

Correlation of Fasting and Postprandial Glucose Levels with Glycosylated Hemoglobin in Diagnosis of Diabetes

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ABSTRACT

Introduction

Diabetes Mellitus describes a group of metabolic disorders characterized by hyperglycemia. Uncontrolled glycemic state often leads to micro and macro vascular complications. Diabetes is the foremost cause of new blindness in adults. Constant screening of the diabetic profile through blood tests of the affected people and prompt actions to control them can help to improve the quality of life of these patients. The study was done to evaluate the correlation between fasting and postprandial plasma glucose levels with glycosylated hemoglobin for diagnosis of diabetes and to determine the prevalence of diabetes in different age groups with sex predilection.

Methods

A descriptive cross sectional study was conducted and the data collection was carried out in the Department of Ophthalmic Pathology and Laboratory Medicine, Biratnagar Eye Hospital. Ethical approval was obtained from Institutional Review Committee of this hospital. All 275 patients who attended the laboratory from January 2019 to June 2019 for fasting plasma glucose, postprandial plasma glucose and glycosylated hemoglobin values estimation were included in this study. The data obtained were computed and analyzed using Statistical Package for the Social Sciences version 20.0

Results

A significant correlation between fasting plasma glucose, postprandial plasma glucose and glycosylated hemoglobin was observed in this study (p value <0.001). The correlation coefficient between fasting plasma glucose and glycosylated hemoglobin ($r= 0.728$) is stronger than the correlation coefficient between postprandial plasma glucose and glycosylated hemoglobin ($r=0.709$).

Conclusions

Fasting plasma glucose correlated better than postprandial plasma glucose with glycosylated hemoglobin.

Keywords: diabetes mellitus; fasting plasma glucose; glycosylated hemoglobin; postprandial plasma glucose.

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INTRODUCTION

Diabetes Mellitus describes a group of metabolic disorders characterized by increased blood glucose levels. It is due to the defect in the insulin release, its action or both and disturbances of fat, carbohydrate and protein metabolism.¹ The hyperglycemic state and the metabolic dysregulation result in complications affecting the kidneys, eyes, nerves and blood vessels.² In the eyes, the uncontrolled diabetes may result in retinopathy, iridopathy, unstable refraction and cataract.³ Early diagnosis and treatment can decrease the morbidity and mortality of the disease. Various laboratory blood tests like fasting plasma glucose, postprandial plasma glucose and glycosylated hemoglobin helps to diagnose and evaluate the diabetic status of the affected people. Hence, this study was done to determine the correlation between fasting and postprandial plasma glucose levels with glycosylated hemoglobin (HbA1c) in diagnosing diabetes mellitus and to find the prevalence of pre-diabetes and diabetes mellitus in different age groups with sex predilection.

METHODS

This descriptive cross sectional study was conducted in the Department of Ophthalmic Pathology and Laboratory Medicine, Biratnagar Eye Hospital. The Institutional Review Committee of this hospital has approved the study. 275 patients who had undergone all the three tests (fasting plasma glucose, postprandial plasma glucose and glycosylated hemoglobin) from January 2019 to June 2019 were included in this study. The fasting plasma glucose test was done after 8-10 hours fast. The postprandial plasma glucose test was done after two hours post regular meal. The fasting and postprandial plasma glucose levels were estimated by enzymatic oxidation method

(GOD-PAP) using HumaStar 200 machine. HbA1c was measured by boronate conjugate assay using HumaMeter A1c machine. Patients aged 21 years and above who underwent all the three tests were included in the study. Any patient below 21 years or who didn't undertake any of the three tests was excluded from the study.

