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Influence of Aging on HbA1C: A Cross-Sectional Study on Diabetic Population Attending a Tertiery Care Center of Central Nepal

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ABSTRACT

Introduction

Diabetes mellitus is increasing day by day throughout the globe. So, early diagnosis of diabetes is crucially important in reduction of the complications. This study was conducted to determine the correlation between glucose monitoring by fasting blood glucose and two hours postprandial blood glucose with glycated hemoglobin (HbA1c) in diabetic patients and evaluate whether glycohemoglobin levels increase with age in both sexes.

Methods

A hospital- based analytical cross-sectional study was carried out from March 2020 to December 2021 in diabetic patients attending at Medicine outpatient department (OPD) of College of Medical College and Teaching Hospital, Bharatpur, Chitwan. The total number patients was 696 people. HbA1c, fasting blood sugar (FBS) and postprandial blood sugar (PPBS) were analyzed. The entire patient's data was collected from the hospital record file. Collected data was enter in to Microsoft excel and then data was analyzed by using SPSS-20 using descriptive and inferential statistics.P-value <0.05 were considered as statistically significant.

Results

Both postprandial blood glucose and fasting blood glucose significantly correlated with HbA1c. Postprandial blood glucose showed better correlation to HbA1c than fasting blood glucose ($r = 0.630$, $P<0.001$ vs. $r =0.452$, $P = 0.05$).

Conclusions

These results showed that postprandial blood glucose correlated better than fasting blood glucose to HbA1c. Thus, postprandial blood glucose predicted overall glycemic control better than fasting blood glucose. Based on our study, we may conclude a significant correlation exist between age and HbA1cin Nepalese population.

Keywords: blood glucose; cross sectional diabetes ; HbA1c

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INTRODUCTION

Diabetes mellitus (DM) describes a common metabolic disorders with of multiple etiology characterized by chronic hyperglycemia. The long–term effects of diabetes mellitus include progressive development of the specific complications of retinopathy with potential blindness, nephropathy, cerebrovascular disease and features of autonomic dysfunction, including sexual dysfunction.[1]

The worldwide prevalence of diabetes among general population was estimated at 150 millions in 1995, and this is projected to increase to 300 million by 2025.[2] Developing countries such as most of the Asian countries are experiencing an accelerated rate in this issue.[3] Nepal is also goingthrough a phase of epidemiological changeover from a higher prevalence of communicable diseases to that of non-communicable diseases andthe prevalence type 2 diabetes is increased speedily.[4] Groups of Nepalese research worker have done their polite studies from different parts of the country on the diverse populations and reported varying prevalence rates ranging from 6.3 to 8.5%.[5]

In order to detect diabetes, fasting blood glucose (FBS) and postprandial blood sugar (PBGS) are used in general. Presently, HbA1c test is recommended to measure the incidence or prevalence of diabetes.[6]. It has been argued that due to problems in standardization and variations in styles of HbA1c test, it is not recommended as a routine test for screening of diabetes. In addition, other factors such as abnormal hemoglobin, anemia and some drugs may affect the results of HbA1c test.[7] Also demographic factors such as race and gender are other effective factors.[8]

The amount of HbA1c is directly dependent on RBC lifespan, which may vary among individuals and different age groups.[10] Thus, HbA1c is considered a weighted measure of the average blood glucose levels during the past 120 days with plasma glucose levels from the preceding 30 days contributing substantially more to the final result compared to plasma glucose levels from the past 90–120 days.[11] Similarly, the HbA1c reference values for the monitoring of glycemia in patients with diabetes do not take the age of the individual into account potentially leading to unnecessary overtreatment with severe consequences.[12]

In this study, after eliminating identifiable diseases or medications known to influence glucose tolerance, we evaluated the changes in glycohemoglobin levels with respect to age in both sexes and investigated whether glycohemoglobin was affected by BMI, physical activity, or family history of diabetes in a large healthy Nepalese population.

METHODS

A hospital- based analytical cross-sectional study was carried out from March 2020 to December 2021in patients with diabetes attending at Medicine outpatient department (OPD) of College of Medical Sciences and Teaching Hospital, Bharatpur, Chitwan. Institutional ethical committee clearance was taken from institutional review committee of College of Medical Sciences. Socio-demographic information of the patients was taken from OPD cards while laboratory parameters were taken from the registry of Central Clinical Laboratory of College of Medical Sciences and Teaching Hospital. The anthropometric measurements (weight and height) were recorded and body mass index (BMI) was calculated on the basis of National Health and Nutritional Examination Survey.

Subjects with the following diseases or conditions were not included in the analysis: 1) various degrees of renal insufficiency (serum

creatinine level >1.5 mg/dl); 2) evidence of significant liver disease; 3) anemia; 4) history of recent surgery, trauma, or illness; 5) pregnancy; 6) any medication intake within 48 hours of the test, 7) significant chronic alcohol intake, and 8) more than 20 cigarettes per day. Total number of diabetic patients consisting of 696 was considered for the analysis. Out of total 696 patients, 413(male) and 283 (female) subjects were available for study. Fasting blood sugar (FBS) and postprandial blood sugar (PPBS) were measured by fully automatic instrument (MISPA, CX). Glycohemoglobin (HbAlc) was measured by using an automatic high-performance liquid chromatography (Lifotronic, H9). All these tests were done in Central Clinical Laboratory under supervision with qualified technicians.

