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Original Article

Third Trimester Glycemic Status and Pregnancy Outcome in Women Attending Antenatal Care in the Buea Health District, South Western, Cameroon: A Prospective Cohort Study

Statut Glycémique au Troisième Trimestre et Issue de la Grossesse chez les Femmes Suivies en Soins Prénatals dans le District Sanitaire de Buea, Région du Sud-Ouest, Cameroun : Une Étude de Cohorte Prospective

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ABSTRACT

Introduction. Glucose intolerance increases perinatal complications, but there is limited research on this topic among non-diabetic pregnant women in Cameroon. This study aimed to assess third-trimester glycemic status and its impact on pregnancy outcomes in the Buea Health District. **Methodology**. A prospective cohort study involving 124 pregnant women was carried out in the Buea Health District (BHD) from December 2023 through May 2024. Socio-demographic characteristics, and pregnancy outcomes were recorded. About 5mls of blood were collected by venipuncture into EDTA and fluoride oxalate tubes for HbA1c and fasting plasma glucose measurement respectively. A Logistic regression analysis was conducted to assess the association between pregnancy outcomes and third trimester glycemic control. **Results.** Third trimester hyperglycemia was present in 12% of pregnant women in the BHD. The percentage of pregnant women with abnormal glycemic status obtained using fasting plasma glucose and glycated heamoglobin (HbA1c) were 32.3% and 11.2% respectively. Women with high third trimester HbA1c percentage had significantly higher odds of having pre-eclampsia (OR=13.429, 95% CI: 0.365-4.845, p = 0.016), abnormal birthweight (OR= 88.000, 95% CI: 2.625-7.465, p < 0.00) and macrosomia (OR=46.000, 95% CI: 2.206-5.700, p < 0.001). Additionally, pregnant women who were hypoglycemic had higher odds of having perineal tear during delivery (OR =6.800, 95% CI=0.211-3.946, p= 0.034). **Conclusion.** Poor third trimester glycemic control (HbA1c) is significantly associated with adverse pregnancy outcomes. Strict glycemic control in pregnancy is therefore an important preventive measure to adverse pregnancy outcomes.

RÉSUMÉ

Introduction. L'intolérance au glucose augmente les complications périnatales, mais peu d'études existent sur ce sujet chez les femmes enceintes non diabétiques au Cameroun. Cette étude visait à évaluer l'état glycémique au troisième trimestre et son impact sur les issues de grossesse dans le district sanitaire de Buea. **Méthodologie**. Une étude de cohorte prospective a été menée auprès de 124 femmes enceintes de décembre 2023 à mai 2024. Des prélèvements sanguins ont permis de mesurer l'HbA1c et la glycémie à jeun. Une analyse de régression logistique a évalué l'association entre le contrôle glycémique et les issues de grossesse. **Résultats.** L'hyperglycémie au troisième trimestre était présente chez 12 % des femmes enceintes dans le DSB. Le pourcentage de femmes enceintes ayant un état glycémique anormal, mesuré par la glycémie à jeun et l'hémoglobine glyquée (HbA1c), était respectivement de 32,3 % et 11,2 %. Les femmes ayant un pourcentage élevé d'HbA1c au troisième trimestre avaient des chances significativement plus élevées d'avoir une pré-éclampsie (OR = 13,429, IC 95 % : 0,365-4,845, p = 0,016), un poids de naissance anormal (OR = 88,000, IC 95 % : 2,625-7,465, p < 0,00) et une macrosomie (OR = 46,000, IC 95 % : 2,206-5,700, p < 0,001). De plus, les femmes enceintes ayant une hypoglycémie avaient des chances plus élevées de subir une déchirure périnéale lors de l'accouchement (OR = 6,800, IC 95 % : 0,211-3,946, p = 0,034). **Conclusion**. Un mauvais contrôle glycémique au troisième trimestre (HbA1c) est significativement associé à des issues de grossesse défavorables. Un contrôle strict de la glycémie pendant la grossesse est donc une mesure préventive importante contre les issues de grossesse défavorables.

