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Keywords: *glycosylated haemoglobin, plasma glucose, correlation.*

GJMR-C Classification : *NLMC Code: WD 200*



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Correlation between Glycosylated Haemoglobin and Plasma Glucose Levels for the Diagnosis and Control of Diabetes Mellitus at a Tertiary Care Hospital in Western Rajasthan

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Background- Conventional methods are inadequate, unreliable, cumbersome and impractical to monitor continuous 24 hours blood glucose level, to overcome this problem development of new test detecting Glycosylated Haemoglobin (HbA1c), indicates plasma glucose level in last 3 months duration hence it is satisfactory tool for assessment of diabetic control. Therefore the present study is planned to know about the glycaemic control of diabetic patient by HbA1c and to know about the various complications. Objectives: To find correlation of Glycosylated Haemoglobin with fasting and post-prandial plasma glucose levels for the diagnosis and control of Diabetes Mellitus. Material and Methods: A hospital based Cross sectional study was conducted at chemical pathology section of Department of Pathology, Mahatma Gandhi and Mathura Das Mathur Hospital, affiliated to Dr. S. N. Medical College, Jodhpur. One hundred diabetic patients attending medical outpatient department of the same institution were included in the study. Results: Total one hundred confirmed diabetic patients with mean age 55.7 ± 12.9 years and sex ratio of 1.85 in favor of males, were included in the study. Among both type of diabetics we found that fasting and post prandial plasma glucose levels had linear relationship with level of glycosylated Haemoglobin and on regression analysis this result was found statistically significant ($p < 0.001$). Patients with greater duration of illness had greater burden of complications. Conclusion: In most of diabetics there was linear correlation between glycosylated Haemoglobin and fasting plasma glucose as well as post prandial plasma glucose.

Keywords : glycosylated haemoglobin, plasma glucose, correlation.

1. INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiencies in insulin secretion and/or insulin action.^[1]

As the incidence and prevalence of diabetes is increasing day by day so the world is facing an

escalating epidemic of diabetes. The prevalence of diabetes in adults worldwide, estimated to be 4% in 1995, is supposed to rise to 5.4% by the year 2025, and is higher in developed countries than in developing countries. The major part of this increase will occur in developing countries so by the year 2025, more than 75% of people with diabetes will reside in developing countries like India, China and U.S.^[1]

Continuous research work has been done in this area of internal medicine, but lack of infirmity and standardization of screening procedure accounts for difficulty in evaluation of prevalence rates of Diabetes. Diabetes is itself a complex disease, moreover variation in diagnostic techniques used all over world makes this task more difficult, but inspite of that a good deal of progress has been made worldwide. In India specially, Western Rajasthan still lots of worked has to be done. One of the main reason for difficulty in resolving this problem is lack of satisfactory method for quantitative assessment of Diabetes control. This problem is not solved by routinely used methods like random blood sugar estimation and intermittent measurement of daily urinary glucose excretions. These methods are inadequate, unreliable, cumbersome and impractical to monitor continuous 24 hours blood glucose levels specially in out-patient setting. The answer to this problem is development of new test detecting Haemoglobin A₁C, indicates plasma glucose level in last 3 months duration hence it is satisfactory tool for assessment of diabetic control. This method is helpful not only for conducting long term studies on the course and effect relationship between diabetic control and late complications but also for day to day management of diabetic patient.

Haemoglobin A₁C, a fast moving minor Haemoglobin component is present in normal persons, but increases in presence of hyperglycemia. HbA₁ is fractionated into HbA_{1a,b,c} by ion exchange column chromatography. Most of these are HbA1C and are most susceptible to the effects of fluctuation in glucose levels. That is why it is most suitable as an indicator of blood glucose control.^[2,3]

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Synthesis of increased amounts of HbA_{1c} has been shown to correlate with glucose control in diabetics.^[4]

As the number of studies done about screening the glycaemic control and early detection of complications are very less specially in western zone of Rajasthan, therefore the present study is planned to know about the glycaemic control of diabetic patient by HbA_{1c} and to know about the various complications.

II. MATERIALS AND METHODS

a) Study design

A hospital based Cross sectional study design was adopted for the study.

b) Study Area

Study was conducted at chemical pathology section of Department of Pathology, Mahatma Gandhi and Mathura Das Mathur Hospital, affiliated to Dr. S. N. Medical College, Jodhpur.

c) Sample size

One hundred diabetic patients attending medical outpatient department of Mahatma Gandhi and Mathura Das Mathur Hospital, Jodhpur were included in the study.

d) Tool and Techniques

Patients attending medical outpatient department of Mahatma Gandhi and Mathura Das Mathur Hospital, Jodhpur were scruted for diabetes mellitus.