The patients were divided as according to their age groups into 21-35years, 36-50years, 51-65years, 66-80years and >80 years. These patients were also categorized into Normal, Pre diabetic and Diabetic using the variables of fasting plasma glucose, postprandial plasma glucose and HbA1c as determined by the American Diabetes Association (ADA). The ADA has established the criteria for diagnosis of diabetes, which states a fasting plasma glucose level of ≥ 126 mg/dl, postprandial plasma glucose level of ≥ 200 mg/dl and HbA1c of $\geq 6.5\%$. Patients are termed pre diabetic if their fasting plasma glucose level is between 100-125 mg/dl, postprandial plasma glucose level between 140-199mg/dl and HbA1c 5.7-6.4%. Patients with fasting plasma glucose < 100 mg/dl, postprandial plasma glucose < 140 mg/dl and HbA1c $< 5.7\%$ are non diabetics.⁴

In this study, the collected data was evaluated by linear regression test to investigate the correlation between fasting plasma glucose, postprandial plasma glucose and HbA1c and t-test was used for comparison of HbA1c with fasting and postprandial plasma glucose. The statistical analysis was done using SPSS 20.0

RESULTS

According to the fasting plasma levels, 54.5% of the 21-35 years age group people fall into the diabetic range. In the age group 36-50 years, 20% are prediabetic and 45.3% are diabetic. The 51-65 years age group consists of 20.7 %

prediabetic and 34.0% diabetic people. The highest percentage of normal individuals was noted in the 66-80 years age group with 59.5%. The oldest age group revealed equal percentage of prediabetic and diabetic patients (Figure 1).

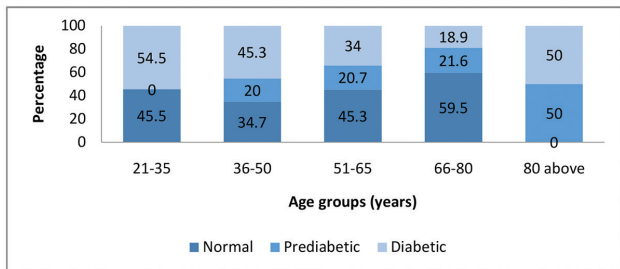


Figure 1. Age wise distribution of normal, pre-diabetic and diabetic people according to fasting plasma levels.

With reference to postprandial plasma glucose levels, 54.5% were diabetic in the youngest age group. The patients of 36-50 years age group were 30.7% prediabetic and 45.3% diabetic. The 51-65 years age group revealed increase in normal individuals (36.7%) than prediabetic (24.7%). The highest percentage of prediabetic (45.9%) was recorded in 66-80 years age group. Patients 80 and above all had diabetes (Figure 2).

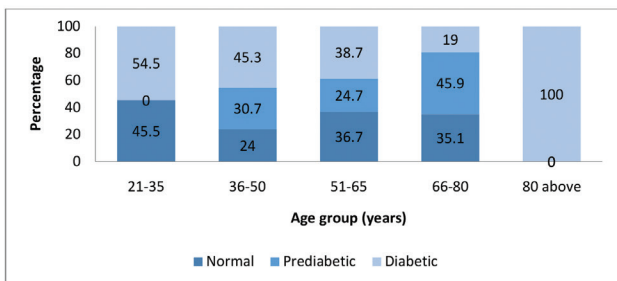


Figure 2. Age wise distribution of normal, pre-diabetic and diabetic people according to postprandial plasma levels.

Taking HbA1c as reference, 63.6% of patients of 21-35 years age group and 81.3% of patients of 36-50 years age group were found to be diabetic. Highest percentage (37.8%) of pre diabetics were found in 66-80 years age group. Patients 80 years and above were all diabetics (Figure 3).

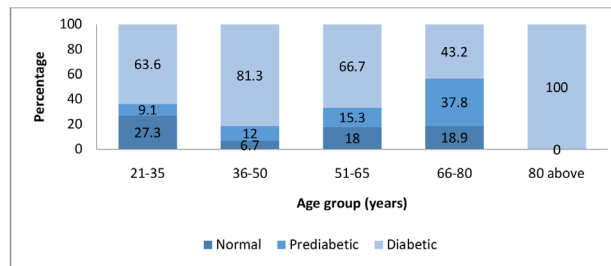


Figure 3. Age wise distribution of normal, pre-diabetic and diabetic people according to glycosylated hemoglobin.

