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A Case-Control Study to Evaluate the Predictive Ability of Hba1c in Detecting Type-II Diabetes Mellitus with Nephropathy

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KEYWORDS

Diabetes type 2, Nephropathy, HbA1c

ABSTRACT:

Objective: To evaluate the predictive ability of HbA1c in detecting type-II diabetes mellitus with nephropathy.

Methods: The present case-control study was conducted in the Department of Biochemistry and General Medicine at S.M.M.H. Medical College and Hospital and Maa Vindhyavasini Autonomous State Society Medical College & Hospital Mirzapur, India. Patients with history of diabetes type 2 with nephropathy; history of diabetes without nephropathy; and no history of diabetes and nephropathy were included in the study. A total of 30 cases and 30 controls were included in the study. HbA1c (glycated hemoglobin) was estimated by commercially available standard kits.

Results: HbA1c was significantly (p=0.0001) higher among cases (9.81±1.33) compared to controls (5.88±2.46). HbA1c >8.0 correctly (efficacy) predicted DM2 with DN among 48.3% cases with sensitivity and specificity of 96.7 (95%CI=90.2-103.1) and 80.0 (95%CI=65.7-94.3) respectively. The AUC was also high (AUC=0.85, 95%CI=0.74-0.96). Linear regression analysis showed that lipid biomarkers such as HDL, LDL, VLDL & total cholesterol-to-HDL ratio as well as BMI and WHR were positive predictors of HbA1c, after adjusted for age and sex. In turn, TC and TG level was a negative predictive factor of HbA1c levels. The increase of 1 unit on TC was associated with a reduction of 0.05 in HbA1c levels. However, all the predictors had no statistical significance (p>0.05).

Conclusion: HbA1c was found to be significantly higher among cases than controls. There was high sensitivity and specificity of HbA1c in diagnosing DM2 with DN.

Introduction

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of different organs especially the eyes, kidneys, nerves, heart and blood vessels (Anonymous, 2013). India leads the world with largest number of diabetic subjects earning dubious distinction of being termed as the "Diabetes capital of the World" (Mohan et al, 2007). According to ICMR-INDIAB study, there are 62.4 million people with

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diabetes and 77 million people with prediabetes (Mohan, 2012). According to International Diabetes Federation, there are 382 million people living with diabetes rocketing to 592 million by 2035. This means one person in ten will have the disease in less than 25 years (Hirst, 2013). In 2015, the International Diabetic Federation estimated that the prevalence of diabetes was 8.8% from ages 20 to 79 years affecting a population of approximately 440 million people. This is predicted to grow to over 550 million people by the year 2035 (International Diabetes Federation, 2015). One of the most important clinical features of diabetes is its association with chronic tissue complications. A short-term increase in hyperglycemia does not result in serious clinical complications. The duration and severity of hyperglycemia is the major causative factor in initiating organ damage. Early morphological signs of renal damage include nephromegaly and a modified Doppler, but the degree of damage is best ascertained from proteinuria and Glomerular filtration rate (GFR) (Zhang et al, 2018). The diagnosis of diabetes mellitus was determined solely by glucose concentration on the basis of the results of two tests: two fasting plasma glucose (FPG) tests, two oral glucose tolerance tests (OGTTs), or one of each performed on separate days close together in time. In 1993, the Diabetes Control and Complications Trial established the importance of HbA_{1c} as an indicator of risk for microvascular complications of diabetes, such as blindness, kidney disease, and nerve damage; however, it was not until 2009 that the International Expert Committee recommended use of HbA_{1c} for diagnosis of diabetes (International Expert Committee, 2009). The rationale for the use of HbA_{1c} for diagnostic purposes is largely based upon data showing that the microvascular complications of diabetes (retinopathy, nephropathy, and neuropathy) tend to occur in patients with $HbA_{1c} \geq 6.5\%$. The strength of the relationship between HbA_{1c} and these complications is as strong as other definitions of diabetes, including FPG or OGTT. The consensus of the committee was that HbA_{1c} screening should be used whenever possible to diagnose diabetes, in part due to its convenience. The present case-control study was conducted to evaluate the predictive ability of HbA1c in detecting type-II diabetes mellitus with nephropathy.

