



Factors Associated with Ophthalmic Complication among Diabetic Patients aged 40 Years or More: Findings of a Hospital-based Study

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Abstract:

Background: Estimates in 2017 indicate that in South-East Asian region, 8.5% of the adult population (82 million people) aged 20-79 years are diabetic. Diabetic Retinopathy is most common among the ophthalmic complications being the fifth leading cause of global blindness. Our objective was to find out the socio-demographic and varied risk factors related to the development of ophthalmic complications in Bangladesh.

Methodology: We conducted a cross sectional study among diabetic patients attending the out-patient department of Bangladesh Institute of Health Science General Hospital from July 2017 to June 2018. The study population included 289 diabetic patients aged ≥ 40 years. The impact of age, physical exercise, duration of diabetes, fasting blood glucose level, treatment with insulin and co-morbidity with hypertension, dyslipidaemia and nephropathy on the likelihood of developing ophthalmic complications was assessed using binary and multivariable logistic regression.

Results: The average age of the patients was 60.2 ± 9.3 years and 181 (63.0%) patients were male. Most of the respondents (97.9%) were suffering from type 2 diabetes. Participants have been suffering from diabetes for on an average of 10.9 ± 7.9 years. From multivariable logistic regression we found that those who had been suffering from diabetes for over 10 years, were almost 4 times more likely to have ophthalmic complications. Patients aged more than 60 years had 3 times greater odds for having ophthalmic complications when adjusted for other variables.

Conclusion: Patients with older age and greater duration of diabetes are more susceptible to ophthalmic complication, thus public health interventions must be formulated accordingly.

Introduction

Diabetes mellitus or simply diabetes, is a chronic condition that occurs when there are raised levels of glucose in the blood because the body cannot produce any or enough of insulin or use insulin effectively. The lack of insulin or the inability of the cells to respond to insulin results in high levels of blood

glucose or hyperglycaemia, the hallmark of diabetes. Hyperglycaemia, if left unchecked for a long term, can cause damage to various body organs, leading to the development of disabling and life-threatening health complications such as cardiovascular disease, neuropathy, nephropathy, and eye disease - leading to retinopathy and blindness.¹

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Estimates in 2017 indicate that in the South-East Asian region, 8.5% of the adult population or approximately 82 million people aged 20-79 years are diabetic. With 1.1 million deaths in 2017 (14% of all mortality), the region had the second-highest number of deaths attributable to diabetes. Globally, Bangladesh is one of the top 10 high-burden countries with diabetes where an estimated 8.4 million people have diabetes and another 7.8 million have pre-diabetes.¹ A meta-analysis showed that the prevalence of diabetes among adults had raised dramatically from 4% in 1995 to 2000, 5% in 2001 to 2005 and 9% in 2006 to 2010.² The prevalence is significantly higher in the urban population compared to rural populations and is skewed towards female and people with higher income and better education.

Multiple ocular diseases are associated with diabetes, which may lead to vision loss. Diabetic Retinopathy is most common among ophthalmic complications. It is the fifth leading cause of global blindness. Retinopathy is an ocular manifestation of the systemic disease which affects up to 80% of all patients with diabetes.³ Studies in different part of the world revealed that complications of diabetes including ophthalmic complications are related with the type of diabetes, duration of the disease, age of the patient, metabolic syndrome including abdominal obesity, prothrombotic state, proinflammatory state, ethnicity, glycaemic control, type of treatment and co-morbidities with other diseases such as hypertension and dyslipidaemia.⁴⁻⁷ In a cross-sectional study in a selected eye outpatient clinic in Bangladesh from

July to October 2014 among 100 diabetes patients presented with eye complaints, it was found that cataract was the predominant complications: 22% patient had unilateral and 20% had a bilateral cataract. 29% patient had retinopathy and rest had refractive error.⁸ In another observational non-interventional cross-sectional study between June to September 2013 at 80 secondary care and 20 tertiary care hospitals in Bangladesh, among 2092 Type 2 Diabetes patients, eye complications were found in 21.7% of cases.⁹

Considering the availability of diabetic patients with the existence of different complications, the present study was planned at Bangladesh Institute of Health Sciences (BIHS) general hospital outpatient department (OPD) to find out the socio-demographic and other risk factors related to the development of ophthalmic complications.