Highest numbers of patients were encountered in the 51-65 years age group. The mean values of HbA1c and fasting plasma glucose were recorded highest in the 21-35 age group patients. The postprandial plasma glucose revealed highest average values in patients of 80 years and above (Table1).

Table 1. Age wise distribution of glucose parameters.

Age group (years) wise		Fasting	PP	HbA1c
21-35	Number of patients	11	11	11
	Mean	140.36	211.45	8.57
	Standard Deviation	69.638	114.056	3.411
36-50	Number of patients	75	75	75
	Mean	136.16	206.03	8.30
	Standard Deviation	59.705	81.102	2.020
51-65	Number of patients	150	150	150
	Mean	121.50	186.50	7.83
	Standard Deviation	57.403	86.212	2.242
66-80	Number of patients	37	37	37
	Mean	100.11	170.57	6.89
	Standard Deviation	34.333	69.882	1.790
More than 80	Number of patients	2	2	2
	Mean	131.50	263.50	7.40
	Standard Deviation	26.163	26.163	1.131
Total	Number of patients	275	275	275
	Mean	123.45	191.24	7.86
	Standard Deviation	56.752	84.389	2.211

The male population was more affected with pre diabetes and diabetes when fasting plasma glucose levels were analyzed (Figure 4).

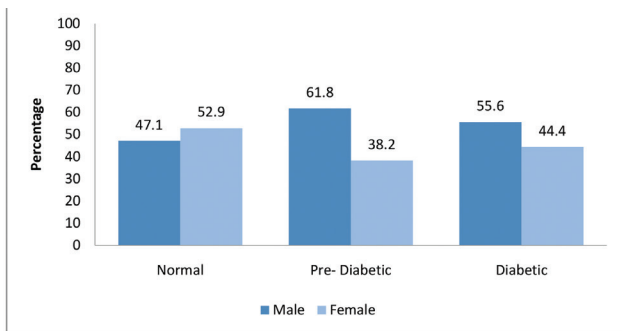


Figure 4. Gender distribution of normal, pre-diabetic and diabetic people according to fasting plasma levels.

The male population was more affected with pre diabetes and diabetes when postprandial plasma glucose levels were analyzed (Figure 5).

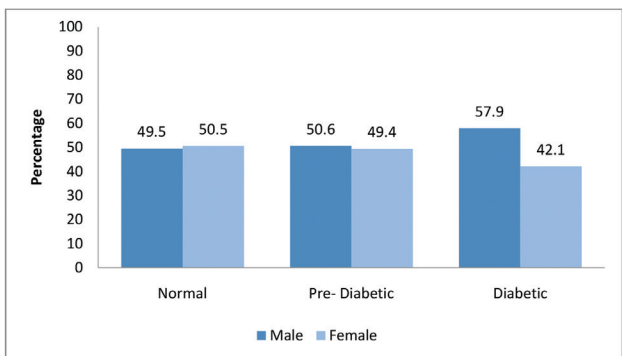


Figure 5. Gender distribution of normal, pre-diabetic and diabetic people according to postprandial plasma levels.

Females were found to be more pre diabetic and males more diabetic when HbA1c test was done (Figure 6).

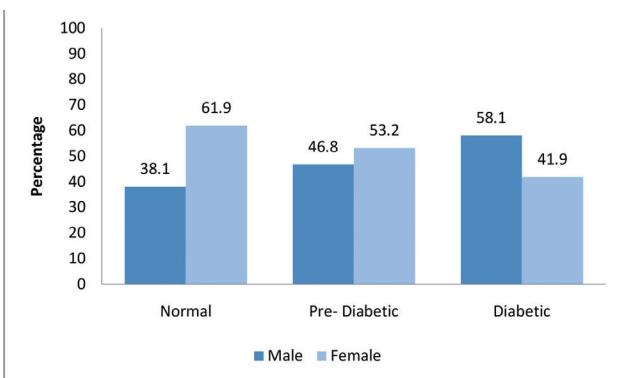


Figure 6. Gender distribution of normal, pre-diabetic and diabetic people according to HbA1c.

