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RELATIONSHIP BETWEEN DURATION OF DISEASE, BMI AND BLOOD GLUCOSE WITH HBA1C LEVELS IN TYPE II DIABETES MELLITUS PATIENTS IN INDIA

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ABSTRACT

Introduction: Type II Diabetes Mellitus is one of the diseases which is expected to reach epidemic proportions in the Indian subcontinent in the coming years. HbA1c levels are used to assess the severity of the disease universally. In the present study we have tried to test for the relationship between the duration of diabetes, BMI of the patients and blood glucose with HbA1c levels.
Material and Methods: 87 Type II Diabetes Mellitus patients were recruited for this study. Their anthropometric and disease history was noted down and HbA1c and blood glucose levels were estimated biochemically.
Statistical Analysis: Data collected was entered in to MS Excel and analyzed by SPSS 25 software for relationship of variables with HbA1c by correlation test and whether these variables are predictors of HbA1c by regression tests.
Result: The duration of diabetes and BMI were not correlated with HbA1c levels, however FBG AND PPG were correlated significantly with HbA1c levels. Also BMI, duration of diabetes, FBG and PPG were found to be independent predictors of HbA1c levels in these patients.
Discussion: BMI and duration of diabetes are not correlated with HbA1c levels in a Type II diabetes mellitus patients but both FBG and PPG were found to be correlated with HbA1c levels. Also if FBG, PPG, BMI and duration of diabetes are known, HbA1c levels can be predicted, showing that these variables can be used to monitor and assess the morbidity of diabetes in these patients.

KEYWORDS : Type II Diabetes Mellitus, NIDDM, BMI, Blood glucose, HbA1c, Indian population

INTRODUCTION

Noncommunicable diseases (NCDs), such as cardio-vascular disease, cerebro-vascular disease, cancer, chronic respiratory diseases and diabetes, are the leading cause of mortality in the world. Diabetes mellitus (DM) is a NCD assuming epidemic proportions in India. There has been a consistent increase in the prevalence of DM in Indian population from 5% in 1980 to 9% in 2014 and it is projected to increase in the future[1]. Risk factors for DM include increased body weight and reduced physical activity. The prevalence of these risk factors in the same year was 21.4% and 12.1% respectively[1]. Diabetes alone accounts for 2% of all deaths among all ages in India[1]. This poses a major public health threat.

Given the large socio-economic and lifestyle differences among different regions of India, it is expected that the prevalence of diabetes would differ among sub-groups of the population. In several multicentric studies conducted in India, the prevalence of Type 2 DM has been estimated as 2.1% in urban areas and 1.5% in rural areas[2]. In other studies, the overall prevalence of DM was 12% [3], 5.9% [4], 33.5% [5] and 4.5% [6] in various samples of Indian population. This is indicative of the consistency of high prevalence of DM among various sub-groups of the Indian population and the urgent need for intervention.

The diagnosis of diabetes is based classically on the Oral Glucose Tolerance Test (OGTT) where the fasting plasma glucose 7 mmol/l (126 mg/dl) or 2 hour plasma glucose 11.1 mmol/l (200 mg/dl) is the current diagnostic criteria[7]. In recent times lot of interest has been generated with regards to glycated hemoglobin (HbA1c). HbA1c is a modified hemoglobin molecule with a stable adduct of glucose that is covalently linked to the N-terminal valine of the beta chain. HbA1c has been proposed as a new test to diagnose diabetes with a value 6.5% to be recommended as the cut point for diagnosis[8,9,10]. There are various advantages of HbA1c over traditional glucose testing because it is independent of last meal, has low variability and shows greater consistency in reflecting glucose levels over the last 8-12 weeks[11]. Based on the above information the aim of our study was to find whether Body Mass Index (BMI), the duration of diabetes, fasting blood glucose (FBG) and postprandial glucose (PPG) were correlated with HbA1c levels and whether these variables could be used to reasonably predict HbA1c in a patient with type 2 DM.

MATERIAL AND METHODS

In this cross sectional study, 87 patients with an established diagnosis of type 2 DM attending an urban outpatient OPD were recruited. All patients were on treatment with oral hypoglycemic agents metformin and/or glimepiride. This study was approved by the ethics committee of Santosh Medical College and Hospital and written, informed consent was obtained from the participating patients.

