



■ Original Research Article

The Role of Early Pregnancy HbA1C in Detecting Gestational Diabetes Mellitus among High-Risk Women in Nigeria.

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ABSTRACT

Background: Gestational Diabetes Mellitus (GDM) is a major cause of maternal and perinatal morbidity and mortality. Early detection and treatment will ensure good pregnancy outcomes. There is paucity of data regarding the use of HbA1c in classifying and managing hyperglycaemia in pregnancy in Nigeria. This study set out to investigate the role of early pregnancy HbA1c values in detecting hyperglycaemia among Nigerian pregnant women. **Materials and Methods:** A total of 125 pregnant women presenting for their booking visits at 20 weeks or less of gestation and having one or more risk factors for GDM were recruited and blood samples were taken for HbA1c and Oral Glucose Tolerance Test (OGTT) determination according to the WHO protocol. **Results:** The mean (SD) age of the study population was 30.4 (5.8) years. The prevalence of Hyperglycaemia in Pregnancy (HIP) from this study after screening at early gestation (<20 weeks) was 15.2% of which 13.3% was classified as GDM. There was a significant correlation between HbA1c and 0-hour glucose ($r=0.412$), 1-hour glucose ($r=0.394$), and 2-hour glucose ($r=0.379$), $P<0.001$. At HbA1c of 5.4% and 5.7%, the sensitivity for detecting HIP was 66.7% and 22.2% respectively and the specificity was 65.9% and 80.5% respectively. At HbA1c of 5.4% and 5.7%, the PPV was 26% and 16.9% respectively while the NPV was 88.2% and 79.7% respectively. **Conclusion:** The study shows a very high prevalence of HIP in early pregnancy among women with high risk for GDM. HbA1c correlated moderately well with glucose levels in early pregnancy. Overall, HbA1c does not have a very robust sensitivity and specificity for diagnosis of HIP when used alone. However, the role appears to be better when used as a marker to rule out HIP in early pregnancy.

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INTRODUCTION

Diabetes in pregnancy is a common medical complication of pregnancy and an important cause of maternal and perinatal morbidity and mortality.^{1, 2} Diabetes mellitus is a metabolic disorder resulting from a varying degree of abnormal metabolism of carbohydrate, protein, and fats with consequent hyperglycaemia due to absolute lack of insulin or insulin resistance.³

Hyperglycaemia detected for the first time in pregnancy can be classified into two groups namely: Diabetes Mellitus in pregnancy and Gestational Diabetes Mellitus. This categorization is based on the degree of hyperglycaemia which is a major determinant of perinatal outcome. GDM may be seen as a form of type 2 diabetes occurring in pregnancy due to an inherent beta cell dysfunction in the patient making her unable to cope with the effect of hormonal changes of pregnancy, and GDM usually resolves after delivery.^{1, 4}

Worldwide Gestational Diabetes Mellitus affects 5% of pregnancies.² Marked variation in gestational diabetes prevalence among different racial/ethnic groups worldwide, with higher prevalence among Native Americans, Asians, African-Americans, and Hispanic populations than among non-Hispanics.^{4, 5}

The diagnosis and categorization of hyperglycaemia in pregnancy is based on an Oral Glucose Tolerance Test (OGTT). There are, however, controversies regarding whether to carry out a risk factor-based screening or a universal screening for all pregnant women. The International Association of Diabetes in Pregnancy Study Group (IADPSG), International Federation of Gynaecology and Obstetrics (FIGO), Australian Diabetes in Pregnancy Society (ADIPS), and the World Health Organization (WHO) recommend the use of OGTT with 75g glucose load for diagnosis of GDM.⁶ The ADA and WHO also recommended the use of glycated haemoglobin (HbA1c) in the first trimester of pregnancy to rule out overt diabetes mellitus.^{7, 8, 9, 10} using a cutoff value of 6.5% (48mmol/mol).^{2, 10, 11.}

The cumbersome nature of OGTT and its discomfort to patients makes this recommendation even more attractive. There is however paucity of data regarding the use of HbA1c in classifying and managing hyperglycaemia in pregnancy in Nigeria. This study set out to investigate the role of early pregnancy HbA1c values in detecting hyperglycaemia among Nigerian pregnant women.

MATERIALS AND METHODS

Study Area

The study was conducted at the Jos University Teaching Hospital (JUTH), a 600-bed tertiary health institution located in Jos, the capital of Plateau State in North

Central Nigeria. The hospital offers services to patients from Plateau state and receives referrals from about 6 neighboring states.

