Original Article

Macro- and micro-vascular complications and their determinants among people with type 2 diabetes in Bangladesh

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ABSTRACT

Objectives: To identify the prevalence of micro- and macro-vascular complications and their associated factors for type 2 diabetes mellitus in Bangladesh.
Methods: This retrospective and cross-sectional study was conducted in six diabetes hospitals, covered urban and rural population. From April to September in 2017, a total of 1253 type 2 diabetes patients aged ≥18 years were recruited. Participants answered a pre-tested electronic questionnaire, and their medical records were reviewed for documented diabetes complications.
Results: Mean age was 55.1 (±12.6) years. Among macrovascular complications, the prevalence of coronary artery disease was found to be 30.5%, 10.1% for stroke and 12.0% for diabetic foot. Among microvascular complications, nephropathy was prevalent among 34.2%, retinopathy among 25.1% and neuropathy among 5.8% of patients. Risk factors found to be associated with one or more of the complications were female gender, higher age, lower education level, an urban area of residence, higher household income, smoking, physical inactivity, hypertension, poor glycaemic control, poor adherence to treatment, longer duration of diabetes, and insulin use.
Conclusion: Diabetes complications are highly prevalent among type 2 diabetes population in Bangladesh. Prevention strategies should focus on increasing physical activity, weight loss, smoking cessation, and more strict control of hypertension and glycaemic level.

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1. Introduction

Diabetes mellitus is a growing problem worldwide, affecting 425 million or 8.8% of adults in 2017. The International Diabetes Federation (IDF) reports that a staggering 79% of adults with diabetes live in low- and middle-income countries [1]. By far the most prevalent type of diabetes, Type 2 Diabetes Mellitus (T2DM) constituted around 90% of all diabetic cases [2]. In Bangladesh, the prevalence of diabetes in adults aged 20—79 years was reported at 6.9%, affecting just below 7 million adults of the population and it is anticipated to increase to 13.7 million by 2045 [1]. The projected increase in prevalence is in line with the epidemiologic transition which Bangladesh is undergoing, whereby its burden of disease shifts from acute infectious and deficiency diseases to non-communicable chronic diseases, such as diabetes [3]. This trend is also seen in the wider context of South Asia, where rapid urbanisation has led to an increasingly sedentary lifestyle, increased intake of dietary fats and more stressful lifestyles. Biological factors have also been found to predispose South Asians to diabetes, and both lifestyle and biological factors are responsible such that South Asians have a 3-fold higher prevalence of diabetes compared to Europeans [4,5]. (see Table 1)

Diabetes mellitus is a disease characterised by either the lack of insulin (Type 1 Diabetes), or loss of insulin sensitivity (T2DM). This results in a chronic hyperglycaemic state, causing an increase in products of glycosylation. These molecules induce inflammation and injury to arterial walls, causing changes in vascular tissue, and promoting atherosclerosis. The resultant narrowing of arteries in turn increases the risk of coronary artery diseases, stroke and peripheral vascular disease, which are termed the macrovascular complications such as coronary artery disease (CAD), stroke and diabetic foot related to T2DM. Smaller blood vessels are also affected by atherosclerotic damage, leading to microvascular complications such as diabetic peripheral neuropathy, retinopathy

Table 1
Demographic characteristics by type of macro and microvascular complications.

