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Neurodevelopmental outcome of neonates with hypoglycemia in Erbil, Iraq

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ABSTRACT

Background and Objectives: Neonatal hypoglycemia is a frequent metabolic disturbance that may result in long-term neurodevelopmental impairment. This study evaluated the neurodevelopmental outcomes of neonates with hypoglycemia in Erbil, Iraq, and identified associated risk factors.

Methods: A prospective observational study was conducted from January 2023 to June 2024 involving 140 neonates with hypoglycemia (blood glucose < 40 mg/dL) admitted to two tertiary hospitals. Neurodevelopmental status was assessed at 6, 12, and 18 months using the Denver II and Bayley III scales.

Results: Among 140 infants (47.9% males; mean gestational age 37.75 ± 1.16 weeks; mean birth weight (BW) 2.73 ± 0.31 kg), 46 (32.9%) had normal development, 48 (34.2%) mild delay, 32 (22.9%) moderate delay, and 14 (10.0%) severe delay. Developmental delay significantly correlated with severity of hypoglycemia ($p < 0.001$), duration > 6 hours (95.4% of delays), low BW (<2.5 kg, $p < 0.001$), prematurity (<37 weeks, $p = 0.006$), and maternal diabetes ($p < 0.001$). Infants without delay had higher mean blood glucose (34.15 ± 2.22 mg/dL) and BW (2.94 ± 0.19 kg) ($p < 0.001$). Motor (38.3%) and language (34.0%) deficits were most common.

Conclusion: Neonatal hypoglycemia, especially when severe, prolonged, or associated with maternal diabetes and low BW, significantly increases the risk of neurodevelopmental delay. Early diagnosis and vigilant glucose management are essential for neuroprotection

Keywords: Bayley Scales, Developmental Disabilities, Gestational Age, Hypoglycemia, Infant

1. INTRODUCTION

The most common metabolic disorder in neonatal intensive care units all over the world is neonatal hypoglycemia (1). This condition poses a significant threat to the developing brain, as glucose serves as the primary energy source for neural tissue during the critical early postnatal period. The immature brain's heightened vulnerability to glucose deprivation stems from its limited glycogen stores, increased metabolic demands, and incomplete development of counter-regulatory mechanisms (2, 3).

The neurodevelopmental consequences of neonatal hypoglycemia have garnered increasing attention from pediatric researchers and clinicians globally. Recent systematic reviews demonstrate compelling evidence linking hypoglycemia to adverse neurological outcomes, including cognitive impairment, motor dysfunction, and behavioral abnormalities that persist well into childhood and beyond (2). The severity and duration of hypoglycemic episodes appear to correlate directly with the extent of neural damage, with prolonged episodes below critical glucose thresholds resulting in irreversible brain injury affecting regions such as the occipital cortex, hippocampus, and basal ganglia (4).

Contemporary research has established clear associations between the severity of hypoglycemic episodes and subsequent developmental delays. Studies employing advanced neuroimaging techniques reveal selective vulnerability of specific brain regions to glucose deprivation, particularly the superficial cortical layers and subcortical structures critical for motor and cognitive function (5). The pathophysiology involves complex mechanisms including excitotoxicity, oxidative stress, and disruption of normal myelination processes, ultimately culminating in neuronal death and permanent structural alterations (4).

Several landmark studies have provided crucial insights into the long-term implications of neonatal hypoglycemia. For instance, the study by Roeper et al. (2024) demonstrated that severe transitional neonatal hypoglycemia was associated with a 4.8-point reduction in full-scale IQ and significantly impaired visual-motor and fine motor functions at mid-childhood follow-up (6). Similarly, recent meta-analytical evidence by Diggikar et al. (2024) revealed that neonatal hypoglycemia significantly increased the risk of neurodevelopmental impairment, with odds ratios of 1.16 in early childhood and 3.67 in mid-childhood, alongside elevated risks for cognitive impairment (OR=2.12), visual-motor dysfunction (OR=3.33), and executive dysfunction (OR=1.99) (2).

The novelty of the present study lies in the comprehensive analysis of neurodevelopmental outcomes in hypoglycemic infants from Erbil, Iraq, where unique demographic characteristics and healthcare delivery systems may produce different risk profiles and outcomes compared to previously studied groups. Therefore, the present study aimed to evaluate the neurodevelopmental outcome of neonates with hypoglycemia in Erbil, Iraq.

