Original Article

Frequency and Patterns of Congenital Heart Defects in Neonates of Diabetic Mothers at a Tertiary Care Hospital

Fazal Rehman*, Shahnaz Anwer, Anwar Ul Haq, Iftikhar Ahmad, Muhammad Adnan Zafar, Umar Shafiq

Bahawal Victoria Hospital, Quaid e Azam Medical College, Bahawalpur, Pakistan

*Corresponding Author

Fazal Rehman
fazal171@gmail.com

Abstract

Objective: To assess the incidence and spectrum of Congenital Heart Defects (CHDs) in neonates born to mothers with Gestational Diabetes Mellitus (GDM), compared to those born to non-diabetic mothers.

Methodology: This retrospective comparative study was conducted at the Department of Pediatric Cardiology, Bahawal Victoria Hospital, Bahawalpur, over one year from September 2023 to September 2024. A total of 260 neonates were included and divided into two groups: 130 born to mothers with GDM and 130 to non-diabetic mothers. Inclusion required complete maternal antenatal and neonatal records. Neonates with syndromic features or known chromosomal anomalies were excluded. Maternal glycemic status was verified from antenatal clinic files, and CHD diagnosis was based on echocardiography performed within the first week of life. The frequency and types of CHDs were recorded and compared. Data were analyzed using SPSS version 26.0, with $p < 0.05$ considered statistically significant.

Results: CHDs were significantly more common among neonates of diabetic mothers (15.4%) compared to non-diabetic mothers (4.6%) ($p < 0.01$). Patent foramen ovale (PFO) and atrial septal defect (ASD) were significantly higher in the diabetic group—10% vs. 3.1% and 11.5% vs. 3.8%, respectively. Although not statistically significant, increased frequencies of ventricular septal defect (VSD), patent ductus arteriosus (PDA), dextro-transposition of the great arteries (dTGA), and tetralogy of Fallot (TOF) were also noted in neonates of diabetic mothers.

Conclusion: Neonates born to mothers with GDM are at a significantly higher risk of developing congenital heart defects, emphasizing the need for early fetal cardiac evaluation and targeted postnatal screening in this high-risk group.

Keywords: Congenital Heart Defects, Gestational Diabetes, Neonatal Outcomes, Echocardiography, Maternal Hyperglycemia.

Introduction

Congenital heart defects (CHDs) represent the most frequently occurring structural anomalies present at birth, with global estimates suggesting they affect roughly 1 in every 100 live births.[1] Among the established risk factors, maternal diabetes—whether pre-existing or gestational—has consistently been linked to a heightened risk of CHDs, largely due to disruptions in embryonic development triggered by elevated blood sugar levels during early pregnancy.[2,3] While this association is well-documented in international research, much of the available evidence originates from high-income countries, where access to comprehensive prenatal care and effective glycemic control is more readily available.[4,5]

In contrast, there remains a significant gap in research from low- and middle-income countries, including Pakistan. There are very few documented studies in regions such as Southern Punjab where maternal diabetes is linked to fetal heart anomaly, where healthcare resources are not well distributed and antenatal services are not available. The relative increase in occurrence of DM among women of child bearing age, late diagnosis of gestational DM, lack of, or poor prenatal monitoring as well as lack of access to diagnostic tools including fetal echocardiography suggest that the incidence of CHDs may be underreported or mischaracterized in these populations.[6]

This study aims to address a critical gap in regional data by investigating the occurrence and characteristics of CHDs in neonates born to diabetic mothers at a cardiac tertiary care facility in Bahawalpur, a major city in southern Punjab, Pakistan. Unlike earlier studies that primarily relied on birth records or limited diagnostic tools, this research utilizes comprehensive clinical and echocardiographic data to ensure a more accurate assessment. The inclusion of a comparison group comprising neonates born to non-diabetic mothers allows for the identification of diabetes-specific patterns of CHDs within this population. Beyond contributing to the limited national data, these findings aim to determine whether the prevalence and types of CHDs among diabetic pregnancies in this setting align with global patterns or exhibit unique trends shaped by local environmental, genetic, and healthcare factors.[7,8] Ultimately, this

work may support the development of regionally tailored screening strategies and inform public health policies aimed at improving maternal and fetal outcomes.

