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Usefulness of HbA1C in differentiating Gestational Diabetes Mellitus and preexisting Diabetes Mellitus in the early stages of pregnancy

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Abstract

Introduction: Diabetes mellitus in pregnancy can cause several complications for the mother and the neonate if left untreated. This study identifies the proportion of undiagnosed pre-existing diabetic pregnant women and the necessity of doing an HbA1C test in the first trimester for its diagnosis.

Methodology: Pregnant women in the first trimester without a history of hypertensive disorders, Diabetes Mellitus in their previous pregnancies were recruited for the studies. Then blood samples were withdrawn from them to perform OGTT and the HbA1C test on booking visit (8-12 weeks of gestation). The results were used to diagnose and find the proportions of pregnant women with pre-existing diabetes mellitus and gestational diabetes mellitus.

Results: The HbA1C test was done for 428 pregnant women and among them, 25 (5.8%) had levels above ≥ 48 mmol/mol (6.5%) and were diagnosed with pre-existing diabetes. Of the 428 pregnant women, only 267 attended the OGTT. Among the 267 pregnant women, 15 had HbA1C levels equal to or more than 6.5% and they were identified to have pre-existing diabetes. Pregnant women diagnosed with gestational diabetes were 34 and the HbA1C of these women was $<6.5\%$. However, the 15 pregnant women who were diagnosed with preexisting diabetes were not identified with gestational diabetes from the OGTT.

Conclusion: HbA1C can be used as a useful tool for screening pre-existing diabetes during pregnancy. Due to the high prevalence of pregnant women with pre-existing diabetes (5.8%) found in this study, it can be recommended to perform a HbA1C test at the booking visit to identify high-risk, pregnant women.

Keywords: HBA1C, OGTT, Pre-existing diabetes, GDM, Pregnant mothers



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INTRODUCTION

Diabetes mellitus is a chronic complex metabolic disorder characterized by high levels of blood glucose and caused by defects in insulin secretion and/or action. The World Health Organization defines Gestational Diabetes Mellitus as any degree of glucose intolerance with onset or first recognition during pregnancy [1]. There are three main types of diabetes including type 1, 2 and gestational diabetes mellitus (GDM).

The widely accepted definition for GDM according to American Diabetes Association (ADA) is any degree of glucose intolerance with onset or first recognition during pregnancy. The definition is applicable even if 'the condition persists after pregnancy'. It does not exclude the possibility that unrecognized glucose intolerance may have antedated or begun concomitantly with the pregnancy [2].

Diagnosis of GDM is done using the Oral Glucose Tolerance Test (OGTT), which is done routinely around 28 weeks of POA in uncomplicated pregnancies in Sri Lanka set up. If the pregnancy is having any risks associated with GDM, this test can be additionally performed in 20 weeks of POA. The glycated hemoglobin test (HbA1C) is not usually performed in Sri Lanka. But the guideline of the National Institute for Health and Care Excellence (NICE), 'Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period (NG3)' which is recommended by the Royal College of Obstetricians and Gynaecologists (RCOG) mentions that HbA1C can be used to identify those who may have preexisting Diabetes [3].

This study identifies the proportion of pregnant women in the first trimester, who visits the Teaching Hospital Peradeniya and are unaware of their pre-existing diabetes condition. The results of this study show whether it is necessary to do a HbA1C test at the booking visit along with the OGTT at 28 weeks, for early diagnosis and better patient management throughout the pregnancy.

METHODS

This cohort study was done at the Teaching Hospital Peradeniya during the time period of 15th December 2016 to 14th December 2017. Pregnant women who participated in the booking visit (8-12 weeks of gestation) and without a history of hypertensive disorders, Diabetes Mellitus 1, Diabetes Mellitus 2, and Gestational diabetes mellitus, Anemia, and Hemoglobinopathy in their previous pregnancies were recruited for the study. Considering the proportion of pregnant mothers affected by GDM in Sri Lanka as 5% [3], to achieve 5% precision and 95% confidence limit, the sample size needed was 800. This was further inflated by 10% to 880 for contingencies [4].