Variables	CAD 30.5% (n = 382)		Diabetic foot 12.0% (n = 150)		Stroke 10.1% (n = 127)		Neuropathy 5.8% (n = 72)		Nephropathy 34.2% (n = 429)		Retinopathy 25.1% (n = 315)	
	%	p-value	%	p-value	%	p-value	%	p-value	%	p-value	%	p-value
Age												
<60 years	23.7	**< 0.001**	12.4	0.475	6.8	**< 0.001**	5.5	0.687	23.9	**< 0.0001**	18.8	**< 0.001**
> = 61 years	44.4		11.0		16.9		6.1		55.6		38.1	
Gender												
Male	31.4	0.432	13.7	**0.045**	11.0	0.261	5.7	0.974	34.8	0.646	21.6	**0.002**
Female	29.4		10.0		9.1		5.8		33.6		29.4	
Education level												
Tertiary	25.4	0.064	12.2	0.863	6.6	**0.047**	4.2	0.218	33.5	**0.021**	25.1	0.295
Secondary	30.7		12.4		12.0		5.5		30.9		23.3	
Up to primary	33.7		11.2		10.0		7.2		39.5		27.7	
Area of residence												
Rural	16.7	**< 0.001**	10.4	0.305	3.5	**< 0.001**	5.6	0.119	13.3	**< 0.001**	11.1	**< 0.001**
Urban	19.1		12.5		12.5		7.4		41.9		30.4	
Household income												
< 20,000 tk	26.2	**0.016**	14.5	0.106	9.8	**0.026**	7.2	0.276	33.8	**< 0.001**	21.7	**< 0.001**
20,000–60,000 tk	31.0		10.9		8.1		5.0		29.2		22.9	
> 60,000 tk	35.9		10.0		13.9		4.9		43.0		33.7	
Active smoking												
Never smoker	29.0	**0.046**	10.7	**0.015**	9.2	**0.050**	5.7	0.916	33.7	0.491	26.6	**0.045**
Ever smoker	34.9		15.7		12.9		5.8		35.8		20.9	
Passive smoking												
No	30.5	0.983	11.5	0.176	10.0	0.639	5.6	0.566	34.8	0.339	25.0	0.745
Yes	30.6		15.0		11.1		6.7		31.1		26.1	
Smokeless tobacco consumer												
No	29.4	0.117	11.3	0.176	9.6	0.207	5.6	0.578	34.1	0.871	25.0	0.801
Yes	34.3		14.3		12.1		6.4		34.6		25.7	
Physical Activity												
Active (≥150 min/week)	23.7	**< 0.001**	10.5	0.107	5.1	**< 0.001**	5.9	0.840	25.3	**< 0.001**	19.4	**< 0.001**
Inactive (<150 min/week)	37.0		13.4		15.0		5.6		42.8		30.6	

and nephropathy [6].

In 2017, diabetes mellitus accounted for 976.9 disability-adjusted life years per 100,000 people in Bangladesh, making it the top 8th cause of death and disability [7]. The disease also costed Bangladesh approximately US$5.3 billion in 2014 [8]. The total annual per capita expenditure on medical care was 6.1 times higher for patients with diabetes than those without diabetes annually [9]. A recent Bangladeshi study further showed that the cost is 1.8–3.4 times higher for patients with the presence of one or more complications compared to those without any complications [10]. Another key challenge to the public health management of diabetes is that a large proportion of diabetics are unaware of their condition. Among Bangladeshi adults with diabetes, a worrying 56.0%, or 3.9 million, are undiagnosed [11]. Late diagnosis of diabetes could increase the risk of complications, and potentially leads to poorer prognosis and quality of life. The high economic burden on the Bangladeshi health care system coupled with the huge impact on the quality of life highlights the importance of early detection and management through the identification of risk factors of T2DM complications.

Globally, the relative risk of micro- and macro-vascular complications among people with diabetes was estimated to be at least 10–20 times higher and 2–4 times higher, respectively, than in people without diabetes mellitus [11]. Several studies have also noted that these complications result from a combination of genetic, metabolic and lifestyle factors [12,13].

More specifically, in South Asia, research showed that newly diagnosed South Asian patients have a higher prevalence of complications compared to Europeans. Macrovascular complications had a prevalence of 15.7% vs. 9.4% while microvascular complications had a prevalence of 27.3% vs. 16.5% [1414]. The significantly higher prevalence of diabetes and its complications has been attributed to various differing biological and lifestyle factors [14].

In Bangladesh, some studies have been conducted to study the prevalence of macrovascular and microvascular complications related to T2DM. Many of these studies observed an increasing trend in both types of complications and identified risk factors for these complications. Advanced age, longer duration of diabetes, hypertension, poor glycaemic control, and a lack of physical exercise were identified as risk factors of macrovascular complications, while increasing age, high hemoglobin A1c (HbA1c), fasting blood glucose (FBG), 2-h post load glucose concentrations (2-hBG) and high blood pressure were significant risk factors for any type of microvascular complications [11,12], where HbA1c, FBG and 2-hBG are markers of plasma glucose levels.

However, many of these studies had a small sample size, and were conducted within a single centre. Some studies were also only conducted on people with diabetes who have had the disease for a specific period of time, and therefore might not be representative of all people with diabetes in Bangladesh. Hence, this study aims to estimate the prevalence of macrovascular and microvascular complications related to T2DM among a sample of patients from urban, semi-urban and rural Bangladesh attending primary to tertiary health care services. We also aim to identify the various risk factors that influence these complications, so they can be tackled early on in treatment. This would lower the risk of developing diabetes-related complications, leading to better health outcomes in the long run.

