The influence of fasting and post-load glucose levels on maternal and neonatal outcomes in women with hyperglycaemia in pregnancy in Uganda: a prospective observational cohort study.

Isaac Sekitoleko[a,b,¶*], Salome Tino(MPH)[a¶], Michael Mubiru[a], Faridah Nansubuga[c], Daniel Zaake[c], Betty Nakabuye[d], Ben Ayiko[e], Herbert Kalema[f], Sarah Nakubulwa[g,h], Musa Sekikubo[g,h], Jack Milln[i],Wisdom P Nakanga[j], Annettee Nakimuli[g,h], Emily L Webb[b], Moffat J Nyirenda[a,b]

[a]MRC/UVRI and LSHTM Uganda Research Unit, Uganda

[b]London School of Hygiene and Tropical Medicine, London, United Kingdom

[c]St. Francis Hospital, Nsambya, Kampala, Uganda

[d]Uganda Martyrs Hospital, Lubaga, Uganda

[e]Entebbe Grade B Hospital, Entebbe, Uganda

[f]Masaka Regional Referral Hospital, Maaka, Uganda

[g]Department of Obstetrics and Gynaecology, School of Medicine, Makerere University College of Health Sciences, Kampala, Uganda

[h]Kawempe Specialized National Referral Hospital, Kampala, Uganda

[i]Queen Mary University of London, London, United Kingdom

[j]National Insititute for Health Research (NIHR), Exeter Clinical Research Faculty, University of Exeter, Exeter, United Kindgom

[¶]These authors contributed equally
[*]Corresponding author

Address for correspondence.

Isaac Sekitoleko

MRC/UVRI and LSHTM Uganda Research Unit

P.O BOX 49, Entebbe

Uganda

Telephone: +256701755373

Email: Isaac.Sekitoleko@mrcuganda.org

Highlights.

- The relative strengths of fasting and post load hyperglycaemia in predicting adverse maternal and neonatal outcomes is unclear.

- Fasting hyperglycaemia was more strongly associated with adverse pregnancy outcomes than post-load hyperglycaemia

- The risk of adverse outcome was even higher in women with elevation of both fasting and post-load glucose levels

Abstract

Aims: The study aims to evaluate the strength of fasting versus post-load glucose levels in predicting adverse outcomes in women with hyperglycaemia in pregnancy (HIP).
Methods: Women attending antenatal clinics in urban and peri-urban Uganda had oral glucose tolerance test between 24 and 28 weeks of gestation to screen for HIP, and were followed up to collect data on maternal and neonatal outcomes. Univariable and multivariable Poisson regression models were used to estimate the relative risk adverse outcome associated with fasting hyperglycaemia alone post-load hyperglycaemia alone, or elevation of both fasting and post-load glucose levels.
Results: We included 3206 participants in the final analysis. HIP is associated with increased risk of Caesarean section, large for gestaional age babies, and neonatal intensive care admission. The risk is highest (2.54-fold compared to normal glycaemic women) when both FBG and post-load glucose levels were elevated. After adjustment for potential confounders, having elevated post-load glucose alone was not associated with increased risk of any of the outcomes, but elevated FBG alone increased the risk of Caesarian section by 1.36-fold.
Conclusion: Fasting hyperglycemia appears to be more strongly associated with adverse pregnancy outcomes than post-load hyperglycaemia, but risk is even higher in women with elevation of both fasting and post-load glucose levels.

Keywords: Hyperglycaemia in pregnancy; gestational diabetes; Oral glucose tolerence; Maternal and neonatal Outcomes; sub-Saharan Africa

1 Introduction

Hyperglycaemic disorders are common in pregnancy, and are associated with a high risk of adverse outcomes in the mother and child.[1, 2] Women with hyperglycaemia in pregnancy (HIP) are more likely to experience preeclampsia, operative delivery, stillbirth and are at increased risk of developing type 2 diabetes mellitus in the long term. Their infants are at higher risk of preterm delivery, congenital abnormalities, macrosomia, neonatal hypoglycaemia and intensive care unit admission. Furthermore, long term intrauterine exposure to maternal hyperglycaemia predisposes the offspring to developing obesity and diabetes later in life.[3]

The majority of cases of hyperglycaemia first detected in pregnancy are due to gestational diabetes mellitus (GDM), while the remainder are classified as diabetes in pregnancy (DIP), either pre-existing type 1 or type 2 diabetes which pre-dates pregnancy or is first identified during testing in the index pregnancy. Recent data from the Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study confirmed that the risk of adverse pregnancy outcomes increases linearly with glucose levels, even among women with glucose values previously considered normal.[2, 4] Moreover, the prevalence of HIP is on the rise consistent with the epidemic increase in diabetes worldwide due to urbanization and changes in lifestyle. Hyperglycaemic disorders in pregnancy will pose a particular public health challenge in low- and middle-income countries, where healthcare systems lack resources for adequate detection and management.[6]

