

Association Between Hypoglycemia During 75-g Oral Glucose Tolerance Test and Perinatal Outcomes: A Prospective Observational Study

Dr. Sahini Sneha

Post Graduate Junior Resident, Department of Obstetrics and Gynaecology, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, India

Email: sahinisneha1211[at]gmail.com

ORCID ID: 0009 0004 1848 4215

Abstract: *Background:* Maternal glucose levels during pregnancy influence fetal growth and perinatal outcomes. While elevated glucose concentrations have been widely studied, the clinical relevance of low glucose values detected during routine 75-g oral glucose tolerance testing (OGTT) remains uncertain. This study aimed to determine whether hypoglycemia during OGTT is associated with gestational age at delivery and perinatal outcomes such as neonatal birth weight. *Methods:* In this prospective observational study, 100 pregnant women undergoing routine 75-g OGTT between 24 and 28 weeks of gestation were enrolled. Women diagnosed with gestational diabetes mellitus according to contemporary international criteria were excluded. Hypoglycemia was defined as any plasma glucose value <70 mg/dL. Participants were categorized into hypoglycemia (n=30) and normoglycemia (n=70) groups. Maternal characteristics and perinatal outcomes were compared using independent sample t-test and Chi-square test. *Results:* Maternal age was significantly lower in the hypoglycemia group (26.3 ± 4.7 vs 28.6 ± 5 years; p=0.032), while body mass index and parity were comparable. Mean gestational age at delivery did not differ significantly (38.2 ± 2.5 vs 38.4 ± 2 weeks; p=0.700). Neonatal birth weight was significantly lower in the hypoglycemia group (2887.5 ± 579 g vs 3138 ± 529 g; p=0.047). Preterm delivery (30% vs 26%; p=0.844), NICU admission (10% vs 13%; p=0.946), and Apgar score <7 at 5 minutes (3% vs 3%; p=0.512) were similar. *Conclusion:* Hypoglycemia during routine 75-g OGTT was associated with lower neonatal birth weight but not with gestational age or short-term neonatal morbidity.

Keywords: Hypoglycemia; Oral glucose tolerance test; Birth weight; Gestational age at delivery; Pregnancy outcomes

1. Introduction

Pregnancy induces substantial metabolic adaptations to support fetal growth and development. Glucose is the principal energy substrate for the fetus, and its placental transport occurs primarily through facilitated diffusion via glucose transporter proteins expressed in trophoblastic membranes.^{1,2} Maternal glucose concentrations therefore directly influence fetal glucose exposure and insulin secretion. Contemporary research supports the concept that fetal growth responds continuously to maternal glycemia, even within ranges traditionally considered physiologically normal.^{3,4}

The prevalence of gestational diabetes mellitus (GDM) has increased globally over the past decade, with estimates ranging from 14% to 20% depending on population characteristics and diagnostic criteria.^{5–7} In India and other low- and middle-income countries, rising maternal age, nutritional transition, sedentary lifestyle, and increasing obesity have contributed to a growing metabolic burden during pregnancy^{6,8,26}. Universal screening using a 75-g oral glucose tolerance test (OGTT) at 24–28 weeks of gestation is therefore recommended by major international organizations.^{9–11}

While the adverse consequences of hyperglycemia- including macrosomia, operative delivery, neonatal hypoglycemia, and long-term cardiometabolic risk—are well established,^{12–14} less attention has been directed toward lower glucose excursions during OGTT. Pregnancy is characterized by progressive insulin resistance, particularly in the second and third trimesters, accompanied by compensatory β -cell adaptation.^{15,16} However, the magnitude of these adaptations

varies considerably between individuals, resulting in heterogeneous glycemic responses to standardized glucose loading.

Emerging evidence suggests that glycemic variability itself may influence placental nutrient sensing pathways, insulin-like growth factor signaling, and fetal growth trajectories.^{17,18,27} Some investigators have reported lower neonatal birth weight among women exhibiting hypoglycemia during glucose testing,^{19–21} whereas others have demonstrated neutral associations with gestational duration or neonatal outcomes.^{22–24} Data from Indian populations remain limited,^{25,26} and prospective evaluations are sparse.