2. Methods

2.1. Study design and study population

This retrospective and cross-sectional study was approved by the Monash University Human Research Ethics Committee, the Ethical Review Committee of the Bangladesh University of Health

Sciences (BUHS) and the Diabetic Association of Bangladesh (BADAS). Data was collected from two tertiary level diabetes hospitals located in the central region of Bangladesh, and two tertiary level diabetes hospitals and two secondary level diabetes hospitals located in the northern region of Bangladesh. These facilities covering professionally mixed patients residing in rural, semi-urban and urban areas.

2.2. Sample selection and data collection

A total of 1253 participants were randomly recruited using systematic random sampling during April to September, in 2017. The target population were adults of both gender and registered T2DM subjects with at least one-year duration of diabetes. People with other forms of diabetes, and pregnant women were excluded. Data was collected via face-to-face interview using a structured questionnaire in a secure web-based application, Research Electronic Data Capture (REDCap [15]). Details regarding sociodemographic which included age, sex, socioeconomic status, educational level, occupational history, physical activity (Global Physical Activity Questionnaire (GPAQ) [16]), smoking history, and diet were collected. Medical history (mental health status, and duration of diabetes) were also collected from all patients. Their anthropometrics (height, weight, hip and waist circumference) and blood pressure were measured and recorded in a standardized way [17].

Clinical information related to T2DM and its complications were retrieved from patients' medical reports which was recorded in their guide book. Documented medical records were used to assess their complications and confirmed both through physicians' notes and reviewing each patient's prescribed medication list. Information on the types and quantities of medication used by each patient were recorded in a copy of a prescription slip which was saved in the REDcap application as an image for future reference. A team of trained data collectors were involved in data collection and execution of each interview. Informed consent was obtained from each participant before their interview.

2.3. Operational definition for identifying complications

Participants were evaluated for CAD by reviewing their medical records, noting any documented diagnosis, prescribed medication or past procedures for CAD. A history of stroke was determined by past diagnoses of irreversible cerebrovascular accident. Additionally, the patient was asked about a possible incident in the previous years. Presence of diabetic foot was assessed by a visual examination of having ulcers or amputations and noting any documented diagnosis of diabetic foot. Nephropathy was defined by estimated glomerular filtration rate of <60 ml/min/1.73 m^2 (calculated from creatinine using the CKD-EPI creatinine equation [17]) and documented diagnosis. Neuropathy was defined using the Michigan Neuropathy Screening Instrument [18] and by the prescribed medication. Retinopathy was defined by documented diagnosis or a past procedure for the treatment of retinopathy.

2.4. Data analysis

Data analysis was carried out using Stata SE version 15.0. Data was summarised and presented as a mean (±standard deviation) for numerical data and frequency and percentage for categorical data. Chi-square test was used to examine associations between each of the complications with patients' demographic and clinical characteristics. Any association was further examined using univariate logistic regression analysis. Potential risk factors with a p-value of 0.1 or less in univariate logistic regression were entered into multiple logistic regression analysis [19]. Stepwise variable

selection method was used to identify the factors related to each of the complications. A p-value of 0.05 or less was considered statistically significant. Multicollinearity and first order interaction effect between covariates were also investigated.

3. Results

3.1. General characteristics

The records of 1253 participants were used in the analysis. Of them, 54.3% (n = 681) were male and 45.7% (n = 572) were female. The mean age ±SD was 55.1 ± 12.6 years and 67.4% were in the below or equal to 60 years age group. About 12.8% of total study subjects were illiterate while the remaining were literate (primary = 19.1%, secondary = 45.2%, tertiary = 22.9%). In terms of area of residence, about three-quarters (73.2%) of participants lived in urban areas while 26.8% in rural areas. With respect to occupation, 2.9% were unemployed, 40.5% were home-makers, 23.6% were retired or of were ill health, and 32.8% were employed. Among macrovascular complications, CAD was present in 30.5%, stroke in 10.1% and diabetic foot in 12.0%. Among microvascular complications, nephropathy was prevalent among 34.2%, retinopathy among 25.1% and neuropathy among 5.8% (data not shown in table).

3.2. Univariate association between risk factors and complications

Inferring from Table 1, risk factors that were significantly associated with one or more diabetes complications include higher age, lower education level, an urban area of residence, higher household income, history of active smoking, history of being a smokeless tobacco consumer, and a low amount of physical activity. It is worthy to note that a history of passive smoking was not significantly associated with any diabetes complications. With regards to gender, the ma gender was significantly associated with diabetic foot while the female gender was significantly associated with retinopathy. Table 2 summarises the clinical characteristics for each macro- and microvascular complications. Poor glycaemic control (HbA1c) was only significantly associated with CAD and no other complications, while a negative family history of diabetes was associated with nephropathy. The prevalence of CAD, stroke, nephropathy and retinopathy is higher among people with hypertension. There was no significant association between waist hip ratio or body mass index and any diabetes complications. A history of dyslipidemia also showed no association with any micro- or macro- vascular complications. Among different modalities of treatment, people on oral hypoglycaemic agent and insulin treatment had a higher prevalence of CAD, stroke, nephropathy and retinopathy, while people on the insulin treatment alone had a higher prevalence of diabetic foot. Other risk factors which were associated with one or more complications include a DM duration of more than ten years and poor adherence with medication.

