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Correlation of Blood Glucose Level, Glycated Hemoglobin, Total Cholesterol and Triacylglycerol Level in Diabetic Patients Attending Tertiary Care Hospital in Eastern Nepal

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Abstract- Background: Measurement of blood glucose level and glycated hemoglobin (HbA_{1c}) are widely used for long term management of diabetes and its complications. Dyslipidemia, an abnormal level of lipids in blood, is frequently associated with diabetes as a strong risk factor for developing cardiovascular disease, and its control can prevent cardiovascular complications. In this study of diabetic patients, we assessed the blood glucose level, HbA_{1c} and estimated average glucose (eAG) to determine the correlation with lipid profiles specifically the total cholesterol(TC) and triacylglycerol(TAG).

Methods: In this retrospective cross sectional study, we analyzed the fasting blood glucose (FBG), postprandial blood glucose (PPBG), HbA_{1c}, TC and TAG level in 726 diabetic patients seen at the biochemistry laboratory, B.P. Koirala Institute of Health Science, Dharan, during January, 2011 to January, 2012. Estimated average glucose (eAG) was calculated from HbA_{1c} using pre-established regression equation ($AG_{mg/dl} = 28.7 \times A1C - 46.7$) proposed by Nathan et al. The correlation coefficient was determined and p value <0.05 was considered statistically significant.

Results: Out of 4,816 samples with lipid profile, we analyzed 726 samples with blood glucose level in the diabetic range, according to American Diabetes Association (ADA) criteria 2010. The median values were FBG 152.5 mg/dl, PPBG 287.0 mg/dl, TC 172.0 mg/dl, TAG 154.0 mg/dl, HbA_{1c} 7.4%. It was found that 9.0% had hypercholesterolemia and 56.7% hypertriglyceridemia according to reference range given in the test kit. There was a significant correlation between FBG with TC, TAG, HbA_{1c} and eAG.

Conclusion: This study shows the association of hyperglycemia defined by elevated FBG with dyslipidemia in diabetic patients. In addition HbA_{1c} not only measures chronic control of blood glucose levels but can also be used to assess the degree of dyslipidemia.

Keywords: blood glucose, glycated hemoglobin, total cholesterol, triacylglycerol, dyslipidemia, nepal.

I. INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia and abnormal carbohydrate, fat and protein metabolism which results from defects in insulin secretion and or insulin action. DM is associated with various acute and chronic complications resulting in systemic damage. (World Health Organization. Dept. of Noncommunicable Disease Surveillance., 1999) Plasma lipid and lipoprotein abnormalities which includes, reduced high density lipoprotein cholesterol (HDL-C), predominance of small dense low density lipoprotein particles (LDL-C) and elevated TAG (also known as lipid triad), are shown to have tight association with DM, especially type 2 DM (T2DM). (Temelkova-Kurktschiev and Hanefeld, 2004) This condition of dyslipidemia is a potential risk factor for atherosclerosis, cardiovascular disease and resulting morbidity and mortality. (Lowe et al., 1997) Therefore, regular monitoring of FBG, PPBG and HbA_{1c} level and adopting suitable therapeutic approaches is imperative in controlling dyslipidemia and lipoprotein disturbances. Effective management of these parameters could provide a beneficial effect against atherosclerosis, cardiovascular complication and resulting adverse consequences. (Ahmed et al., 2008) According to World Health Organization (WHO) and ADA, the value of FBG, PPBG and HbA_{1c} are considered as important criteria for the diagnosis for DM. However, HbA_{1c} is also used to assess long term monitoring of blood glucose level. (American Diabetes, 2010) We have used ADA criteria 2010 to categorize patients into diabetic and non-diabetic. (American Diabetes, 2010) Based on these criteria, FBG level (126 mg/dL or

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PPBG level (200 mg/dL or HbA_{1c} 6.5%) were classified as diabetic.

The relationship between estimated average glucose level (eAG) and HbA_{1c} have been shown by many studies, and various equations have been obtained. (Nathan DM, 2007, Sacks et al., 2002, Rohlfing et al., 2002) In the present study we have used Nathan's regression equation (Nathan DM, 2007), as recommended by the ADA, to calculate the eAG level using HbA_{1c} value. This was then used to study the relationship with FBG level and lipid profile in diabetic patients.