In the Indian context, where dual burdens of undernutrition and rising metabolic disease coexist, subtle variations in maternal glycemia may have distinct implications for fetal growth patterns.²⁶ Unlike populations characterized predominantly by obesity-driven insulin resistance, metabolic profiles in Indian women may reflect a complex interaction between body composition, micronutrient status, and genetic susceptibility. Despite the increasing prevalence of GDM in India, relatively few studies have examined the clinical significance of glucose values falling below conventional thresholds during routine screening. This gap in evidence highlights the need for prospective evaluation within diverse populations.

Given increasing recognition of maternal metabolic phenotype and fetal programming mechanisms,^{27–29} clarifying the clinical significance of hypoglycemia during routine OGTT is important. The present study therefore aimed to evaluate whether hypoglycemia during 75-g OGTT

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is associated with gestational age at delivery and neonatal birth weight.

Beyond immediate perinatal outcomes, there is increasing recognition that intrauterine metabolic exposure may influence long-term cardiometabolic risk through developmental programming mechanisms.^{27–29} Subtle variations in maternal glycemia, even within non-diabetic ranges, may alter fetal pancreatic development, insulin sensitivity, and adipocyte differentiation. While hyperglycemia has been implicated in promoting fetal hyperinsulinemia and accelerated growth, it remains uncertain whether lower glucose excursions during pregnancy exert reciprocal effects on fetal metabolic regulation. Clarifying whether hypoglycemia during routine screening reflects a benign physiological variant or a metabolically distinct phenotype is therefore clinically relevant, particularly in populations undergoing rapid epidemiological transition.²⁶

2. Materials and Methods

This prospective observational study was conducted at a tertiary care teaching hospital between January 2024 and December 2025 after obtaining approval from the Institutional Ethics Committee. Written informed consent was secured from all participants prior to inclusion.

Pregnant women between 24 and 28 weeks of gestation undergoing routine universal screening with a 75-g oral glucose tolerance test (OGTT) were enrolled consecutively in order to reflect routine antenatal practice and reduce selection bias. Women diagnosed with gestational diabetes mellitus (GDM) according to internationally accepted criteria^{9–11} were excluded so that the study population represented normoglycemic pregnancies without overt dysglycemia. Additional exclusion criteria included pre-existing diabetes mellitus, chronic hypertension, thyroid dysfunction, renal disease, multiple gestation, and other systemic disorders known to influence fetal growth.

After an overnight fast of at least 8 hours, venous blood samples were collected at fasting and at 1 hour and 2 hours following ingestion of 75 g of anhydrous glucose dissolved in water. Plasma glucose levels were measured using standardized enzymatic methods in a quality-controlled laboratory participating in internal and external assurance programs. Hypoglycemia was defined as any plasma glucose value <70 mg/dL, consistent with internationally accepted definitions of clinically significant hypoglycemia. This cutoff was selected to ensure comparability with prior studies evaluating low glucose responses during pregnancy.

Maternal demographic and obstetric characteristics, including age, body mass index, and parity, were recorded at enrollment. Participants were followed prospectively until delivery, and neonatal outcomes were obtained from hospital records to ensure accuracy and minimize recall bias. Missing data were negligible, and complete delivery outcomes were available for all participants.

The primary outcomes were gestational age at delivery and neonatal birth weight. Secondary outcomes included preterm

delivery (<37 weeks), mode of delivery, admission to the neonatal intensive care unit (NICU), and Apgar score at 5 minutes.

Continuous variables were expressed as mean \pm standard deviation and assessed for normal distribution before analysis. Between-group comparisons were performed using independent sample t-test for continuous variables and Chi-square test for categorical variables. A two-tailed p value <0.05 was considered statistically significant. Statistical analyses were conducted using SPSS software.

3. Results

A total of 100 pregnant women were included in the final analysis. Of these, 30 (30%) exhibited at least one hypoglycemic value (<70 mg/dL) during the 75-g OGTT, while 70 (70%) demonstrated normoglycemic responses.

Baseline Maternal Characteristics

Maternal age was significantly lower in the hypoglycemia group compared with the normoglycemia group (26.3 \pm 4.7 years vs 28.6 \pm 5 years; p=0.032). There was no statistically significant difference in body mass index between groups (25.8 \pm 3.9 kg/m² vs 27.5 \pm 5.2 kg/m²; p=0.076). The proportion of primigravida women was also comparable (23% vs 36%; p=0.326). Overall, baseline demographic and obstetric characteristics were similar between the two groups. (Table I)