3.3. Multivariable association between risk factors and macrovascular complications

The results of the multiple logistic regression analysis with stepwise removal for the association between each of the macrovascular complications are shown in Table 3. Smoking, past or present and presence of hypertension increased the odds of CAD by 1.6-fold (95% CI, 1.1 to 2.3) and 3.6-fold (95% CI, 2.4 to 5.4) respectively. Patients with poor glycaemic control were also found to be at greater odds, 2.2-fold ((95% CI, 1.3 to 3.7), and those with education levels below tertiary standards were 1.8–2.1 times as likely to develop this complication. Increased odds of CAD were also observed among those with aged 61 years or above, with higher

Table 2
Clinical characteristics by type of macro and microvascular complications.

Variables	CAD 30.5% (n = 382)		Diabetic foot 12.0% (n = 150)		Stroke 10.1% (n = 127)		Neuropathy 5.8% (n = 72)		Nephropathy 34.2% (n = 429)		Retinopathy 25.1% (n = 315)	
	%	p-value	%	p-value	%	p-value	%	p-value	%	p-value	%	p-value
DM Duration												
≤ 5 years	20.1	< **0.001**	10.6	0.316	5.7	< **0.001**	4.9	0.703	16.6	< **0.001**	12.2	< **0.001**
6–10 years	26.8		11.0		7.5		6.1		26.5		19.0	
≥ 11 years	40.0		13.6		14.9		6.1		51.3		37.9	
Family history of diabetes												
No	32.0	0.121	11.7	0.692	9.6	0.418	5.7	0.976	36.6	**0.016**	25.4	0.800
Yes	27.7		12.5		11.1		5.8		29.8		24.7	
Modality of treatment												
Oral tablet	22.2	< **0.001**	8.6	**0.025**	7.2	**0.006**	4.9	0.459	20.8	< **0.001**	16.0	< **0.001**
Insulin	21.8		14.9		5.8		8.1		25.3		16.1	
Oral and insulin	36.4		13.6		12.4		6.0		43.2		31.6	
Medication adherence												
Adequate	27.0	**0.041**	10.5	0.222	5.6	< **0.001**	5.4	0.655	32.6	0.352	20.4	**0.003**
Inadequate	32.5		12.8		12.8		5.9		35.2		27.9	
Hypertension												
No	13.7	< **0.001**	10.5	0.245	3.8	< **0.001**	5.4	0.680	17.7	< **0.001**	12.6	< **0.001**
Yes	39.8		12.8		13.6		6.0		43.4		32.1	
Dyslipidaemia												
No	28.8	0.078	13.3	0.045	9.9	0.692	6.9	0.011	25.3	0.880	34.6	0.746
Yes	33.6		9.4		10.6		3.5		24.9		33.6	
Body mass index												
Normal	28.5	0.394	11.9	0.678	9.0	0.700	5.6	0.962	32.4	0.721	24.2	0.323
Overweight/Obese	31.1		11.1		8.3		5.5		33.5		27.1	
Waist/hip ratio												
Normal	7.1	0.098	7.1	0.803	0.0	0.289	21.4	0.004	14.3	0.297	28.6	0.607
High	26.8		9.1		7.5		4.7		26.7		22.8	
Glycaemic control (HbA1c)												
Control (≤6.9%)	15.4	< **0.001**	8.2	0.590	7.1	0.930	4.4	0.315	29.1	0.284	16.5	0.159
Uncontrolled (≥7%)	28.2		9.5		7.0		6.3		25.3		21.1	

income and with more than ten years of DM history. Only the two variables, being smoker and past or present insulin user in combination of oral hypoglycaemic agent were at 60% and 40% increased odds of diabetic foot respectively. In the context of stroke, patients staying in urban region had 2.3-fold higher odds (95% CI, 1.2 to 4.6) and that was 3.0-fold (95% CI, 1.6 to 5.5) higher among hypertensive patients. Furthermore, smoking (OR, 1.7; 95% CI, 1.1 to 2.8), being physically inactive (OR, 2.4; 95% CI, 1.5 to 3.8), and inadequate medication adherence (OR, 2.5; 95% CI, 1.5 to 4.3) were associated with stroke. Other variables, being aged 61 years and above, having attained a maximum of secondary education and having diabetes for more than ten years also increased the odds of stroke.