Study Design

This was a prospective Observational study.

Study Population

This study was conducted among pregnant women presenting for their first antenatal visits (Booking visits) at the Jos University Teaching Hospital (JUTH), Jos-Nigeria. The average number of booked antenatal clients was 2821 per annum.

Sampling Technique

This involved recruiting consecutively consenting pregnant women who met the inclusion criteria until the sample size was attained. This study was conducted between February 2018 and October 2018.

Inclusion Criteria

Women recruited for this study were pregnant mothers aged 18 years and above who were 20 weeks or less of gestation presenting for their first antenatal (Booking) visits. They were pregnant women with risk factors for Gestational Diabetes Mellitus as follows: women with a history of diabetes mellitus in first-degree relatives; recurrent pregnancy losses; previous history of GDM; history of IUFD or stillbirth; and previous foetal macrosomia, others were women with a history of shoulder dystocia in previous delivery; obesity; polycystic ovary syndrome and previous history of impaired glucose tolerance, who signed a written informed consent.

Exclusion Criteria

Patients excluded from this research were those with the following characteristics: pregnant women who do not have risk factors for GDM; pregnant women who were beyond 20 weeks of gestation; pregnant women known to have diabetes mellitus before conception; those with anaemia and any form of haemoglobinopathy, and those that do not consent for the study.

Sample Size Determination

The sample size was arrived at using the formula for calculating the minimum sample size for an infinite population as stated below¹²

$$n = z^2 \cdot p \cdot q / d^2$$

Where, n= minimum sample size

z= the standard normal variate at a confidence level of 95% = 1.96

p= prevalence of GDM in a previous study done in Jos North = 8.3%²⁰ = 0.083

$$q = 1 - p$$

d= expected difference or expected error = 5% = 0.05

Therefore,

$$n = z^2 \cdot p \cdot (1 - p) / d^2$$

$$n = (1.96)^2 \times 0.083(1 - 0.083) / 0.05^2$$

$$n = 3.84 \times 0.083(0.917) / 0.0025$$

$$n = 0.29226624 / 0.0025$$

$$n = 116.9, \text{ approximated to } 117$$

The sample size was made up to 125.

Data Collection

Data was collected using a prefilled questionnaire involving detailed history, physical examination, and investigations. The history included: age, parity, marital status, level of education of woman, occupation of the woman, ethnicity, residence, gestational age, recurrent miscarriages, preterm delivery, intrauterine foetal death, stillbirth, and foetal macrosomia; others include previous GDM or IGT, family history of Diabetes Mellitus, and history of PCOS. On physical examination, the weight, height, blood pressure, and symphysio-fundal height (SFH) were taken.

Blood Sampling and Handling

During a 2-hour OGTT, blood was collected into fluoride oxalate bottles for glucose determination from each participant following an overnight 10-12 hours fast. Five ml of venous blood was collected (Fasting sample) before administration of 75g glucose in 300 ml of water. This was aliquoted into EDTA specimen tubes for HbA1c and fluoride oxalate tubes representing 0-hour sampling for glucose measurement. The sampling was repeated at 1 and 2 hours for glucose measurement. The blood for glucose assay was separated within 1 hour of collection by centrifuging at 4000 rpm for 5 minutes. Plasma glucose was assayed within 4 hours of sampling. The sample for HbA1c assay was collected in EDTA bottles and stored at -70°C to be assayed within 60 days of collection.^{13, 14}

Biochemical Analysis

Blood samples were analyzed for glucose by colorimetric analysis using commercial kits on an automatic Cobas C111 chemistry analyzer (Roche Diagnostics GmbH, Sandhofer Strasse 116, Mannheim, Germany). HbA1C was analyzed by Cobas commercial kit Catalogue number: 04498577190 (Tina-quant Hemoglobin A1c Gen.3) on the Cobas C311 automatic chemistry analyzer (Roche Diagnostics GmbH, Sandhofer Strasse 116, Mannheim, Germany).

Data Analysis

All statistical analysis was performed using SPSS software (version 16.0). Frequencies and percentages were computed for demographic and educational characteristics, and presented in tables. Comparison of means was done by independent T-test and Person correlation was used to assess the correlation between continuous variables. The Receiver Operative Characteristic Curve (ROC curve) was used to assess the sensitivity and specificity of HbA1C in predicting GDM at various cut-off values. A P-value of less than 0.05 was taken as significant.

