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Review Article

The long-term impact of maternal diabetes on neonatal health and lifelong well being

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ABSTRACT

Maternal diabetes (MD), including gestational diabetes mellitus (GDM) and pre-existing type 1 diabetes mellitus (T1DM) or type 2 diabetes mellitus (T2DM), affects a significant proportion of pregnancies worldwide Emerging evidence suggests that MD include physical complications from cognitive and neurodevelopmental disorders (NDDs) within the offspring. Methods: This qualitative study utilized secondary literature data analysis published from 2017 to 2023. Data sources included peer-reviewed journals, databases, and reports focusing on MD during pregnancy and its impact on neurodevelopment disorders (NDDs). Inclusion criteria encompassed studies exploring associations between MD [T1DM, T2DM, GDM, and pre-GDM-not otherwise specified (PGDM-NOS)] and cognitive outcomes in children. Exclusion criteria omitted studies before 2017 or lacking detailed diabetes and clinical data. Qualitative synthesis indicated that offspring of mothers with diabetes during pregnancy face increased risks for cognitive and NDDs. Analysis of maternal age distribution revealed distinct prevalence patterns across diabetes types, emphasizing age-related risk differences. Children exposed to MD exhibited higher prevalence rates of ASD (3.2% vs. 2.0%), intellectual disability (ID) (2.7% vs. 0.9%), and attention deficit hyperactivity disorder (ADHD) (6.3% vs. 4.3%) compared to unexposed peers, underscoring significant associations between MD and NDDs. MD during pregnancy poses substantial risks to neonatal health and lifelong well-being, notably increasing the likelihood of NDDs in offspring. These findings advocate for tailored healthcare strategies addressing MD-related risks to mitigate adverse neurodevelopmental outcomes.

Keywords: MD, NDDs, ID, ADHD

INTRODUCTION

Gestational diabetes mellitus (GDM) is well established as a major threat factor for various adverse outcomes in offspring from infancy to adulthood approximately 15% of pregnancies worldwide face the complications of GDM. Several observational investigations have associated MD having a heightened threat of NDDs within the offspring, and have noted the impact of fetal hyperglycemia in effects on neurodevelopment, especially in severe pregnancy is suggested as a helpful mechanism.[1] Congenital defects are three times more common in diabetic pregnancies, particularly when maternal blood sugar control (HbA1c>7%) is inadequate during the critical first trimester of organ development.[2] Poor glycemic control in pre-existing diabetes significantly heightens the risk of congenital abnormalities.[2]

Studies by Arabin et al suggest that GDM diagnosed prior to 26 gestational weeks may heighten the threat of ASD in children, highlighting the potential timing-dependent effects of maternal hyper-glycemia on neurodevelopmental outcomes.[3] However, while ASD, ADHD, and ID are highly heritable conditions, factors

like maternal age, which correlates strongly with GDM and T2DM, may confound these associations due to shared genetic predispositions. Furthermore, the depiction is further complicated by the genetic overlap between psychiatric disorders and conditions such as autoimmune diseases such as T1DM.[4] Deficiencies of essential nutrients such as iron, docosahexaenoic acid (DHA) are also significantly involved in the etiology of NDDs ASD, ID, and ADHD throughout childhood not only but as occurrence time same shows greater severity, more diverse needs, and worse prognosis compared to single NDD diagnoses. The chief goal of the investigation was to gauge the bearing of MD on neonatal health and their life-long well-being over time, focusing on the incidence, ubiquity and linked threat factors of arthritis in children with MD especially during pregnancy and raising standards be clear and identify strategies for early intervention and prevention.

LITERATURE RESEARCH

This study employed a qualitative method approach, focusing on secondary data analysis from existing literature published from 2017 to 2023. The qualitative analysis synthesized data indicating that offspring of mothers with diabetes during pregnancy face heightened risks for cognitive and NDDs, alongside well-established metabolic risks associated with MD.

Data collection

Data sources included peer-reviewed journals, databases, and reports that provided detailed insights into characteristics, health parameters, and links across MD along with NDDs in neonatal. These studies probed the links across MD throughout pregnancy (including T1DM, T2DM, GDM, and PGDM-NOS) and NDDs in offspring.

