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A Study of Correlation between Type 2 Diabetes Mellitus and Glycosylated Haemoglobin in a Tertiary Care Centre

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Abstract

Background: Diabetes is a silent killer. Looking at the alarming presence of diabetes and its morbidity and mortality in India, we need to diagnose this metabolic disorder accurately and at the earliest. We have carried out this study to determine correlation of fasting blood glucose, post meal blood glucose and glycosylated haemoglobin in type 2 Diabetes Mellitus and to find the cut off value of glycosylated haemoglobin to diagnose type 2 diabetes mellitus. **Materials and Methods:** A cross sectional study was carried out among 298 cases of type 2 Diabetes Mellitus attending a tertiary care centre in Maharashtra during August 2018 to August 2020. **Results and Conclusions:** Majority were males and in the age group of 41 to 50 years. Fasting Blood Glucose (FBS) and Postprandial Blood Glucose (PPBS) are strongly correlated to Glycosylated Haemoglobin (HbA1c). Association between FBS and PPBS is statistically significant. Correlation of PPBS and HbA1c is stronger than that of FBS and HbA1c. Cut off level of HbA1c is higher in the study subjects in comparison to standard cut off value of 6.5%.

Keywords: Fasting Blood Glucose, Glycosylated Haemoglobin, Postprandial Blood Glucose, Type 2 Diabetes Mellitus

1. Introduction

Diabetes, "the disease of millennium" is recognised by raised blood sugar which causes, over a time lethal injuries to the myocardium, arterial endothelial linings, retina, nephrons and myelin sheath of neurons[1]. Diabetes is the leading cause of visual loss, myocardial infarction, cerebrovascular episodes and lower extremities amputation[2].

Globally, the prevalence of diabetes in the adult age group over 18 years of age increased from 4.7% in year 1980 to 8.5% in year 2014[2]. Prevalence of diabetes in India is 8.8% as reported by International Diabetic Federation. India was the first in the list of countries with high prevalence of diabetes in the world and hence is called as the capital for DM[1].

Type 2 diabetes is the commonest type of DM, almost 90-95% and is usually seen in adults. It is speculated that about one third of type 2 diabetics remain undiagnosed to the extreme occurrence of the complications. So, early diagnosis and treatment becomes very necessary to prevent complications.

Fasting Value of Blood Sugar (FBS), Post Meal Value of Blood Sugar (PPBS), Random Blood Sugar (RBS) and HbA1C are the laboratory tests to diagnose type 2 diabetes. Fasting is specified as no food intake for at least 8 hours. FBG ≥126 mg/dl (7.0 mmol/l) is considered as diabetes. Two hours plasma glucose PPBG ≥200 mg/dl (11.1 mmol/l), in an Oral Glucose Tolerance Test (OGTT), is diagnosed as diabetes. The test is executed as described by the World Health Organization, delivering a glucose bolus comprising of the equivalent of 75 g

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anhydrous glucose added in potable water. In a patient with characteristic symptoms of hyperglycemia or a situation of hyperglycemic crisis, a random plasma glucose value ≥200 mg/dl (11.1 mmol/l) is diagnosed as diabetes. HbA1C ≥6.5% is diagnostic of diabetes. HbA1C is now routinely recommended as one of the established criteria for testing and monitoring glycemic control, especially in type 2 Diabetes Mellitus[3]. It is a measure of blood glucose level over 8-12weeks[2].

The WHO consultation concluded that HbA1c can be utilised as a diagnostic test for Diabetes Mellitus. Below 6% HbA1c is regarded as normal, 6 to 6.5% as pre-diabetes and 6.5% or above as diagnostic of diabetes[2]. Diagnosis of diabetes according to New ADA guidelines: Level of HbA1c ≤5.6% is normal, 5.7 to 6.4% is pre-diabetes and ≥6.5% is diabetes[2].

However, in most of the nations across the world, varied testing strategies and cut off ranges of HbA1c are argued upon till date[4]. Also there are ethnic differences in HbA1C levels, which necessitates an own standard of care regarding patient population[5].

Hence this study is done to see the correlation of DM and HbA1c and to find out the cut-off value of HbA1c in Type 2 Diabetes Mellitus in a tertiary care centre.

2. Aims and Objectives

1. To study the correlation of DM and HbA1c and
2. To find out the cut-off value of HbA1c in Type 2 Diabetes Mellitus in a tertiary care centre.

