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Original Article

Dyslipidaemia as a risk factor for erectile dysfunction in type 2 diabetes mellitus patients



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ABSTRACT

Background: Despite epidemiological studies worldwide have documented erectile dysfunction (ED) as a major complication of type 2 diabetes Mellitus (T2DM) in men, only limited research reported on determinants of ED in this population. The study aimed at examining the association of ED with dyslipidaemia in T2DM patients.

Methods: The study enrolled 813 consecutive eligible adult male T2DM patients attending the endocrinology departments of a tertiary teaching hospital in Bangladesh. Sexual function was assessed using modified International Index of Erectile Function (IIEF) in face-to-face interview and collected along with sociodemographic information. Diabetes and lipid profile and treatment history were collected from patient's treatment records. Association of ED with dyslipidaemia was assessed using multivariable logistic regression adjusting for potential confounders.

Result: Prevalence of ED among the T2DM patients was very high (72.7%), of which around half had moderated-to-severe ED. Odds of having dyslipidaemia among T2DM patients with ED is 2.3 times higher than those without. The odds increased by approximately 3 fold for an abnormal High Density Lipoprotein level and by 2.7 fold for abnormal Low Density Lipoprotein.

Conclusion: Dyslipidaemia was associated with increased ED risk among T2DM. Abnormal lipoprotein level particularly were found to pose greater risk.

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1. Introduction

Erectile dysfunction (ED) affects more than 150 million men worldwide, with that number is expected to more than double to 322 million men by 2025 [1]. Men experiencing this sexual disorder have demonstrated severe deficits within their personal relationships, self-confidence and overall quality of life [2]. Individuals with diabetes mellitus were found to have greater susceptibility of developing ED [3,4] with ED occurring in more than 50% of

individuals with diabetes [5]. With around 422 million cases worldwide [6], people with diabetes are the largest group of people at risk of ED.

Despite epidemiological studies worldwide have documented ED as a major complication of type 2 diabetes mellitus (T2DM) in men, only limited research reported on the determinants of ED in this population [7,8]. Fredman et al. [3] studied medical and psychosocial correlates of ED, demonstrating a specific pattern of ED occurrence in diabetic patients. In men with diabetes, ED occurs earlier, is more severe and is associated with a poorer quality of life than in general population [9]. This suggests that a separate set of risk factors may operate in the pathogenesis of ED in men with diabetes.

Several studies into ED in general population have exhibited an association between ED and dyslipidaemia [3,10,11]. Studies in

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laboratory animal also supports the role of lipid profile abnormality in the pathogenesis of ED [12,13]. Although a well-founded pathogenesis of ED is yet to be agreed, considerable biomedical research increasingly pointing towards a vascular mechanism [14–17] where lipid abnormality is likely to play an important role. Besides, ED has been reported to have link with metabolic syndrome [18]. This link between diabetes, ED and metabolic syndrome also provides basis for a possible role of lipid profile in the causal pathway in ED among diabetic patients. This study aimed to examine the possible association of dyslipidaemia with risk of ED in patients with T2DM.

2. Method

The study was conducted in Endocrinology department of the Bangabandhu Sheikh Mujib Medical University (BSMMU) hospital. A total of 813 eligible adult male T2DM patients with no known anomaly or injury in the genitourinary anatomy were included in the study during July 2015 to December 2015. The study received approval from the ethical review board of BSMMU. Patients had their diabetes diagnosed in less than 1 year, not staying with spouse during past six months, suffering from a debilitating chronic disease or condition including psychiatric illness were excluded. Informed written consent was from each of the participant prior to interview. In-depth interview of the study participants were conducted to collect sociodemographic data using pretested interview schedule. Relevant data on diabetes and other coexisting illness, lipid profile, and drug history were collected from the patient's treatment record. Anthropometry was assessed using standard operating procedure. World health organization (WHO) guideline

was used for diagnostic criteria for diabetes [19], overweight [20] (BMI 25–30 kg/m²), obese [20] (BMI > 30 kg/m²). Glycosylated haemoglobin (HbA1c) above 7% was used as criteria for poor glycaemic control [21]. Abnormal level in one or more of the four measured lipid parameters was considered as the operational definition for dyslipidaemia in the study. While reading lipid profile, total cholesterol ≥ 200 mg/dl, low-density lipoprotein (LDL) ≥ 160 mg/dl, triglyceride (TG) was ≥ 150 mg/dl and high-density lipoprotein (HDL) < 40 mg/dl was considered as abnormal [22].

