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Normal Values of Hemoglobin A_{1c} in Sudanese healthy pregnant ladies in Khartoum state 2017: A pilot Study

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Abstract: The research aimed to measure HbA_{1C} in normal Sudanese non-diabetic pregnant women attending antenatal care at Ribat University Hospital, Khartoum state during the period from Sep 2017 to Nov 2017, and to explore the effect of pregnancy on $HbA_{1C.}$ A Cross sectional facility based study was conducted in The National Ribat University hospital during the period from Sep 2017 to Nov 2017 among the Normal Sudanese pregnant, non-diabetic females of ages between 18-40 years. Twenty women were included as a pilot, ten of them at first trimester and ten at third trimester. Correlations between the variables were estimated and P value less than 0.05 was considered statistically significant and used to determine the relationship between the Multiple factors of pregnancy and HbA1c level. The mean value of HbA1c at first trimester of pregnancy was found to be 4.7% with a range of (3.5% - 5.5 %) and the mean value of HbA1c at third trimester of pregnancy was found to be 3.98% with a range of (2.8% - 5.4%). The mean value of HbA1c in normal pregnancy was found to be 4.37% with a range of (2.8% - 5.5 %). There was no correlation between normal FBG, Hb level, daily caloric intake, age, PH. of DM, PH. of GDM, family history of DM and the level of HbA1c. According to this study the mean value of HbA1c in Sudanese healthy pregnant women is 4.37 found within the normal Sudanese values of HbA1c. HbA1c is lower in the third trimester compared to first trimester.
Keywords: HbA1c, Hb, FBG, PH, GDM, DM.

INTRODUCTION

In pregnancy: the pregnant mother undergoes significant anatomical and physiological changes in order to nurture and accommodate the developing foetus and prepare the mother for labor and be ready delivery [1].

$HbA_{1c.}$ Glycated proteins are formed during the no enzymatic reaction of glucose and amino groups of proteins. Hemoglobin A1c is formed by the condensation of glucose with the N-terminal valine residue of each beta-chain of hemoglobin A. The amount of glycated hemoglobin in blood depends on both life-span of red blood cells and blood glucose concentration.

American medical association added HbA_{1C} as a criterion in the diagnosis of diabetes mellitus and considered 6.5% as the cut off point for diagnosis [2-5]. Good glycemic control around the time of conception is necessary to optimize outcome of Pregnancy [6,7]. The major advantage of HbA1c is the lack of impact of fluctuating glucose after meals and with illness [8].

However, a lot of factors and several conditions should be considered which can affect the level of HbA1c: Color, pregnancy, Hb, FH of DM and PH of GDM, conditions where the RBCs life span is substantially shorter ,…etc.

Black persons have higher HbA1c levels than white persons across the full spectrum of glycemia, and the differences increase as glucose intolerance worsens [8,9].

The hormonal changes are due to pregnancy induced systemic vasodilatation and increased vascular capacitiance. Blood volume begins to increase as early as 6 weeks of gestation [10,11].

The increase in red cell and hemoglobin mass is reported to be maximum at 12-28 weeks of pregnancy rise in plasma volume more as compared to increase in the red cell mass (40% vs. 20% respectively)[12].

So advise the pregnant women to maintain the hemoglobin level at or above 11 g/dl and should not be

allowed to fall below 10.5 g/dl in any trimester to prevent the complications of aneamia [13].

Anemia is a common problem worldwide and has higher prevalence among pregnant females as is estimated to be about 38% compared to 29% of non-pregnant women[14].

A low level of HbA1c may be seen in anemia which shortens the RBCs life span. There is fasting hypoglycemia due to fetal consumption, postprandial hyperglycemia, and hyperinsulinemia due to anti-insulin factors. This response is consistent with pregnancy-induced state of peripheral insulin resistance, the purpose of which is to ensure a sustained supply of glucose to fetus to meet its growth demand. Hyperinsulinemia and insulin resistance are most marked in the third trimester of pregnancy [15]. In a normal pregnancy, between 6 to 10 weeks, there is a decrease in the fasting blood glucose and this continues throughout pregnancy [15].

For the previous 30 years, investigators have attempted to determine whether the glycated hemoglobinA1c (HbA1c) level during pregnancy may be used as a screening or diagnostic test for gestational diabetes (GDM) [16, 17]. One of the studies says the pregnant women had a low HbA1C, particularly in the first trimester of pregnancy. This might implicate that for prevention of congenital malformations and macrosomia in diabetic pregnant women and HbA1C should be below 5% in the first trimester of pregnancy and below 6% in the third trimester [6,8,18].

The more recent studies have indicated that the HbA1c level during pregnancy may predict GDM in women at high risk for diabetes. The New Zealand Ministry of Health recommends that an HbA1c test be offered to all pregnant women at booking as part of the first antenatal blood screen to detect GDM[20].