Table I: Baseline Maternal Characteristics of the Study Population

Variable	Hypoglycemia group (n=30)	Normoglycemia group (n=70)	p value
Maternal age (years) (mean \pm SD)	26.3 \pm 4.7	28.6 \pm 5	0.032
Body mass index (kg/m ²) (mean \pm SD)	25.8 \pm 3.9	27.5 \pm 5.2	0.076
Primigravida n (%)	7 (23%)	25 (36%)	0.326

OGTT Glycemic Values

Fasting, 1-hour, and 2-hour plasma glucose values were significantly lower in the hypoglycemia group compared with the normoglycemia group (p<0.001 for all comparisons), confirming distinct glycemic response patterns following glucose loading. (Table II)

Table II: Oral Glucose Tolerance Test Values in Study Groups

OGTT parameter (mean \pm SD)	Hypoglycemia group (mean \pm SD)	Normoglycemia group (mean \pm SD)	P value
Fasting plasma glucose (mg/dL)	75.2 \pm 5	81.2 \pm 5	<0.001
1-hour plasma glucose (mg/dL)	99.4 \pm 20.5	127.4 \pm 20.5	<0.001
2-hour plasma glucose (mg/dL)	75.5 \pm 21.1	108 \pm 19	<0.001

Primary Outcomes

Mean gestational age at delivery did not differ significantly between the hypoglycemia and normoglycemia groups (38.2 \pm 2.5 weeks vs 38.4 \pm 2 weeks; p=0.700). The rate of preterm delivery (<37 weeks) was similar (30% vs 26%; p=0.844).

Mean neonatal birth weight was significantly lower in the hypoglycemia group (2887.5 ± 579 g) compared with the normoglycemia group (3138 ± 529 g; $p=0.047$), corresponding to an approximate mean difference of 250 g. (Table III)

Table III: Comparison of Primary and Secondary Pregnancy Outcomes among groups

Outcome	Hypoglycemia group (n= 30)	Normoglycemia group (n= 70)	P value
Gestational age at delivery (weeks) (mean \pm SD)	38.2 ± 2.5	38.4 ± 2	0.7
Birth weight (grams) (mean \pm SD)	2887.5 ± 579	3138 ± 529	0.047
Preterm delivery n (%)	9 (30%)	18 (26%)	0.844

Secondary Outcomes

There was no significant difference in mode of delivery between groups ($p=0.72$). NICU admission occurred in 10% of neonates in the hypoglycemia group and 13% in the normoglycemia group ($p=0.946$). An Apgar score <7 at 5 minutes was observed in 3% of neonates in both groups ($p=0.512$). (Table IV)

Table IV: Additional Maternal and Neonatal Outcomes among groups

Variable	Hypoglycemia group (n = 30)	Normoglycemia group (n = 70)	P value
Mode of delivery –			0.72
Vaginal n (%)	17 (57%)	44 (63%)	
Caesarean n (%)	13 (43%)	26 (37%)	
NICU admission n (%)	3 (10%)	9 (13%)	0.946
Apgar score <7 at 5 min n (%)	1 (3%)	1 (3%)	0.512

4. Discussion

In this prospective observational study, hypoglycemia during routine 75-g OGTT was associated with a statistically significant reduction in neonatal birth weight, while gestational age at delivery and immediate neonatal outcomes remained unaffected. These findings add to the growing body of evidence suggesting that maternal glycemic responses influence fetal growth across a biological continuum rather than solely at hyperglycemic thresholds.

Glucose is the primary metabolic substrate available to the fetus, and placental transfer occurs predominantly via facilitated diffusion through glucose transporter proteins, especially GLUT1. Fetal insulin secretion, stimulated by maternal glucose exposure, functions as a key anabolic hormone regulating intrauterine growth.^{12–14} Elevated maternal glucose levels are well established to promote fetal hyperinsulinemia and accelerated somatic growth. In contrast, the physiological implications of lower maternal glucose excursions remain less clearly defined. A reduced maternal–fetal glucose gradient could theoretically attenuate fetal insulin stimulation, resulting in modest reductions in adipose deposition and overall growth velocity. The approximately 250 g difference in mean birth weight

observed in our cohort may reflect such subtle metabolic modulation rather than overt pathological growth restriction.

Importantly, although birth weight was statistically lower in the hypoglycemia group, this difference did not translate into increased rates of preterm birth, NICU admission, or low Apgar scores. The absence of adverse short-term neonatal outcomes suggests that the magnitude of growth difference was clinically modest. Similar observations have been reported in contemporary studies evaluating low glucose values during OGTT.^{19–21} However, other investigations have demonstrated neutral associations between hypoglycemia during glucose testing and perinatal outcomes.^{22–24} The heterogeneity across studies likely reflects differences in population characteristics, maternal body composition, nutritional patterns, and metabolic phenotype.