Sexual function of the study participants were assessed using 6-item Modified International Index of Erectile Function (IIEF) [23]. The questionnaire was translated to Bengali and was pre-tested prior to the commencement of data collection. The questionnaire has shown excellent internal consistency (Cronbach's alpha = 0.91) in detecting ED in the study population.

Responses to each of the six items were constructed on a 5-point Likert scale from 1 to 5. A score of '0' was allocated for those patients who were not involved in any sexual activity in past 30 days and were excluded from the analysis. Total EF score was generated by adding the scores of each of the six items. ED was categories based on the NIH consensus panel classification and the scoring guideline [24,25]. A score of 6–10 was classified as severe ED, 11–16 as moderate ED, 17–21 as mild to moderate ED, 22–25 as mild ED and 26–30 as no ED.

Relative frequency was tabulated for qualitative attributes and summary statistics (mean \pm SD) were generated for quantitative attributes. Association of ED categories with patients' sociodemographic characteristics, diabetes status and comorbidities was

Table 1
Socio-demographics characteristics of study subjects (n = 737).

Characteristics	Frequency	Percentage (%)
Age (years)		
21–40	114	15.5
41–50	199	27.0
51–60	225	30.5
>60	199	27.0
Mean (\pm SD)	52.8 (\pm 10.3)	
Education		
Up to primary	71	9.6
Secondary	166	22.5
Higher secondary	146	19.8
Graduate and above	354	48.0
Income (tk/Month)		
<20000	186	25.2
20000–30000	364	49.4
>30000	187	25.4
BMI (Kg/M ²)		
<18.5	12	1.6
18.5–25	418	57.0
25–29.9	273	37.2
>30	30	4.1
Mean (\pm SD)	24.4 (\pm 3.1)	
WHR		
Normal	351	47.6
Raised	386	52.4
Smoking		
Smoker	150	20.4
Quitted	217	29.4
Never-smoker	370	50.2
Smokeless tobacco		
Consumer	99	13.4
Quitted	77	10.4
Never-consumer	561	76.2

Table 2
Distribution of the study subjects by diabetes and lipid profile.

Diabetes and lipid profile	Frequency	Percentage
Duration of DM (years)		
0–5	323	43.8
6–10	199	27.0
11–15	118	16.0
>15	93	13.2
Mean (\pm SD)	8.26 (\pm 6.3)	
Hb1Ac level		
Hb1Ac < 7	165	22.4
Hb1Ac > 7	572	77.6
Comorbidities		
None	576	78.2
One	124	16.8
> One	37	5.0
Current treatment for DM		
MNT	79	10.7
OHA	353	47.9
OHA + Insulin	169	22.9
Insulin	136	18.5
Any dyslipidaemia		
Present	471	63.9
Absent	266	36.1
Total cholesterol (mg/dl)		
<200	481	65.3
>200	256	34.7
HDL (mg/dl)		
>40	463	62.8
<40	274	37.2
LDL (mg/dl)		
<160	555	75.3
≥ 160	182	24.7
TG		
<150	410	55.6
>150	327	44.4

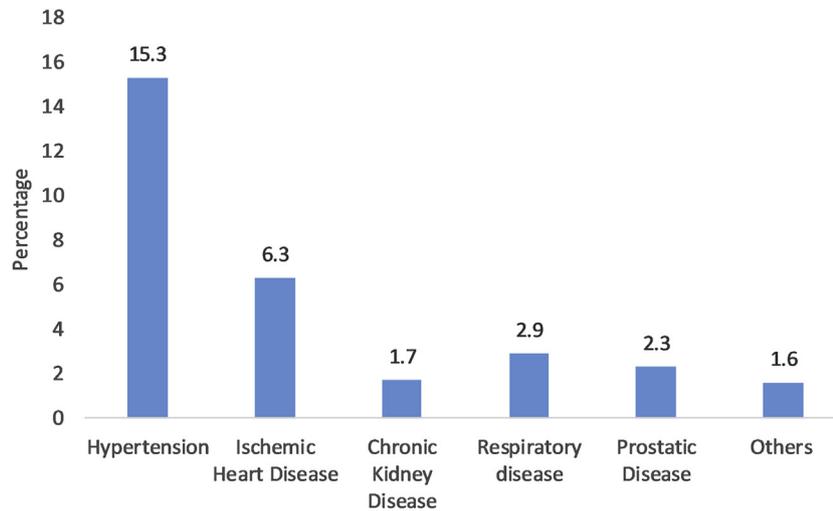


Fig. 1. Distribution of the patients by comorbidities.

assessed using chi-square test. Association of ED with dyslipidaemia was assessed using multivariable logistic regression adjusting for potential confounders. Odds ratio (OR) and 95% confidence interval of dyslipidaemia and individual lipid parameters were generated through multivariable logistic regression entering individual candidate predictor simultaneously with plausible confounders namely age, education, income, duration of diabetes and

glycaemic control status.

