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Assessment of BMI, Duration of Diabetes, Fasting lipids, S. Creatinine, and Microalbuminuria in Glycemic Control: A 10 year's follow-up study

Mohammad Zubair[1,2]✉, Marai Mohammed Alamri[3]

Diabetes is directly associated with various life-threatening diseases like renal failure and cardiac disruption. Similarly, hypertension is accompanied by diabetes, which can lead to microalbuminuria or diabetic nephropathy. Therefore, the study has aimed to assess BMI, duration of diabetes, fasting lipids, serum creatinine, and microalbuminuria to control glucose levels. A cross-sectional analysis of 500 type 2 diabetic subjects was conducted among North Indian population visiting endocrine clinic of Rajiv Gandhi Centre for Diabetes & Endocrinology (RGCDE), Faculty of Medicine of J. N. Medical College Hospital, Aligarh Muslim University Aligarh, India. The patients reported to endocrine clinic in the year 1999–2012. The findings have shown that there is a significant association between HbA1c and neuropathy (p = 0.03), LDL-C and HbA1c (p = 0.031), triglyceride and HbA1c (p = 0.000) and type of medication and HbA1c (p = 0.014). However, there was no significant correlation between diabetes duration and glycemic control.

INTRODUCTION

Diabetes is associated with a group of metabolic diseases and is characterized by hyperglycemia. It usually occurs as a result of insulin action or insulin secretion. Chronic hyperglycemia of diabetes can result in long-term dysfunction, damage and failure of heart, kidneys, eyes, blood vessels and nerves. There are several pathogenic processes that are involved in the development of diabetes. It results in the destruction of β-cells of pancreas, causing certain abnormalities that further result in the resistance of insulin action. Usually, such resistance in insulin action is due to the inadequate insulin secretion as well as due to minimum tissue responses to insulin. In most of the cases, impairment of insulin secretion and flaws in insulin action coexist in the same patient[1]. That is why; it is often unclear that which abnormality is causing hyperglycemia.

Diabetes long-term complications include nephropathy, leading to renal failure, potential loss of vision, cardiovascular symptoms, amputations, and sexual dysfunction. Usually, diabetic patients are accustomed to hypertension as well as abnormalities of lipoprotein metabolism. There are two major cases of diabetes. In the first case, the deficiency of insulin secretion is identified. Whereas, in second case, the cause of diabetes is focused due to the combination of resistance in insulin action and an unsatisfactory insulin secretory response. In second case, a degree of hyperglycemia is enough to cause various functional changes, and for so can result in late detection of diabetes[2]. Meanwhile, it is possible that the abnormality in carbohydrate metabolism is demonstrated by the help of measuring plasma glucose in state of fasting.

Type 2 diabetes mellitus is also referred as adult-onset diabetes, usually comprises of people, who have insulin resistance and have minimum insulin deficiency. People with this type of diabetes are mostly obese to some degrees. Moreover, ketoacidosis seldom occurs among patients, and this disease is mostly linked with the stress of another illness[3]. This type of diabetes may go undetected for a long time before the symptoms starts to show up. Such form of diabetes gradually develops with the increase in obesity, age, and lack of physical activity. Mostly, it is found among women with gestational diabetes mellitus (GDM) or people with hypertension. When it comes to GDM in most cases, the issue resolves once the delivery is done, but the possibility of unrecognized glucose intolerance may occur and such possibility cannot be ignored easily.

Immune-mediated diabetes usually occurs due to autoimmune destruction of β-cells in pancreas. Furthermore, in this sort of diabetes, the rate of destruction may vary. Usually, destruction of β-cells is rapid, when it comes to infants and children as compared to adults. In the state of fasting, level of hyperglycemia may increase abruptly due to an infection or when stress is taken. Whereas, adults may succeed in preventing ketoacidosis for many years that means that they will solely depend on insulin for survival. In idiopathic diabetes, the patients are having permanent insulinopenia and are at risk of ketoacidosis. But, this type of diabetes is only found among patients, who have Asian or African ancestry[4]. In this form of diabetes, patients usually suffer from episodic ketoacidosis and exhibit insulin deficiency from time to time.