HIP is detected by oral glucose tolerance test (OGTT) performed between 24 and 28 weeks of gestation, but in most low resource settings (LMIC), wider use of OGTT is not feasible or applicable; instead, use of fasting blood glucose (FBG) alone is a common practical screening approach.[7] However, the effectiveness of such a strategy in preventing adverse pregnancy outcomes is unclear, in part, because the strenghth of association between FBG or post-load (1- and/or 2hr) OGTT glucose levels and burden of adverse outcomes of HIP is unknown; while some reports suggest that fasting hyperglycaemia plays a predominant role, [8-10] other studies have suggested that post-load levels are more predictive than FBG for neonatal outcomes such as macrosomia and hypoglycaemia.[11-13]. Importantly, most of this research has been in high-income countries where screening is an established part of care with clearly defined national guidelines. We urgently need data from LMIC, because presentation of hyperglycaemia and the healthcare systems in these regions are different from those in high-income countries.[14, 15]

We therefore undertook a large study of pregnant women attending antenatal care in urban and peri-urban health facilities in Uganda to examine the effects of HIP on three major pregnancy outcomes, namely Caesarean delivery, large for gestational age (LGA) and neonatal admission to intensive care unit (NICU), and to assess the relative impact of fasting and post-load OGTT glucose levels.

2 Subjects.

Pregnant women aged 18 years or older and between 24 and 28 weeks of gestation were enrolled from the hospital antenatal clinics. Those known to have existing diabetes, with multiple pregnancy, significant medical condition (heart failure, renal disease, severe anaemia and pre-eclampsia) or unable to give informed consent were excluded from the study. Women provided written informed consent to take part in the study.

3 Material and Methods.

3.1 Setting

This was an observational prospective cohort study conducted in five hospitals in peri-urban and urban areas in Uganda from 13th June 2018 to 31st October 2019. The five hospitals included both public (government-funded where healthcare is free at point of care) and private (where individuals pay for services received) facilities.

3.2 Data collection

Standardised questionnaires were used to collect data on socio-demographic and lifestyle factors (including age, level of education, smoking status and alcohol use). Questionnaires also covered family, medical (including HIV status) and reproductive history (parity, gravidity and complications in prior pregnancies). Weight and height were measured using calibrated Seca scales and stadiometers. After 30 minutes of rest, three seated blood pressure measurements, with 5 minutes' rest in between, were collected on the right arm using portable sphygmomanometers (OMRON-Healthcare-Co HEM-7211-E-Model-M6; Kyoto, Japan).

OGTT was performed following 8 hours of overnight fast; a fasting venous blood glucose was collected in sodium fluoride vacutainer, and participants were then given 82.5g glucose monohydrate (equivalent to 75g anhydrous glucose) dissolved in 300ml of water. Repeat venous blood samples were taken at 60 and 120 minutes. Samples were immediately centrifuged and separated, and plasma kept on ice. All samples were analysed centrally at the MRC/UVRI and LSHTM Clinical and Diagnostics Laboratory in Entebbe (using Roche cobas 6000 analyser), within 4 hours of collection, or stored at -80ºC for subsequent analysis.

Women with hyperglycaemia in pregnancy were notified and invited to meet the local obstetric team for further management. Data on adverse maternal and neonatal outcomes, including caesarean birth,

large for gestation age and neonatal intensive care admission, were extracted from mothers' hospital case notes at the time of delivery and/or at delivery were retrieved from the hospital case notes and discharge forms by trained health personnel using data extraction forms.

3.3 Definitions

Maternal overweight or obesity was defined as BMI of greater than 25kg/m^2 or 30kg/m^2, respectively. Hypertension was defined as systolic BP≥140mmHg or diastolic BP≥90mmHg. HIP was diagnosed according to WHO 2013 criteria as either GDM: FBG ≥5·1 and ≤6·9 mmol/L or 1HR glucose ≥10·0mmol/L or 2HR glucose ≥8·5and <11·0mmol/L; or DIP: FBG ≥7·0mmol/L or 2HR ≥11·1mmol/L. Macrosomia was defined as birthweight >4kg.

Adverse pregnancy outcomes of interest were caesarean birth, large for gestational age (LGA) defined as birth weight greater than 90th percentile and neonatal intensive care unit admission (NICU) defined as whether or not a baby was admitted into the intensive care unit. We also derived a composite adverse outcome binary variable defined as experiencing at least one of the three adverse outcomes versus experiencing none of the three adverse outcomes.