3. Results

Of the 813 participants who participated in the interview, 76 subjects answered, “No sexual activity” in the past 1 month and were excluded from further analysis. Table 1 shows the

Table 3
Association of age, duration of DM and complication status with ED.

Variable	No ED	Mild ED	Mild – Moderate ED	Moderate ED	Severe ED	P Value ^a
Age (years)						<0.001
21–40	55 (45.6%)	27 (23.7)	18 (15.8%)	13 (11.4%)	4 (3.5%)	
41–50	67 (33.7%)	51 (25.6%)	41 (20.6%)	30 (15.1%)	10 (5.0%)	
51–60	53 (23.6%)	35 (15.6%)	56 (24.9%)	55 (24.4%)	26 (11.6%)	
>60	29 (14.6%)	16 (8.0%)	32 (16.1%)	66 (33.2%)	56 (28.1%)	
Education						<0.001
Up to Primary	26 (34.2%)	7 (9.2%)	20 (26.3%)	18 (23.7%)	5 (7.0%)	
Secondary	27 (16.8%)	41 (24.7%)	24 (14.9%)	45 (28.0%)	24 (14.9%)	
High secondary	37 (25.3%)	21 (14.4%)	18 (12.3%)	37 (25.3%)	33 (22.6%)	
Graduate & above	111 (31.4%)	60 (16.4%)	66 (24.5%)	9 (10.6%)	23 (8.6%)	
Income						<0.001
<20000	36 (19.4%)	24 (12.9%)	38 (20.4%)	61 (32.8%)	27 (14.5%)	
20000–30000	98 (26.9)	61 (16.8%)	75 (20.6%)	79 (21.7%)	51 (14.0%)	
>30000	67 (35.8%)	44 (23.5%)	34 (18.2%)	24 (12.8%)	18 (9.6%)	
Duration of DM (years)						<0.001
0–5	100 (31.0%)	90 (27.9%)	52 (16.1%)	55 (8.0%)	26 (8.0%)	
6–10	56 (28.1%)	22 (11.2%)	45 (22.6%)	49 (13.6%)	27 (13.6%)	
11–15	29 (24.6%)	8 (6.8%)	31 (26.3%)	27 (22.9%)	23 (19.5%)	
>15	16 (16.5%)	9 (9.3%)	19 (19.6%)	33 (34.0%)	20 (20.6%)	
Comorbidities						0.657
None	156 (27.1%)	107 (18.6%)	113 (19.6%)	125 (21.7%)	75 (13.0%)	
One	33 (26.6%)	15 (12.1%)	25 (20.2%)	33 (26.6%)	18 (14.5%)	
> One	12 (32.4%)	7 (18.9%)	9 (24.3%)	6 (16.2%)	3 (8.1%)	
DM control						<0.001
Hb1Ac <7	66 (40.0%)	33 (20.0%)	27 (16.4%)	26 (15.8%)	13 (7.9%)	
Hb1Ac >7	135 (23.6%)	96 (16.8%)	120 (21.0%)	138 (24.1%)	83 (14.5%)	
Smoking status						0.369
Smoker	40 (26.7%)	24 (16.0%)	28 (18.7%)	40 (26.7%)	18 (12.0%)	
Quitted	53 (24.4%)	34 (15.7%)	48 (22.1%)	45 (20.7%)	37 (17.1%)	
Never-smoker	108 (29.2%)	71 (19.2%)	71 (19.2%)	79 (21.4%)	41 (11.1%)	
Smokeless tobacco						0.038
Consumer	25 (25.3%)	9 (9.1%)	15 (15.2%)	32 (32.3%)	18 (18.2%)	
Quitted	17 (22.1%)	16 (20.8%)	20 (26.0%)	14 (18.2%)	10 (13.0%)	
Never-consumer	159 (28.3%)	104 (18.5%)	112 (20.0%)	118 (21.0%)	68 (12.1%)	

^a p values were generated through chi-square test for assessing univariate association.

sociodemographic and anthropometric characteristics of the subjects. The mean (\pm SD) age of the patients was 52.8 ± 10.3 years. Information pertaining to a subject's diabetes and lipid profile are presented in Table 2. Overall 63.9% of the participants had at least one lipid parameter abnormal. The mean (\pm SD) duration of diabetes among the study subjects was 8.26 ± 6.3 years and uncontrolled diabetes based on HbA1c levels was found in 77.6% of participants. Comorbidities were found in 21.8% of subjects and the most prevalent comorbidity was hypertension (15.3%) followed by ischemic heart disease (6.2%) (Fig. 1).