2. METHODS AND MATERIALS

Study design and setting

This prospective observational study was conducted at Maternity Teaching Hospital and Raparin Pediatric Hospital in Erbil, Iraq, over a period of 18 months, from January 2023 to June 2024.

Participants

The study population comprised neonates admitted to the neonatal intensive care units (NICUs) of the participating hospitals who were diagnosed with hypoglycemia during the early neonatal period. Participants were selected through consecutive sampling, whereby all eligible neonates meeting the inclusion criteria during the study period were enrolled after obtaining informed written consent from their parents or legal guardians. The sample size was determined based on previous similar studies (7). Therefore, 140 neonates were enrolled to ensure adequate statistical power.

The study included singleton neonates with documented hypoglycemia (blood glucose (BG) <40 mg/dL or <2.2 mmol/L) measured by a laboratory-based analyzer (Roche Cobas c311) within the first 72 hours of life, gestational age (GA) ≥35 weeks, birth weight (BW) ≥1,800 g, and parental consent for participation and follow-up. Exclusion criteria included major congenital or chromosomal anomalies, severe perinatal asphyxia (Apgar <3 at 5 minutes or resuscitation >10 minutes), confirmed metabolic disorders, severe infections requiring prolonged antibiotics, parental refusal or inability to attend follow-ups, transfer before completion of management, or relocation outside the study area.

Data Collection

Data collection was initiated immediately upon diagnosis of hypoglycemia and continued through structured follow-up assessments at predetermined intervals. A comprehensive, pre-designed data collection form was utilized to systematically record demographic information, maternal characteristics, perinatal factors, and clinical parameters. Demographic data included infant's sex, date of birth, GA determined by last menstrual period and confirmed by early ultrasound examination, BW measured using calibrated electronic scales (Seca 374, Seca GmbH, Germany), and mode of delivery. Maternal information encompassed age, parity, presence of gestational diabetes mellitus, pre-existing diabetes, hypertensive disorders, and medications administered during pregnancy and labor.

Blood glucose measurements were obtained using capillary blood samples analyzed with a point-of-care glucometer (Accu-Chek Performa, Roche Diagnostics, Switzerland) for initial screening, with all hypoglycemic readings confirmed through venous blood samples analyzed using the laboratory-based Roche Cobas c311 chemistry analyzer. The severity of hypoglycemia was classified as mild (BG 30-40 mg/dL), moderate (20-30 mg/dL), or severe (less than 20 mg/dL). The duration of hypoglycemia was calculated from the time of first documented low glucose reading until sustained normoglycemia (BG greater than 45 mg/dL) was achieved for at least 12 consecutive hours. All hypoglycemic episodes, their management protocols including intravenous dextrose administration rates, and time to glucose normalization were meticulously documented.

Neurodevelopmental assessments were conducted by trained pediatricians and developmental specialists at 6, 12, and 18 months of corrected age using standardized, validated assessment tools. The Denver Developmental Screening Test II (DDST-II) was employed as the primary screening instrument, supplemented by the Bayley Scales of Infant and Toddler Development, Third Edition (BSID-III) for infants showing suspected delays or abnormalities. The DDST-II evaluated four

developmental domains: gross motor, fine motor-adaptive, language, and personal-social skills. Developmental outcomes were categorized as normal development, mild developmental delay (performance 1-2 standard deviations below the mean in one or more domains), or moderate to severe developmental delay (performance more than 2 standard deviations below the mean or delays in multiple domains). All assessments were performed in a quiet, comfortable environment with parents present, and each evaluation session lasted approximately 45-60 minutes.

Ethical Considerations

The protocol received approval from the research ethics committee of ministry of health. Written informed consent was obtained from parents or guardians prior to undertaking the research in accordance with regulatory and ethical standards. Participation was voluntary and participants were free to withdraw at any time without compromising care. Confidentiality was maintained through coded identifiers and data access was restricted. The study adhered to the Declaration of Helsinki (2013) and applicable local regulations.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation (SD). Associations between categorical variables were examined using the Chi-square test or Fisher's exact test when appropriate. Mean differences among groups were compared using one-way analysis of variance (ANOVA). Post-hoc Tukey tests were applied for multiple comparisons. A p-value <0.05 was considered statistically significant.

