Associations of Demographic, Clinical and Laboratory Profiles of Patients with type II Diabetes Mellitus with its Microvascular Complications in Bangladesh

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ABSTRACT

Objective: The aim of this study was to investigate the associations of makers from demographic, clinical, and laboratory profiles with microvascular complications in a cohort of type II diabetic population in Bangladesh.

Methods: In this cross-sectional study 103 participants [47 Men and 56 Women; Age 40~70 years] having type II diabetes for more than 10 years were randomly recruited during their routine visits to a major Diabetic Hospital in Dhaka, Bangladesh. The associations of prevalence of microvascular complications [Cardiac Autonomic Neuropathy(CAN), Diabetic Peripheral Neuropathy(DPN), Diabetic Nephropathy(Nep), Diabetic Retinopathy(Ret)] with demographic, clinical, and laboratory profiles were assessed by multivariate logistic regression ($p<0.05$ and Odds ratio (OR)> 1.0).

Results: The prevalence rates of CAN, DPN, Ret and Nep were 68%, 43.69%, 6.8%, and 4.8% respectively. The overall prevalence of diabetic-associated microvascular complication is 94.36% in this cohort of diabetic patients. BMI ($p=0.0330$, OR=1.90) and HbA1c ($p=0.0535$, OR=3.08) were found to be the most significant risk factors in the development of all microvascular complications. However, HbA1c for CAN; HbA1c, Microalbuminuria and Urinary creatinine for DPN; years of Diabetes, Systolic blood pressure and albumin creatinine ratio for Nep, HbA1c and Microalbuminuria for Ret were found to be most significantly associated in this Diabetes patients' cohort.

Conclusion: The proportion of microvascular complications was found to be significantly high among patients with Type II diabetes mellitus in this cohort. Controlling HbA1c could help reduce all four types of complications. However, controlling microalbuminuria could prevent DPN and Ret. This emphasizes the need for screening and prevention program toward early, symptomless identification of type II diabetes microvascular complications.

Keywords: microvascular complications; cardiac autonomic neuropathy; diabetic peripheral neuropathy; diabetic nephropathy; diabetic retinopathy; demographic, clinical, and laboratory profiles.

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1. Background

Diabetes is called 'silent killer' that killed 1.6 million people in 2016 making it the 5th leading cause of deaths worldwide[1]. Global impact of type 2 diabetes prevalence in low and middle-income countries was estimated to be 415 million in 2015 and predicted to rise to 642 million in 2040[2]. Type 2 diabetes mellitus has been rapidly rising worldwide over the past three decades, particularly in developing countries including Bangladesh[3]. Type 2 diabetes prevalence in Bangladesh will be more than 50% by the next 15 years, placing Bangladesh as the 8th highest diabetic populous country in the world[4]. A study suggests that diabetic prevalence will be more than double between 2020 to 2030[5]. IDF Diabetes Atlas has estimated that if nothing is done, the number of diabetes may rise to 629 million in 2045[6] which should be double of 151 million[7] from 2000 to 2025[8].

The prevalence of diabetes was higher in rural areas[9] but it is high for males in urban areas whereas lower in rural areas compared to females in Bangladesh[10, 11]. Neuropathies are a common persistent complication of both types of diabetes mellitus which conferred morbidity and mortality to diabetic patients. CAN is associated with an increased risk of mortality[12, 13]. A study including 1171 patients with type 1 and type 2 diabetes mellitus using predefined HRV and spectral analysis of R-R intervals reported abnormal findings for 34.3% of type 2 patients[14]. Neuropathy is the most common microvascular complications of both type 1 and type 2 diabetes mellitus[15–17]. A study found that 19.7% of total registered type 2 patients have DPN conducted in the outpatient section of BIRDEM Hospital, Dhaka, Bangladesh. The prevalence of DPN among type 2 diabetic patients are much higher in Europe. A study concludes that 32.1% of diabetic patients in the United Kingdom, 17.6% in Turkey and 35.4% in Spain have DPN[18]. The prevalence of DPN increases with the age of the patient and also with the diabetic duration[19, 20]. A multi-country study conducted in Asia shows that 58.6% prevalence of micro or macroalbuminuria indicating an impending pandemic of diabetic renal and cardiovascular diseases in Asia[21]. A cross-sectional study with 836 rural Bangladeshi patients shows a high prevalence of retinopathy in Bangladesh[22]. Results from 35 studies from 1980 to 2008 with 22,896 subjects with diabetes showed that the global prevalence for any Ret was 34.6% (95% CI 34.5 – 34.8)[23].

Analyses of the exponential trend revealed an increase in diabetes prevalence among the urban and rural population at a rate of 0.05% and 0.06% per year, respectively[24]. Increasing age, hypertension, and higher BMI were found to be significant risk factors in the urban and rural community of Bangladesh[25]. But the patients with diabetic type II in Bangladesh have limited knowledge of its risk factors, cause and also management[26, 27]. Depressive diabetic symptoms were found in 29% of male and 30.5% of female participants with diabetes and 6.0% of male and 14.6% of female subjects without diabetes[28].

The current study had two main objectives: (1) to determine the prevalence of type 2 diabetes complications in a cohort with type II diabetes recruited from a major hospital in Dhaka, Bangladesh; and (2) to investigate the risk factors from demographic, laboratory and clinical variables of diabetes related microvascular complications and comorbidities.

