The Journal of Teachers Association

ISSN 1019-8555 (Print) & ISSN 2408-8854 (Online)
Frequency: Bi-Annual
DOI: https://doi.org/10.62469/taj.v037i02.014

OPEN ACCESS

Website: www.tajrmc.com
Email: editor@tajrmc.com
Volume-37 | Issue-2 | Jul-Dec 2024

Status of Hemoglobin A1C Among Pregnant in Comparison to Non-Pregnant Women in Rajshahi City

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Abstract: ***Background:*** The time a fetus develops inside a woman's uterus is known as pregnancy, and it typically lasts for 40 weeks. To maximize the benefits of pregnancy, good glycemic control must be maintained throughout. ***Methods:*** This cross-sectional type of comparative study was carried out in the Department of Physiology in Rajshahi Medical College, Rajshahi and data were collected from the Maternity and Child Welfare Centre (MCWC), Rajshahi over a period of 1 year from January 2019 to December 2019 among the pregnant and non-pregnant women to assess the hemoglobin A1c during the 3rd trimester of pregnancy. Prior to the commencement of the study approval was taken from the Ethical Review Committee (ERC). A semi-structured questionnaire and laboratory support were used to gather information from 120 women by convenient sampling technique. ***Results:*** The results showed that plasma HbA1c was 4.8 ± 0.4% in pregnant women and 5.6 ± 0.5% in non-pregnant women and it was statistically highly significant ($p < 0.001$). So, regular monitoring of HbA1c in pregnant women should be done to avoid adverse pregnancy outcomes. ***Conclusions:*** The study indicated that nondiabetic women with pregnancy had significantly lower HbA1c compared with non-pregnant women.

Keywords: 3rd trimester pregnancy and Hemoglobin HbA1c.

Original Research Article

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How to cite this article:
Begum B, Rupa SN, Sayem ASM, Mahmuda S, Tasu TS, Kabir F, Islam MJ; Status of Hemoglobin A1C Among Pregnant in Comparison to Non-Pregnant Women in Rajshahi City. Taj 2024;37 (2): 106-111.

Article history:
Received: August 17, 2024
Revised: October 10, 2024
Accepted: November 12, 2024
Published: December 01, 2024

Article at a glance:

Study Purpose: *The purpose of this study was to investigate whether hemoglobin A1c during 3rd trimester of pregnancy differs from non-pregnant women of Rajshahi City.*

Key findings: *The mean plasma HbA1c (%) level of the pregnant women was lower than the non-pregnant women.*

Newer findings: *The plasma HbA1c was significantly lower in pregnant women than the non-pregnant women ($p < 0.001$).*

Abbreviations: *ADA: American Diabetes Association, ERC: Ethical Review Committee, hPL: Human placental lactogen and hPGH: Human placental growth hormone.*

INTRODUCTION

As a physiological state, pregnancy lasts from the time of conception to the time of delivery. The female body goes through a lot of hormonal and metabolic changes during that period.[1] Worldwide, more than 200 million fertile women conceive each year, and the majority of these pregnancies end happily. Glycemic changes occur in pregnant women as a result of hormonal and metabolic changes. Changes in blood HbA1c have

been linked to gestational age throughout pregnancy.[2] Haemoglobin is glycosylated to generate glycated haemoglobin, or HbA1c. A person's glycemic status during the previous two to three months is represented by its value. As per the American Diabetes Association (ADA) Guidelines-2018, a normal pregnancy is associated with a slightly lower HbA1c than a typical non-pregnant woman, possibly because of greater red blood cell turnover. HbA1c levels in non-pregnant women were normal, 4.5-5.7% in early pregnancy, and 4.4-5.6% in late pregnancy. Blood glucose concentration and red blood cell life span both affect the amount of glycated hemoglobin in blood.[3] In the worst-case scenario, an elevated HbA1c level is linked to an increased risk of intrauterine growth retardation, congenital defects, fetal obesity, premature deliveries, diabetes mellitus, hypertension, atherosclerosis, preeclampsia, ischemic heart disease, and mortality. The absence of effects from changing blood sugar levels after meals and during illness is the main benefit of HbA1c.[4] Newer red blood cells are exposed to lower glucose concentrations because there is a reduction in fasting blood glucose throughout a normal pregnancy, which lasts for six to ten weeks. Furthermore, pregnancy significantly shortens the RBC life span. It is therefore reasonable to anticipate lower HbA1c readings during pregnancy than in the non-pregnant condition.[5]