Anthropometric parameters: A detailed history including all vital parameters was taken initially from all the patients and duly noted down. Age was taken as completed years on the medical records. Height was measured using a standard stadiometer with subject standing in erect posture with the heel and back against the wall without footwear. The readings were taken to nearest 0.1 cm. Weight was recorded in kilograms (kgs) using a calibrated portable weighing machine (Avery) with a capacity of 120 kg and a sensitivity of 0.05 kg without shoes while bearing weight on both feet. Body mass index was calculated as the ratio of weight in kgs divided by the square of height in meters [weight(kg)/height(m)^2]. Duration of diabetes was taken as the time duration from the first date of diagnosis of diabetes to the day of the study in years.

Biochemical parameters: Oral Glucose Tolerance test was prescribed to the patients and fasting blood glucose and post prandial glucose were estimated in the plasma by Glucose oxidase-peroxidase method[12]. For estimation of HbA1c, blood in EDTA vial was used and it was estimated by modified ion-exchange high performance liquid chromatography method[13] using an automated, calibrated chemistry analyzer.

Statistical Analysis:

Data collected by the various methods was entered in to the Microsoft Excel file for further analysis. SPSS 25.0 for Mac (IBM Corp, Armonk, N.Y, U.S.A) software was used for statistical analysis of the data. Data was first tested for normal distribution using standard tests. As our data did not have a normal distribution, the correlation of BMI, Duration of disease, FBG and PPG with HbA1c was analyzed using Spearman's correlation independently. Linear regression was applied to BMI, duration of diabetes, FBG and PPG to determine whether they were predictors of HbA1c values.

RESULTS:

Out of the 87 patients, 51 were males and 36 were females. As shown in table 1, the mean age of the study population was 54 years with a range of 30-80 years. The mean duration of diabetes in the study population was 7 years. The mean BMI was 27.4 kg/m^2 with range of 17-49 kg/m^2. Patients had a mean FBG of 160 mg/dl and a mean PPG of 244 mg/dl. Finally, the mean HbA1c was 8.4% with a maximum value of up to 15%.

When PPG values were correlated with HbA1c values, it was found to be significant with correlation coefficient of 0.458 and p-value at 0.01 as shown in table 2. Similarly, there was a significant correlation between FBG and HbA1c values with a correlation coefficient of 0.482 and p value at 0.01 as shown in table 3. Correlation studies between BMI values and HbA1c values did not yield any significant results. Similarly, there was no significant correlation between duration of

diabetes with HbA1c values.

When linear regression was applied to test for a relationship between BMI, duration of diabetes, FBG and PPG on HbA1c values, it was observed that all of these variables were predictors for the HbA1c value. As can be seen in Figure 1, the predicted values of HbA1c on the basis of these variables lie very close to the actual values of HbA1c on y-axis and x-axis respectively. We can see from Figure 2 that if the FBG value is known ,we can predict the HbA1c value in a linear manner which is statistically significant $p<0.05$. Ten such results have been plotted in the figure which establish a linear relationship.

DISCUSSION:

The majority of this study population were in the age group of 40 to 60 years which is the middle age category. This is similar in pattern to the global data where the majority of diabetes morbidity and mortality occurs between 30-70 years of age[1]. Again, the gender distribution of the data in our study showed a majority of the patients were males which was also consistent with the global data[1]. This is also corroborated at national level in the study by Mohan V et al. showing that the percentage of males with diagnosed diabetes were more than females[2]. The duration of diabetes ranged from 1 year to as long as 13 years. Increased duration of diabetes is associated with increased HbA1c values in studies by Arnetz et al.[15] and Kilpatrick et al.[16]. In our study, no correlation was seen between HbA1c and duration of diabetes. Kabadi et al. also found no significant relationship between duration of diabetes and blood glucose which may explain this observation[17]. The BMI of the patients ranged from 23 to 31 kg/m^2. BMI was also not correlated with HbA1c values. This is in contrast to studies where it is shown that increased BMI increases the risk of diabetes and increases insulin resistance[18]. However, the reason behind lack of correlation between BMI and HbA1c may be due to the complex role of BMI and glucose metabolism where free lipids may be deposited in hepatocytes which may alter glucose metabolism[19].

