Clinical Ophthalmology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

Ophthalmic Changes in the Offspring of Pregnant Women with Gestational Diabetes Mellitus or Diabetes Mellitus – A Systematic Review

Yushuai Liu[1], Jiashuang Yan[2], Mu Li[1], Dan Zhao[1]

[1]Department of Ophthalmology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, 430022, People's Republic of China; [2]Wuhan University of Science and Technology, Wuhan, Hubei, 430081, People's Republic of China

Correspondence: Dan Zhao, Email zd2017hust@163.com

Background: Gestational diabetes mellitus (GDM) affects 5.8% to 25.1% of pregnant women and is associated with a range of adverse perinatal outcomes, including intrauterine growth restriction, prematurity, neonatal respiratory distress, and adiposity. Offspring of mothers with GDM or diabetes mellitus (DM) are also at elevated risk for long-term metabolic complications, such as obesity, dyslipidemia, and type 2 DM. While systemic and structural anomalies—including congenital heart disease, skeletal malformations, and renal agenesis—have been well documented, limited attention has been paid to ophthalmic consequences. Accordingly, this study aims to summarize current evidence on the impact of maternal GDM/DM on the ocular development and long-term visual outcomes in offspring.

Methods: A review was conducted, integrating findings from studies describing ocular abnormalities in offspring born to mothers with GDM/DM.

Results: GDM/DM during pregnancy may contribute to a spectrum of ocular anomalies in offspring, including hypoplasia of the iris stroma, vascular tortuosity and dilation of the iris vessels, optic nerve hypoplasia, decreased macular thickness and volume, and an increased risk of long-term ophthalmic morbidity such as refractive errors.

Conclusion: Given the range of potential ophthalmic abnormalities in offspring of mothers with GDM/DM, regular ocular screening and long-term follow-up are recommended. Further research is warranted to better understand the underlying mechanisms and to develop evidence-based screening protocols.

Keywords: gestational diabetes mellitus, offspring, ophthalmic changes, congenital malformations, long-term ophthalmic morbidity

Introduction

Gestational diabetes mellitus (GDM) is defined as first occurred or recognized glucose intolerance during pregnancy, in spite of the requirement for insulin therapy, degree of the metabolic disorder, or duration of the condition after pregnancy.[1,2] Women with GDM show evidence of metabolic dysfunction before conception, such as increased insulin resistance and pancreatic β-cell defects. Following pregnancy and the related metabolic changes (increased insulin resistance and demand for pancreatic β-cell response due to the release of placental factors), the effect of insulin in inhibiting endogenous glucose (primarily hepatic glucose) generation and promoting glucose consumption by peripheral skeletal muscle and adipose tissue is weakened, leading to clinical hyperglycemia. Maternal hyperglycemia increases placental transfer of glucose and (fetal) β-cell secretagogues to the fetus, resulting in fetal hyperinsulinemia. Subsequently, fetal hyperinsulinemia can cause fetal metabolic re-programming and further short-term and long-term pathological changes, such as overgrowth, adiposity, and metabolic dysfunction, in later life.[1]

Recent large-scale studies have provided updated insights into the global and regional burden of diabetes in women and its impact on pregnancy. According to the Global Burden of Disease (GBD) Study 2021, the global prevalence of diabetes increased from 5.9% (5.5–6.3) in 2021 to 9.5% (9.0–9.9) in 2050, influencing more than 1.27 billion (1.19–1.35)

Received: 13 February 2025
Accepted: 28 July 2025
Published: 18 August 2025

individuals. Furthermore, the sub-analysis specifically investigating female trends reported that in 64 countries and territories (31.4%), age-standardised diabetes prevalence was higher in females than in males, with more than 20% excess observed in Azerbaijan, Haiti, Laos, Mauritania, Zimbabwe, and Belize. In contrast, in central sub-Saharan Africa, male prevalence was significantly higher (1.40 times; 95% CI: 1.30–1.48), while central Latin America, southern sub-Saharan Africa, and the Caribbean showed >10% higher prevalence in females.[3] A 2024 pooled analysis of 1108 population-representative studies involving 141 million participants further confirmed the steady rise in diabetes prevalence, indicating that in 2022, an estimated 828 million (95% credible interval 757–908) adults had diabetes. In women, although some high-income countries such as Japan, Spain, and France experienced a decline in female diabetes prevalence—possibly linked to stable or decreasing obesity rates—most regions demonstrated rising trends. Between 1990 and 2022, age-standardised diabetes prevalence increased with high certainty in 131 countries for women, doubling in 66 of them. The most substantial increases were observed in countries spanning Southeast Asia, South Asia, North Africa, and the Caribbean.[4] These findings reflect a growing challenge to maternal health worldwide. In terms of pregnancy-specific outcomes, gestational diabetes mellitus (GDM) remains one of the most prevalent complications. A 2024 meta-analysis including 1.55 million pregnancies in the United States and Canada reported an overall GDM prevalence of 6.9% (95% CI: 5.7–8.3), with 13.7% (95% CI: 10.7–17.3) diagnosed using one-step OGTT and 5.2% (95% CI: 4.4–6.1) using the two-step approach. In addition, the study highlighted the potential of continuous glucose monitoring and alternative biomarkers such as HbA1c to detect glycemic abnormalities even among women with normal OGTT results, offering promising ways for earlier and more accurate GDM diagnosis.[5] These statistics reflect growing public health concerns and provide critical context for evaluating the long-term consequences of GDM, including ophthalmic sequelae in affected offspring.