3.4. Multivariable association between risk factors and microvascular complications

Presented in Table 4 are the results of the multiple logistic regression analysis for risk factors of microvascular complications nephropathy and retinopathy. Having hypertension (OR, 2.6; 95% CI, 1.9 to 3.6) and being physically inactive (OR, 1.7; 95% CI, 1.3 to 2.3) were positively associated with diabetic nephropathy. Staying in urban region (OR, 3.2, 95% CI, 2.1 to 4.7) also increased the odds of having retinopathy. Other variables which were related to retinopathy includes being aged 61 years and over, having diabetes for more than ten years, and being on both oral hypoglycaemic agent and insulin. On the other hand, a positive family history of diabetes and having a monthly household income of 20,000 to 60000tk reduced the odds for nephropathy complications by 30% and 40% respectively. A series of factors were found to be associated with the development of diabetic retinopathy. Living in urban region (OR, 2.1; 95% CI, 1.3 to 3.2), being physically inactive (OR, 1.4; 95% CI, 1.0 to 2.1) and inadequate medication adherence (OR, 1.4; 95% CI, 1.0 to

2.1) were the factors associated with elevated odds of diabetic retinopathy. Further, female patients, patients older than 60 years, having diabetes for more than ten years and being on both oral hypoglycaemic and insulin were other associated factors to retinopathy.

4. Discussion

Diabetes is a major global health problem in the recent decades, and its complications, while very detrimental, have risks which can be reduced with proper measures. Diabetes is also an increasingly significant health issue in Bangladesh, but studies on prevalence of its microvascular and macrovascular complications, and their risk factors are relatively limited in Bangladesh, hence the purpose of this paper. This study results showed that, overall, complications were present in 63.4% of all participants. This is broken down into 14.8% of participants with only macrovascular complications, 20.7% with only microvascular complications, as well as 27.9% with both types of complications. Importantly, the study found that these complications had strong association with patients' demographics, lifestyle modification factors and co-morbidities.

Coronary artery disease was found to be the most prevalent macrovascular complication, with a prevalence rate of 30.5%. This is within the global prevalence range of 12%–31.7% [1]. Past studies conducted in Bangladesh also found CAD to be of highest prevalence, amongst all macrovascular complications [12,20]. Similarly, in rural India, a study found CAD prevalence to be the highest amongst macrovascular complications at 32.3% [21], while another study conducted in United Arab Emirates also found CAD to be the most prevalent macrovascular complication [22]. On the other hand, stroke was found to be the least prevalent macrovascular complication in our study group, with a prevalence of 10.1%. This falls within the global prevalence range of 4%–12% [23]. A study in

Table 3
Adjusted association between each of the macrovascular complications and potential risk factors.

Variables	CAD[a]			Diabetic foot[b]			Stroke[c]		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Age									
<60 years	Reference			Reference			Reference		
>= 61 years	1.6	1.1–2.3	0.009	–	–	–	1.8	1.1–2.8	0.009
Education level									
Tertiary	Reference			Reference			Reference		
Secondary	1.8	1.1–2.8	0.008	–	–	–	1.6	1.1–2.5	0.028
Up to primary	2.1	1.3–3.5	0.002	–	–	–	–	–	–
Household income									
< 20,000 tk	Reference			Reference			Reference		
20,000–60,000 tk	1.5	1.0–2.3	0.029	–	–	–	–	–	–
> 60,000 tk	2.3	1.4–3.7	<0.001	–	–	–	–	–	–
DM Duration									
≤ 5 years	Reference			Reference			Reference		
6–10 years	–	–	–	–	–	–	–	–	–
≥ 11 years	1.5	1.1–2.2	0.012	–	–	–	1.7	1.1–2.7	0.018
Area of residence									
Rural	Reference			Reference			Reference		
Urban	–	–	–	–	–	–	2.3	1.2–4.6	0.011
Modality of treatment									
Oral tablet	Reference			Reference			Reference		
Insulin	–	–	–	–	–	–	–	–	–
Oral and insulin	–	–	–	1.4	1.0–2.1	0.045	–	–	–
Active smoking									
Never smoker	Reference			Reference			Reference		
Ever smoker	1.6	1.1–2.3	0.015	1.6	1.1–2.4	0.008	1.7	1.1–2.8	0.017
Physical activity									
Active (>= 150 min/week) (ref)	Reference			Reference			Reference		
Inactive (<150 min/week)	–	–	–	–	–	–	2.4	1.5–3.8	<0.001
Hypertension									
No	Reference			Reference			Reference		
Yes	3.6	2.4–5.4	<0.001	–	–	–	3.0	1.6–5.5	<0.001
Medication adherence									
Adequate	Reference			Reference			Reference		
Inadequate	–	–	–	–	–	–	2.5	1.5–4.3	0.001
Glycaemic control (HbA1c)									
Control (≤6.9%)	Reference			Reference			Reference		
Uncontrolled (≥7%)	2.2	1.3–3.7	0.002	–	–	–	–	–	–