Prior consent was taken of all patients included in the study. A self prepared semistructured Proforma was used to obtain complete clinical picture of patients. The Proforma comprised of three parts, part one consisting of epidemiological profile and detailed history regarding diabetes mellitus, part two consisting of complete physical examination and part three consisting

of complete investigations regarding diabetes mellitus as well as other body system functions.

The diagnostic criteria were based on WHO study group criteria (i.e. fasting plasma glucose ≥ 126 mg/dl or 2 hours post glucose level ≥ 200 mg/dl).^[5]

Quantitative estimation of glycosylated Haemoglobin (HbA₁) in blood by cation exchange resin chromatography method. From the value of HbA₁, HbA_{1c} was calculated using the formula $[HbA_{1c} = (HbA_1 - 6.14) / 1.23]$.

e) Exclusion Criteria

1. Patients with recent onset diabetes (<6 months).
2. Patients within 1 month of any coronary vascular event.
3. Patients with recent acute illness (<3 months).
4. Patients of liver disease, gout and hypothyroidism.
5. Alcoholic patients.
6. Patients on lipid lowering agents, niacin, neomycin, estrogen, HRT, corticosteroids and stanozolol.
7. Pregnancy.

f) Data Analysis

Data was entered and analyzed by using Microsoft Exel and SPSS Version 16.0 and appropriate statistical tests were applied to find out statistically significant difference.

III. RESULTS

Total one hundred confirmed diabetic patients were included in the study. Patients belonged to 14 -85 years age group (mean age 55.7 ± 12.9 years). Majority 65(65%) of patients were males and patients between 41-60 years were most commonly (49%) affected. Majority 86(86%) of the patients belong to diabetes mellitus type-2. (Table 1)

Table 1: Distribution of type of diabetes according to age group

Age	Type of Diabetes		Total
	Type 1 Diabetes Mellitus	Type 2 Diabetes Mellitus	
0-20	1 (7.14)	0 (0)	1 (1)
21-40	9 (64.28)	2 (2.32)	11 (11)
41-60	3 (21.43)	46 (53.49)	49 (49)
61-80	1 (7.14)	37 (43.02)	38 (39)
>80	0 (0)	1 (1.17)	1 (1)
	14 (100)	86 (100)	100 (100)

Among Both Type-1 DM and Type-2 DM patients most common presenting symptoms was polyuria (92.85% in Type-1 and 95.34% in Type-2) followed by Polyphasia (85.71% in Type-1 and 91.86% in Type-2), Polydypsia (85.71% in Type-1 and 86.04% in Type-2), Weakness (64.28 in Type-1 and 61.62% in

Type-2) and Weight loss (57.14% in Type-1 and 61.62% Type-2).

Majority of 8(57.12%) Type-1 diabetics and 43(50%) of Type-2 diabetics were having more than 9% glycosylated Haemoglobin. (Table 2)

Table 2: Distribution of levels of glycosylated Haemoglobin according to presence of clinical presentations

Clinical Presentation	Glycosylated Haemoglobin							Total
	≤7.0	7.1-8.0	8.1-9.0	9.1-10.0	10.1-11.0	11.1-12.0	>12.0	
Polyphagia	15 (16.49)	21 (23.08)	7 (7.69)	14 (15.38)	7 (7.69)	7 (7.69)	20 (21.98)	91 (100)
Polydipsia	16 (18.39)	20 (22.99)	5 (5.75)	13 (14.94)	8 (9.19)	7 (8.04)	18 (20.69)	87 (100)
Polyuria	18 (18.95)	23 (24.21)	5 (5.26)	15 (15.79)	8 (8.42)	8 (8.42)	18 (18.95)	95 (100)
Weight Loss	12 (19.67)	10 (16.39)	5 (8.19)	10 (16.39)	5 (8.19)	8 (13.11)	11 (18.03)	61 (100)
Weakness	8 (12.91)	12 (19.35)	4 (6.45)	9 (14.52)	7 (11.29)	6 (9.68)	16 (25.81)	62 (100)

Among both type of diabetes with increasing fasting plasma glucose, level of glycosylated Haemoglobin increases and on regression analysis this result was found statistically significant ($p < 0.001$). In case of Type-1 diabetes mellitus only 2(14.28%) patients having fasting plasma glucose level below 140 mg/dl and their glycosylated Haemoglobin was less than 7.0%. While only 3(21.42%) patients having fasting plasma glucose level more than 300 mg/dl and their

glycosylated Haemoglobin was more than 11.0%. In case of Type-2 diabetes mellitus only 12(13.95%) patients having fasting plasma glucose level below 140 mg/dl and their glycosylated Haemoglobin was less than 7.0%. While only 7(8.14%) patients having fasting plasma glucose level more than 300 mg/dl and their glycosylated Haemoglobin was more than 11.0%. (Figure 1)

