

Correlation Between HbA1c, Serum Magnesium (Mg) and Lipid Profile in Type 2 Diabetic Foot Ulcer and without Foot Ulcer Patients – a Cross-Sectional Study

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Abstract::

Introduction : Diabetes mellitus, especially Type 2, is a common metabolic problem in Bangladesh with serious complications like diabetic foot ulcer. The relationship between HbA1c, serum magnesium, and lipid profile in type 2 DFU patients was examined in this study.

Aim of the study: The aim of this study was to examine the correlation between HbA1c, serum Magnesium, and lipid profile in type 2 diabetic foot ulcer and without foot ulcer patients.

Methods: This cross-sectional study was conducted in the Department of Biochemistry and Molecular Biology, BIRDEM Academy, Dhaka, Bangladesh during the period from January 2018 to December 2018

Result: In total 120 respondents who were adult male and female were included in the study. In our study, we found that the majority of our patients (58.3%) were aged

between 41-50 yrs. in group II. We found the percentage of male and female participants were 66.7% and 33.3% in group I and 51.7% and 48.3% in group II respectively. The negative correlation was found between serum magnesium with fasting plasma glucose and Triacylglycerol in group I. The significant positive correlation was found between serum Mg and HDL-c ($r=0.443$; $p<0.01$) in group I.

Conclusion: Diabetes Mellitus, notably Type 2, poses challenges in Bangladesh, including Diabetic Foot Ulcer (DFU). This study explores links between HbA1c, serum magnesium, and lipid profile in Type 2 DFU patients, potentially guiding early interventions and improving diabetic care outcomes.

Key words: HbA1c, Serum Magnesium, Lipid Profile, Type 2 DFU

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Introduction:

Diabetes mellitus (DM) is a chronic metabolic disease due to insufficient insulin production or action or both, causing elevated blood glucose level and harm to many of body's systems, especially blood vessels and nerves¹ In Bangladesh, the prevalence of DM was 7.1 million in

2015 and is projected to increase to 13.6 million by 2040. Type 1 DM accounts for about 5%, and Type 2 DM accounts for 90-95% of all Diabetes Mellitus cases.² Type 1 DM results from autoimmune destruction of β -cells of pancreas, while Type 2 is due to progressive insulin

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secretion defect and resistance.³ Persistent high blood glucose leads to long-term vascular complications, including microvascular and macrovascular issues in Type 2 diabetes.

Diabetic foot ulcers are a major complication of diabetes, causing significant morbidity and hospital admissions.⁴ Around 1-4% of type 2 diabetic patients develop foot ulcer yearly, leading to gangrene and amputation.^{5,6} Contributing risk factors include micro and macro angiopathy, peripheral neuropathy, and ischemia.⁷ HbA1c is a crucial indicator of glycemic control, reflecting average glucose level over two months.⁸ The ADA and EASD recommend an HbA1c level $\leq 6.5\%$ as a diagnostic criteria for diabetes.⁹ Regular monitoring of blood glucose and HbA1c is standard practice in diabetes management now a days,¹⁰ as good glycemic control reduces the complication risk.¹¹ Elevated HbA1c levels indicate poorly controlled diabetes and an increased risk of complications.¹²

Magnesium is important cation for carbohydrate metabolism and enzyme actions.^{13,14} Low magnesium in type 2 diabetes affects glycemic control and insulin sensitivity.¹⁵ Several factors like diet, insulin resistance, and medications contribute to hypomagnesemia.^{13,16,17} Hypomagnesemia is linked to diabetic complications, including neuropathy and diabetic foot ulcer.¹⁸ Magnesium level should be controlled and magnesium supplementation is beneficial for diabetic foot ulcer patients.¹⁹ Diabetes also disrupts lipid metabolism, leading to changes in cholesterol, Triacylglycerol, HDL-c, and LDL-c levels.²⁰ Low magnesium is associated with dyslipidemia and hypertension,²¹ and studies link it to reduced HDL-c level.²² Diabetic foot ulcer patients show elevated total cholesterol, triacylglycerol, and LDL-c, and lower HDL-c levels.²⁰ These factors contribute to cardiovascular risk and vascular damage.²³ The aim of the study was to evaluate the correlation between HbA1c, serum Magnesium (Mg), and lipid profile in individuals diagnosed with type 2 diabetes, regardless of whether they had foot ulcer or not.