II. MATERIALS AND METHODS

We analyzed one-year retrospective data (January 2011 to January 2012) from the Department of Clinical Laboratory Services and Laboratory Medicine, BPKIHS, Dharan. Out of 4,816 samples with a lipid profile only 726 samples containing both lipid profiles with their respective blood glucose levels or HbA_{1c} levels were included in this analysis. The parameters for the diagnosis of diabetes as per the criteria proposed by ADA were FBG ≥ 126 mg/dL or PPBG ≥ 200 mg/dL or $HbA_{1c} \geq 6.5\%$ [5]. FBG and PPBG was measured by auto Analyzer (Vitalab™ Selectra E) using Glucose Oxidase-Peroxidase (GOD-POD) and HbA_{1c} level were measured by Nycocard reader™ II based on immuno chromatographic principle. Serum TC and serum TAG were also measured in auto Analyzer (Vitalab™ Selectra E) based upon the principle of Cholesterol Oxidase-Peroxidase (CHOD-PAP) and Glycerol Oxidase-Peroxidase (GPO-PAP) respectively.

III. ETHICAL CLEARANCE

Permission was granted for the use of medical data, taken from medical records section of B.P. Koirala Institute of Health Sciences (BPKIHS), Dharan. The ethical clearance for this study was approved from the Institutional Ethical Review Board of BPKIHS, Dharan, Nepal.

IV. STATISTICAL ANALYSIS

The normality of data was checked by Kolmogorov-Smirnov test. We applied Spearman's rank correlation test as all data obtained were non-normal. Comparison of age and sex with other parameters was done by Man Whitney-U test. A p-value ≤ 0.05 was considered statistically significant.

V. RESULT

Among 726 subjects, 50.7% (n=368) were males and 49.3% (n=358) were females. The median values were FBG 152.5 mg/dL, PPBG 287.7 mg/dL, TC 172.0 mg/dL, TAG 154.0 mg/dL and HbA_{1c} 7.4% (see table 1). Of the diabetic patients, 18.9% (n=137) had

underlying borderline high cholesterol, 9.0% (n=65) were hypercholesteromic and 56.7% (n=412) were hypertriglyceremic (see table 2).

A nonparametric procedure, the Spearman's rank order correlation coefficient (i.e., Spearman's rho) was computed to assess the relationship among FBG, PPBG, TC, TAG and HbA_{1c} . We found a statistically significant correlation between FBG and TC ($r=0.145$, $n=626$, $p<0.01$), FBG and TAG ($r=0.159$, $n=626$, $p<0.01$), PPBG and TC ($r=0.135$, $n=509$, $p<0.01$), PPBG and TAG ($r=0.147$, $n=509$, $p<0.01$), HbA_{1c} and TC ($r=0.54$, $n=286$, $p<0.01$) and HbA_{1c} with TAG ($r=0.126$, $n=323$, $p<0.05$) (see table 3).

A scatter plot between FBG and HbA_{1c} (see Figure 1), HbA_{1c} and TC (see Figure 2) and HbA_{1c} and TAG (see Figure 3) are presented to summarize these results. In contrast to other parameters, females were found to have higher median total cholesterol (178 mg/dL) than males (168 mg/dL) which was statistically significant $p\leq 0.007$. There was no significant difference between two age groups (>40 and <40 years) for TC, TAG, blood glucose level and HbA_{1c} (data not shown).

We also calculated estimated average blood glucose (eAG) level of all samples with HbA_{1c} values and found a significant correlation between FBG and eAG. There was also a significant correlation of eAG with TC ($p\leq 0.04$, $r=0.161$), TAG ($p\leq 0.024$, $r=0.126$) and PPBG ($p\leq 0.001$, $r=0.448$).

VI. DISCUSSION

Our study provides evidence of connection in elevated blood glucose level and HbA_{1c} with dyslipidemia in diabetic patients. The HbA_{1c} measurement is used to determine the average level of glycemic control over the previous 8–12 weeks; this measurement is accepted as a gold-standard measurement of chronic glycaemia. (American Diabetes, 2010) We found a significant correlation among FBG with PPBG ($p<0.01$, $r=0.686$), TC ($p<0.01$, $r=0.145$), TAG ($p<0.01$, $r=0.159$) and HbA_{1c} ($p<0.01$, $r=0.54$) in accordance with the findings of Ito *et al* (Ito et al., 2000) and Khan *et al*. (Khan et al., 2007)

We also calculated eAG from the values of HbA_{1c} using the formula derived from Nathan ($AG_{mg/dl} = 28.7 \times HbA_{1c} - 46.7$). (Nathan DM, 2007) The eAG will help the health care providers to clearly interpret the result of HbA_{1c} .

