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*Research Article*

# Neurodevelopmental Outcome in Infants of Gestational Diabetic Mother in a Tertiary Care Hospital, Dhaka, Bangladesh

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## Abstract

Background: Diabetes Mellitus (DM) is one of the most common metabolic complications of pregnancy, with negative influences on maternal and fetal health. Infants of Diabetic Mothers (IDMs) are prone to develop both early and late complications. Evidences shows that diabetes in pregnancy have strong association with long-term adverse effects on brain development in babies born to mothers with gestational diabetes mellitus. Very few studies were done in this subcontinent regarding association of gestational diabetes mellitus and infant's neurodevelopmental outcome. This study will help to find out this associations and thus to reduce poor neurodevelopmental outcome in infants of diabetic mothers by early detection and providing proper early childhood stimulation.

Objective: To assess the neurodevelopmental outcome of infants born to mother with gestational diabetes mellitus.

Methodology: This prospective observational study was conducted in the department of Neonatology and Institute of Pediatric Neurodisorder and Autism (IPNA), BSMMU, from March 2022 to September 2023. Neonates (N= 52) born at or after 34 weeks of gestation and born to gestational diabetic mother were enrolled in this study. Consent was taken from guardians. The newborns fulfilling the inclusion criteria were followed up for neurodevelopmental assessment at their 9 months of age by clinical psychologists assigned from Institute of Pediatric Neurodisorder and Autism (IPNA), BSMMU, who were blinded about infant's diagnosis. Bayley scales of infant and toddler development (BSID III) was used for developmental assessment. In the Bayley III, cognitive development, expressive and receptive language and fine and gross motor development all were evaluated at 9 months of age. All data were recorded in a preformed questionnaire and analyzed by Statistical Package for Social Sciences (SPSS), version 25.

Results: According to inclusion and exclusion criteria 58 newborn were enrolled and their blood samples were sent at 24 to 48 hours of age to see the laboratory parameters of metabolic and hematological profile. Among them 6 patients lost to follow up, so 52 infants were followed up for neurodevelopmental outcome at 9 months of age. Among the baseline characteristics of mother and neonate 48% mother needed drugs for glycemic control, while others were on dietary modification and 75% of the mothers had good glycemic control. Most of the neonate were born at term and were age appropriate, 18 patients needed NICU admission. Among the neonatal laboratory parameters hyperbilirubinemia was most common (30.8%) and hypoglycemia was second most common found in 15.4% of newborns. The most common morbidity was sepsis (17.3%). Overall adverse neurodevelopmental outcome was found among 14 (26.9%) neonate and 38 (73.1%) neonates had favorable outcome. Use of

drugs and poor maternal glycemic control were found statistically significant in between adverse and favorable groups. (p-value- 0.041 and 0.000). Among the neonatal clinical parameters only hypoglycemia was found statistically significant in between these two groups. (p-value- 0.014) Multivariate logistic regression among these predictive factors showed only maternal poor glycemic control was significantly associated with adverse neurodevelopmental outcome (p-value=0.001).
Conclusion: Maternal gestational diabetes can adversely affect on their infants neurodevelopment. Among the adverse outcome of three domains language delay was most common. Neonatal hypoglycemia, maternal poor glycemic control and use of drugs for GDM are significant predictors of adverse neurodevelopmental outcome in infants of gestational diabetic mother. Among them maternal poor glycemic control was significantly associated with adverse neurodevelopmental outcome.