Material and Methods

The present case-control study was conducted in the Department of Biochemistry and General Medicine at S.M.M.H. Medical College and Hospital and Maa Vindhyavasini Autonomous State Society Medical College & Hospital Mirzapur, India. Patients with history of diabetes type 2 with nephropathy; history of diabetes without nephropathy; and no history of diabetes and nephropathy were included in the study. A total of 30 cases and 30 controls were included in the study. HbA1c (glycated hemoglobin) was estimated by commercially available standard kits.

Statistical Analysis

The results are presented in frequencies, percentages and Mean±SD. The Chi-square test was used to compare categorical variables between cases and controls. The Unpaired t-test was used to compare HbA1c level between cases and controls. The receiving operating curve (ROC) analysis was carried out. The area under the curve (AUC) with its 95% confidence interval (CI) was calculated. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) with its 95% CI was calculated. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

Results

Table-1 shows the basic characteristics of patients of Type-II Diabetes Mellitus with Nephropathy. There was no significant (p>0.05) difference in the basic characteristics of patients between the groups showing comparability of the groups in terms of basic characteristics of patients. HbA1c was significantly (p=0.0001) higher among cases (9.81±1.33) compared to controls (5.88±2.46) (Table-2). Table-3 & Fig.1 shows the predictive values of HbA1c in predicting DM-2 with DN. HbA1c >8.0 correctly (efficacy) predicted DM2 with DN among 48.3% cases with sensitivity and specificity of 96.7 (95%CI=90.2-103.1) and 80.0 (95%CI=65.7-94.3) respectively. The AUC was also high (AUC=0.85, 95%CI=0.74-0.96). There was poor correlation of HbA1c with lipid profile among DM-2 with DN (Table-4). In Table 5, linear regression analysis showed that lipid biomarkers such as HDL, LDL, VLDL & total cholesterol-to-HDL ratio as well as

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BMI and WHR were positive predictors of HbA1c, after adjusted for age and sex. In turn, TC and TG level was a negative predictive factor of HbA1c levels. The increase of 1 unit on TC was associated with a reduction of 0.05 in HbA1c levels. However, all the predictors had no statistical significance (p>0.05).

Table-1: Basic Characteristics of Patients of Type-II Diabetes Mellitus with Nephropathy

Basic Characteristics	Cases (n=30)	Controls (n=30)	p-value[1]
Age in years, Mean±SD	54.50±9.91	53.70±12.20	0.78
Gender, no. (%)	-	-	-
Male	16 (53.3)	14 (46.7)	0.60
Female	14 (46.7)	16 (53.3)	
Height in cms, Mean ±SD	1.66±0.09	1.63±0.08	0.14
Weight in kgs, Mean ±SD	76.53±17.48	70.33±12.14	0.11
BMI in kg/mtr^2, Mean ±SD	27.89±7.70	26.61±5.92	0.47
WHR, Mean ±SD	1.02±0.08	0.96±0.22	0.15
[1]Unpaired t-test/Chi-square test			

Table-2: Comparison of HbA1c Between the Groups

Groups	HbA1c (Mean±SD)
Cases	9.81±1.33
Controls	5.88±2.46
p-value[1]	0.0001*
[1]Unpaired t-test, *Significant	

Table-3: Predictive Values of HbA1c in Predicting DM-2 with DN

HbA1c cutoff	Cases		Controls		Total	
	No.	%	No.	%	No.	%
>8.0	29	48.3	6	10.0	35	58.3
≤8.0	1	1.7	24	40.0	25	41.7
Total	30	50.0	30	50.0	30	100.0
Predictive values, % (95%CI)	-	-	-	-	-	-
Sensitivity	96.7 (90.2-103.1)					
Specificity	80.0 (65.7-94.3)					
PPV	82.9 (70.4-95.3)					
DNV	96.0 (88.3-103.7)					
AUC	0.85 (0.74-0.96)					
%age are from total cases, CI-Confidence interval, PPV-Positive predictive value, DNV-Negative predictive value, AUC-Area under the curve						

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Fig-1: ROC Curve showing Sensitivity and Specificity of HbA1c in Predicting DM-2 with DN