The mean values of all three glucose parameters were higher in males compared to female

population (Table 2).

Table 2. Gender wise distribution of glucose parameters.

Gender wise		Fasting	PP	HbA1c
Male	Number of patients	146	146	146
	Mean	126.89	197.70	8.15
	Standard Deviation	55.715	84.206	2.271
Female	Number of patients	129	129	129
	Mean	119.55	183.93	7.53
	Standard Deviation	57.873	84.324	2.101
Total	Number of patients	275	275	275
	Mean	123.45	191.24	7.86
	Standard Deviation	56.752	84.389	2.211

Taking both fasting and postprandial plasma glucose estimates into consideration, 121(44.0%) patients are normal by fasting glucose levels, whereas 91 patients (33.1%) are normal by postprandial glucose levels. More patients (28.0%) were prediabetic by postprandial levels than fasting (20.0%). Postprandial levels labeled 107 (38.9%) patients as diabetic while fasting recorded 99 (36.0%) patients as diabetic. However, 86 (31.3%) patients were found to be diabetics when both fasting and postprandial levels were analyzed together. For those with normal fasting levels, 3.3% had diabetes and 32.2% had prediabetes according to postprandial status (Table 3). A significant correlation was seen between the two parameters (Figure 7).

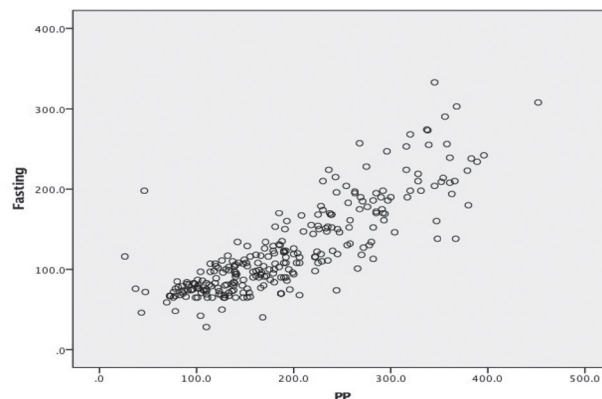


Figure 7. A scatter plot of fasting plasma glucose versus postprandial plasma glucose.

Table 3. Fasting versus Postprandial glucose levels.

			PP categorization			Total
			Normal	Pre diabetic	Diabetic	
Fasting Categorization	Normal	Count	78	39	4	121
		% within Fasting Categorization	64.5%	32.2%	3.3%	100.0%
		% of Total	28.4%	14.2%	1.5%	44.0%
	Prediabetic	Count	12	26	17	55
		% within Fasting Categorization	21.8%	47.3%	30.9%	100.0%
		% of Total	4.4%	9.5%	6.2%	20.0%
	Diabetic	Count	1	12	86	99
		% within Fasting Categorization	1.0%	12.1%	86.9%	100.0%
		% of Total	.4%	4.4%	31.3%	36.0%
Total		Count	91	77	107	275
	% within Fasting Categorization	33.1%	28.0%	38.9%	100.0%	
	% of Total	33.1%	28.0%	38.9%	100.0%	

Taking both fasting and HbA1c estimates into consideration, 121(44.0%) patients were normal by fasting glucose levels, whereas 42 patients (15.3%) were normal by HbA1c. More patients (20.0%) were prediabetic by fasting levels than HbA1c (17.1%). HbA1c labelled 186 (67.6%) patients as diabetic while fasting recorded 99

(36.0%) patients as diabetic. However, 94 (34.2%) patients were found to be diabetics when both fasting and HbA1c levels were analyzed together. For those with normal fasting levels, 24.8% had prediabetes and 41.3% had diabetes according to HbA1c status (Table 4). A significant correlation was seen between the two parameters (Figure 8).

Table 4. Fasting plasma glucose versus HbA1c.

