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Association of HbA1c, Creatinine and Lipid Profile in Patients with Diabetic Foot Ulcer

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Abstract: Diabetic foot ulcer is a major disabling complication of Diabetes Mellitus and often precedes lower extremity amputation. The descriptive correlational study aimed to identify the relationship of HbA1c, lipid profile and creatinine in diabetic foot ulcer attending Chittagong Diabetic General Hospital, Chittagong, Bangladesh. One hundred blood-samples each from the patient groups having DFU and without DFU of varying ages were collected for analysis. The HbA1c, Creatinine and lipid profile of the subjects were measured with standard methods. These data along with the information of patients' age and gender were subjected to different statistical analysis by SPSS to evaluate the association of those parameters in DFU patients. It was found that approximately all foot ulcer patients have HbA1c level uncontrolled with 86% of them having HbA1c level =8.86%. Unlike the DFU-patients, 88% of patients without DFU have HbA1c level controlled, but others are not free from risk of foot ulcer. The data analysis also revealed that, the HbA1c, Creatinine, Cholesterol, LDL and TG levels are significantly higher in DFU-patients (10.50% and 1.77 mg/dl, 216.52 mg/dl, 152.31 mg/dl and 149.61 mg/dl respectively) than that of in patients without DFU (6.55%, 1.034 mg/dl, 152.18 mg/dl, 96.53 mg/dl, 107.13 mg/dl respectively) having just the opposite result for HDL. The correlational study confirmed a strong to very strong positive correlation among the values of HbA1c, Creatinine, Cholesterol, LDL and TG in DFU-patients where HDL showed a very strong negative correlation with those parameters. So HbA1c and Creatinine may be major factors in diabetic foot ulcer management.

Key words: DFU · HbA1c · Creatinine · Lipid Profile

INTRODUCTION

The increasing incidence of Diabetes mellitus which represents a group of chronic diseases characterized by high levels of blood glucose resulting from defects in insulin action, production or both has become a major health concern worldwide. Worldwide, the number of cases of diabetes has been estimated to be 171 million and by 2025, this number is projected to reach 366 million [1]. Diabetic foot infections are one of the major long term complications of Type 2 diabetes as 1-4% of people with type 2 diabetes develop a foot ulcer each year and it can result in gangrene and lower extremity amputation associated with socioeconomic impact [2, 3] and a significant mortality [4]. Patients with diabetes are 25 times more likely to lose a leg than those without the condition and up to 70% of all leg amputations occur in people with diabetes. The result is that a leg is lost to diabetes every 30 seconds somewhere in the world [5, 6]. An investigation by The Global Lower Extremity Amputation Study Group revealed that 25%-90% of all amputations were associated with diabetes [7]. In developing countries like Bangladesh the prevalence of DFU consumes as much as 40% of the healthcare resources available for diabetes where it was estimated as 20% for developed countries [8]. The Diabetes mellitus is associated with an increased total mortality, cardiovascular Morbimortality and Kidney disease in the general population [9, 10]. But in our knowledge, there was no correlational study among the indicators of those diseases was done for Bangladeshi patients.

While there are no guidelines to use HbA1c as a screening tool, physicians consider its elevated value as an indicator of diabetes mellitus. In most labs, the normal

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range of Hemoglobin A1c (HbA1c) for non diabetic patients is 4-5.9 % where in poorly controlled diabetes, its 8.0% or above and in well controlled patients it's less than 7.0% [11]. Another important consideration about the diabetes mellitus is that, approximately one third of people with diabetic kidney disease may get cardiovascular risks and mortality [12, 13]. Creatinine has been found to be a fairly reliable indicator of kidney function especially in urgent laboratory investigations. In this context, association of HbA1c with Lipid profile and Creatinine levels in the patients with diabetic foot ulcer can be significant in the study of diabetic foot ulcer management and treatment.

Thus we aimed our study to identify the relationship of HbA1c, creatinine and lipid profile in diabetic foot ulcer.

METHODS AND MATERIALS

The study was carried out during the period of September 2011 to June 2012 in Chittagong Diabetic General Hospital, Khulshi, Chittagong, Bangladesh. A total number of 100 subjects with DFU and 100 subjects without DFU were selected on the basis of the availability in the hospital and their consent. The patients with serious comorbid diseases and the history of using drugs significantly affecting glucose metabolism were excluded from the study. The information regarding their age and gender was also collected.

Collection of Blood Samples: 10 ml of Fasting blood was collected. Then the patient was given 75 g of glucose in 250-300 ml of water and advised to drink in 5 min. The next blood sample was taken 2 hours (2h) after glucose load. After 10-15 minutes blood sample was centrifuged for 10 minutes at 3000 rpm to obtain serum. Fasting and 2h serum glucose was measured in the same day. Subjects were finally selected from fasting and 2h serum glucose values that fulfilled the inclusion criteria of this study. Serum was kept frozen at -70°C for future analysis.

Laboratory Analysis: 5µl of blood was taken to analyze HbA1c and was estimated according to boronate affinity assay by NycoCard (Axis-Shield, Norway). The results were read within 5 minute. Creatinine concentration in the sample was measured using using Jaffe's method described by Bowers and Wong [14]. Cholesterol was determined by Cholesterol Oxidase -Peroxidase method [15], triglycerides by Trinders Glycerol Phosphate Oxidase-Peroxidase method [16], HDL by Poly ethylene glycol [PEG] precipitation method [17] and LDL cholesterol by calculation method according to Freidewald Formulae [18]. Creatinine and lipid profile measurement used kits and reagents from Siemens Healthcare Diagnostics Inc. Newark, DE 19714, U.S.A.