2. Research Design and Methods

2.1 study type

Cross-sectional study of Bangladeshi patients from Dhaka with type II diabetes. We followed the STROBE cross-sectional reporting guidelines[29].

2.2 inclusion and exclusion criteria

Inclusion criteria include: Bangladeshi national, diagnosis of type II diabetes mellitus, above 40 years of age, able to give consent and also the diabetes duration not be less than10 years. Exclusion criteria include: Stroke history, having any heart disease, not able to give consent, diabetes duration less than 10 years and the presence of any other pathophysiology that may lead to one or more similar complications such as cancer.

2.3 participants and complications

One hundred and three (47 males and 56 females), unrelated patients of age more than 40 years and having diabetes for more than 10 years with type 2 diabetes were randomly selected and enrolled in the study during routine visits to the BIHS[30] Hospital between 18th December 2017 to 26th April 1018. This hospital is one of the most visited

hospitals for diabetic patients in Bangladesh. Among 103 subjects, 70 were able to complete a diagnostic test for all 4 complications (CAN, DPN, Nephropathy, and Retinopathy).

In this study, the selected patients have been diagnosed with complications such as CAN, DPN, Nep, and Ret. The presence of these complications was confirmed by a qualified physician, based on the criteria outlined by the report of the WHO consultation group[31].
Diagnosis of cardiac autonomic neuropathy was obtained from Ewing test, that included five tests: deep breathing, lying to standing, Valsalva maneuver, lying to standing BP, and sustained handgrip BP[32].

Diagnosis of diabetic peripheral neuropathy was obtained from a nerve conduction velocity (NCV) test[33–35]. There were several tests for recognizing polyneuropathy, CTS (carpal tunnel syndrome), peroneal neuropathy and other types of neuropathies.
Diagnosis of nephropathy was set by the ACR (albumin creatinine ratio) level >30 mg/mmol for microalbuminuria, and >300 mg/mmol for macroalbuminuria[36]. Diagnosis of retinopathy was obtained from the fundus image test and classified according to WHO criteria[37]. Fundus imaging is a process where 3-D retinal semi-transparent tissues projected onto the imaging plane is obtained using reflected light and represented in 2-D[38].

2.4 types of variable

2.4.1 Demographic and clinical variable

Demographic data were collected at the time of enrollment from the patients. We measured the waist circumference, height, and weight at the time of enrollment and listed the value for the diabetic duration, age, gender, smoking history, and smokeless tobacco history. All of these data were verified from the necessary and relevant documents. Clinical data were measured at the time of enrollment. The blood pressure was measured on the first day before starting their Ewing test. If the systolic blood pressure is >130mm Hg and diastolic blood pressure is >80 mm Hg or taking antihypertensive medications, it called as hypertension. Dyslipidemia was diagnosis from the medications of the patient or by checking the history of dyslipidemia of that patient.

Table 1 Demographic and Clinical profile of patients

Demographic variables						
Variables and their subdivisions	Male		Female		All	
	Mean ± SD	N (%of M)	Mean ± SD	N (% of F)	Mean ± SD	N(% of total)
Patients		47(45.63)		56(54.37)		103(100)
Age (years)	57.70±9.78	47(100)	54.60±7.93	56(100)	56.01±8.91	103(100)
≥40-49	44.8±3.22	*10(21.28)*	45.6±2.95	*15(26.79)*	45.28±3.02	*25(24.27)*
≥50-59	53.2±2.7	*15(31.91)*	52.86±3.17	*22(39.29)*	53±2.95	*37(35.92)*
≥60	66.63±4.78	*22(46.81)*	63.73±3.79	*19(33.93)*	65.29±4.54	*41(39.80)*
CAN	58.74±9.63	31(65.95)	53.32±7.40	37(66.07)	55.79±8.85	68(66.01)
DPN	58.95±10.33	21(44.68)	52.58±6.33	24(42.85)	55.55±8.93	45(43.68)
Nep	58.5±10.37	12(25.53)	54.37±8.75	16(28.57)	56.14±9.52	28(27.18)
Ret	56.8±11.64	5(10.63)	47.5±0.707	2(3.571)	54.14±10.54	7(6.796)
BMI (kg/m2)	25.53±3.47	47(100)	27.93±5.08	56(100)	26.84±4.56	103(100)
Underweight: <18.5	0	0(0)	0	0(0)	0	0(0)
Normal: ≥ 18.5-24.99	23.54±1.45	**27(57.45)**	22.93±1.69	17(30.36)	23.31±1.56	44(42.72)
Overweight: ≥ 25.0-29.99	26.54±1.03	15(31.91)	27.58±1.32	**24(42.86)**	27.18±1.31	39(37.86)
Obese: ≥ 30	33.23±4.09	5(10.638)	34.18±4.77	15(26.79)	33.94±4.52	20(19.42)