Of the 737 men included in the analysis, 536 (72.7%) reported varying degrees of ED, 129 (17.5%) of them had mild ED, 147 (19.9%) had mild-to-moderate ED, 164 (22.3%) had moderate ED and 96 (13%) had severe ED. Table 3 illustrates the univariate association of patient characteristics with ED. The patients with diabetes and ED were significantly older ($p < 0.001$), less educated ($p < 0.001$), poorer ($p < 0.001$), had a longer duration of diabetes ($p < 0.001$) and reported poorer diabetes control ($p < 0.001$). Fig. 2 depicts an increasing trend of ED with increasing age and duration of diabetes and with decreasing income.

Dyslipidaemia ($p < 0.001$) was significantly associated with ED after adjusting for age, education, income, duration of diabetes and diabetes control. Diabetic patients with ED were 2.3 times (adjusted OR-2.3; 95% CI: 1.6–3.2) more likely to have dyslipidaemia in comparison to those with no ED. Although, individually each parameter of lipid—total cholesterol ($p < 0.001$), LDL ($p < 0.001$), HDL ($p < 0.001$) and TG ($p < 0.001$)—were also found to be associated with ED; however the odds ratios were greater with abnormality in the lipoproteins. The odds increased by approximately 3 fold (adjusted OR-2.97; 95% CI: 1.97–4.52) for an abnormal High Density Lipoprotein level and by 2.7 fold (adjusted OR-2.69; 95% CI: 1.65–4.37) for abnormal Low Density Lipoprotein (Table 4).

4. Discussion

Our study confirmed the presence of established risk factors for ED including older age, lower educational attainment, co-existing illnesses, longer duration of diabetes and poor diabetes control in Bangladeshi diabetic patients. The study confirms dyslipidaemia as a significant risk factor of ED among these patients. The association of ED was found to be stronger with lipoprotein level abnormality particularly.

The association between diabetes and dyslipidaemia in our study is consistent with the finding of the ED study of Italian men [26]. The dyslipidaemia seen in patients with diabetes—atherogenic dyslipidaemia—have a distinct pattern and is characterized by higher triglyceride and abnormal lipoproteins level, particularly lower level of HDL [27]. This form of dyslipidaemia includes two criteria for the diagnosis of metabolic syndrome which has been demonstrated as a risk factor for ED [28]. This association between ED and lipoprotein abnormality found in our study, may represent a big picture that the atherogenic dyslipidaemia is an intermediate factor of causal link between ED and metabolic syndrome. Study by Esposito et al. showed a higher prevalence of ED among men with the metabolic syndrome [29]. Discussion on the link between metabolic syndrome and ED is beyond the remit of this study; however, it is worth exploring the link in future research. Despite obesity being an established factor, it did not appear as significant predictor in our study. This is probably due to low prevalence of obesity ($BMI > 30 \text{ kg/m}^2$) in our study population, which is as low as 4.1%.

The higher occurrence of both ED and dyslipidaemia is evident in Bangladeshi men with diabetes. Reason for higher dyslipidaemia may be rooted in the dietary practice of the population; where high carbohydrate rich diet is traditionally popular. Our findings may have direct implications in the treatment of ED, particularly in a