[a] Adjusted for age, level of education, area of residence, household income, active smoking, smokeless tobacco, physical activity, duration of diabetes, medication adherence, modality of treatment, family history of DM, hypertension, glycaemic control, dyslipidaemia, and waist/hip ratio (area under the receiver operating characteristic curve: 73.6%, Hosmer-Lemeshow goodness-of-fit test p-value: 0.988).

[b] Adjusted for gender, household income, active smoking, smokeless tobacco, physical activity, modality of treatment, BMI, and dyslipidaemia (area under the receiver operating characteristic curve: 56.8%, Hosmer-Lemeshow goodness-of-fit test p-value:0.033).

[c] Adjusted for age, level of education, area of residence, household income, active smoking, smokeless tobacco, physical activity, duration of diabetes, medication adherence, modality of treatment, BMI, hypertension, and dyslipidaemia (area under the receiver operating characteristic curve: 78.3% and the Hosmer-Lemeshow goodness-of-fit test p-value:0.835).

Bangladesh also reported a similar prevalence of 11.0% [23]. While literature both within and outside of Bangladesh do not completely agree, it is consistent that the least prevalent macrovascular diabetes complication is one of either stroke or diabetic foot [12,20,21,24]. Our study showed that prevalence of diabetic foot was 12.0%. This is slightly higher than 6.4% global prevalence of diabetic foot among people with T2DM [25]. This is also slightly higher than other studies in Bangladesh and other parts of Asia, with prevalence ranging from 7.2% to 11.6% [12,22,26–28].

For microvascular complications, our study showed the prevalence of nephropathy to be highest at 34.2%. While this prevalence is within the global prevalence range of 12%–55% amongst all diabetic patients [1], past studies in Bangladesh reported a slightly lower prevalence of nephropathy [13,29]. Elsewhere in Asia, a study conducted on the Northwest Indian population found a nephropathy prevalence of 30.2% [28], while the prevalence of nephropathy was found to be 15% [27] in Saudi Arabia. Neuropathy was the least prevalent microvascular complication in our study, affecting 5.8% of our study's subjects, falling below the global prevalence range of 16%–66% [1]. Previous studies in Bangladesh reflected higher prevalence of neuropathy [13,30]. A study in Doha also showed

results like our study, where neuropathy was the least prevalent microvascular complication, but with a higher prevalence of 15.3% [31]. The low prevalence of neuropathy reflected in our study was possibly due to the underdiagnoses of neuropathy, thus reflecting the need for improvements in neuropathy screening among people with T2DM in Bangladesh. In our study, diabetic retinopathy had a moderately high prevalence of 25.1%. This is slightly lower than the global prevalence of 35.0% [1], consistent with other studies in Bangladesh which also reported prevalence rates of diabetic retinopathy lower than the global prevalence [13,32]. The prevalence of diabetic retinopathy consistently falling below the global prevalence may be attributed to the finding that Asian countries typically have a lower prevalence of diabetic retinopathy than their Western counterparts, as reported by a review article by Lee et al. [33]. Furthermore, the asymptomatic nature of the complication means that people only seek medical help when their vision becomes significantly impaired, and their daily activities are affected [33]. This may also lead to underdiagnoses of retinopathy.

Among all the participants of this study, 25.9% had a smoking history. It was shown in our results that smokers, past and present, have a higher risk of all three macrovascular complications, with

Table 4
Adjusted association between each of the microvascular complications and potential risk factors.