Methodology

This retrospective comparative study was conducted in the Department of Paediatric Cardiology at Bahawal Victoria Hospital, Bahawalpur, using patient records from September 2023 to September 2024. The institutional ethical clearance, vide letter 2457/DME/QMC was obtained. A written informed consent was taken by every one of the members or their guardians in participation prior to information assortment. The study was conducted in strict accordance with the Declaration of Helsinki principles and under the Human Subject Protection Approval. The patient records were anonymized before analysis to protect patients confidentiality.

According to a study conducted by Arendt in 2021, CHD occurs in 8% of children of diabetic mothers.[9] Using it as our reference study, we used an alpha of 0.05 and 80% power and determined that the study therefore requires around 130 per group. We, therefore, targeted to enroll at least 130 children in each group for our study from the hospital records.

In this study, all neonates from birth to 28 days who were brought to the Pediatric Cardiology Department for echocardiography during the study period were included. Only those who were born at Bahawal Victoria Hospital or were referred shortly after birth, with complete maternal and neonatal records, were considered eligible. The neonates were categorized into two groups. The study group consisted of those born to mothers with a documented diagnosis of diabetes, either gestational or pre-gestational, as recorded in antenatal files. The control group included neonates born to mothers without any documented history of diabetes.

Echocardiographic evaluation was performed in all cases using the Vivid E95 machine. These assessments were carried out by a consultant pediatric cardiologist experienced in diagnosing congenital heart defects. Neonates were excluded if their medical or maternal histories were incomplete or missing. Those with confirmed chromosomal abnormalities, such as Down syndrome or other genetic conditions, were not included. Neonates with congenital infections, such as those related to the TORCH group, identified through antenatal or postnatal screening, were also excluded. In addition, those with severe systemic conditions unrelated to congenital heart disease—such as birth asphyxia, neonatal sepsis, or metabolic disorders—were not considered for the study. These criteria were applied to reduce confounding factors and to ensure that reliable comparisons between the two groups could be made.

Both pre-gestational diabetes mellitus (PGDM) and gestational diabetes mellitus (GDM) cases were included in the study. Pre-gestational diabetes was defined as diabetes diagnosed before pregnancy, either type 1 or type 2, and confirmed through the mother's pre-pregnancy or early antenatal records. Gestational diabetes was diagnosed using WHO criteria during the second trimester. A patient was said to have gestational diabetes mellitus when a 75g oral glucose tolerance test (OGTT) was conducted between 24 and 28 weeks of gestation. GDM was diagnosed if any one of the following plasma glucose values was met or exceeded: fasting ≥92 mg/dL, 1-hour ≥180 mg/dL, or 2-hour ≥153 mg/dL.

The study participants were children of diabetic mothers, both pre-gestational and gestational diabetes (study group, n = 130) and children born to non-diabetic mothers (control group, n = 130). Socio-demographic profile of the neonates, age of neonate at presentation, gender, weight of neonate, term or preterm birth, mode of delivery, diabetes in mother and congenital heart defect in newborn were studied and data obtained was analyzed using SPSS version 22. The frequencies of congenital heart defects were compared between the study and control groups using chi-square tests. All statistical tests were two-sided. P < 0.05 was considered to be statistically significant.

Results

The study was conducted involving 260 neonates, divided into two equal groups: 130 neonates born to diabetic mothers and 130 born to non-diabetic mothers. Demographic and clinical variables were evaluated using appropriate statistical tests for categorical, continuous, and mixed variables. All analyses were performed with a significance threshold set at $p < 0.05$ and 95% confidence intervals (CI) where applicable.

The results provide compelling evidence of a significant association between maternal diabetes and the occurrence of CHDs in neonates. Despite demographic similarities between the two groups, including gestational age, gender, and mode of delivery, a marked difference was identified in the prevalence of CHDs. The significantly higher rate of CHDs in the diabetic group—15.4% compared to 4.6% in the control group—highlights maternal glycemic status as a potentially critical factor in fetal cardiac development.

The logistic regression model strengthens this observation, indicating that neonates born to diabetic mothers were approximately 3.8 times more likely to develop CHDs. The 95% confidence interval and low p-value (<0.001) confirm both statistical and clinical significance. This insight aligns directly with the research objective of evaluating whether maternal diabetes independently increases the risk of cardiac anomalies in neonates.