INTRODUCTION

Diabetes mellitus (DM) remains an enormous public health problem worldwide. According to the International Diabetes Federation (IDF), about 10% of global health expenditure is spent on diabetes, and by the year 2045, the number of people diagnosed with diabetes will rise to 700 million [1]. In Cameroon, the prevalence of diabetes in adults in urban areas is currently estimated to be 6-8%, with the main drivers being increasing age, overweight, sedentary lifestyle and obesity with as many as 80% of people living with diabetes currently undiagnosed in the population [2]. Diabetes mellitus in pregnancy may be pre-existing, insulin-dependent (0.5%), non-insulin dependent (2%), gestational (3–6%) and a consequence of the pregnancy itself [3].

The pregnancy of a healthy woman is physiologically associated with resistance to the action of insulin on glucose uptake and consumption by maternal peripheral tissues. This physiological resistance to insulin action during pregnancy becomes more apparent in the second trimester, and insulin resistance increases progressively to term [4]. When resistance to maternal insulin action becomes overwhelmed, maternal hyperglycemia occurs and gestational diabetes mellitus in pregnancy may set in [5]. There is a rise in the prevalence of diabetes during pregnancy, along with an increase in the prevalence of diabetes in the general population. It is estimated that 16.9% of pregnancies globally are affected by hyperglycemia in pregnancy using the World Health Organization (WHO) criteria, equating to 21.4 million of 127.1 million live births to women [5].

Fasting plasma glucose is indicative of short-term glycemic control and is highly correlated with diabetic complications. Glycated haemoglobin (HbA1c) measurements are more meaningful as they provide an assessment of glycemic control over the previous 2-3 months, unlike blood glucose measurements obtained at a single point in time and influenced by diet, exercise and drug adherence in the previous few hours. HbA1c is also associated with diabetic complications [6]. Until very recently, only a handful of epidemiological studies have evaluated maternal glycemic control in pregnancy.

Poor glycemic control is associated with a greater risk of short- term maternal and neonatal complications such as an increased risk for spontaneous preterm birth, caesarean sections, macrosomia, metabolic complications, shoulder dystocia, stillbirth and pre-eclampsia [7]. Few studies have evaluated the relationship between maternal glycemic control and pregnancy outcomes. Evaluation of glycemic status especially during the third trimester is of paramount importance as appropriate control measures can be taken to avoid unwanted feto-maternal outcomes

MATERIALS AND METHODS

Study design

This was a prospective cohort study carried out in the Buea Health District, Fako Division, South West Region of Cameroon. The Buea Health District comprises seven health areas that in turn have several antenatal care and maternity units catering for maternal and child health. This study spanned a period of five months from December 2023 through May 2024.

Study population

This study included pregnant women who attended antenatal care in the Buea Health District. Eligibility for recruitment to this study were; pregnant women aged between 21 and 40 years, at third trimester gestation, resident in Buea who gave birth in Buea and singleton pregnant women attending ANC at the selected health facilities. The study excluded women with multiple gestation, gestational diabetes and those with complicated pregnancies such as threatened abortion.

Sampling

Five health areas out of seven in the Buea Health District were selected by simple random sampling. The number of participants recruited in each health facility was obtained by probability proportionate to size sampling and participants were recruited by a consecutive convenient sampling method.

Data collection

A structured and pretested questionnaire was used to document participants' sociodemographic (age, religion, marital status, educational level and income level), clinical (diabetic status, parity, gravidity and family history of diabetes) and anthropometric (weight, height, calculated BMI) data. Additionally, pregnancy outcomes including pre-eclampsia, macrosomia, caesarean sections, preterm delivery, birth weight and stillbirth were recorded.

Participants' height was measured with them barefoot using a portable stadiometer and recorded to the nearest 0.1 cm. Participants' body weight were measured with them wearing light clothing, using a calibrated scale and recorded to the nearest 0.1 kg. Body mass index (BMI) was calculated using the formula weight (kg) divided by the square of height (m2). Systolic and diastolic blood pressures (SBP/DBP) were measured three times using mercury sphygmomanometers following a 10-minute rest, and the average of the readings was recorded. Fasting blood sample (5mL) was collected into fluoride oxalate and EDTA test tubes via venipuncture. Blood in the fluoride oxalate tube was centrifuged at 5000 rpm for 5 minutes and plasma obtained was used to measure fasting plasma glucose concentration. FPG levels were measured by an enzymatic colorimetric method at 510nm wavelength using reagent from SGM Italia, Rome, Italy. EDTA whole blood was used to measure HbA1c levels by immunofluorescence method using commercially available reagent by AeHealth Diagnostics, London, United Kingdom. BMI categories were defined as follows: normal ($18.5 \leq BMI < 24$ Kg/m2), overweight ($24 \leq BMI < 28$ Kg/m2), and obese ($BMI \geq 28$Kg/m2).