Statistical Analysis: Data produced from laboratory procedures was analyzed using SPSS 16.0 for Windows. The students' t test was performed to evaluate the significance of difference in values of HbA1c, Creatinine, Cholesterol, HDL, LDL and TG between the diabetic patient groups with and without DFU. Pearson's correlation test was done in order to test any correlation among the values of the above parameters in patients with DFU.

RESULT

The statistical analysis showed the mean value of the HbA1c (%) for the patients with Diabetic Foot Ulcer (DFU) was 10.50 (Table-1) where 86% of those patients have the HbA1c of =8.86%. In addition, 78% and 75% of the total patients with DFU were found male and aged more than 50 respectively. Student's t test revealed that the level of HbA1c, Creatinine, Cholesterol, LDL and TG are significantly higher in patients with DFU than that of the patients without DFU where the value of HDL is significantly higher in patients without DFU than that of the patients with DFU (Table 1).

Pearson's correlation test (Table 2) showed that the values of HbA1c have highly positive correlation with the values of Creatinine, Cholesterol, LDL and TG. In the contrary, HDL level contain highly negative correlation with other parameters ($p<0.01$).

Table 1: HbA1c, Creatinine, Cholesterol, HDL, LDL and TG values in patients with and without DFU (Mean±SD).

Parameter	Patient with Diabetic foot ulcer	Patient without Diabetic foot ulcer
HbA1c (%)	10.50±1.5502*	6.55±0.99178
Creatinine (mg/dl)	1.77±0.44117*	1.034±0.23154
Cholesterol	216.52±27.36757*	152.18±16.99826
HDL	34.78±3.88729	37.46±4.18368*
LDL	152.31±23.59372*	96.53±10.78312
TG	149.61±16.71192*	107.13±11.96627

*significantly higher ($p<0.05$)

Table 2: Correlation of Creatinine and Lipid Profile with HbA1c in patients with Diabetic DFU

		HbA1c	Creatinine	Cholesterol	HDL	LDL	TG
HbA1c	Pearson Correlation	1	.692**	.792**	-.932**	.862**	.976**
	Sig. (2-tailed)		.000	.000	.000	.000	.000
	N	100	100	100	100	100	100
Creatinine	Pearson Correlation	.692**	1	.736**	-.796**	.819**	.766**
	Sig. (2-tailed)	.000		.000	.000	.000	.000
	N	100	100	100	100	100	100
Cholesterol	Pearson Correlation	.792**	.736**	1	-.838**	.878**	.847**
	Sig. (2-tailed)	.000	.000		.000	.000	.000
	N	100	100	100	100	100	100
HDL	Pearson Correlation	-.932**	-.796**	-.838**	1	-.941**	-.970**
	Sig. (2-tailed)	.000	.000	.000		.000	.000
	N	100	100	100	100	100	100
LDL	Pearson Correlation	.862**	.819**	.878**	-.941**	1	.932**
	Sig. (2-tailed)	.000	.000	.000	.000		.000
	N	100	100	100	100	100	100
TG	Pearson Correlation	.976**	.766**	.847**	-.970**	.932**	1
	Sig. (2-tailed)	.000	.000	.000	.000	.000	
	N	100	100	100	100	100	100

**. Correlation is significant at the 0.01 level (2-tailed).

DISSCUSSION

Uncontrolled HbA1c level is considered to be a strong indicator of uncontrolled glucose level in blood. This study evaluated the level of HbA1c levels in diabetic patients having foot ulcers and without foot ulcer. The high percentage of the diabetic patients with DFU (86%) may be significant observation in the management of DFU. This finding can be correlated to the fact that diabetic mellitus being a metabolic disorder causes the altered protein and lipid metabolism and thereby abnormal granulation tissue formation. It can also significantly supports the findings of Goldin A. *et al* who indicated that increased glucose levels in the body end up in uncontrolled covalent bonding of aldose sugars to a protein or lipid without any normal glycosylation enzymes [19]. The accumulation of these products called advanced glycation end product (AGEs) over the surface of cell membranes occurs on extracellular matrix proteins and alter the properties of matrix proteins such as collagen, vitronectin and laminin results in increased stiffness and increased synthesis of granulation tissue [19-22].

CONCLUSION

The data indicates that almost all the patients with DFU have Creatinine level =1.23 mg/dl with an average value of 1.77 mg/dl where normal range is 0.6-1.2 mg/dl. So increase of creatinine level with a possibility of kidney dysfunction may be associated with diabetic foot ulcer (DFU). The most significant findings of this study are that, with the increase of HbA1c level Creatinine, Cholesterol, LDL and TG level increases in DFU patients. It was also found that HDL level decrease with the increase of HbA1C level in patients with DFU. Another important finding is that, In case of foot ulcer patient HbA1c, Creatinine, Cholesterol, LDL and triglycerides level were found higher than those of patients without foot ulcer where it was opposite in case of HDL. The data analysis also indicates that male persons are at the greater risk of foot ulcer than those of female person [23-25]. It was also found that foot ulcer more frequently occurs in the patient aged more than 50.

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