3.4 Statistical analysis

Pregnancies were categorised into 4 categories; 1) Pregnancies without HIP, 2) HIP pregnancies with elevated FBG only, 3) HIP pregnancies with elevated post-load glucose only i.e. at 1 hour and or 2 hours, and 4) HIP pregnancies with elevated values using both FBG and post-load glucose. Participants' baseline characteristics and adverse maternal and neonatal outcomes were summarized using frequencies and proportions for categorical variables, both overall and stratified by pregnancy category as defined above. Based on the distribution of each variable, continuous variables were summarized using means (standard deviation) or medians (interquartile ranges). To compare baseline characteristics between the three hyperglycaemic groups we used the chi-squared test for categorical variables. For continuous variables, the ANOVA and Kruskal-Wallis H test were used to compare means and medians, respectively.

Using pregnancies without HIP as the reference group, we used generalised linear models to fit univariable and multivariable Poisson regression models with robust error variances in order to estimate the relative risk (RR) of experiencing adverse pregnancy outcomes associated with elevated FBG alone, elevated post-load glucose alone, or elevation of both values (FBG, and post-load glucose) compared to normoglycaemic pregnancies as the reference group. Crude and adjusted risk ratios together with the respective 95% confidence intervals are reported. The multivariable regression

models were adjusted for gestational age at enrolment, BMI, mother's age, gravidity, family history of diabetes and child's sex at birth as a priori confounding factors. To further investigate the independent effects of elevated FBG and elevated post-load glucose on pregnancy outcomes, the multivariable regression models were repeated, but now including elevated FBG and elevated post-load glucose as separate explanatory variables, and adjusting for each other. All analyses were conducted in STATA 15.1 (College Station, Texas).

3.5 Ethical approval

This research project was approved by the research and ethics committee of the Uganda Virus Research Institute (approval GC/127/19/04/625) and the Uganda National Council for Science and Technology (approval HS2340). Informed written consent was obtained before enrolling participants into the study.

3.6 Patient and public involvement

Patients, community representatives and policy makers are engaged at different stages of our research including formulating research questions. We have community advisory groups to facilitate our engagement with the community.

4 Results

The study enrolled 3852 participants at baseline. Amongst these, 0.4% (n=14) had missing baseline laboratory data. Of the 3838 participants with complete data, 91.5% (n=3511) were normoglycaemic and 8.5% (327) were hyperglycaemic. Of the normoglycaemic and hyperglycaemic participants, 17.2% (n=605) and 8.3% (n=27) delivered outside study hospitals. Overall, among participants with complete baseline data (demographic and laboratory data) (n=3838), 632 (16.5%) did not deliver at study hospitals **(Figure 1).** Participants who either had missing baseline laboratory data or deliveries outside study designated hospitals were excluded from final analyses. Participants excluded from the final analysis had similar baseline characteristics to those included **(Supplemental Table 1).**

Of the 3206 participants included in the final analysis, 2906 were normoglycaemic and 300 were diagnosed with HIP, of which 258 (86.0%) and 42 (14%) were GDM and DIP cases, respectively. In addition, amongthose diagnosed wih HIP, 170 (56.7%) had elevated FBG only, 73 (24.3%) had elevated post-load glucose only, and 57 (19.0%) had both elevated FBG and post-load glucose values. Participants with elevated FBG only were younger than participants who had elevated post-load glucose or both elevated FBG and elevated post-load glucose. The prevalence of obesity was highest

among participants with both elevated FBG and post-load glucose, and lowest in participants with elevated FBG only. Median upper-arm circumference, and systolic and diastolic blood pressure were also highest in those who had elevation of both FBG and post-load glucose. Primigravida was less common among those with both elevated FBG and post-load glucose compared to the other groups. **(Table 1).**

4.1 Adverse outcomes.

Of the participants included in the final analysis (n=3206), 45.5% (n=1458) experienced at least one of the adverse pregnancy outcomes. The prevalence of any adverse outcome was higher among women with HIP, compared to those with normoglycaemia (54.3% and 44.6%, respectively); all three adverse outcomes were more common in women who had HIP than in women with normoglycaemia, with caesarean delivery the most prevalent **(Table 2).** Amongst those with HIP, 36.3% (n=109) had a caesarean delivery, 24.0% (n=72) had LGA babies, and 16.0% (n=48) had babies admitted in ICU, compared to 27.6%, 18.6% and 10.8%, respectively, among women with normoglycaemia. Among women with HIP, the risk of experiencing at least one of the three adverse pregnancy outcomes was highest among participants with elevation of both FBG and post-load glucose (68.4%), lower among those with elevated FBG only (52.9%) and lowest among those with elevated post-load glucose only (46.6%)**.** Risks of each individual adverse outcome were also highest in participants with both elevated FBG and post-load glucose, compared to women with elevated FBG only or women with elevated post-load glucose levels only **(Table 2).**