**Keywords:** Gestational Diabetes Mellitus; Infant of Diabetic Mother; Neurodevelopmental Outcome

## Introduction

Diabetes Mellitus (DM) is one of the most common medical complications in pregnancy that substantially influences children's health. About 1- 14% of all pregnancies are complicated by diabetes mellitus, among them 90% are GDM [1]. The global prevalence of GDM is 14.7% based on the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria [2]. A study done in Bangladesh to determine the prevalence of GDM for the first time among women in Bangladesh by using the World Health Organization (WHO) and the new American Diabetes Association (ADA) criteria which showed that the prevalence of GDM was 9.7% according to WHO criteria and 12.9% according to the ADA criteria [3]. But overall prevalence of GDM in Bangladesh is 35%, based on WHO (2013) criteria [4]. Also, World Health Organization (WHO) has been predicted that between 1995 and 2025, prevalence of diabetes will increases by 35% in the world wide. According to the 7th International Diabetes Federation Diabetes Atlas in 2015, 20.9 million (16.2%) live births were affected with hyperglycemia in pregnancy and around 85.1% of those were because of GDM. So, now it has become a serious public health issue. Women in Asian countries display the highest prevalence of GDM. About 17% of Asian women are likely to develop GDM in comparison to 4% of European and white American women [5]. Gestational Diabetes Mellitus (GDM) is defined as glucose intolerance which begins during 2nd trimester of pregnancy, from 24 to 28 weeks, but high risk mothers may affect earlier. Though, in some cases GDM may be of pre-existing diabetes, that were yet undiagnosed [6]. The hormonal changes of the body are related to the pathophysiology and etiology of GDM. With the progression of gestation as insulin sensitivity decreases it results increase of blood glucose levels. So, to maintain the normal blood glucose, the body compensates it by increasing insulin secretion. So, when the body will no longer be able to adapt with this new circumstances and thus, when the endocrine system is unable to produce adequate insulin, GDM occurs [7]. Both maternal and fetal perinatal morbidity and mortality is also high among GDM mothers in Bangladesh [8]. Gestational diabetes can interact with the infant's micronutrient status, birth anthropometrics and has effect even on the offspring's neurodevelopment. Brain development in fetus and in early childhood is very important as it determines their lifelong performance in various neuropsychological domains such as cognition, language and motor functions [9]. It has been observed that the last trimester of pregnancy is the most important period of neuronal determination, synaptogenesis and dendritic arborization [10]. It is evidenced that maternal diabetes have serious harmful effects on the developing fetus and during pregnancy, the hyperglycemic environment of the intrauterine life negatively impacts fetal neural development [11,12]. The growth spurt of the brain occurs approximately from the beginning of the third trimester of pregnancy and a diabetic pregnancy generates an adverse intrauterine environment which can cause neurodevelopmental impairment of the fetus and thus induces critical limitations on its future cognitive abilities either in infancy or in childhood [13]. Various studies have addressed the question of possible brain damage induced by diabetes during the second half of pregnancy, which may result in deficits in cognitive function. Some studies also suggested that GDM adversely affect the motor functions of offspring [14]. A literature review showed that, GDM is a powerful risk factor for motor developmental delay and was associated with reduced motor development in children [15]. Poor motor development in infants and children may have long-term negative consequences for a child's future development and often indicative of more generalized developmental delays and disabilities in children [16,17]. Also several studies have suggested that children born to mothers with gestational diabetes develop language delay, impaired recognition memory, poor motor development and neuropsychological impairment at different stages of childhood [18]. It is evidenced by several studies that, the fetal exposure to maternal diabetes during pregnancy later increase the risk for reduced language abilities in the child and shown in several studies that intrauterine exposure to maternal diabetes can initiate negative language outcomes for children [11]. Early diagnosis of these developmental disabilities is a critical responsibility of pediatric professionals. This prospective study is done to evaluate the neurodevelopmental outcome in all the three domains in infants of mother having gestational diabetes and to identify the risk factors associated with abnormal outcome.

**Material and Methods**

*Study Design*

Prospective observational study.

*Place of Study*

Department of Neonatology and Institute of Pediatric Neurodisorder and Autism (IPNA), Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, Bangladesh.

*Study Population*

Newborns born at or after 34 weeks of gestation to a mother with gestational diabetes mellitus delivered in BSMMU.

*Selection of Patient*

*Inclusion criteria:*

- All inborn neonates born to mother with gestational diabetes at or after 34 weeks of gestational age.

*Exclusion criteria:*

- Major congenital anomalies
- Syndromic manifestations
- Perinatal asphyxia with moderate to severe encephalopathy
- Out born infants of diabetic mother
- Infants born to mother with pregestational diabetes
- Parental refusal to come for follow up

*Sample Size*

52

This prospective observational study was conducted over a period of eighteen months in the Department of Neonatology and Institute of Pediatric Neurodisorder and Autism (IPNA), BSMMU, Shahbag, Dhaka after approval of IRB. Gestational diabetic pregnancy were assessed for eligibility by reviewing OT list and mother's file. Verbal consent was taken from father and legal guardian of possible eligibility of the newborn. Thesis activities were briefly explained including possible enrollment and follow up. After delivery written consent was taken from parents and legal guardian and assurance about confidentiality was given. During reviewing of mother's file those with incomplete information or data were excluded from this study.

All pregnant women with a positive oral glucose tolerance test at 24–28 weeks of gestation or later, were considered as GDM by obstetrician. Diagnosis was done as per the International Association of Diabetes and Pregnancy Study Groups (IADPSG) 2010 criteria: fasting glucose ≥ 5.1 mmol/L (92 mg/dL) or 2-hour glucose ≥ 8.5 mmol/L.

All inborn neonates born to mothers with gestational diabetes mellitus and gestational age more or equal to 34 weeks from postnatal ward and if admitted in NICU both were enrolled. Gestational age was calculated by from first day of Last Menstrual Period (LMP). In case of unavailability of LMP, first trimester ultrasonogram scan was used.

Data about maternal history i.e. age, parity, OGTT, FBS, HbA1C, drugs uses for diabetes in pregnancy, status of glycemic control, multiple gestation, pregnancy induced hypertension, preeclampsia, maternal risk factors for sepsis like PROM, UTI, chorioamnionitis all were collected using a structured questionnaire.

Neonatal records regarding gestational age, mode of delivery (vaginal/cesarean), information regarding perinatal depression at birth, APGAR score at 1$^{st}$ and 5$^{th}$ minutes were collected by using structured questionnaire. The newborn's weight was taken without clothing soon after birth on a digital weighing scale (Beurer Baby scale BY 80, Germany) with a precision of ± 5 gm.

A detailed physical examination of the newborn to assess the general condition with emphasis on birth trauma, cardiac, respiratory system examination were carried out at birth. All required information for each neonate were recorded in a data

collection form. For blood sugar, samples were obtained from the heel of foot by prick method by resident doctors and checked on glucometer according to NICU protocol. Abnormal values if found were also checked by corresponding blood glucose (RBS) from laboratory.