			HbA1c Categorization			Total
			Normal	Pre diabetic	Diabetic	
Fasting Categorization	Normal	Count	41	30	50	121
		% within Fasting Categorization	33.9%	24.8%	41.3%	100.0%
		% of Total	14.9%	10.9%	18.2%	44.0%
	Prediabetic	Count	1	12	42	55
		% within Fasting Categorization	1.8%	21.8%	76.4%	100.0%
		% of Total	.4%	4.4%	15.3%	20.0%
	Diabetic	Count	0	5	94	99
		% within Fasting Categorization	0%	5.1%	94.9%	100.0%
		% of Total	0%	1.8%	34.2%	36.0%
Total		Count	42	47	186	275
	% within Fasting Categorization	15.3%	17.1%	67.6%	100.0%	
	% of Total	15.3%	17.1%	67.6%	100.0%	

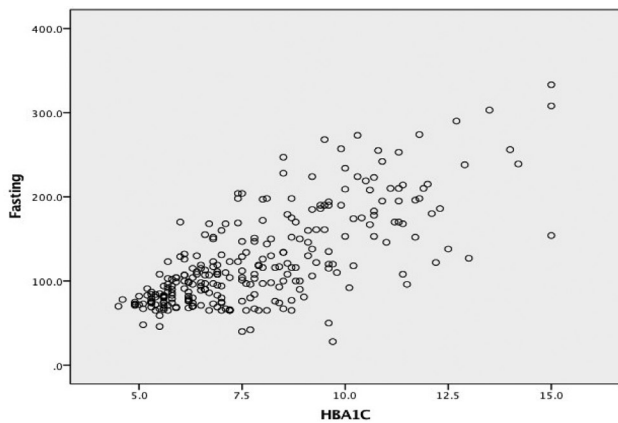


Figure 8. A scatter plot of fasting plasma glucose versus HbA1c.

Taking both postprandial and HbA1c estimates into consideration, 91(33.1%) patients were normal by postprandial glucose levels, whereas 42 patients (15.3%) were normal by HbA1c. More patients (28.0%) were prediabetic by postprandial levels than HbA1c (17.1%). HbA1c labelled 186 (67.6%) patients as diabetic while postprandial recorded 107 (38.9%)

patients as diabetic. However, 101 (36.7%) patients were found to be diabetics when both postprandial and HbA1c levels were analyzed together. For those with normal postprandial levels, 40.4% had prediabetes and 18.8% had diabetes according to HbA1c status (Table 5). A significant correlation was seen between the two parameters (Figure 9).

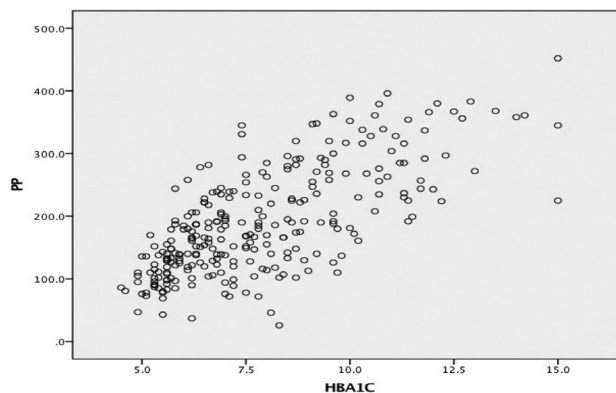


Figure 9. A scatter plot of postprandial plasma glucose versus HbA1c.

Table 5. HbA1c versus Postprandial plasma glucose.

		PP categorization				
			Normal	Prediabetic	Diabetic	Total
HbA1c Categorization	Normal	Count	37	5	0	42
		% within HbA1c Categorization	88.1%	11.9%	0%	100.0%
		% of Total	13.5%	1.8%	0%	15.3%
	Prediabetic	Count	19	22	6	47
		% within HbA1c Categorization	40.4%	46.8%	12.8%	100.0%
		% of Total	6.9%	8.0%	2.2%	17.1%
	Diabetic	Count	35	50	101	186
		% within HbA1c Categorization	18.8%	26.9%	54.3%	100.0%
		% of Total	12.7%	18.2%	36.7%	67.6%
Total	Count	91	77	107	275	
	% within HbA1c Categorization	33.1%	28.0%	38.9%	100.0%	
	% of Total	33.1%	28.0%	38.9%	100.0%	

The correlation coefficient between fasting plasma glucose and HbA1c ($r=0.728$) is stronger than the correlation coefficient between postprandial plasma glucose and HbA1c ($r=0.709$) using Pearson's correlation coefficient. The p value between the three glucose parameters was estimated. A significant correlation was noted between them (p value <0.001) (Table 6).

