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Original Article

Burden of macro- and micro-vascular complications of type 2 diabetes in Bangladesh

Afsana Afroz [a], Khurshid Alam [b], Md Nassif Hossain [a], Animesh Biswas [c], Liaquat Ali [c], Dianna J. Magliano [a,d], Baki Billah [a,*]

[a] Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, Australia
[b] School of Population and Global Health, The University of Western Australia, Perth, Australia
[c] Bangladesh University of Health Sciences (BUHS), Dhaka, Bangladesh
[d] BakerIDI Heart and Diabetes Institute, Melbourne, Australia

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ABSTRACT

Objective: The aim was to estimate the burden of macro- and micro-vascular complications on hospitalisation and healthcare cost among people with type 2 diabetes mellitus in Bangladesh.
Methods: A cross-sectional study was carried out in 2017. A total of 1253 patients were recruited from six hospitals. Information related to cost and complications of type 2 diabetes were collected. Multiple logistic and non-parametric regression analyses were performed to evaluate the effect of complications on hospitalisation and average annual cost.
Results: Overall, 63.4% of the participants had complications of which 14.8% and 20.7% had macro- and micro-vascular complications respectively and 27.9% had both. Use of insulin, presence of both hypertension and dyslipidaemia, coronary artery diseases, stroke, nephropathy, and retinopathy were significantly associated with hospitalisation. Further, use of oral hypoglycaemic agent with a combination of insulin, presence of coronary artery diseases, stroke, nephropathy, and retinopathy increased the average annual cost.
Conclusion: The prevalence of macro- and micro-vascular complications were very high in Bangladesh and majority of them are key drivers for hospitalisation and increased healthcare cost. An improvement of primary prevention strategy for complications is urgently needed which in turn will reduce the long-term healthcare cost for type 2 diabetes in Bangladesh.

1. Introduction

Diabetes mellitus and its related complications are a growing health and economic burden worldwide. The global prevalence of diabetes was estimated to be 8.8% among adults aged 20–79 years in the year 2017 [1]. About 79% of them were living in low- and middle income countries. It has been projected that by the year 2045 the global prevalence of diabetes will reach to about 9.9%. The largest increase will take place in regions where economies are moving from low income to middle income levels [1].

Diabetes is strongly associated with both macro- and micro-vascular complications [2]. The disease and its associated complications pose a severe economic burden on individuals as well as on the healthcare system. Expenditure on healthcare for people with diabetes are on average two-fold higher than that of people without diabetes [3]. To treat and prevent diabetes and its related complications, USD727 billion was spent in the year 2017 globally, which represents an 8% increase compared to that of the 2015 estimate [1].

A study conducted in the USA showed that the prevalence of uncontrolled diabetes increased from 35.8% to 44.5% between the year 1988 and 2000 [4]. The increasing prevalence of uncontrolled diabetes leads to an increase in the prevalence of diabetes related macro- and micro-vascular complications. This imposes a significant economic burden on healthcare systems, and above all, on individuals with diabetes and their families [1]. Detailed data on global estimates of diabetes related complications are limited. However, in some high income countries, where data are available,

* Corresponding author. Department of Epidemiology and Preventive Medicine, School of Public Health and Preventive Medicine, Monash University, 553 St. Kilda Rd., Level 4, Melbourne, VIC, 3004, Australia.
E-mail address: baki.billah@monash.edu (B. Billah).

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the prevalence of complications vary enormously [1]. A few studies [5–8] in Bangladesh investigated the prevalence of microvascular complications (nephropathy, retinopathy and neuropathy) of type 2 diabetes. However, none of the study investigated the macrovascular complications (coronary artery disease, stroke and diabetic foot).

Each complication results in different type of resource utilisation, thus have an independent economic impact. Poorly controlled diabetes leading to complications results in frequent hospitalisations [1] which escalates the cost further [9,10]. The Cost of Diabetes in Europe-Type II study [9] and study conducted in the USA [10] reported that the hospitalisation cost due to diabetes related complications ranges between 50% and 55% of the total cost of diabetes care. In order to prioritise the resource allocation for the prevention of complications, policymakers need a clear information about their individual impact on healthcare. In Bangladesh, there is a paucity of research-based evidence that addressed the burden of diabetes related macro- and micro-vascular complications on hospitalisation and average annual cost of diabetes care.

Thus, the aim of this study was to explore the association of hospitalisation as well as average annual cost with macro- and micro-vascular complications among people with type 2 diabetes mellitus (T2DM) in Bangladesh. This study findings will be useful to suggest recommendations in advocating and developing complication specific diabetes management plan.

2. Methodology

2.1. Study design and study population

This study has been approved by the Monash University Human Research Ethics Committee and the ethics committee of the Diabetic Association of Bangladesh (BADAS). The BADAS (a not-for-profit but mostly self-sustained social welfare organisation) has 61 affiliated hospitals and centres across Bangladesh that provide health services to majority of the people with diabetes in the country. Six hospitals were selected from the central and northern regions of the country which provide primary to tertiary level cares to rural-urban and professional mix population. Since the socio-economic status of people living in northern and southern regions in the country are very similar, no hospital were selected from the southern region.