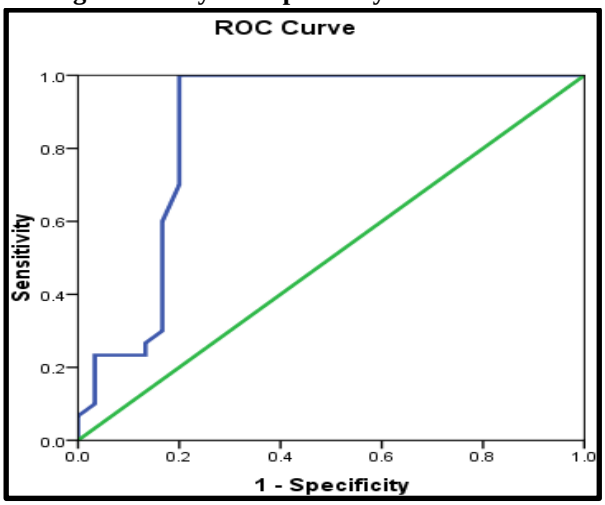

Table-4: Correlation of HbA1c with Lipid Profile among Patients of DM-2 with DN

Lipid profile	HbA1c	
	Correlation coefficient	p-value
TC	-0.14	0.45
TG	-0.05	0.78
HDL	0.07	0.69
LDL	-0.07	0.68
VLDL	0.02	0.91
TC/HDL	-0.18	0.33

Table-5: Multivariate Linear Regression Analysis with HbA1c as a Dependent Variable

Predictors of HbA1c	Beta Coefficient	95%CI	p-value
BMI	0.03	-0.11 to 0.18	0.63
WHR	0.47	-8.29 to 9.18	0.91
TC	-0.05	-0.36 to 0.25	0.71
TG	-0.004	-0.02 to 0.01	0.69
HDL	0.23	-1.67 to 2.14	0.79
LDL	0.03	-0.04 to 0.10	0.42
VLDL	0.01	-0.06 to 0.07	0.84
TC/HDL	0.44	-8.29 to 9.18	0.91

Discussion

In the present study, HbA1c was significantly (p=0.0001) higher among cases (9.81±1.33) compared to controls (5.88±2.46). Gantala et al (2018) showed that the mean HbA1c levels of type 2 DN found to be more than that of controls which was found significant at ($p<0.01$). The finding of this study was consistent with the reports by Timothy and Peter (2000) where variations in HbA1c levels were strongly associated with DN in patients with type 2 diabetes. Previous studies have shown that patients with HbA1c >8% are at higher risk for renal diseases (Jawa et al, 2004).

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HbA1c is considered to be the gold standard for measurement of glycemic control. It is also a predictor of diabetic complications (Jha et al, 2010). Study by Williams & Garg (2014) have revealed a significant association of HbA1c with clinical stages of diabetic nephropathy, where higher HbA1c levels were associated with stage 3 and stage 4 and increased risk of mortality in diabetic nephropathy patients. Previous studies by Kawanami et al (2016) and Chehade et al (2013) have shown that dyslipidemia facilitates glomerulosclerosis under diabetic conditions. Dyslipidemia complicated with diabetes has been shown to be involved in the development of type 2 DN. Dyslipidemia in type 2 diabetes is characterized by an increase in VLDL, LDL and TG and a decrease in HDL (Mooradian, 2009; Parveen et al, 2016). Rai et al (2017) found that HbA1c levels in T2DM without any complications were 6.92 ± 1.40, in T2DM with nephropathy was 8.93 ± 2.35 and in controls was 5.45 ± 0.50. T2DM without any complications and T2DM with nephropathy had statistically significant higher levels of HbA1c when compared to controls, which was statistically significant ($p < 0.001$). In this study, linear regression analysis showed that lipid biomarkers such as HDL, LDL, VLDL & total cholesterol-to-HDL ratio as well as BMI and WHR were positive predictors of HbA1c, after adjusted for age and sex. In this study, HbA1c >8.0 correctly (efficacy) predicted DM2 with DN among 48.3% cases with sensitivity and specificity of 96.7 (95%CI=90.2-103.1) and 80.0 (95%CI=65.7-94.3) respectively. The AUC was also high (AUC=0.85, 95%CI=0.74-0.96). Su et al (2018) showed that ROC analysis revealed that the optimal cutoff value of HbA1c to indicate DPN was 15.15%, and its corresponding sensitivity and specificity were 66.67% and 65.73%, respectively.[1-18]

Conclusion

HbA1c was found to be significantly higher among cases than controls. There was high sensitivity and specificity of HbA1c in diagnosing DM2 with DN.

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