Objectives

The objective of this study was to investigate the potential correlations between HbA1c, serum Magnesium (Mg), and lipid profile in individuals with type 2 diabetes, both with and without foot ulcer.

Methodology & Materials

This was a cross-sectional study and was conducted in the Department of Biochemistry and Molecular Biology, BIRDEM Academy, Dhaka, Bangladesh during the period from January 2018 to December 2018.

A total of 120 patients who were male and female, aged 30 years above were included in the study. Among them, 60 were previously diagnosed Type 2 diabetic patients with foot ulcer were selected as Group I and another 60 were previously diagnosed Type 2 diabetic patients without foot ulcer were selected as Group II. Data were collected through structured questionnaire and review of patients clinical and biochemical records. We included patients having type 2 diabetes with and without foot ulcer and excluded who were not eligible for the study. Type 2 diabetes mellitus was diagnosed according to WHO criteria. Diagnosed cases of type 2 diabetic foot ulcer patients were selected from inpatient and outpatient departments of medicine and surgery. Height and weight were measured and recorded in the questionnaire. Blood pressure was also measured. At first 5 ml blood sample was collected from each study subject after an overnight fasting of 10-12 hours. From this blood sample, 1.5 ml was delivered in a fluoride tube for estimation of fasting plasma glucose and another 1.5 ml was delivered in a EDTA tube for HbA1c estimation and remaining 2 ml in red tube for measurement of serum magnesium and lipid profile.

Statistical Analysis: All data were recorded systematically in preformed data collection form and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Statistical analysis was carried out by using Statistical analysis was done by using SPSS (Statistical Package for Social Science) Version 23 for windows 10. P value < 0.05 was considered as statistically significant. Ethical clearance was obtained from BIRDEM to undertake the current study.

Results:

Table-I

Distribution of age in Group I (type 2 diabetes with foot ulcer) and Group II (type 2 diabetes without foot ulcer) of the study subjects (N=120)

Age	Group I		Group II	
	Frequency	Percentage	Frequency	Percentage
31-40	8	13.3	12	20
41-50	18	30	35	58.3
>50	34	56.7	13	21.7

Table 1 shows the distribution of age in Group I and Group II. In Group I, most of the study participants were more than 50 years age group (56.7%) and in Group II, the study participants belonging to the age group (41-50) year were more prevalent (58.3%).

Figure 1 shows gender distribution of study subjects of Group I and Group II. This study found that in Group I,

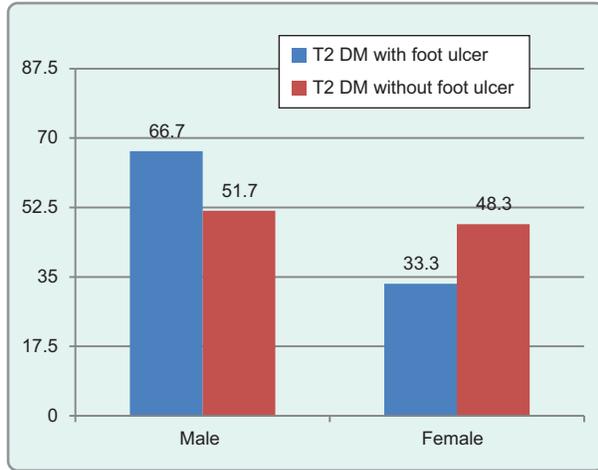


Fig.-1: Gender distribution in Group I (type 2 diabetes with foot ulcer) and Group II (type 2 diabetes without foot ulcer) of the study subjects.

percentage of male and female participants were 66.7% and 33.3% respectively. In Group II percentage of male participants were more prevalent than female (51.7% vs 48.3%).

Table 2 shows that high hemoglobin A1c (HbA1c $\geq 7.5\%$) was significantly more affected by diabetic foot ulcer than

compared with near normal HbA1c (61.6% vs 31.9%; $\chi^2=10.10$; $p < 0.001$). As for serum magnesium, we found the prevalence of hypomagnesaemia was more in group I (69.6%) and in group II, it was 30.4%.