4.2 Association between HIP and adverse outcomes.

Compared to normoglycaemic participants, and after adjusting for gestational age at enrolment, BMI, mother's age, gravidity, family history of diabetes and child's sex at birth, participants with elevated FBG only had higher risk of having a caesarean birth (RR: 1.36, 95% CI: 1.05 – 1.76), but the risks of having a LGA baby or neonatal ICU admission were similar to normoglycaemic participants. In contrast, both in crude and adjusted analyses, having elevated post-load glucose alone was not associated with increased risk of any of the adverse outcomes. However, participants who had elevation of both FBG and post-load glucose were at significantly higher risk of both LGA and neonatal ICU admission; compared to normoglycaemic mothers, participants with elevated FBG and post-load glucose had 1.74 times the risk of giving birth to large babies (RR: 1.74, 95% CI: 1.12 – 2.68), and 2.07 times the risk of having their babies being admitted in ICU (RR: 2.07, 95% CI: 1.23 – 3.47) (**Figure 2).** Considering elevated FBG and elevated post-load glucose as independent predictors of adverse pregnancy outcome in regression models, the inclusion of elevated post-load glucose in models in addition to elevated FBG improved the fit of the models (p-values 0.001, 0.003, 0.03 and

0.001 for any adverse outcome, Caesarean section, LGA and NICU admission, respectively), thus confirming that having elevated values for both fasting and post-load glucose was more predictive of adverse outcomes than elevated values for fasting glucose alone.

5 Discussion

In this study, we show that HIP is associated with increased risk of Caesarean section, LGA and neonatal ICU admission, and that the risk is highest when the mother has elevations in both FBG and post-load glucose on OGTT. After adjustment for a number of potential confounders, having elevated post-load glucose alone was not associated with increased risk of any of the outcomes, but elevated FBG without elevated post-load glucose increased the risk of Caesarian section, while elevations in both FBG and post-load glucose was associated with increased risk of LGA and neonatal admission to ICU.

Our data are in accord with reports from other populations where fasting hypoglycaemia has been shown to be more important in determining pregnancy outcomes, responsible for a twofold higher risk of adverse events, compared to elevated post-load glucose.[2, 8, 9, 16]

The mechanisms that make fasting hyperglycaemia particularly important in determining the risk of adverse pregnancy outcomes are unclear; they may be related to the total burden of hyperglycaemia to which the mother and developing fetus are exposed. In addition, elevated FBG may represent more generalized metabolic arrangement that leads to increased risk of pregnancy complications.[17-19] Interestingly in our study, obesity (which is known to induce metabolic changes and is associated with increased maternal outcomes) was not more prevalent in mothers with isolated elevation of FBG.

Although post-load hyperglycaemia in the absence of elevated fasting blood glucose was not associated with adverse pregnancy outcomes, its presence significantly increased the risk of adverse pregnancy outcomes in mothers who also had elevated FBG. This underscores the importance of identifying and managing both fasting hypoglycaemia and post-prandial hypoglycaemia in women during pregnancy.[2] Intriguingly, participants who had elevation of both fasting post-load glucose had a significantly higher blood pressure levels, suggesting a more generalised disorder.

Our study has a number of strengths: it is one of the largest and most rigorous of its kind on HIP in Africa and, to our knowledge, the first to investigate the relative associations between FBG or post-load glucose elevetions and adverse pregnancy outcomes. Participants were recruited from both public

and private health facilities, thus are likely to be generalisable to similar urban and peri-urban settings. However, there are also some limitations. A sixth of women enrolled in the study did not deliver in the study facilities and were therefore lost to follow-up, which may introduce bias to the outcomes reported; however, the baseline characteristics of these participants were similar to those who were retained in the study. Women diagnosed with HIP were referred for management by their clinicians, rather than through a study protocol; the intensity of treatment was therefore likely to be variable and not under study control. LGA was calculated using gestational age at delivery, based on either early obstetric ultrasound scan or last menstrual cycle at booking. Estimation of gestational age is difficult in this setting; this would have affected women with and without HIP. For the other outcomes (Caesarean delivery and admission to neonatal ICU), we relied on healthcare records rather than active investigation by the study team. We did not have data on previous operative delivery, so we could only report Caesarean delivery, rather than primary Caesarean delivery. The study was performed in urban and peri-urban central Uganda which may reduce generalisability to rural populations.