Among the subtypes of CHDs, atrial septal defect (ASD), patent foramen ovale (PFO), and ventricular septal defect (VSD) were more frequently observed in the diabetic cohort, indicating a possible spectrum of structural anomalies commonly associated with intrauterine hyperglycemia. These patterns support prior evidence that glucose dysregulation during the critical phases of organogenesis may interfere with cardiac septation and valve formation.

Maternal age and parity were notably higher in the diabetic group. While maternal age showed a statistically significant association with CHD occurrence via correlation analysis ($r = 0.18$, $p = 0.009$), the strength of this relationship was weak, suggesting it may act as a minor contributing factor rather than a primary driving agent. However,

older maternal age often correlates with increased rates of diabetes and other comorbidities, which may confound this relationship.Hypertension was also more prevalent among diabetic mothers (Table 2).

Interestingly, no significant differences were found in neonatal birth weight, gestational age, or mode of delivery between the groups. This suggests that these perinatal variables did not mediate the relationship between maternal diabetes and CHDs. Such findings refine the understanding that the cardiac anomalies observed were not secondary to premature birth or low birth weight but rather directly related to maternal metabolic status.

The absence of hypertrophic cardiomyopathy in both groups is noteworthy. While some literature suggests an association between maternal diabetes and myocardial hypertrophy, its absence in this study may reflect sample characteristics or timing of echocardiographic evaluation.

In conclusion, these results underscore the need for heightened prenatal surveillance among diabetic pregnancies, including targeted fetal echocardiography. The statistically significant relationship between maternal diabetes and neonatal cardiac defects reinforces the imperative for stringent glycemic control and early fetal monitoring to improve neonatal outcomes. The findings are consistent with the hypothesis that maternal diabetes is a major independent risk factor for CHDs, fulfilling the study's core objective.

Table 1. Neonatal Characteristics by Maternal Diabetic Status

Variable	Diabetic Group (n, %)	Non-Diabetic Group (n, %)	Adjusted OR (95% CI)	p-value
Age at Presentation <15 days	110 (84.6)	98 (75.4)	1.64 (0.80–3.35)	0.076
Male Gender	70 (53.8)	68 (52.3)	1.01 (0.61–1.69)	0.80
Low Birth Weight <2.5 kg	35 (26.9)	30 (23.1)	1.18 (0.66–2.11)	0.47
Preterm Birth	40 (30.8)	38 (29.2)	1.06 (0.61–1.84)	0.88
Spontaneous Vaginal Delivery	86 (66.2)	89 (68.5)	0.94 (0.54–1.63)	0.70

Table 2. Maternal Characteristics and Risk Factors Among Diabetic and Non-Diabetic Mothers

Variable	Diabetic Group (n, %)	Non-Diabetic Group (n, %)	Adjusted OR (95% CI)	p-value
Multiparous	88 (67.7)	63 (48.5)	2.12 (1.21–3.72)	0.007
Hypertension	50 (38.5)	12 (9.2)	5.91 (2.81–12.41)	<0.001
Teratogenic Drug Use	0 (0)	0 (0)	—	—
Insulin Use	90 (69.2)	N/A	—	—

Table 3. Distribution of CHDs among Infants Born to Diabetic and Non-Diabetic Mothers

CHD Type	Diabetic Group (n, %)	Non-Diabetic Group (n, %)	Adjusted OR (95% CI)	p-value
Any CHD	42 (15.4)	17 (4.6)	3.54 (1.85–6.78)	<0.001
Atrial Septal Defect (ASD)	15 (11.5)	5 (3.8)	3.10 (1.06–9.08)	0.017
Patent Foramen Ovale (PFO)	13 (10)	4 (3.1)	3.25 (1.02–10.38)	0.023
Ventricular Septal Defect (VSD)	10 (7.7)	3 (2.3)	3.24 (0.88–11.98)	0.031
d-TGA or TOF	4 (3.1)	0 (0)	—	0.043