Statistical Analysis

The entire patient's data was collected from the hospital record file. Collected data was enter in to Microsoft excel and then data was analyzed by using SPSS-20. Data was analyzed by using descriptive and inferential statistics. In the descriptive statistics for the categorical variable mean and SD was calculated while for categorical variables were expressed in term of percentage. In the inferential statistics to find the association between categorical variables chi-square test were used while for continuous variables correlation was calculated. Also, to fine the association between one continuous variable with more than two categorical outcome variables one way ANOVA was used. P-value less than 0.05 were considered as statistically significant.

RESULTS

A total of 696 adult subjects were enrolled in the OPD in College of Medical Science, Bharatpur for cross-sectional study. Regarding sex out of total patients, 413 patients were male and 283 patients were female Table 1. It has been found from Table-1 that out of total patients, 59.3% male patients and 40.7% female patients were diabetes.

Table 1. Age and Sex distribution of the participant.

Participant	Sex		Age			
	Frequency	Percent	Mean	SD	Minimum	Maximum
Male	413	59.3	55.65	14.39	16	88
Female	283	40.7	53.29	13.35	19	86
Total (n)	696	100.0	54.69	14.01	16	88

Table 2 represented the age and gender distribution of the participant. To evaluate the relationship between HbA1cand age in both sexes, we considered the patient from 20-80

Table 2. Age group wise and gender distribution of the study participant.

Age	Male		Female		Over all
	Frequency	Percentage	Frequency	Percentage	
<20 years	2	0.5	2	0.71	4
20-40 years	65	15.7	54	19.08	119
40-60 years	192	46.5	141	49.82	333
60 years and above	154	37.3	86	30.39	240
Total	413	100.0	283	100.00	696

years and they were divided into four groups with age of 20years interval. Maximum diabetic population has been found in 40 – 60 years age group. Females comprised 49.82 %(n=141) whereas male were 46.5 %(n=192) diabetic.

case (n=453,65.1%) and PPBS -based case (n=498, 71.6%) respectively. HbA1c averaged value was 7.19±1.72. 48.4% of patients had values < 6.5 % and 51.6% had values ≥ 6.5 % (Table 5).

Age and gender wise value of study variable data

Table 4. Distribution of diabetic patients by fasting glucose levels.

Fasting Blood Sugar level	**Number**	**Percentage**
Normal (<6.7 mmol/l	243	34.9
High (>6.8 mmol/l)	453	65.1
Mean±SD (mmol/l)	6.84±2.12	
Postprandial Blood Sugar level		
Normal (<11.1 mmol/l	198	28.4
High (>11.2 mmol/l)	498	71.6
Mean±SD (mmol/l)	13.04±3.89	

Table 5. Result of HbA1c study Participant.

Result	**Frequency**	**Percent**	**Mean ±S.D**	**Range**
<6.5	337	48.4	7.19±1.72	4.5 -12.10
≥6.5	359	51.6		
Total	696	100.0		

BMI of both genders were studied, showed in Table 3. The data were classified based on BMI values, which clearly indicated the maximum population were high body mass index (>25g/m2, n=374).

Table 3. BMI of the participant.

BMI	**Frequency**	**Percentage**
<18.5 kg/m2	64	9.2
18.5-24.99 kg/m2	258	37.1
>25 kg/m2	374	53.7

Both Postprandial and fasting blood glucose were represented in Table 4. Plasma glucose averaged 6.8±2.12mmol/lin the fasting state and most subjects had blood glucose level >6.8mmol/l. Postprandial average plasma glucose was 13.04±3.89 mmol/l and most subjects had blood glucose level >11.2 mmol/l in postprandial state. As recorded data, the number of FBS -based

analyses and displayed in Table 6. Independent t-test was done to find out the association among age and sex and insignificant p- value was found more than 0.05 in all variables respectively. Based on this finding, the association of FBS, PPBS and HbA1c with variables sex, BMI and age were significant.

HbA1c levels with different age groups in both the genders was highly reproducible and association found was found to be statistically significant as all the p-values were <0.005 (Table 7). HbA1c ≥ 6.5 increased the chance of diabetes in 40- 60 age groups in both genders.

Correlation between HbA1c levels with different variables in both the genders was highly significant. Table 6includes descriptive statistics of HbA1c according to different age and average blood glucose among both

Table 6. Age and Gender wise value of study variables.