In our study, 21.8% of participants with HIP had elevated post-load glucose only. This is in keeping with data from non-pregnant populations in sub-Saharan Africa that have shown that when OGTT is used to screen for diabetes, a high proportion (at least 30%) of cases display post-load hyperglycaemia only; these individuals would be missed if only fasting glucose is measured [20] [21, 22]. Similarly, screening approaches that employ FBG only (which is common in resource poor settings) to screen for HIP in pregnancy would miss a significant proportion of cases. The pathogenesis of this isolated postprandial hyperglycaemia and how it progresses or leads to complications is unknown; our finding that elevations in post-load glucose alone are not associated with adverse pregnancy outcomes is reassuring. In summary, risk of adverse outcome was highest among women with elevation of both fasting and post-load glucose levels, and screening approaches including both tests may be required.

6 Acknowledgements

We acknowledge the commitment of hospitals and participants towards the study activities.

Contributors

MJN had the initial idea and developed the conceptual framework. IS and EW did the data analysis. IS and ST drafted the manuscript. All authors contributed to the design or data collection, and commented on drafts and revisions.

Declaration of interests

We declare no competing interests.

Funding

This work was supported by the UK Medical Research Council (MRC) and the UK Department for International Development (DFID) under the MRC/DFID Concordat agreement, through a strategic award to MJN (Project Reference: MC_UP_1204/16)

Data sharing statement

The data underlying this article will be shared on reasonable request to the corresponding author.

7 References

[1] Farrar D. Hyperglycemia in pregnancy: prevalence, impact, and management challenges. Int J Womens Health. 2016;8:519-27.
[2] Group HSCR, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358:1991-2002.
[3] Nijs H, Benhalima K. Gestational Diabetes Mellitus and the Long-Term Risk for Glucose Intolerance and Overweight in the Offspring: A Narrative Review. J Clin Med. 2020;9.
[4] Coustan DR, Lowe LP, Metzger BE. The hyperglycemia and adverse pregnancy outcome (HAPO) study: can we use the results as a basis for change? J Matern Fetal Neonatal Med. 2010;23:204-9.
[5] Hu FB. Globalization of diabetes: the role of diet, lifestyle, and genes. Diabetes Care. 2011;34:1249-57.
[6] Goldenberg RL, McClure EM, Harrison MS, Miodovnik M. Diabetes during Pregnancy in Low- and Middle-Income Countries. Am J Perinatol. 2016;33:1227-35.
[7] Colagiuri S, Falavigna M, Agarwal MM, Boulvain M, Coetzee E, Hod M, et al. Strategies for implementing the WHO diagnostic criteria and classification of hyperglycaemia first detected in pregnancy. Diabetes Res Clin Pract. 2014;103:364-72.
[8] Black MH, Sacks DA, Xiang AH, Lawrence JM. Clinical outcomes of pregnancies complicated by mild gestational diabetes mellitus differ by combinations of abnormal oral glucose tolerance test values. Diabetes Care. 2010;33:2524-30.
[9] Ehrlich SF, Crites YM, Hedderson MM, Darbinian JA, Ferrara A. The risk of large for gestational age across increasing categories of pregnancy glycemia. Am J Obstet Gynecol. 2011;204:240 e1-6.
[10] Feng H, Zhu WW, Yang HX, Wei YM, Wang C, Su RN, et al. Relationship between Oral Glucose Tolerance Test Characteristics and Adverse Pregnancy Outcomes among Women with Gestational Diabetes Mellitus. Chin Med J (Engl). 2017;130:1012-8.
[11] Jovanovic-Peterson L, Peterson CM, Reed GF, Metzger BE, Mills JL, Knopp RH, et al. Maternal postprandial glucose levels and infant birth weight: the Diabetes in Early Pregnancy Study. The National Institute of Child Health and Human Development--Diabetes in Early Pregnancy Study. Am J Obstet Gynecol. 1991;164:103-11.
[12] Combs CA, Gunderson E, Kitzmiller JL, Gavin LA, Main EK. Relationship of fetal macrosomia to maternal postprandial glucose control during pregnancy. Diabetes Care. 1992;15:1251-7.