There are such cases as well, where people have higher blood glucose level; but still they do not meet the criteria of diabetes. Such

[1]PhD(Micro), PDF(Medicine), MRSB(U.K.). Assistant Professor, Department of Medical Microbiology, Faculty of Medicine, University of Tabuk, Tabuk 71491, Kingdom of Saudi Arabia; [2]Former DSK-PDF, Rajiv Gandhi Centre for Diabetes & Endocrinology, Faculty of Medicine, J. N. Medical College Hospital, Aligarh Muslim University Aligarh, India; [3]Department of Surgery, Faculty of Medicine, University of Tabuk, Tabuk, Kingdom of Saudi Arabia
✉*Corresponding author:* Dr. Mohammad Zubair
(mohammad_zubair@yahoo.co.in), ORCID ID: 0000-0002-5787-7845

Table 1 Baseline characteristic of participants

N =500	Total	HbA1c <6.9		HbA1c ≥ 6.9		P value
	N	N	%	n	%	
Male	205	31	38.7	174	41.8	0.782
Female	291	49	61.2	242	58.1	
Duration of Diabetes(years)						
≤15	184	29	36.2	155	36.5	0.839
>15	316	52	65.0	264	63.4	
Neuropathy	500					
Absent	439	63	45.0	376	90.3	0.03
Present	61	18	22.5	43	10.3	
LDL-C (mg/dl)						
≤100	176	37	46.2	139	33.4	0.031
>100	324	44	55.0	280	67.3	
Triglycerides (mg/dl)						
≤200	426	69	86.2	357	85.8	0.000
>200	74	12	15.0	62	14.9	
BMI (kg/m^2)						
Obese ≥25	254	41	51.2	213	51.2	0.172
Overweight (23—24.9)	86	20	25.0	66	15.8	
Normal (18.5—22.9)	129	17	21.2	112	26.9	
Lean (<18.5)	31	3	3.7	28	6.7	
CAD	62	13	16.2	49	11.7	0.506
S. Creatinine						
>0.6—≤1.2)	263	39	49.0	223	53.6	0.401
>1.2	196	41	51.5	196	47.1	
Type of Medication						
Metformin Only	87	15	18.7	72	17.3	0.014
Sulfonylurea Only	27	11	13.7	16	3.8	
Mixed Oral	145	23	28.7	122	29.3	
Insulin only	42	18	22.5	24	5.7	
Insulin+oral	190	13	16.2	177	42.5	

LDL:low-density lipoproteins, CAD: Coronary artery disease, Mixed Oral medications: (Metformin, Sulfonylureas, Thiazolidinediones & Ecosprin), BMI: Body mass index.

people were accustomed to have impaired fasting glucose (IFG). People with IFG are pre-diabetes and are at high risk of developing diabetes. IFG is mostly associated with obesity, low cholesterol, and hypertension[5]. Therefore, exercises are resulted in 5-10% loss of body weight and ensured delay in the development of diabetes.

The injurious effects of hyperglycemia are divided into macrovascular complications and microvascular complications. It is; therefore, essential for the physicians to understand the relation between diabetes and vascular disease. The most common form of microvascular complication of diabetes is diabetic retinopathy. It is responsible for the rapid growth in cases that are solely associated with blindness. Microvascular complications usually depend on the severity and duration of hyperglycemia. As per study, a person with type 1 diabetes would show an evidence of retinopathy within 20 years of diagnosis; whereas, retinopathy will begin to develop as early as 7 years in a patient with type 2 diabetes[1]. Furthermore, the complications that are associated with macrovascular are coronary artery disease, stroke and peripheral arterial disease.

Microalbuminuria is one of the first symptoms of kidney diseases, caused by diabetes mellitus. It is discovered, when the albumin level in the urine exceeds 30 mg per 24 hours. Microalbuminuria test is helpful for diagnosing certain symptoms of renal diseases. Progression to diabetic nephropathy can be prevented with early treatment of microalbuminuria. Microalbuminuria is of utmost importance as it plays a vital role in clinical finding. Moreover, it is not only associated with progression to overt proteinuria, but also cardiovascular events. Additionally, diabetes lowers good cholesterol and raises the triglyceride and bad cholesterol levels. Moderately, high levels of cholesterol and hypertension is a fatal combination for arteriosclerotic cardiovascular disease and diabetic nephropathy. Chronic hyperglycemia condition causes major malfunctioning and impairment of many organs like the heart, kidney, blood vessels and the eyes[6]. Tissues that are most unprotected from the prolonged plasma glucose levels include β-cells of pancreas and vascular endothelial cells.