Methodology

Study Design

This study was conducted following cross-sectional design among diabetic patients attending the outpatient department of Bangladesh Institute of Health Science General Hospital located at Durussalam, Mirpur in Dhaka city from July 2017 to June 2018

Study Population

Our study population included diabetic patients aged 40 years or more. For the selection of study participants, we followed the predetermined inclusion and exclusion criteria (**Table 1**).

Table 1. List of inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> • Diabetic patients of both sexes aging 40 years or more • Provided consent and willing to undertake a 20 minutes interview 	<ul style="list-style-type: none"> • aged less than 40 years • Severely ill patients • Psychologically abnormal patients

Sample Size

We calculated sample size following this formula:

$$n = \frac{z^2 pq}{d^2}$$

Where, n = Desired sample size.

Z = Standard normal deviate, critical value of normal distribution was 1.96.

P = prevalence of ophthalmic complications among diabetic patients from a previous study on a hospital based population in Bangladesh²³ was 21.7%.

$$q = (1-p) \text{ i.e. } = (1-0.217) = 0.783$$

d = Confidence level at 95%, was 0.05

Thus, required sample size was = $(1.96)^2 (0.217) (0.783) / (0.05)^2 \sim 261$ participants. To avoid non-response, 10% of the calculated value was added and thus we collected information from 289 participants.

We selected these participants using systematic random sampling technique. On an average 150 patients with diabetes used to report to the outpatient department of Bangladesh Institute of Health Science general hospital. It was planned to interview 10 patients on every working day. So, every $(150 \div 10)$ 15th patient was selected for an interview. In the case of a patient not consistent with inclusion criteria, the next patient was selected.

We used a pre-tested semi-structured questionnaire to collect information. The questionnaire was pre-tested among 12 patients in a diabetes centre located at a nearby area for clarity, accuracy, ambiguity and was modified accordingly before collecting information from the study participants. After explaining the purpose, objectives, perspectives, benefits, risks, and burdens of the study to the respondent (patients and companions) written consent was obtained and then relevant information were collected by the researcher himself through face to face interview by asking questions in Bengali maintaining privacy as much as possible. Each day approximately 10 participants were invited. Height and weight of the patient, type of diabetes, glycaemic status and treatment of diabetes were noted in the checklist from the diabetes guide book of the respondents. It was made clear to the respondents that they were at liberty to answer and not to answer any question. They were assured that under no circumstance finding of the interview and other information would be disclosed to any unauthorized person or authority.

Ethical permission:

We obtained ethical approval of the research protocol from the Armed Forces Medical Institute under Directorate General Medical Services. Following that, a formal application with all the relevant papers was submitted to the director of Bangladesh Institute of Health Science General Hospital seeking permission to collect data from the Outpatient Department of the hospital. The director of the hospital gave written permission to collect data. No financial incentive was offered to the participants.

Data Analysis

Data analysis was done by computer with the help of “Statistical Package for Social Science” (SPSS software, version 19). Descriptive statistics like

frequency distribution, mean, range, standard deviation etc. were calculated by SPSS program. For inferential statistics, tests such as Chi-square test, Binary logistic regression, Multinomial logistic regressions were done to find out any association between different variables. Initially, categorical variables were described as number and proportions for socio-demographic variables and co-morbidities including other risk factors for ophthalmic complications. To determine the association between selected variables, chi-squared (χ^2) test was done. The impact of age, physical exercise, personal habits, duration of diabetes, fasting blood glucose level, treatment with insulin and co-morbidity with hypertension, dyslipidaemia and nephropathy on the likelihood of developing ophthalmic complications was assessed using binary logistic regression. Then multivariable logistic regression models were fitted to adjust for potential confounding variables.