Major GDM risk factors include maternal overweight and obesity, late childbearing, a medical history of GDM, family history of type 2 diabetes mellitus (DM), and ethnicity.[1] Pregnant women with GDM may also be more susceptible to other diseases, such as type 2 diabetes mellitus (DM), cardiometabolic dysfunction, hypertension, increased cardiovascular risks, increased incidence rate of cardiovascular events, metabolic syndrome, kidney diseases, liver diseases, retinal dysfunction and diseases, certain neoplastic diseases.[1,6–15] Thus, we conclude that pregnant women with GDM may have various lesions involving multiple organs and systems.

Several retrospective and prospective observational studies have indicated that GDM is closely associated with poor maternal and offspring outcomes. The perinatal complications of GDM include polyhydramnios, preeclampsia, macrosomia, surgical delivery, birth canal lacerations, shoulder dystocia, neonatal hypoglycemia, jaundice, and perinatal mortality in some cases of untreated GDM.[1,16–22] For instance, Pettitt et al first highlighted in a cohort of Pima Indian women that maternal hyperglycemia during the third trimester was significantly correlated with increased risks of perinatal mortality, macrosomia, toxemia, and cesarean delivery.[16] Beischer et al showed that early identification and treatment of maternal hyperglycemia could significantly reduce perinatal mortality, underscoring the importance of antenatal screening.[17] Casey et al reported that women with GDM had higher incidences of hypertensive disorders, cesarean delivery, and shoulder dystocia compared with the general obstetric population.[18] Aberg et al linked impaired glucose tolerance to increased fetal mortality in preceding siblings, suggesting long-term interpregnancy risks.[19] Persson and Hanson also identified elevated rates of neonatal complications—such as fetal, asphyxia, and transient tachypnea —among infants born to mothers with GDM.[20] Subsequent large-scale studies further reinforced these findings. Jensen et al, in a cohort of 3260 Danish women, demonstrated that hyperglycemia detected via a 75-g oral glucose tolerance test was associated with increased risk of adverse maternal and perinatal outcomes (eg, macrosomia, spontaneous preterm delivery, hypertensive complications, and neonatal hypoglycaemia, etc).[21] The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study led by Metzger et al, involving more than 23,000 women, established a continuous relationship between maternal glucose levels and adverse pregnancy outcomes—including birth weight above the 90th percentile, cord-blood serum C-peptide level above the 90th percentile, and neonatal hypoglycemia—even below traditional diagnostic thresholds.[22] Collectively, these findings revealed the significant impact of GDM on maternal and neonatal health and emphasize the need for early detection and timely intervention to improve pregnancy outcomes.

Compared with infants born to mothers without DM, those born to mothers with pre-pregnancy DM or GDM were more likely to have congenital anomalies.[23] Liu et al reported that neonates born to mothers with GDM had a two to three

times greater chance of suffering from congenital heart disease and congenital anomalies of the kidneys and urinary tracts, especially in male neonates.[24] Using magnetic resonance imaging to investigate the brain function, a case-control study in preterm infants born to mothers with GDM reported that compared with infants born to mothers without GDM, the brains of infants born to mothers with GDM tended to have multiple decreased fractional anisotropy, indicating microstructural white matter abnormalities.[25] Although pregnant hyperglycemia might have a significant impact on fetal neurodevelopment and on offspring cognition,[26] there is still no solid evidence confirming the independent negative effect of maternal GDM on cognitive function in the offspring of pregnant women with GDM.[27,28] Therefore, further studies in this field are needed.

Increasing evidence now clearly shows that offspring exposed in utero to maternal hyperglycemia—particularly GDM—experience long-term alterations, including increased adiposity, insulin resistance, hypertension, and early cardiac functional changes. Josefson et al reported a 54% higher obesity risk and marked impairments in insulin sensitivity among GDM-exposed subjects aged 10–14 years,[29] and a clinical study within the Danish National Birth Cohort indicated that adolescent offspring of women with GDM has increased adiposity among 9 to 16 girls.[30] HAPO FUS study indicated that exposure to higher levels in utero is significantly associated with childhood glucose and insulin resistance independent of maternal and childhood BMI and family history of diabetes.[31] Besides insulin resistance, in utero exposure to diabetes confers an additional independent risk for the development of T2DM and/or cardiovascular disease (eg, higher systolic blood pressure) later in life. Another prospective cohort study also confirmed that maternal DM is a risk factor for high blood pressure in offspring at the age of 10 (systolic: β, 1.48; 95% CI, 0.36–2.59; and diastolic: β, 0.86; 95% CI, 0.05–1.71).[32] Except hypertension, intrauterine exposure to maternal diabetes was also associated with higher morbidity and risk related to cardiovascular disease by offspring up to 35 years old (adjusted hazard ratio [HR] 1.42, 95% confidence interval [CI] 1.12–1.79).[33] Besides GDM, the offspring of women with prior diabetes is also associated with some adverse neurocognitive and behavioural outcomes. In one Swedish retrospective cohort study, a parental history of T1 diabetes is associated with 29% elevated risk of attention deficit/hyperactivity disorder.[34] Maternal pregestational diabetes mellitus combined with severe obesity will not only increase the risk for attention-deficit/hyperactivity disorder and conduct disorder (HR = 6.03; 95% CI = 3.23–11.24), but also for autism spectrum disorder (HR = 6.49; 95% CI = 3.08–13.69) in their offspring.[35] In terms of behavioral and intellectual development, maternal diabetes may also have negative effect on neurodevelopment, IQ and educational attainment.[36–38]