3. Materials and Methods

This study was a cross sectional observational type of study, done in the Department of Pathology in a tertiary care centre during August 2018 to August 2020.

All those coming to tertiary care hospital and satisfying the eligibility criteria and giving the informed consent were enrolled in the study.

3.1 Inclusion criteria

The patients referred to the Central Clinical Laboratory, suspected of having type 2 Diabetes Mellitus, 40 to 70 years old, irrespective of the gender.

3.2 Exclusion criteria

- Already diagnosed cases of type 2 Diabetes Mellitus who came for follow up.
- Conditions which affect the glycosylated haemoglobin assessment by HPLC method such as:
- Iron and vitamin B 12 deficiency.
- Hemoglobinopathy.
- Chronic renal failure.
- Alcoholism
- Post splenectomy
- Hyperbilirubinemia
- Hypertriglyceridemia
- Haemolytic anemia

RBS, FBS and PPBS were measured by the technique of glucose oxidase peroxidase principle and HbA1C was measured by the High Performance Liquid Chromatography principle. Data was collected in microsoft excel and was analysed using SPSS 22. Institutional ethical approval was taken before starting the study.

4. Results

Table 1. Gender wise distribution of patients

Gender	No. of patients	% of patients
Male	169	56.71
Female	129	43.29
Total	298	100.00

It is observed from Table no.1 that the study population comprised of 169 [56.71%] males and 129 [43.29%] females.

Table 2. Distribution of patients as per age

Age groups	Patient Numbers	% of patients
41-50 yrs	120	40.27
51-60 yrs	95	31.88
61-70 yrs	83	27.85
Total	298	100.00
Mean age	54.10	
SD age	9.98	

Table 2 shows number of patients as per age. Patients in the age group of 41-50 years were maximum i.e., 40.27%. The mean age was 54.19 ± 9.98 years.

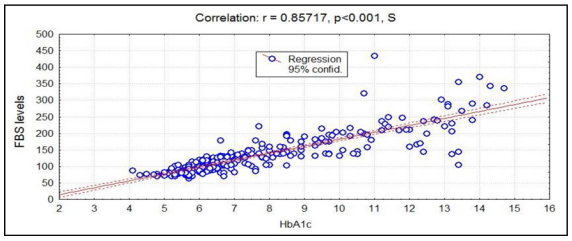


Figure 1. Scatter diagram of correlation between HbA1c and FBS.

A positive and significant correlation was observed between HbA1c and FBS levels (r = 0.8572, p<0.05) at 5% level of significance (Figure 1).

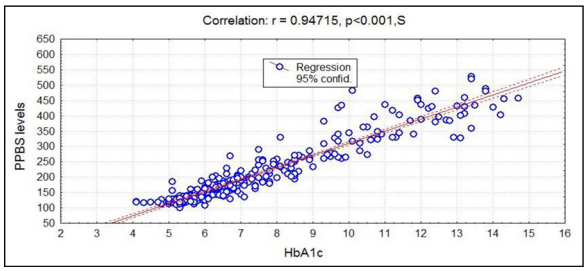


Figure 2. Scatter diagram of correlation between HbA1c and PPBS.

A positive and statistically significant correlation was found between HbA1c and PPBS levels (r = 0.9471, p<0.05) at 5% level of significance (Figure 2).

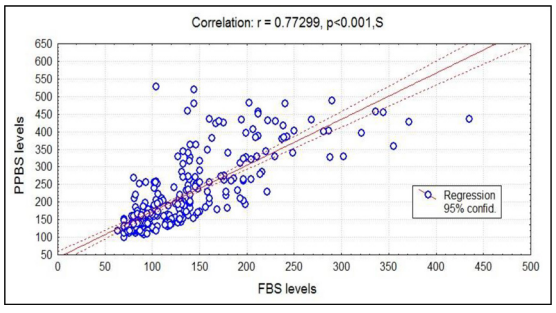


Figure 3. Scatter diagram of correlation between FBS and PPBS levels.

A positive and statistically significant correlation was found between FBS and PPBS levels (r = 0.7730, p<0.05) at 5% level of significance (Figure 3).