CAN	26.26±3.71	31(65.95)	27.94±5.82	37(66.07)	27.17±5.01	68(66.01)
DPN	25.52±3.56	21(44.68)	28.75±5.01	24(42.85)	27.24±4.64	45(43.68)
Nep	26.17±4.22	12(25.53)	29.18±5.60	16(28.57)	27.89±5.19	28(27.18)
Ret	26.79±5.53	5(10.63)	26.29±2.09	2(3.571)	26.65±4.60	7(6.796)
History of hypertension		27(57.45)		**35(62.5)**		**62(60.19)**
History of dyslipidemia		14(29.79)		**21(37.5)**		**35(33.98)**
Smoking history		9(19.15)		0(0)		**9(8.74)**
Smokeless tobacco history		10(21.28)		17(30.357)		**27(26.21)**
Clinical variables						
Name of the Variables and their subdivisions	Male		Female		All	
	Mean ± SD	N (%of M)	Mean ± SD	N (% of F)	Mean ± SD	N(% of total)
Diabetes duration (years)	16.17±6.07	47(100)	15.55±5.76	56(100)	15.83±5.88	103(100)
≥10-19	13.54±2.76	37(78.72)	12.60±2.64	41(73.21)	13.05±2.73	78(75.73)
≥20-29	24±3.116	8(17.02)	22.30±1.93	13(23.21)	22.95±2.52	21(20.39)
≥30	33.5±2.12	2(4.26)	32±2.828	2(3.57)	32.75±2.22	4(3.88)
CAN	16.54±6.20	31(65.95)	16.13±6.01	37(66.07)	16.32±6.05	68(66.01)
DPN	17.33±7.43	21(44.68)	**14.16±4.80**	24(42.85)	15.64±6.30	45(43.68)
Nep	18.91±8.11	12(25.53)	16.81±6.63	16(28.57)	17.71±7.24	28(27.18)
Ret	13±2.828	5(10.63)	17.5±3.535	2(3.571)	14.28±3.49	7(6.796)
Waist Circumference (cm)	90.84±8.61	47(100)	97.38±9.46	56(100)	94.39±9.61	103(100)
Men ≥90	97.40±6.7	23(48.94)				
Women ≥80			97.72±9.19	**55(98.21)**		
CAN	92.09±8.47	31(65.95)	96.58±9.30	37(66.07)	94.54±9.15	68(66.01)
DPN	92.64±8.13	21(44.68)	**98.63±9.07**	24(42.85)	95.84±9.06	45(43.68)
Nep	91.22±6.71	12(25.53)	97.31±9.80	16(28.57)	94.70±9.00	28(27.18)
Ret	89.91±5.26	5(10.63)	93.98±14.36	2(3.571)	91.07±7.53	7(6.796)
Systolic blood pressure(mmHg)	141.2±19.5	47(100)	136.0±20.14	56(100)	138.4±19.94	103(100)
≤119	108±5.29	4(8.51)	108.3±8.96	12(21.43)	108.2±8.03	16(15.53)
≥120-139	129.2±6.67	19(40.43)	130.1±4.98	19(33.93)	129.7±5.82	38(36.89)
≥140-159	148.2±7.52	15(31.91)	148.3±5.71	19(33.93)	148.2±6.47	34(33.01)
≥160	169.6±9.72	9(19.15)	171.3±6.40	6(10.714)	170.3±8.33	15(14.56)
CAN	145.0±20.16	31(65.95)	134.0±21.30	37(66.07)	139.0±21.35	68(66.01)
DPN	148.5±20.82	21(44.68)	134.8±15.96	24(42.85)	141.2±19.43	45(43.68)
Nep	153.0±15.16	12(25.53)	136.1±17.22	16(28.57)	143.4±18.19	28(27.18)
Ret	158.6±16.14	5(10.63)	137.5±17.67	2(3.571)	152.5±18.21	7(6.796)

Diastolic blood pressure(mmHg)	78.97±9.86	47(100)	76.42±11.96	56(100)	77.59±11.07	103(100)
≤79	71.36±7.45	22(46.81)	67.96±6.98	32(57.14)	69.35±7.30	54(52.43)
≥80-89	82.73±2.83	19(40.43)	83.81±3.08	16(28.57)	83.22±2.95	35(33.98)
≥90-99	94±3.39	5(10.64)	94.14±2.61	7(12.5)	94.08±2.81	12(11.65)
≥100	100±0	1(2.13)	105±0	1(1.79)	102.5±3.54	2(1.94)
CAN	78.45±11.40	31(65.95)	75.48±12.76	37(66.07)	76.83±12.16	68(66.01)
DPN	78.19±12.23	21(44.68)	76.87±10.63	24(42.85)	77.48±11.29	45(43.68)
Nep	74.91±13.48	12(25.53)	75.93±10.81	16(28.57)	75.5±11.79	28(27.18)
Ret	84.6±10.13	5(10.63)	72.5±3.54	2(3.571)	81.14±10.27	7(6.796)

2.4.2 Laboratory data

The laboratory data were taken from the laboratory of the hospital after the enrollment and some were taken after the completion of 24-hour Holter recording. Laboratory test parameters are hemoglobin A1c (HbA1c), microalbuminuria, urinary creatinine, and albumin creatinine ratio. The data and its basic analysis are shown in Table 2.