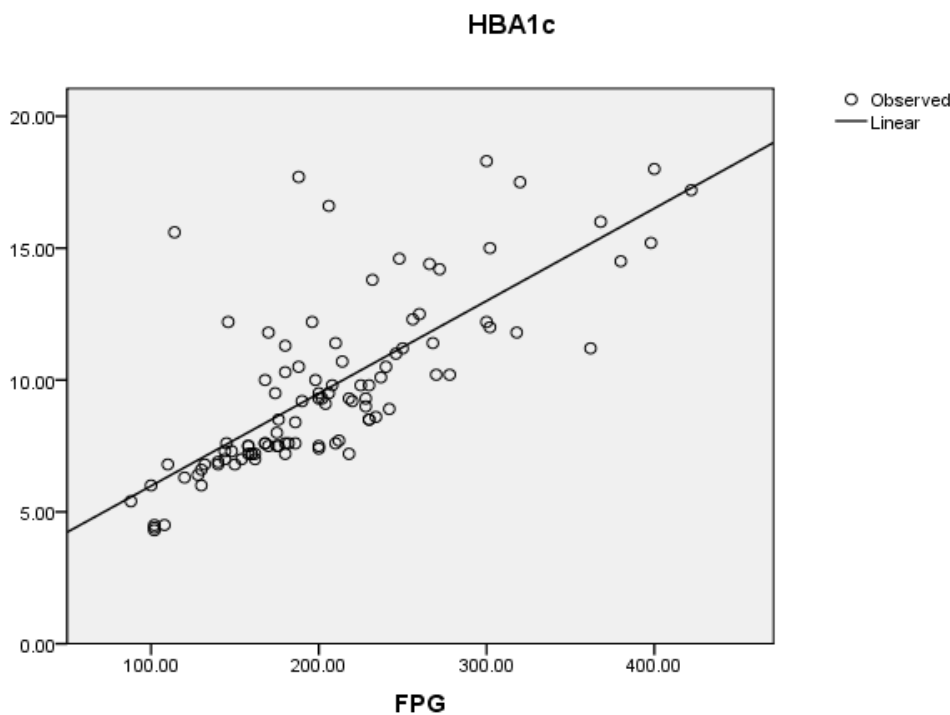


Figure 1 : Showing linear relationship between fasting plasma glucose and glycosylated Haemoglobin level

Among both type of diabetes with increasing post prandial plasma glucose, level of glycosylated Haemoglobin increases and on regression analysis this result was found statistically significant ($p < 0.001$). In case of Type-1 diabetes mellitus 6(42.95%) patients having post prandial plasma glucose level below 220

mg/dl and their glycosylated Haemoglobin was less than 8.0%. While 4(28.57%) patients having post prandial plasma glucose level more than 300 mg/dl and their glycosylated Haemoglobin was more than 11.0%. In case of Type-2 diabetes mellitus 27(31.4%) patients having post prandial plasma glucose level below 220

mg/dl and their glycosylated Haemoglobin was less than 9.0%. While only 13(15.12%) patients having post prandial plasma glucose level more than 300 mg/dl and

their glycosylated Haemoglobin was more than 11.0%. (Figure 2)