Body Mass Index is a value that is calculated by taking the weight of the body and dividing it with the square of the body weight and is expressed in units of kg/m^2. It simply means that if an individual's BMI is between 18-25, then the person is in a safer zone. If the BMI is between 25-30, the individual is considered overweight, and if the BMI is above 30, the person is in the danger zone and is considered obese. BMI and physical inactivity are independent risk factors in the development of type 2 diabetes mellitus. The study aims to assess BMI, duration of diabetes, fasting lipids, serum creatinine, and microalbuminuria to control glucose levels.

MATERIAL AND METHODS

A cross-sectional analysis of 500 type 2 diabetic subjects was conducted among North Indian population visiting endocrine clinic of Rajiv Gandhi Centre for Diabetes & Endocrinology (RGCDE), Faculty of Medicine of J. N. Medical College Hospital, Aligarh Muslim University Aligarh, India. The patients reported to endocrine clinic in the year 1999–2012. Type 2 diabetes was defined according to the expert

Table 2 Risk Factors associated with BMI after adjustment

	Obese [≥25 kg/m^2]	Over weight [23-24.9 kg/m^2]	Normal [18.5-22.9 kg/m^2]	Lean [<18.5 kg/m^2]
N	**254 (50.8%)**	**86 (17.2%)**	**129 (25.8%)**	**31 (6.2%)**
Gender distribution				
Male	83 (32.6%)	43 (50%)	64 (49.6%)	15 (48.4%)
Female	171 (67.3%)	43 (50%)	65 (50.4%)	16 (51.6%)
Age Distribution (years)				
<60	199 (78.3%)	70 (81.4%)	104 (80.6%)	24 (77.4%)
≥60	55 (21.7%)	16 (18.6%)	25 (19.4%)	7 (22.6%)
Duration of Diabetes (>15 years)	169 (66.5%)	56 (65.1%)	71 (55%)	20 (64.5%)
Co-morbid conditions				
LDL-C (mg/dl)	49.50 ± .490	41.23 ± 0.445	61.70 ± 0.457	55.54 ± 0.505
HDL-C (mg/dl)	44.13 ± 3.34	43.27 ± 2.92	91.8 ± 44.87	44.755 ± 6.68
Triglycerides	182.71 ± 16.072	182.24 ± 15.080	184.09 ± 14.91	179.19 ± 14.160
S. Creatinine	1.44 ± 0.498	1.46 ± 0.501	1.51 ± 0.501	1.51 ± 0.50
Treatment type				
Metformin Only	212 (83.5%)	79 (91.9%)	98 (76%)	12 (38.7%)
Sulfonylurea Only	145 (57.1%)	44 (51.2%)	70 (54.3 %)	10 (32.3%)
Mixed Oral	178 (70.3%)	61 (71.5%)	84 (65.1%)	11 (35.5%)
Insulin only	106 (41.7%)	33 (38.4%)	73 (56.6%)	23 (74.2%)
Insulin+oral	142 (56%)	47 (54.9%)	78 (60.8%)	17 (54.8%)

LDL:low-density lipoproteins, HDL: High-density lipoprotein, CAD: Coronary artery disease, Mixed Oral medications: (Metformin, Sulfonylureas, Thiazolidinediones & Ecosprin).

committee on the diagnosis and classification of diabetes. The patients diagnosed with diabetes before the age of 25 and started insulin around the time of diagnosis were excluded to minimize inclusion of type 1 diabetes patients. The patients with self-reported diabetes were not included because age at diagnosis could not be determined in these cases. 60 patients enrolled in the year 1999–2000 did not report in the successive. However, the final analysis was conducted among 500 patients of type 2 diabetes attending clinic regularly over a period of 10 years for evaluation of glycemic and non-glycemic targets. None of these patients were insured. They were paying the cost of investigation and purchasing medicine on their own; however, consultation charges were free to the patients. They were followed up at 3-monthy intervals with all patients undergoing anthropometric measurements (BMI = weight in kg/ height in m^2), diet and lifestyle advise by a diabetic educator and consultation by a qualified endocrinologist. Fasting and postprandial plasma glucose, A1c % (3 monthly), besides evaluation of SMBG (in 50% of these patients regularly) were performed. Fasting lipids, serum creatinine and microalbumin were assessed annually. The treatment was modified as per the investigation report.

