



## HbA1c in Healthy Sudanese Pregnant Women in Reference to Body Mass Index

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### Abstract

A descriptive, cross sectional study conducted in Sudan, Khartoum state in Yastabsheron obstetric hospital during the period from February to June 2011. Analytical and statistical methods were applied to estimate the concentration of HbA1c in apparently healthy pregnant Sudanese women as well as in apparently healthy non-pregnant Sudanese women to assess the difference in the results which may be caused by physiological and biochemical change that occur in blood of maternal ladies, so pregnant women can get a good report and interpretation of the results obtained. Blood samples were taken from a total of 90 apparently healthy pregnant women (test group) and 30 apparently healthy non-pregnant women (control group), then samples were analyzed for HbA1c by using affinity chromatography method, and results were recorded in addition to their age, body mass index and the number of pregnancies, then results were statistically analyzed.

Result showed that, the mean concentration of the HbA1c in cases group was  $(4.407 \pm 1.044)\%$  in first trimester,  $(4.797 \pm 0.621)\%$  in second trimester and  $(4.823 \pm 0.616)\%$  in third trimester, and  $(5.660 \pm 0.461)\%$  in control group with a P value of 0.00, indicating the 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.

On the other hand, the study showed that there was a significant weak positive correlation between HbA1c concentration with all of body mass index and the age of pregnant women, but an insignificant weak positive correlation with the number of pregnancies. The study concluded that, Healthy pregnant women have lower HbA1c concentrations than non-pregnant women which can be attributed to the decrease in plasma glucose values and to the shortened erythrocyte life span that occur during pregnancy. The body mass index and age affect the concentration of HbA1c, but it is not affected by the number of pregnancies. So the reference intervals for HbA1c in pregnant women should therefore be lower than those currently in use for non-pregnant women.

**Keywords:** HbA1c; Body Mass Index

### Introduction

Pregnancy is a major endocrine event in the female lifespan, involving wide-ranged and often dramatic changes in the metabolism of various hormones [1]. It is a normal physiological phenomenon with many biochemical changes that assist the nurturing and with many survival of the fetus.

As gestation progresses, reference ranges for the concentration of many biochemical parameters change significantly from those

found in the non-pregnant state. Gestation-specific reference ranges are essential for correct interpretation of tests used in screening, diagnosis, and monitoring during pregnancy [2].

Strict glycemic control is essential to minimize the maternal and fetal morbidity and mortality of pregnancies complicated by diabetes [3-5].

In addition to home blood glucose measurement, which may not always reflect the true average blood glucose level [6], HbA1c is a

useful parameter in metabolic regulation [7-10]. Thus, supplementation with HbA1c, as is common outside pregnancy, seems appropriate.

Before pregnancy, the target for metabolic control in women with diabetes is HbA1c values near the normal range [11]. However, the upper normal range of HbA1c during normal pregnancy is only sparsely investigated with different methods [12], mainly in late pregnancy [13,14], and reference ranges are generally established from the non-pregnant state.

Increased third-trimester HbA1c levels are associated with an increased risk of preeclampsia [5], macrosomia [3] and stillbirth [4], leading to speculations that the target for HbA1c in pregnancy should be even lower than outside pregnancy to prevent adverse events.

Obesity, diabetes and glycaemic control are inter-linked, weight gain is associated with worsening diabetic control and can be exacerbated by therapies aimed at controlling hyperglycemia. Some studies observed that there is a strong relationship between increasing BMI and HbA1c across all age groups [15]. There is a need to establish the reference range of HbA1c during normal Pregnancy with an internationally recognized diabetes Control and Complications Trial (DCCT)-aligned method. In this study, we evaluated the normal upper range of HbA1c during pregnancy in reference to BMI.

## Objectives

### General objective

To assess HbA1c in healthy Sudanese pregnant women in reference to BMI.

### Specific objectives:

- To measure HbA1c in pregnant women at 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> trimester compared to non-pregnant women.
- To assess the effect of body mass index on HbA1c levels in pregnant women
- To correlate HbA1c to age of pregnant women and the number of pregnancies.