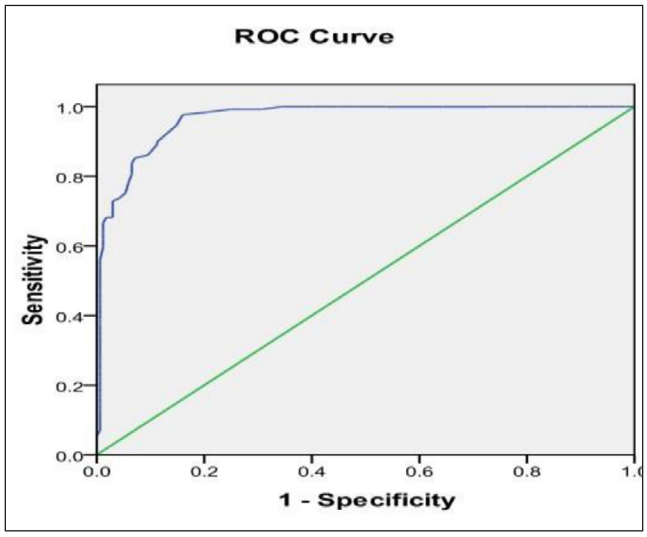
4.1 Receiver Operating Characteristic (ROC) Curve analysis for cut off of HbA1c

FBS more than or equal to 126 mg /dl is taken as diagnostic of Diabetes Mellitus.

Area under the curve**:**

Area	Std. Error	p-value	Asymptomatic 95% of Confidence Interval	
			Lower Bound	Upper Bound
0.966	0.009	0.0001,S	0.948	0.984

Figure 4. ROC Curve:



Range of cut-off value for HbA1C**:**2.10 – 16.70

Cut-off value for Maximum sensitivity and specificity = till the value of 6.15% of HbA1c we can get 100% sensitivity. But the specificity is 66%. As we increase the cut off value of HbA1c, the sensitivity starts decreasing and specificity increases. At the level of 6.8 of HbA1c, sensitivity and specificity both are about 89%. Here we get the maximum sensitivity and specificity. So the cut off level of 6.8% of Hb1Ac will be the best value to diagnose DM (Table 3 & Figure 4).

Table 3. Coordinates of the Curve

Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
6.0500	1.000	0.402
6.6500	0.946	0.148
6.7500	0.915	0.124

6.8450	0.899	0.112
6.8950	0.891	0.112
6.9500	0.860	0.095

ROC analysis of HbA1C: PPBS
PPBS more than or equal to 200 is taken as DM.
Area under the curve

Area	Std. Error	p-value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.979	0.007	0.0001,S	0.966	0.992

Range of Cut off value for HbA1C:2.10 – 16.70

Cut-off Value for Maximum Sensitivity and Specificity = Here also the value of 6.15% of HbA1c gives sensitivity as 100% to diagnose DM. As we increase the cut off value of HbA1c the sensitivity starts decreasing and specificity increases.

7.05% of Hb1Ac gives the sensitivity of 92% and specificity of 90% (Table 4).

Table 4. Coordinates in this Curve

Positive if More Than or Equal To[a]	Sensitivity	1 – Specificity
6.0500	1.000	0.457
6.1500	1.000	0.403
6.2500	0.991	0.371
6.3500	0.982	0.323
6.4500	0.982	0.280
6.5500	0.982	0.231
6.6500	0.964	0.210
6.7500	0.955	0.172
6.8450	0.955	0.151
6.8950	0.955	0.145
6.9500	0.938	0.118
7.0500	0.920	0.102
7.1500	0.920	0.086

Thus, in our study, cut off value of HbA1c is 6.89% according to FBS and 7.05% according to PPBS. In both cases, we have higher cut off value of HbA1c as compared to standard value of 6.5% to diagnose Diabetes mellitus.

5. Discussion

This study is an observational cross sectional one, done on 298 cases of type 2 diabetes coming to a tertiary care hospital. Diabetes is a chronic disorder with profound metabolic derangements. It is becoming one of the commonest non-infectious and non-malignancy related cause of mortality and morbidity[6,7]. Males are more likely to get type 2 DM. Study by Nordostrom et al.[8] reported that the occurrence of type 2 diabetes was 14.6% in males and 9.1% in females which was statistically significant (P < .001). Our study also is in accordance with this, showing 169 [56.71%] males and 129 [43.29%] females.

Most common age of diagnosed type 2 diabetes is more than or equal to 45 years. Present study also shows the mean age of 54.19 ± 9.98 years and major number of patients were in the age range of 41-50 years i.e.,75.57% followed by 51-60 years i.e. 31.88%. Similarly, Mohammadi et al.[9] reported mean age as 44 years. The mean age of the patients was 50.11 ± 11.18 years in a study conducted by Fahrukh et al.[10] in a tertiary care hospital.