The long-term effects of GDM, including childhood adiposity and cardiometabolic risks, have also been reported. Offspring born to women with GDM was suggested to have higher BMI z-scores, higher systolic and diastolic blood pressures, higher rates of childhood overweight and obesity, higher lipid profile levels, and higher insulin and insulin resistance levels than those born to women without GDM.[8] In addition, other studies have indicated that, compared with their counterparts, offspring born to women with GDM had greater Carotid Intima-Media Thickness, higher cardiac output and stroke volume, reduced mitral E/A ratio, and decreased total peripheral resistance in early childhood and adolescence.[39,40] Compared with GDM, pre-existing diabetes (type 1 or type 2 DM) is typically associated with a longer duration and greater severity of hyperglycemia, and thus may lead to more profound fetal programming effects.[41–43]

Although numerous studies have investigated the effect of GDM on multiple organs and tissues, little is known about ophthalmic changes in the offspring of pregnant women with GDM/DM. A recent study confirmed that medically treated GDM is an independent risk factor for long-term ophthalmic morbidity,[44] indicating the important effect of GDM/DM on ophthalmic changes. Accordingly, in this review, we summarize the effect of GDM/DM on the ophthalmic development of the offspring of pregnant women with GDM/DM, including iris changes, optic nerve hypoplasia, retinal changes, and long-term ophthalmic morbidity such as refractive errors.

Methods

The bibliographic searches were performed in PubMed, from inception to June 2025, written in English. The primary search strategy was (gestational diabetes) OR (diabetes) OR (diabetes in pregnancy) AND (offspring) OR (children) OR (neonate) AND (ophthalmic) OR (congenital malformations) OR (long-term ophthalmic morbidity) OR (ocular) OR (eye). Following the literature search, two independent reviewers were involved in the literature screening and data

extraction process. Any discrepancies were resolved through discussion or consultation with a third senior reviewer. This approach ensured accuracy and consistency in data collection.

In this review, we aimed to explore the potential ophthalmic consequences in offspring born to mothers with GDM/DM. Based on the PICO framework:

Population (P): Offspring of women with GDM/DM;

Intervention (I): Intrauterine exposure to maternal GDM/DM;

Comparison (C): Offspring of normoglycemic pregnancies (mothers without GDM or diabetes);

Outcome (O): Ophthalmic abnormalities and developmental changes, and long-term risks such as refractive errors.

Iris Changes

The iris is composed of three components: the iris pigmented epithelium, iridial muscles, and iris stroma.[45] The iris root is attached to the ciliary body and corneal-scleral junction, which is also called the iridocorneal angle. During embryogenesis, the iris originates from both the optic cup and periocular mesenchyme.[45] After birth, the iris is still immature and undergoes certain developmental changes: the surface of the iris stroma is formed into crypts and hillocks; the color is altered as stromal melanocytes produce pigmentations, the iris vessel changes in its caliber and course, and the innervation of the pupil becomes mature.[46] GDM could affect the morphology and development of the iris. Ricci et al performed routine ophthalmic examinations of 600 full-term neonates, including 66 born to mothers with GDM, and found that more than half of the infants born to diabetic mothers revealed significant tortuosity and dilatation of the iris vessels, and this changes in iris vessel resolved spontaneously within 14 days after birth. In addition, 90% and 85% of newborns in the diabetic group showed hypoplasia of the iris stroma and changes in pupil dynamics, respectively.[47]

Optic Nerve Hypoplasia

Optic nerve hypoplasia (ONH) is a nonprogressive congenital disease. Histologically, it is characterized by selective tortuosity of the major retinal veins and abnormally small and pale optic discs with a surrounding area of pigmented sclera, which could result in the "double ring" sign.[48,49] Both unilateral and bilateral optic nerve hypoplasia can be observed, and bilateral cases are generally accompanied by significant blindness and infantile nystagmus, while unilateral cases are accompanied by sensory esotropia (more commonly) or exotropia (less commonly).[48] ONH is often associated with certain clinically important central nervous system/endocrine abnormalities that belong to the disease spectrum of septo-optic dysplasia. Septo-optic dysplasia is a congenital syndrome with developmental abnormalities of the optic nerves, cerebral hemispheres, and midline brain structures.[49–51]