Clinical variables

Several clinical variables associated with worse glycemic control as covariates have been considered. BMI (weight in kg divided by height in m^2) was categorized as 'lean' (<18.5 kg/m^2), 'normal' (18.5–22.9 kg/m^2), 'overweight' (23.0–24.9 kg/m^2) and 'obese' (>25 kg/m^2). Duration of diabetes was calculated from the patient's report of age at diabetes diagnosis subtracted from current age. Diabetes treatment was classified into categories of metformin only, sulfonylurea only, mixed oral medications (Metformin, Sulfonylureas, Thiazolidinediones & Ecosprin), or insulin plus oral medications. The data obtained through this procedure was analyzed through descriptive statistics.

Ethical Clearance

This study was approved Bio-Ethical Committee (BEC) of Faculty of Medicine, Aligarh Muslim University, Aligarh on August 2013, registered under Drug Controller General of India (DCGI), Government of India under registration Number: ECR/419/Inst/UP/2013 issued under Rule 122DD.

RESULTS

The results have shown 500 patients with diabetic foot ulcers have participated in the study. Table 1 has shown the baseline characteristics of participants on the basis of HbA1c. The findings have shown that there is a significant association between HBA1c and neuropathy (p = 0.03), LDL-C and HbA1c (p = 0.031), triglyceride and HbA1c (p = 0.000) and type of medication and HbA1c (p = 0.014).

Table 2 has presented risk factors related with BMI after adjustment of BMI. The findings have shown that duration of diabetes is main risk factor in the Obese category, LDL-C is the main factor in the overweight category. The findings have indicated that total 254 patients were obese (50.8%), 86 patients were overweight (17.2%), 129 patients were normal (25.8%), and 31 patients were lean (6.2%).

Table 3 has represented the risk factors associated with creatinine clearance. The findings have shown risks based on microalbuminuria, mild to moderate reduced CCre and severe reduced CCre treatment. The correlation between BMI, HbA1c and serum creatinine is presented in Figure 1. The findings have indicated that LDL-C and triglycerides are positively and significantly associated with HbA1c. On the contrary, the findings have indicated that there is an insignificant and negative correlation between BMI and serum creatinine with baseline characteristics (Table 4).

DISCUSSION

The present study has assessed factors including BMI, duration of diabetes, fasting lipids, serum creatinine, and microalbuminuria to control glycemic levels through cross-sectional analysis. The findings have clearly revealed significant association between HbA1c and neuropathy (p = 0.03), LDL-C and HbA1c (p = 0.031), triglyceride and HbA1c (p = 0.000) and type of medication and HbA1c (p = 0.014).

Table 3 Risk factors associated with Creatinine Clearance after adjustment

	Category A: no nephropathy or microalbuminuria only; CCre≥90 ml/min/1.73m^2	**Category B:** mild to moderate reduced CCre, CCre: 30–89 ml/min/1.73m^2	**Category C:** severe reduced CCre or need for renal replacement treatment, CCre < 30ml/min/1.73m^2
N	**54**	**379**	**67**
Gender distribution			
Male (referent)	21 (38.8%)	158 (41.6%)	26 (38.8%)
Female	33 (61.1%)	221 (58.3%)	41 (61.1%)
Age Distribution (years) *<60*	43 (79.6%)	308 (81.2%)	46 (68.6%)
Duration of Diabetes (*>15* years)	38 (70.3%)	227 (59.8%)	51 (76.1%)
BMI (kg/m^2)			
Obese	24 (44.4%)	163 (43.0%)	67 (100%)
Over weight	19 (35.1%)	67 (17.6%)	0 (0%)
Normal (referent)	10 (18.5%)	119 (31.3%)	30 (44.7%)
Lean	37 (68.5%)	0 (0%)	0 (0%)
CAD	6 (11.1%)	51 (13.4%)	5 (7.4%)

CAD: Coronary artery disease, BMI: Body mass index.