Table 6. Correlation between fasting plasma glucose, postprandial plasma glucose and glycosylated hemoglobin.

		Fasting	PP	HbA1c
Fasting	Pearson Correlation	1	.840**	.728**
	Sig. (2-tailed)		.000	.000
PP	Pearson Correlation	.840**	1	.709**
	Sig. (2-tailed)	.000		.000
HbA1c	Pearson Correlation	.728**	.709**	1
	Sig. (2-tailed)	.000	.000	

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

DISCUSSION

Glycosylated hemoglobin (HbA1c) is a form of hemoglobin which is chemically linked to a sugar molecule. Most monosaccharides like glucose non-enzymatically bond with hemoglobin (Hb) when present in the blood stream of the humans. The rate of formation of glucose bound Hb (glycated hemoglobin) is directly proportional to the amount of glucose present in the body at that time. HbA1c reflects an average blood glucose level of 2-3 months, as the red blood cells remain in circulation for maximum of 120 days. It can be used as a diagnostic test for diabetes mellitus and as assessment test for monitoring glycemic control in diabetes people. In this study, considering HbA1c as the parameter, the prevalence of diabetes are 63.6% and 81.3% in 21-35 years and 36-50 years age groups respectively. Among 66-80 years age group,

37.8% are prediabetics and 43.2% are diabetics. According to a study in Nepal, diabetes was present in 14.6% of people ≥ 20 years old in urban and 2.5% in rural areas. Among those > 40 years old, diabetes was present in 18.3% in urban and 3.3% in rural areas.⁵ Studies by Nitesh K K et al.,⁶ reported the prevalence of diabetes were 16.22% in 30-40 years age group, 24.32% in 41-50 years age group, 43.34% in 51-60 years age group and 16.2% in 61-70 years age group respectively. This study also revealed the mean average of HbA1c and fasting plasma glucose levels are higher in younger generation compared to the elderly ones. It is noted that most elderly people diagnosed with diabetes are under medications and close follow up maintaining the glycemic status. But the younger generations are unaware of their diabetic status, as no screening has been done, with the existing misconception that diabetes is the disease of the old. With increasing urbanization, food habits, sedentary life style, the rate of prevalence of diabetes in younger people has been increasing worldwide. In USA and UK, type 2 DM have affected people less than 19 years. In Japan, 50-75% of people aged 10-29 years have type 2 DM.⁷ Development of type 2 DM at young age leads to early exposure to the harmful effects of hyperglycemia and vascular complications. Life expectancy is reduced by eight years if type 2 DM is diagnosed in a person at age 40.⁸ As a result, our future generations may have to tolerate the morbidity and mortality of the disease at the peak of their productive years. This will in-turn affect the health care systems and economy of the countries across the world. This study also revealed that the mean average of postprandial plasma levels is higher in elderly patients. This is in concordance with the study by Lim et al.,⁹ which hypothesized that it might be because of increased beta cell insufficiency in elder generation. The presence of hypoglycemia thus may have lead to defensive eating and

overcorrection of hypoglycemia finally resulting in postprandial hyperglycemia. This study also concluded male population being more affected by diabetes than female. Similar findings have been reported by other studies.^{6,10-11}