2.2. Sample selection

A total of 1253 participants were recruited using probability proportional to size and systematic random sampling methods from April to September 2017. The target population was adults of either gender with a minimum one year duration of T2DM. People with other types of diabetes or pregnant women were excluded.

2.3. Data collection

Participant's socio-demographics and all information related to the cost of diabetes care were collected using a structured questionnaire in a secured web-based application known as Research Electronic Data Capture (REDCap) [11]. Clinical information related to T2DM and its complications in the previous year were retrieved from patient's medical records (guidebook) using a data extraction check-list. Patient's complication status was ensured by asking the patients and reviewing their documented medical records and prescribed drug list confirmed by the allocated medical doctor to the patient. A team of trained data collectors was involved in face-to-face interviewing of each patient. Before the interview, a signed consent was obtained from each patient. Data was collected from the out-patient department (OPD) of the selected hospitals. However, individual who were referred to hospital admission from the outpatient department, their hospitalisation related data was collected prospectively from record of the in-patient department (IPD).

2.4. Operational definition for identifying complications

Coronary artery disease (CAD) was defined by reviewing the medical records of documented diagnosis, prescribed medication or any procedure that was undertaken as a treatment of CAD. Stroke was defined by reviewing the documented diagnosis of an irreversible cerebrovascular accident as well as by asking the patient about any incidence in the previous years. Diabetic foot was defined by visual examination of ulcers or amputations and documented diagnosis of diabetic foot. Nephropathy was defined by an estimated glomerular filtration rate <60 ml/min/1.73 m^2 [12] and a documented diagnosis from the medical records. Neuropathy was defined using the Michigan Neuropathy Screening Instrument [13] and by the prescribed medication. Retinopathy was defined by documented diagnosis or a procedure undertaken for the treatment of retinopathy.

2.5. Cost calculation

The total cost of care was calculated using the standard micro-costing approach and considering societal perspective during the year 2017 [14]. Direct and indirect costs endured by the participants were taken into account in calculating the total cost. All costs attributed to resource utilisation were calculated in Bangladeshi Taka (BDT) and then converted into USD considering a mid-year currency exchange rate for the year 2017 (US$1 = BDT80).

In order to estimate direct cost, bottom-up methodology [15] was used for primary data collection. Direct cost was divided into direct medical and non-medical costs. Direct medical cost included costs of hospitalisation, out-patient consultancy, medicine, laboratory tests, and other services. Direct non-medical cost included costs of transportation and meal en-route to hospital. The unit cost of each direct cost component was multiplied by quantities of medical services that were used during the previous year and then the total direct cost was calculated adding up all the medical and non-medical cost components. The indirect cost included productive time loss of the patients and their attendants. The human capital approach [16] was adopted to estimate indirect cost for those who were currently in a formal workforce or housewives. In order to perform sensitivity analysis, minimum wage rate of Bangladesh [17] and then again median monthly income of the study participants were used to calculate the productivity loss of housewives. The total cost was calculated adding up total direct and total indirect costs.

2.6. Statistical analysis

The descriptive statistics included mean with standard deviation, median with percentiles and frequency with percentage. Normality test of cost data was performed using histogram, Q-Q plot and Shapiro-Wilk test. Nonparametric Mann–Whitney *U* test and Kruskal-Wallis test were used respectively for comparing two groups and more than two groups. A multiple logistic regression analysis was used to identify the factors related to hospitalisation. Furthermore, multiple non-parametric regression analyses (50th percentile (median), 75th percentile and 90th percentile) were performed to explore the relationship of average annual cost with macro- and micro-vascular complications. Sensitivity analyses were performed to investigate the robustness of total estimated

cost. All the statistical tests were considered significant at 5% level, and the presented p-values were two-tailed. Data was analysed using the statistical software package, Stata SE version 15.

3. Results

3.1. Socio-demographic and clinical characteristics

Table 1 showed the socio-demographic and clinical characteristics of the study participants (n = 1253). Among them, 54% were male with a mean age of 55.1 years (±12.5). Nearly half (46%) of participants had a secondary level education and 22.9% had a tertiary level education. About 41% of participants were employed and about a quarter (23.8%) were housewives. Three-fourths of participants resided in urban areas, 12.9% in semi-urban areas and 13.9% in rural areas. About a quarter (25.7%) of participants had a monthly household income of USD375 or less. The mean duration of T2DM was 10.7 years (±7.7), with 43.5% had a duration of more than 10 years. Nearly three-fifths of participants (58.6%) managed their glycaemic level using a combination of oral hypoglycaemic agent (OHA) and insulin, 34.5% using OHA only and 6.9% using insulin only. About two-thirds (62%) of participants had poor glycaemic control (HbA1c ≥ 8%) and 19.8% had fair glycaemic control (HbA1c 7–7.9%). More than half (55.8%) of participants were moderately adhering to medication, followed by 37.1% with good and only 6.9% with poor adherence. About a half (48.5%) of participants had one or two diabetes related complications, 15.2% had three or more and 36.3% had no complication. Hypertension (HTN) was presented among 41.8% of participants, 12% had dyslipidaemia and 22.6% had both HTN and dyslipidaemia.

3.2. Prevalence of complications

Fig. 1 shows the prevalence of T2DM related macro- and micro-vascular complications. Overall, 63.4% of patients had one or more macro- and/or micro-vascular complications. The prevalence of macrovascular complications of CAD, stroke and diabetic foot were respectively 30.5%, 10.1% and 12%, while that for microvascular complications of nephropathy, neuropathy, and retinopathy were 34%, 5.7% and 25.1% respectively.

