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Distribution of Glycated Hemoglobin According to Gender, Age and Body Mass Index in Sudanese Adults without Diabetes

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Original Research Article

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Abstract: Glycated Hemoglobin (Hb A_{1c}) is now used largely for DM control. Hb A_{1c} is influenced by many risk factors; these include BMI, physical activity, age, ethnicity, diet and smoking. The determinants of Hb A_{1c}values in Sudanese have not been studied despite their utmost value in DM control. The objective of this study is to evaluate age, gender and body mass index as determinants of glycated hemoglobin in non-diabetic Sudanese population. A cross sectional study was conducted during 2016-2018 in Sudan covering Khartoum state, Northern state, Gezira state, Red Sea state and North Darfur state, on adults of ages between 20-60 years and not known to be diabetic or suffering from any chronic illness.1097 participants were assessed by a questionnaire covering age, gender and other demographic and social characteristics. BMI was calculated after measuring weight and height by standard scales. A sample of 5 ml venous blood was taken for FBG to exclude DM and measurement of Hb A_{1c} using a modified ELISA reader known as Cobas Integra 800 (Roch) machine. Correlations between the variables were estimated and P value < 0.05 was considered statistically significant. There is a positive correlation between HbA_{1c} and gender; female subjects had higher values than male subjects. The mean of HbA_{1c} in females was 4.6 ±0.9 % which was more than the mean in males 4.5 ±1.0 % with significant p value of 0.03. There are slight differences in HbA_{1c} levels between the age groups, the oldest (more than 50 years) having the lowest values (4.4%) and those with group of age between 35-50 years have the highest value (4.7%). HbA_{1c} levels were found to be higher (4.8%) in those having BMI more than 30. There was no significant correlation between $HbA_{1\ c}$; age, weight and BMI (r =.009, .010, =-.032) and the p values were 0.7, 0.7 , 0.33.respectively . There was intermediate correlation between HbA_{1c} and Height (r) =0.13 with significant p value of 0.00. This study showed significant higher HbA_{1c} levels in females compared to males. Age and BMI have no significant effect on the HbA_{1c} levels in Sudanese population but there was a significant correlation with height.

Keywords: $HbA_{1c,}$ BMI, Age, Gender.

INTRODUCTION

Different studies have shown variations in the normal ranges of Glycated Hemoglobin (Hb A_{1c}) according to the effect of age, gender and body mass index (BMI). In 1982 Arnetz *et al.*, performed a small study on 48 subjects above 50 years old, sub-divided into three age groups. They observed significant differences in HbA_{1c} levels between the groups, the oldest having the highest values [1]. A large French study on 3240 individuals in a working population in 1989, the Telecom study which was conducted by Simon *et al.*, concluded that age independently influenced HbA_{1c} [2].

Association of Hb A_{1c} with age has been compared by Pani *et al.*, who performed a cross-sectional analysis of Hb A_{1c} across age categories in 2,473 non-diabetic persons between 1991-1996. They stated that their results established clearly that Hb A_{1c} increases with age, even after multivariate adjustments for sex, fasting, and 2-hour post-load glucose and suggested that non-glycemic factors may contribute to the relationship of Hb A_{1c} with age [3]. In 1996 Kilpatrick *et al.*, performed a study regarding the age and $HbA_{1c}$and they reported that HbA_{1c} showed a positive linear relationship with age in non-diabetic individuals, whereas fructosamine did not [4]. On the

other hand In contradiction to the previous studies; in 1988 Kabadi found no significant relationship between age, fasting plasma glucose (FPG) and glycated hemoglobin [5]. Also, in March 1999 Wiener et al. performed a cross-sectional analysis to resolve whether hemoglobin A_{1c} levels in normal subjects increase with age; they measured HbA_{1c} in 399 subjects undergoing routine oral glucose tolerance test (OGTT). They found no significant correlation between HbA_{1c} and age, therefore, they could not see any need for age-specific reference ranges for Hb A_{1c} [6].

High Body mass index (BMI) is known as an important risk factor for diabetes, with higher BMI causing insulin resistance and thereby higher levels of glycaemia. Simon *et al.*, found higher level of Hb A_{1c} in obese persons (defined as BMI > 30 kg/m2), but after adjustment for age, the relation between BMI and Hb A_{1c} was no longer significant [2]. Modan et al. found no significant correlation between BMI and Hb A_{1c} [7], but in contrast, in the cross section study conducted by Boeing *et al.*, it was found that obesity was related with higher Hb A_{1c} levels [8].