Table 4 Correlation of BMI, HbA1c and Serum Creatinine

	BMI	**HbA1c**	**Serum Creatinine**
N			
Gender distribution Male (referent)	0.056	0.058	0.050
Age Distribution (years) <60	-0.015	-0.085	-0.028
Co-morbid conditions			
LDL-C (mg/dl)	0.054	0.096*	0.037
Triglycerides	-0.004	-0.106*	-0.028
BMI (kg/m^2)	1	0.042	-0.012
S. Creatinine	0.060		1
HDL-C			
Treatment type			
Metformin Only	0.009	0.368	0.642
Sulfonylurea Only	0.008	0.385	0.466
Mixed Oral	0.008	0.376	0.554
Insulin only	0.205	0.795	0.884
Insulin+oral	0.106	0.585	0.719

LDL-C:low-density lipoproteins, Mixed Oral medications: (Metformin, Sulfonylureas, Thiazolidinediones & Ecosprin), CAD: Coronary artery disease, BMI: Body mass index.

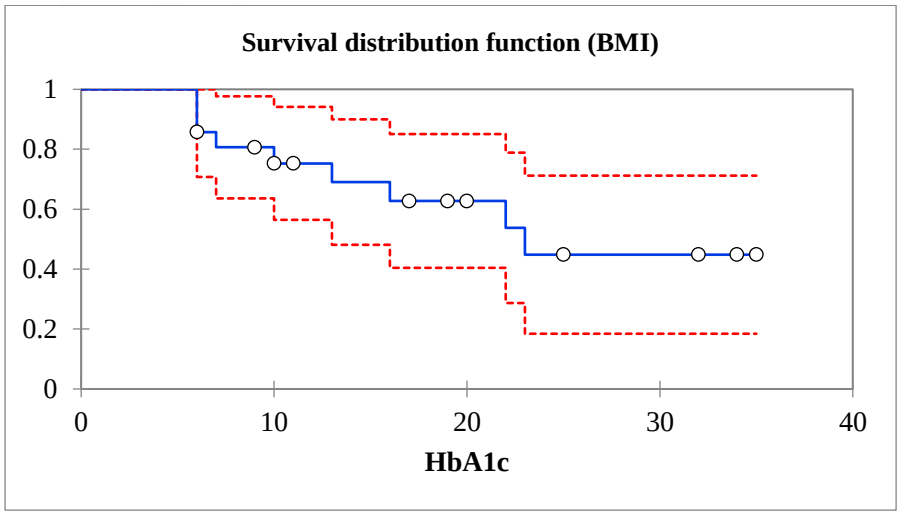

Figure 1 (a) Kaplan Meier curve of BMI in diabetic patients with HbA1c

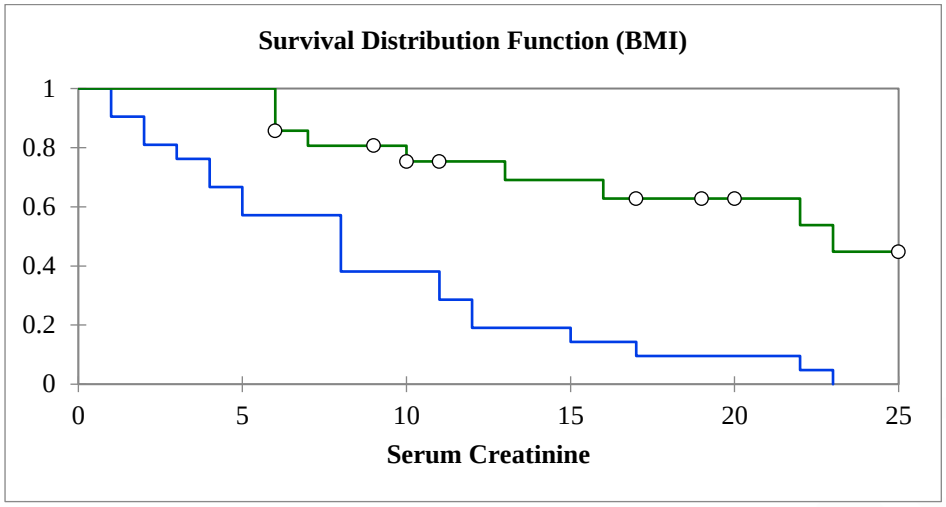

Figure 1(b) Kaplan Meier curve of BMI in diabetic patients with Serum creatinine

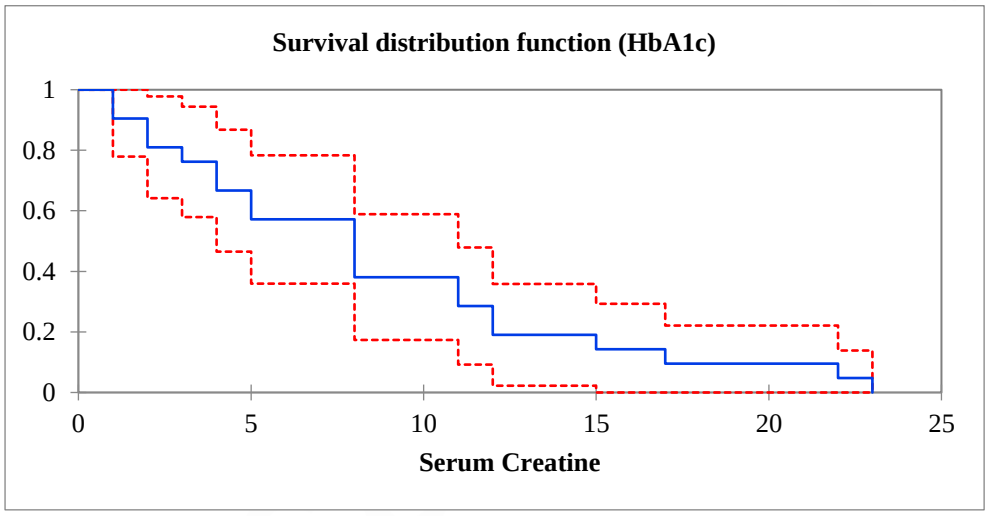

Figure 1(c) Kaplan Meier curve of HbA1c in diabetic patients with Serum Creatinine

Nonetheless, the results showed insignificant correlation between diabetes duration and glycemic control.

In some cases, diabetes has developed but not in an advanced state that it causes hyperglycemia, causing impaired fasting glucose. Glycemia in people can be controlled by the means of exercise and weight reduction and these patients require insulin to complete the task. Moreover, people with enhanced β-cells destruction and no proper insulin secretion require insulin for survival. The metabolic abnormality can relapse, enhance, or stay as it is[7]. Therefore, the severity of metabolic process and its treatment is pointed out through certain degree of hyperglycemia. It is not necessary that all of the patients with diabetes fit into a single class. Usually, it all depends on the circumstances that exist during the diagnosis phase. For instance, a patient with Gestational Diabetes Mellitus (GDM) may show the sign of hyperglycemia even after the delivery is done. Likewise, a person, who has been treated with thiazides, can later on develop diabetes[4,8].