Results

We collected information from 289 patients. The average age of the patients was 60.2 ± 9.3 years and 181 (63.0%) patients were male. Majority of the patients (73.7%) were living in an urban area. The socio-demographic characteristics of the respondents are given in Table II.

Table II. Socio-demographic characteristics

Variables	
Age (years)	60.2±9.3
Sex (Female, %)	37
Level of formal education	
Primary education	76 (26.3%)
Secondary or equivalent	53 (18.3%)
Higher secondary or equivalent	44(15.2%)
Graduation and above	68 (23.6%)
Area of residence	
Urban	213 (73.7)
Rural	43 (14.9)
Semi- urban	33 (11.4)
Occupational status	
Unemployed	24 (8.3)
Service Holder	32 (11.0)
Retired	112 (38.8)
Business	45 (15.6)
Home Maker	76 (26.3)
Monthly income (BDT)	
≤ 20000	74 (25.6)
20001 - 40000	114 (39.4)
40001 - 60000	72 (24.9)
> 60000	29 (10.0)

Most of the respondents (97.9%) were suffering from type 2 diabetes and others (2.1%) were suffering from type 1 diabetes. Among all the participants, about half of them had normal body weight (47.4%), almost 40.0% of the respondents were overweight and 11.4% were obese. They have been suffering from diabetes for an average of 10.9±7.9 years. About forty percent of the patients developed diabetes within 45 years of age. The mean (±SD) age onset of diabetes was 49.1±9.4 years. The clinical characteristics of the patients are given in Table III.

Table III. Clinical characteristics

Variables	n= 289
BMI category (%)	
Underweight	1.4
Normal Weight	47.4
Over Weight	39.8
Obese	11.4
Average age of onset of diabetes (years)	49.1±9.4
Onset of diabetes (%)	
40-45 y	40.1
46-50 y	20.8
51-55 y	13.8
56- 60 y	12.1
>61 y	13.1
Duration of diabetes	
<10 years	56.4
>10 years	43.6
Presence of ophthalmic complication (%)	
No complication	60.5
Single complication	35.3
2 or more complications	4.2
Presence of co-morbidities (%)	
No co-morbidity	15.2
Single co-morbidity	27.0
Two co-morbidities	37.7
Three or more co-morbidities	20.1
Fasting blood glucose	
≤ 6.0	15.4
> 6.0	84.6
2 Hours ABF glucose level	
≤ 8.0	15.7
> 8.0	84.3
HbA _{1c} level	
≤ 7.0	18.6
> 7.0	81.4
Follow up visit to a clinician (%)	
No regular follow-up	29.4
Once in a month	9.0
Once in every 3 Months	45.3
Once in every 6 Months	11.4
Once per year	4.9

Out of 289 respondents, 184 patients (63.7%) had a positive family history of diabetes. Among them, 175 (60.6%) had diabetes in 1st blood relatives. Total 131 patients (45.3%) were treated with oral hypoglycaemic agents and 119 patients (41.2%) received a combination of oral hypoglycaemic agents and Insulin. Among 289 diabetes patients, 245 (84.8%) patients had one or more co-morbidities like hypertension, dyslipidaemia, nephropathy etc. Hypertension was present in 198 patients (mean duration 8.4±6.8 years), dyslipidaemia in 175 patients (mean duration 4.5 ±4.1 years) and nephropathy was present 65 patients (mean duration 3.4±3.3 years).

Among 289 respondents, 114 (39.5%) patients had ophthalmic complications. Ninety-three patients (32.2%) had a complication with cataract only, 7 had cataract with retinopathy and 2 had cataract with glaucoma. Five patients had retinopathy only and 2 had glaucoma only. Rest of the patients has mixed complications. Table 4 presents the characteristics related to ophthalmic complications.