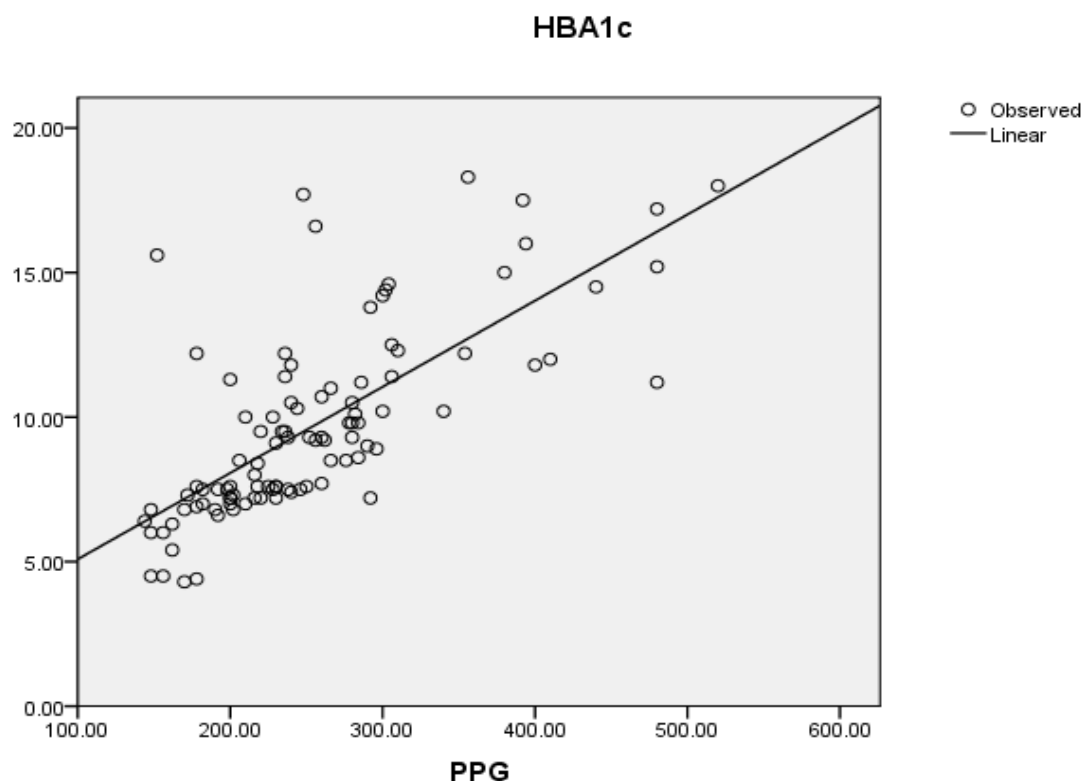


Figure 2: Showing linear relationship between post prandial plasma glucose and glycosylated Haemoglobin level

In case of diabetes mellitus type-1 majority 10(71.42%) of patients had complications. Among these 3(21.42%) patients had Retinopathy followed by Nephropathy, Neuropathy and Cardiovascular diseases in 2(14.28%) patients and Skin related complications in 1(7.14%) patients. Among these patients with complications, majority 6(60%) of patients had duration of illness more than 5 years.

In case of diabetes mellitus type-2 majority 56(65.11%) of patients had complications. Among these 33(38.37%) patients had Nephropathy followed by Cardiovascular diseases in 27(31.4%) patients, Skin

related complications in 20(23.56%) patients, Neuropathy in 18(20.93%) patients, Retinopathy in 16(18.6%) patients and cerebrovascular accident in 1(1.16%) patients. Among these patients with complications, majority 40(70.46%) of patients had duration of illness more than 5 years.

Most common complication among diabetes mellitus was nephropathy (38%) and least common complication was cerebrovascular accident (2%). As greater the duration of diabetes, the burden of complications also increases. (Table 3)

Table 3: Status of complications in diabetes mellitus patients according to duration

Complications	Duration		
	≤5	>5	Total
Neuropathy	10 (17.85%)	14 (31.81%)	24 (24%)
Nephropathy	18 (32.14%)	20 (45.45%)	38 (38%)
Retinopathy	10 (17.85%)	15 (34.09%)	25 (25%)
CVA	2 (3.57%)	0 (0%)	2 (2%)
CVD	13 (23.21%)	20 (45.45%)	33 (33%)
Skin	13 (23.21%)	13 (29.54%)	26 (26%)

Note: Figures are overlapping.

In case of type-1 diabetes mellitus, all type of complications except CVA were found in patients with Glycosylated Haemoglobin level more than 11.0%.

In case of type-2 diabetes mellitus, majority of the patients having Glycosylated Haemoglobin level more than 9.0% presented with complications.

Among all cases majority 57(57%) patients did not had albuminuria, while 43(43%) patients had albuminuria either microalbuminuria and /ormacroalbuminuria . (Table4)

Table 4: Status of albuminuria according to Glycosylated Haemoglobin levels

Albuminuria	Glycosylated Haemoglobin							Total
	≤7.0	7.1-8.0	8.1-9.0	9.1-10.0	10.1-11.0	11.1-12.0	>12.0	
Nonalbuminuric	17	19	4	10	1	2	4	57(57%)
Microalbuminuric	0	5	2	5	7	5	12	36(36%)
Macroalbuminuric	0	1	1	0	0	1	4	7(7%)
Total	17	25	7	15	8	8	20	100(100%)

IV. DISCUSSION

Present study was conducted at chemical pathology section of Department of Pathology, Mahatma Gandhi and Mathura Das Mathur Hospital, affiliated to Dr. S. N. Medical College, Jodhpur and One hundred diabetic patients attending medical outpatient department of Mahatma Gandhi and Mathura Das Mathur Hospital, Jodhpur were included in the study.