Concerning gender and Hb A_{1c}; Faerch *et al*., [9] and Gulliford *et al.*, [10] both found higher levels of Hb A_{1c} in men compared to women, but other studies found no sex-related differences in Hb A_{1c} [4, 7]. In women, Hb A_{1c} levels rose particularly at the age of menopause and the use of oral contraceptives or estrogens made no difference [2].

Hb $A_{1c}$is influenced by many other factors; these include physical activity, ethnicity, diet and smoking [11].

In Khartoum state at 2016 Ali *et al*., performed a Cross-sectional study on 20 non-diabetic adult males of ages between 35-45 years and found a weak correlation between Hb A_{1c} : age and BMI [12]. Another cross-sectional study done in Khartoum state at 2016 by Fadul et al. on 20 non-diabetic adult females, with ages between 35-45 years and found no correlation between Hb A_{1c} and BMI [13].

It is well known that the normal values used in Sudanese laboratories are mainly derived from European studies. Differences in the normal values in Sudan have been documented in some hematological values [14, 15], respiratory function tests parameters [16], Renal functions test [17] and serum electrolytes [18]. In Khartoum state at 2018 Ali *et al.*, performed a large Cross-sectional study on 444 healthy non diabetic Sudanese adults and found the mean of HbA_{1c} was 4.2±1.8% and with a range of 1.2 – 6.5% [19].

Currently, there are no known big scale studies conducted to investigate the determinant of HbA_{1c} range in Sudanese people; could there be a difference in the mean of Hb A_{1c} in Sudanese population according to effect of age, gender and BMI is clearly a valid a question.

METHODS

A Cross sectional study was conducted during 2016-2018 on Healthy Sudanese subjects of both sexes with age group 20 -60 years. 1163 Healthy Sudanese adult volunteers were included, and the study covered Khartoum state, Northern state, Gezira state, Red Nile state and North Darfur state. The exclusion criteria of this study included: Pregnant ladies, abnormal FBG , Diabetes mellitus, Hypertension , Renal failure, Liver disease , Cancer, Chronic diseases (cardiac diseases, TB, asthma, thyroid disorders), Hematological disorders., Recent acute diseases (Malaria, typhoid fever..), Lactation., History of recent surgery or splencetomy, History of schistosomiasis, hemoglobinopathies, blood disorders and Subjects not consenting. Written consents were obtained from all participants after fully explaining to them the project. A questionnaire was filled by all volunteers to obtain the data about name, age, address, medical history, drug use, and lifestyle. Weight, height, and blood pressure were measured with standard techniques. Complete clinical examination was performed. After informed consent, five ml of venous blood was collected by a standard procedure from each participant under complete aseptic conditions in the morning and after an overnight fasting.2.5 ml was placed in fluoride oxalate containers, and then used for FBG measurement with auto analyzer A 15. The remaining 2.5 ml was placed in EDTA container and used for HbA_{1c} analysis. (Icteric, lipemic, hemolyzed or bacterially contaminated samples were not used). $HbA_{1c}$was measured using modified ELISA reader known as COPAS Integra 800using commercial reagent kits from Roche Company. All techniques and equipment were standardized. All data collected in this study was analyzed using the SPSS computer programs. Correlation Coefficient (r) was used for continuous numerical variables and Student t test and (ANOVA) statistics was used for categorical variables. $P \leq 0.05$ was considered significant.

Ethical Consideration

Ethical Approval of this study was obtained from the Federal Ministry of Health in Sudan (FMOH) and The National Ribat University (NRU). The objectives of the study were explained to all individuals participating in the study. An informed consent was obtained from each participant in the study.

RESULTS

A total of 1096 volunteers were identified as eligible; according to the inclusion criteria and approved to be enrolled after filling the consent, questionnaire and were fit on the physical examination.

67 subjects (5.7%) were excluded due to high fasting blood glucose (FBG) and they were not known to be diabetics.

73.7% of the study sample were females and 24.8% were males. Mean of age was 25.2 ± 9.3 years, BMI was 22.8 ± 4.8 and Hb $A_{1c}$was 4.6 ± 0.9.