2.5 statistical analysis

Demographic variable (such as gender, height, age, weight, smoking history, tobacco history, and diabetes duration), clinical measurement (waist circumference, BMI, systolic blood pressure, and diastolic blood pressure), measured laboratory values (such as HbA1c, microalbuminuria, urinary creatinine, albumin creatinine ratio) were all summarized as mean ±SD for men, women and also both combined. For determining the interrelation between complications and data from demographic, clinical and laboratory tests, a stepwise logistic regression analyses were performed for development of complications (complications vs no complications, CAN vs no CAN, DPN vs no DPN, Nep vs no Nep, and Ret vs no Ret) using MATLAB (MATLAB2018a). Further by using the same software, the best model selected for input to a multivariate logistic regression model from each stepwise analysis to exclude the effects of contradicting factors. The findings were presented as estimates, standard errors, odds ratio (OR), 95% confidence interval (95% CI) and probability (p-value). Odds Ratio and Confidence Interval were calculated in MATLAB using the beta estimates and standard errors. The significance (p-value) level was set at less than 0.05.

Table 2 Laboratory variable of patients

Types and their variables	Male		Female		All	
	Mean ± SD	N (%of M)	Mean ± SD	N (% of F)	Mean ± SD	N(% of total)
HbA1c(%,mmol/mol)						
Not specified	9.066±1.944	47(45.63)	8.621±1.453	56(54.37)	8.824±1.701	103(100.0)
Optimal: <7		2(4.26)		8(14.29)		10(9.71)
Fair: 7-8		12(25.53)		11(19.64)		23(22.33)
High: >8		33(70.21)		37(66.07)		70(67.96)
CAN	9.213±1.790	31(45.59)	8.716±1.491	37(54.41)	8.943±1.640	68(66.02)
Optimal: <7		1(3.23)		4(10.81)		5(7.35)
Fair: 7-8		6(19.35)		8(21.62)		14(20.59)
High: >8		24(77.42)		25(67.57)		49(72.06)
DPN	9.291±1.988	21(46.67)	8.930±1.667	24(53.33)	9.098±1.810	45(43.69)
Optimal: <7		2(9.52)		3(12.50)		5(11.11)
Fair: 7-8		3(14.29)		4(16.67)		7(15.56)
High: >8		16(76.19)		17(70.83)		33(73.33)
Nephropathy	9.9750±2.221	12(42.86)	8.763±1.902	16(57.14)	9.282±2.094	28(27.18)

Optimal: <7		1(8.33)		3(18.75)		4(14.29)
Fair: 7-8		1(8.33)		4(25.00)		5(17.86)
High: >8		10(83.33)		9(56.25)		19(67.86)
Retinopathy	10.720±3.334	5(71.43)	11.100±1.980	2(28.57)	10.829±2.846	7(6.80)
Optimal: <7		0(0.00)		0(0.00)		0(0.00)
Fair: 7-8		2(40.00)		0(0.00)		2(28.57)
High: >8		3(60.00)		2(100.00)		5(71.43)
Microalbuminuria (mg)						
Not specified	60.6164±99.490	47(46.08)	49.571±82.123	55(53.92)	54.661±90.247	102(99.03)
Optimal: <30		34(72.34)		38(69.09)		72(70.59)
Microalbuminuria: 30-300		10(21.28)		15(27.27)		25(24.51)
Macro albuminuria: >300		3(6.38)		2(3.64)		5(4.90)
CAN	88.439±113.172	31(45.59)	56.981±93.199	37(54.41)	71.322±103.204	68(66.02)
Optimal: <30		18(58.06)		25(67.57)		43(63.24)
Microalbuminuria: 30-300		10(32.26)		10(27.03)		20(29.41)
Macro albuminuria: >300		3(9.68)		2(5.41)		5(7.35)
DPN	121.925±124.49	21(47.73)	55.2565±87.479	23(52.27)	87.075±110.720	44(42.72)
Optimal: <30		10(47.62)		15(65.22)		25(56.82)
Microalbuminuria: 30-300		8(38.10)		7(30.43)		15(34.09)
Macro albuminuria: >300		3(14.29)		1(4.35)		4(9.09)
Nephropathy	210.308±91.414	12(42.86)	144.519±98.407	16(57.14)	172.7143±99.417	28(27.18)
Optimal: <30		0(0.00)		1(6.25)		1(3.57)
Microalbuminuria: 30-300		9(75.00)		13(81.25)		22(78.57)
Macro albuminuria: >300		3(25.00)		2(12.50)		5(17.86)
Retinopathy	158.62±140.295	5(71.43)	136.15±178.691	2(28.57)	152.20±136.247	7(6.80)
Optimal: <30		2(40.00)		1(50.00)		3(42.86)
Microalbuminuria: 30-300		2(40.00)		1(50.00)		3(42.86)
Macro albuminuria: >300		1(20.00)		0(00.00)		1(14.28)
Urinary Creatinine (mg/dl)						
Not specified	194.46±139.83		130.87±117.85		160.17±131.70	102(99.03)
Target 20-320 mg/dl		41(87.23)		50(90.91)		91(89.22)
Non-Target >320mg/dl		6(12.77)		4(7.27)		10(9.80)
CAN	236.15±150.39	31(45.59)	123.28±107.24	37(54.41)	174.74±139.68	68(66.02)
Target 20-320 mg/dl		25(80.65)		34(91.89)		59(86.76)
Non-Target >320mg/dl		6(19.35)		2(5.41)		8(11.76)
DPN	236.84±160.20	21(47.73)	157.52±149.63	23(52.27)	195.34±158.11	44(42.72)
Target 20-320 mg/dl		17(80.95)		20(86.96)		37(84.09)
Non-Target >320mg/dl		4(19.05)		3(13.04)		7(15.91)
Nephropathy	256.43±205.44	12(42.86)	152.65±77.99	16(57.14)	197.13±152.68	28(27.18)
Target 20-320 mg/dl		9(75.00)		16(100.0)		25(89.29)
Non-Target >320mg/dl		3(25.00)		0(0.00)		3(10.71)
Retinopathy	211.36±55.58	5(71.43)	159.95±135.98	2(28.57)	196.67±75.96	7(6.80)
Target 20-320 mg/dl		5(100.0)		2(100.0)		7(100.0)
Non-Target >320mg/dl		0(0.00)		0(0.00)		0(0.00)