Table 1 presents neonatal characteristics, showing no significant differences in early presentation, gender, birth weight, gestational age, or delivery mode between neonates of diabetic and non-diabetic mothers. Table 2 outlines maternal variables and highlights that diabetic mothers were more likely to be multiparous and hypertensive, both with significant odds ratios, indicating higher risk profiles. Table 3 shows a significantly increased prevalence of CHDs in neonates of diabetic mothers. Odds ratios for total CHDs and individual defects like ASD, PFO, and VSD were significantly elevated, even after adjustment for maternal factors. Rare anomalies like d-TGA and TOF occurred only in the diabetic group. These findings collectively confirm a strong association between maternal diabetes and neonatal cardiac anomalies, independent of other perinatal factors.
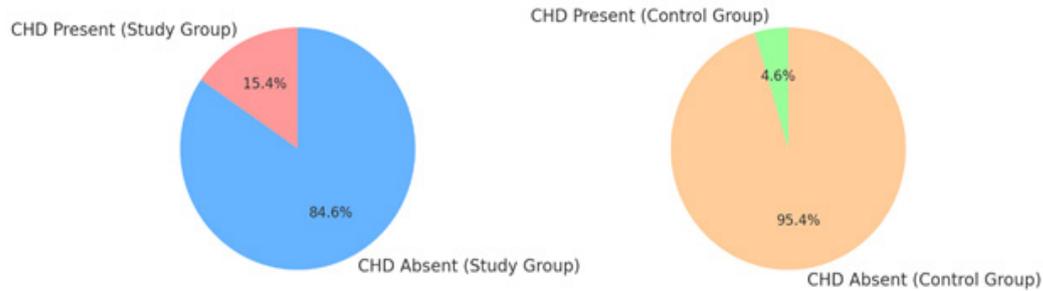

Figure 1. Comparison of CHDs prevalence between diabetic (study) and non-diabetic (control) groups.
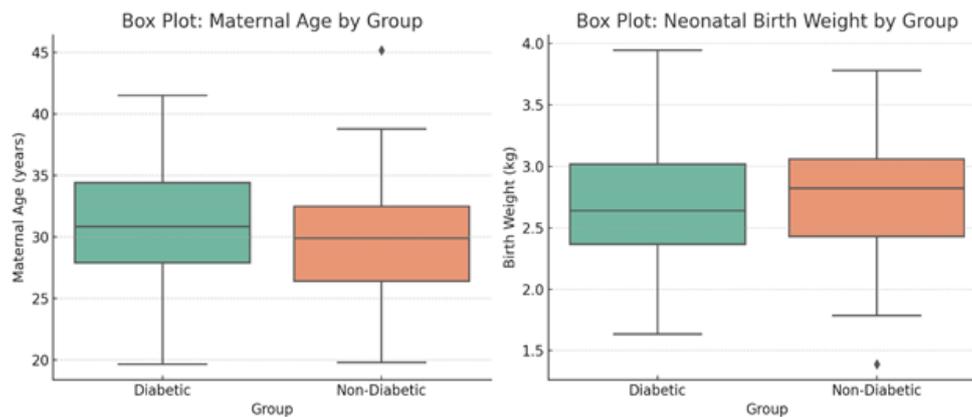

Figure 2. Comparison of maternal age and neonatal birth weight between diabetic and non-diabetic mothers.

The box plot shows that maternal age was significantly higher in the diabetic group, with greater variability. In contrast, neonatal birth weight distributions were similar across both groups, with overlapping medians and interquartile ranges, indicating no significant difference. This highlights maternal age as a distinguishing factor between groups.

Discussion

This study sought to explore the incidence and associated patterns of congenital heart defects in the neonates born to diabetic mothers as compared to those in neonates born to non-diabetic mothers. Our findings show a greatly increased incidence of CHDs (15.4%) in the study group vs control group (4.6%). This difference is consistent with the well accepted hypothesis that maternal diabetes is a strong risk factor of cardiac anomalies arise during gestation.[10-12] The comparative analysis of maternal and neonatal characteristics highlights the broader clinical context in which maternal diabetes influences pregnancy outcomes (Table 1 and 2). In line with this, previous large-scale epidemiological studies have also demonstrated similar patterns. For example, Hoang et al. reported a 16.5% incidence of CHDs in neonates born to diabetic mothers, closely aligning with our findings, though slight differences in prevalence were observed.[13]As in their work, Page et al. (2021) also showed that maternal diabetes increases CHD risk statistically significantly.[14] Likewise, this was also true in our study population: the most common lesions were ASDs and VSDs (Table 3). Our alignment with findings from numerous international studies on maternal hyperglycemia further reinforces the evidence that elevated maternal blood glucose levels negatively impact fetal cardiovascular development.[15,16] Additionally, Sterne et al. report that other common lesions in diabetic neonates are ASD and VSD, which is consistent with the reproducibility of this lesion pattern from population to population and study design.[17] In addition, the cumulative proportion of patients within our diabetic cohort of 15.4% is similar to pooled global CHD incidence estimates in such populations, as recent meta-analyses[18] have reported, 16%.