Ethical Consideration

Ethical clearance was obtained from the Ethical Committee of Jos University Teaching Hospital (JUTH) on the 26th of September, 2017 with Registration Number: JUTH/DCS/ADM/127/XXV302 . The nature, aim, and objective of the study were explained to each participant, and informed consent was duly signed before being recruited. Participants who opted out of the study had their opinions respected and no victimization of any kind was mated on them.

RESULTS

Table 1 shows the socio-demographic characteristics of the participants. Most of the women were at least 30 years old (52.8%). The mean (SD) age was 30.4 (5.8) years. Most of them (80.8%) have had at least one pregnancy while 17.6% of them were primigravidae and 24.8% of the study participants were grand-multiparous. A significant number of the study participants (65.6%) were within 14-20 weeks of gestation at the time of first testing, while 12.8% were less than 10 weeks of gestation at first testing. The mean (SD) weight of the study group was 74.2 (16.2) kg. The frequency of HIP was 15.2% of which 13.3% was classified as GDM.

Table 1: Socio-Demographic Characteristics Of Study Participants

Characteristics	Frequency	Percent
Age (years)	Mean ± SD =30.4±5.8	
<20	3	2.4
20-29	56	44.8
30-39	60	48.0
40-49	6	4.8
Gravidity		
1	22	17.6
2-4	70	56
≥5	31	24.8
Missing	2	1.6
Weight (Kg)	Mean ± SD =74.2±16.2	
Gestation at baseline OGTT (week)		
≤10	16	12.8
10-13	27	21.6
14-20	82	65.6
<i>HIP</i>	19	15.2
<i>GDM</i>	16	13.3
<i>DM</i>	3	2.4

SD=Standard Deviation

Table 2: Correlation Between HbA1c and Glucose

Characteristics	R	p-value
0hr Glucose (mmol/L)	0.412	< 0.001
1hr Glucose (mmol/L)	0.394	< 0.001
2hr Glucose (mmol/L)	0.379	< 0.001

Table 2 describes the correlation between HbA1c and Glucose at different OGTT time points. There was a significant correlation between HbA1c and 0-hour glucose, 1-hour glucose, and 2-hour glucose with $P < 0.001$. The correlation coefficient was strongest at 0 hours ($r = 0.412$) and weakest at 2 hours ($r = 0.379$).

Table 3: Comparison of Mean HbA1C with GDM Status Using Independent t-test

Characteristics	HIP	NORMOGL YCEMIC	T-test	P-value
Age (years)	33 ± 5.7	30 ± 5.8	2.129	0.035*
Gravidity	3.47 ± 1.8	3.39 ± 2.0	0.873	0.079
Weight (Kg)	88.9 ± 17.5	88.9 ± 14.9	3.912	< 0.001
0- hour Glucose (mmol/L)	6.20 ± 1.57	4.46 ± 0.43	9.694	< 0.001
1- hour Glucose (mmol/L)	9.27 ± 3.49	6.05 ± 1.39	6.974	< 0.001
2 - hour Glucose (mmol/L)	8.9 ± 3.49	5.84 ± 1.04	7.556	< 0.001
HbA1C (%)	5.8 ± 1.0	5.2 ± 0.7	2.119	0.037*

Significant= $P < 0.05$: * Significant

Table 3 compares levels of HbA1c in participants with GDM and those without GDM. Pregnant Women were significantly older and likely to have more weight than their non-GDM counterparts. The mean glucose levels and HbA1c were significantly higher among GDM women compared to those without GDM. However, the observed difference in mean HbA1c was statistically significant ($P < 0.05$).

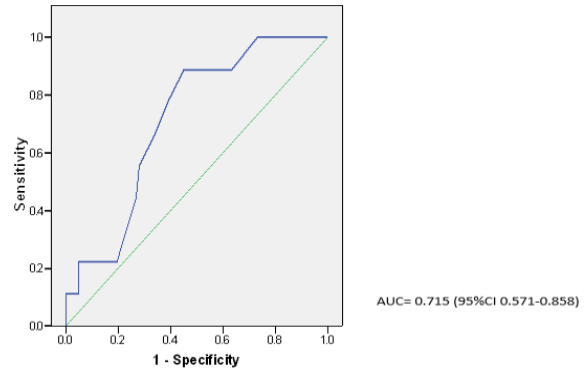


Figure 1: ROC Curve of HbA1c to predict GDM

Figure 1 shows the ROC Curve of HbA1c to predict hyperglycaemia in pregnancy. The Area under the Curve (AUC) was 0.715 (95% CI 0.571-0.858).