Albumin Creatinine Ratio (mg/mmol)						
Not Specified	32.09±52.45	47(46.08)	39.28±74.58	55(53.92)	35.97±65.11	102(99.03)
Optimal: <3		12(25.53)		10(18.18)		22(21.57)
Borderline high: 3-30		23(48.94)		29(52.73)		52(50.98)
High: >30		12(25.53)		16(29.09)		28(27.45)
CAN	44.35±60.99	31(45.59)	45.36±86.19	37(54.41)	44.90±75.22	68(66.02)
Optimal: <3		7(22.58)		6(16.22)		13(19.12)
Borderline high: 3-30		12(38.71)		20(54.05)		32(47.06)
High: >30		12(38.71)		11(29.73)		23(33.82)
DPN	60.73±68.22	21(47.73)	35.97±51.28	23(52.27)	47.79±60.55	44(42.72)
Optimal: <3		6(28.57)		5(21.74)		11(25.00)
Borderline high: 3-30		4(19.05)		11(47.83)		15(34.09)
High: >30		11(52.38)		7(30.43)		18(40.91)
Nephropathy	105.960±57.952	12(42.86)	111.404±109.675	16(57.14)	109.071±89.771	28(27.18)
Optimal: <3		0(0.00)		0(0.00)		0(0.00)
Borderline high: 3-30		0(0.00)		0(0.00)		0(0.00)
High: >30		12(100.0)		16(100.0)		28(100.0)
Retinopathy	86.567±87.999	5(71.43)	58.923±61.616	2(28.57)	78.671±77.312	7(6.80)
Optimal: <3		0(0.00)		0(0.00)		0(0.00)
Borderline high: 3-30		2(40.00)		1(50.00)		3(42.86)
High: >30		3(60.00)		1(50.00)		4(57.14)

3. Results

3.1 demographic, clinical, and laboratory profiles

Demographic, and clinical data, major comorbidities with type II diabetes are shown in table 1 and laboratory profiles are shown in table 2. There were 47 (45.63%) male patients and 56 (54.37%) female patients. The mean age of the patients was 56 years (±8.913), the mean age of the male and female patients was 57.1 years (±9.78) and 54.6 years (±7.93), respectively. It is consistent with the finding that the diabetic population in Bangladesh, as well as south Asia, are comparatively younger than west[39, 40]. The sub-variables under 'Age' shows that 46.8% of the male subjects are greater than 60 years old but about 40% female subjects aged between 40 to 50 though overall patient shows the increasing prevalence for a higher age. A study in Spain also shows that an increase in patient age increases the prevalence of diabetic complications[18]. 27(57.45%) males, 35(62.50%) females, and total 62(60.19%) patients had a history of hypertension (mean systolic blood pressure was 138.4 mm Hg). A total of 35(33.98%) patients had dyslipidemia where 14(29.79%) were male and 21(37.5%) were female. A very low number of patients 9(8.74%) had a smoking history where everyone was male. Also, overweight condition (42.86%) is common for female diabetic patients. Having waist circumference higher than 80cm for more than 98% female subjects. 57.45% of male subject has normal weight. Though obesity is relatively common for female patients (27%), a total of 20(19.42%) patients had obese (BMI (mean body mass) index = 33.94 kg/m^2, mean waist circumference = 90.84 cm for male and 97.38 cm for female. For the retinopathy patients, waist circumference was 89.91 cm for male and 93.98 cm for female) where 15 (26.79%) were female and 5(10.638%) were male.

More than 67% of patients for any types of complication had a high HbA1c (mean HbA1c = 8.824, for male mean HbA1c = 9.066, and female mean HbA1c = 8.621 for the patients with CAN). The retinopathy patients had very high HbA1c (mean HbA1c = 10.829, for male mean HbA1c = 10.720, and for female mean HbA1c = 11.100). Microalbuminuria was found in 25(24.51%) of patients where 10 were male and 15 were female. In the case of nephropathy total of 22(78.57%) patients had microalbuminuria. All the retinopathy patients had a creatinine level of 20 to 320 mg/dl. Mean ACR (albumin creatinine ratio) for the patients is 35.967 mg/mmol where 47(46.08%) male had the mean ACR of 32.092 mg/mmol and 55(53.92%) female had the mean ACR of 39.280 mg/mmol.

Neuropathy is the most common complication in Bangladeshi diabetic type 2 patients of more than 40 years' old who have diabetes duration of more than 10 years. Besides, there are a very few retinopathy patients so it implies that the rate of retinopathy in Bangladeshi diabetes type 2 patients is very low.

