in blood pressure (BP) control during follow-up in both males and females, reflecting effective cardiovascular risk management. Similar findings have been reported in previous studies showing that optimized antihypertensive therapy and regular follow-up improve blood pressure control in patients with T2DM [11, 27, 28]. Although ejection fraction (EF) showed a mild declining trend over one year, the changes were not statistically significant, indicating relatively preserved cardiac systolic function throughout the study period. In accordance, previous studies reported that early cardiovascular management in T2DM may help maintain stable cardiac function despite ongoing metabolic risk factors [29, 30].

A high prevalence of hypertension (82%) during final follow-up was observed among the study participants, with many patients requiring multiple antihypertensive agents, reflecting the difficulty of blood pressure control in patients with T2DM. Previous studies have shown that diabetic patients frequently require combination therapy to achieve target blood pressure levels due to increased cardiovascular and renal risk [27, 28]. A proportion of normotensive patients were receiving ACEIs or ARBs

because of proteinuria, consistent with current recommendations supporting renin-angiotensin system blockade for renal protection and reduction of diabetic nephropathy progression even in the absence of hypertension [31, 32].

We found a modest reduction in HbA1c levels over one year in both sexes, although the changes were not statistically significant. Female participants consistently exhibited higher HbA1c values, which may reflect poorer glycemic control and greater metabolic risk among women with T2DM [33, 34]. Lipid parameters including- total cholesterol (TC), LDL cholesterol, and triglycerides (TG) showed gradual improvement during follow-up, although not significant, suggesting beneficial effects of ongoing treatment and lifestyle modification. Similar trends have been reported in diabetic cohorts receiving standard lipid-lowering therapy [35]. However, HDL cholesterol declined significantly over time, indicating worsening protective lipid status, which may contribute to persistent cardiovascular risk despite improvement in other lipid fractions [36].

The present study demonstrated significant improvement in hemoglobin (Hb) levels in both male and female participants during follow-up, suggesting partial correction of anemia with ongoing management. However, females consistently had lower hemoglobin levels than males, which is consistent with previous reports in patients with T2DM and chronic kidney disease (CKD) [37, 38]. Renal parenchymal changes on ultrasonography (USG) increased progressively over time in both sexes, indicating gradual progression of diabetic nephropathy despite treatment. Although the changes were not statistically significant, similar previous study have shown that structural renal abnormalities may progress gradually and correlate with long-term renal impairment in diabetic patients [39]. A significant rise in serum creatinine among female participants over the follow-up period suggests progressive decline in renal function, possibly reflecting greater susceptibility to diabetic nephropathy progression in women [40]. Although proteinuria increased overall during the study period, the change was not statistically significant, which may be attributable to the renoprotective effects of ongoing anti-proteinuric therapy [32].

A subset of patients receiving angiotensin-converting enzyme inhibitor (ACEI) and angiotensin II receptor blocker (ARB) demonstrated worsening renal function at six months. Improvement in serum creatinine following discontinuation suggests that advanced renal impairment may predispose to transient hemodynamic decline with renin-angiotensin system blockade [41]. Although ACEIs and ARBs are renoprotective in diabetic nephropathy, their benefits

may become limited in advanced kidney dysfunction and therefore require close monitoring of renal function [32].

To summarize- this prospective cohort study of Bangladeshi patients with T2DM demonstrated progressive worsening of both microvascular and macrovascular complications over one year. Diabetic retinopathy and peripheral vascular disease showed significant progression, while neuropathy and ischemic heart disease increased gradually. Blood pressure control and hemoglobin levels improved during follow-up, although glycemic and lipid control remained suboptimal, particularly among females. Renal involvement progressed with increasing serum creatinine, proteinuria, and ultrasonographic renal changes despite treatment. A subset of patients receiving ACEI/ARB therapy experienced transient deterioration of renal function, especially at higher baseline creatinine levels. Overall, the findings highlight the importance of early screening, strict metabolic control, cardiovascular risk reduction, and close renal monitoring in patients with T2DM.

### **Conclusion**

This study concluded that, despite adequate prescription a large number of patients remain beyond the targeted glycemic control among Bangladeshi T2DM patients. Both microvascular and macrovascular complications increased progressively over time among male and female participants with T2DM. Although significant improvement in blood pressure control and hemoglobin levels was observed and lipid control remained suboptimal, particularly among females. Renal parameters indicated progressive renal dysfunction and worsening proteinuria during follow-up, more pronounced in female participants. The study also demonstrated an initial decline in renal function following initiation of anti-proteinuria therapy, with partial recovery after drug withdrawal. These findings highlight the need for comprehensive long-term monitoring and optimized management strategies to reduce both microvascular and macrovascular complications in patients with T2DM.

### **Limitations**

The study was limited by 12-month follow-up, its observational design, recruitment from tertiary-care centers, lack of detailed assessment of lifestyle factors, medication adherence, and socioeconomic variables. These limitations may have influenced the observed progression of diabetic complications and limit the generalizability of the findings.

### **Recommendation**

Longer-term multicenter studies with comprehensive risk factor assessment are warranted.

### **Conflicts of interest**

All authors declared that they have no competing interest regarding this publication.

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