3. RESULTS

A total of 140 neonates with hypoglycemia were included in the study in Erbil, Iraq. Of these, 67 (47.9%) were males and 73 (52.1%) were females. The majority were delivered vaginally, accounting for 113 (80.7%), while 27 (19.3%) were delivered by cesarean section. The mean BW was 2.73 ± 0.31 kg, and the mean GA was 37.75 ± 1.16 weeks. The mean BG level recorded was 28.75 ± 6.86 mg/dL. Regarding the severity of hypoglycemia, 40 (28.6%) had mild, 71 (50.7%) had moderate, and 29 (20.7%) had severe hypoglycemia.

Table 1. Baseline Characteristics and Clinical Profiles of Neonates with Hypoglycemia.

Variables		N	%
Sex	Male	67	47.9
	Female	73	52.1
Mode of Delivery	Vaginal	113	80.7
	Cesarean	27	19.3
BW (kg)	Mean ± SD	2.73 ± 0.31	
GA (weeks)	Mean ± SD	37.75 ± 1.16	
BG (mg/dL)	Mean ± SD	28.75 ± 6.86	
Severity Hypoglycemia	Mild	40	28.6
	Moderate	71	50.7
	Severe	29	20.7
Final Outcome	Mild Delay	48	34.2
	Normal	46	32.9
	Moderate	32	22.9
	Severe	14	10.0

Concerning neurodevelopmental outcomes, 46 (32.9%) neonates had normal development, while 48 (34.2%) showed mild delay, 32 (22.9%) had moderate delay, and 14 (10.0%) exhibited severe developmental delay (Figure 1).

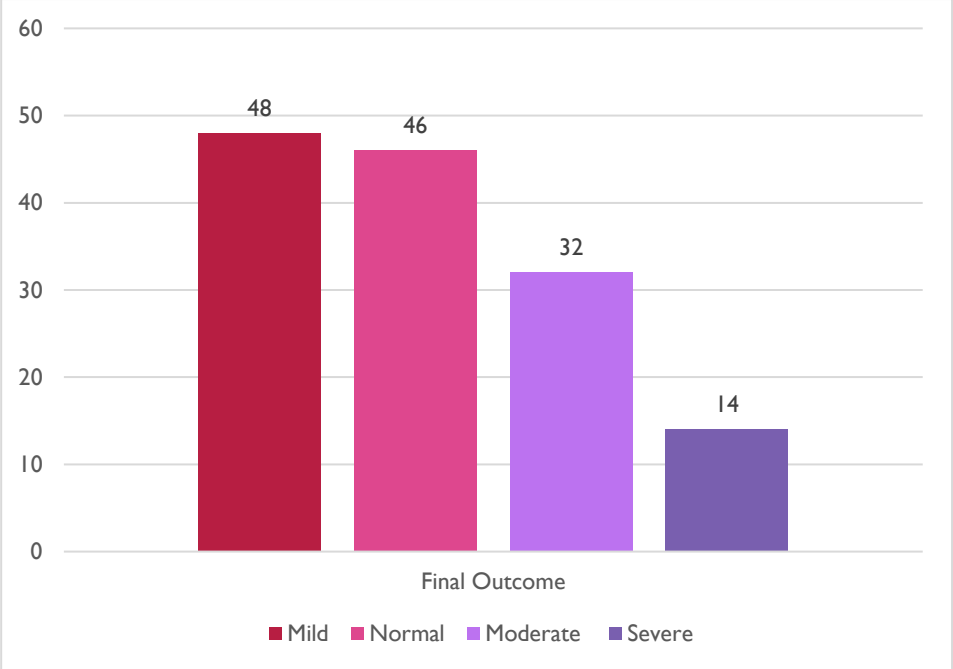

Figure 1. Neurodevelopmental outcomes.

A significant association was observed between the severity of neonatal hypoglycemia and neurodevelopmental outcomes ($p < 0.001$). Among infants with mild hypoglycemia, the majority 35 (87.5%) exhibited mild developmental delay, while only 3 (7.5%) had normal outcomes and 2 (5.0%) showed moderate delay, with none presenting severe delay. In the moderate hypoglycemia group, 43 (60.6%) infants demonstrated normal development, whereas 13 (18.3%) each experienced either mild or moderate delay, and 2 (2.8%) had severe delay. In contrast, severe hypoglycemia was strongly associated with adverse outcomes, as 17 (58.6%) of these neonates had moderate delay and 12 (41.4%) had severe delay, with no cases of normal or mild developmental outcomes.

