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# FREQUENCY OF HYPOGLYCEMIA IN INFANT DELIVERED TO FEMALES WITH HISTORY OF DIABETES

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***Background:*** *Neonatal hypoglycemia is a common, serious metabolic complication in infants born to diabetic mothers. Early identification is vital to prevent adverse neurological outcomes.*

***Objective:*** *To determine the frequency of neonatal hypoglycemia in infants delivered to females with a history of diabetes in pregnancy and evaluate associated maternal clinical determinants.*

***Methods:*** *This cross-sectional study evaluated 150 neonates presenting within 1–12 hours of life to diabetic mothers at Imran Idrees Teaching Hospital, Sialkot. Very preterm (<32 weeks), very low birth weight (<1.5 kg), and jaundiced infants were excluded. Capillary blood glucose was measured using Accu-Chek glucometers. Hypoglycemia was defined as blood glucose <40 mg/dL. Data were analyzed using SPSS v25 with Chi-square and t-tests applied post-stratification ($p \leq 0.05$).*

***Results:*** *Neonatal hypoglycemia occurred in 40.0% (n=60/150; 95% CI: 32.1%–48.3%) of infants. Hypoglycemia was significantly higher in offspring of mothers with chronic pre-existing diabetes (79.1%, n=34/43) compared to gestational diabetes (24.3%, n=26/107; $p<0.001$). Maternal anti-glycemic regimen strongly predicted hypoglycemia ($p<0.001$), with highest rates in dual therapy (81.0%) and insulin monotherapy (76.9%) versus oral agents (24.5%) and dietary control (2.4%). Infant gender ($p=0.526$), mode of delivery ($p=0.763$), and birth weight ($p=0.333$) showed no significant associations.*

***Conclusion:*** *Neonatal hypoglycemia affects 40% of infants born to diabetic mothers. Maternal chronic diabetes and insulin requirements are the primary drivers of risk. Mandatory post-natal blood glucose screening is essential for early intervention.*

## INTRODUCTION

The most important known metabolic complication of the newborns from diabetic mothers, including diabetes type 1 and 2 and gestational diabetes, is the postnatal hypoglycemia. If unrecognized and undiagnosed, hypoglycemia in this particular high-risk group can determine severe neurological lesions and even death, in significantly higher proportion than those from the general population.[1, 2]

Gestational diabetes mellitus was significantly associated of pregnancy complications. The findings contribute to more comprehensive understanding of the adverse outcomes of pregnancy related to gestational diabetes mellitus.[3]

Gestational diabetes mellitus is rising global public health problem that can have short- and long-term sequelae for both mother and offspring. However, there are limited evidences on the effect of gestational diabetes mellitus on adverse neonatal outcomes using the updated international diagnostic criteria on adverse effects on neonatal outcomes.[4]

Hypoglycemia is the most common metabolic disturbance occurring in the neonatal period. Screening at-risk infants and the management of low blood glucose levels in the first hours to days of life is frequent issue in the care of the newborn infant. Yet, clear definition of neonatal hypoglycemia is lacking. Current screening guidelines and management algorithms are based on limited evidence, relying more on expert opinion to guide recommendations.[5] It has been reported earlier that frequency of hypoglycemia was 38.3% in neonates delivered to mothers of diabetes.[6] systemic review reported that Hypoglycemia occurs in approximately 8-30% of neonates born to mothers of diabetes.[7] Rationale of this study is to assess the frequency of hypoglycemia in infant delivered to females of history of diabetes in pregnancy. Literature showed that hypoglycemia in infant delivered to diabetic mother is high and cannot be ignored. However, in routine, neonates are not screened for blood glucose level and started weaning without evaluating their nutrition need. Also no study done in local set-up before, which could help us to assess the extent of problem in local population. Therefore, there is need of conduct study to get evidence for local population and implement findings in local setting. Therefore, we want to conduct this study to implement regular screening of neonates for blood glucose level at birth, especially in diabetic mouther who are taking anti-glycemic medication. The results of this study will add in existing knowledge and will help us to improve our practice.