Table 3 shows the Lipid profile among Group I and Group II. The study found that the mean value of TC was 177.01 ± 27.83 , TAG was 170.21 ± 56.01 , that of LDL-c was 99.31 ± 32.31 and HDL-c was 30.40 ± 9.93 in group I; in group II the mean value of TC, TAG, LDL-c and HDL-c were 161.23 ± 28.35 , 149.30 ± 46.95 , 87.60 ± 21.44 and 37.91 ± 7.48 respectively. This study also found that the mean value of TC, TAG, LDL-c were significantly higher in Group I than Group II ($p < 0.01$, $p < 0.05$, $p < 0.05$ respectively), on the other hand the mean value of HDL-c was significantly lower in Group I than Group II ($p < 0.001$).

Table 4 shows the correlation of serum magnesium with other biochemical variables in Group I and Group II (type 2 diabetes with and without foot ulcer). In this study, in Group I significant negative correlation was found between serum magnesium with fasting plasma glucose and Triacylglycerol ($r = -0.296$; $p = 0.022$ and $r = -0.280$; $p = 0.030$) respectively. However, significant positive correlation was found between serum magnesium with high density lipoprotein cholesterol (HDL-c) level ($r = 0.443$; $p = 0.001$). As for Group II, the serum magnesium was negatively correlated with fasting plasma glucose ($r = -0.176$, $p = > 0.05$), TC ($r = -0.029$, $p = > 0.05$), TG ($r = -$

Table-II
HbA1c and Serum magnesium status in type 2 diabetic with and without foot ulcer patients (n=120)

Group		Group I (DM with foot ulcer) (%)	Group II (DM without foot ulcer) (%)	p-value
HbA1c	Within reference ($< 7.5\%$)	15 (31.9%)	32 (68.1%)	0.001
	Uncontrolled ($\geq 7.5\%$)	45 (61.6%)	28 (38.4%)	
Serum magnesium	Hypomagnesaemia (< 0.70 mg/dl)	39 (69.6%)	17 (30.4%)	0.001
	Within reference (≥ 0.70 mg/dl)	21 (32.8%)	43 (67.2%)	

Table-III
Lipid profile of Group I (type 2 diabetes with foot ulcer) and Group II (type 2 diabetes without foot ulcer)

Lipid profile	T2 DM with foot ulcer (n=60) Mean \pm SD	T2 DM without foot ulcer (n=60) Mean \pm SD	p value
Total cholesterol (TC) (mg/dl)	177.01 ± 27.83	161.23 ± 28.35	0.003
Triacylglycerol (TAG) (mg/dl)	170.21 ± 56.01	149.30 ± 46.95	0.029
Serum LDL-cholesterol (mg/dl)	99.31 ± 32.31	87.60 ± 21.44	0.021
Serum HDL-cholesterol (mg/dl)	30.40 ± 9.93	37.91 ± 7.48	0.001

Table-IV
Correlation of serum magnesium level (mmol/L) with other biochemical variables in Group I and Group II (type 2 diabetes with and without foot ulcer).

Variables	With foot ulcer DM patients		Without foot ulcer DM patients	
	r	P value	R	p value
Fasting plasma glucose	-0.296	0.022	-0.176	>0.05
Total cholesterol (TC)	0.053	0.687	-0.029	
Triacylglycerol (TAG)	-0.280	0.030	-0.143	
LDL cholesterol	0.044	0.740	0.014	
HDL cholesterol	0.443	0.001	-0.04	

Table-V
Correlation of HbA1c (%) level with other biochemical variables in Group I and Group II (type 2 diabetes with and without foot ulcer).

Variables	With foot ulcer DM		Without foot ulcer DM	
	r	p value	r	p value
Total cholesterol (TC)	0.094		0.134	>0.05
Triacylglycerol (TAG)	0.023		0.144	
LDL cholesterol	0.008		0.160	
HDL cholesterol	-0.066		-0.055	

0.143, $p = >0.05$), HDL-c ($r = -0.04$, $p = >0.05$) respectively.