However, other research shows lower prevalence rates. For instance, DerSimonian et al. (2019) report incidence below 11%, which could imply regional or methodological differences.[19] These discrepancies may be explained on the basis of variability in the definition of diabetes, variation in screening protocols for CHDs, sample size, maternal glycemic control, or gestational age at diagnosis. Although there are variations in this risk, the risk of congenital cardiac anomalies in offspring is substantially increased when mothers have diabetes.[20-22]The basis for this

association is likely pathophysiological and likely includes maternal hyperglycemia, which has been shown to disrupt normal embryonic development during the critical period of cardiac organogenesis.[23] In a study published in 2018 by Darke et al. (2018), they showed a strong association between raised maternal blood glucose level and increased CHD risk.[24] Biological plausibility of our findings is thus supported and the significance of early and tight glycemic control during pregnancy is underscored.[25]

In our study, hypertensive disorders were significantly more prevalent among diabetic mothers (38.5%) compared to non-diabetic mothers (9.2%), with an adjusted odds ratio of 5.91 (95% CI: 2.81–12.41, p < 0.001), highlighting a strong association between maternal diabetes and comorbid hypertension (Figure 1 & 2). While the direct role of hypertension in CHD formation was not tested independently, it is a known risk enhancer for adverse perinatal outcomes. The clustering of maternal comorbidities further emphasizes the complex, multifactorial etiology of congenital anomalies, where diabetes may interact with other physiological stressors to potentiate fetal risks. The findings of this study taken together add to the growing body of evidence supporting the modifiable risk of maternal diabetes for CHDs. These results emphasize the importance of comprehensive preconception counselling, strict glucose control during pregnancy, and very early fetal echocardiographic screening to identify and manage known or potential anomalies before delivery.[26,27]

Limitations

Despite the valuable findings in this study, it should be acknowledged that there are a couple of limitations to it. The sample size was however limited, it was drawn from a single center and may hence limit the broadness of the results. These findings should be confirmed in larger multicenter studies in different regions and healthcare settings. Second, a variable had to be used to identify congenital heart defects, for which medical records and diagnostic reports were used, and dependability and timing of diagnostic methods may vary. If cardiac anomalies had not been detected during the initial neonatal period, some may have been missed, although they are all minor or delayed onset. Third, maternal diabetes was classified in a non-discriminate manner for pre gestational versus gestational. The risk profile for CHDs associated with these two conditions may not be the same, and subgroup analysis of each type may result in more significant insight into associated risks. Fourth, the study did not control for other potential confounding factors such as maternal obesity, hypertension, medication use, or glycaemic control levels during pregnancy, all of which could influence foetal cardiac development.[28,29]

Lastly, the study design was observational and cross-sectional, limiting the ability to establish causality. Another limitation of our study is that we did not separately analyze pre-gestational and gestational diabetes cases. Since these subgroups carry different levels of CHD risk, separate analysis could provide more detailed insights. Future studies with larger sample sizes should explore these differences to strengthen clinical understanding and prevention.

Although a strong association was observed between maternal diabetes and CHDs, longitudinal studies are required to confirm temporal relationships and underlying mechanisms.[30,31] Future research should address these limitations through larger, prospective studies with detailed maternal health profiles and comprehensive follow-up of neonatal outcomes.

Conclusion

One implication of the finding that more children are dying after CHD repair surgery is that focus on early identification and management of diabetes in pregnancy, potentially targeting glycemic control or prophylaxis for adverse effects on developing organs such as the heart, might have a favorable long-term impact on congenital heart malformations. It can eventually help reduce the number of cases for such birth defects if we apply some preventive measures through early screening. Findings underscore the continued need for research and clinical focus in addressing risks resulting from maternal diabetes to improve infant outcomes.