Table 2. Neurodevelopmental Outcomes by Severity of Hypoglycemia

Severity of Hypoglycemia	Final Outcome				p-value
	Mild Delay	Normal	Moderate Delay	Severe Delay	
Mild	35 (87.5%)	3 (7.5%)	2 (5.0%)	0 (0.0%)	<0.001
Moderate	13 (18.3%)	43 (60.6%)	13 (18.3%)	2 (2.8%)	
Severe	0 (0.0%)	0 (0.0%)	17 (58.6%)	12 (41.4%)	

Among the 94 children who exhibited developmental delays, motor function was the most frequently affected domain, observed in 36 (38.3%) cases. Language development was delayed in 32 (34.0%) children, while cognitive delays were identified in 30 (31.9%). Additionally, multiple domains were affected concurrently in 29 (30.9%) children (Table 3).

Table 3. Developmental Domains Affected Among Children with Delays (n=94)

Developmental Domain Affected	N	%
Motor	36	38.3
Language	32	34.0
Cognitive	30	31.9
Multiple Domains	29	30.9

Several significant risk factors were identified as contributing to developmental delay among neonates with hypoglycemia. Maternal diabetes showed a strong association, as all 29 (100%) infants born to diabetic mothers experienced developmental delay ($p < 0.001$), contrasting with 46 (41.4%) without delay among those born to non-diabetic mothers. Low BW (<2.5 kg) was likewise a major factor, with 66 (98.5%) delayed cases compared to only 1 (1.5%) without delay ($p < 0.001$). Prematurity (<37 weeks) also played a role, as 14 (100%) preterm infants exhibited delays, whereas 46 (36.5%) term infants had normal development ($p = 0.006$). The duration of hypoglycemia demonstrated a significant relationship as well: delays occurred in 62 (95.4%) neonates with prolonged hypoglycemia (>6 hours) compared to only 32 (42.7%) delays among those with shorter episodes (<6 hours) ($p < 0.001$) (Table 4).

Table 4. Risk Factors Associated with Developmental Delay.

Risk Factor		No Delay (n=46)	Developmental Delay (n=94)	P-value
Maternal Diabetes	No	46 (41.4%)	65 (58.6%)	<0.001
	Yes	0 (0.0%)	29 (100%)	
Low BW (<2.5 kg)	No	45 (61.6%)	28 (38.4%)	<0.001
	Yes	1 (1.5%)	66 (98.5%)	
Preterm (<37 weeks)	No	46 (36.5%)	80 (63.5%)	0.006
	Yes	0 (0.0%)	14 (100%)	
Duration	>6 hours	3 (4.6%)	62 (95.4%)	<0.001
	<6 hours	43 (57.3%)	32 (42.7%)	
Mode of Delivery	Vaginal	38 (33.6%)	75 (66.4%)	0.691
	Cesarean	8 (29.6%)	19 (70.4%)	

Analysis using one-way ANOVA revealed significant differences in key clinical parameters between neonates with and without developmental delay. Infants with normal development had a higher mean BW (2.94 ± 0.19 kg) compared to those with developmental delay (2.62 ± 0.30 kg, $p < 0.001$). Similarly, the mean GA was greater among those without delay (38.06 ± 0.67 weeks) than in those with delay (37.33 ± 1.12 weeks, $p < 0.001$). BG levels were also markedly higher in the no-delay group (34.15 ± 2.22 mg/dL) compared to the delay group (26.11 ± 6.81 mg/dL, $p < 0.001$) (Table 5).

Table 5. Comparison of Mean Clinical Parameters between Neonates with and without Developmental Delay.

