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CLINICAL ARTICLE

Maternal hyperglycemia and adverse pregnancy outcomes in Dar es Salaam, Tanzania

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ABSTRACT

Objective: To evaluate maternal glucose levels during pregnancy as a predictor of adverse perinatal outcomes in Dar es Salaam, Tanzania. *Methods:* Random blood glucose measurements were analyzed from 3383 pregnant women enrolled in a randomized trial to assess the impact of multivitamins on pregnancy outcomes in Dar es Salaam between August 2001 and July 2004. Information on maternal and neonatal morbidity was recorded at monthly study visits, delivery, and 6 weeks postpartum. Binomial regression and generalized estimating equations were used to determine the relationship between elevated glucose (>7.8 mmol/L) and pregnancy outcomes. *Results:* In total, 25 women had elevated glucose (0.7%). Hyperglycemia was associated with an increased risk of delivery before 37 weeks [relative risk (RR), 2.11; 95% confidence interval [CI], 1.07–4.13; $P = 0.03$), delivery before 34 weeks (RR, 4.15; 95% CI, 1.43–12.03, $P = 0.009$), incident gestational hypertension (RR, 2.90; 95% CI, 1.24–6.76; $P = 0.01$), low birth weight (RR, 2.87; 95% CI, 1.18–6.99; $P = 0.02$), reduced newborn head circumference (mean difference, −1.57; 95% CI, −2.51 to −0.62; $P = 0.001$), and fetal loss (RR, 3.38; 95% CI, 1.13–10.08; $P = 0.03$). *Conclusion:* Maternal hyperglycemia is uncommon among pregnant Tanzanian women, but nonetheless seems to increase the risk of several adverse perinatal outcomes.

1. Introduction

Both gestational and pre-gestational diabetes have well-known deleterious consequences for mothers and neonates, including pregnancy-induced hypertension [1,2], stillbirth [1–4], perinatal death [1,4–6], cesarean delivery [5,7], preterm delivery [1,5–8], high and low birth weight [1,5,7], and both large-for-gestational age and small-for-gestational age (SGA) outcomes [6,8]. Considerable evidence also shows that milder hyperglycemia as an antecedent to overt diabetes can lead to adverse pregnancy outcomes [3,7,9–11].

The management of diabetic pregnancies may be a growing concern in sub-Saharan Africa, where diabetes has received comparatively little attention. Estimates of the prevalence of gestational diabetes in this region are scarce and have varied from 0% to 13.9% [1,11–13]. Impaired glucose tolerance, a precursor to diabetes, has been reported as 0% among pregnant women in Tanzania [14,15] and 7.3% among those in South Africa [16].

Predictions indicate that, between 2010 and 2030, sub-Saharan Africa will experience the largest percentage increase in diabetes of any region [17]. The prevalence of diabetes among adults in sub-Saharan Africa is expected to increase from 3.8% to 4.7% during this time, which will translate to 11.8 million new cases. As a result, increasing numbers of women in this region will enter pregnancy with abnormal glucose regulation or will experience its onset during gestation and subsequently face a substantial risk of pregnancy complications.

The aim of the present study was to examine the effect of plasma glucose levels in pregnancy on adverse perinatal outcomes within a cohort of women who were previously enrolled in a randomized controlled trial of daily multivitamin supplementation (vitamins B, C, and E) versus placebo in Dar es Salaam, Tanzania, [18].

2. Materials and methods

The present study retrospectively analyzed data from pregnant women who were enrolled in a double-blind, randomized, placebo-controlled trial at participating prenatal clinics in Dar es Salaam, Tanzania, between August 1, 2001, and July 31, 2004 [18]. Ethics approval for the trial was obtained from the institutional review boards of Muhimbilli University of Health and Allied Sciences in Dar es Salaam, Tanzania, and Harvard School of Public Health in Boston, MA, USA. Written informed consent was obtained from all women.

Women eligible for the original trial were HIV-negative, had a pregnancy of 12–27 weeks of gestation, and were planning to stay in Dar es

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Salaam for at least 1 year after delivery. The present analysis included only women who had available glucose measurements (supply limitations precluded the measurement of glucose levels for every trial participant).

Glucose was measured in plasma drawn from participants at regularly scheduled study visits to prenatal clinics. Most (90%) samples were obtained between 22–34 weeks of gestation. Glucose testing was performed with the Roche Hitachi 911 chemistry analyzer (Roche Diagnostics, Indianapolis, IN, USA).

Individuals with abnormal glucose levels were referred for treatment as per standard of care. Because only random plasma glucose levels were available, it was not possible to follow conventional guidelines for the diagnosis of gestational diabetes or impaired glucose tolerance. Instead, glucose levels exceeding 7.8 mmol/L (140 mg/dL) were considered to be elevated. This cutoff value represents the typical upper threshold for peak postprandial glucose during pregnancy [19]. The follow-up period for the present analysis began at the time of glucose measurement and ended at 6 weeks postpartum.

Information on sociodemographic characteristics was collected through maternal interviews at baseline. Gestational age was determined by the physician using the date of the last menstrual period. At each monthly visit, participants underwent physical examination and anthropometric assessments. Study nurses recorded single values for systolic and diastolic blood pressure at each visit with a mercury sphygmomanometer while participants were at rest. Routine laboratory tests were conducted as described elsewhere [18].

Maternal complications included preterm delivery, severe preterm delivery, hypertension, cesarean delivery, and severe anemia. All deliveries that occurred before 37 weeks of gestation were considered preterm. Those that occurred before 34 weeks were considered severely preterm. Hypertension was defined as a systolic blood pressure of 140 mm Hg or more or a diastolic blood pressure of 90 mm Hg or more at any time during pregnancy. Cesarean delivery was recorded by the research midwives who attended to participants during labor.