A study has shown that there is a direct relationship between vascular diseases and diabetes; therefore, the importance of controlling hyperglycemia is understated[5]. Diabetes can lead to life-threatening diseases like cardiac disruption and renal failure. Hypertension accompanied by diabetes can lead to microalbuminuria or diabetic nephropathy. Albumin is amongst the first protein that leaks, when the kidney is not performing at its optimal level. Early kidney damage can be treated by keeping the glycemic level in control. Among the diabetic patients, the levels of serum creatinine are low as compared to the non-diabetic individuals. A study conducted by Tsuda et al.[9] examined the consequences and factors that are linked with overestimation of renal failure among the diabetic patients. The results showed that renal function is overestimated through the difference in values of glomerular filtration rate as the glycemic controls worsened.

Since a major proportion of population is suffering from diabetes worldwide, there is an added emphasis to evaluate the rate of achieving treatment targets and the occurrence of complications experienced by these patients. In a large cross-sectional nationwide study, a total of 9956 patients with type 2 diabetes mellitus were surveyed and evaluated for the prevalence of neuropathy, nephropathy and retinopathy. The results revealed the rates of achieving treatment targets for HbAlc, blood pressure and lipids were 52.9 %, 46.8% and 65.5% respectively. The results also showed that the rate of achieving target diminished with the increasing duration of diabetes in spite of the increase in the use of diabetes medications. There was less prevalence of complications in patients that achieved the treatment targets[10].