The research protocol was presented to the chosen women, and formal informed consent was acquired.

Despite the fact that we did not perform therapies, the research protocol was explained to the selected women and informed written consent was obtained. Following that, blood samples were withdrawn from the pregnant women on their booking visit (8-12 weeks of gestation) in order to complete the HbA1C and OGTT test. Indeed, the HbA1C test was used as a control measure following the OGTT test to corroborate the results. Both tests were done on all participants who were selected for this study and the OGTT test was done just after the HbA1C test.

Patients with positive HbA1C test results were not considered to have pre-existing diabetes. No therapies were administered until GDM was confirmed by positive OGTT test results. We recommended individuals to a follow-up OGTT inquiry at the 28th week of POA if the HbA1C was positive but the OGTT was negative. In addition, we identified high-risk individuals based on their family history. And asked them to bring PPBS with them on the next visit instead of waiting till the 28th week of POA. Meanwhile, they have advocated for lifestyle adjustments, including dietary alterations.

Individuals were diagnosed with GDM if the OGTT results were positive so that the appropriate treatments could be delivered in accordance with

the NICE recommendation. To minimize errors, we employed the same kits, labs, and healthcare staff for all participants and each of the results were recorded independently in the diagnosing method. Test results were analyzed according to the NICE guidelines and the values were presented as Mean \pm SD for each parameter. Women with HbA1C values equal to or above 6.5% were considered to have pre-existing diabetes [2,5]. Diagnostic criteria for gestational diabetes is being positive for one or both of the results of the OGTT test done, which include fasting blood sugar and 2-hour blood sugar value after taking 75 grams of glucose. If the fasting blood sugar value is greater than 5.2 mmol/l or if the blood sugar value taken in 2 hours after consuming 75g of glucose is greater than 7.7 mmol/l, the pregnant women were diagnosed with GDM [5].

RESULTS

The total number of pregnant women in the first trimester recruited for the study was 428 and the HbA1C test was performed for all of them. Among them, 25 (5.8%) had HbA1C values equal to or above 6.5% and were diagnosed with pre-existing diabetes.

Pregnant women who participated in the OGTT test were 267. Since both HbA1C and the OGTT results at the booking visit were needed for the analysis, they were taken as the study population and others were excluded.

Among the 267 pregnant women, 15 had HbA1C levels equal to or more than 6.5% and they were identified to be at risk of developing pre-existing diabetes. Pregnant women diagnosed with gestational diabetes were 34. However, the 15 pregnant women who were diagnosed with risk of preexisting diabetes were not identified as women with gestational diabetes from the OGTT test.

Table 01 – Diabetic and normal pregnant women identified from the HbA1C test and the OGTT done at first trimester.

		OGTT	
		Normal	Gestational Diabetic
HbA1C	Normal	218	34
	Diabetic	15	0

As shown in the table 2, the mean value of the HbA1C results of the pregnant women who were identified with pre-existing diabetes was 6.70% and in the normal population it was 5.20%. For the OGTT (fasting) and the OGTT (2 hour), Gestational diabetic population had mean values of 5.41 mmol/l and 8.85 mmol/l respectively. The mean values of the OGTT (fasting) and the OGTT (2 hour) in the normal population was 4.13 mmol/l and 5.08 mmol/l respectively.

Table 02 – Mean values of the HbA1C tests and the OGTT tests done at the booking visit.