Table IV. Patient Characteristics related to ophthalmic complication

Variables	n= 114	p
	Ophthalmic complication present	
	Number (%)	
Age (y)		
≤ 60	36 (31.6)	
> 60	78 (68.4)	0.001
Sex		
Male	72 (63.2)	
Female	42 (36.8)	0.881
BMI category (%)		
Underweight	3 (2.6)	
Normal Weight	58 (50.9)	
Over Weight	42 (36.8)	
Obese	11 (9.6)	0.318
Habit of Physical Exercise(days/week)		
≤ 5	74 (64.9)	
> 5	40 (35.1)	0.038
Age of onset of diabetes		
≤ 45	47 (41.2)	
46 - 50	21 (18.4)	
51- 55	14 (12.3)	
56 - 60	14 (12.3)	
> 60	18 (15.8)	0.757

Table IV. (Contd.)

Variables	n= 114 Ophthalmic complication present Number (%)	<i>p</i>
Duration of diabetes		
≤ 10	39 (34.2)	0.001
> 10	75 (65.8)	
Fasting blood glucose (mmol/l)		
≤ 6.11	24 (21.1)	0.046
> 6.11	88 (77.2)	
Require insulin treatment		
Treatment without Insulin	47 (41.2)	0.048
Treatment with Insulin/ Insulin Combination	67 (58.8)	
Co-morbidities present		
Hypertension	88 (77.2)	0.010
Dyslipidaemia	68 (59.6)	0.807
Nephropathy	40 (35.1)	0.001

We have used unadjusted and adjusted logistic regression to explore the association of ophthalmic complication with several factors. The results are given in Table V.

Table V. Results from multivariable regression model

Factors	Adjusted OR	<i>p</i> -value
Age		
>60 y	3.314	.000
<60y		
Physical Exercise		
(> 5days/week)	1.574	.113
(< 5days/week)		
Fasting Blood Glucose Level		
(≥ 6.11)	0.568	.133
(≤ 6.11)		
Duration of Diabetes		
(>10 Years)	3.736	.000
(<10 Years)		
Presence of Co-morbidities	1.465	.398

From multivariable logistic regression, we found that both age and duration of diabetes were positively associated with occurring of ophthalmic complication among our study participants. Those patients who had been suffering from diabetes for over 10 years, were almost 4 times more likely to have ophthalmic complications. Furthermore, patients with age more than 60 years had 3 times greater odds for having ophthalmic complications when adjusted for other variables.

Discussion:

Our study objective was to identify the socio-demographic and other risk factors including comorbidities related to the development of ophthalmic complications among patients coming to a tertiary care hospital situated in Dhaka Bangladesh. We found that higher age and longer duration of diabetes were significantly associated with the occurrence of ophthalmic complications among this study participants.

Diabetes is one of the largest health emergencies of the 21st century and globally, high blood glucose is the third highest risk factor for premature mortality, after high blood pressure and tobacco use.¹⁰ Bangladesh is one of the top 10 high-burden countries with diabetes where an estimated 8.4 million people have diabetes and another 7.8 million have pre-diabetes.¹ Unfortunately, despite all the treatment presently available, the outcome for patients with diabetes remains disappointing. Long term complications of diabetes still cause significant morbidity and mortality.

Several studies have reported that complication of diabetes including ophthalmic complications are associated with the type of diabetes, duration of the disease, age of the patient, metabolic syndrome including abdominal obesity, ethnicity, glycaemic control, type of treatment and co-morbidities with other disease such as hypertension and dyslipidaemia.⁴⁻⁷

A range of ocular diseases is associated with diabetes, which often leads to vision loss. Diabetic retinopathy is the most common ophthalmic complications. Other ocular conditions directly associated with diabetes are - cataract, anterior ischemic optic neuropathy, diabetic papillopathy and ocular movement disorders. Diabetes is a known risk factor for the development of glaucoma

and ocular ischemic syndrome and it is considered as a possible risk factor in other ocular conditions such as retinal vein occlusion, retinal arteriolar emboli, retinal artery occlusion and some corneal diseases.¹¹