3.3. Diabetes related complications and average annual cost (cost-of-illness)

Table 2 showed the OPD and IPD costs by complications, comorbidities and glycaemic control. The cost was higher for patients with the presence of CAD (USD33.3, p = 0.032), nephropathy (USD61.1, p = 0.010) and retinopathy (USD82.4, p = 0.001) in

Table 1
Socio-demographic and clinical characteristics of the study participants.

Variables		n (%) or mean ± standard deviation	
Age		55.1	±12.5
Gender	Male	681	54.3
	Female	572	45.6
Education	Illiterate	161	12.8
	Primary level	239	19.1
	Secondary level	566	45.2
	Tertiary level	287	22.9
Work status	Unemployed	36	32.8
	Employed	411	40.5
	Housewife	508	23.8
	Retired	298	2.9
Area of residence	Rural/Semi-urban	336	26.8
	Urban	917	73.2
Monthly household income (USD)	≤250	447	35.7
	251–750	497	39.7
	751 and above	309	24.6
Onset of diabetes	≤40 years	503	40.1
	40–60 years	644	51.4
	≥61 years	106	8.5
Duration of diabetes	Total	10.9	±7.7
	≤5 years	360	28.7
	6–10 years	348	27.8
	≥11 years	545	43.5
Mode of treatment	OHA	432	34.5
	Insulin	87	6.9
	Combination	734	58.6
Family history of diabetes	Yes	433	34.6
	No	820	65.4
HbA1c (%)	Good control (≤6.9%)	182	18.2
	Fair control (7–7.9%)	198	19.8
	Poor control (≥8%)	621	62.0
Adherence to medication	Good	466	37.2
	Moderate	700	55.9
	Poor	87	6.94
Number of complication	No complication	458	36.6
	1 to 2	613	48.9
	3 or more	182	14.5
History of co-morbidity	No comorbidity	296	23.6
	HTN	524	41.8
	Dyslipidaemia	151	12.0
	HTN + Dyslipidaemia	283	22.6

OHA = oral hypoglycaemic agent; HTN=Hypertension.

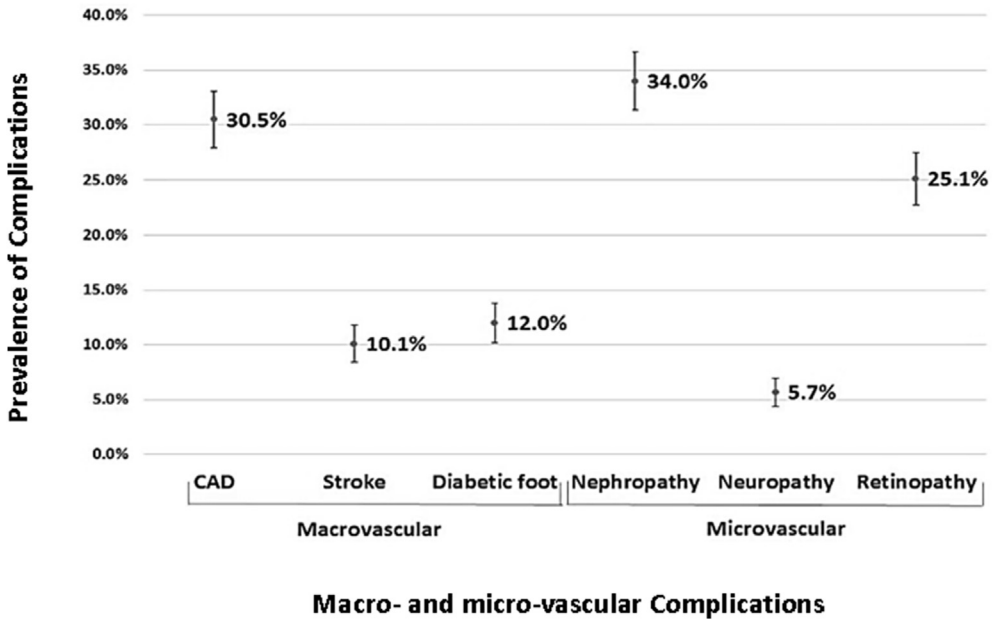

Fig. 1. Prevalence of major macro- and micro-vascular complications.

Table 2
Cost-of-illness (average annual cost) for diabetes related complications, comorbidities and glycaemic control.