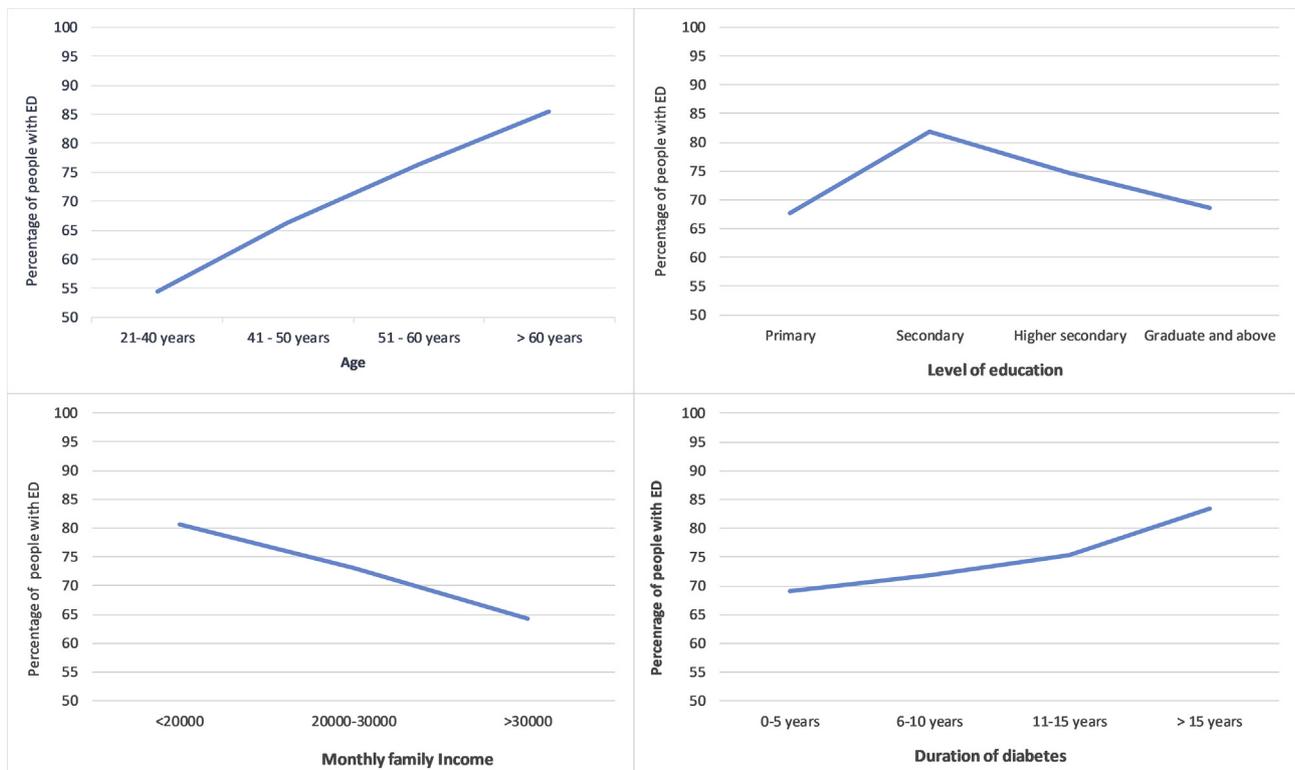


Fig. 2. Distribution of ED by patient characteristics.

Table 4
Association of lipid profile of the patients with ED.

Variable	No ED Frequency (%)	ED Frequency (%)	Adjusted OR (95% CI) ^a	P value
Dyslipidaemia				
Normal	152 (72.4%)	58 (27.6%)	Referent	
Dyslipidaemia	178 (33.8%)	349 (66.2%)	2.26 (1.6–3.2)	<0.001
Cholesterol				
Normal	149 (31.0%)	332 (69.0%)	Referent	
Raised	52 (20.3%)	204 (79.7%)	1.75 (1.19–2.57)	0.004
HDL				
Normal	164 (35.4%)	299 (64.6%)	Referent	
Low	37 (13.5%)	237 (86.5%)	2.97 (1.95–4.52)	<0.001
LDL				
Normal	176 (31.7%)	379 (68.3%)	Referent	
Raised	25 (13.7%)	157 (86.3%)	2.69 (1.65–4.37)	<0.001
TG				
Normal	137 (33.4%)	273 (66.6%)	Referent	
Raised	64 (19.6%)	263 (80.4%)	1.83 (1.27–2.64)	<0.001

^a Adjusted for age, education, income, duration of diabetes and diabetes control.

population with such high prevalence of dyslipidaemia. Correction of dyslipidaemia may significantly improve endothelium-mediated responses in the arteries of corpus cavernosum in patients with ED and thus may result in improved erectile function [30]. The treatment may also result in increased corporeal blood flow and flow-mediated endothelium-dependent dilatation by improving endothelial function [31]. Furthermore, statins are found to increase vascular sensitivity to sildenafil, a popular treatment for erectile dysfunction, improved the efficacy of oral sildenafil in men who did not initially succeed [32].

One limitation of the study is that the study subjects were recruited from a referral endocrinology centres that may result in pooling of patients with longer diabetes duration, with poorer glycaemic control and even with more complications. We used HbA1c levels, which is typically only relevant for a few months as a surrogate for overall diabetes control. Contrastingly, the strengths of the study is the use of a validated measure of erectile dysfunction.

In conclusion, dyslipidaemia appeared as a significant predictor of ED among T2DM patients. More specifically abnormal lipoprotein level poses greater risk of ED among diabetic subjects.

Disclosure

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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