## Materials and Methods

- **Study approach:** Quantitative study
- **Study design:** The scope of this study is to estimate HbA1c in healthy pregnant Sudanese women in reference to BMI. This study is a descriptive cross sectional case control study.
- **Study area:** This study was carried out in Khartoum state in Yastabsheron obstetric hospital.

- **Study period:** Study was carried during the period from February to May 2011.
- **Study population:** Ninety (90) samples had been collected from apparently healthy pregnant Sudanese women who represent the test group and 30 samples had been collected from apparently healthy non pregnant Sudanese women who represent a control group.
- **Exclusion criteria:** Pregnant women with family history of diabetes, history of gestational diabetes, diabetes and anemia excluded.
- **Ethical consideration:** Permission of this study was obtained from the local health authorities in Yastabsheron obstetric hospital.
  - The objectives of the study were explained to all individual participating in this study.
  - An informed consent was obtained from all participants.
  - Health education was provided to all participants.
- **Data collection and clinical measurement:**
  - Interview with the test group and the control group were done to obtain the clinical data.
  - Clinical assessment was done by a medical doctor.
  - A questionnaire was designed specifically to obtain information's which help in either including or excluding certain individuals in or from the study respectively.

## Measurement of body mass index

The following anthropometric parameters were taken into consideration

### Weight and height:

- Weight was recorded to the nearest kilograms (kg) with the subject standing on the weighing machine without shoes. The same weighing machine used for all participants and the machine was tested with known set of weights for any error.
- Height was recorded with the subject erect, bare footed feet together, back and heels against the upright bar of height scale.
- The height measurement equipment consists of a vertical bar with a steel tape attached perpendicularly to the vertical bar which was brought down snugly on the examinees head.
- Weight was recorded in (kg) where as height was recorded in (cm).

**BMI**

- BMI was calculated from the formula:
- Weight in kilograms \square of height in meters.

**Collection of blood samples**

- Venous blood specimens "3ml" were collected from participants, using tourniquet, disposable syringe and spirit for sterilization of the area of collection.
- The collected blood was drawn into EDTA containers, gently mixed.
- Blood samples were preserved at 2-8°C for one week prior to analysis.
- Obtained blood samples were tested for determination of HbA1c using iron exchange chromatography method.
- No special patient preparation is required. Fasting specimens are not required. No special additives or preservatives other than anticoagulants are required.

**Methodology**

**Instrument used for measurement:** Nycocard reader II.

**Materials required**

Syringes, EDTA containers alcohol, cotton and complete hba1c (Nycocard) kit.

**Measurement of HbA1c****Principle**

- Nycocard HbA1c is a boronate affinity assay. The kit contains test devices with a porous membrane filter, test tube pre-filled with reagent and a washing solution. The reagent contains agent that lyses erythrocytes and precipitates hemoglobin specifically, as well as a blue boronic acid conjugate that binds cis-diols of glycosylated hemoglobin, when blood is added to the reagent, the erythrocytes immediately lyse. All hemoglobin precipitates. The boronic acid conjugates binds to the cis-diol configuration of glycosylated hemoglobin, the precipitates is evaluated by measuring the blue (glycosylated hemoglobin) and the red (total hemoglobin) color intensity with the Nycocard READER II, the ratio between them being proportional to the percentage of HbA1c in the sample(www.axis-shield.com/Nycocard-HbA1c).

**Procedures**

- Five  $\mu\text{L}$  of whole blood were mixed with R1/Reagent in the test tube, Incubated for 2 minutes, the test tube re-

mixed and 25  $\mu\text{L}$  of the reaction mixture were applied to the test device, then 25  $\mu\text{L}$  washing solution added, and the test results read by the Nycocard reader II (www.axis-shield.com/Nycocard-HbA1c).

**Quality control**

Reagents, standard were checked for storage, stability and preparation before starting work.

**Data analysis**

Collected data were analyzed by a computer system using statistical package for social science (SPSS) program using the One-Way ANOVA, independent (t test) and correlation tests.