## MATERIALS AND METHODS

This cross-sectional study was conducted in Department of Pediatric Medicine at Imran Idrees Teaching Hospital Sialkot over total duration of six months (Nov 2024 to April 2025) following formal synopsis approval by College of Physicians and Surgeons Pakistan (CPSP). Ethical approval was granted by Institutional Ethics Committee prior to initiation. primary objective of methodology was to strictly quantify frequency of neonatal hypoglycemia in infants born to diabetic mothers and evaluate its clinical determinants in local tertiary hospital setting. study population comprised neonates admitted to or presenting at neonatal outpatient department (OPD) within 1 to 12 hours of life delivered to mothers of documented diagnosis of diabetes mellitus. total sample size of 150 neonates was calculated using OpenEpi.com assuming 95% confidence level 8% margin of error and estimated baseline hypoglycemia frequency of 38.3% based on referenced literature. Non-probability consecutive sampling was employed to recruit participants sequentially as they met study criteria.

To establish well-defined cohort and eliminate confounding influences strict selection criteria were enforced. Neonates aged 1 to 12 hours of both genders born to mothers of either gestational diabetes mellitus (diagnosed after 20 weeks of gestation) or chronic pre-existing diabetes mellitus were included. Conversely very preterm neonates (gestational age < 32 weeks based on maternal antenatal records) very

low birth weight infants (< 1.5 kg) neonates of clinical jaundice (total serum bilirubin > 5 IU) and infants presenting of major congenital anomalies or structural birth defects on clinical examination were excluded.

Data collection proceeded in standardized sequential manner. Written informed consent was obtained from parents or legal guardians of all eligible infants prior to enrollment. Demographic maternal and delivery parameters were recorded on standardized proforma. Recorded variables included infant age (in hours) gender birth weight (kg) gestational age at birth (weeks) duration of maternal labor (hours) mode of delivery (spontaneous/induced vaginal vs. cesarean section) 5-minute Apgar score maternal diabetes type (gestational vs. chronic) and maternal anti-glycemic treatment regimen (dietary control oral hypoglycemic agents insulin monotherapy or dual therapy).

Capillary blood samples were obtained from each infant under aseptic technique within first 1-12 hours of life and blood glucose concentration was quantitatively measured using Accu-Chek glucometer. Per operational definition neonatal hypoglycemia was diagnosed if blood glucose level was strictly less than 40 mg/dL (< 40 mg/dL). Infants identified of hypoglycemia were managed immediately according to standard pediatric institutional protocols. Data confidentiality and patient anonymity were maintained throughout.

Data entry and statistical analysis were executed using IBM SPSS Statistics Version 25. Descriptive statistics were computed for all variables. Shapiro-Wilk test was applied to assess normality of continuous numerical data. Continuous variables were expressed as Mean ± Standard Deviation (SD) for normally distributed parameters and median of interquartile ranges for non-normal distributions. Categorical variables (gender mode of delivery maternal diabetes type anti-glycemic treatment and hypoglycemia status) were reported as absolute frequencies (n) and percentages (%). dataset was stratified by age gender birth weight gestational age maternal diabetes type anti-glycemic regimen delivery mode labor duration and Apgar score. Post-stratification Chi-square ($\chi^2$) tests were executed to compare stratified groups for hypoglycemia occurrence. two-tailed p-value ≤ 0.05 was considered statistically significant.

**RESULTS**

The total of 150 neonates fulfilling all pre-defined inclusion and exclusion criteria were successfully evaluated. Data were processed to determine primary frequency of neonatal hypoglycemia and analyze secondary demographic and clinical relationships.

**Primary Outcome: Frequency of Neonatal Hypoglycemia**

Among 150 infants delivered to mothers of history of diabetes 60 infants were diagnosed of neonatal hypoglycemia based on presentation blood glucose < 40 mg/dL establishing overall primary study frequency of 40.0% (95% CI: 32.1% - 48.3%). remaining 90 infants (60.0%) were normoglycemic (≥ 40 mg/dL).

**Table 1: Frequency Distribution of Neonatal Hypoglycemia (N = 150)**

| Outcome Category | Operational Definition | Frequency (n) | Percentage (%) |
|---|---|---|---|
| **Neonatal Hypoglycemia** | **Blood Glucose < 40 mg/dL** | **60** | **40.0%** |
| Normoglycemia | Blood Glucose ≥ 40 mg/dL | 90 | 60.0% |
| **Total** | — | **150** | **100.0%** |

Observed 40.0% frequency of neonatal hypoglycemia validates study rationale and aligns of internationally published rates (38.3% reported by Begum et al. 2018). These findings confirm that acute early postnatal glucose

drop is widespread metabolic issue in infants born to diabetic mothers in local population highlighting critical need for mandatory blood glucose screening protocols immediately following birth.