Previous studies have indicated a relationship between ONH and certain gestational conditions, including primioarity, prematurity, young maternal age, GDM, and alcohol/tobacco abuse.[49,52–55] However, the exact pathogenesis of ONH remains unclear. Previous genetic investigations have suggested a potential role of HESX1 and SOX2 gene mutations in the pathogenesis of ONH. However, the rate of these mutations is less than 1%. Thus, further genetic studies in this field are needed.[48,56–58] Besides genetic studies, GDM could also influence the development of the optic nerve and be the reason for ONH.[48] Female sex, short gestation duration, low birth weight, and poor maternal DM control may increase the risk of ONH,[56] and maternal type 1 DM is associated with hypoplasia of the superior segmental optic nerve in offspring.[59–65]

Retinal Changes

High levels of circulating glucose and DM were confirmed to have adverse effects on the eye, such as non-proliferative and proliferative diabetic retinopathy, macular edema, faster formation and progression of cataracts, and higher risk for glaucoma. Furthermore, there was a close correlation between the control of DM and the risk of DM-related ophthalmic complications, suggesting that the morbidity of ophthalmic complications decreased significantly with strict control of DM.[44,66] However, whether good glycemic control could prevent the short-term and long-term ophthalmological complications in the offspring of pregnant women with GDM/DM still needs further investigations. One study systematically tested the changes in the retinal structure of offspring of pregnant women with GDM/DM; among them, 1741 offspring underwent an adequate quality retinal nerve fiber layer (RNFL) scan and 1687 offspring underwent an

adequate-quality macular scan. The results revealed that offspring of pregnant women with GDM/DM had significantly thinner inner and outer macula and macular volume than offspring from non-diabetic pregnancies. However, central macular thickness, foveal minimum thickness, and RNFL thickness were not significantly different between the offspring of pregnant women with and without GDM.[67]

A recent cohort study by Khoshtinat et al reported that GDM was significantly associated with an increased risk of retinopathy of prematurity (ROP) in preterm infants.[68] Among 1161 infants studied, 76.5% of eyes in the GDM group showed ROP or incomplete retinal vascularization, and 13.5% developed severe ROP—both rates significantly higher than in the hypertensive disorders of pregnancy group. These associations remained significant after adjusting for gestational age and birth weight. The authors suggested that intrauterine hyperglycemia may impair retinal angiogenesis via vascular endothelial growth factor dysregulation, increasing vulnerability to severe ROP. These findings support the need for enhanced postnatal retinal screening in infants born to mothers with GDM.

In parallel, recent studies employing optical coherence tomography (OCT), optical coherence tomography angiography (OCTA), and fundus autofluorescence (FAF) have revealed microscopic changes involving the microvascular environment and the macula in GDM patients.[69,70] These noninvasive imaging modalities offer promising tools for detecting early retinal changes in both mothers with GDM and their offspring, underscoring their potential role in ongoing ophthalmic surveillance.

Long-Term Ophthalmic Morbidity

In terms of long-term ophthalmic morbidity, GDM requiring medication was reported to be an independent risk factor. The risk of long-term ophthalmic morbidity is significantly higher in the offspring of pregnant women with GDM. Among the long-term complications, refractive error has often been reported. The offspring of pregnant women with GDM had a three-fold higher rate of refractive error than the control group (offspring of pregnant women without GDM). Although the GDM-induced refractive error is relatively easy to manage, if it is not detected in a timely manner, it could further result in amblyopia and/or accommodative strabismus, disturbance of acquisition of fine motor skills, and even learning problems.[44,71]

Another up to 25-years follow-up study found that pregnancy with DM is associated with an increased risk of high refractive error in their offspring. Compared with those without diabetic complications, the increased risks were more pronounced among offspring of mothers with diabetic complications, which suggesting that positive glucose control in mothers with GDM/DM or pre-gestational diabetes is crucial for reducing high refractive error risk in offspring.[72]

A recent focused review by Guo et al provided additional support for the link between maternal hyperglycemia and refractive error development in offspring.[73] Their findings highlighted several structural and functional consequences of intrauterine hyperglycemia, including thinner macular regions, increased axial length, and thicker central corneas in neonates. Moreover, both human and animal studies demonstrated that intrauterine exposure to hyperglycemia impairs retinal cone cell development, disrupts Pax6 expression, and increases oxidative stress, ultimately affecting the trajectory of postnatal visual maturation.

Conclusions

The etiology of GDM is related to a volumetric increase in circulating glucose during pregnancy.[74] GDM can increase the risk of metabolic morbidity in newborns. However, if good metabolic management is performed, the incidence rate of congenital malformations does not differ from that in non-diabetic populations.[75]

The primary aim of GDM/DM treatment is the prevention of fetal overgrowth and pregnant complications, which is normally achieved by dietary regulation and physical activity involvement, because dietary regulation and physical activity involvement could minimize the postprandial glucose elevation and the requirement for medication interventions.[1] As mentioned above, although ophthalmic complications of GDM/DM are not commonly reported, they are still not rare in the clinic, and clinicians can encounter them at times.