3.2 complications of type 2 diabetes

Overall, more than one clinically diagnosed complications were present in 99 subjects out of 103 diabetes cohort included in this study. Most of the subjects had CAN (66.02%) followed by diabetic peripheral neuropathy (43.69%), nephropathy (27.18%) and retinopathy (6.8%). Those patients who had retinopathy also had CAN and DPN. The rate of retinopathy complication is very low. Only 7 retinopathy patients were found. 5 patients out of them had all type of complication and the rest two had CAN and DPN. So, we can conclude that Ret is the final stage of type 2 diabetes mellitus complication in Bangladesh. We did not find any subject with only Nep or only Ret. If a patient had Ret, we can say that he/she had CAN and DPN both or CAN, DPN and Nep all. The average diabetic duration of male patients with CAN and DPN are high (17.33 years for CAN and 18.91 years for DPN) but lower for retinopathy (13 years). Female patients with retinopathy had a high diabetic duration of 17.5 years. They did not check DM until they became very ill. So their reported DM duration is from the day "they" found out first not the form the actual moment of DM development. The overall result indicates a high prevalence of complications in Bangladeshi type II diabetes patients.

3.3 risk factors for complications

To assess the association between any complication (as an outcome) and all demographic, clinical and laboratory variables of the patients, a simple logistic regression test was performed in MATLAB. Here complication is a response variable whether demographic, clinical and laboratory variables of the patients are predictor variable. We found several predictor variables were significantly associated with different complications by this approach.

Therefore, for determining the best model for each complication analysis we performed stepwise multiple logistic regression analyses (see Research Design and Methods).

The most significant predictor risk factors were BMI (p=0.0330, OR=1.90) and HbA1c (p=0.0535, OR=3.08) for the development of microvascular complications as shown in table 3. This was shown in a different study before[41].

Table 3 Association between clinical and laboratory variables with type II diabetes complications

Variable Names	Estimates	SE	OR(95% CI)	p
Complications VS No Complications				
Age	-0.0545	0.0573	0.95 (0.68 to 1.14)	0.3418
BMI	0.6438	0.3021	1.90 (1.13 to 17.22)	0.0330*
Diabetes Duration	0.1152	0.1314	1.12 (0.72 to 2.36)	0.3806
Diastolic BP	-0.0105	0.0460	0.99 (0.79 to 1.20)	0.8183
Systolic BP	0.0305	0.0288	1.03 (0.94 to 1.22)	0.2891
Waist Circumference	-0.0227	0.0218	0.98 (0.86 to 1.05)	0.2954
HbA1c	1.1265	0.5836	3.08 (0.96 to 186.37)	0.0535*
Microalbuminuria	0.0674	0.0891	1.07 (0.78 to 1.75)	0.4493
ACR	0.0305	0.0341	1.03 (0.91 to 1.25)	0.3708
Urinary creatinine	0.0142	0.0105	1.01 (0.98 to 1.08)	0.1778
CAN VS no CAN				
Age	0.0133	0.0421	1.01 (0.85 to 1.24)	0.7525
BMI	0.1819	0.1324	1.19 (0.83 to 2.76)	0.1693

Diabetes Duration	0.1855	0.1096	1.20 (0.93 to 2.51)	0.0905
Diastolic BP	-0.0107	0.0319	0.98 (0.84 to 1.12)	0.7383
Systolic BP	0.0141	0.0187	1.01 (0.94 to 1.12)	0.4484
Waist Circumference	0.0011	0.0155	1.00 (0.93 to 1.07)	0.9405
HbA1c	0.7476	0.3544	2.11 (1.12 to 27.69)	0.0349*
Microalbuminuria	0.0072	0.0061	1.01 (0.99 to 1.05)	0.2378
ACR	0.0036	0.0066	1.00 (0.98 to 1.04)	0.5852
Urinary creatinine	0.0016	0.0029	1.00 (0.99 to 1.02)	0.5778
DPN VS no DPN				
Age	-0.0085	0.0276	0.99 (0.86 to 1.11)	0.7586
BMI	0.0462	0.0546	1.04 (0.87 to 1.42)	0.3972
Diabetes Duration	-0.0502	0.0415	0.95 (0.73 to 1.07)	0.2265
Diastolic BP	0.0098	0.0215	1.01 (0.93 to 1.12)	0.6498
Systolic BP	0.0206	0.0127	1.02 (0.99 to 1.11)	0.1055
Waist Circumference	-0.0086	0.0104	0.99 (0.93 to 1.03)	0.4076
HbA1c	0.5441	0.2042	1.72 (1.39 to 8.79)	0.0077*
Microalbuminuria	0.0086	0.0034	1.01 (1.00 to 1.04)	0.0118*
ACR	0.0039	0.0039	1.00 (0.99 to 1.03)	0.3097
Urinary creatinine	0.0043	0.0021	1.00 (1.00 to 1.02)	0.0462*
Nep VS no Nep				
Age	-0.0113	0.0293	0.99 (0.85 to 1.11)	0.6977
BMI	0.0342	0.0524	1.03 (0.85 to 1.37)	0.5137
Diabetes Duration	0.0852	0.0436	1.09 (0.99 to 1.48)	0.0505*
Diastolic BP	-0.0223	0.0231	0.98 (0.85 to 1.05)	0.3342
Systolic BP	0.0265	0.0135	1.03 (1.00 to 1.13)	0.0490*
Waist Circumference	-0.0058	0.0110	0.99 (0.94 to 1.04)	0.5985
HbA1c	0.3320	0.1706	1.39 (0.99 to 4.63)	0.0516
Microalbuminuria	0.0535	0.0140	1.05 (1.06 to 1.20)	0.0001*
ACR	21.4514	0.0164	2.07e9 (2.62e21 to 3.04e21)	0**
Urinary creatinine	0.0015	0.0017	1.00 (0.99 to 1.01)	0.3467
Ret VS no Ret				
Age	-0.0610	0.0569	0.94 (0.67 to 1.12)	0.2838
BMI	-0.1375	0.1446	0.87 (0.38 to 1.39)	0.3417
Diabetes Duration	-0.0564	0.0878	0.94 (0.59 to 1.30)	0.5203
Diastolic BP	0.0247	0.0382	1.02 (0.89 to 1.25)	0.5172