Babies who developed clinical jaundice were followed with serial transcutaneous bilirubin levels measured by Transcutaneous Bilirubinometer (Model: Dregger JM-103). When transcutaneous bilirubin exceeded sending level, then 1.5 ml of venous blood was sent in a plain tube to the Department of Biochemistry and Molecular Biology of BSMMU for measuring Total Serum Bilirubin by spectrophotometric method using a fully automated analyzer (SIEMENS Healthneers Atellica CH Analyzer, Germany).

All babies were investigated to see hematocrit, Serum. Calcium, Serum. Magnesium at their 24-48 hours of age, 4 ml blood was taken into 2 tubes: (each tube containing 2 ml blood). EDTA (ethylene diamine tetra acetic acid) tube for HCT which is sent to Laboratory Medicine Department of BSMMU and analyzed by cell counter method in a automated analyzer.

The other blood sample was sent in a plain tube for calcium and magnesium and sent to the Department of Biochemistry and Molecular Biology, BSMMU. The blood was centrifuged at ×3000 RPM for 5 min and the serum was collected. S. Calcium and S. magnesium were measured by atomic absorption spectrometry method.

In case of admitted patient data about duration of hospital stay, features of sepsis, shock, respiratory distress were collected and documented in a data collection form. During and prior to discharge again a brief counseling regarding the study that neurodevelopmental follow up at 9 months of age for neurodevelopmental assessment was done, communication procedure was explained and contact no was given.

After discharge regular communication was maintained by monthly phone calls and by WhatsApp text with parents up to 9 months of age to ensure follow up. Among enrolled newborn those who were admitted in NICU were followed in IPNA as per NICU, BSMMU protocol.

Detailed neurodevelopmental assessment was done at 9 months of postnatal age using Bayley Scales of Infant and Toddler Development third edition by clinical psychologists assigned from the department of Institute of Pediatric Neurodisorder and Autism (IPNA), who were blinded about infant's clinical information. In the Bayley III the cognitive, receptive and expressive language, gross and fine motor developmental score of preterm infants were evaluated. In BSID III for assessment of raw score for cognitive domain 91 items, for receptive and expressive language domain 23 and 49 items respectively and from fine and gross motor domain respectively 66 and 72 items were seen. By assessing these items, psychologists derives raw scores for each domain which later converted to scaled scores and then to composite scores from BSID manual. It took between 45-60 minutes to do the whole assessment.

Developmental delay was classified as "delayed" if a Bayley III composite score below 70 on any of the subscales. Outcome was recorded as "favorable'' outcome if normal neurologic development and "adverse" developmental outcome defined as delay in one or more developmental domains: cognition, receptive and expressive language and gross and fine motor functions.

*Statistical Analysis*

After collecting the data, it was entered in a personal computer. Then edited, analyzed, plotted and were presented in graphs and tables. Categorical data were expressed as frequency and percentage and statistical test were done by chi-square test and quantitative data were expressed as mean ± SD and statistical test were done by student t test. Some categorical and quantitative data were also presented by graph and chart. Logistic regression analysis was used to test the association of variables with outcome. Statistical analyses were performed using the Statistical Package for Social Sciences for windows version 25 (SPSS.25), (IBM, USA). P-value <0.05 was considered as level of significance.

**Results**

A total of 123 newborns were screened for eligibility during delivery. Out of them 64 were excluded due to missing data in mother's file, not giving consent for blood sampling and denial for follow up visits. Later on 59 patients remained for final

assessment. One newborn who was admitted in NICU died during hospital stay, so lastly 58 enrolled newborn's blood samples were sent at 24 to 48 hours of age for analysis. Among them 6 patients lost to follow up, so finally 52 infants were followed up and assessed for neurodevelopmental outcome at 9 months of age (Fig. 1).

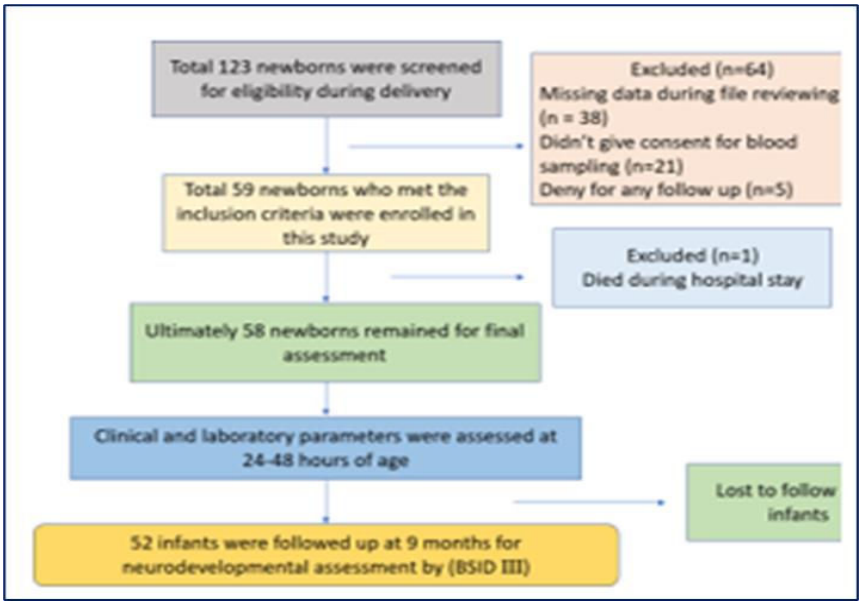


**Figure 1:** Flow chart of patient enrollment.

Baseline characteristics of the mothers of studied neonates are presented in Table 1. Mean maternal age was 27.36+ 5.18 years. Among them 56.1% were multipara, most of them (65.2%) had singleton pregnancy and had LSCS (83.3%). Fifty mothers (75.8%) got complete course of antenatal steroid.