Future research should focus on several key areas:

1. Longitudinal Cohort Studies: There is a need for large-scale, prospective, longitudinal studies that follow children from birth to adulthood to evaluate the onset, progression, and persistence of ophthalmic abnormalities associated with maternal GDM/DM. These studies should also evaluate the influence of glycemic control during pregnancy on visual outcomes.
2. Mechanistic Investigations: The exact biological mechanisms by which maternal hyperglycemia affects fetal ocular development remain poorly understood. Future studies should explore the molecular and epigenetic pathways involved in retinal neurogenesis, optic nerve development, and vascular remodeling.
3. Imaging-based Early Detection: Advanced imaging modalities such as OCT, OCTA, and FAF should be systematically used to screen and monitor subtle ophthalmic changes in offspring at high risk, even in the absence of overt visual symptoms.
4. Interventional Strategies: Studies should examine whether early interventions (eg, visual training, optical correction, or even systemic metabolic control in offspring) can ameliorate the long-term visual sequelae of GDM/DM.
5. Impact of Severity and Treatment Type: Differentiating the ophthalmic outcomes in offspring born to mothers with diet-controlled vs insulin-treated GDM/DM may provide insight into the dose-response relationship between hyperglycemia and ocular development.

In summary, considering the potential ophthalmic changes in the offspring of mothers with GDM/DM, regular and systematic ophthalmologic examinations are recommended. Previous studies with follow-up durations of up to 18 and even 25 years have demonstrated associations between maternal diabetes during pregnancy and long-term ophthalmic morbidity in offspring.[72] These findings suggest that follow-up should extend at least into early adulthood. However, there is a lack of research regarding optimal follow-up intervals and standardized screening protocols. Further investigation is needed to guide clinical practice and establish evidence-based strategies for preventing visual impairment in this high-risk population.

Abbreviations

GDM, Gestational diabetes mellitus; DM, diabetes mellitus.

Data Sharing Statement

The dataset(s) supporting the conclusions of this article is (are) included within the article.

Funding

This study was supported by the National Natural Science Foundation of China under Grant 82000893.

Disclosure

The authors report no conflicts of interest in this work.

References

1. McIntyre HD, Catalano P, Zhang C, Desoye G, Mathiesen ER, Damm P. Gestational diabetes mellitus. *Nat Rev Dis Primers*. 2019;5(1):47. doi:10.1038/s41572-019-0098-8
2. Cho NH, Shaw JE, Karuranga S, et al. Idf diabetes atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabet Res Clin Pract*. 2018;138:271–281. doi:10.1016/j.diabres.2018.02.023
3. GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the global burden of disease study 2021. *Lancet*. 2023;402(10397):203–234. doi:10.1016/S0140-6736(23)01301-6
4. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes prevalence and treatment from 1990 to 2022: a pooled analysis of 1108 population-representative studies with 141 million participants. *Lancet*. 2024;404(10467):2077–2093. doi:10.1016/S0140-6736(24)02317-1
5. Eades CE, Burrows KA, Andreeva R, Stansfield DR, Evans JM. Prevalence of gestational diabetes in the United States and Canada: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2024;24(1):204. doi:10.1186/s12884-024-06378-2
6. Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. *Lancet*. 2009;373(9677):1773–1779. doi:10.1016/S0140-6736(09)60731-5
7. Yogev Y, Xenakis EM, Langer O. The association between preeclampsia and the severity of gestational diabetes: the impact of glycemic control. *Am J Obstet Gynecol*. 2004;191(5):1655–1660. doi:10.1016/j.ajog.2004.03.074