Table 5 shows correlation of HbA1c level with other biochemical variables in Group I and Group II (type 2 diabetes with and without foot ulcer). In this study Group I, the HbA1c was positively correlated with TC ($r = 0.094$, $p = >0.05$), TAG ($r = 0.023$, $p = >0.05$) and LDL-c ($r = 0.008$, $p = >0.05$). However, negative correlation was found between HbA1c with high density lipoprotein cholesterol (HDL-c) level ($r = -0.066$, $p = >0.05$). As for Group II, the HbA1c was positively correlated with TC ($r = 0.134$, $p = >0.05$), TAG ($r = 0.144$, $p = >0.05$), LDL—c ($r = 0.160$, $p = >0.05$) respectively.

Discussion:

The cross-sectional study was conducted in the Department of Biochemistry and Molecular Biology, BIRDEM Academy, Dhaka, Bangladesh during the period from January 2018 to December 2018 to estimate HbA1C, serum Magnesium and lipid profile level in type 2 diabetic foot ulcer and without foot ulcer patients. A total of 120 subjects were selected in this study according to inclusion and exclusion criteria. Among them 60 diagnosed type 2 diabetic foot ulcer patients were placed in Group I and another 60 diagnosed type 2 diabetic patients without foot ulcer were placed in Group II. In this study we found that the majority (56.7%) of our patients of Group I were aged more than 50 years and 58.3% of our patients of Group II were aged between 41-50 years. [Table-1] In the study male respondents were found more

than female in both Groups. In Group I there were 66.7% male and 33.3% female, whereas in Group II male and female participants were 51.7% and 48.3% respectively. [Figure-1] The mechanism behind could be that male were less insulin sensitive than female due to more hepatic and visceral fat than women.²⁴ This finding was similar with this study where we found more male participants (66.67%) than female (34.4%) of type 2 diabetic foot ulcer group.²⁵ Another study also found male participants more predominant than female in their study (67% and 33% respectively).²⁶ In our study we found uncontrolled glycemia is considered as the strongest indicator of development of diabetic complications. Frequency of uncontrolled HbA1C was higher in Group I than Group II (61.6% and 38.4% respectively). Frequency of hypomagnesaemia was also higher in group I than group II (69.6% and 30.4% respectively). In a study by Rodriguez Moran and Guerrero Romeo, it was observed that 93.9% of patients with diabetic foot ulcer had hypomagnesaemia in contrast to 73.1% of diabetic patients without foot ulcer.²⁷ Regarding lipid profile, we found the mean value of Total cholesterol (TC), Triacylglycerol (TAG), Low density lipoprotein cholesterol (LDL-c) and High density lipoprotein cholesterol (HDL-c) in Group I were 177.01 ± 27.83 (mg/dl), 170.21 ± 56.01 (mg/dl), 99.31 ± 32.31 (mg/dl) and 30.40 ± 9.93 (mg/dl) respectively, whereas the mean value of TC, TAG, LDL-c and HDL-c in Group II were 161.23 ± 28.35 (mg/dl), 149.30