Diabetes Mellitus leads to various complications like cardiovascular diseases, neuropathy, retinopathy nephropathy etc. All the complications are mainly due to persistent hyperglycemia[7]. Hence, monitoring of glucose level becomes the mainstay of treatment of type 2 DM. Many clinical trials which were randomized and prospective, in type 2 Diabetes Mellitus, have shown that reducing high level of glycemia significantly reduced the microvessel related complications of diabetes[11]. Pathological tests to diagnose hyperglycemia are fasting blood glucose level, random blood glucose level, post meal blood glucose level and HbA1c level[6],

Out of various parameters, HbA1c is a reliable indicator of chronic hyperglycemia. It has a definite role in management of DM[7]. It is preferable because of the following points: 1. Patients don't need to abstain from food intake, 2. HbA1c denotes a glycaemia over a longer period than plasma glucose level, 3. Laboratory diagnostic modalities are now standardised and are trustworthy and 4. Errors in the measurement of HbA1c are infrequent[12]. Hyperglycemia leads to glycation of various proteins such as HbA1c, formed during the non-enzymatic joining of glucose moiety to haemoglobin, which is considered to denote the overall or average mean glucose level over the course of last 8–12 weeks, the time duration being taken by the 120-days existence of the red blood cells. The value of HbA1c precisely predicts diabetes related complications

as it reflects more ominous glycation related sequelae of diabetes[13–15].

The HbA1c is a precise and easy-to-do laboratory test with on-the-spot values availability and thus, can be a good diagnostic approach in establishing the diagnosis but it cannot be employed as the only screening test because of its low sensitivity. Therefore Fasting Blood Glucose Value (FBS) and Post Prandial Blood Glucose Value (PPBS) should also be performed. Fasting blood glucose is a relatively cheaper test and the preferred test for the diagnosis of DM in clinical practice. Many reports are available showing the significant correlation between glycohemoglobin A1c levels and fasting blood glucose levels[16]. In this study, we observed that there was a significant correlation between FBS and HbA1c levels ($r = 0.8572$, $p<0.05$). Shwetha, et al.[16] also found significant correlation of FBS with HbA1c.

In our study, a positive and significant correlation was observed between HbA1c and PPBS levels ($r = 0.9471$, $p<0.05$) at 5% level of significance which is in accordance with the results found by Shwetha, et al.[16]. The correlation of HbA1c was marginally better with PPBS than that with FBS. Similar result was found by Shwetha et al. in their study[16]. Ketema, et al.[17] and Rosendiani, et al.[18] also found better correlation between PPBS and HbA1c than FBS and HbA1c.

We also found that a positive and significant correlation was present between FBS and PPBS levels ($r = 0.7730$, $p<0.05$) at 5% level of significance. Thus all the blood sugar levels and HbA1c levels were significantly correlated with each other as also found in previous studies[16,19–22].

In spite of the fact that HbA1c has been trusted upon for the diagnosis of Diabetes Mellitus, in a number of nations worldwide, some testing methodologies and cut off ranges are still being scrutinised and debated[17]. Radhakrishna P, et al.[23] has stated that ≥ 6.5 % is a simple and trustworthy alternative to blood glucose test for diagnosing Diabetes Mellitus. Cut off level of HbA1c to diagnose DM may be community specific and may differ with race, ethnicity, age, gender and community prevalence of DM[24].

Our study has shown a cut off value of 6.89% for HbA1c according to FBSL with a sensitivity and specificity of 89%. Cut off value was best at 7.05% for HbA1c according to PPBSL with a sensitivity and specificity of 92% and 90% respectively.

6. Conclusion

Fasting blood glucose value and post prandial blood glucose values are strongly correlated to HbA1c.

Association between fasting blood glucose value and post prandial blood glucose value is statistically significant.

Correlation of post prandial blood glucose value and HbA1c value is stronger than that of fasting blood glucose and HbA1c.

Cut off level of HbA1c is slightly higher in the study population as compared to the standard cut off value of 6.5%.

7. Recommendations

We need to do further study in general population using random samples from the community.

Large sample studies are recommended to check the cut off levels of HbA1c.

8. Limitations

It is a hospital based study and the results obtained cannot be generalized.

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