8. Li LJ, Huang L, Tobias DK, Zhang C. Gestational diabetes mellitus among asians - a systematic review from a population health perspective. *Front Endocrinol*. 2022;13:840331. doi:10.3389/fendo.2022.840331
9. Burlina S, Dalfra MG, Chilelli NC, Lapolla A. Gestational diabetes mellitus and future cardiovascular risk: an update. *Int J Endocrinol*. 2016;2016:2070926. doi:10.1155/2016/2070926
10. Daly B, Toulis KA, Thomas N, et al. Increased risk of ischemic heart disease, hypertension, and type 2 diabetes in women with previous gestational diabetes mellitus, a target group in general practice for preventive interventions: a population-based cohort study. *Plos Med*. 2018;15(1):e1002488. doi:10.1371/journal.pmed.1002488
11. Retnakaran R. Hyperglycemia in pregnancy and its implications for a woman's future risk of cardiovascular disease. *Diabet Res Clin Pract*. 2018;145:193–199. doi:10.1016/j.diabres.2018.04.008
12. Retnakaran R, Shah BR. Role of type 2 diabetes in determining retinal, renal, and cardiovascular outcomes in women with previous gestational diabetes mellitus. *Diabetes Care*. 2017;40(1):101–108. doi:10.2337/dc16-1400
13. Kramer CK, Campbell S, Retnakaran R. Gestational diabetes and the risk of cardiovascular disease in women: a systematic review and meta-analysis. *Diabetologia*. 2019;62(6):905–914. doi:10.1007/s00125-019-4840-2
14. Wang Y, Yan P, Fu T, et al. The association between gestational diabetes mellitus and cancer in women: a systematic review and meta-analysis of observational studies. *Diabetes Metab*. 2020;46(6):461–471. doi:10.1016/j.diabet.2020.02.003
15. Li LJ, Kramer M, Tapp RJ, et al. Gestational diabetes mellitus and retinal microvasculature. *BMC Ophthalmol*. 2017;17(1):4. doi:10.1186/s12886-016-0398-7
16. Pettitt DJ, Knowler WC, Baird HR, Bennett PH. Gestational diabetes: infant and maternal complications of pregnancy in relation to third-trimester glucose tolerance in the Pima indians. *Diabetes Care*. 1980;3(3):458–464. doi:10.2337/diacare.3.3.458
17. Beischer NA, Wein P, Sheedy MT, Steffen B. Identification and treatment of women with hyperglycaemia diagnosed during pregnancy can significantly reduce perinatal mortality rates. *Aust N Z J Obstet Gynaecol*. 1996;36(3):239–247. doi:10.1111/j.1479-828X.1996.tb02703.x
18. Casey BM, Lucas MJ, Mcintire DD, Leveno KJ. Pregnancy outcomes in women with gestational diabetes compared with the general obstetric population. *Obstet Gynecol*. 1997;90(6):869–873. doi:10.1016/S0029-7844(97)00542-5
19. Aberg A, Rydhstrom H, Kallen B, Kallen K. Impaired glucose tolerance during pregnancy is associated with increased fetal mortality in preceding sibs. *Acta Obstet Gynecol Scand*. 1997;76(3):212–217. doi:10.1111/j.1600-0412.1997.tb07847.x
20. Persson B, Hanson U. Neonatal morbidities in gestational diabetes mellitus. *Diabetes Care*. 1998;21 Suppl 2:B79–84.
21. Jensen DM, Damm P, Sorensen B, et al. Proposed diagnostic thresholds for gestational diabetes mellitus according to a 75-g oral glucose tolerance test. Maternal and perinatal outcomes in 3260 Danish women. *Diabet Med*. 2003;20(1):51–57. doi:10.1046/j.1464-5491.2003.00857.x
22. Metzger BE, Lowe LP, Dyer AR, et al. Hyperglycemia and adverse pregnancy outcomes. *N Engl J Med*. 2008;358(19):1991–2002.
23. Wu Y, Liu B, Sun Y, et al. Association of maternal prepregnancy diabetes and gestational diabetes mellitus with congenital anomalies of the newborn. *Diabetes Care*. 2020;43(12):2983–2990. doi:10.2337/dc20-0261
24. Liu X, Liu G, Wang P, et al. Prevalence of congenital heart disease and its related risk indicators among 90,796 Chinese infants aged less than 6 months in tianjin. *Int J Epidemiol*. 2015;44(3):884–893. doi:10.1093/ije/dyv107