| Parameter | Value (N=52) |
|---|---|
| **Maternal Age in years,** Mean ± SD | 29.52+ 5.32 |
| **Type of Gestation, n (%)** | |
| Single | 42(65.2) |
| Multiple | 10 (34.8) |
| **Mode of delivery, n (%)** | |
| NVD | 5 (9.6) |
| LSCS | 47 (90.4) |
| **Hypertension, n (%)** | |
| Yes | 18 (34.6) |
| No | 34 (65.4) |
| **Polyhydramnios, n (%)** | |
| Yes | 6 (11.5) |
| No | 46 (88.5) |
| **Drugs used in GDM, n (%)** | |
| Yes | 25 (48.1) |
| No | 27 (51.9) |
| **Glycemic Control, n (%)** | |
| Good | 39 (75) |
| Poor | 13 (25) |
| Qualitative data were presented as number and percentage, Quantitative data were presented as mean ± SD, NVD - Normal Vaginal Delivery, LSCS - Lower Segment Cesarean Section, GDM- Gestational Diabetes Mellitus, SD - Standard Deviation. | |

**Table 1:** Maternal baseline characteristics of neonates (N=52).

Baseline characteristics of the studied neonates were presented in Table 2. Mean gestational age was 36.54 ± 1.63 weeks and mean birth weight was 2722.5 ± 660 gram. Most of the neonates belonged to term (51.9%) and normal birth weight (> 2500 g). Male and female ratio was 1.1:1. Most of them were appropriate for gestational age (65.4%). Five newborns had intrauterine growth restriction, about one third (34.6%) neonates needed neonatal intensive care admission, eight newborn had APGAR score less than 7/10 at 1st minute after birth.

| Parameter | Value (N=52) |
|---|---|
| **Gestational Age in weeks,** Mean ± SD | 36.54 ± 1.63 |
| **Gestational age category (weeks) n (%)** | |
| Preterm (34 to <37 weeks) | 25 (48.1) |
| Term (≥ 37 weeks) | 27 (51.9) |
| Birth weight in grams, Mean ± SD | 2722.5 ± 660 |
| **Birth weight category, n (%)** | |
| LBW (1500-2499 g) | 16 (30.8) |
| NBW (≥ 2500 g) | 36 (69.2) |
| **Fetal growth at birth, n (%)** | |
| Small for gestational age | 12 (23.1) |
| Appropriate for gestational age | 34 (65.4) |
| Large for gestational age | 6 (11.5) |
| **Intra Uterine Growth Restriction, n (%)** | |
| Yes | 5 (9.6) |
| No | 47 (90.4) |
| **Gender of the baby, n (%)** | |
| Male | 27 (51.9) |
| Female | 25 (48.1) |
| **Apgar score < 7/10 at 1st minute, n (%)** | **8 (15.4%)** |
| **NICU admission, n (%)** | |
| Yes | 18 (34.6) |
| No | 34 (65.4) |
| Qualitative data were presented as number and percentage, Quantitative data were presented as mean ± SD LBW- Low Birth Weight, NBW- Normal birth weight, NICU- Neonatal Intensive Care Unit. | |

**Table 2:** Neonatal baseline characteristics of studied neonates (N=52).

Clinical characteristics of enrolled neonates were shown in Table 3. Near about one third had hyperbilirubinemia (31%), thereafter hypoglycemia and polycythemia was found in 15% neonates, hypocalcemia was in 13.5% and few neonates had hypomagnesemia (9.6%). The most common morbidity of the studied newborns was sepsis (17.3%), thereafter respiratory distress (11.5%), around 4% patients had seizure and 2% newborn developed shock as a complication. Fig. 2 is showing the percentage of metabolic, hematological and clinical findings among studied neonates.

| Clinical Characteristics | Value(N=52) |
|---|---|
| Hyperbilirubinemia, n (%) | 16 (30.8) |
| Sepsis, n (%) | 9 (17.3) |
| Hypoglycemia, n (%) | 8 (15.4) |
| Polycythemia, n (%) | 8 (15.4) |
| Hypocalcemia, n (%) | 7 (13.5) |
| Respiratory distress, n (%) | 6 (11.5) |
| Hypomagnesemia, n (%) | 5 (9.6) |
| Seizure, n (%) | 2 (3.8) |
| Shock, n (%) | 1 (1.9) |
| Qualitative data were presented as number and percentage (%) | |