### Baseline Demographic and Clinical Characteristics

sample comprised 79 male infants (52.7%) and 71 female infants (47.3%). Shapiro-Wilk test was applied to assess normality across continuous parameters. Birth weight gestational age and blood glucose demonstrated normal distributions ($p > 0.05$) while age at presentation duration of labor and Apgar score deviated from normality ($p < 0.05$).

**Table 2: Descriptive Statistics of Continuous Study Variables (N = 150)**

| Variable | Mean | Std. Deviation | Median | Min - Max | Shapiro-Wilk p-value |
|---|---|---|---|---|---|
| Age at Presentation (hours) | 6.94 | 3.49 | 7.00 | 1.00 - 12.00 | < 0.001 |
| Birth Weight (kg) | 3.22 | 0.44 | 3.24 | 1.74 - 4.50 | 0.571 |
| Gestational Age (weeks) | 37.56 | 1.52 | 37.55 | 34.10 - 41.50 | 0.578 |
| Duration of Labor (hours) | 9.67 | 3.62 | 9.00 | 4.00 - 16.00 | < 0.001 |
| Apgar Score (5 minutes) | 8.27 | 0.83 | 8.00 | 7.00 - 10.00 | < 0.001 |
| Blood Glucose Level (mg/dL) | 42.83 | 11.88 | 41.50 | 20.00 - 73.00 | 0.148 |



### Maternal Clinical Profile and Stratification Analysis

Gestational diabetes mellitus was diagnosed in 107 mothers (71.3%) whereas chronic pre-existing diabetes was present in 43 mothers (28.7%). Maternal anti-glycemic treatments included oral hypoglycemics in 49 cases (32.7%) dietary control in 41 cases (27.3%) insulin monotherapy in 39 cases (26.0%) and dual therapy (oral + insulin) in 21 cases (14.0%). Post-stratification Chi-square tests revealed highly significant associations between maternal diabetic parameters and neonatal outcome.

**Table 3: Post-Stratification Chi-Square Analysis for Neonatal Hypoglycemia**

| Factor | Sub-category | Hypo-glycemia (n=60) | Normo-glycemia (n=90) | Total (N=150) | Rate (%) | $\chi^2$ Value | p-value |
|---|---|---|---|---|---|---|---|
| Type of Diabetes | Chronic Diabetes | 34 | 9 | 43 | **79.1%** | 36.091 | **< 0.001*** |
| | Gestational Diabetes | 26 | 81 | 107 | **24.3%** | | |
| Anti-Glycemic Meds | Both (Oral + Insulin) | 17 | 4 | 21 | **81.0%** | 65.842 | **< 0.001*** |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Insulin Monotherapy | 30 | 9 | 39 | **76.9%** | | |
| | Oral Hypoglycemics | 12 | 37 | 49 | **24.5%** | | |
| | Dietary Control | 1 | 40 | 41 | **2.4%** | | |
| Infant Gender | Male | 34 | 45 | 79 | **43.0%** | 0.402 | **0.526** |
| | Female | 26 | 45 | 71 | **36.6%** | | |
| Delivery Mode | Vaginal Delivery | 35 | 49 | 84 | **41.7%** | 0.091 | **0.763** |
| | Cesarean Section | 25 | 41 | 66 | **37.9%** | | |

**Comparison of Continuous Parameters by Hypoglycemic Status**

Independent sample t-tests were performed to evaluate differences in continuous parametric measures between hypoglycemic and normoglycemic cohorts.

**Table 4: Comparison of Continuous Variables Between Outcome Groups**

| Parameter | Hypoglycemic (n=60) | Normoglycemic (n=90) | t-statistic | p-value |
|---|---|---|---|---|
| Blood Glucose Level (mg/dL) | 31.40 ± 5.98 | 50.44 ± 8.13 | -15.553 | **< 0.001*** |
| Birth Weight (kg) | 3.18 ± 0.45 | 3.25 ± 0.42 | -0.971 | 0.333 |
| Gestational Age (weeks) | 37.42 ± 1.62 | 37.65 ± 1.45 | -0.922 | 0.358 |
| Duration of Labor (hours) | 8.77 ± 3.30 | 10.27 ± 3.73 | -2.528 | **0.013*** |
| Apgar Score (5 minutes) | 8.25 ± 0.79 | 8.28 ± 0.86 | -0.200 | 0.842 |



**Impact of Maternal Diabetes Subtype:** Infants delivered to mothers of chronic pre-existing diabetes suffered significantly higher hypoglycemia rate (79.1%) compared to those born to mothers of gestational diabetes (24.3% $p < 0.001$). Chronic maternal hyperglycemia results in prolonged fetal pancreatic exposure inducing pancreatic beta-cell hyperplasia and post-partum hyperinsulinemia.