In the present study the average age of the respondents was about 60 years, which is relatively higher than the contemporary and similar studies. In a 2013 study, Latif et al.⁹ found the mean age was 51.3 ± 11.0 years. In another study in a similar setting in 2012 by Sultana et al.¹², the mean age was 53.2 ± 10.5 years. The reason for the higher average age might be due to the selection criteria of the respondents. Only diabetes patients above 40 years were included in the present study and at the same time, the average life expectancy of Bangladeshi people has also increased. For a similar reason, a higher proportion of older people has also been found in the present study. The proportion of respondent age up to 45 years was 5.5% which is less than what was found (8.2%) in the study by Ahmed et al.¹³ In the present study proportion of respondents between 46-65 years was 65.8% and above 65 years was 28.7% which was 74.6% and 17.2% respectively in the study by Ahmed et al.¹³

Among 289 diabetes patients in the present study, 97.9% had type 2 and rest 2.1% had type 1 diabetes. This finding is consistent with other studies from the country.^{12,13} In the current study, the mean age of onset of diabetes was 49.1 ± 9.4 years. About forty percent of the respondents developed diabetes within 45 years of age. In the study by Latif et al. [9] the mean age of diabetes onset was 42.1 ± 14.2 years which is less than the findings of the present study. The finding in the study by Sultana et al.¹² was similar to the present study and it was 46.9 ± 9.9 years. The variation might be due to the selection criteria of which varied from study to study.

The mean duration of diabetes among the respondents was 10.9 ± 7.9 years in the present study. In the study by Latif et al.⁹ the mean duration of diabetes was 7.9 ± 10.4 . Sultana et al.¹² found the mean duration of diabetes as 6.3 ± 5.6 years and 80% of the respondents had a duration up to 10 years. The finding in the present study revealed that the mean duration was much longer and the proportion of respondents with longer duration was more than previous studies. This

might be attributed to the selection criteria in the present study. Diabetes patients above 40 years participated in the present study. Moreover, the proportion of elderly participants was higher in the present study.

The presence of selected co-morbidity was studied in the present study. The selected diseases were: hypertension, dyslipidaemia, nephropathy, heart disease and anaemia. The presence of the above co-morbidities was recorded from the diabetes guide book of the respondents as diagnosed by doctors. Only nephropathy was recorded basing on the serum creatinine level when it was found persistently higher than normal level (> 1.4 mg/dl) and management was given by a physician.

A higher proportion of hypertension (68.5%) was found in this study as compared to the study finding by Latif et al. [9] where hypertension was found in 56.4% of patients. Nath et al.⁸ found 71% of the T2DM patients had hypertension. In the DiabCare Bangladesh, 2008 study hypertension was found in 47% of diabetes patients and in 1998 study this percentage was 35.8% of T2DM patients which indicated a gradual increase in this co-morbidity in Bangladeshi patients.⁹ Kahloun et al. [14] in their study in Tunisia found hypertension as co-morbidity in 37.5% of diabetic patients and in the study by Soleymani et al.¹⁵ in Iran this percentage was 22.1%. The above finding indicated that the prevalence of hypertension among diabetes patients are increasing in Bangladesh and it is much higher than other countries like Iran and Tunisia.

Presence of heart disease was found in 12.8% of the respondents in the present study which was mainly ischemic heart disease or a history of myocardial infarction for which the patient was under treatment. In most of the studies among patients suffering from diabetes and/or its complications, heart disease has also been leveled as a macrovascular complication of diabetes rather than co-morbidity. In the study by Latif et al. [9], myocardial infarction was found in 5.2% of patients and in the study by Sultana et al.¹² myocardial infarction was found in 6.0% of respondents. These proportions are less than that in the present study. The reason might be that the IHD without myocardial infarction cases were excluded in those studies. Or it might be due to the increase in the

prevalence of heart diseases among diabetes patients in Bangladesh.