Newborn growth parameters included birth weight, SGA status, crown–heel length, head circumference, and placental weight. After delivery, research midwives weighed neonates and placentas to the nearest 10 g and measured newborn length and head circumference to the nearest 0.1 cm. Neonates weighing less than 2500 g were categorized as low birth weight. Those weighing more than 4000 g were categorized as macrosomic. SGA status was defined as a birth weight below the 10th percentile for gestational age. US standards were used as the "reference population" because they might provide a better reflection of growth potential unaffected by nutritional deprivation than local norms [18]. Fetal and perinatal mortality outcomes included fetal loss (any death occurring before delivery), stillbirth (deaths occurring at 28 gestational weeks or more), perinatal death (deaths that occurred between 28 weeks of gestation and 1 week following delivery) and early infant deaths (deaths that occurred before 6 weeks postpartum).

All statistical analyses were performed via SAS version 9.2 (SAS Institute, Cary, NC, USA). Relative risks (RRs) and 95% confidence intervals (CIs) were determined by using binomial regression specified with the log-link function for all dichotomous outcomes. In most cases, however, the log-binomial models failed to converge and were replaced with log-Poisson models, which provide consistent but not fully efficient estimates of the RR and its CIs [20]. Continuous endpoints were assessed with generalized linear models with the use of the identity link and Gaussian variance function.

For models of hypertension in pregnancy, a generalized estimating equation model with a compound symmetry working correlation matrix was used to account for repeated measures of blood pressure [21]. Women with hypertension at baseline were excluded from the analysis of this outcome. A generalized estimating equation model with a compound symmetry working correlation matrix was also specified for analyses of birth outcomes to account for correlations due to twinning. All analyses of birth outcomes were restricted to live births. Restricted cubic splines [22] were used to model continuous glucose levels in relation to the outcomes of interest.

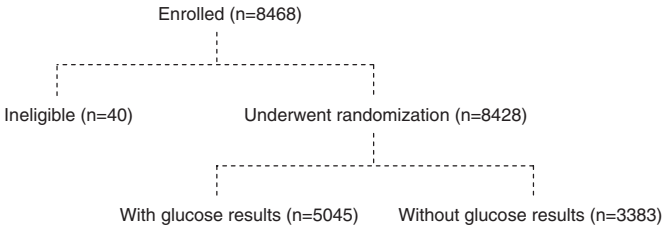

Fig. 1. Derivation of the study population.

All multivariate models included age (<20 years, 20 to <25 years, 25 to <30 years, ≥30 years), nearest body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) measurement prior to the time of glucose testing (<18.5 kg/m^2, 18.5–24.9 kg/m^2, 25.0–29.9 kg/m^2, ≥30.0 kg/m^2), quartiles of nearest mid-upper arm circumference measurement prior to the time of glucose measurement, Filmer–Pritchett wealth score below median (yes/no), and receipt of multivitamins during the larger trial (yes/no).

In addition, for each separate outcome, the following characteristics were considered to be potential confounders if they predicted the outcome in univariate analysis at a *P* value of 0.20 or less: literacy (yes/no); marital status (yes/no); dependence on others for economic support (yes/no); low daily per capita food expenditure (yes/no); education (0–4, 5–7, 8–11, ≥12 years); frequency of meat or fish intake (<1 per month, 1–3 times per month, about once/week, 2–4 times per week, 5–7 times per week); gravidity (0, 1, ≥2); gestational age at time of glucose measurement (<25 weeks, ≥25 weeks); weight gain from study entry to the time of glucose measurement (<3 kg, 3 to <6 kg, 6 to <9 kg, ≥9 kg); quartiles of nearest triceps skin fold thickness measurement prior to time of glucose testing; nearest hemoglobin measurement prior to time of glucose measurement (<8.5 g/dL, 8.5–10.9 g/dL, ≥11.0 g/dL); smoking (yes/no); year of recruitment (2001, 2002, 2003, 2004); district of recruitment (Ilala, Temeke, Kinondoni); history of a low birth weight newborn (yes/no) history of hypertension during the current pregnancy (yes/no; for analysis of hypertension); family history of hypertension (yes/no; for analysis of hypertension); family history of diabetes (yes/no); history of fetal loss (yes/no; for analyses of fetal and infant mortality); Missing indicators were used to retain observations in the analyses for variables where more than 1% of total observations were missing [23]. Observations containing missing values for model covariates with 1% or fewer total observations missing were

Table 1
Comparison of baseline characteristics between women with glucose data available and those without.[a]

Characteristic	Glucose results available (n = 3383)	Glucose results unavailable (n = 5045)
Age, y	25.2 ± 5.0	25.1 ± 5.0
Literate	88	87
Completed secondary education	5	5
Married or cohabitating	89	88
Economically dependent on others	98	98
Low daily per capita expenditure on food	36	42
Filmer–Pritchett wealth score less than median	48	48
Nulliparous	47	45
Gestational age, wk	21.5 ± 3.3	21.0 ± 3.5
BMI	24.5 ± 3.6	24.6 ± 3.9
Mid-upper arm circumference, cm	26.3 ± 3.2	26.5 ± 3.3
Triceps skin fold thickness, mm	18.6 ± 6.5	19.0 ± 6.7
Received multivitamin regimen	51	49

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters).

[a] Values are given as mean ± SD or percentage.