**Role of Maternal Medication Regimen:** Maternal requirement for exogenous insulin monotherapy (76.9%) or dual therapy (81.0%) served as strongest clinical predictor of neonatal hypoglycemia ($p < 0.001$). In contrast mothers whose glucose was managed solely via dietary modification had extremely low neonatal hypoglycemia incidence (2.4%). This highlights that maternal exogenous insulin dependency directly mirrors fetal hyperinsulinemic state.

**Lack of Gender and Delivery Mode Bias:** Neither infant gender ($p = 0.526$) nor mode of delivery ($p =$

0.763) demonstrated statistically significant differences in hypoglycemia development indicating that metabolic risk is driven primarily by maternal glycemic control rather than mechanical or demographic variables.

**Birth Weight and Gestational Age Independence:** No statistically significant differences were observed in birth weight ($p = 0.333$) or gestational age ($p = 0.358$) between hypoglycemic (3.18 kg) and normoglycemic (3.25 kg) infants confirming that hypoglycemia risk cuts across birth weight spectrums in diabetic pregnancies.

## DISCUSSION

Transition from intrauterine to extrauterine life represents critical physiological adaptation requiring neonate to shift rapidly from continuous transplacental maternal glucose transfer to autonomous endogenous glucose production through glycogenolysis and gluconeogenesis. In infants delivered to diabetic mothers (IDMs) this delicate homeostatic mechanism is severely disrupted by maternal-fetal metabolic dysregulation. present cross-sectional study was undertaken at Imran Idrees Teaching Hospital Sialkot to evaluate frequency of neonatal hypoglycemia among infants born to diabetic mothers and to identify primary clinical determinants modulating this risk within our local population.

In our study cohort of 150 neonates primary outcome demonstrated neonatal hypoglycemia (blood glucose < 40 mg/dL) frequency of 40.0% (n = 60) within first 1 to 12 hours of life. This finding validates initial study premise and confirms that acute early glucose instability remains dominant metabolic complication in local neonatal care. observed 40.0% rate is consistent of regional and international literature which reports neonatal hypoglycemia frequencies ranging between 30% and 45% among IDMs. For instance recent prospective multi-center study by Sharma et al. (2022) identified neonatal hypoglycemia in 38.6% of infants born to diabetic mothers attributing this high burden to sub-optimal maternal glycemic control during third trimester[8]. Similarly Al-Jassim et al. (2021) reported 41.2% incidence of transient hypoglycemia among IDMs in tertiary care setting[9]. subtle elevation in our observed rate relative to historical controls can be explained by delayed maternal diagnosis limited access to continuous glucose monitoring and inconsistent compliance of dietary and pharmacological interventions prior to delivery in regional settings[10].

Pathophysiologically high occurrence of hypoglycemia in IDMs is best explained by classical Pedersen hypothesis. Maternal hyperglycemia leads to sustained transplacental glucose diffusion into fetal circulation triggering fetal pancreatic beta-cell hyperplasia and chronic hyperinsulinemia[11]. Following delivery abrupt clamping of umbilical cord terminates maternal glucose influx while neonate's hyperinsulinemic state persists. High circulating fetal insulin levels suppress hepatic glycogenolysis and gluconeogenesis while simultaneously augmenting peripheral tissue glucose uptake culminating in rapid post-partum glycemic drop.

Post-stratification analysis in our study revealed profound statistically significant association between maternal diabetes subtype and occurrence of neonatal hypoglycemia ($\chi^2 = 36.091$ $p < 0.001$). Infants born to mothers of chronic pre-existing diabetes exhibited striking hypoglycemia frequency of 79.1% (n = 34/43) whereas those born to mothers of gestational diabetes mellitus (GDM) had significantly lower frequency of 24.3% (n = 26/107). This disparity is biologically plausibly grounded in duration and severity of maternal glycemic exposure[12]. Pre-existing diabetes exposes developing embryo and fetus to maternal hyperglycemia throughout organogenesis and entire gestation resulting in more pronounced pancreatic beta-cell hypertrophy and

impaired counter-regulatory hormonal responses (such as glucagon and epinephrine secretion) post-delivery. Conversely GDM typically manifests during second or third trimester (after 20 weeks of gestation) shortening duration of fetal hyperinsulinemic conditioning. These findings mirror those of Martinez-Cruz et al. (2023) who observed that infants of mothers of pregestational Type 1 and Type 2 diabetes were 3.2 times more likely to develop severe neonatal hypoglycemia than those of mothers of GDM[13].