Complications	Average annual cost Without hospitalisation (OPD)		Average annual cost With hospitalisation (IPD)	
	Median (25th p, 75th p)	p-value	Median (25th p, 75th p)	p-value
Macrovascular				
CAD				
No	359.9 (256.1, 509.1)	**0.032**	1189.9 (838.2, 1948.5)	0.272
Yes	393.2 (289.5, 509.1)		1281.1 (932.6, 2009.0)	
	CD 33.3		CD 91.2	
Stroke				
No	366.6 (265.3, 507.2)	0.513	1221.6 (857.7, 1856.2)	**0.006**
Yes	345.1 (233.7, 504.1)		1558.2 (1018.3, 2505.4)	
	CD 21.5		CD 336.6	
Diabetic foot				
No	364.1 (256.6, 505.7)	0.074	1179.8 (859.5, 1855.5)	**0.001**
Yes	425.8 (287.5, 516.8)		1130.2 (1130.2, 2958.4)	
	CD 30.9		CD 49.6	
Microvascular				
Nephropathy				
No	358.3 (255.7, 499.4)	**0.010**	1060.8 (727.7, 1652.9)	**0.001**
Yes	419.4 (295.5, 520.5)		1337.2 (953.7, 2043.8)	
	CD 39.8		CD 276.4	
Neuropathy				
No	366.6 (261.2, 504.2)	0.861	1277.6 (876.8, 1996.7)	0.503
Yes	356.4 (267.5, 559.4)		1022.0 (877.1, 1954.1)	
	CD 6.3		CD 255.6	
Retinopathy				
No	356.7 (255.9, 496.6)	**0.001**	1268.7 (897.9, 2097.6)	0.167
Yes	439.1 (321.2, 549.8)		1224.4 (857.5, 1902.6)	
	CD 65.3		CD 44.3	
Comorbidity				
None	324.3 (231.1, 502.8)	**0.001**	1283.4 (858.8, 1206.2)	0.994
HTN	387.5 (285.9, 526.9)		1230.8 (880.2, 1996.6)	
Dyslipidaemia	320.0 (237.0, 452.8)		1281.1 (876.5, 1630.2)	
HTN + Dyslipidaemia	387.1 (286.0, 503.3)		1227.2 (887.6, 2009.0)	
Glycaemic status (HbA1c %)				
Good control (≤6.9%)	307.3 (222.4, 466.5)	**0.001**	1198.3 (775.3, 1964.8)	0.612
Fair control (7–7.9%)	343.3 (264.8, 496.4)		1210.3 (893.1, 1658.7)	
Poor control (≥8%)	383.8 (275.7, 521.4)		1110.8 (858.7, 1551.1)	

CD = cost difference; Mann–Whitney *U* test and Kruskal-Wallis test were used respectively for comparing two groups and more than two groups.
p-values is significant (p<0.05).

comparison with those without these complications. Furthermore, the hospitalisation cost was higher for patients who had the event of stroke (USD336.6, p = 0.006) and nephropathy (USD276.4, p = 0.001). Participants with the presence of comorbidity as well as poor glycaemic control had higher (p = 0.001) OPD cost.

The cost ratio by the complication status presented in Table 3 showed that the ratio was 1.9-fold for patients with the presence of one or more complications compared to those without any complication. The ratio increased progressively as the number of complications increased. Patients with one, two and three or more complications (irrespective of macro- or micro-vascular) had 1.3-fold, 2.4-fold and 3.4-fold higher cost respectively. The presence of macro- and micro-vascular complications individually increased the cost ratio by 1.3-fold and 1.7 fold respectively and the ratio increased by 3.1-fold with the presence of both.

3.4. Relationship of hospitalisation with complications

Table 4 showed the results of multiple logistic regression analysis that identified the factors related to hospitalisation. The odds of hospitalisation increased by 6.1-fold (95% CI: 3.9–9.3) and 2.5-fold (95% CI: 1.5–3.8) for patients with the presence of nephropathy and retinopathy respectively. Furthermore, patients with stroke had 4.3-fold higher (95% CI: 2.1–8.7) odds (95% CI: 1.5–3.9) of hospitalisation and that was 2.5-fold higher for those with CAD. Patients with an onset of T2DM at aged 61 years or above had 2.3-fold increased odds to be hospitalised (95% CI: 1.1–4.9). The odds of hospitalisation was also higher for patients who were treated with insulin only (OR: 5.3, 95% CI: 2.1–13.1) or with a combination of OHA and insulin (OR: 2.9, 95% CI: 1.7–5.1). Compared to patients resided in urban areas, rural patients had 10% less odds to be hospitalised and compared to low income group that was 45% less for middle income group.

Table 4
Multiple logistic regression analysis: determinants of hospitalisation.

Variables	OR	p-value	95% CI
Gender (ref: male)rowhead			
Female	1.3	0.122	0.91–2.13
Onset of diabetes (ref: ≤40 years)rowhead			
41–60 years	0.8	0.433	0.53–1.32
≥61 years	2.3	0.031	1.07–4.92
Area of residence (ref: Urban)rowhead			
Rural/Semi-urban	0.1	0.001	0.02–0.12
Monthly household income (ref: USD≤250)rowhead			
USD251-750	0.45	0.002	0.27–0.74
USD751 and above	0.74	0.367	0.42–1.26
Mode of treatment (ref: OHA)rowhead			
Insulin	**5.3**	**<0.001**	2.17–13.1
OHA + Insulin	**2.9**	**<0.001**	1.71–5.06
HbA1c (ref: controlled ≤6.9%)rowhead			
Uncontrolled	1.3	0.363	0.72–2.37
Comorbidity (ref: no)rowhead			
HTN	1.4	0.293	0.75–2.57
Dyslipidaemia	0.6	0.328	0.25–1.57
HTN + Dyslipidaemia	1.3	0.349	0.71–2.62
Macrovascular complicationsrowhead			
CAD (ref: no)rowhead			
Yes	**2.5**	**<0.001**	1.59–3.97
Stroke (ref: no)rowhead			
Yes	**4.3**	**<0.001**	2.13–8.75
Diabetic foot (ref: no)rowhead			
Yes	1.7	0.144	0.87–3.32
Microvascular complicationsrowhead			
Nephropathy (ref: no)rowhead			
Yes	**6.1**	**<0.001**	3.94–9.35
Neuropathy (ref: no)rowhead			
Yes	1.2	0.770	0.45–2.92
Retinopathy (ref: no)rowhead			
Yes	**2.5**	**<0.001**	1.57–3.89

p-values is significant (p<0.05).