Insulin resistance is elevated during a typical pregnancy. Increased levels of estrogen, progesterone, human placental lactogen (hPL), human placental growth hormone (hPGH), cortisol, TNF, ILs, and other substances are thought to be a mediating factor in the decline in maternal insulin sensitivity. Because mothers who are insulin resistant use lipids rather than carbohydrates for energy, the fetus receives less carbohydrates.[6] For pregnant non-diabetic women, the HbA1c reference intervals were 4.0%–5.5%, while for non-pregnant controls, they were 4.8%–6.2%. For non-diabetic pregnant women, the cutoff values for HbA1c were 3.8–5.5% at 15–24 weeks, 4.0–5.5% at 25–27 weeks, and a little but substantial increase to 4.4-5.5% at 28–36 weeks.[7] Although it is not well defined during pregnancy, the typical reference interval for HbA1c is well established in adults. In a report by Worth et al.,[8] the HbA1c levels were found to be increased in pregnancy. A similar increase was also seen in another study done by Vintzileos et al.,[9]. On the other hand, a study conducted by Fadel et al.,[10] showed no significant change in HbA1c level in pregnancy. This was in good agreement with the study by O'Shaughnessy et al.,[11]. Furthermore, there are another set of studies, which show that HbA1c levels are lower in the pregnancy state. Nielsen et al.,[12] demonstrated a decrease in the upper reference limit of HbA1c from 6.3% before pregnancy to 5.7% in early pregnancy and 5.6% in the third trimester. Radder et al.,[13] have also reported a fall in the HbA1c levels during pregnancy. In all three trimesters of a typical pregnancy, HbA1c is lower than it is in non-pregnancy.[14]

It was evident from the aforementioned research that there is ongoing debate regarding typical HbA1c levels during pregnancy. In order to attain adequate glycemic control and consequently attempt to reduce neonatal mortality and morbidity, it was crucial to carry out additional research in this field. While routine examinations are performed in Bangladesh as part of prenatal checkups, routine HbA1c testing is necessary to prevent numerous unfavorable consequences. In order to implement the necessary control measures and prevent an unintended feto-maternal consequence, the study's objective was to assess the HbA1c level throughout the third trimester of pregnancy.

METHODS

This was a cross-sectional type of comparative study at the Department of Physiology, Rajshahi Medical College, Rajshahi from January 2019 to December 2019 to assess HbA1c among pregnant and non-pregnant women in rajshahi city. Pregnant women and non-pregnant healthy women of 3rd trimester were included in this study. A convenient sampling technique was used and the total sample size was 120 (60 in each group). Consulting with the supervisor and reviewing the previous published literature researcher developed the semi-structured questionnaire for the study. Then to finalize the procedure and to evaluate the effectiveness of the questionnaire a pretest was carried out among 10 pregnant and non-pregnant women. After pretest, some correction was done and the questionnaire was finalized for data collection. The pregnant and

non-pregnant women were enrolled in this study after considering inclusion and exclusion criteria. Complete history taking and physical examination was done after taking informed consent and recorded in a preformed questionnaire. After 12 hours overnight fasting by all the women 4ml of fasting venous blood sample was collected from the median cubital vein by disposable syringe with all aseptic precautions.

All efforts were made to collect data accurately. After collecting data, data were checked to detect errors and to maintain validity. Then data were cleaned by editing, coding, recoding and categorizing. Then data were imputed into SPSS software. Qualitative variables were described by frequency and percentage, while quantitative variables were described by the mean and standard deviation. Differences in continuous variables were determined by unpaired t-test. All statistical analysis was done by SPSS software, version 24. A p-value < 0.05 was considered statistically significant for all tests.

RESULT

Age and BMI were 24.7±4.4 years & 26.3±3.5 kg/m^2 in pregnant women and 26.1±5.8 years & 27.6±4.5 kg/m^2 in non-pregnant women, respectively (Table 1).

Table 1: Age and BMI of study subjects (n=120)

Variables	Pregnant (n=60)	Non-pregnant (n=60)
Age (years)	24.7 ± 4.4	26.1 ± 5.8
BMI (kg/m^2)	26.3±3.5	27.6±4.5

Data were shown as mean ± SD.

Pregnant women with primipara and multipara were 31(51.7) and 29 (48.3), respectively but majority of the non-pregnant subjects were nulliparous (Table 2).

Table 2: Parity of study subjects (n=120)

Parity	Pregnant (n=60)	Non-pregnant (n=60)
Nullipara	0 (0)	33 (55.0)
Primipara	31(51.7)	24 (40.0)
Multipara	29 (48.3)	3 (5.0)

Pregnant women with preterm (<37 weeks) and term (≥ 37 weeks) pregnancy were 59 (98.3%) and 1 (1.7%), respectively. Here, majority of the pregnant women were at preterm (Figure 1).

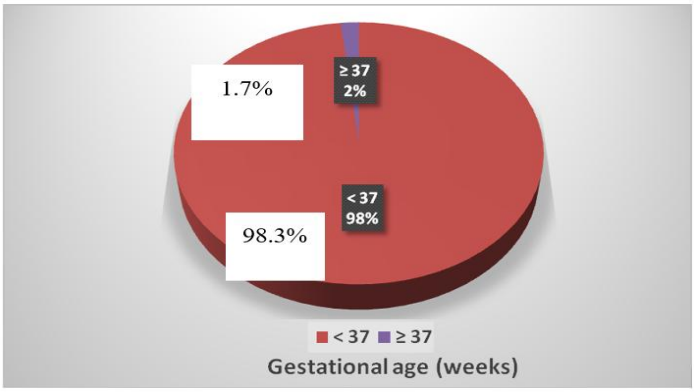

Figure 1: Gestational age of pregnant subjects (n=60).