Gender	Result (HbA1c)		Fasting Blood Sugar level		Postprandial Blood Sugar level		BMI	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Male	7.17	2.68	7.23	2.14	12.75	3.26	25.69	5.15
Female	7.26	2.36	7.12	1.88	12.72	3.28	25.23	5.14
P-value	0.673		0.153		0.86		0.675	
Age								
<20 Years	8.09	0.51	11.74	2.64	6.95	0.82	22.43	5.02
20-40 years	7.13	1.01	12.87	2.31	7.27	2.53	25.20	5.10
40-60 years	7.11	0.97	12.76	2.22	7.04	2.23	25.76	5.10
>60 Years	7.31	0.97	12.68	2.26	7.43	2.98	25.37	5.28
P-Value	0.25		0.123		0.33		0.45	

Table 7. Association between gender and age with HbA1c.

	Result		Chi-Square	P-value
Sex	**<6.5**	**≥6.5**		
Male	200	213	1.57	0.99
Female	137	146		
Age Group				
<20	2	2	12.73	0.005*
20 to 40	70	49		
40 to 60	140	193		
60 and above	125	115		
Total	337	359		

*Statistically significant at 5% level of significance

Table 8. Correlation between Hb1Ac with different variables.

Correlation of HBA1c	Age	BMI	FBS	PPBS
	0.402	0.374	0.602	0.432
Coefficient of determination (r^2)	0.161	0.139	0.362	0.186
P-value	0.035*	0.006*	0.021*	0.035*

genders. Both postprandial and fasting blood glucose significantly correlated with HbA1c. Postprandial glucose showed better correlation to HbA1c than fasting blood glucose (r= 0.602, p=0.021vs r=0.42,p=<0.035) (Table 8).Age and BMI were comprised against HbA1C values showed positive correlation. Pearson's correlation co-efficient was 0.161, p<0.035for age and 0.139, p<0.00 for BMI.

*Statistically significant at 5% level of significance

DISCUSSION

People with diabetes have a major risk of macrovascular and microvascularcomplications, which can be a considerable burden to the patient, families and society.[12] Proper glycemic control is the best strategy to prevent and delay the progression of diabetes complication and improve the quality of life.[13] Current studies inNepal reported that the prevalence of pre-diabetesand type 2 diabetes increaseextremely due to various factors like obesity,poor physical activities, lifestyle changes associated with urbanization and deterioration of the ecological environment .It is also possible that people with diabetes may move to urban areas after diagnosis to be closer to hospitals, perhaps staying with urban family members.[14]

Our results showed that both FBS and PPBS correlated significantly with HbA1c values. PPBS correlated more strongly with HbA1c in comparison with FBG. This result is consistent with various other studies that have found in their studies that postprandial glucose levels correlate better with HbA1c values than fasting blood glucose. [15, 16]Also we found that 65.1.0 % male have FBS >6.8 mmol/l and 71.6% have PPBS >11.2 mmol/l. Similarly the HbA1c (≥6.5%) was found in large population (51.6%).We also found thatthe maximum population (n=374, 53.7%) have high BMI (>25 kg/m2).

Our main goal in this study whether HbA1C increases with age in male and female. Regarding this objective we examined 696 diabeticsubjects and observed thatHbA1C levels are increasing with age in both gender. This observation is parallel to that in previous studies in Japan and USA.[17, 18] Our closer observation revealed that the age-dependent elevation pattern of HbA1c in ≥60 years of age population, which is comparable to the result found in a working male Japanese population described by Hashimoto et al.[17]It has also been observed that the mean HbA1C level was significantly higher in male gender than females (p<0.99) and these findings were similar to other reportedwork.[19]We also found that mean FBS and PPBS level was significantly (p<.005) elevated in different age groups with poor glycemic control (HbA1c≥6.5%) which is corroborated with the study reported by Khattabet et al [20] In this study, moderate correlation was observed between HbA1c and fasting plasma glucose (r=0.602) and postprandial glucose (r=0.432), this finding is reliable with other studies reported by Sikariset et al. and Ketemaetet al[21,22] In our study, HbA1c was significantly higher in men than women under 60 years of age. Between 20 and 34 years of age, hormonal changes during the menstrual cycle may account for the differences in glycohemoglobin levels in men and women.But at older ages, these levels are virtually identical.

A possible explanation for the observed association of higher HbA1C with increasing age in individuals with normal glucose tolerance is that factors unrelated to glucose metabolism are affecting HbA1C levels due to accumulation of toxic metabolic products during ageing process and pathophysiology of number of disease, like Alzheimer disease, diabetes, and lung diseases.[23, 24]

CONCLUSIONS

The results suggest that both fasting blood glucose and postprandial blood glucose correlated significantly with HbA1c andthere was better correlation between HbA1c and postprandial blood glucose. Our study demonstrated that, although the HbA1c test was marginally more specific but less sensitive than the fasting glucose test, at the given cutoff points the accuracies of two tests were equivalent. Basedon our study, we may concluded a significant correlationexist between age and HbA1cin Nepalese men and

women. Although the study was performed in COMSTH, Bharatpur city, we need to extrapolate our findings to different parts of Nepal.

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