With respect to HbA_{1c} value based on sex, there was positive correlation between HbA_{1c} and gender; female subjects had higher values than male subjects. The mean of HbA_{1c} in females was 4.6 ±0.9 % and the mean in males was 4.5 ±1.0% with significant p value of 0.03 (Figure-1).

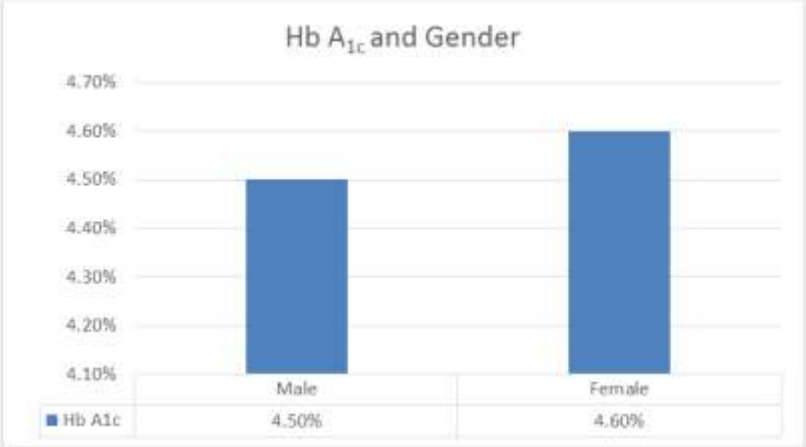

Fig-1: HbA_{1c} level in Sudanese males and females (n=1096)

There was no correlation between HbA_{1c}; age , weight and BMI (*r*) =.009, .010, =-.032 and the p value was 0.7, 0.7 , 0.33.respectively . There was intermediate correlation between HbA_{1c} and Height(*r*) =0.13 with significant p value of 0.00 (Table-1).

Table-1: HbA_{1c} Correlations with age, weight, height and BMI in Sudanese population

		Hb A_{1c}	Age	BMI	weight	Height
HbA_{1c}	Pearson Correlation	1	.009	-.032	.010	.131**
	Sig. (2-tailed)		.772	.335	.777	.000

There were slight differences in HbA_{1c} levels between the age groups, the oldest (more than 50 years) having the lowest values (4.4%) and those with group of age between 35-50 years have the highest value (4.7%). HbA_{1c} levels was found to be higher (4.8%) in those having BMI more than 30.

DISCUSSION

HbA_{1c} measurement is one of the diagnostic tests used in the diagnosis of diabetes and monitoring hyperglycemia in uncontrolled diabetic patients. HbA_{1c} is a relevant predictor of diabetes related complications and of mortality [20]. As HbA_{1c} is now used largely for DM control, the factors that influence the HbA_{1c} reference intervals of healthy adults Sudanese have been addressed by this study.

There is positive correlation between HbA_{1c} and gender; female subjects had higher values than male subjects. This finding agrees with studies of Simon [2], Faerch [9] and Gulliford [10] and disagree with Kilpatrick [4] and Modan [7] studies.

There is no statistical correlation between age and Hb A_{1c}. These findings were in agreement with the study of Kabadi *et al.*, [5] and Wiener *et al.*, [6] which showed no significant correlation between HbA_{1c} with age and disagree with Arnetz [1], Simon [2], Pani *et al.*, [3] and Kilpatrick [(4)]studies. The mean of Hb A_{1c} in the age group of more than 50 years old was less than in the other age groups, a finding different from the previous studies [1-4] which showed an increased level with age and it needs further elaboration.

It has been shown in this study that there is no correlation between Hb A_{1c} and BMI. This result agree with Simon *et al.*, [2], Modan *et al.*, [7] and, Fadul *et al.*, [13] and disagree with Boeing *et al.*, [8] study which showed that obesity was found to be related with higher Hb A_{1c} levels and Ali *et al.*,. [12] who showed positive correlation between Hb A_{1c} and BMI. The findings of this study do not support that the Hb A_{1c} is influenced by BMI, but we have observed that the level of HbA_{1c} was found to be higher in those having BMI more than 30; but they were a small group, and this could be elaborated more with obese subjects

The significant positive association between height and Hb A_{1c} need further analysis and studies to search for the exact effect, explanation and investigate the other variables like Hb, sex hormones and growth hormone.

In conclusion this study showed significant variations in HbA_{1c} levels according to effect of gender. Age and BMI have no effect on the HbA_{1c} levels in Sudanese population.

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