Fasting and postprandial glucose were found to have a significant correlation with HbA1c values in our study. Gupta et al. have also reported a significant correlation of FBG with HbA1c values in Type 2 DM patients[20]. Similar correlation was noted between FBG and HbA1c values in diabetics in a study by Ghazanfari et al.[21]. Correlation between plasma glucose and HbA1c was also seen in a study by Rohlfing et al.[22]. Postprandial glucose was also correlated with HbA1c values in our study. Similar results by other authors have also shown that postprandial plasma glucose is correlated with HbA1c between 7.3%-9.2%, and with fasting blood glucose at HbA1c more than 9.3%[24]. The difficulty associated with postprandial glucose is that it depends on before meal blood glucose, time of the meal and type of the meal and thus is very vague[21]. On the basis of these observations, we can conclude that both FBG and PPG are correlated with HbA1c values.

In the next part of our study, we applied linear regression to study the relationship between BMI, duration of diabetes, FBG and PPG with HbA1c values. We have observed a significant relationship where BMI, duration of diabetes, FBG and PPG were predictors of HbA1c values. Figure 1 shows the graph obtained using these variables to predict HbA1c when compared to the actual values. Figure 2 shows the predicted value of HbA1c based on known values of FBG. As can be seen from the figure, HbA1c values show a linear relationship and can be predicted accurately. A similar study by Rohfling et al.[21] also showed a predictive relationship of mean plasma glucose with HbA1c values. In our study, the new finding is that not only plasma glucose but also BMI of the patient and duration of diabetes is involved in predicting the value of HbA1c in Type 2 diabetes mellitus patients.

Table1. Anthropometric and biochemical variables of Type 2 DM patients

Variables	MeanSD
Age(years)	54.611.4
Duration(years)	7.26.1
BMI(Kg/m^2)	27.44.8
FBG(mg/dl)	160.565.9
PPG(mg/dl)	244.196.8
HbA1c(%)	8.41.9

Table 2. Correlation between PPG and HbA1c values.

			HBA1C	PPG
Spearman's rho	HBA1C	Correlation Coefficient	1.000	.458**
		Sig. (2-tailed)	.	.000
		N	82	81
	PPG	Correlation Coefficient	.458**	1.000
		Sig. (2-tailed)	.000	.
		N	81	81

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

Table 3. Correlation between FBG and HbA1c values.

			HBA1C	FBG
Spearman's rho	HBA1C	Correlation Coefficient	1.000	.482**
		Sig. (2-tailed)	.	.000
		N	82	81
	FBG	Correlation Coefficient	.482**	1.000
		Sig. (2-tailed)	.000	.
		N	81	81

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

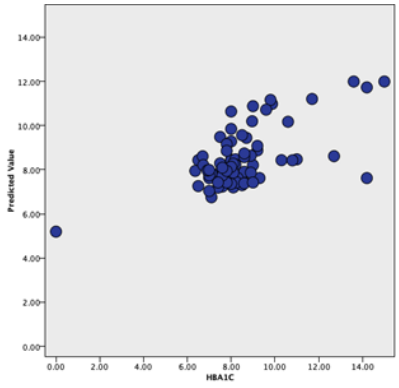

Figure 1. Predicting HbA1c values from BMI, Duration, FBG and PPG.

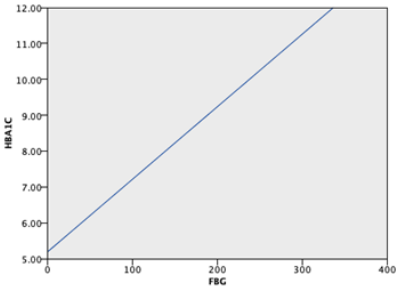

Figure 2. Linear regression between FBG and HbA1c

CONCLUSION:

HbA1c may be used together in conjunction with plasma glucose values for monitoring Type 2 DM as it is also dependent on BMI, duration of disease and blood glucose levels all of which are intimately involved in the pathogenesis and morbidity and mortality associated with Type 2 Diabetes Mellitus. HbA1c is a useful marker because it shows an average value of blood glucose for 120 days out of which 50% of its value reflects the last 30 days blood glucose and only 10% of its value reflects last 90-120 days blood glucose[23].

Limitations of the study:

The study sample population was heterogenous in terms of age, duration of disease and degree of glycemic control. Diabetes being a disease with a high prevalence, number of patients should have been more. A larger sample size would be needed to predict the role of BMI and duration of diabetes together with blood glucose in predicting HbA1c values in Type 2 DM.

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