**Table 3:** Laboratory parameters and Clinical characteristics of neonates (N=52).

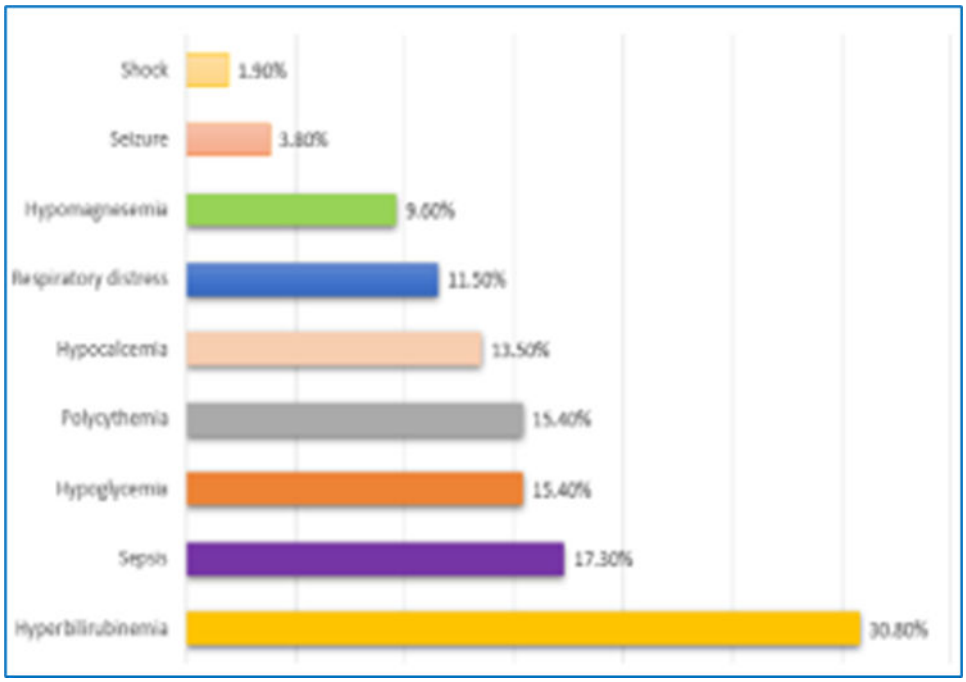


**Figure 2:** Metabolic, hematological and clinical findings among studied neonates (N=52).

The overall neurodevelopmental outcome of the infants of diabetic mother is shown in Fig. 3. Most of the infants (n=38) had favorable outcome, which is 73.1% of studied neonates. More than one fourth (26.9%) infants (n=14) had adverse neurodevelopmental outcome.

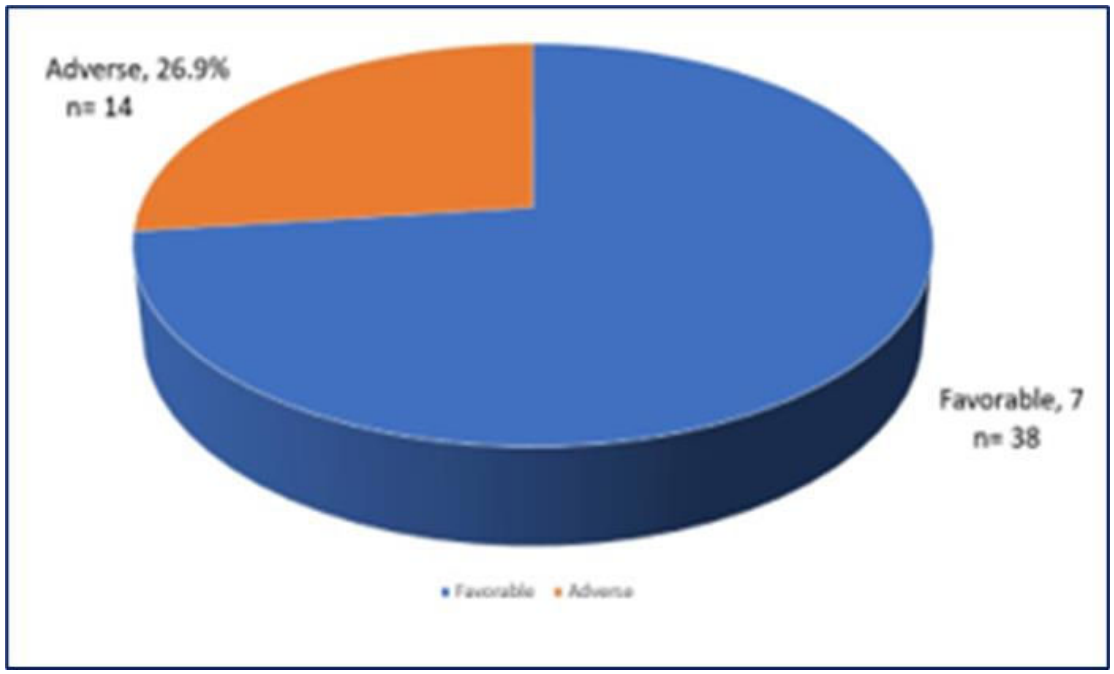


**Figure 3:** Neurodevelopmental outcome of studied neonates (N=52).

Most of the newborns had favorable outcome, 98% in cognition, 79% in language and 90% in motor development. Among the adverse outcome of three domain, 2% had cognitive delay, around one fourth had language delay (21.2%) and few had delay in motor domain (9.6%). (Table 4). In Fig. 4 is showing the difference between adverse and favorable outcome among the three domains.

| Parameters | Value (N=52) |
|---|---|
| **Cognition, n (%)** | |
| Favorable (score, 70-160) | 51 (98.1) |
| Adverse (score, 40-69) | 1 (1.9) |
| **Language, n (%)** | |
| Favorable (score, 70-160) | 41 (78.8) |
| Adverse (score, 40-69) | 11 (21.2) |
| **Motor, n (%)** | |
| Favorable (score, 70-160) | 47 (90.4) |
| Adverse (score, 40-69) | 5 (9.6) |
| Qualitative data were presented as number and percentage (%) | |