In our study, 44% and 33.1% of the total cases were termed normal under fasting and postprandial criteria respectively but only 15.3% were found non diabetic using HbA1c based criteria. For those with normal fasting levels, 24.8% had prediabetes and 41.3% had diabetes according to HbA1c status. Also, for those with normal postprandial levels, 40.4% had prediabetes and 18.8% had diabetes according to HbA1c status. This discordant result may be because of short term and momentarily alterations in dietary habits, fasting, exercise or use of medications. These methods happen to decrease the plasma glucose levels in a short period of time but not HbA1c. This shows there is a high chance of poor glycemic control in the patients included in this study. This also may indicate that these patients may have prepared themselves only for the hospital visiting days.¹² Our study also concluded that 17.1% and 67.6% of the total cases were prediabetics and diabetics using HbA1c which supports the conclusion that HbA1c identified more people at risk compared to plasma levels as reported in other studies.¹³⁻¹⁶

HbA1c and plasma glucose provide different information and have varied advantages and disadvantages. The plasma glucose levels indicate the blood glucose at that given moment, is relatively convenient and cheap. But a single reading of plasma glucose may be affected due to stress, alcohol, dehydration and steroids.¹⁷⁻¹⁸ On the other hand, HbA1c is a better indicator of glycemic exposure, provides average plasma values of 8-12 weeks and is a reliable index for estimation of longterm complications. It doesn't require fasting or timed samples or any

preparations. It has a less biological variability and less preanalytical instability.¹⁹ But it may be influenced by conditions like red cell turnover, hemoglobin subtype, hypertriglyceridemia, chronic alcoholic status and ethnicity irrespective of glucose concentration levels.²⁰⁻²¹

If clinically unsure, it is advised to repeat the same test immediately with new blood sample for confirmation. If two different tests results are above the diagnostic levels, diabetes is confirmed. But, if discordant results are obtained, the test whose result is above the diagnostic threshold should be repeated again and final diagnosis should be made on basis of the results of the repeated confirmatory test. Also due to the preanalytic and analytic variability of the different tests, a test whose result was above the diagnostic cut point when repeated can yield result below the diagnostic cut point. This happens most likely in 2 hour postprandial estimation, more likely in fasting values and least likely in HbA1c.²¹

After the ADA 2010 recommendation, there has been a gradual increase in using HbA1c as a diagnostic test for diabetes mellitus and has been considered a reliable biomarker in diagnosis and prognosis of diabetes.²² HbA1c test is widely used and accepted as the means of retrospectively analyzing the mean glycemic status. But in developing countries like Nepal, where majority of the population is below the poverty line, HbA1c may be expensive for them. Also the test may be unavailable or still not properly standardized in these places. So, the idea of correlation of fasting and postprandial plasma glucose with HbA1c may be helpful in keeping the glycemic value under control. As a result, various research studies have been ongoing to determine the relative contribution of fasting and postprandial glucose levels as well. In this regard, our study revealed fasting

and postprandial glucose levels are significantly correlated with glycosylated hemoglobin ($p < 0.001$). However, fasting glucose level has a stronger correlation coefficient ($r = 0.728$) than postprandial glucose level (0.709). These findings are in accordance to findings of Saiedullah et al.,²³ and Gupta S et al.,²⁴ On the other hand, Rosediani et al.,²⁵ Shrestha et al.,²⁶ and Swetha et al.,²⁷ have concluded that postprandial glucose levels correlated better with glycosylated hemoglobin in comparison to fasting glucose levels.

CONCLUSIONS

This study shows that the prevalence of diabetes mellitus is exponentially increasing in the young generation. People with risk factors and family history should screen their diabetic profile and those with the disease should regularly monitor their glycemic status. In this study, though both fasting and postprandial plasma glucose levels correlated significantly with

glycosylated hemoglobin, the former showed better correlation with HbA1c than the latter.

LIMITATIONS

Glycosylated hemoglobin varies in conditions of anaemia, hemoglobinopathies, alcoholism, chronic renal failure, hyperbilirubinaemia, hypertriglyceridemia, splenectomy which are not taken in consideration in our study. The present study was carried out in a small sample size. HbA1c and plasma glucose tests were carried on a single day. However, several glucose readings over a period of several weeks can be better correlated to HbA1c than a single glucose reading on a single day.

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Conflict of Interest: None.

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