Systolic BP	0.0318	0.0218	1.03 (0.97 to 1.18)	0.1450
Waist Circumference	-0.0172	0.0202	0.98 (0.88 to 1.05)	0.3943
HbA1c	0.6592	0.2675	1.93 (1.36 to 15.26)	0.0137*
Microalbuminuria	0.0087	0.0035	1.01 (1.00 to 1.04)	0.0143*
ACR	0.0055	0.0039	1.00 (0.99 to 1.03)	0.1603
Urinary creatinine	0.0012	0.0025	1.00 (0.99 to 1.01)	0.6252

3.3.1 CAN

We found only HbA1c (p=0.0349, OR=2.11) as a significant risk factor predictor for CAN that is also significant for type 1[42] diabetes. Diabetic duration (p=0.0905, OR=1.20) has also the tendency to influence the cardiac autonomic neuropathy (CAN), the most common complication in Bangladeshi patients having type 2 diabetes.

3.3.2 DPN

Similarly, microalbuminuria (p=0.0118, OR=1.01), urinary creatinine (p=0.0462, OR=1.00) were found to be significant risk factor where HbA1c (p=0.0077, OR=1.72) was found to be the most significant predicting risk factor for DPN complication of type 2 diabetes in Bangladesh. It is consistent with other finding that age and diabetic duration is insignificant [15, 43–48] here since all the patients are more than 40 years of age and the diabetic duration is minimum of 10 years.

3.3.3 Nep

ACR (p=0, OR=2.07e9) was found to be the most significant risk factor predictor whether microalbuminuria (p=0.0001, OR=1.05) was also a significant risk factor predictor and systolic blood pressure was also found to be a significant predictor risk factor for diabetic nephropathy (Nep). Systolic BP is also significant (p=0.049, OR=1.03). Hemoglobin A1c (p=0.0516, OR=1.39) and diabetic duration (p=0.0505, OR=1.09) both can be considered as significant variable to predict nephropathy. A previous study shows that systolic blood pressure (OR 1.04, 95% CI 0.78-1.53), serum creatinine (OR 1.04, 95% CI 0.96-1.87) and, HbA1c (OR 1.12, 95% CI 0.89-2.01) are the predictive variables of diabetic nephropathy patient in a hospital in Bangladesh[26].

3.3.4 Ret

In the case of diabetic retinopathy (Ret), HbA1c (p=0.0137, OR=1.93) and microalbuminuria (p=0.0143, OR=1.01) were found to be a significant risk factor predictor. A previous study in Bangladesh shows a 5.4% prevalence of retinopathy patients[22] and we have 6.8% of retinopathy patients with type 2 diabetes.

4. Discussion

4.1 Prevalence of Microvascular Complications in Bangladesh

Our data reveal a high regularity of complications associated with type II diabetes patients in Bangladesh. The annual cost of type II diabetes microvascular complication treatment is approximately US$314[49] as the report of WHO, where the annual household income per capita is approximately $601 on December 2016[50]. Now, the prevalence of diabetes has more than doubled in Bangladesh. More than 94% of the investigated cohort had diabetic complications, where over 60% of the patients had two or more complications with CAN, and 5.633% of patients had all the complications. The most common clinically detected single complication was CAN (66.02%) in our studies. Furthermore, CAN was found in all age groups. DPN is also a common complication of type 2 diabetes in Bangladesh. About 43.69% of patients had DPN in this study. A previous study in Bangladesh had found 19.7% of DPN patients in BIRDEM hospital[18]. Nephropathy was also common for patients who had microalbuminuria and high ACR. About 33.80% of patients had diabetic nephropathy. CAN is common with diabetic type 2 nephropathy patients[51] and an association between CAN and nephropathy will increase the risk of mortality[52]. The prevalence of diabetic retinopathy in Bangladesh is very low as compared to other population such UAE population having retinopathy of 13.36% of its Diabetic cohort[53].

4.2 Major risk factors

Age, diabetic duration, and BMI were the most functional predictors for the development of microvascular complications, while HbA1c and ACR were found to be potential predictors for the evolution of type II diabetes complications, especially when the duration of type II diabetes is considered. A study shows that age, BMI, and systolic BP are found to be the significant risk factors for Bangladeshi rural patients with type II diabetes[54] which was also found significant for CAN of type 1 diabetes[55]. HbA1c was found to be a single potential predictor for CAN. Other studies also found HbA1c as significant with other predictors[53, 56]. HbA1c levels are significantly higher for diabetics, shown in another paper[57]. Other studies show that HbA1c and diabetic duration are the significant risk factors for DPN with type II diabetic subject[44, 47]. Other results also reveal that HbA1c is a significant risk factor along with microalbuminuria and creatinine levels for type II diabetic patients with DPN.