± 46.95 (mg/dl), 87.60 ± 21.44 (mg/dl) and 37.91 ± 7.48 (mg/dl) respectively. This study also found that the mean value of TC, TAG, LDL-c were significantly higher in Group I than in Group II ($p < 0.05$), on the other hand the mean value of HDL-c was significantly lower in Group I than in Group II ($p < 0.05$). This finding was consistent with Hasan et al. (2013) who found the level of TC, TAG & LDL-c significantly higher in diabetic foot ulcer patients than that of patients without foot ulcer. They also found significantly lower HDL-c in type 2 diabetic foot ulcer patients than diabetic patients without foot ulcers.²⁸ Some study showed that elevated triacylglycerol and decreased HDL-c levels are the most common lipid metabolism disorders in diabetic patients, and claim that LDL-c level is relatively similar to non-diabetic individuals.²⁹ In our study group I, significant negative correlation was found between serum magnesium with fasting plasma glucose ($r = -0.296$) and Triacylglycerol ($r = -0.280$) respectively and group II was negatively correlated with fasting plasma glucose ($r = -0.176$), TC ($r = -0.02$), TAG ($r = -0.143$), HDL-c ($r = -0.04$) respectively. [Table-IV] The study found that the serum magnesium level was negatively correlated with postprandial plasma glucose level.³⁰ This study is reinforced by previous studies who reported that serum magnesium deficiencies were present in patients with type 2 DM, showing a strong relationship with foot ulcer.³¹ We found the patients with diabetic foot ulcer had positive correlation of HbA1c level with TC ($r = 0.094$), TAG ($r = 0.023$), LDL-c ($r = 0.008$). It was also found that patients without diabetic foot ulcer had positive correlation of HbA1c level with TC ($r = 0.134$), TAG ($r = 0.144$), LDL-c ($r = 0.160$) respectively. [Table-V] This finding was similar with the finding of Keskek et al (2013) who also found negative correlation between serum magnesium with fasting serum glucose and HbA1C level.³² No correlation was found between HbA1C and other biochemical variables. But in another study of Hasan et al. (2013) found positive correlation between HbA1C and TC, TAG and negative correlation with HDL-c in diabetic foot ulcer patients. It was observed that complications of diabetes mellitus are associated with high HbA1C, low serum magnesium level and dyslipidemia. Consequently, we determined that low serum magnesium level is associated with high level of blood glucose, HbA1C and also high TC, TAG, LDL-c and low HDL-c levels. Uncontrolled diabetes and low HDL-C level are important risk factors for atherosclerosis, which contribute to the development of foot ulcer. Neuropathy, another risk factor for diabetic foot ulcers, can develop from high glucose level due to magnesium deficiency.²⁸ We also found a significant relationship

between HbA1c and FBS level, which is in line with findings of some other studies.^{33,34,35} Except for LDL-c level, we found significant relationship between HbA1c, FBS, cholesterol and triacylglycerol levels. Pujari found a statistically significant correlation between HbA1c level and dyslipidemia.³⁵ In Oman, Al-Alawi reported a correlation between improved dyslipidemia and HbA1c control.³⁶ In a similar study in India, reported a significant positive correlation between HbA1c, total cholesterol, triacylglycerol, HDL-c and LDL-c levels.³⁷ In 2013, Parial et al. reported that 86% of patients and almost all patients with foot ulcer had high HbA1c levels (8.88 mg/dl), while 88% of patients without diabetic foot ulcer had satisfactory HbA1c level. HbA1c, total cholesterol, LDL-c and triacylglycerol levels had a significant positive correlation with diabetic foot ulcer, indicating major contributing factor for diabetic foot ulcer. In a study in India on females patients with type 2 diabetes, HbA1c had a positive correlation with total cholesterol ($r = 0.414$) and LDL-c ($r = 0.8686$) levels, which is consistent with our findings.³⁸ In a study by Mahajan and Koley, HbA1c had a significant positive correlation with blood glucose, total cholesterol, triacylglycerol, LDL-c and HDL-c levels.³⁹ In Pakistan, Naeem et al. found that female diabetic patients had significantly increased systolic and diastolic blood pressure, total cholesterol and LDL-c level compared to male patients.⁴⁰ So along with glycemic control, magnesium level should be maintained in patients with DM, with or without foot ulcer and dietary supplementation of magnesium in addition with classical therapies for diabetes may help in prevention or delaying diabetic complications. Oral magnesium supplementation may improve insulin sensitivity and metabolic control in type 2 DM with lower serum magnesium levels thus reducing the risk of both micro and macrovascular complications. It has also a beneficial effect on lipid profile of diabetic patients.³¹

Limitations of the study

Our study was a single center study so we cannot draw conclusions regarding causality. We could only study a few adverse effects within a short study period. There are many things that could have been included here such as the patients with H/O cerebrovascular accident, chronic systemic disease, other endocrine disorders and peripheral arterial disease.

Conclusion and recommendations

Diabetes Mellitus, especially Type 2, presents a significant challenge in Bangladesh, with Diabetic Foot Ulcer (DFU) as a major complication. In this study we explored the relationship between HbA1c, serum

magnesium, and lipid profile in Type 2 DFU patients. The findings could offer insights into early screening and interventions, reducing the burden of DFU-related complications on both individual and society. This research has the potential to reshape diabetic care and improve the quality of life for many.

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