In our study, we found a significant correlation between eAG and FBG similar to the findings of Bozkaya *et al* (Bozkaya et al., 2010). Diabetic patients can have many lipid abnormalities including hyper chylomicronaemia, elevated levels of very low density lipoprotein cholesterol (VLDL-C), low density lipoprotein cholesterol (LDL-C) and triglycerides, and low levels of high- density lipoprotein cholesterol (HDL-C). (Haffner, 1998) All of these lipid abnormalities are predisposing

factors for atherosclerosis and cardiovascular disease. (Haffner et al., 1998, Pyorala et al., 1987) In diabetes, these conditions arise due to impaired metabolism, especially glucose metabolism leading to hyperglycemia and dyslipidemia. Thus, controlling hyperglycemia can minimize these lipid disorders and subsequent vascular conditions. (Marcus, 2001, Lehto S et al., 1997) Considering the importance of these parameters, we assessed lipid parameters in diabetes. We were only able to include TC and TG in lipid profile due to the variation in methods of analysis in our laboratory for HDL-C, VLDL-C, and LDL-C.

Similar to the finding from Esteghamati *et al* (Esteghamati et al., 2006), we found higher level of TC in females than in males which was significant. This was in contrast to the finding of Mengesha *et al* (Mengesha, 2006). Except for TC levels, which tend to be higher in females, there was no significant difference between males and females with regard to the other plasma lipid levels. The eAG calculated from HbA_{1c} also showed good correlation with FBG, TC and TAG.

VII. CONCLUSION

Our study shows that dyslipidemia is associated with elevated blood glucose level either acutely or chronically. In addition, the value of HbA_{1c} can also indicate eAG. Thus, the adverse effect of hyperglycemia and associated dyslipidemia must not be underestimated in diabetes. Bearing this in mind, continuous monitoring of glucose and lipid profile in diabetic patients is essential. All of these are effective in assessing hyperglycemic and dyslipidemic condition, as shown by our study.

VIII. COMPETING INTERESTS

The author(s) declare that they have no competing interests.

IX. AUTHORS' CONTRIBUTIONS

MKT and PRS conceived and designed the study, participated in literature review and drafted the manuscript. PRS also conducted the statistical analyses. ND and SK collected the data and participated in literature review. ML and NB provided expertise and reviewed drafts. MKT and PRS contributed equally to this work. All authors read and approved the final manuscript.

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Table 1 : Biochemical parameters of diabetic patients

Parameters		Male (n=368)	Female (n=358)	Total
FBS(mg/dL) (n=626)	Median	155	151	153
	(25 th ; 75 th Percentile)	(132 ; 208)	(131 ; 207)	(132 ; 207)
PPBS (mg/dL) (n=509)	Median	300	279	287
	(25 th ; 75 th Percentile)	(240 ; 387)	(234 ; 359)	(236 ; 376)
TC(mg/dL)* (n=726)	Median	168	178	172
	(25 th ; 75 th Percentile)	(139 ; 195)	(142 ; 211)	(140 ; 203)
TAG (mg/dL) (n=726)	Median	152	157	154
	(25 th ; 75 th Percentile)	(101 ; 234)	(110 ; 217)	(105 ; 225)
HbA _{1c} (%) (n=323)	Median	7.3	7.4	7.4
	(25 th ; 75 th Percentile)	(6.2 ; 9.1)	(6.6 ; 9.3)	(6.3 ; 9.2)

*significant at the level $p < 0.05$

Abbreviation; FBG= Fasting Blood Glucose, PPBG= Postprandial Blood Glucose, TC=Total Cholesterol, TAG=Triacylglycerol

Table 2 : Distribution of lipid parameters among diabetic patients by gender

Lipid parameters		Male (n=368)		Female (n=358)		Total (n=726)	
		n	%	n	%	n	%
*TC (mg/dl)	Desirable	288	78.3	236	65.9	524	72.2
	Borderline high	57	15.5	80	22.3	137	18.9
	Hypercholesterolemia	23	6.3	42	11.7	65	9.0
TAG (mg/dl)	Normal	167	45.4	147	41.1	314	43.3
	Hypertriglyceridemia	201	54.6	211	58.9	412	56.7

*Significant at the level $p < 0.01$

Abbreviation; TC=Total Cholesterol, TAG=Triacylglycerol

TC Desirable <200 mg/dL, Borderline high 200-239 mg/dL and Hypercholesterolemia >240 mg/dL. TG Normal <140 mg/dL and Hypertriglyceridemia >140 mg/dL.