In the current study, 39.5% of patients had one or more of the selected ophthalmic complications: most common complication found was cataract (36.0%) followed by retinopathy (5.2%). Glaucoma was present in 1.7% cases. In a study by Nath et al.⁸ cataract was found as the predominant complication: 22% patient had unilateral and 20% had bilateral cataract. 29% had retinopathy and the rest of the diabetic patients had a refractive error. Eye complication was found in 21.7% of T2DM patients in the study by Latif et al.⁹ cataract (9%) and nonproliferative diabetic retinopathy (8.7%) were most common. In the study by Sultana et al.¹² cataract was found in 19% and diabetic retinopathy was found in 14% of diabetic patients. The study by Latif et al (2011) revealed that cataract (12.9%) was the most common eye complication in diabetic patients and advanced diabetic eye diseases were found in 2.1% of study subjects. In DiabCare Bangladesh study 1998, the prevalence of ophthalmic complications among diabetic patients were: cataract 13%, advanced diabetic eye disease 0.7%, retinopathy 10.8%. The study by Kahloun et al.¹⁴ found that cataracts (32.6%), open-angle glaucoma (2.7%), diabetic retinopathy (26.3%) and diabetic macular oedema (8.7%) were present as complication among diabetic patients in their study. In the present study, the proportion of cataract was higher which might be attributed to the older age of the study subjects but the proportion of retinopathy was fairly lower than those found in other studies. An infrequent and irregular ophthalmic examination might be the reason for this finding. Nath et al.⁸ conducted the study at eye outdoor of a hospital which might be the reason for a higher percentage of ophthalmic complication.

The present study found that 56.9% of the respondents aged more than 60 years developed an ophthalmic complication ($p < 0.001$). A similar finding was observed in the study by Kahloun et al.¹⁴ in Tunisia, where visual impairment in diabetic patients was significantly associated with age 60 years or more ($p < 0.001$). Association of age with the development of retinopathy was also observed in the study by Ahmed et al.¹⁶ Nadarajan et al.¹⁷ found that the prevalence of diabetic retinopathy was more among more than 60 years age group patients ($p = 0.032$).

In this study, we found that after adjusting for several possible predictors, only the age of the respondents and duration of diabetes mellitus were the significant risk factors for developing ophthalmic complications. It was revealed that patients with diabetes for more than 10 years and patients with age > 60 years were almost 4 times and 3 times more likely to develop ophthalmic complications respectively. Kahloun et al.¹⁴ found similar results in Tunisia. They found that duration of diabetes for more than ten years was associated with visual impairment in diabetic patients ($p < 0.001$). Mohan et al. observed a high prevalence of complications related to Type 2 diabetes in patients with long-standing diabetes (9.9 ± 5.5 years) [5]. The study by Latif et al.⁹ also observed that the duration of type 2 diabetes and age were strongly correlated with selected diabetes complications. Not only in the developing world, but diabetic retinopathy is also one of the key reasons for blindness in 20-74 years aged adults in the developed nations like United States of America.¹⁸ Type 2 DM has been associated with a greater percentage of patients with visual loss.¹⁹ Total duration and control of diabetes has been found to be significantly related to the incidence of diabetic retinopathy. As per Wisconsin epidemiologic study of diabetic retinopathy (WESDR),²⁰ the general 10-year incidence of DR was 74% and 64% of people with baseline DR developed more severe DR.²¹

The findings of this study need to be interpreted in light of the study limitations. Due to the cross-sectional observational nature of the study, it was not possible to exclude completely the effect of selection bias. The patients attending the hospital may not be representative of the country as a whole. As the patients need to pay for screening for eye complication, there is a possibility that the actual number of patients with ophthalmic complication could not be identified.

Conclusion:

From this study this is evident that patients with older age and greater duration of diabetes are more susceptible to ophthalmic complication. As life expectancy is increasing in the country, we can only assume that the prevalence of diabetes and its associated debilitating complications will also increase in the future, which will impose a serious public health burden on our already fragile and

resource-constrained health system. Public health policy and interventions must be formulated to delay the onset of diabetes to reduce the burden of such enervating chronic condition.

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Author's contribution

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Quazi Md Rashid-Un-Nabi, Mostafa A. Sumon and Sk Akhtar Ahmad. The first draft of the manuscript was written by Quazi Md Rashid-Un-Nabi and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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