Variable	Neuropathy[a]			Nephropathy[b]			Retinopathy[c]		
	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Age									
<60 years	Reference			Reference			Reference		
>= 61 years	–	–	–	2.4	1.8–3.3	<0.001	2.5	1.7–3.6	<0.001
Gender									
Male	Reference			Reference			Reference		
Female	–	–	–	–	–	–	1.7	1.2–2.4	0.003
DM Duration									
≤5 years	Reference			Reference			Reference		
6–10 years	–	–	–	–	–	–	–	–	–
≥11 years	–	–	–	2.3	1.7–3.2	<0.001	2.3	1.5–3.3	<0.001
Family history of diabetes									
No	Reference			Reference			Reference		
Yes	–	–	–	0.7	0.5–0.9	0.029	–	–	–
Area of residence									
Rural	Reference			Reference			Reference		
Urban	0.5	0.2–0.9	0.028	3.2	2.1–4.7	<0.001	2.1	1.3–3.2	0.001
Household income									
<20,000 tk	Reference			Reference			Reference		
20,000–60,000 tk	–	–	–	0.6	0.4–0.8	0.003	–	–	–
>60,000 tk	–	–	–	–	–	–	–	–	–
Modality of treatment									
Oral tablet	Reference			Reference			Reference		
Insulin	–	–	–	–	–	–	–	–	–
Oral and insulin	–	–	–	1.7	1.2–2.4	<0.001	1.4	1.0–2.1	0.039
Medication adherence									
Adequate	Reference			Reference			Reference		
Inadequate	–	–	–	–	–	–	1.4	1.0–2.1	0.035
Hypertension									
No	Reference			Reference			Reference		
Yes	–	–	–	2.6	1.9–3.6	<0.001	–	–	–
Physical activity									
Active (>= 150 min/week) (ref)	Reference			Reference			Reference		
Inactive (<150 min/week)	–	–	–	1.7	1.3–2.3	<0.001	1.4	1.0–2.1	0.031
Waist/hip ratio									
Normal	Reference			Reference			Reference		
High	0.2	0.1–0.7	0.015	–	–	–	–	–	–

[a] Adjusted for age, gender, area of residence, waist/hip ratio, and dyslipidaemia (area under the receiver operating characteristic curve: 60.1%, Hosmer-Lemeshow goodness-of-fit test p-value: 0.842).

[b] Adjusted for age, gender, level of education, area of residence, household income, active smoking, smokeless tobacco, physical activity, duration of diabetes, medication adherence, modality of treatment, family history of DM, BMI, and hypertension (area under the receiver operating characteristic curve: 80.9%, Hosmer-Lemeshow goodness-of-fit test p-value: 0.542).

[c] Adjusted for age, gender, level of education, area of residence, household income, active smoking, smokeless tobacco, physical activity, duration of diabetes, medication adherence, modality of treatment, BMI and glycaemic control (area under the receiver operating characteristic curve: 75.0%, Hosmer-Lemeshow goodness-of-fit test p-value: 0.759).

60–70% increased odds of CAD, diabetic foot and stroke. This is consistent with extensive literature worldwide [34—361]. Also, this study does not associate smoking as a significant risk factor for microvascular complications. Current literature differs across studies, but largely agree that smoking aggravates diabetic nephropathy [37,38]. It is however unclear if smoking is an independent risk factor for diabetic neuropathy and retinopathy [38,39]. While our study did not find an association between smoking and microvascular complications, it should nevertheless be discouraged by health practitioners as it is a major risk factor for macrovascular complications, which lead to high mortality rates.

The American Diabetes Association recommends adults with diabetes to engage in more than 150 min of moderate-to-vigorous intensity exercise over a week [40]. An alarming 51.2% majority of our participants did not reach this level of physical activity. The results in this study suggest that participants with inadequate physical activity are positively associated with stroke, nephropathy, and retinopathy, increasing the risk of each complication by 140%, 70%, and 40% respectively. This is supported by a meta-analysis conducted which showed that inactive individuals have 37% higher risk of stroke incidence or mortality compared to active individuals [41]. A Finnish study on diabetes also corroborated our

findings that physical inactivity was more common in patients with nephropathy and retinopathy [42]. However, such findings may be in part due to the patients' diminished ability to exercise with complications present. Thus, patients should be educated regarding the benefit of exercise for prevention of diabetes complications, and they should be motivated to maintain a minimum of 150 min physical exercise per week.

In this study, hypertension was shown to be an independent risk factor for CAD, stroke, and nephropathy, with poor hypertension control increasing the risks of these complications by 3.6-fold, 3.0-fold and 2.6-fold respectively. The study also showed that 64.4% of all the participants were clinically hypertensive, suggesting poor control within the diabetic population in Bangladesh. The relationship between hypertension and atherosclerotic complications like stroke and CAD is thoroughly explored in literature, with elevations in both diastolic and systolic blood pressure beyond normal ranges increasing the risks of CAD and strokes [43,44], a finding that was similarly reflected in our study. Thus, hypertension should be a key target for intervention amongst patients with diabetes in order to reduce the risk of further macro- and micro-vascular complications.