Patients were categorized into three groups based on their fasting plasma glucose levels: normoglycemic (70-100 mg/dL), hypoglycemic (<70mg/dL) and hyperglycemic (>100mg/dL). HbA1c categories were defined as low (<4.0%), normal (4.0-6.5%) and high (>6.5%). Additionally, macrosomia was defined as birth weight greater than 4kg regardless of fetus gestational age,

preterm as babies born alive before 37 weeks of pregnancy, pre-eclampsia as a blood pressure of 140/90 mm Hg or greater after 20 weeks gestation in a woman with previously normal blood pressure and proteinuria, underweight babies as babies with less than 2kg birth weight and healthy babies as babies with birth weight between 2-3.9kg.

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences Version 26.0 for Windows ((SPSS, Inc., Chicago, IL, USA). Categorical variables are presented as frequencies and percentages, and continuous variables as mean ± standard deviation. The association between pregnancy outcomes and glycemic control was assessed using logistic regression analysis with results presented as odds ratios (OR) and 95% confidence intervals (CI). P< 0.05 was considered statistically significant.

Ethical consideration

Ethical approval for this study was obtained from the Institutional Review Board of the Faculty of Health Sciences, University of Buea (Reference N: 2023/ 1157-02/UB/SG/IRB/FHS), adhering to the principles outlined in the Helsinki Declaration. An administrative clearance was granted by the Regional Delegation of Public Health, South West Region. Furthermore, approval was obtained from the director of BRH and the chief of centers of the selected health facilities. Participation in this study was voluntary after a written informed consent was given by participants. The use of sterile material for sample collection and appropriate procedures to reduce risk of injury were strictly implemented. Patients' anonymity and confidentiality were respected and data collected were utilized only for research purposes.

RESULTS

Socio-demographic characteristics of study population

A total of one hundred and twenty-four (124) pregnant women were recruited in this study (table I).

Table I: Socio-demographic characteristics of participants

Variable	Category	N	%
Age group (years)	21-30	85	68.5
	31-40	39	31.5
	Total	124	100
Marital status	Married	84	67.7
	Single	40	32.3
	Total	124	100
Educational level	Primary	10	8.1
	Secondary	74	59.7
	Tertiary	40	32.3
	Total	124	100
Income (XAF)	<50000	52	41.9
	50001-100000	54	43.5
	100001-200000	8	6.5
	>200000	10	8.1
	Total	124	100

Most of them were aged between 21-30 years representing 68.5% of the study population. The majority of the participants were married representing 67.7% and most (54.9%) had a secondary school level of education. Most participants earned a monthly income between 50,000 – 100,000 XAF representing 43.5% as shown in Table I.

Clinical and anthropometric characteristics of study population

In this study, the majority of the women had glycated hemoglobin levels within normal (53.2%) and a normal weight (47.6%). The majority of the pregnant women (79.1%) had been pregnant not more than three times and 85.5% had had less than two live births. The majority of the women (76.6%) had no family history of diabetes mellitus as shown in Table II.

Table II: Clinical and anthropometric characteristics of study population

Variable	Category	N	%
Hemoglobin levels (g/dL)	Low	58	46.8
	Normal	66	53.2
	Total	124	100
BMI (kg/m²)	Normal	59	47.6
	Overweight	40	32.3
	Obese	25	20.1
	Total	124	100
Diabetic status	Non-diabetic	124	100
Gravidity	<3	98	79.1
	>3	26	20.9
	Total	124	
Parity	<2	106	85.5
	>2	18	14.5
	Total	124	
Family history of diabetes mellitus	Yes	21	16.9
	No	95	76.6
	I don't know	8	6.5
	Total	124	100

Assessment of third trimester glycemic control parameters

In this study, eighty-four participants had normal FPG concentrations (67.7%), twenty-five (20.2%) were hypoglycemic and fifteen (12.1%) were hyperglycemic. One hundred and eight participants (87.1%) had normal HbA1c levels, seven had low HbA1c levels (5.6%) and seven (5.6%) had high levels of HbA1c. This is shown in Table III.