**Table 4:** Neurodevelopmental Outcome of enrolled neonates in follow up at 9 months of age (N= 52).

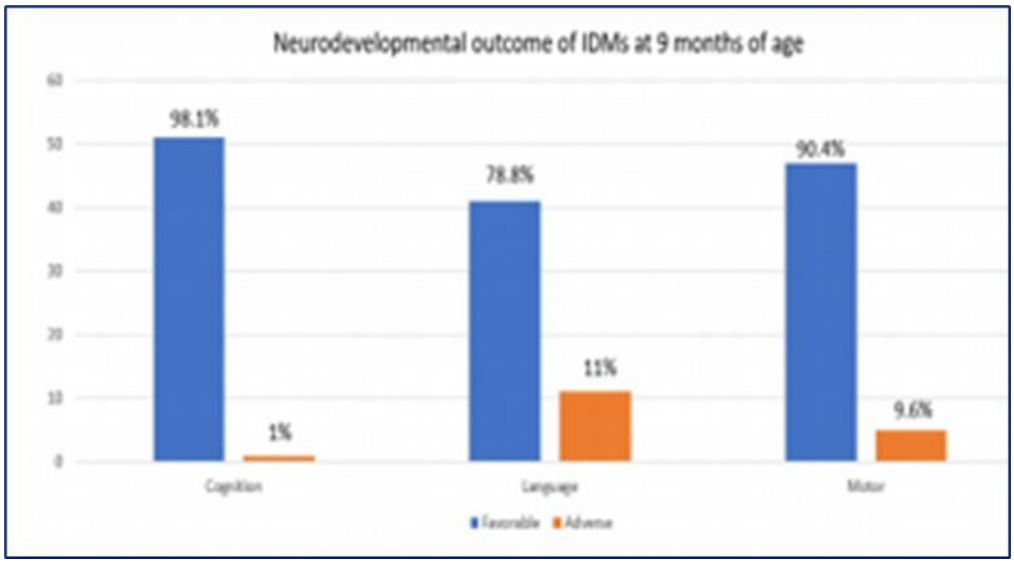


**Figure 4:** Neurodevelopmental outcome of infants at 9 months follow up.

Qualitative data were presented as number and percentage, Quantitative data were presented as mean ± SD. Statistical test: Chi square test and Independent t-test.

Maternal parameters were compared between the favorable and adverse outcome group. There were significant difference between two groups in respect to drugs (insulin or OHA) used in gestational diabetes mellitus and maternal glycemic control. (p-value- 0.041 and 0.000). Regarding other parameters such as maternal age, mode of delivery and hypertension there were no significant difference found (Table 5).

| Parameter | Favorable (n=38) | Adverse (n=14) | P-value |
|---|---|---|---|
| **Maternal Age in years,** Mean ± SD | 29.37± 5.12 | 29.93±6.01 | 0.740 |
| **Mode of delivery, n (%)** | | | |
| NVD | 4 (10.5) | 1 (7.1) | 0.714 |
| LSCS | 34 (89.5) | 13 (92.9) | |
| **Hypertension, n (%)** | | | |
| Yes | 11 (28.9) | 7 (50.0) | 0.157 |
| No | 27 (71.1) | 7 (50.0) | |
| **Drugs used in GDM, n (%)** | | | |
| Yes | 15 (39.5) | 10 (71.4) | **0.041** |
| No | 23 (60.5) | 4 (28.6) | |
| **Glycemic Control, n (%)** | | | |
| Good | 35 (92.1) | 4 (28.6) | 0.000 |
| Poor | 3 (7) | 10 (71.4) | |

**Table 5:** Comparison of Maternal factors between adverse and favorable outcome group (N= 52).

Qualitative data were presented as number and percentage, Quantitative data were presented as mean ± SD.

*Statistical Test*

Chi square test and Independent t-test Neonatal baseline characteristics were compared between the favorable and adverse outcome group. There were no significant difference between two groups in respect to birth weight, gestational age category, fetal growth at birth, intrauterine growth restriction, gender distribution, APGAR score and need for NICU admission (Table 6).

| Parameter | Favorable (n=38) | Adverse (n=14) | p-value |
|---|---|---|---|
| **Gestational Age in weeks,** Mean ± SD | 36.5 ± 1.5 | 36.64 ± 1.9 | 0.782 |
| **Gestational age category (weeks) n (%)** | | | |
| Preterm (34 to <37 weeks) | 19 (50.0) | 5 (35.7) | 0.500 |
| Term (≥ 37 weeks) | 18 (47.4) | 9 (64.3) | |
| **Birth weight in grams,** Mean ± SD | 2751.84 ±634.4 | 2642.86 ±745.0 | 0.602 |
| **Fetal growth at birth, n (%)** | | | |
| Small for gestational age | 8 (21.1) | 4 (28.5) | 0.568 |
| Appropriate for gestational age | 26 (68.4) | 8 (57.2) | 0.448 |
| Large for gestational age | 4(10.5) | 2(14.3) | 0.707 |
| Intra Uterine Growth Restriction, n (%) | 2 (5.3) | 3 (21.4) | 0.079 |
| **Gender of the baby, n (%)** | | | |
| Male | 22 (57.9) | 5 (35.7) | 0.156 |
| Female | 16 (42.1) | 9 (64.3) | |
| Apgar score <7/10 at 1$^{st}$ minute, n (%) | 5 (13.2%) | 3 (21.4%) | 0.463 |
| **NICU admission, n (%)** | | | |
| Yes | 13 (34.2) | 5 (35.7) | 0.919 |
| No | 25 (65.8) | 9 (64.3) | |