3.5. Relationship of average annual cost (or cost-of-illness) with complications

Multiple median (50th percentile) regression analysis results presented in Table 5 showed that patients with the presence of stroke and CAD had respectively USD241.8 (p < 0.001, 95% CI: 113.6–315.8) and USD83.3 (p = 0.009, 95% CI: 21.02–145.6) higher cost compared to those without these complications. Also, the presence of nephropathy increased the cost by USD215.1 (p < 0.001, 95% CI: 152.6–279.5) and it increased by USD84.3 (p = 0.015, 95% CI: 15.43–152.2) for patients who had retinopathy. Patients using a combination of OHA and insulin to control hyperglycaemia were subject to USD134.3 (p < 0.001, 95% CI: 76.70–191.6) higher cost in comparison with those using OHA only. Similarly, patients in a high income group spent USD74.5 (p < 0.034, 95% CI: 5.73–143.22) more than the lower income group.

The 75th as well as 90th percentile regression analyses were also performed to explore the key factors of cost for the patients within the top 25% and 10% of spending (Table 5). The 75th percentile regression analysis showed that patients with the presence of CAD, stroke and nephropathy spent respectively USD180.8 (p = 0.003, 95% CI: 61.6–300.0), USD332.1 (p = 0.001, 95% CI: 138.7–525.5) and USD537.7 (p < 0.001, 95% CI: 416.3–659.1) more

Table 3
Cost ratio by complications status.

Variable	Number (%)	Average annual cost		
		Median (25th p, 75th p)	p-value	Ratio
Complication statusrowhead				
Absent	458 (36.6)	359 (255.7, 524.3)	**<0.001**	1:1
Present	795 (63.4)	705 (393.1, 1360.4)		1:1.9
Number of complicationrowhead				
Absent	Reference			
One	352 (28.1)	473.4 (299.9, 806.5)	**<0.001**	1:1.3
Two	261 (20.8)	888.3 (475.9, 1432.8)		1:2.4
Three and more	182 (14.5)	1206.1 (723.8, 2043.8)		1:3.4
Types of complicationsrowhead				
Absent	Reference			
Macrovascular	186 (14.8)	451.6 (289.5, 810.7)	**0.001**	1:1.3
Microvascular	259 (20.7)	596.5 (364.1, 1088.8)		1:1.7
Micro and macrovascular	350 (27.9)	1048.4 (557.5, 1777.3)		1:3.1

Mann–Whitney *U* test and Kruskal-Wallis test were used respectively for comparing two groups and more than two groups.
p-values is significant (p<0.05).

Table 5
Multiple non-parametric regression analysis: determinants of overall average annual cost.

Variables	50th percentile (median) regression			75th percentile regression			90th percentile regression		
	Beta	p-value	95% CI	Beta	p-value	95% CI	Beta	p-value	95% CI
Gender (ref: male)									
Female	49.13	0.061	−2.25–100.53	32.44	0.518	−65.91–130.8	−12.77	0.902	−216.04–190.5
Onset of diabetes (ref: ≤40 years)									
41–60 years	−36.97	0.183	−91.3–17.43	−18.27	0.731	−122.3–85.8	−28.98	0.792	−244.16–186.2
≥61 years	−37.30	0.490	−143.2–68.67	−8.86	0.932	−211.6–193.9	110.88	0.604	−308.27–530.0
Area of residence (ref: Urban)									
Rural/Semi-urban	−54.03	0.068	−70.86–46.42	−52.48	0.354	−163.6–58.6	−132.01	0.260	−361.6–97.66
Monthly household income (ref: USD≤250)									
USD251-750	−12.21	0.683	−70.86–46.42	−8.23	0.886	−120.5–103.9	35.97	0.761	−195.9–167.9
USD751 and above	74.48	0.034	5.73–143.22	120.28	0.073	−11.27–251.8	218.4	0.115	−53.48–490.2
Mode of treatment (ref: OHA)									
Insulin	57.42	0.270	−44.76–159.6	**233.35**	**0.019**	37-79-428.9	309.65	0.133	−94.49–713.8
OHA + Insulin	**134.3**	**<0.001**	76.70–191.6	**170.78**	**0.002**	60.50–281.1	**312.7**	**0.007**	84-78-540.6
HbA1c (ref: controlled ≤6.9%)									
Uncontrolled	23.26	0.508	−45.71–92.24	−7.10	0.916	−139.1–124.9	11.12	0.936	−261.68–283.9
Comorbidity (ref: no)									
HTN	18.94	0.579	−48.12–86.02	29.18	0.656	−99.17–157.5	44.43	0.742	−220.8–309.7
Dyslipidaemia	−20.80	0.639	−107.9–66.30	−15.69	0.853	−182.3–150.9	−38.28	0.827	−382.7–306.2
HTN + Dyslipidaemia	10.12	0.799	−67.84–88.06	−6.71	0.930	−155.8–142.5	−27.85	0.859	−336.1–280.4
Macrovascular complications									
CAD (ref: no)									
Yes	**83.31**	**0.009**	21.02–145.6	**180.8**	**0.003**	61.60–300.0	**379.91**	**0.003**	133.5–626.3
Stroke (ref: no)									
Yes	**241.75**	**<0.001**	113.6–315.8	**332.14**	**0.001**	138.7–525.5	**466.09**	**0.022**	66.38–865.7
Diabetic foot (ref: no)									
Yes	41.23	0.357	−46.5–129.0	−6.85	0.936	−174.8–161.1	168.69	0.341	−178.4–515.8
Microvascular complications									
Nephropathy (ref: no)									
Yes	**215.11**	**<0.001**	152.6–279.5	**537.71**	**<0.001**	416.3–659.1	**1062.4**	**<0.001**	811.5–1313.3
Neuropathy (ref: no)									
Yes	−18.90	0.728	−125.6–87.8	−22.45	0.829	−226.7–181.8	−15.50	0.943	−437.6–406.6
Retinopathy (ref: no)									
Yes	**84.31**	**0.015**	15.43–152.2	59.47	0.369	−70.43–189.4	13.65	0.921	−254.8–282.1