[13] de Veciana M, Major CA, Morgan MA, Asrat T, Toohey JS, Lien JM, et al. Postprandial versus preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy. N Engl J Med. 1995;333:1237-41.
[14] Natamba BK, Namara AA, Nyirenda MJ. Burden, risk factors and maternal and offspring outcomes of gestational diabetes mellitus (GDM) in sub-Saharan Africa (SSA): a systematic review and meta-analysis. BMC Pregnancy Childbirth. 2019;19:450.
[15] Macaulay S, Dunger DB, Norris SA. Gestational diabetes mellitus in Africa: a systematic review. PLoS One. 2014;9:e97871.
[16] Ryan EA, Savu A, Yeung RO, Moore LE, Bowker SL, Kaul P. Elevated fasting vs post-load glucose levels and pregnancy outcomes in gestational diabetes: a population-based study. Diabet Med. 2020;37:114-22.
[17] Stuebe AM, Landon MB, Lai Y, Spong CY, Carpenter MW, Ramin SM, et al. Maternal BMI, glucose tolerance, and adverse pregnancy outcomes. Am J Obstet Gynecol. 2012;207:62 e1-7.
[18] Catalano PM, McIntyre HD, Cruickshank JK, McCance DR, Dyer AR, Metzger BE, et al. The hyperglycemia and adverse pregnancy outcome study: associations of GDM and obesity with pregnancy outcomes. Diabetes Care. 2012;35:780-6.
[19] Scholtens DM, Bain JR, Reisetter AC, Muehlbauer MJ, Nodzenski M, Stevens RD, et al. Metabolic Networks and Metabolites Underlie Associations Between Maternal Glucose During Pregnancy and Newborn Size at Birth. Diabetes. 2016;65:2039-50.
[20] Motala AA, Esterhuizen T, Gouws E, Pirie FJ, Omar MAK. Diabetes and other disorders of glycemia in a rural South African community: prevalence and associated risk factors. Diabetes care. 2008;31:1783-8.
[21] Chinenye S, Young EE. Isolated postprandial hyperglycemia in type 2 diabetic patients in a Nigerian Tertiary Health Center. Indian journal of endocrinology and metabolism. 2012;16:604-8.
[22] Levitt NS, Unwin NC, Bradshaw D, Kitange HM, Mbanya JC, Mollentze WF, et al. Application of the new ADA criteria for the diagnosis of diabetes to population studies in sub-Saharan Africa. American diabetes association. Diabet Med. 2000;17:381-5.