Inclusion and exclusion criteria

Inclusion criteria include investigations conducted between January 2017 and December 2023. Studies focusing on MD in pregnancy, secondary data analysis, or systematic literature review and its association with NDDs in children were conducted. Further investigating of the impact of MD (T1DM, T2DM, GDM, and PGDM-NOS) on cognitive and neurodevelopmental outcomes in children was also done. Studies that report on the incidence of autism spectrum disorder (ASD), and ID, along with ADHD, or related outcomes in mothers of children who have been involved in diabetes mellitus is reported.

Exclusion criteria based on studies published before January 2017 or after December 2023. Studies not directly addressing the relationship between MD and NDDs in offspring and those studies lacking detailed information on MD types, gestational weeks at diagnosis, or comprehensive clinical data necessary to assess the associations with neurodevelopmental outcomes.

Data analysis

The data analysis focused on qualitative analysis on secondary data analyses published between January 2017 and December 2023.The neuro disorders parameters were investigated in MD such as ASD, ID, and ADHD among offspring of mothers having numerous kinds of diabetes. The analysis also focused on maternal age distribution and the timing of GDM and deficiency of nutrients diagnosis to assess their impact on cognitive and neurodevelopmental outcomes in children.

OBSERVATIONS

The qualitative analysis revealed that data suggest that offspring of mothers with diabetes across pregnancy are at heightened threat for cognitive disorders and NDDs, in addition to the well-known metabolic risks associated with MD. The analysis of maternal age distribution among mothers with various types of diabetes reveals distinct patterns. For mothers under 25 years old, prevalence is similar between those without diabetes (19.0%) and those with T1DM (19.3%), but significantly lower for T2DM (5.9%), GDM (10.0%), and PGDM-NOS (12.4%). Ages 25-29 constitute a majority, with 34.1% in the unexposed group, 33.0% in T1DM, 18.8% in T2DM, 25.3% in GDM, and 28.6% in PGDM-NOS. Ages 30-34 show stable proportions across types: 30.9% unexposed, 29.9% T1DM, 32.5% T2DM, 33.2% GDM, and 34.0% PGDM-NOS. Mothers aged 35-39 are 13.4% unexposed, 14.7% T1DM, 30.1% T2DM, 23.8% GDM, and 19.4% PGDM-NOS, with T2DM having a higher prevalence. Those aged 40 and above are least prevalent: 2.6% unexposed, 3.1% T1DM, 12.7% T2DM, 7.7% GDM, and 5.6% PGDM-NOS. These insights emphasize the necessity for tailored healthcare strategies considering age-related risk differences among mothers with diabetes, potentially mitigating risks for cognitive and NDDs in their offspring.

MD AND THE FETAL BRAIN

In addition to the neonatal period, the 2022 NHMS revealed that 20% of children below the age of 5 were experiencing stunted growth, while 46% were suffering from anaemia. The impact of iron deficiency on brain development varies based on the timing of deficiency (early or late pregnancy, and first 6 months of life, or even later in infancy), resulting in variable aberrations in motor, and cognitive, or even neurophysiological development. Disturbances within maternal lipid metabolism have been associated with all forms of diabetes throughout pregnancy, resulting in impaired transfer of vital lipids from the mother to the growing foetus. DHA, being an omega-3 fatty acid, is essential for the formation and maintenance of neural tissue, alongside retina, and mitochondrial membranes, and cerebral cortex, along with brain function. Research conducted on animals has demonstrated that a lack of omega-3 fatty acids causes a drop in DHA levels within

the cerebral cortex, which causes the development of learning difficulties. In contrast, research conducted on humans has demonstrated that supplementing with DHA during pregnancy improves problem-solving abilities and sustained attention in infants.

IMPACT OF MD ON NDDS

The data on children born between 1987 and 2010 indicate the prevalence of NDDs among those exposed to diverse types of MD throughout pregnancy. Among children unaffected by NDDs, 94.3% were unexposed to MD, while the rates for those exposed to T1DM, T2DM, GDM, and PGDM-NOS were 91.9%, 90.7%, 92.9%, and 92.6%, respectively.

For any ASD, the prevalence was 2.0% in unexposed children, 2.9% in those exposed to T1DM, 3.2% in those exposed to T2DM, 2.8% in those exposed to GDM, and 2.5% in those exposed to PGDM-NOS. The prevalence of any ID was 0.9% in unexposed children, compared to 1.7%, 2.7%, 1.5%, and 1.5% in children exposed to T1DM, T2DM, GDM, and PGDM-NOS, respectively.