p-values is significant (p<0.05).

than those without these complications. This differences were much higher for the 90th percentile regression, which showed that the presence of CAD, stroke and nephropathy increased the cost by USD379.9 (p = 0.003, 95% CI: 133.5–626.3), USD466.1 (p = 0.022, 95% CI: 66.38–865.7) and USD1062.4 (p < 0.001, 95% CI: 811.5–1313.3) respectively. Furthermore, both 75th and 90th percentile regression analyses revealed that patients treated with insulin only or with a combination of OHA and insulin had significantly higher cost compared to those treated with OHA only.

3.6. Sensitivity analysis

The results of sensitivity analysis confirmed that the estimated total average annual cost was robust between the use of minimum wage rate of Bangladesh and the median wage of study participants. Furthermore, the cost variation between the selected hospitals was homogeneous which demonstrates that the cost was not driven by a single hospital.

4. Discussion

Diabetes related complications are the salient threat on the global economy especially on the economy of the resource limited countries including Bangladesh. There is a dearth of evidence on the burden of macro- and micro-vascular complications of T2DM on hospitalisation and total healthcare cost in Bangladesh, hence the purpose of this study. This study results showed that overall 63.4% of participants had complications of which 14.8% had macrovascular complications, 20.7% had microvascular complications and 27.9% had both. The presence of CAD, stroke, nephropathy, and retinopathy increased the likelihood of hospitalisation in multi-fold and they had an independent impact on higher healthcare cost.

The estimated prevalence of each complication in this study was comparable to that of the global estimates for working people with diabetes aged between 20 and 65 years. The prevalence of CAD (30.5%) was within the range of the estimated global prevalence (12%–31.7%) [1] and that of diabetic foot (12%) was comparable with other Asian countries namely India [18] and Thailand [19], but higher than the global estimate of 6.4% [1]. It should be noted that the global prevalence of diabetic foot varied between 3% in Oceania to 13% in North America [1]. Poorly controlled blood glucose level causes damage to the nerves, which places the people with diabetes at 10 times higher risk of developing nephropathy [1]. In this study, the prevalence of nephropathy was 34% which resembles the estimated global prevalence of 39% [20]. This study showed that 5.7% of participants had neuropathy which was much lower than the estimated global prevalence (16%–66%) [1]. This may be due to the asymptomatic nature of this complication that keeps patients as undiagnosed. Furthermore, in Bangladesh, the healthcare cost is mostly out-of-pocket and hence, generally, people seek medical help when the complication incurs some obstacle to their daily living. Retinopathy is another microvascular complication which is commonly prevalent among people with T2DM and it is a leading cause of blindness for these people [1]. This study showed that the prevalence of retinopathy is 25.1%, which is less than the global prevalence of 35% [1]. This difference again may be due to the silent progression of retinopathy and unmet financial involvement for regular screening.

The cost of diabetes care is significantly associated with the level of complications that lead to hospitalisation. In this study, the OPD

cost was significantly higher for patients with the presence of CAD, nephropathy and retinopathy as they require frequent OPD follow-up. Hospitalisation cost was higher for patients with stroke and nephropathy which may be related to higher treatment cost and prolonged hospital stay. A study conducted in the USA also reported that nephropathy and cardiovascular diseases were the most prevalent among people with diabetes and were associated with predominantly higher costs [21]. The economic impact of managing T2DM with CAD and nephropathy is likely to be higher as the patients may require high resource treatment options.

Our study results showed that the patients who were treated with a combination of insulin and OHA were more likely to be hospitalised and had a higher cost which is supported by previous studies [22,23]. The higher spending for patients using insulin with a combination of OHA can be justified by the higher cost of insulin. Additionally, patients are generally prescribed for insulin in combination with OHA when the monotherapy fails to maintain the blood glucose level within the clinically recommended range. Furthermore, the progression of diabetes increases the likelihood of acquiring diabetes complications that require multiple modalities of treating hyperglycaemia.