The research aimed to measure HbA_{1C} in normal Sudanese non-diabetic pregnant women attending antenatal care at Ribat University Hospital, Khartoum state during the period from Sep 2017 to Nov 2017, and to explore the effect of pregnancy on $HbA_{1C.}$

METHODS

A cross sectional facility based study was conducted in The National Ribat University hospital during Sep 2017 to Nov 2017 among the Normal Sudanese pregnant, non-diabetic females of ages between 18-40 years. Twenty women were included as a pilot, ten of them at first trimester and ten at third trimester. After their consent they were assessed via a questionnaire covering age, educational level, chronic illness, gestational age of pregnancy, past history of GDM, family history of DM, daily caloric intake for the last three days and smoking history. Arterial blood pressure was checked for each volunteer to exclude hypertension. Blood samples were analyzed for FBG (to exclude DM), Hb level and glycosylated hemoglobin level by colorimetric reaction using machine COBAS INTEGRA 400 plus A1C analyzer. Correlations between the variables were estimated and P value less than 0.05 were considered statistically significant.

RESULTS

Analytical performance

The analytical quality of HbA1c measurements performed locally in the same center was evaluated by analysis of HbA1c value.

HbA1c reference intervals

Within the framework of a study of pregnant women we evaluated the HbA1c concentrations in 2 different categories of participants. Among the 20 pregnant women, we distinguished those with first and third trimester separately. Each of the 2 categories of pregnant women had mean HbA1c values. The mean of HbA_{1c} results for first trimester is 4.77 with standard deviation of 0.60 (Table 1).

The maximum value was 5.5% and the minimum was 3.5% (table 1).

The mean of HbA1c results for third trimester is 3.98% with standard deviation of 1.03 (Table 1). The maximum value was 5.4% and the minimum was 2.8% (table 1).

Table-1: HbA_{1c} reference intervals in first trimester and first trimester healthy pregnant women

Group	n[a]	Range (minimum–maximum)	Median HbA_{1c} %
First trimester	10	3.5%-5.5%	4.77% ± 0.60
Third trimester	10	2.8% - 5.4%	3.98% ± 1.03
During all pregnancy	20	2.8%-5.5%	4.3750%

n[a]: no. of women participate in this group.

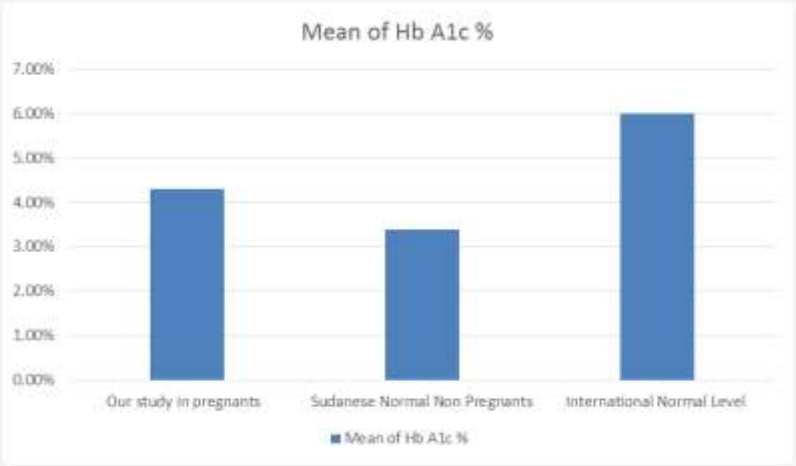

Fig-1: HbA_{1c} Mean Values Comparison

In Fig. 1: Comparison between our study, the normal mean of HbA_{1C} in Sudanese Normal adult nonpregnant female SNNP was 3.4% and the range was (1.4%-5.3%) and the Normal International Standard mean of HbA_{1C} in nonpregnant female ranging between (4%- 6%).

Table-2: (Table 2) shows the all P-values between the 2 groups

Variables	P-value HbA1c First Trimester	P-value HbA1c Third Trimester	Statistical significance
FH.of DM	0.442	0.340	Insignificant
PH.Of GDM	-	0.189	Insignificant
Nutrition	0.472	0.189	Insignificant
Kal	0.442	0.333	Insignificant
Sys. Bp	0.364	0.444	Insignificant
Dia. Bp	0.220	0.468	Insignificant
Hb	0.265	0.189	Insignificant
FBG	-	-	Insignificant

A small decrease in HbA1c values was observed at late trimester of pregnancy and within the Sudanese HbA1c value.

No correlation was found between FBG, Hb level, daily calorie intake, PH. of GDM, FH. of DM and the level of HbA1c. Table 2 shows that the all P-values are greater than (0.05).

DISCUSSION

In this study, we determine the normal level of HbA1c in normal healthy Sudanese pregnant women and to analysis the effect of pregnancy on HbA1c and to observe the relationship between HbA1c values and the main factors which can affect the level of HbA1c in Cross sectional facility based studies. It is predominately focused on early-pregnancy and third-trimester HbA1c levels,

More recent studies have linked the HbA1c level to adverse pregnancy outcomes using different cutoff points for the HbA1c level [21,22]. During pregnancy, the HbA1c level exhibits biphasic changes, with decreases between the first trimester and mid-pregnancy, followed by increases in the third trimester [23].