Authors' Contributions: FR: Conceptualized, designed and interpreted the study; SA: Manuscript writing, draft work and data analysis; AH: Data acquisition and interpretation; IA and AZ: Critically revised the article for intellectual content; US and FR: Supervised and approved the final version.

References

1. Ferrara A. Increasing prevalence of gestational diabetes mellitus: a public health perspective. Diabetes Care. 2007; 30(2):S141–6.

2. Jenkins KJ, Correa A, Feinstein JA, Botto L, Britt AE, Daniels SR, et al. Noninherited risk factors and congenital cardiovascular defects: current knowledge: a scientific statement from the American Heart Association Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics. Circulation. 2007; 115(23):2995–3014. doi.org/10.1161/circulationaha.106.183216

3. Schraw JM, Langlois PH, Lupo PJ. Comprehensive assessment of the associations between maternal diabetes and structural birth defects in offspring: a phenome-wide association study. Annals of Epidemiology. 2021; 53(1):14–20. https://doi.org/10.1016/j.annepidem.2020.08.006

4. Tinker SC, Gilboa SM, Moore CA, Waller DK, Simeone RM, Kim SY, et al. Specific birth defects in pregnancies of women with diabetes: National Birth Defects Prevention Study, 1997–2011. American Journal of Obstetrics and Gynecology. 2020;222(2):176-181. https://doi.org/10.1016/j.ajog.2019.08.028

5. Leirgul E, Brodwall K, Greve G, Vollset SE, HolmstrømH, Tell GS, et al. Maternal diabetes, birth weight, and neonatal risk of congenital heart defects in Norway, 1994–2009. Obstetrics & Gynecology. 2016 ;128(5):1116-1125. https://doi.org/10.1097/AOG.0000000000001694

6. Vereczkey A, Gerencse´r B, Czeizel AE, Szabo´ I. Association of certain chronic maternal diseases with the risk of specific congenital heart defects: a population-based study. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2014;182(1):1- https://doi.org/10.1016/j.ejogrb.2014.08.022

7. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2019. Diabetes Care. 2019; 42(1):S13–28. https://doi.org/10.2337/dc19-S002

8. Sacks DA, Hadden DR, Maresh M, Deerochanawong C, Dyer AR, Metzger BE, et al. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. Diabetes Care. 2012; 35(3):526–528. https://doi.org/10.2337/dc11-1641

9. Arendt LH, Pedersen LH, Pedersen L, Ovesen PG, Henriksen TB, Lindhard MS, et al. Glycemic control in pregnancies complicated by pre-existing diabetes mellitus and congenital malformations: a Danish population-based study. Clinical epidemiology. 2021;23(1):615-626. https://doi.org/10.2147/CLEP.S298748

10. Wu Y, Liu B, Sun Y, Du Y, Santillan MK, Santillan DA, et al. association of maternal prepregnancy diabetes and gestational diabetes mellitus with congenital anomalies of the newborn. Diabetes Care. 2020; 43(12):2983–2990. https://doi.org/10.2337/dc20-0261

11. Yang G-R, Dye TD, Li D. Effects of pre-gestational diabetes mellitus and gestational diabetes mellitus on macrosomia and birth defects in upstate New York. Diabetes research and clinical practice. 2019;155(1):107811.https://doi.org/10.1016/j.diabres.2019.107811

12. Chen L, Yang T, Chen L, Wang L, Wang T, Zhao L, et al. Risk of congenital heart defects in offspring exposed to maternal diabetes mellitus: an updated systematic review and meta-analysis. Archives of Gynecology and Obstetrics. 2019;300(12):1491-1506. https://doi.org/10.1007/s00404-019-05376-6

13. Hoang TT, Marengo LK, Mitchell LE, Canfield MA, Agopian AJ.Original findings and updated metaanalysis for the association between maternal diabetes and risk for congenital heart disease phenotypes. American Journal of Epidemiology. 2017;186(1):118-128. https://doi.org/10.1093/aje/kwx033

14. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. British Medical Journal. 2021;372(1):1-1https://doi.org/10.1371/journal.pmed.1003583

15. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. Journal of the American Medical Association. 2000;283(15):2008-2012.https://doi.org/10.1001/jama.283.15.2008