This study further showed that living in urban regions resulted

in a higher risk of stroke, nephropathy, and retinopathy compared to living in rural regions. Living in an urban environment is associated with a 2.3-, 3.2- and 2.1-fold increase in risk of stroke, nephropathy and retinopathy respectively. Studies outside and within Bangladesh have also shown similar results for stroke, retinopathy and nephropathy [13,45,46]. This result of increased prevalence of certain complications in urban areas has been attributed to the fact that urbanisation is associated with a higher calorie food intake and increased stresses, and these are risk factors for diabetes and its complications [47]. This shows that environmental factors have a strong influence on the prevalence of diabetes and its complications. Bangladesh is facing rapid urbanisation in recent times, and hence targeting environmental risk factors for diabetic complications in urban areas would be of relevance in Bangladesh.

In our study, longer duration of diabetes was found to be an important risk factor for CAD, stroke, nephropathy and retinopathy. Having a diabetes duration of more than ten years was associated with a 1.5-, 1.7-, 2.3- and 2.3-fold increase in the risk of CAD, stroke, nephropathy and retinopathy respectively over those with a disease duration of five years and under. This is supported by studies which have also shown that a longer duration of diabetes leads to increased prevalence of certain macrovascular and microvascular complications [48–50]. Patients with a long history of diabetes are more likely to be at advanced stages of the disease. They are subject to a longer duration of the atherosclerotic process, thus driving the increased development of both macro- and microvascular complications. This therefore reflects the importance of screening of complications in patients who have had a longer history of T2DM, by general practitioners.

Our study showed that poor medication adherence leads to a 2.5- and 1.4-fold increase in the risk of stroke and retinopathy respectively. Our results are corroborated by past studies, which show a significantly lower incidence of developing new macrovascular and microvascular complications in patients with good medication adherence [51]. In light of this, when faced with patients with poorly controlled T2DM, clinicians should first consider counselling them on improving medication adherence, before increasing their medication dosage. This would in turn lead to a lower risk of developing diabetes complications.

Advanced age was similarly identified as a risk factor for the development of diabetes complications. Being more than 60 years of age was associated with a 1.6- and 1.8-fold increase in the risk of macrovascular complications such as CAD and stroke, respectively. It was also associated with a 2.4- and 2.5-fold increase in the risk of microvascular complications such as nephropathy and retinopathy, respectively which is reflected in other studies [52]. Clinicians are hence recommended to place more importance on screening for diabetes complications in this group of patients.

However, in our study, a traditionally known risk factor of a high waist-to-hip ratio (WHR) was shown to have no association with micro- and macrovascular complications but was protective for neuropathy. While many studies have shown a link between obesity and neuropathy [53,54], some studies have suggested that WHR is not an independent risk factor of neuropathy. These findings probably suggest that WHR is a risk of neuropathy mainly through an influence on other complication risk factors.

4.1. Strengths and limitations

Having an extensive sample size, this is one of the largest studies conducted in Bangladesh across a wide social demographic range that was surveyed. Data was collected from all primary, secondary and tertiary levels of health care, covering patients residing in rural, semi urban and urban areas. This study also evaluates all the macro- and microvascular complications of diabetes across a wide range of modifiable lifestyle factors as well as non-modifiable risk factors, allowing the independent risk of each individual factor to be established. Our study has a few limitations. Firstly, a few data obtained were self-reported and hence subjective. A cross-sectional study also does not allow the establishment of causality.

5. Conclusion

Our study demonstrated that among macrovascular complications, CAD was the most prevalent while among microvascular complications, nephropathy was the most prevalent. We also found that numerous lifestyle factors such as smoking, level of physical activity, and poor medication adherence can be important risk factors for both microvascular and macrovascular complications. Certain social demographics such as age, rural or urban area of residence were also found to be risk factors associated with diabetes complications. Clinical risk factors for diabetes complications we explored included the duration of diabetes and a history of hypertension. We recommend that screening and investigation be implemented early during the diagnosis of diabetes to identify the above risk factors so that they can be targeted early with an individualised treatment and management strategy to prevent the onset of complications. Further studies are needed to verify the above findings and to explore effective tools to predict patients' risk profile in developing complications upon diagnosis as this will be helpful in the early prevention of these complications.

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Author's contribution

Concept and design (AA, BB), acquisition of data (AA), interpretation of data and drafting the manuscript (WZ, AJWL, DXJL), critically review to improve the content and final approval of version to be submitted (AA, BB). All authors have read and approved the manuscript.

Disclosure

The authors have not declared any conflicts of interest.

Availability of data

The data sets generated during and/or analysed during the current study are available from the corresponding author upon reasonable request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.07.046.

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