Pregnancy is characterized by progressive insulin resistance driven by placental hormones such as human placental lactogen, progesterone, cortisol, and placental growth hormone.^{15,16} To maintain euglycemia, pancreatic β -cells undergo adaptive hyperplasia and increase insulin secretion. However, the magnitude of these adaptations varies between individuals. Women demonstrating hypoglycemia during OGTT may represent a subgroup with relatively preserved insulin sensitivity or an exaggerated insulin secretory response to glucose loading. Rather than indicating pathology, such responses may reflect a distinct metabolic phenotype within the spectrum of normal pregnancy adaptation.

Beyond maternal insulin dynamics, placental nutrient sensing mechanisms may also play a role. Experimental evidence indicates that placental transport capacity adapts dynamically in response to maternal metabolic signals.^{17,18,27} Alterations in glucose availability can influence expression of nutrient transporters and signaling pathways involved in growth regulation, including the insulin–like growth factor axis. Even modest shifts in maternal glucose patterns could therefore influence fetal growth trajectory without necessarily affecting gestational duration or neonatal adaptation.

The lack of difference in gestational age between groups is particularly noteworthy. Preterm birth is commonly associated with inflammatory, vascular, or endocrine disturbances. Our findings do not suggest that isolated hypoglycemia during OGTT is linked to these pathways. Similarly, comparable NICU admission rates and Apgar scores indicate preserved neonatal physiological transition.

From a clinical perspective, these findings have practical implications. Current international guidelines emphasize identification and management of hyperglycemia during pregnancy,^{9–11} given its well-documented association with adverse outcomes. In contrast, low glucose values during OGTT are not addressed in standard recommendations. The present study suggests that isolated hypoglycemia during screening should not automatically prompt concern for immediate obstetric or neonatal risk in otherwise uncomplicated pregnancies. Instead, such findings may represent physiological variability in maternal glucose handling.

The relevance of these findings may be particularly important in populations undergoing rapid nutritional and epidemiological transition, such as India.²⁶ Coexistence of undernutrition and rising metabolic disease creates a complex maternal metabolic landscape. Subtle variations in maternal glycemia may therefore have population-specific implications for fetal growth patterns. Additional multicentric studies across diverse Indian populations would be valuable in clarifying these relationships.

The long-term implications of hypoglycemic responses during pregnancy remain uncertain. Developmental programming research indicates that intrauterine metabolic exposure can influence offspring insulin sensitivity, adiposity distribution, and cardiometabolic risk later in life.^{28,29} Whether lower maternal glucose excursions confer protective, neutral, or adverse long-term metabolic effects requires longitudinal follow-up studies.

The strengths of this study include its prospective design and standardized glucose testing performed as part of routine antenatal care, enhancing clinical applicability. Consecutive recruitment reduced selection bias and improved representativeness of real-world practice. However, several limitations should be acknowledged. The sample size was modest, which may limit power to detect smaller differences in secondary outcomes. The single-center setting may limit generalizability to other populations. Furthermore, OGTT reflects glucose handling under standardized conditions rather than continuous daily glycemic exposure. Incorporating continuous glucose monitoring in future research could provide more comprehensive insight into maternal glycemic patterns.

Overall, our findings suggest that hypoglycemia during routine 75-g OGTT is associated with modest reductions in neonatal birth weight without evidence of short-term neonatal harm. These results support a measured interpretation of low glucose values during screening and highlight the need for further research into the broader spectrum of maternal metabolic phenotypes during pregnancy.

5. Conclusion

In this prospective observational study, hypoglycemia detected during routine 75-g oral glucose tolerance testing was associated with a modest reduction in neonatal birth weight but was not linked to differences in gestational age at delivery or short-term neonatal morbidity. These findings suggest that isolated hypoglycemia during antenatal glucose screening may reflect physiological variation in maternal metabolic response rather than an immediate obstetric or neonatal risk factor.

Given the increasing emphasis on maternal glycemic profiling in pregnancy, further large-scale and longitudinal studies are warranted to determine whether hypoglycemic responses during OGTT represent a distinct metabolic phenotype with long-term implications for offspring health.

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