The data for any ADHD showed a prevalence of 4.3% in unexposed children. For those exposed to MD, the prevalence was 6.1% for T1DM, 6.3% for T2DM, 5.0% for GDM, and 5.7% for PGDM-NOS. Specifically for ASD only, the rates were 0.9% (unexposed), 1.2% (T1DM), 1.5% (T2DM), 1.3% (GDM), and 0.9% (PGDM-NOS).

For ADHD only, the prevalence was 3.3% in unexposed children, 4.5% in those exposed to T1DM, 4.6% in those exposed to T2DM, 3.6% in those exposed to GDM, and 4.3% in those exposed to PGDM-NOS. The combined presence of ASD and ADHD was observed in 0.8% of unexposed children, 1.2% of those exposed to T1DM, 1.0% of those open to T2DM, 1.0% of those open to GDM, and 1.1% of those open to PGDM-NOS.

For ID without ASD, the rates were 0.6% (unexposed), 1.1% (T1DM), 2.0% (T2DM), 1.0% (GDM), and 1.0% (PGDM-NOS). Finally, for ID with ASD, the prevalence was 0.3% in unexposed children, compared to 0.6%, 0.8%, 0.6%, and 0.5% in those exposed to T1DM, T2DM, GDM, and PGDM-NOS, respectively.

These statistics highlight the heightened risk of NDDs in children born to mothers with various types of diabetes. Grasping said associations is fundamental for developing preventive strategies and tailored interventions to support the affected children and their families

ADHD INCIDENCE AND RISK IN RELATION TO MD

Incident cases of ADHD totalled 323, constituting 10.3% of the sample population. Incident cases of ASD were recorded at 36, representing 1.15% of the sample population. Among children born to mothers having T2DM, 275 cases (8.8%) were noted.

The incidence of ADHD in pregnancies affected by GDM was 7.81 cases per 1,000 person-years, compared to 4.66 cases per 1,000 person-years in non-GDM pregnancies, demonstrating a statistically noteworthy difference ($p<0.05$). The adjusted hazard ratio (HR) for ADHD risk in GDM pregnancies was 1.64 (95% CI, 1.31 to 2.05), indicating a significant increase in risk.

Children of mothers with T2DM exhibited ADHD rates of 14.2%, compared to 10% in those without T2DM, with a statistically significant difference ($p=0.029$). ADHD rates varied significantly based on the history of GDM and T2DM: GDM-/T2DM-: 8.7%; GDM-/T2DM+: 9.8%; GDM+/T2DM-: 12.9%; GDM+/T2DM+: 15.4%

These statistics underscore the heightened incidence and risk of ADHD inside children born to mothers with various types of diabetes, highlighting the importance of monitoring and potentially intervening during such pregnancies to mitigate these risks effectively.

DISCUSSION

The qualitative analysis underscores that offspring born to all mothers with diabetes during pregnancy face heightened risks of cognitive and NDDs. As discussed, prevalence of MD under age 25 is comparable to those without diabetes and T1DM, but notably lower for T2DM, GDM, and PGDM-NOS. In contrast, the age group of 25-29 years constitutes a majority across all groups, while those aged 30-34 years show stable proportions. Mothers aged 35-39 years have higher prevalence rates, particularly in the T2DM group, and those aged 40 and above are least prevalent but more pronounced in T2DM. Consistent with the study by (Kelstrup et al) corroborate our results, demonstrating similar patterns of increased risk across different types of MD and age groups as a results 30 to 40 years mothers show significant prevalence rate ($p<0.05$) in T2DM.[5]

Other finding indicates deficiency of iron and essential elements such as DHA play import role in neuro development disorder. Similar study finding suggest that Iron deficiency, a common complication in MD, impacts brain development by altering gene expression critical for synaptic plasticity and neurodevelopmental pathways, emphasizing the need for early intervention strategies to mitigate long-term cognitive risks. Also, suggested critical role of iron and DHA in fetal brain development, underscoring the importance of managing MD to mitigate neurodevelopmental risks in offspring (Perea et al).[6]