Table 4: Sensitivity, Specificity, and Predictive Values of HbA1c for GDM at booking/baseline OGTT

HbA1C levels	Sensitivity	Specificity	Positive Predictive value	Negative Predictive Value
5.1%	0.889	0.439	0.221	0.937
5.4%	0.667	0.659	0.260	0.882
5.7%	0.222	0.805	0.169	0.797
6.0%	0.222	0.854	0.214	0.806
6.5%	0.222	0.951	0.448	0.822

PPV=Positive Predictive Value, NPV=Negative Predictive Value

In table 4, The Sensitivity, Specificity and Predictive Values of HbA1c at different cut-off values for predicting HIP. At HbA1c of 5.4% and 5.7%, the sensitivity for detecting HIP was 66.7% and 22.2% respectively and the specificity was 65.9% and 80.5% respectively. At HbA1c of 5.4% and 5.7%, the PPV was 26% and 16.9% respectively while the NPV was 88.2% and 79.7% respectively.

DISCUSSIONS

Gestational Diabetes Mellitus is a common condition of obstetric importance and early diagnosis is crucial for intervention and improved outcome. Several studies have evaluated screening and diagnosis of GDM and a few are

focusing on early diagnosis of GDM. This study set out to investigate the role of early pregnancy HbA1c values in predicting GDM. It is worthy of note that the prevalence of HIP from this study after screening at early gestation (<20 weeks) was 15.2% of which 13.3% was classified as GDM. This was higher than the reported combined first and second-trimester prevalence of 13.3% considering that conventional testing is usually done at 24-28 weeks.¹⁵ The prevalence of GDM reported ranged from 1-14% globally depending on the population studied and the diagnostic criteria used.¹⁶⁻¹⁷

A study conducted in 2012 in Jos, reported the prevalence of GDM as 8.3%, however, the diagnosis was made using the WHO 1999 diagnostic criteria¹⁸. In a more recent study Imoh et al, reported a comparable prevalence of 15.7% using similar diagnostic criteria (WHO 2013) among pregnant women in the second to early third trimester.¹⁹ However, our findings in early pregnancy suggest a more likely higher prevalence which is in keeping with the projection of increasing metabolic and non-communicable diseases in developing countries^{20, 21}.

A plausible explanation for this is the epidemiological transition and increasing adoption of Western lifestyles in developing countries such as ours.²² The significance of this finding is that efforts to screen and diagnose GDM should be intensified in antenatal care given the complications attributable to GDM. Our finding is a wake-up call that early screening may pick up quite a large number of women with GDM to improve outcomes.

The mean HbA1c in this study was higher than that obtained in a similar study with a mean (SD) of 4.8 (0.4)²³. The HbA1c had a moderate but statistically significant correlation with glucose levels at fasting ($r=0.413$), 1hr ($r=0.394$), and 2hr ($r=0.379$) time points $P < 0.001$. This suggests that other factors may influence the relationship between HbA1C and glycaemic status in early pregnancy. Several clinical and analytical interferences on HbA1C assay may affect the relationship between HbA1C and glucose²⁴. For instance, iron deficiency anaemia which is common in women in pregnancy in Nigeria is associated with higher HbA1C levels. Red cell survival, liver and renal disease, impact of race and age, and vitamin C intake are other factors that affect HbA1C levels²⁴. The strongest correlation was found with fasting glucose. This was similar to the finding in the same study where the strongest correlation between HbA1c and glucose was with fasting glucose.

On the contrary, in a systematic review of 14 articles by Ketema EB et al, seven of the articles reviewed showed a stronger correlation between postprandial glucose levels and HbA1c than with fasting glucose levels.²⁵ Women with GDM at booking had significantly higher HbA1c levels compared to those without. This is in keeping with several studies that found

significantly higher HbA1c levels in GDM subjects compared to non-GDM subjects²⁶⁻²⁸. For Instance, in our study, mean HbA1c in GDM and non-GDM at booking was 5.8 (1.0) % and 5.2 (0.7) % and Renz Et al found mean HbA1c in GDM (5.5%) to be significantly higher than in non GDM women (5.1%).²⁷

The finding from this study showed that the AUC for detecting GDM using a ROC curve was 0.715 (95% CI 0.571-0.858). This was higher than the finding of Kui Wu et al, where the AUC was 0.563 (95% CI 0.50–0.625)²⁶. The closer the AUC is to 1.0, the better the utility of the predictive ability of the marker. From these findings, HbA1c has a moderately good predictive ability for GDM in early pregnancy. This predictive ability may improve as some of the study participants may develop GDM in the latter part of pregnancy.