Moreover, a recent study indicated that the mid-pregnancy HbA1c level was associated with various adverse pregnancy outcomes in high-risk Taiwanese women and May investigated as a predictor of GDM[19]. At Dec. 2016, the study enrolled 1,989 pregnant Taiwanese women determined that the optimal cut-off point of the HbA1c level to predict GDM was 5.7% [19].

The study was done in Japan during the first trimester and between 24 and 28 weeks of pregnancy. The subjects were 749 pregnant women. Of the 749 subjects, 22 (2.9%) tested positive for GDM. Of those 22 patients, 14 were diagnosed with GDM in the first trimester (63.6%) and eight in the second trimester (36.4%). This finding suggests the importance of screening for glucose intolerance in the first trimester [24].

In Japan, from April 2014, it has been decided to adopt the National Glycohemoglobin Standardization Program (NGSP) value, which is used by many

countries globally, as the first step toward internationalization [25].

The International Association of Diabetes and Pregnancy Study Groups (IADPSG) were diagnosed GDM at first-trimester with an HbA1c level 5.7 - 6.4%[26]. An Indian study has shown the mean HbA1c in pregnant Indian women with normal glucose tolerance to be 5.36+/-0.36%. **(27)**

The HbA1c value should be kept between 4.5% and 5% for minimal adverse outcomes it may well be useful to keep the blood sugar values, irrespective of fasting or postprandial levels, to below 101 mg/dl, in the third trimester[28]. In a study done by, HbA1c values in diabetic pregnancy are lower than in nonpregnant diabetic subjects and the mean value in pregnant nondiabetic was 4% ± 0.7% [29.

Lower concentration of HbA1c facilitates oxygen delivery to the fetus – HbA1c has decreased affinity for 2, 3-bisphosphoglycerate and increased affinity for oxygen. Average HbA1c was found to be 5.1% ± 0.4% in early pregnancy ($P < 0.001$) and 5.0% ± 0.3% ($P < 0.001$) in late pregnancy [29,30].

The Italian study was involved Five Italian Diabetic Care Units , the HbA1c reference intervals were 4.0%–5.5% for pregnant nondiabetic women and 4.8%–6.2% for nonpregnant controls. The conclusion of this study was healthy pregnant women have lower HbA1C concentrations than nonpregnant women. The reference intervals for HbA1c in pregnant women should therefore be lower than those currently in use[31].

Other study was conducted in Sudan, Khartoum state, result showed that, the mean concentration of the HbA1c in cases group was (4.407±1.044) % in first trimester, (4.797±0.621) % in second trimester and (4.823±0.616) % in third trimester, and (5.660±0.461%) in control group with a highly significant difference between the two groups. The study also showed that the mean concentration of HbA1c of the first trimester is lower than that of the second and third trimesters, but there was no significant difference between the mean concentration of the second and third trimester [32].

In more recent study, the normal range value for HbA1c in Sudanese female between (1.4 % – 5.3%) witches was found to be different from the international values [4]. In our study, the mean of HbA1c in Sudanese healthy pregnant women is 4.37±92% found within the normal Sudanese values of HbA1c. HbA1c is lowered at third trimester than first trimester.

Our findings demonstrated the decrease of HbA1c level during pregnancy similar to some previous studies. The early pregnancy HbA1c level was 4.77 ±.60 and the late pregnancy HbA1c level was 3.98% ±1.03 although the differences between the two levels were found within the normal range of Sudanese HbA1c level witch different from international range.

We observed a small decrease in HbA1c values in the late of pregnancy. Controversial data are reported in the literature about this point: some authors confirmed this finding [33], whereas others did not detect differences among trimesters [34]. Or reported an additional increase in HbA1c values in late pregnancy. [22, 31, 35] All these finding support a possible relationship between HbA1c and gestational age.

These lower HbA1c concentrations found in the late of pregnancy might be related to the decrease in plasma glucose values and to the shortened erythrocyte life span that occur during pregnancy or due to low Hb in most of women participate in this study.

CONCLUSION AND RECOMMENDATIONS

The normal range values for HbA1c in pregnant Sudanese women are between (2.8%-5.5%). HbA1c is not affected by daily calorie intake, Hb level, FBG, PH of DM, PH of GDM or Family History of DM may be due to the small sample

The current study comprised a single-center study; thus, additional design studies are required. The results provided supporting evidence for recent reports that recommended measured the HbA1c level at early pregnancy as one of blood screening base line tests, and follow the level especially in high risk women.

The mean HbA1c level 4.37±92% may be used as a prognostic biomarker for predict of GDM in Sudanese pregnant women.

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Conflicts of interest

There are no conflicts of interest.

Ethical approval

The study was approved by the National Ribat University hospital.

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