Another major qualitative analysis, supported by data on NDDs among children born to mothers with diabetes, reveals compelling associations that warrant attention. Our study aligns with previous research indicating heightened prevalence rates of NDDs, counting ASD, ID,

and ADHD, among offspring exposed to MD during pregnancy. The ubiquity rates of ASD, ID, and ADHD were consistently higher among children exposed to various types of MD compared to those unexposed. Specifically, the prevalence of ASD ranged from 2.0% (unexposed) to 3.2% (T2DM), ID from 0.9% (unexposed) to 2.7% (T2DM), and ADHD from 3.3% (unexposed) to 6.3% (T2DM). These statistics underscore the significant impact of MD on neurodevelopmental outcomes, emphasizing the need for targeted interventions and preventive strategies. Our study corroborates previous findings showing that PGDM is linked with an elevated risk of ASD in offspring. Chen et al observed that GDM diagnosed at ≤26 weeks gestational age (wkGA) was linked to the highest risk of ASD, contrasting our finding where diagnosis between 27 and 30 wkGA showed the greatest risk, possibly influenced by differing GDM screening protocols.[7] Regarding ID, Ornoy et al found a stronger link with PGDM likened to GDM, consistent with our results studies examining ADHD also align with our findings, Muhammad although did not find associations with GDM, particularly after considering timing of exposure.[8,9]

Few studies (Rodolaki et al) have explored the concurrent occurrence of ASD, ID, and ADHD in offspring of mothers with diabetes and suggested that the association between PGDM/GDM and ASD may be largely explained by their co-occurrence with ID, highlighting an etiological distinction for ASD with ID as a distinct group.[10] Our findings support this distinction, noting strong associations with outcomes counting ID regardless of co-occurring NDDs. Chen et al study, similarly found increased ADHD risk in offspring of mothers having T1DM, particularly when excluding cases with secondary diagnoses of ID, and ASD, or even Tourette syndrome, consistent with our findings focusing on ADHD without ASD along with/or ID.[11]

The discussion highlights significant associations between MD-both, PGDM and GDM-and increased threats of NDDs in offspring, our findings support existing literature on the heightened risk profiles across different MD types, underscoring the need for tailored healthcare strategies to mitigate these risks effectively. Additionally, our study contributes to understanding the nuanced relationships between MD, timing of exposure, and the specific neurodevelopmental outcomes observed in children.

CONCLUSION

In conclusion, our study underscores the significant association between MD and heightened risks of cognitive and NDDs in offspring, including ASD, ID, and ADHD. The findings emphasize the need for tailored healthcare strategies, particularly considering age-related risk variations among mothers with different types of diabetes.

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REFERENCES

1. Neiger R. Long-term effects of pregnancy complications on maternal health: a review. J Clin Med. 2017;6(8):76.
2. Armengaud JB, Ma RC, Siddeek B. Offspring of mothers with hyperglycaemia in pregnancy: The short term and long-term impact. What is new? Diabetes Res Clin Pract. 2018;145:155-66.
3. Arabin B, Baschat AA. Pregnancy: an underutilized window of opportunity to improve long-term maternal and infant health-an appeal for continuous family care and interdisciplinary communication. Front Pediatr. 2017;5:69.
4. Patel R, Patel M, Patel Z. Current Status of Machine Learning and Artificial Intelligence in Cervical Cancer Screening and Diagnosis: A Systematic Review. Glob Acad J Med Sci. 2024;6(1):38-48.
5. Kelstrup L, Bytoft B, Hjort L, Houshmand-Oeregaard A. Diabetes in pregnancy: Long-term complications of offsprings. In Gestational diabetes, Karger Publishers. 2020;28:201-22.
6. Perea V, Urquizu X, Valverde M, Macias M,. Influence of maternal diabetes on the risk of neurodevelopmental disorders in offspring in the prenatal and postnatal periods. Diabetes Metabol J. 2022;46(6):912-22.
7. Chen KR, Yu T, Lien YJ, Chou YY. Childhood neurodevelopmental disorders and maternal diabetes: A population-based cohort study. Develop Med Child Neurol. 2023;65(7):933-41.
8. Ornoy A, Becker M, Weinstein-Fudim L. Diabetes during pregnancy: a maternal disease complicating the course of pregnancy with long-term deleterious effects on the offspring. a clinical review. Int J Molecular Sci. 2021;22(6):2965.
9. Muhammad Ismail HI. Preventing Childhood Neurodisability. Malays J Med Sci. 2023;31(2):1-5.
10. Rodolaki K, Pergialiotis V, Iakovidou N. The impact of maternal diabetes on the future health and neurodevelopment of the offspring: a review of the evidence. Front Endocrinol. 2023;14:1125628.
11. Chen S, Zhao S, Dalman C, Karlsson H. Association of maternal diabetes with neurodevelopmental disorders: autism spectrum disorders, attention-deficit/hyperactivity disorder and intellectual disability. Int J Epidemiol. 2021;50(2):459-74.

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