A study was performed in patients with type 2 diabetes mellitus to examine the relationship of Triglyceride variability with the occurrence of microalbuminuria. A total of 457 normoalbuminuric outpatients participated in observational retrospective study. The level of lipids,

HbAlc and microalbuminuria was measured three times a year. Furthermore, the standard deviation of triglyceride adjusted for the number of visits and the standard deviation of triglyceride was calculated. A case-controlled sensitivity analysis was conducted to confirm the results of the cohort study. It was concluded that microalbuminuria and triglycerides were directly related in patients with type 2 diabetes. Additionally, it was found that the high triglycerides affected the microalbuminuria incidence. Consequently, it was concluded that a predictor of incident microalbuminuria was a higher intraindividual triglyceride variability. It was recommended that a better control of dyslipidemia could help protect against diabetic nephropathy[11].

A study indicated that 284 asymptomatic patients with type 2 diabetes were examined about coronary atherosclerosis and microalbuminuria. It was performed by using coronary computed tomography angiography and 24-hour urine albumin measurements. Between 30-300 mg per day of urinary albumin excretion is considered to be microalbuminuria. Besides, maximum intraluminal stenosis that is equal to or more than 50% is considered to be an obstructive Coronary Artery Disease (CAD). The use of segment stenosis score, segment involvement score, atheroma burden obstructive score and coronary artery calcium score were used to evaluate the data. It was discovered that patients with microalbuminuria were more susceptible to have obstructive Coronary Artery Disease (CAD). Furthermore, microalbuminuria was linked with higher SIS (p= 0.029), SSS (p=0.011), ABOS (p=0.010). Conversely, microalbuminuria was not linked with higher CACS (p=0.058)[12].

The present study has shown that increased BMI is a significant risk factor leading to the onset of diabetes as the results showed that 254 patients were obese (50.8%), 86 patients were overweight (17.2%), 129 patients were normal (25.8%), and 31 patients were lean (6.2%). Similar to this, a study conducted by Firouzi et al.[13] identified the risk factors associated with poor glycemic control among the patients with type 2 diabetes mellitus. The results depicted that majority of the subjects suffering diabetes mellitus were overweight and obese with specifically abdominal obesity. These individuals consumed low intake of calcium, fiber, and vitamin C. It has also been revealed increased prevalence of poor glycemic control among the diabetic patients is due to lack of appropriate physical activity and high intake of different medications. Another similar study investigated the relationship between BMI and suboptimal glycemic control among the patients with type 1 and type 2 diabetes mellitus[14]. The results showed that as compared to the patients with BMI less than 25, the number of patients with BMI greater than 25 was higher. It was also emphasized that variety of factors like; HbA1c levels, diet, physical activities, and BMI help to achieve targeted glycemic control[14].

Kim et al.[12] evaluated the status of glycemic control among diabetic patients, who are given metformin and sulfonylurea for more than three months that was measured by HbA1c. The results depicted that glycemic control among majority of the patients was not satisfactory, despite of receiving combined metformin and sulfonylurea therapy. These patients are at high risk of developing nephropathy, retinopathy, and chronic diabetic condition along with minimal chance to achieve target HbA1c[12]. These results are consistent with the present study as the findings showed significant relationship between HBA1c and neuropathy (p = 0.03), LDL-C and HbA1c (p = 0.031), triglyceride and HbA1c (p = 0.000) and type of medication and HbA1c (p = 0.014). Another study conducted by Cheneke et al.[15] assessed different risks and complications among diabetic individuals by using HbA1c. The results showed poor glycemic control among the patients, who were on treatment indicating increased risk of developing diabetic complications[16]. Therefore, in agreement with the present study, it is important to trace the cause of poor glycemic control to mitigate the problem.

CONCLUSION

The study has aimed to assess HbA1c, BMI, duration of diabetes, fasting lipids, serum creatinine, and microalbuminuria to control glucose levels. The results have shown a statistically significant correlation between BMI and triglyceride and LDL-C; and HbA1c and however, there was no significant correlation between serum creatinine and BMI with other characteristics. The insignificant finding between these characteristics restricts to examine the positive association for BMI and serum creatinine.

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Authors' Contribution
MZ and MAA have mutually coordinated for this research. Though, MZ was responsible for the finalization and correspondence of this research.

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Conflict of Interest
MZ and MAA declare no conflict of interest.

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