25. Xuan DS, Zhao X, Liu YC, et al. Brain development in infants of mothers with gestational diabetes mellitus: a diffusion tensor imaging study. *J Comput Assist Tomogr*. 2020;44(6):947–952. doi:10.1097/RCT.0000000000001110
26. Anderson JL, Waller DK, Canfield MA, Shaw GM, Watkins ML, Werler MM. Maternal obesity, gestational diabetes, and central nervous system birth defects. *Epidemiology*. 2005;16(1):87–92. doi:10.1097/01.ede.0000147122.97061.bb
27. Fraser A, Lawlor DA. Long-term health outcomes in offspring born to women with diabetes in pregnancy. *Curr Diab Rep*. 2014;14(5):489. doi:10.1007/s11892-014-0489-x
28. Clausen TD, Mortensen EL, Schmidt L, et al. Cognitive function in adult offspring of women with gestational diabetes--the role of glucose and other factors. *PLoS One*. 2013;8(6):e67107. doi:10.1371/journal.pone.0067107
29. Josefson JL, Catalano PM, Lowe WL, et al. The joint associations of maternal bmi and glycemia with childhood adiposity. *J Clin Endocrinol Metab*. 2020;105(7):2177–2188. doi:10.1210/clinem/dgaa180
30. Grunnet LG, Hansen S, Hjort L, et al. Adiposity, dysmetabolic traits, and earlier onset of female puberty in adolescent offspring of women with gestational diabetes mellitus: a clinical study within the Danish National Birth Cohort. *Diabetes Care*. 2017;40(12):1746–1755. doi:10.2337/dc17-0514
31. Scholtens DM, Kuang A, Lowe LP, et al. Hyperglycemia and adverse pregnancy outcome follow-up study (HAPO FUS): maternal glycemia and childhood glucose metabolism. *Diabetes Care*. 2019;42(3):381–392. doi:10.2337/dc18-2021
32. Miranda JO, Cerqueira RJ, Barros H, Areias JC. Maternal diabetes mellitus as a risk factor for high blood pressure in late childhood. *Hypertension*. 2019;73(1):e1–e7. doi:10.1161/HYPERTENSIONAHA.118.11761
33. Guillemette L, Wicklow B, Sellers EAC, et al. Intrauterine exposure to diabetes and risk of cardiovascular disease in adolescence and early adulthood: a population-based birth cohort study. *CMAJ*. 2020;192(39):E1104–E1113. doi:10.1503/cmaj.190797
34. Ji J, Chen T, Sundquist J, Sundquist K. Type 1 diabetes in parents and risk of attention deficit/hyperactivity disorder in offspring: a population-based study in Sweden. *Diabetes Care*. 2018;41(4):770–774. doi:10.2337/dc17-0592
35. Kong L, Norstedt G, Schalling M, Gissler M, Lavebratt C. The RISK OF OFFSPRING PSYCHIATRIC DISORDERS IN THE SETTING OF MATERNAL OBESITY AND DIABetes. *Pediatrics*. 2018;142(3):e20180776. doi:10.1542/peds.2018-0776
36. Fraser A, Nelson SM, Macdonald-Wallis C, Lawlor DA. Associations of existing diabetes, gestational diabetes, and glycosuria with offspring IQ and educational attainment: the Avon longitudinal study of parents and children. *Exp Diabetes Res*. 2012;2012:963735. doi:10.1155/2012/963735
37. Bytoft B, Knorr S, Vlachova Z, et al. Long-term cognitive implications of intrauterine hyperglycemia in adolescent offspring of women with type 1 diabetes (the EPICOM study). *Diabetes Care*. 2016;39(8):1356–1363. doi:10.2337/dc16-0168
38. Rizzo T, Metzger BE, Burns WJ, Burns K. Correlations between antepartum maternal metabolism and intelligence of offspring. *N Engl J Med*. 1991;325(13):911–916. doi:10.1056/NEJM199109263251303
39. Krishnaveni GV, Veena SR, Jones A, et al. Exposure to maternal gestational diabetes is associated with higher cardiovascular responses to stress in adolescent indians. *J Clin Endocrinol Metab*. 2015;100(3):986–993. doi:10.1210/jc.2014-3239
40. Hoodbhoy Z, Mohammed N, Aslam N, et al. Is the child at risk? Cardiovascular remodelling in children born to diabetic mothers. *Cardiol Young*. 2019;29(4):467–474. doi:10.1017/S1047951119000040