Table III: Third trimester glycemic control of pregnant women using FPG and HbA1c

Variable	Category	N	%
FPG (Reference interval: 70- 100 mg/dL)	Normal	84	67.7
	Hypoglycemia	25	20.2
	Hyperglycemia	15	12.1
	Total	124	100
HbA1c (Reference interval: 4.0-6.5%)	Normal	108	87.1
	Low	7	5.6
	High	7	5.6
	Total	124	100

Biochemical and anthropometric measurements of study participants

In this study, most of the women had hemoglobin levels, glycated hemoglobin levels and fasting plasma glucose levels within normal range (10.5 g/dL, 5.4 % and 88.3 mg/dL respectively). Most of the participants were class 1 obese (Mean BMI of 31.6± 0.45 kg/m2) and most of the participants had babies with healthy birthweight (3.38 kg). This is shown in table IV.

Table IV: Biochemical and anthropometric parameters of study participants

	N	Mean ± SD	Reference Interval
Age (years)	124	28.13 ± 5.43	
Hb levels (g/dL)	124	10.52 ± 0.11	11.5-13.5
BMI (kg/m²)	124	31.63 ± 0.45	18.5-24.9
HbA1c (%)	124	5.42 ± 0.06	4.5-6.5
FPG (mg/dL)	124	88.3 ± 2.06	70-110

Assessment of pregnancy outcomes in study population

Out of the one hundred and twenty-four pregnant women recruited in this study, one hundred and nine (87.9%) pregnancy outcomes were assessed. Forty participants (36.7%) had caesarean deliveries, four (3.7%) had pre-eclampsia, three (2.8%) had preterm delivery, seventeen (15.6%) had abnormal babies with birth weight, ten (9.2%) had babies with macrosomia and eight (7.3%) participants had perineal tear during delivery (Table V).

Table V: Assessment of pregnancy outcomes in study population

Outcome	N	%
Caesarian delivery	40	36.7
Pre-eclampsia	4	3.7
Preterm delivery	3	2.8
Underweight babies	2	1.8
Overweight babies	15	13.8
Macrosomia	10	9.2
Perineal tear	8	7.3

Association between glycemic control and pregnancy outcomes

There was a significant relationship between third trimester HbA1c and preterm delivery (p =0.0201) where participants with low HbA1c levels had fifteen times the odds of having a preterm delivery [crude Odds ratio (cOR) = 15.66, 95% CI 0.463- 5.397] compared to those who had a normal glycemic status (p = 0.043). Also, women with high HbA1c levels had thirteen times the odds [OR = 13.429, 95% CI 0.365 – 4.845, p=0.016] of having pre-eclampsia compared to those with a normal glycemic status (p=0.016). Participants with high HbA1c levels had eighty-eight times the odds of having babies with an abnormal birth weight [cOR = 88.0, 95% CI 2.625 – 7.465] (p <0.001). Women who had high HbA1c values had forty-six times the odds of having babies with macrosomia compared to women with a normal glycemic status [cOR = 46.00, 95% CI 2.206, 5.700] (p <0.001). There was no significant relationship between third trimester FPG levels and preterm delivery, pre-eclampsia, birthweight and macrosomia. In this study, participants with hypoglycemia had six times the odds of having perineal tear during delivery [cOR= 6.8, 95% CI 0.211 – 3.946] compared to those with normal FBG levels (p=0.034). There was a significant relationship between third trimester HbA1c and perineal tear. These are shown in table VI.