16. Rothman KJ, Greenland S, Lash TL. Modern epidemiology. 3rd edition. Philadelphia:Lippincott Williams & Wilkins;2014;25(2):178-181.https://doi.org/10.1097/EDE.0000000000000062

17. Sterne JA, Herna´n MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. British Medical Journal. 2016; 355(1):4919. https://doi.org/10.1136/bmj.i4919

18. Hamling J, Lee P, Weitkunat R, Ambu¨hl M. Facilitating meta-analyses by deriving relative effect and precision estimates for alternative comparisons from a set of estimates presented by exposure level or disease category. Statistics in medicine. 2008;27(7):954-970. https://doi.org/10.1002/sim.3013

19. DerSimonian R, Laird N.Meta-analysis in clinical trials. Controlled Clinical Trials.1986; 7(3):177–188.https://doi.org/10.1016/0197-2456(86)90046-2

20. Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses.British Medical Journal.2003; 327(7414):557–560.https://doi.org/10.1136/bmj.327.7414.557

21. Deeks JJ, Higgins JP, Altman DG, Cochrane Statistical Methods Group. Analysing data and undertaking meta-analyses.Cochrane handbook for systematic reviews of interventions.2019;23(!):241-284:https://training.cochrane.org/handbook/archive/v6/chapter-10

22. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test.British Medical Journal.1997; 315(7109):629–634.https://doi.org/10.1136/bmj.315.7109.629

23. Allen LA, Cannings-John RL, Evans A, Thayer DS, French R, Paranjothy S, et al. Pregnancy in teenagers diagnosed with type 1 diabetes mellitus in childhood: a national population-based e-cohort study. Diabetologia.2020;63(1):799–810. https://doi.org/10.1007/s00125-019-05063-w

24. Darke J, Glinianaia SV, Marsden P, Bell R. Pregestational diabetes is associated with adverse outcomes in twin pregnancies: a regional register-based study. Acta Obstetricia et Gynecologica Scandinavica. 2016;95(3):339-46. https://doi.org/10.1111/aogs.12825

25. Garne E, Loane M, Dolk H, Barisic I, Addor MC, Arriola L, et al. Spectrum of congenital anomalies in pregnancies with pregestational diabetes. Birth Defects Research Part A: Clinical and Molecular Teratology. 2012 ;94(3):134-140. https://doi.org/10.1002/bdra.22886

26. Bell R, Glinianaia SV, Tennant PWG, Bilous RW, Rankin J. Peri-conception hyperglycaemia and nephropathy are associated with risk of congenital anomaly in women with pre-existing diabetes: a population- based cohort study. Diabetologia. 2012; 55(2):936–947. https://doi.org/10.1007/s00125-012-2455-y

27. Macintosh MC, Fleming KM, Bailey JA, Doyle P, Modder J, Acolet D, et al. Perinatal mortality and congenital anomalies in babies of women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland: population-based study. British Medical Journal. 2006;333(7560):177. https://doi.org/10.1136/bmj.38856.692986.AE

28. Raitio A, Tauriainen A, Leinonen MK, Syva¨nen J, Kemppainen T, Lo¨yttyniemi E, et al. Maternal risk factors for gastroschisis: a population-based case-control study. Birth Defects Res. 2020;112(13):989-995. https://doi.org/10.1002/bdr2.1703

29. Mowla S, Gissler M, Ra¨isa¨nen S, Kancherla V. Association between maternal pregestational diabetes mellitus and spina bifida: a population-based case-control study, Finland, 2000–2014. Birth Defects Research. 2020 Jan 15;112(2):186-95.. https://doi.org/10.1002/bdr2.1624

30. Hilde´n K, Hanson U, Persson M, Magnuson A, Simmons D, Fadl H. Gestational diabetes and adiposity are independent risk factors for perinatal outcomes: a population based cohort study in Sweden. Diabetic Medicine. 2019; 36(2):151–157. https://doi.org/10.1111/dme.13843

31. Ludvigsson JF, Neovius M, So¨derling J, Gudbjo¨ rnsdottir S, Svensson AM, Franze´n S, et al. Periconception glycaemic control in women with type 1 diabetes and risk of major birth defects: population based cohort study in Sweden. British Medical Journal. 2018; 362: (1).2638. https://doi.org/10.1136/bmj.k2638