Table 3 : Correlation between FBS, PPBS, TC, TAG and HbA_{1c} in diabetic patients

Parameters		FBS	PPBS	TC	TAG
PPBS	r value	0.686**			
	n	409			
TC	r value	0.145**	0.135**		
	n	626	509		
TAG	r value	0.159**	0.147**	0.438**	
	n	626	509	726	
HbA _{1c}	r value	0.54**	0.448**	0.161**	0.126*
	n	286	242	323	323

Spearman's rank correlation

*significant at the level $p < 0.05$

**highly significant at the level $p < 0.01$

Abbreviation; FBG=Fasting Blood Glucose, PPBG=Postprandial Blood Glucose, TC=Total Cholesterol, TAG=Triacylglycerol

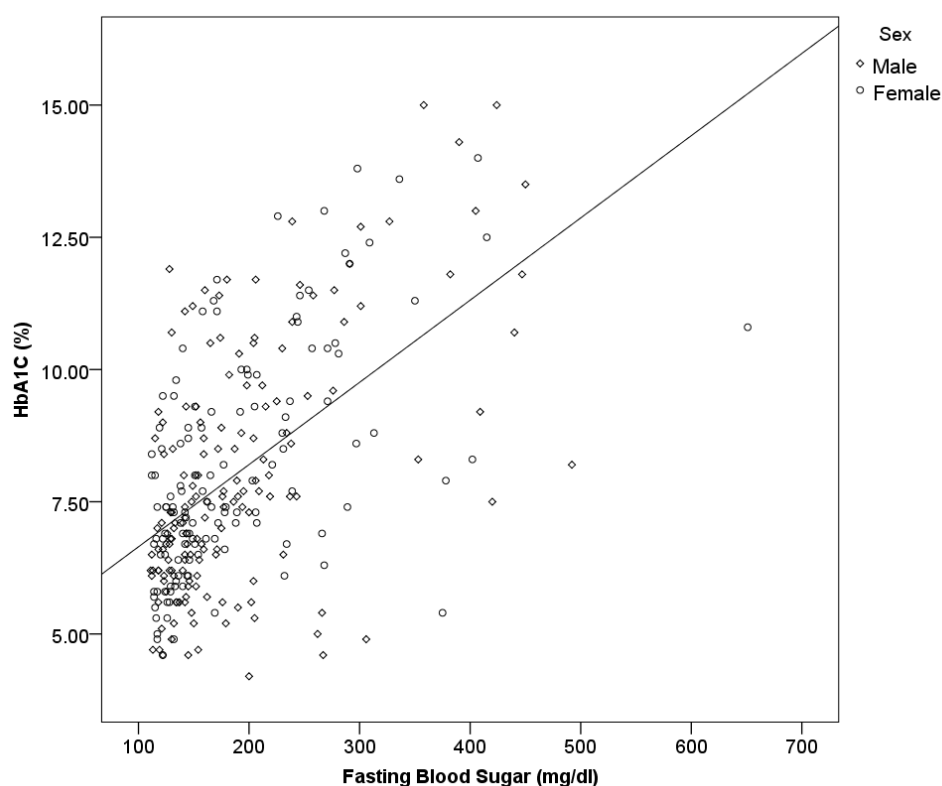


Figure 1: Correlation between HbA_{1c} level and FBS in diabetic patients

Spearman's rho correlation=0.540; $p < 0.001$

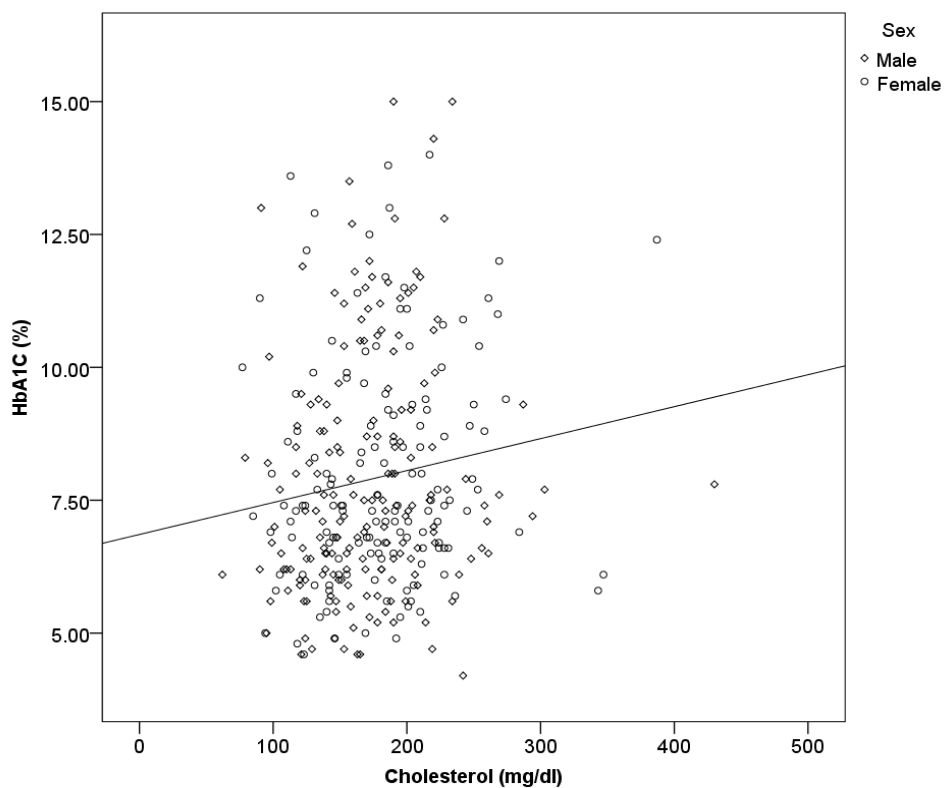


Figure 2 : Correlation between HbA_{1c} level and TC level in diabetic patients
Spearman's rho correlation=0.161; $p=0.004$

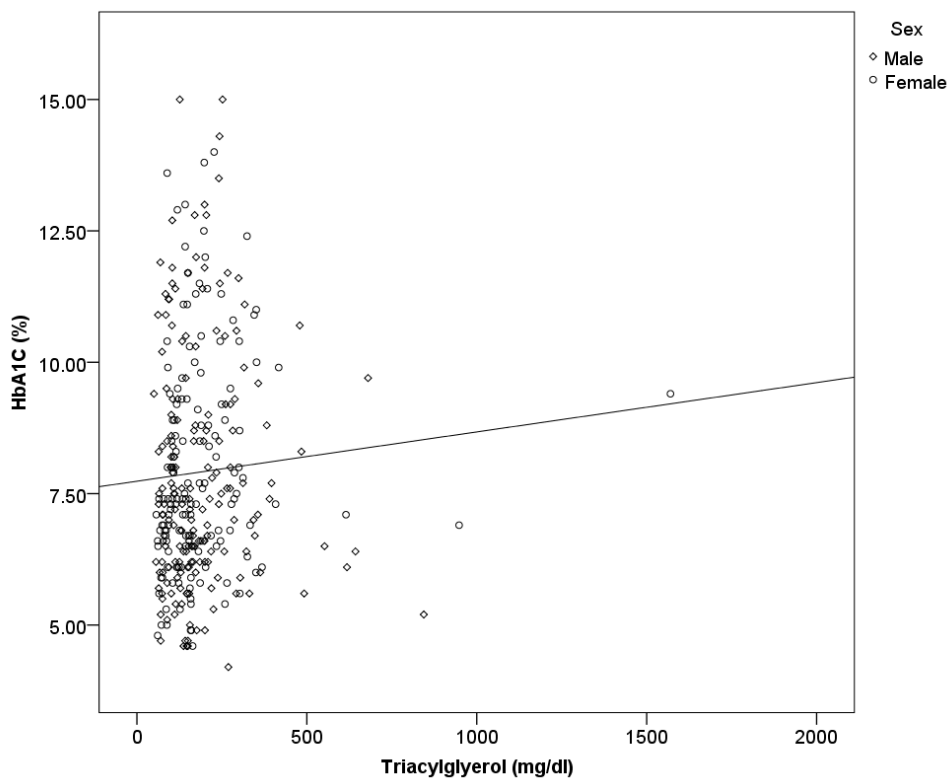


Figure 3 : Correlation between HbA_{1c} level and Triacylglycerol level in diabetic patients
Spearman's rho correlation=0.126; $p=0.024$