The cut-off for diagnosing Impaired Glucose Tolerance in the non-pregnant is 5.7%. The result from this study shows that at an HbA1C value of $\geq 5.7\%$, the sensitivity for detecting GDM up until 28 weeks is only about 22.2% while the specificity is about 80.5 % meaning that about 20% of the women will be wrongly classified as GDM. The PPV was 16.9% meaning that for a positive HbA1c result $\geq 5.7\%$, only about 17 % of the women will have GDM. The NPV of 79.7% suggests that for a negative result, only about 20% of the women will be wrongly classified as GDM indicating that HbA1c may rather be best used to exclude the occurrence of HIP in pregnant women with cut-off values below 5.7%.

In a similar manner, at HbA1c of 5.4%, the sensitivity and specificity were 66.7% and 65.9% respectively, and PPV and NPV of 26.0% and 88.2% accordingly. This implies that only about a quarter of those with a positive test result at that cut-off will have GDM, i.e. 70% of women with HbA1c values $\geq 5.4\%$ will be wrongly diagnosed to have GDM and about 12% of those with HbA1c below 5.4% will be wrongly classified as having GDM.

Limitations

A limitation of this study is that the participants were not followed up beyond 28 weeks of gestation to determine if they developed HIP in the index pregnancy therefore, we do not know how many of the women may eventually have GDM later in pregnancy. Although we excluded women with obvious anaemia and any form of haemoglobinopathy in this study, we are not able to control the overall influence of external factors in HbA1c levels no matter how minute.

CONCLUSIONS

The findings from our study show a very high prevalence of HIP in early pregnancy among women with high risk

for GDM. This suggests that the majority of women with increased risk for GDM are likely to manifest hyperglycaemia early in pregnancy. HbA1c correlated moderately well with glucose levels in early pregnancy. Overall, HbA1c does not have a very robust sensitivity and specificity for diagnosis HbA1C when used alone. However, the utility appears to be better when used as a marker to rule out HIP in early pregnancy.