8 Figures and tables with legends.

Figure 1. Participant flow in the study

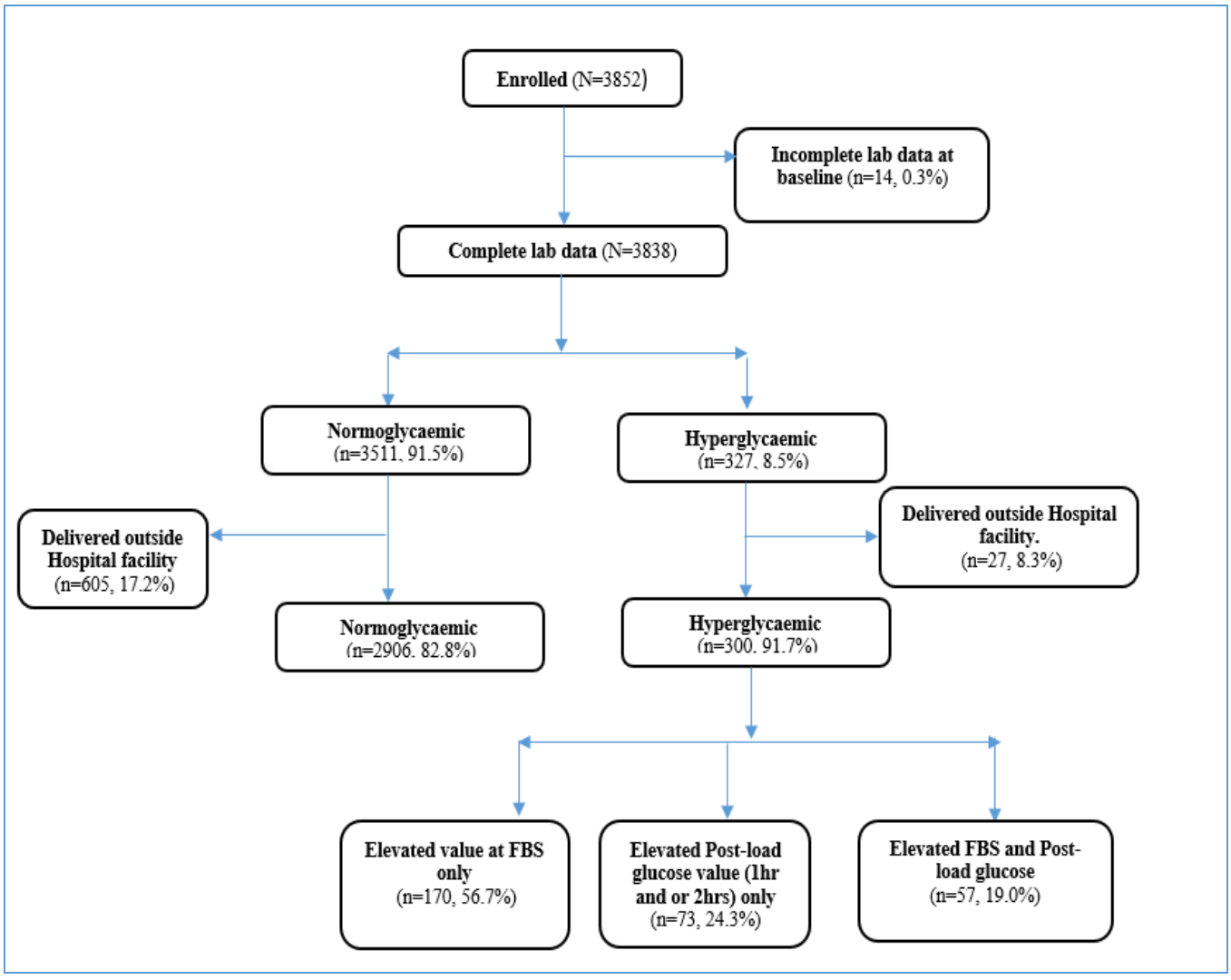


Table 1. Maternal characteristics, obstetrical and neonatal outcomes

Variables		Elevated Blood glucose			
	Non-Elevated glucose at both fasting, and 1-hr & or 2-hrs	**Elevated FBG only**	**Elevated post-load glucose i.e. 1-hr and or 2-hrs only**	**Elevated FBG and elevated post-load glucose (1-hr & or 2-hrs**	**P-value**
Gestational age at enrolment, Mean ± SD	26.0±**1.25**	26.0±**1.02**	26.0±**1.21**	26.1±**1.21**	0.797
Maternal age, Median(IQR)	26 (23-30)	27.0 (24-33)	29 (24-34)	31 (28 - 36)	<0.001
MUAC, median (IQR)	28.4 (26.1 – 31.3)	30.0 (27 – 34)	31.1 (28 – 33)	34 (31 – 37.2)	<0.001
Maternal income, median(IQR)	210,000 (95,000 – 450,000)	300,000 (100,000 – 600,000)	275,000 (100,000 – 500,000)	300,000 (100,000-500,000)	0.481
Systolic Blood pressure, mean (SD)	104.0 (10.4)	104.7 (11.1)	105.8 (10.6)	111.1 (9.3)	<0.001
Diastolic Blood Pressure, mean (SD)	67.3 (8.4)	68.4 (9.0)	69.3 (9.4)	73.9 (7.3)	<0.001
HIV, n(%)					
Negative	2744 (94.4)	156 (91.8)	71 (97.3)	53 (93.0)	
Positive	162 (5.6)	14 (8.2)	2 (2.7)	4 (7.0)	0.288
Maternal BMI, n (%)					
Below 25 kg/m^2	1024 (35.2)	43 (25.3)	15 (20.6)	3 (5.3)	
Overweight	1123 (38.6)	57 (33.5)	25 (34.3)	11 (19.3)	
Obese	759 (26.1)	70 (41.2)	33 (45.2)	43 (75.4)	<0.001
Family history of DM, n (%)					
No	1979 (73.8)	108 (68.8)	47 (66.2)	32 (59.3)	
Yes	704 (26.2)	49 (31.2)	24 (33.8)	22 (40.7)	0.442
Gravidity, n (%)					
1	938 (32.3)	42 (24.7)	19 (26.0)	7 (12.3)	
2-4	1641 (56.5)	96 (56.5)	45 (61.6)	33 (57.9)	
Above 4	327 (11.3)	32 (18.8)	9 (12.3)	17 (29.8)	0.068
Gender of the Neonates, n (%)					
Male	1305 (49.0)	100 (62.1)	30 (47.6)	29 (53.7)	
Female	1357 (51.0)	61 (37.9)	33 (52.4)	25 (46.3)	0.121