**Results**

During February to May 2011, a total of 90 pregnant women (at the different three trimesters (first, second and third) of pregnancy admitted to Yastabsheron obstetric hospital and a total of 30 females (non- pregnant women) were randomly selected to conduct this study. The two groups were apparently healthy women and they were free of any disorders that can affect the concentration of HbA1c. Blood samples were taken from each subject, samples were analyzed for determination of HbA1c concentration and results were recorded in addition to their age, body mass index and the number of pregnancies.

The results obtained were statistically analyzed, using the One-Way ANOVA, independent (t test) and correlation. The level of significance was expressed as  $P < 0.05$  for significant, and  $P < 0.01$  for highly significant.

Table 1 showed that, the mean concentration of the HbA1c in cases group was ( $4.407 \pm 1.044$ )% in first trimester, ( $4.797 \pm .621$ )% in second trimester and ( $4.823 \pm .616$ )% in third trimester), and ( $5.660 \pm .461$ )% in control group with a P value of 0.00, indicating the highly significant difference between the two groups.

Table 2 showed the significant difference between the mean concentration of HbA1c of first (4.407%) and second trimesters (4.797%).

Table 3 showed the significant difference between the mean concentration of HbA1c of first (4.407%) and third trimesters (4.823%).

Table 4 showed the insignificant difference between the mean concentration of HbA1c of second (4.797%) and third trimesters (4.823%).

Variable	Cases group N =90			Control group N= 30	P value
	First trimester	Second trimester	Third trimester		
HbA <sub>1c</sub> %	4.407 (± 1.044) %	4.797 (± .621) %	4.823 (± .616) %	5.660 (± .61) %	0.00

**Table 1:** Summarizes comparison of means of HbA<sub>1c</sub> % between study and control groups:

The mean difference is significant at the 0.05 level.

The table shows the mean ±SD, range in brackets () and probability (P) value.

Variable	Stage of pregnancy	N	Mean	Std. Deviation	Sig.
HbA <sub>1c</sub> %	First trimester	30	4.407	1.0448	.013
	Second trimester	30	4.797	.6217	

**Table 2:** Summarizes comparison of means of HbA<sub>1c</sub> % between first and second trimester:

The mean difference is significant at the 0.05 level.

Variable	Stage of pregnancy	N	Mean	Std. Deviation	Sig.
HbA <sub>1c</sub> %	First trimester	30	4.407	1.0448	.011
	Third trimester	30	4.823	.6163	

**Table 3:** Summarizes comparison of means of HbA<sub>1c</sub> % between first and third trimester:

The mean difference is significant at the 0.05 level.

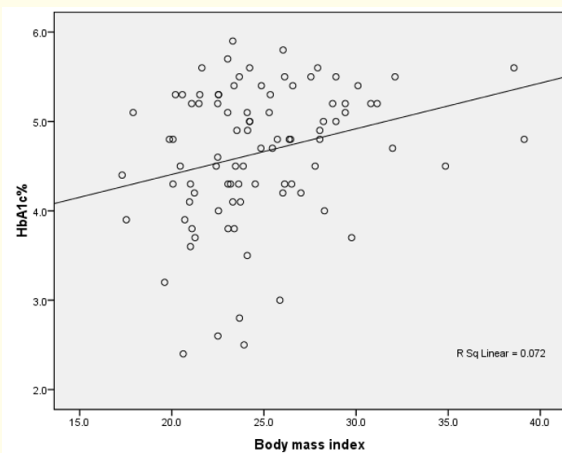
Variable	Stage of pregnancy	N	Mean	Std. Deviation	Sig.
HbA <sub>1c</sub> %	Second trimester	30	4.797	.6217	.955
	third trimester	30	4.823	.6163	

**Table 4:** Summarizes comparison of means of HbA<sub>1c</sub> % between second and third trimester:

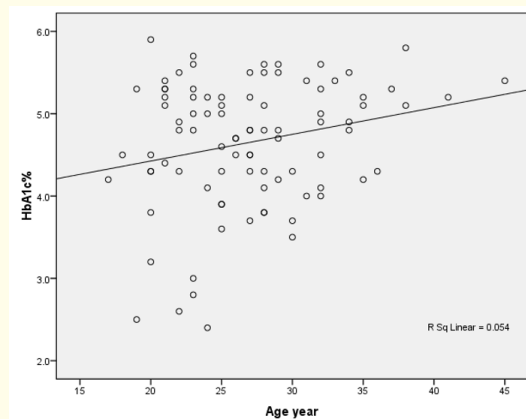
The mean difference is significant at the 0.05 level.