**Table 6:** Comparison of neonatal baseline characteristics between adverse and favorable outcome group (N= 52).

Multivariate regression analysis of factors affecting neurodevelopmental outcome in the studied newborns showed only maternal glycemic control was significantly associated with adverse neurodevelopmental outcome among the studied neonates. (p-value=0.001) (Table 7).

| Factors | 95% C.I. | | | p-value |
|---|---|---|---|---|
| | Odds ratio | Lower | Upper | |
| **Hypoglycemia** | 3.401 | 0.353 | 32.76 | 0.289 |
| **Drugs used in GDM** | 5.028 | 0.794 | 31.85 | 0.086 |
| **Glycemic control** | 25.05 | 3.954 | 158.7 | 0.001 |

**Table 7:** Multivariate logistic regression analysis of factors affecting neurodevelopmental outcome in enrolled neonates (N=52).

**Discussion**

It is well established that diabetes has been associated with maternal and perinatal morbidity and mortality both in short and long term. In this prospective observational study, 52 infants of gestational diabetic mother were recruited to see the association

between GDM and child's neurodevelopment and they were followed up at their 9 months of age. To justify whether any maternal factors and neonatal complications affecting the neurodevelopment of infant, some maternal factors and newborn's clinical, metabolic and hematological profile were seen. Newborn who developed any co-morbidities like sepsis, jaundice and/or respiratory distress were admitted in NICU and other's were kept mother's side in the postnatal ward. Both were followed up according to NICU protocol during hospital stay. Neonatal hypoglycemia, maternal poor glycemic control and maternal use of drugs for GDM was the predictive factors of adverse neurodevelopment. Among the predictive factors such as hypoglycemia, no baby developed symptomatic hypoglycemia as because early introduction of frequent feeding was ensured. Mother who needed drugs Mother who needed drugs for GDM either took insulin or Metformin as oral hypoglycemic agent. Though most of the mother had good glycemic control, adverse outcome was mostly found among the infants of mother who had poor glycemic control and it was significantly associated with adverse developmental outcome in this study. This study includes newborn with gestation 34 weeks or more, as less than 34 weeks neonates are more vulnerable to develop several serious co morbidities like sepsis, respiratory distress, jaundice, perinatal asphyxia, congenital anomalies, specially in this subcontinent. Similarly, in a multicenter study done in Montreal, Canada and Dublin, Ireland, they also excluded gestation of less than 32 weeks to avoid poor developmental outcome due to other co-morbidities [5]. In this study, the mean gestational age was 36.54 ±1.63 weeks. It is close to a previous study, where the mean gestational age was 37.92 ± 1.65 [19]. In the present study, the mean birth weight was 2722.5 ± 660 g which was lower than the previous study where the mean birth weight was 3596 ± 494 g [22]. This difference can be explained by that, in their study they recruited more number of obese mother getting insulin. In this study, lower segment cesarean section was needed in 90.4% cases which was quite higher than the previous study where LSCS was needed only for 51.1% cases [15]. This higher percentage of the LSCS may be explained by the fact, that this study was conducted in a tertiary care hospital, where most of the complicated pregnancies were dealt by the Feto-maternal medicine unit, with necessitating LSCS. However, a study explained that if LSCS done electively, it is associated with improved neonatal outcomes in terms of better APGAR scores at 5 minutes [15]. This findings was consistent with the present study, that this study found no low 5 min APGAR score among studied neonates.

In this study, more than half neonates were delivered at term (51.9 %), on the other hand a previous study found preterm deliveries were higher (51.1%) [20]. This difference can be explained by the fact that, in their study all diabetic mothers were with coexisting medical complications like pregnancy induced hypertension, chronic heart and renal disease. In this study 65.4% babies were AGA which is quite similar to a previous study done in Tamil Nadu, India, where they found 68% babies were age appropriate [21]. Maternal factors responsible for poor neurodevelopmental outcome in infants were evaluated in this study. As maternal complications, this study found (34.6 %) mother were hypertensive which is consistent with a previous study which showed that up to 10-30 % of women with gestational diabetes may develop hypertension in pregnancy [22]. In this study, 11.5 % mother had polyhydramnios which is similar to a previous study where they found that incidence of polyhydramnios is 11.6% [23]. In this study, 48.1% mother needed insulin or oral hypoglycemic agent as medication, where a study showed 57.1% mother needed insulin [24]. This contradictory findings can be explained by higher number of obese mother were included in their study. This study showed 13% diabetic mother had poor glycemic control which is differed from the previous study done in Tamil Nadu, India in 2018, where they got 58.1% mother had poor glycemic control [21]. This difference may be due to the fact that, they included all the mother getting insulin who were obese and overweight. When neonatal clinical and laboratory parameters were seen, this study found hypoglycemia was the second most common complication present in 15.4 % of patients. This result is not consistent with the result of a study where they found hypoglycemia was the most common complication among IDM and seen in 71.4% of neonates [25]. This difference can be explained by the fact that, this study was done in a tertiary level hospital where all the babies were strictly followed up in postnatal ward and frequent feeding was ensured and blood glucose level was checked routinely, which decreased the chance of developing hypoglycemia. Several studies have agreed that the incidence of hypoglycemia in infants of gestational diabetic mother was 12.9% to 59.4% [26-28]. In the present study hyperbilirubinemia was found as the most common complication seen in 30.8% of neonate where in a previous study they found 66.7% hyperbilirubinemia in IDM [25]. This larger difference may be due to strict monitoring of jaundice by measuring serial transcutaneous bilirubin and frequent follow up in this tertiary level hospital reduce the severity of jaundice. This study found polycythemia in 15.4 % cases, this findings was quite near to a study where they found 11% cases of polycythemia in IDMs [15]. In the present study 13.5% IDMs developed hypocalcemia, where in another study they found hypocalcemia in 22% of IDMs [15]. This difference may be explained by the fact, that they included most of the preterm babies in their study. Regarding clinical parameter this study found sepsis was the most common (17.3%) and respiratory distress was the second most common (11.5%) morbidities among IDMs, which differed from the study done in California, Los Angeles, where they showed respiratory distress