The actual economic burden of diabetes remains underestimated if the cost of diabetes related complications had not been taken into account [24,25]. This study showed that patients with the presence of any complication experienced almost double healthcare cost compared to those without complication. Previous studies [26,27] also supported this finding where per patient cost increased between 2 and 3.5-fold with the presence of complications. Moreover, this study results showed that cost increased considerably as the number of complications increased and that was 3-fold higher with the presence of both macro- and microvascular complications compared to patients without complication. This finding is consistent with that of other studies [19,22,28,29].

Furthermore, this study results showed that patients with CAD, stroke, nephropathy and retinopathy were more likely to be hospitalised. These findings are similar to that in studies conducted by Williams et al. [28], Bhattacharyya et al. [22,30] and Chaikledkaew et al. [23]. As was evidenced by the multiple non-parametric regression analysis, each of the above complications increased the cost significantly and they are the key contributors for higher average annual cost per person. This can be due to the increased severity of the compilations and their resource-intensive treatment options. In addition, use of OHA in a combination with insulin appeared as an increased cost contributor which was similar to that of the previous studies [19,23,26,27,29,30]. The cost related to treating CAD, stroke and nephropathy progressively increased starting from the top 50% cost bracket, and this difference widens more towards the top 25% and 10% of patients. Early diagnosis and intensified treatment for these complications can be a way to avoid hospitalisation. This may result in a relatively large economic saving, thereby calling for tailored preventive interventions.

The International Diabetes Federation guidelines provide emphasis on comprehensive management plan including health education about the importance of positive lifestyle modification, effective monitoring for blood glucose and lipids, and regular screening for complications for people with T2DM [1]. In current practice, all the hospitals under the umbrella of the BADAS have health educators to educate patients on management plan including the benefits of positive lifestyle changes. Patients are also receiving advice for regular screening of complications. However, in general, patients are less likely to engage with this advice due to the out-of-pocket costs for screening and monitoring which lacks government subsidisation. Out-of-pocket access to healthcare is a factor that is closely related to household economic status. In Bangladesh, people have to pay out-of-pocket to secure their health and more than 12% of households have to borrow money or sell household assets to pay healthcare costs related to chronic diseases [31]. The healthcare financing in Bangladesh is still predominantly prioritised by maternal and child health programs [32] and NCDs especially diabetes and hypertension are being paid less attention. This study findings demonstrated that the economic burden of T2DM along with its complications will increase if preventive measures are not implemented. Hence, people with T2DM should be under the coverage of screening and monitoring programs on a regular basis. They should be advocated for positive lifestyle changes and better control of diabetes. Finally, these programs should be subsidised by the government so that every patients get an opportunity to access the service.

This study has some strengths and limitations. The strength of this study was that it has included a representative large sample covering professional mix patients living in urban, semi-urban and rural areas. Patients were recruited from multiple hospitals that provide primary to tertiary levels healthcare facilities and data collection using electronic questionnaire confirmed the data quality. Information regarding T2DM related complications was confirmed by the proper documentation of diagnosis and allocated medical doctors. This study captured all possible costs related to T2DM and its complications. At the same time, it has the limitation that this hospital based prevalence of complications may differ from a community-based study. Hence, generalizability of this study results may be limited to patients attending the hospitals under the BADAS and hospitals similar to this study hospitals. Due to cross-sectional study design, it was difficult to measure the severity of the complication that may influence the cost estimation.

5. Conclusion

While it is understood that prevention or a delayed onset of compilations for patients with T2DM leads to a reduction of healthcare cost on disease management, the findings of this study highlight the main cost contributors that require attention to maximise health outcomes for the T2DM population in Bangladesh. Access to robust monitoring and subsidised early screening programs for T2DM patients can help greatly to minimise the economic burden of macro- and micro-vascular complications related to this growing epidemic.

Author's contribution

Concept and design (AA, BB), acquisition of data (AA, AB, LA), interpretation of data and drafting the manuscript (AA, BB), critically review to improve the content and final approval of version to be submitted (AA, NH, BB, DM, KA, LA). All authors have read and approved the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.03.001.

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Disclosure

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Availability of data

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

References

[1] Cho Nam Han, Kirigia Joses, Mbanya Jean Claude, Ogurstova Katherine, Guariguata Leonor, Rathmann Wolfgang, et al. IDF DIABETES ATLAS Eighth edition. 2017.

[2] Association AD. Economic costs of diabetes in the US in 2012. Diabetes Care 2013;36(6):1797. Diabetes Care 2013; 36: 1033–1046.

[3] Cho NH, Whiting D, Forouhi N, Guariguata L, Hambleton I, Li R, et al. IDF DIABETES ATLAS. seventh ed. International diabetes federation; 2015 Hallado en http://www_idf_org/diabetesatlas/5e/es/prologo.

[4] Koro CE, Bowlin SJ, Bourgeois N, Fedder DO. Glycemic control from 1988 to 2000 among US adults diagnosed with type 2 diabetes: a preliminary report. Diabetes Care 2004;27(1):17–20.

[5] Akhter A, Fatema K, Ahmed SF, Afroz A, Ali L, Hussain A. Prevalence and associated risk indicators of retinopathy in a rural Bangladeshi population with and without diabetes. Ophthalmic Epidemiol 2013;20(4):220–7.