Variables	No Delay (n=46)	Developmental Delay (n=94)	P-value
BW (kg)	2.94 ± 0.19	2.62 ± 0.30	<0.001
GA (weeks)	38.06 ± 0.67	37.33 ± 1.12	<0.001
BG (mg/dL)	34.15 ± 2.22	26.11 ± 6.81	<0.001

4. DISCUSSION

Neonatal hypoglycemia is a condition that causes a major metabolic challenge to the newborn period that can have long, term neurodevelopmental outcomes (2). The research work of the present study was to figure out the correlation between the severity of hypoglycemia and later development delay of the 140 neonates in Erbil, Iraq. Results showed that 67.1% of infants with neonatal hypoglycemia were involved in the case of neurodevelopmental delay and there was a substantial link between the severity of hypoglycemia and developmental outcomes. The study showed that children's motor skills were most frequently affected (38.3%) followed by language skills (34.0%) and cognitive skills (31.9%) and the number of domains that were simultaneously impacted was 30.9% of cases.

According to the latest systematic reviews and meta, analyses that study neonatal hypoglycemia and neurodevelopmental outcomes, these results are in correspondence. Diggikar et al. (2024) undertaking a very broad meta, analysis, pointed out that the neurodevelopmental impairment was notably more in early and mid, childhood for infants that suffered neonatal

hypoglycemia where cognitive impairment was the major one (OR = 2.12; 95% CI = 1.79, 2.52) and at the same time, visual, motor impairment was found to be elevated (OR = 3.33; 95% CI = 1.14, 9.72) (2). The conclusions made by Mahrous et al. (2025) in their very recent systematic review, are also very much in line with this. They claim that extreme hypoglycemia, particularly if it is early, onset or recurrent, is always linked to the appearance of co, morbidities such as motor dysfunction, delayed cognitive abilities, and executive function impairments (8). Moreover, the finding of the current study that 100% of severe hypoglycemia cases resulted in either moderate (58.6%) or severe (41.4%) developmental delays is in accord with these results and signals the vital role of extreme glucose depletion in the developing brain.

The predominance of motor function impairment observed in this study (38.3% of delayed cases) is consistent with emerging literature on domain-specific effects of neonatal hypoglycemia. Recent research has specifically identified fine motor function as particularly vulnerable to hypoglycemic injury, with boys showing greater susceptibility. A longitudinal study by Roeper et al. (2024) found that severe transitional hypoglycemia was associated with significantly lower performance in visual-motor and fine motor functions, with affected children scoring 4.8 points lower on full-scale IQ assessments (6). This sex-specific vulnerability aligns with findings from multiple studies suggesting that male infants may be at higher risk for motor developmental delays following hypoglycemic episodes, possibly due to differences in brain maturation patterns and metabolic responses (9).

This research has revealed that developmental delays (98.5% of cases) are closely related to the occurrence of low BW. This connection basically depicts the complex interaction between fetal growth restriction and glucose stability. A meta-analyses performed recently have been very consistent in their results, namely they have pointed out that low BW is a major factor leading to neonatal hypoglycemia along with neurodevelopmental deficits later on (1). The association seems to be due to the fact that infants born with growth restriction have low glycogen reserves, immature counter-regulatory mechanisms, and they most often have other perinatal risk factors alongside. The results of this study link prolonged hypoglycemia duration (>6 hours) with 95.4% of developmental delays, issue the message of extreme importance to the situation and even more so, early diagnosis and immediate treatment program, thus a very strong support for the recently proposed guidelines cumulating in more stringent monitoring and intervention practice (10, 11).

The study's identification of maternal diabetes as a universal risk factor (100% of affected infants showing developmental delay) reflects well-established pathophysiological mechanisms. Contemporary research continues to demonstrate that infants of diabetic mothers face elevated risks for both immediate hypoglycemic complications and long-term neurodevelopmental consequences. The consistency of this finding across multiple studies underscores the importance of optimal maternal glycemic control and intensive neonatal monitoring in this high-risk population (12).

The study's clinical parameter differences between groups with and without developmental delays provide important insights into prognostic indicators. The significantly lower mean BG levels in the delayed group (26.11 ± 6.81 mg/dL vs 34.15 ± 2.22 mg/dL, $p < 0.001$) support emerging evidence for higher treatment thresholds. Recent research suggests that traditional glucose thresholds may be insufficient to prevent neurodevelopmental sequelae, with some experts advocating for treatment initiation at glucose levels ≥47 mg/dL rather than the conventional 40-45 mg/dL. The GA and BW differences observed between groups further emphasize the multifactorial nature of neurodevelopmental risk in hypoglycemic infants, highlighting the need for individualized risk assessment and management strategies (6, 8).