REFERENCES

1. Karen Reed. Diabetes DG, Syndrome M. Introduction to Diabetes - Diagnosis and Treatment. 2015;
2. Hughes RCE, Moore MP, Gullam JE, Mohamed K, Rowan J. An Early Pregnancy HbA 1c 5.9% (41 mmol/mol) Is Optimal for Detecting Diabetes and Identifies Women at Increased Risk of Adverse Pregnancy Outcomes. 2014;37 (November): 2953–9.
3. Amod A, Ascott-Evans BH, Berg GI, Blom DJ et al, SEMDSA Guideline for the Management of Type 2 Diabetes (Revised). 2012; 17(2).
4. Anderberg E, General oral Glucose Tolerance Test during Pregnancy, An Opportunity for Improved Pregnancy Outcome and Improved future. 2010.
5. Ugege WE, Abasiattai AM, Umoiyoho AJ, Utuk NM. The prevalence of gestational diabetes among antenatal attendees in a tertiary hospital in south –south Nigeria. International Journal of Medical and Health Research 2015; Vol 1 (1): 72-79.
6. Ellen K, Mbbs LI. Use of Fasting Plasma Glucose and Haemoglobin A1c in Screening for Gestational Diabetes Mellitus in High-risk Antenatal Patients in Hong Kong. 2014;14(1):31–7.
7. Bhavadharini B, Uma R, Saravanan P, Mohan V. Screening and diagnosis of gestational diabetes mellitus – relevance to low and middle income countries. Clin Diabetes Endocrinol [Internet]. 2016;1–8. Available from: <http://dx.doi.org/10.1186/s40842-016-0031-y>.
8. Bhavadharini B, Mahalakshmi MM, Deepa M, Harish R, Malanda B. Elevated glycated hemoglobin predicts macrosomia among Asian Indian pregnant women (WINGS 9) Original Article Elevated glycated hemoglobin predicts macrosomia among Asian Indian pregnant women (WINGS-9). 2016; (December).
9. RACGP, General Practice Management of type 2 diabetes 2014.
10. WHO guideline and classification of Hyperglcaemia in pregnancy 2013;12–3.
11. Donovan L, Hartling L, Muisé M, Guthrie A, et al. Screening Tests for Gestational Diabetes : A Systematic Review for the US Preventive Services Task Force. Annals of Internal Medicine Review 2017;159(2).
12. Kothari CR second edition In New Age International Publishers: Sampling Fundamentals In Research Methodology: methods and Techniques 2004 p
13. Little R, Rohlfing C, Hanson S, Connolly S, Higgins T et al. Effects of Hemoglobin (Hb) E and HbD Traits on Measurements of Glycated Hb (HbA1C) by 23 Methods. Clinical Chemistry 2008;54(8):1277–1282
14. Little RR, Roberts WL. A Review of Variant Hemoglobins Interfering with Hemoglobin A1C Measurement. Journal of Diabetes Science and Technology 2009; 3(3):446-451.
15. Ewenighi CO, Nwanjo HU, Dimkpa U, Onyeausi JC, Nnatuanya IN, Onoh LU, Et al. Prevalence Of Gestational Diabetes Mellitus; Risk Factors Among Pregnant Women (In Abakaliki Metropolis, Ebonyi State Nigeria.). NJIRM 2013; 4: 56-61
16. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2010; 33(Suppl. 1): S62–S69
17. Schneider S, BOCKC, Wetzel M, Maul H, Loerbroks A. The prevalence of gestational diabetes in advanced economies. J Perinat Med. 2012;40:511-520.
18. Anzaku AS, Musa J. Prevalence and associated risk factors for gestational diabetes in Jos, North-central, Nigeria.. Arch Gynecol Obstet. 2013 May;287(5):859-63. doi: 10.1007/s00404-012-2649-z.
19. Imoh LC, Asorose AS, Odo AI, Aina DO, Abu AO, Ocheke AN. Modification of WHO diagnostic criteria for gestational diabetes: implications for classification of hyperglycemia in pregnancy. Int J Reprod Contracept Obstet Gynecol 2017;6:2716-23.
20. GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2015;385(9963):117-171. doi:10.1016/S0140-6736(14)61682-2.
21. Macaulay S, Dunger DB, Norris SA. Gestational Diabetes Mellitus in Africa: A Systematic Review. 2014 Jun 3; 9(6):e97871. doi: 10.1371/journal.pone.0097871
22. Coetzee EJ. Pregnancy and diabetes scenario around the world: Africa. International J Gynecol Obstet. 2009;104:S39-S41
23. Rollins G. Assessing the Role of HbA1c in Gestational Diabetes. Available from <https://www.aacc.org/Publications/Clinical-Laboratory-Strategies/2012/Assessing-the-Role-of-HbA1c-in-Gestational-Diabetes.aspx>. Assessed on 10th October 2018.
24. Radin MS, Pitfalls in Hemoglobin A1c Measurement: When Results may be Misleading. J Gen Intern Med. 2014 Feb;29(2):388-94. Doi: 10.1007/s11606-013-2595-X. Epub 2013 Sep 4. PMID: 24002631; PMID: PMC3912281.
25. Ketema EB and Kibret KT Correlation of fasting and postprandial plasma glucose with HbA1c in assessing glycaemic control; systematic review and meta-analysis. Archives of Public HealthThe official journal of the Belgian Public Health Association 2015;73:43
26. Wu, K., Cheng, Y., Li, T., Ma, Z., Liu, J., Zhang, Q., & Cheng, H. The utility of HbA1c combined with haematocrit for early screening of gestational diabetes mellitus. Diabetology & Metabolic Syndrome. 2018;10:14. doi:10.1186/s13098-018-0314-9.
27. Renz PB, Cavagnoli G, Weinert LS, Silveiro SP, Camargo JL. HbA1c Test as a Tool in the Diagnosis of Gestational Diabetes Mellitus. Wagner B, ed. PLoS ONE. 2015;10(8):e0135989. doi:10.1371/journal.pone.0135989.
28. Kumru P, Arisoy R, Erdogdu E, Demirci O, Kavrut M , Ardic C, et al. Prediction of gestational diabetes mellitus at first trimester in low-risk Pregnancies. Taiwanese Journal of Obstetrics & Gynecology 55 (2016) 815e820