Table VI : Association between glycemic control and pregnancy outcomes

Parameter	Category	cOR	95% CI	P value
Preterm delivery				
HbA1c	Low	15.667	0.463-5.397	0.043
	High	0.023	477.612	0.997
Pre-eclampsia				
HbA1c	Low	0.045	377.420	0.996
	High	13.429	0.365-4.845	0.016
Birthweight				
HbA1c	Low	3.667	1.769-3.489	0.284
	High	88.000	2.625-7.465	<0.001
Macrosomia				
HbA1c	Low	0.203	168.146	0.994
	High	46.000	2.206-5.700	<0.001
Perineal Tear				
FPG	Hypoglycemia	6.800	0.211-3.946	0.034
	Hyperglycemia	5.231	0.535-3.849	0.113

DISCUSSION

This study was aimed at determining the relationship between glycemic control and birth outcomes in pregnant women attending ANC in the Buea Health District. In this

study, third trimester hyperglycemia was found in 12% of pregnant women where FPG measurements indicated more women with abnormal glycemic status compared to measurements obtained for HbA1c (32% and12% respectively). The pregnancy outcomes identified and assessed in this study were; caesarean delivery, pre-eclampsia, preterm delivery, birth weight, macrosomia and perineal tear. High third trimester HbA1c levels significantly prompted high odds of having pre-eclampsia, abnormal birthweight and babies with macrosomia.

Most pregnant women (67.7% and 87.1% using FPG and HbA1c values respectively) had glycemic status within the normal range with respect to FPG having a mean value of (88.3±2.06) and HbA1c having a mean value of (5.42±0.06). Also, FBG values indicated more pregnant women with abnormal glycemic status compared to values obtained for HbA1c (32.3% and 11.2% respectively). This could be attributed to the fact that glycated hemoglobin levels are representative of glycemic status for longer periods which may not be influenced by brief episodes of hyperglycemia in the participants. Also, data suggest that HbA1c levels can be influenced by pregnancy which affects red cell turnover as new erythrocytes formed will be exposed to a lower time-averaged glucose concentration and the degree of glycosylation might therefore be less [8]. Findings from the current study also reveal that, 32.3% of study population did not know their diabetic status meanwhile, 12.1% of pregnant women were diagnosed of third trimester hyperglycemia. The findings of this study reveal a lower proportion of pregnant women with hyperglycemia compared to reports from a study carried out in Yaounde, Cameroon in which a 31% prevalence of hyperglycemia in pregnant women which was significantly associated with neonatal macrosomia was reported [9]. The difference in the reported prevalence of hyperglycemia could be due to differences in the lifestyle of pregnant women. The birth outcomes identified amongst pregnant women in this study were normal vaginal delivery (55.6%), caesarian section (36.7%), preeclampsia (3.7%), macrosomia (9.2%), perineal tear (7.3%), birth weight (84.4% healthy weight, 1.8% underweight, 13.8% overweight) and preterm delivery (2.8%). Results from a similar study in China, reported a 21.6% of preterm delivery, 25.8% of macrosomia and 10.5% of preeclampsia [10]. Another study carried out in Kenya to assess average third trimester FPG and pregnancy outcomes in diabetic pregnancy, reported 25.2% of macrosomia, 16.2% of stillbirth, 41.5% preterm delivery, 30.2% postpartum hemorrhage, 17.1% of neonatal hypoglycemia, 83.3% of perineal trauma [11]. The difference in the reported frequencies of occurrence of the pregnancy outcomes could be due to use of diabetic pregnant women as target population in the latter study. The present study also observed no association (p=0.562) between glycemic control and mode of delivery. However, pregnant women with hyperglycemia and high HbA1c levels [OR= 0.718, 95% CI 0.816-1.463] had less chances of giving birth through normal vaginal delivery. There is mounting body of evidence that maternal glycemic control during pregnancy is associated with mode of delivery. The effect of maternal glycemic control in causing operative delivery seems minor, and they could be attributed to cofounders such as obesity, and an older maternal age [9], which could explain the case in this study. In the present study, there was a significant association between HbA1c and preterm delivery (p=0.020) which indicated that low HbA1c significantly (p=0.043) prompted high odds of preterm delivery [OR=15.667, 95% CI 0.463-5.397]. This finding differs from that reported in a study done in Saudi Arabia where pregnant women with high HbA1c levels had shorter gestational periods [10]. Although the implication of glycemic status (hyperglycemia and high HbA1c) in the occurrence of preterm birth has not been fully elucidated, it is suggested that preterm birth in poor glycemic control is directly associated with the pathophysiology of polyhydramnios [12]. The difference in observed relationship between glycemic control and preterm delivery in pregnant women in this study, could be due to the influence of other factors that are involved in the pathophysiology of polyhydramnios that were not assessed. The present study also reveals that there was a significant association (p= 0.008) of third trimester HbA1c and pre-eclampsia which indicated that high HbA1c levels significantly (p= 0.016) prompted higher chances of having pre-eclampsia than women with normal HbA1c [OR = 13.42, 95% CI 0.365-4.845] unlike third trimester FPG which was not significantly associated with pre-eclampsia (p value 0.081). This is similar to findings from a study carried out in Shanghai, on maternal glycemic parameters and adverse pregnancy outcomes where FPG was not significantly associated with preeclampsia unlike HbA1c which was significantly associated with pre-eclampsia and women with high HbA1c values had 5 times the odds of having preeclampsia during pregnancy [13]. The pathophysiology of preeclampsia remains elusive. Current theories suggest that the clinical features of this syndrome are caused by systemic maternal endothelial dysfunction resulting from a combination of preexisting maternal risk factors and abnormal placental development. These maternal characteristics may contribute to oxidative stress, inflammation and vascular dysfunction, all of which have been implicated in the etiology of pre-eclampsia [14]. Compared to women who have normotensive pregnancies, women who develop preeclampsia are more insulin resistant prior to pregnancy, in the first and second trimesters, and years after pregnancy. There was also a significant association between third trimester HbA1c levels and birthweight (p <0.001) where high HbA1c levels significantly prompted high odds of having babies with abnormal birthweight [OR= 88.0, 95% CI 2.625-7.465] similar to a finding obtained from a study in Ethiopia in 2021 with significantly high odds of pregnant women with high HbA1c 5having babies with abnormal birthweight [1]. Another study carried out in Saudi Arabia reported that pregnant women with high HbA1c levels significantly had high odds of having babies with abnormal birthweight [9]. In the current study, there was a significant association