Plasma HbA1c of pregnant women was 4.8 ± 0.4% and non-pregnant women was 5.6 ± 0.5% and it was statistically highly significant ($p < 0.001$) (Table 3).

Table 3: Glycemic status of study subjects (n=120)

Variables	Pregnant (n=60)	Non-pregnant (n=60)	p-value
Plasma HbA1c (%)	4.8 ± 0.4	5.6 ± 0.5	< 0.001***

Data are shown as mean ± SD. Statistical analysis was done by unpaired 't'-test (independent sample 't' test). *** = statically significant ($p<0.001$).

DISCUSSION

Pregnancy causes drastic changes in maternal physiology, psychology and metabolism. This cross-sectional comparative study has been conducted to evaluate any alteration of HbA1c during pregnancy. For that purpose, 60 pregnant women and 60 non-pregnant women at 3rd trimester were selected by convenient sampling technique. During pregnancy, maternal fasting hypoglycemia occurs due to fetal consumption and postprandial hyperglycemia occurs due to anti insulin factors, oral glucose tolerance test may show an abnormal pattern. HbA1c is the gold standard indicator of glycemic status. If a pregnant woman is associated with GDM, the level of HbA1c should be 5.7-6.4% (According to the International Association of Diabetes and Pregnancy Study Groups). It is more marked in second and third trimester of pregnancy. But in normal healthy pregnant women have lower HbA1c concentrations than non-pregnant women. HbA1c has decreased affinity for 2,3 bisphosphoglycerate and increased affinity for oxygen, lower concentration of plasma HbA1c facilitates oxygen delivery to the fetus.

Age is one of the factors which can affect serum HbA1c. So that age matched cases and controls were taken in order to remove one of the major confounding factor[1]. In the current study, it was found that HbA1C level significantly lower in pregnant women than non-pregnant women. Our findings are in good agreement with Siddig et al.[4], Shobha et al.[15], Versantvoort et al.[14], O'Connor et al.[16], Mosca et al.[7], Radder and Roosmalen[13], Nielsen et al. [12], O'Kane et al.[17]. These lower HbA1c concentrations found in pregnancy might be related to the decrease in plasma glucose values and to the shortened erythrocyte life span that occur during pregnancy. During normal pregnancy a decrease in fasting blood glucose occurs early in pregnancy and is sustained during the remaining part of pregnancy. Erythrocyte life span is decreased during normal pregnancy due to 'emergency hemopoiesis' in repose to elevated erythropoietin levels. New erythrocytes may be exposed to lower average concentration of glucose due to sustained fasting hypoglyacemia. The HbA1c value should be kept between 4.5% and 5% for minimal adverse outcomes in the third trimester.[15] As HbA1c has decreased affinity for 2, 3-biphosphoglycerate and increased affinity for oxygen, lower concentration of HbA1c facilitates oxygen delivery to the fetus.[4] Our evaluation of HbA1c reference intervals in pregnancy was performed on a consistent number of women by use of a DCCT aligned HbA1c method. Our result was conflicting with Worth et al.[8] where the study design was different or there were some methodological difficulties. Diabetes in pregnant women is associated with increased occurrence of both fetal and maternal adverse events including macrosomia, congenital malformations, spontaneous abortion, perinatal mortality and preeclampsia. In this study, we determine the effect of pregnancy on HbA1c, it is predominantly focused on third trimester HbA1c levels.

One of the strengths of our study was that we have included only healthy women who were relatively free from any disease. So, it was possible for us to detect any minute change of HbA1c parameters due to pregnancy.

One of the weaknesses of our study was that we have done a cross-sectional study on small sample size. We included only 3rd trimester of pregnant women in our study. Hence trimester variation regarding to the changes of HbA1c parameters could be studied to get better results.

CONCLUSION

HbA1c can indeed be utilized for the monitoring of glycemic level, as a screening test, even in nondiabetic pregnancies in our clinical practice.

Acknowledgements

Contribution of the women who participated in the study was acknowledged for their co-operation in data collection for this manuscript.

Authors' contributions

BB, SNR, ASMS, SM: Concept and design, data acquisition, interpretation and drafting. BB, TST, FK and MI: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

Declarations

Funding

The authors received no financial support for the research, authorship and/or publication of this article.

Conflict of interest: Authors declared no conflict of interest.

Ethical approval

Ethical approval of the study was obtained from the Ethical Review Committee from Rajshahi Medical College, Rajshahi. Informed consent was taken from all women. All the study methodology was carried out following the relevant ethical guidelines and regulations.

Consent for publication: Taken

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The Journal of Teachers Association
Abbreviated Key Title: TAJ
Official Journal of Teachers Association Rajshahi Medical College