In our study majority 67(67%) of patients belong to 45-65 years age group, while only 16(16%) patients were of more than 65 year of age. In congruence to our results study conducted by King et al^[7] found that majority of the patients belonged to middle age (45-65 years) group in developing countries like india and majority of diabetic patients are in the older age category (≥ 65 years) in developed countries. So in developing countries, these patients will have more years of life to develop chronic complications of diabetes, which undoubtedly will have major implications with respect to health care needs, resource utilization and cost.

Age of 10(71.44%) Type-1 Diabetic patients were below 40 years of age while only 2(2.32%) of Type-2 diabetics were belonging to this group and 84(97.68%) Type-2 diabetics were more than 40 years age group. Similar to our findings, study conducted by La Porte R.E. et al.^[6] found that majority (85-89%) of the patients belong to Type-2 diabetes mellitus and usually occurs in adults over 35 years of age while Type-1 diabetes accounts for 0.2 to 1.5 percent of patients and especially afflicts children and young adults.

Among both type of diabetes there was strong correlation between levels of glycosylated Haemoglobin and fasting plasma glucose(p<0.001) and with increasing fasting plasma glucose, level of glycosylated Haemoglobin increases and on regression analysis this result was found statistically significant(p<0.001). Similar to our results Tossapompong et al^[7-10]. Also found significant correlation between glycosylated

Haemoglobin level and fasting plasma glucose (p<0.1), but in contrast to our result their correlation was poor.

In present study majority (28.57%) of type-1 DM patients had fasting plasma glucose level between 141-180 mg/dl. Similar to our results Masram S. W. et al^[11] also observed mean fasting plasma glucose level 169.47 mg/dl. In our study majority (28.57%) of type-1 DM patients had HbA1c level more than 12%. In contrast to our result Masram S. W. et al^[11] observed mean HbA1c level 9.1%.

In present study majority (27.90%) of type-2 DM patients had fasting plasma glucose level between 181-220 mg/dl. Similar to our results Masram S. W. et al^[11] also observed mean fasting plasma glucose level 223.82 mg/dl. In our study majority (25.58%) of type-2 DM patients had HbA1c level more than 7.1-8.0%. In contrast to our result Masram S. W. et al^[11] observed mean HbA1c level 11.06%.

There was strong correlation between post prandial plasma glucose and level of glycosylated Haemoglobin (p<0.001) in both types of diabetic patients in the present study and similar to our results Masram S. W. et al^[11] also found strong correlation between post prandial plasma glucose and level of glycosylated Haemoglobin (p<0.001).

In present study majority (28.57%) of type-1 DM patients had post meal plasma glucose level between 180-220 mg/dl. Similar to our results Masram S. W. et al^[11] also observed mean fasting plasma glucose level 243.93 mg/dl. In our study majority (28.57%) of type-1 DM patients had HbA1c level more than 12%. In contrast to our result Masram S. W. et al^[11] observed mean HbA1c level 9.1%.

In present study majority (30.23%) of type-2 DM patients had fasting plasma glucose level between 221-260 mg/dl. Similar to our results Masram S. W. et al^[10] also observed mean fasting plasma glucose level 269.94 mg/dl. In our study majority (25.58%) of type-2 DM patients had HbA1c level more than 7.1-8.0%. In contrast to our result Masram S. W. et al^[11] observed mean HbA1c level 11.06%.





Most common complication was nephropathy (38%) followed by cardiovascular disease (33%), skin diseases(26%), retinopathy(25%), neuropathy(24%) and cerebrovascular accident(2%) in present study and similar to our result *Masram S. W. et al⁽¹¹⁾* also found CVD in 33% and CVA in only 6.9% diabetics. In contrary to our finding *Masram S. W. et al⁽¹¹⁾* found neuropathy in 60% and retinopathy in 15.4% diabetics.

Present study showed 43% of diabetic had albuminuria either microalbuminuria or macroalbuminuria. Similar to our result *Deepak Parchwani et al⁽¹²⁾* also found microalbuminuria in 30% of diabetics.

V. CONCLUSION

In most of diabetics there was linear correlation between glycosylated Haemoglobin and fasting plasma glucose as well as post prandial plasma glucose. With increased duration of illness burden of complications also increases. We concluded that most of diabetic patients having high level of glycosylated Haemoglobin, also had one or more diabetic complications. Glycosylated Haemoglobin did not correlate well with blood glucose level estimated at one point of time. Glycosylated Haemoglobin is a better index for diagnosis and control of diabetes and for early detection of complications.

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