secondary crucial clinical determinant identified in our investigation was maternal anti-glycemic treatment regimen ($\chi^2 = 65.842$ $p < 0.001$). Neonates whose mothers required exogenous insulin monotherapy or combination/dual therapy (oral agents plus insulin) experienced hypoglycemia rates of 76.9% (n = 30/39) and 81.0% (n = 17/21) respectively. In sharp contrast infants born to mothers managed strictly of dietary control experienced extremely low hypoglycemia incidence of 2.4% (n = 1/41) while those whose mothers were managed on oral hypoglycemic agents demonstrated moderate rate of 24.5% (n = 12/49). Maternal insulin requirement during pregnancy serves as direct clinical proxy for severe underlying maternal insulin resistance and marked glycemic variability[14]. Mothers requiring high daily units of insulin or escalation to dual therapy typically exhibit higher postprandial glucose peaks which drive exaggerated fetal hyperinsulinemia. Furthermore recent insights by Weber et al. (2022) suggest that maternal insulin regimen intensity correlates directly of impaired neonatal fatty acid oxidation and blunted ketone body production depriving newborn brain of alternative metabolic substrates during early hypoglycemia. low incidence seen in our dietary control subgroup highlights that well-managed mild gestational dysglycemia carries minimal risk of profound neonatal metabolic derangement[15].

Regarding demographic and mechanical confounding factors our analysis showed no statistically significant differences in neonatal hypoglycemia frequencies across infant gender ($\chi^2 = 0.402$ $p = 0.526$; 43.0% in males vs. 36.6% in females) or mode of delivery ($\chi^2 = 0.091$ $p = 0.763$; 41.7% in vaginal delivery vs. 37.9% in cesarean section)[16]. Similarly continuous parameters such as mean birth weight (3.18 ± 0.45 kg in hypoglycemic vs. 3.25 ± 0.42 kg in normoglycemic infants $p = 0.333$) gestational age (37.42 ± 1.62 vs. 37.65 ± 1.45 weeks $p = 0.358$) and 5-minute Apgar scores (8.25 ± 0.79 vs. 8.28 ± 0.86 $p = 0.842$) were comparable between both outcome groups. These findings are clinically reassuring as they indicate that neonatal hypoglycemia in IDMs is governed almost exclusively by maternal-fetal metabolic dynamics rather than mechanical or perinatal asphyxial stresses. Work by Chen et al. (2024) similarly concluded that birth weight category alone is poor isolated predictor of hypoglycemia in IDMs when maternal antenatal glucose profiles are controlled[17].

Interestingly statistically significant difference was observed in duration of labor between groups (8.77 ± 3.30 hours in hypoglycemic vs. 10.27 ± 3.73 hours in normoglycemic infants $p = 0.013$). Shorter labor duration in hypoglycemic group may reflect higher proportion of planned elective surgical deliveries or rapid induced labor in high-risk diabetic pregnancies resulting in less stress-induced endogenous catecholamine surge prior to delivery which normally stimulates early neonatal gluconeogenesis[18].

### Clinical Implications and Recommendations

high prevalence (40.0%) of neonatal hypoglycemia observed in this study underscores urgent necessity of establishing standardized institutional protocols for routine point-of-care blood glucose monitoring in all infants born to diabetic mothers regardless of birth weight or delivery mode[19]. Blood glucose screening should be initiated within 30 to 60 minutes of life and repeated prior to feeds during first 24 to 48 hours. Special clinical vigilance must be directed toward neonates delivered to mothers of chronic pre-existing diabetes or those requiring insulin therapy during pregnancy. Early initiation of breastfeeding or oral

dextrose gel administration in high-risk infants can prevent severe asymptomatic glucose drops and reduce unnecessary neonatal intensive care unit (NICU) admissions[20].

### Study Limitations

This study has several noteworthy limitations. First its single-center cross-sectional design at tertiary teaching hospital may introduce selection bias as high-risk diabetic mothers are more frequently referred to our institution. Second maternal HbA1c levels during third trimester were not uniformly available for all participants to correlate exact long-term glycemic control of neonatal outcomes. Third blood glucose was measured using point-of-care capillary glucometers; while standard practice in clinical settings confirmation via laboratory plasma hexokinase methods provides greater accuracy at very low glucose thresholds. Future multi-center prospective studies incorporating continuous glucose monitoring data and long-term neurodevelopmental follow-up are recommended.

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