was more common and near about 48%, this bigger difference can be explained by the fact that they recruited all the newborns below 34 weeks in their study and respiratory distress is common in preterm babies [29]. This study showed neurodevelopmental outcome at 9 months by BSID III where cognitive, expressive and receptive language, fine and gross motor development was seen. There are several studies done in different subcontinent to see the neurodevelopmental outcome but they use other scale to assess the outcome like Bruininks Oseretzky test, Wechsler Preschool and Primary Scale of Intelligence, Ages and Stages Questionnaire (ASQ), TanakaBinet IQ scores and BSID II(mental developmental index and psychomotor developmental index). So far, only two studies used BSID III to see the outcome among diabetic mother.

This study found overall adverse outcome in 26.9% infants among them 1.9% had cognitive delay, which differed from the study where they found 6.5% delay in cognitive skills [12]. This difference may be in respect to the fact, that in this study more number of mother had good glycemic control. Also some author given this explanation that cognitive ability of offspring born to mothers with well controlled diabetes is usually normal unless complicated by other comorbidities [30]. The present study got 9.6% infants with motor delay, which was also lower from a study, where they found 14.6% and another study found 12.6% delay in motor development [12,31]. This lower percentage in this study also can be explained by this fact that having more number of mother with good glycemic control in this study. This study found language delay in 11% infants, this result differed in respect of lower percentage from the study where they found 26% of children born to diabetic mothers having low language abilities [19]. But this findings was in agreement with some studies in terms of that all these studies including the present study found a higher incidence of developmental language delay in infants born to diabetic mothers [19,24,32]. This finding was contradicting by a study where they found that children born to mothers with diabetes had a higher risk of developmental delay mainly in gross motor skills [33]. In a contrary, when some studies done with older children, showed no significant differences in developmental outcomes among the diabetic mother [32]. This can be explained by the statement given by a study where they stated that, younger children have poorer neurological functions as there is a gap in maturation of central nervous system, but older children can compensate for slight motor impairment as because this gap will compensate with age [30]. This statement was established in some studies as they didn't find any difference in cognitive scores in older children from 4 to 13 years born to GDM mothers [34,35]. When neonatal factors were compared with adverse and favorable outcome only hypoglycemia was found significantly associated with adverse outcome. This findings was consistent with a systematic review by where they found that neonatal hypoglycemia was significantly associated with developing long lasting adverse neurodevelopmental outcome.36 When maternal factors were compared with adverse and favorable outcome, maternal poor glycemic control and maternal use of drugs for GDM where found significantly associated with adverse outcome. In contrast with this findings a study showed that no significant difference was associated with maternal use of drugs for GDM [37]. This can be explained by the fact, that they only studied with the mother where on medication either oral (metformin) or insulin. When multivariate logistic regression was done among these factors only poor glycemic control was found significantly associated with adverse neurodevelopmental outcome. This finding was in agreement with several studies and systematic review [7,11,19]. Like this study, several studies were done to see the neurodevelopmental outcome among infants born to mother with gestational diabetes and most of the study was consistent with this statement that maternal gestational diabetes can adversely effect neurodevelopmental outcome of infants. Which is consistent with the findings of present study.

**Conclusion**

Maternal gestational diabetes can adversely affect on their infants neurodevelopment. Among the adverse outcome of three domains language delay was most common. Neonatal hypoglycemia, maternal poor glycemic control and use of drugs for GDM are significant predictors of adverse neurodevelopmental outcome in infants of gestational diabetic mother. Among them maternal poor glycemic control was significantly associated with adverse neurodevelopmental outcome.

**Limitations of the Study**

Long term follow-up couldn't be done. BSID III was not done by single clinical psychologist. Single follow up was done.

**Recommendations**

Further multicenter prospective studies with larger sample size and longer follow up can be done to give better insight of neurodevelopmental outcome of infants of diabetic mother. Each and every diabetic mother should enrolled in follow up clinic to identify the later co-morbidities of infant as well as neurodevelopment at earliest possible time hence intervention can be provided for better quality of life of the infants of diabetic mother.

**Conflict of Interest**

The authors declare that they have no conflict of interest.

**Author Contribution**

Contributed to concept and design, analysis and interpretation of data and drafting and revising of article; analysis and interpretation of data and revising article for intellectual content. All authors contributed to final approval of version to be published.

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