[6] Rahim MA, Mitra P, Haque HF, Samdani TS, Zaman S, Uddin KN. Prevalence of chronic kidney disease stages 3-5 among patients with type 2 diabetes mellitus in Bangladesh. IMCJ Med Sci 2017;11(1):19–24.

[7] Hoque S, Muttalib M, Islam MI, Happy TA. Evaluation of different HbA1c levels to assess the risk of peripheral neuropathy among type 2 diabetic patients along with other conventional risk factors. Bangladesh Med Res Counc Bull 2017;42(2):95–103.

[8] Mørkrid K, Ali L, Hussain A. Risk factors and prevalence of diabetic peripheral neuropathy: a study of type 2 diabetic outpatients in Bangladesh. Int J Diabetes Dev Ctries 2010;30(1):11.

[9] Massi-Benedetti M. The cost of diabetes in Europe-Type II: the CODE-2 study. Diabetologia 2002;45(7):S1–4.

[10] Association AD. Economic costs of diabetes in the US in 2007. Diabetes Care 2008;31(3):596–615.

[11] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42(2):377–81.

[12] Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150(9):604–12.

[13] Moghtaderi A, Bakhshipour A, Rashidi H. Validation of Michigan neuropathy screening instrument for diabetic peripheral neuropathy. Clin Neurol Neurosurg 2006;108(5):477–81.

[14] Drummond MF, McGuire A. Economic evaluation in health care: merging theory with practice. Oxford: OUP; 2001.

[15] Rice DP. Estimating the cost of illness. Am J Public Health Nation's Health 1967;57(3):424–40.

[16] Moore R, Mao Y, Zhang J, Clarke K. Economic burden of illness in Canada, 1993. Chronic Dis Inj Can 1997;18(2):1F.

[17] List Of Minimum Wages By Country. https://en.wikipedia.org/wiki/List_of_minimum_wages_by_country. [Accessed 13 January 2018].

[18] Shobhana R, Rama Rao P, Lavanya A, Viswanathan V, Ramachandra A. Cost burden to diabetic patients with foot complications—a study from southern India. JAPI 2000;48(12):1147–50.

[19] Chatterjee S, Riewpaiboon A, Piyauthakit P, Riewpaiboon W, Boupaijit K, Panpuwong N, et al. Cost of diabetes and its complications in Thailand: a complete picture of economic burden. Health Soc Care Community 2011;19(3):289–98.

[20] Parving H-H, Lewis J, Ravid M, Remuzzi G, Hunsicker L. Prevalence and risk factors for microalbuminuria in a referred cohort of type II diabetic patients: a global perspective. Kidney Int 2006;69(11):2057–63.

[21] Brown JB, Pedula KL, Bakst AW. The progressive cost of complications in type 2 diabetes mellitus. Arch Intern Med 1999;159(16):1873–80.

[22] Bhattacharyya SK. Predicting hospitalisation of patients with diabetes mellitus. Pharmacoeconomics 1998;13(5):519–29.

[23] Chaikledkaew U, Pongchareonsuk P, Chaiyakunapruk N, Ongphiphadhanakul B. Factors affecting health-care costs and hospitalizations among diabetic patients in Thai public hospitals. Value Health 2008;11(s1).

[24] Norlund A, Apelqvist J, Bitzén PO, Nyberg P, Scherstén B. Cost of illness of adult diabetes mellitus underestimated if comorbidity is not considered. J Intern Med 2001;250(1):57–65.

[25] Morsanutto A, Berto P, Lopatriello S, Voinovich D, Gelisio R, Mantovani LG. Major diabetes complications have an impact on total annual medical cost of type 2 diabetes. Diabetes Care 2004;27(7):1841–2.

[26] Bakst A, Wisner C, Kirsch J, Hood S, Mera R, editors. The cost of diabetes in Europe-Type 2 Study: micro-and macrovascular complications and disease progression are primary independent drivers of increased costs in diabetes. Diabetologia. New York, NY 10010 USA: Springer-Verlag 175 Fifth ave; 2000.

[27] Schmitt-Koopmann I, Schwenkglenks M, Spinas GA, Szucs TD. Direct medical costs of type 2 diabetes and its complications in Switzerland. Eur J Public Health 2004;14(1):3–9.

[28] Williams R, Van Gaal L, Lucioni C. Assessing the impact of complications on the costs of Type II diabetes. Diabetologia 2002;45(1):S13–7.

[29] Riewpaiboon A, Pornlertwadee P, Pongsawat K. Diabetes cost model of a hospital in Thailand. Value Health 2007;10(4):223–30.

[30] Bhattacharyya SK, Else BA. Medical costs of managed care in patients with type 2 diabetes mellitus. Clin Ther 1999;21(12):2131–42.

[31] Rahman MM, Gilmour S, Saito E, Sultana P, Shibuya K. Self-reported illness and household strategies for coping with health-care payments in Bangladesh. Bull World Health Organ 2013;91(6):449–58.

[32] Chowdhury AMR, Bhuiya A, Chowdhury ME, Rasheed S, Hussain Z, Chen LC. The Bangladesh paradox: exceptional health achievement despite economic poverty. Lancet 2013;382(9906):1734–45.