Test	Status	Mean \pm SD
HbA1C	(+) ve	6.70 \pm 0.41 %
	(-) ve	5.20 \pm 0.73 %
OGTT (fasting)	(+) ve	5.41 \pm 1.32 mmol/l
	(-) ve	4.13 \pm 0.84 mmol/l
OGTT (2hour)	(+) ve	8.85 \pm 1.85 mmol/l
	(-) ve	5.08 \pm 1.24 mmol/l

DISCUSSION

This study targeted to identify the proportion of pregnant women in the first trimester who were unaware of their pre-existing diabetes and the proportion was found to be 5.8%. Having undiagnosed diabetes mellitus can cause several complications such as abnormalities in fetal growth, prematurity, maternal and fetal morbidity, prone to caesarian sections as well as long-term complications for the mother and the neonate [6,7]. HbA1C is a test that can be done without preparing the person by fasting for 8 hours for the test. In addition, it is less complicated and consumes a lesser time when compared to OGTT. Since the proportion of pregnant women who were unaware of their pre-existing diabetes is high (5.8%) in this study, it can be recommended to perform a HbA1C test for all the pregnant women in their first trimester. This would help to identify women with diabetes mellitus and the complications in pregnancy can be minimized by early management.

Out of the 34 pregnant women who were diagnosed with gestational diabetes mellitus in this study did not have HbA1C levels above \geq 48 mmol/mol (6.5%) and were not diagnosed with

pre-existing diabetes. Similar results were obtained by a recent study done in Brazil, where only five women were presented with HbA1C levels ≥ 48 mmol/mol (6.5%), among 86 pregnant women diagnosed with GDM from the OGTT test [8]. Our study results showed that 15 of the women who had HbA1C values above ≥ 48 mmol/mol (6.5%) had normal OGTT results. This result is supported by a recent Australian study, where high HbA1C results were found in a pregnant population with normal OGTT results [9]. The study done in Brazil found out that the pregnant women who were diagnosed with Diabetes by the HbA1C would not have been identified with diabetes by the OGTT alone [10]. Several factors affect HbA1C levels during pregnancy. Several physiological changes occur where the plasma volume increases more rapidly than the rate of production of red blood cells. This haemodilution process during pregnancy can reduce the HbA1C levels, giving false negative results ⁽¹¹⁾. Iron deficiency is commonly observed during pregnancy, and this extends the lifetime of red blood cells increasing the HbA1C levels [11,12]. Thus, high HbA1C levels would be noted in anemic pregnant women giving a false positive result. Previous studies have shown that there could be a 1-1.5% relative rise in the HbA1C level due to iron deficiency [13].

Traditionally OGTT test is done in Sri Lanka hospitals at 28 weeks of gestation to identify gestational diabetes mellitus. HbA1C is a useful test that can be used to identify women with pre-existing diabetes at the early stages of pregnancy. However, it is needed to carry out more research to improve the cut-off values of HbA1C and to come up with better screening strategies to diagnose pre-existing diabetes during pregnancy. When it comes to treatments, 15 pregnant moms are at risk of having pre-existing Diabetes Mellitus and 34 have Gestational Diabetes Mellitus. Among them, we must give both populations the necessary education about lifestyle change. Despite the fact that therapies were not provided for the risk group of Participants, the above-mentioned further investigations were aimed to confirm the diagnosis in the following visit. So, during that time, we advised mothers to make lifestyle changes. On the other hand, The GDM

mothers were treated according to the NICE guideline along with dietary modifications.

We were unable to attain the projected sample size due to the high costs of the kits we were utilizing, and we were unable to cover the calculated sample because of insufficient funds. However, the majority of similar studies have been done by using between 200 - 300 participants [14], [15]. Therefore, as we discuss earlier our sample size (297 participants) would not be affected by the results since other studies also conduct by using a similar number of participants.

CONCLUSION

HbA1C can be used as a useful tool for the screening of pre-existing diabetes in early pregnancy. Due to the high prevalence of pregnant women with pre-existing diabetes (5.8%) found in this study, it can be recommended to perform a HbA1C test at the booking visit to identify high-risk pregnant women.

Author declaration

Authors' contributions:

Prof. Chaminda Kandauda – Conceptualization, Methodology, Resources, Supervision, manuscript preparation

Prof. Sampath Tennakoon – Formal analysis

Thejana Gunathilake – Investigation, manuscript preparation

B.G.T. Hansamali – manuscript review and edit.

Conflicts of Interest:

No conflicts of interest declared by the authors.

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