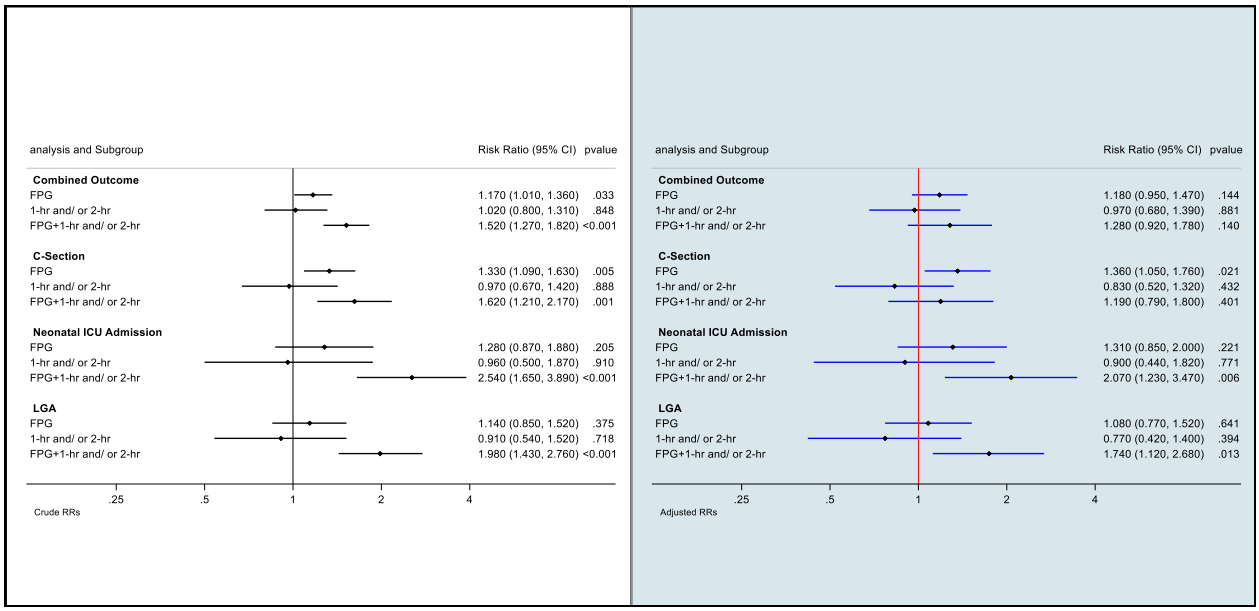
MUAC-Mid upper arm circumfrance, BMI-Body Mass Index, IQR-interquartile Range and DM- Diabetes Mellitus

Table 2. Adverse pregnancy and neonatal outcomes by number of elevated glucose values.

Variable	Normoglycaemia (n=2906)	Elevated FBG only (n=170)	Elevated Post-load glucose only (n=73)	Elevated FBG and Post-load glucose (n=57)	All women with HIP (n=300)	All participants (n=3206)
Composite adverse outcome[1], n(%)	1295 (44.6)	90 (52.9)	34 (46.6)	39 (68.4)	163 (54.3)	1458 (45.5)
Caesarean delivery, n (%)	802 (27.6)	64 (37.7)	20 (27.4)	25 (43.9)	109 (36.3)	911 (28.4)
LGA n(%)	541 (18.6)	38 (22.4)	12 (16.4)	22 (38.6)	72 (24.0)	613 (19.1)
Neonatal ICU admission,	315 (10.8)	24 (14.1)	8 (11.0)	16 (28.1)	48 (16.0)	363 (11.3)

[1]Any versus none of Caesarean delivery, LGA or neonatal ICU admission

Figure 2. Un-adjusted and Adjusted Risk Ratios and 95% confidence intervals for experiencing adverse maternal outcomes (C-Section, Neonatal ICU Admission, and LGA) according to elevated fasting and 1 hour & or 2 hour values.



Adjusted for gestational age at enrolment, BMI, mother age, gravidity, family history of diabetes and child's sex at birth.

Supplemental Table 1. Baseline Characteristics of paricipants.

Variables	Participants with complete data included in main model (n=2641)	Missing outcome data (n=1197)
Gestational age at enrolment, Mean ± SD	26.0**±1.24**	25.9 **±1.33**
Maternal age, Median(IQR)	26 (23 - 30)	24 (21 - 28)
MUAC, median (IQR)	28.7 (26.2 – 31.7)	27.6 (25.6 – 30.5)
Maternal income, median(IQR)	240,000 (100,000-464,000)	150,000 (50,000 –300,000)
Systolic Blood pressure, mean (SD)	104.2 (10.5)	104.8 (9.2)
Diastolic Blood Pressure, mean (SD)	67.5 (8.5)	66.5 (8.0)
HIV, n(%)		
Negative	3024 (94.3)	578 (91.5)
Positive	142 (5.7)	54 (8.5)
Maternal BMI, n (%)		
Below 25 kg/m^2	1085 (33.8)	267 (42.3)
Overweight	1216 (38.0)	237 (37.5)
Obese	905 (28.2)	128 (20.3)
Family history of DM, n (%)		
No	2166 (73.1)	457 (77.1)
Yes	779 (26.9)	136 (22.9)
Gravidity, n (%)		
1	1006 (31.4)	230 (36.4)
2-4	1815 (56.6)	336 (53.2)
Above 4	385 (12.0)	66 (10.4)