between HbA1c and macrosomia (p<0.001) which was further indicative that high HbA1c levels significantly prompted high odds [OR= 46, 95% CI 2.206 – 5.700]. This is similar to reports from the study done in Saudi Arabia and another study carried out in Ethiopia [10, 15] which reported that women with high HbA1c levels significantly had high odds of having babies with macrosomia. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) as well as most interventional and cohort studies evaluating the perinatal outcome of maternal hyperglycemia report an increased odd of macrosomia. Macrosomia usually occurs with excess neonate's adiposity and neonatal hypoglycemia at birth [16]. In fact, excess maternal blood glucose is transported to the fetal circulation through the placenta. This is firstly responsible for increase in blood glucose which excessively stimulates insulin production. Fetal hyperinsulinemia then induces hypoglycemia observed in the neonate through its anabolic and glycogenolytic pathways. Anabolic reactions are also responsible for excess adiposity and macrosomia. Macrosomia can lead to obesity and even diabetes mellitus in the mother as well as in the infant [14]. Nonetheless, in this study, hypoglycemia significantly (p=0.034) prompted high odds of perineal tear during delivery than normal FPG levels [OR= 6.8, 95% CI 0.211-3.946]. There was no significant association between third trimester HbA1c levels and perineal tear (p=0.280). This was different from the Saudi Arabian study that reported that high HbA1c levels significantly had high odds of perineal tear during delivery [17].

CONCLUSION

There is a low prevalence of dysglycaemia amongst pregnant women in the BHD. Caesarean delivery, preterm delivery, perineal tear, pre-eclampsia, macrosomia and abnormal birthweight are the most common pregnancy outcomes among pregnant women in the Buea Health District. There is a significant association between third trimester glycemic control (HbA1c) and preterm delivery, pre-eclampsia, birthweight and macrosomia in pregnant women attending ANC in the Buea Health District. Strict glycemic control in pregnancy is recommended as an important preventive measure to adverse feto-maternal outcomes

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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