5. CONCLUSIONS

This study demonstrated a strong relationship between neonatal hypoglycemia and subsequent neurodevelopmental delay among infants in Erbil, Iraq. Two-thirds (67.1%) of affected neonates exhibited developmental delays, which were significantly correlated with the severity and duration of hypoglycemia. Severe hypoglycemia led exclusively to moderate or severe developmental impairment, with motor, language, and cognitive domains most commonly affected. Low BW, prematurity, prolonged hypoglycemia, and maternal diabetes emerged as major risk factors. Infants with higher BW, later GA, and higher mean BG levels were more likely to have normal development. These findings emphasize the critical importance of early detection, prompt correction, and rigorous monitoring of hypoglycemia, particularly in high-risk neonates, to mitigate long-term neurodevelopmental consequences.

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REFERENCES

[1] Kebede SD, Kassaw A, Aytenew TM, Agmas K, Kefale D. Prevalence of prolonged transitional neonatal hypoglycemia and associated factors in Ethiopia: A systematic review and meta-analysis. PLOS ONE. 2025;20(2):e0316464. https://doi.org/10.1371/journal.pone.0316464

[2] Diggikar S, Trif P, Mudura D, Prasath A, Mazela J, Ognean ML, et al. Neonatal Hypoglycemia and Neurodevelopmental Outcomes-An Updated Systematic Review and Meta-Analysis. Life (Basel, Switzerland). 2024;14(12):1618. https://doi.org/10.3390/life14121618

[3] Sharma A, Davis A, Shekhawat PS. Hypoglycemia in the preterm neonate: etiopathogenesis, diagnosis, management and long-term outcomes. Translational pediatrics. 2017;6(4):335-48. https://doi.org/10.21037/tp.2017.10.06

[4] De Angelis LC, Brigati G, Polleri G, Malova M, Parodi A, Minghetti D, et al. Neonatal Hypoglycemia and Brain Vulnerability. Frontiers in endocrinology. 2021;12:634305. https://doi.org/10.3389/fendo.2021.634305

[5] Paulsen ME, Rao RB. Cerebral Effects of Neonatal Dysglycemia. Clinics in perinatology. 2022;49(2):405-26. https://doi.org/10.1016/j.clp.2022.02.008

[6] Roeper M, Hoermann H, Körner LM, Sobottka M, Mayatepek E, Kummer S, et al. Transitional Neonatal Hypoglycemia and Adverse Neurodevelopment in Midchildhood. JAMA network open. 2024;7(3):e243683. https://doi.org/10.1001/jamanetworkopen.2024.3683

[7] Ghazala N, Bala A, Ansari MA. Neurodevelopmental Outcomes in Children with Neonatal Hypoglycemia. International Journal of Current Pharmaceutical Review and Research. 2025;17(8):577-81.

[8] Mahrous RFA, Hassanin SHA, Elbashir REE, Elseed HG, Elnour SEA, Elsayid NN, et al. Neonatal Hypoglycemia and Long-Term Pediatric Neurodevelopmental Outcomes: A Systematic Review. Cureus. 2025;17(6):1-11. https://doi.org/10.7759/cureus.86183

[9] Rasmussen AH, Wehberg S, Pørtner F, Larsen AM, Filipsen K, Christesen HT. Neurodevelopmental outcomes after moderate to severe neonatal hypoglycemia. European journal of pediatrics. 2020;179(12):1981-91. https://doi.org/10.1007/s00431-020-03729-x

[10] Garg M, Devaskar SU. Exploring the long-term impacts of neonatal hypoglycemia to determine a safe threshold for glucose concentrations. European journal of pediatrics. 2025;184(4):263. https://doi.org/10.1007/s00431-025-06082-z

[11] De Rose DU, Perri A, Maggio L, Salvatori G, Dotta A, Vento G, et al. Neonatal hypoglycemia and neurodevelopmental outcomes: Yesterday, today, tomorrow. European journal of pediatrics. 2024;183(3):1113-9. https://doi.org/10.1007/s00431-023-05405-2

[12] Rodolaki K, Pergialiotis V, Iakovidou N, Boutsikou T, Iliodromiti Z, Kanaka-Gantenbein C. The impact of maternal diabetes on the future health and neurodevelopment of the offspring: a review of the evidence. Frontiers in endocrinology. 2023;14:1125628. https://doi.org/10.3389/fendo.2023.1125628.