Hypertension is the most common risk factor present in the patients. Type II diabetes patients with hypertension have a higher probability of having microvascular complications. 130/80 mm Hg for recommended target level, and greater than 120 mm Hg for abnormal pressure level was set for systolic blood pressure for patients with diabetes mellitus[31, 47]. In this study, the mean systolic blood pressure is 138 mmHg. The average systolic blood pressure for the male is 141 mmHg and for the female is 136 mmHg. From a previous report, Asians should achieve this target level (130/80 mm Hg) for owing the stronger association of hypertension, kidney disease, and stroke[58]. Current study reported that the higher levels of systolic and diastolic blood pressure may be supplementary variables, to the elevated levels of HbA1c, ACR and urinary creatinine, toward explaining the high percentage of complications observed in this cohort, since hypertension has been shown to be associated with CAN, DPN, Ret, Nep as well as peripheral vascular disease. The link between good glycemic control and the low occurrence of microvascular complications in patients with type II diabetes is well established[59, 60]. Our study shows the prevalence of obesity among type II diabetes patients, support another study[61]. A study reveals that “The high rate of vitamin D deficiency is another factor associated with both obesity and type II diabetes”, and many females from Bangladesh have a deficiency of vitamin D especially those who had diabetes[62, 63]. Patients should be aware to control obesity and glycemic levels.
However, obesity is also common in type II diabetic patients in Bangladesh. About 20(19.42%) patients had obesity where 15 were male and 5 were female. High LDL-cholesterol, low HDL-cholesterol, and triglycerides are the usual patterns for dyslipidemia in patients with type II diabetes[64]. We had 37.5% male and 29.79% female who had dyslipidemia, observed from their history and medications. Microalbuminuria was significantly abnormal in about 24.51% of the patients, but 78.58% of nephropathy patients had microalbuminuria. The prevalence of microalbuminuria was 24.9% and macroalbuminuria was 5.3% found by ten years following diagnosis of diabetes[65]. Cholesterol and HbA1c constitute the high-risk factors for diabetic nephropathy[66], hypertension and dyslipidemia are also found to be significant risk factors in a study[67]. Albumin creatinine ratio is also significant for diabetic retinopathy patients in Bangladesh. In our study, 100% of diabetic nephropathy patients had high ACR (>30mg/mmol). 67.96% of diabetic patients had high HbA1c where 73.33% diabetic peripheral neuropathy patients and also 72% cardiac autonomic neuropathy patients had high HbA1c, supports another study[68]. We find higher HbA1c in the case of female patients than males. 77% of female cardiac autonomic neuropathy patients and 76% of female diabetic peripheral neuropathy patients had high HbA1c. Working-age adults with retinopathy has the higher probability of blindness, especially in patients with longer diabetes duration[69]. In this study, HbA1c, BMI, obesity, ACR, and microalbuminuria were the remarkable risk factors for the growth of microvascular complications[70]. Dyslipidemia is a well-known risk factor for the evolution of diabetic retinopathy.

4.3 Key message to health community in Bangladesh

1. HbA1c is a recognized screening test for diabetic mellitus. This study suggest that it can be used to predict development of microvascular complications in these patients.

2. As HbA1c is not dependent on fasting state, opportunity exist for its utilization at the community level for screening of diabetes microvascular complications.

3. Improvement of glycemic control, weight management and early detection of nephropathy through screening can be reduce frequent complications related to diabetes mellitus.

5. Conclusion

This study explored the present status of microvascular complications of type II diabetes in Bangladesh. Higher comorbidities and microvascular complications were found as compared with neighboring countries, most likely, due to the increased levels of hypertension, and obesity. Control of hemoglobin and obesity needs more observations and care. This study also suggests high HbA1c could be related to CAN; high HbA1c, Microalbuminuria, and Urinary creatinine could be related to DPN; years of Diabetes, Systolic blood pressure and albumin creatinine ratio could be related to Nep, high HbA1c and Microalbuminuria could be related to Ret. These may be useful predictor risk factors for the development of diabetic complications. In a word, this study has identified the main trends in microvascular complications among Bangladeshi type II diabetes patients. Bangladesh has a high prevalence of the disease and the maximum of its population are poor. Considering this, our study can contribute more effective screening and improved treatment techniques in the future.

6. List of Abbreviations

CAN – cardiac autonomic neuropathy
DPN – diabetic peripheral neuropathy
Nep – nephropathy
Ret – retinopathy
NCV – nerve conduction velocity
CTS – carpal tunnel syndrome
ACR – albumin creatinine ratio

Declarations

ethical consideration

The study was approved by the Ethical Review Committee of Bangladesh University of Health Sciences (BUHS/BIO/EA/17/01) and conforms to the ethical principles outlined in the Declaration of Helsinki and Ministry of Health and Family Welfare of Bangladesh.

author consent

Each patient agreed to take part in this study and gave signed consent after a brief session to explain aims and methods. This article has not been published previously and it is not under consideration for publication elsewhere. This publication is approved by all authors.

data statement

Data could be shared with any other researchers working in non-profit organizations under research agreement.

conflict of interest

Authors declare that there is no conflict of interest with any third parties or institutions.

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