Figure 1 showed the correlation between HbA1c and body mass indexes in cases group (r= 0.268) (p-value = 0.011).

Figure 2 showed the correlation between HbA1c and age in cases group (r= 0.232) (p. value = 0.028)

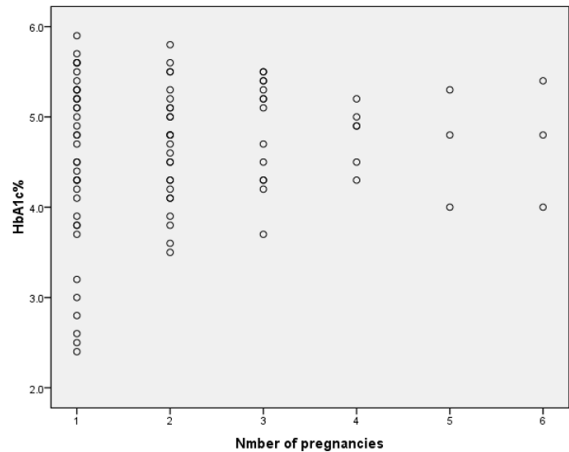


**Figure 1:** The scatter plot of HbA1c concentrations and body mass index showed the significant weak positive correlation on this fig. (r: 0.268), (p.value:0.011).



**Figure 2:** The scatter plot of HbA1c concentrations and age showed the weak positive significant correlation on this fig. (r:0.232), (p.value:0.028).

Figure 3 showed the correlation between HbA1c and number of pregnancies in cases group ( $r=0.130$ ) ( $p. \text{value} = 0.221$ ).



**Figure 3:** The scatter plot showed the insignificant weak positive correlation between HbA1c concentrations and the number of pregnancies on this fig. ( $r: 0.130$ ), ( $p.\text{value}:0.221$ ).

## Discussion

The present study was carried out in order to measure the concentration of HbA1c in pregnant women at the different stages of pregnancy as well as in non pregnant women to detect if there are any differences between results and to ensure proper interpretation of laboratories result may obtained for the whole study group.

Elevated HbA1c is associated with increased risk of adverse pregnancy outcomes (e.g., abortion, stillbirth, and congenital abnormalities) [16]. Some previous study found that even a slightly raised HbA1c level was positively associated with an increased risk of major congenital abnormalities [17].

The statistical analysis showed that the mean concentration of HbA1c in pregnant women in the different trimesters of pregnancy was lower than the mean of non-pregnant women.

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.

On the other hand, the study showed that there was a significant weak positive correlation between HbA1c concentration with all of body mass index and the age of pregnant women, but an insignificant weak positive correlation with the number of pregnancies.

In comparison to a previous study, there was an agreement between this study and the study was conducted by Andrea Mosca, *et al.* for determination of HbA1c in Healthy pregnant women in which Healthy pregnant women have lower HbA1c concentrations than non-pregnant women, due to the decrease in plasma glucose values and to the shortened erythrocyte life span that occur during pregnancy. So the reference intervals for HbA1c in pregnant women should therefore be lower than those currently in use [18]. Also, this study agrees with another previous study, which was conducted by C Jacques, *et al.* in which they estimate HbA1c in different stages of healthy pregnant women, and found that HbA1c levels progressively decreased during the first 25 weeks of pregnancy, then remained stable [19].

The study also agreed with the study of Nilsen J R., *et al.* which found that HbA1c was significantly decreased early in pregnancy and further decreased in late pregnancy compared with age-matched non pregnant women [20-70].

## Conclusion

Healthy pregnant women have lower HbA1c concentrations than non-pregnant women which can be attributed to the decrease in plasma glucose values and to the shortened erythrocyte life span that occur during pregnancy. The body mass index and age affect the concentration of HbA1c, but it is not affected by the number of pregnancies. So the reference intervals for HbA1c in pregnant women should therefore be lower than those currently in use for non-pregnant women.

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