41. Seneviratne SN, Rajindrajith S. Fetal programming of obesity and type 2 diabetes. *World J Diabetes*. 2022;13(7):482–497. doi:10.4239/wjd.v13.i7.482
42. Monteiro LJ, Norman JE, Rice GE, Illanes SE. Fetal programming and gestational diabetes mellitus. *Placenta*. 2016;48 Suppl 1:S54–S60. doi:10.1016/j.placenta.2015.11.015
43. Catalano PM. The impact of gestational diabetes and maternal obesity on the mother and her offspring. *J Dev Orig Health Dis*. 2010;1(4):208–215. doi:10.1017/S2040174410000115
44. Walter E, Tsumi E, Wainstock T, Spiegel E, Sheiner E. Maternal gestational diabetes mellitus: is it associated with long-term pediatric ophthalmic morbidity of the offspring? *J Matern Fetal Neonatal Med*. 2019;32(15):2529–2538. doi:10.1080/14767058.2018.1439918
45. Davis-Silberman N, Ashery-Padan R. Iris development in vertebrates; Genetic and molecular considerations. *Brain Res*. 2008;1192:17–28. doi:10.1016/j.brainres.2007.03.043
46. Spierer A, Isenberg SJ, Inkelis SH. Characteristics of the iris in 100 neonates. *J Pediatr Ophthalmol Strabismus*. 1989;26(1):28–30. doi:10.3928/0191-3913-19890101-07
47. Ricci B, Scullica MG, Ricci F, Santo A. Iris vascular changes in newborns of diabetic mothers. *Ophthalmologica*. 1998;212(3):175–177. doi:10.1159/000027271
48. Brodsky MC. Optic nerve hypoplasia: "neural guidance" and the role of mentorship. *J Neuro-Ophthalmol*. 2020;40 Suppl 1:S21–28. doi:10.1097/WNO.0000000000001003
49. Mohney BG, Young RC, Diehl N. Incidence and associated endocrine and neurologic abnormalities of optic nerve hypoplasia. *JAMA Ophthalmol*. 2013;131(7):898–902. doi:10.1001/jamaophthalmol.2013.65
50. Acers TE. Optic nerve hypoplasia: septo-optic-pituitary dysplasia syndrome. *Trans Am Ophthalmol Soc*. 1981;79:425–457.
51. Birkebaek NH, Patel L, Wright NB, et al. Optic nerve size evaluated by magnetic resonance imaging in children with optic nerve hypoplasia, multiple pituitary hormone deficiency, isolated growth hormone deficiency, and idiopathic short stature. *J Pediatr*. 2004;145(4):536–541. doi:10.1016/j.jpeds.2004.06.041
52. Borchert M, Garcia-Filion P. The syndrome of optic nerve hypoplasia. *Curr Neurol Neurosci Rep*. 2008;8(5):395–403. doi:10.1007/s11910-008-0061-7
53. Garcia ML, Ty EB, Taban M, David RA, Rogers D, Traboulsi EI. Systemic and ocular findings in 100 patients with optic nerve hypoplasia. *J Child Neurol*. 2006;21(11):949–956. doi:10.1177/08830738060210111701
54. Zeki SM, Dutton GN. Optic nerve hypoplasia in children. *Br J Ophthalmol*. 1990;74(5):300–304. doi:10.1136/bjo.74.5.300
55. Hellstrom A, Wiklund LM, Svensson E. The clinical and morphologic spectrum of optic nerve hypoplasia. *J Aapos*. 1999;3(4):212–220. doi:10.1016/S1091-8531(99)70005-4
56. Borchert M. Reappraisal of the optic nerve hypoplasia syndrome. *J Neuroophthalmol*. 2012;32(1):58–67. doi:10.1097/WNO.0b013e31824442b8
57. McNay DE, Turton JP, Kelberman D, et al. Hesx1 mutations are an uncommon cause of septooptic dysplasia and hypopituitarism. *J Clin Endocrinol Metab*. 2007;92(2):691–697. doi:10.1210/jc.2006-1609
58. Mellado C, Poduri A, Gleason D, et al. Candidate gene sequencing of lhx2, hesx1, and sox2 in a large schizencephaly cohort. *Am J Med Genet A*. 2010;152A(11):2736–2742. doi:10.1002/ajmg.a.33684
59. Landau K, Bajka JD, Kirchschlager BM. Topless optic disks in children of mothers with type i diabetes mellitus. *Am J Ophthalmol*. 1998;125(5):605–611. doi:10.1016/S0002-9394(98)00016-6
60. Donat JFG. Septo-optic dysplasia in an infant of a diabetic mother. *Arch Neurol*. 1981;38(9):590–591. doi:10.1001/archneur.1981.00510090084012
61. Nelson M, Lessell S, Sadun AA. Optic nerve hypoplasia and maternal diabetes mellitus. *Arch Neurol*. 1986;43(1):20–25. doi:10.1001/archneur.1986.00520010016013
62. Foroozan R. Superior segmental optic nerve hypoplasia and diabetes mellitus. *J Diabetes Complications*. 2005;19(3):165–167. doi:10.1016/j.jdiacomp.2004.09.003
63. Kim RY, Hoyt WF, Lessell S, Narahara MH. Superior segmental optic hypoplasia. *Arch Ophthalmol*. 1989;107(9):1312–1315. doi:10.1001/archopht.1989.01070020382040
64. Kaur S, Jain S, Sodhi HB, Rastogi A, Kamlesh. Optic nerve hypoplasia. *Oman J Ophthalmol*. 2013;6(2):77–82. doi:10.4103/0974-620X.116622
65. Petersen RA, Holmes LB. Optic nerve hypoplasia in infants of diabetic mothers. *Arch Ophthalmol*. 1986;104(11):1587. doi:10.1001/archopht.1986.01050230025014
66. Aiello LP. Diabetic retinopathy and other ocular findings in the diabetes control and complications trial/epidemiology of diabetes interventions and complications study. *Diabetes Care*. 2014;37(1):17–23. doi:10.2337/dc13-2251
67. Tariq YM, Samarawickrama C, Li H, Huynh SC, Burlutsky G, Mitchell P. Retinal thickness in the offspring of diabetic pregnancies. *Am J Ophthalmol*. 2010;150(6):883–887. doi:10.1016/j.ajo.2010.06.036
68. Khoshtinat N, Moayeri M, Fakhredin H, et al. Association of hypertensive disorders of pregnancy and gestational diabetes mellitus with developing severe retinopathy of prematurity. *Int J Retina Vitreous*. 2025;11(1):52. doi:10.1186/s40942-025-00635-y
69. Al-Dwairi R, Altal O, Fares M, et al. Utility of fundus autofluorescence and optical coherence tomography in measuring retinal vascular thickness, macular density, and ophthalmic manifestations in women with gestational diabetes mellitus. *Life*. 2024;14(12):1596. doi:10.3390/life14121596
70. Pota ÇE, Doğan ME, Bülbül GA, Sanhal CY, Pota A. Optical coherence tomography angiography evaluation of retinochoroidal microvascular circulation differences in pregnant women with pregestational and gestational diabetes mellitus. *Exp Clin Endocrinol Diabetes*. 2024;132(9):522–530. doi:10.1055/a-2316-3903
71. Alvarez-Bulnes O, Mones-Llivina A, Cavero-Roig L, et al. Ophthalmic pathology in the offspring of pregnant women with gestational diabetes mellitus. *Matern Child Health J*. 2020;24(4):524–529. doi:10.1007/s10995-020-02887-6
72. Du J, Li J, Liu X, et al. Association of maternal diabetes during pregnancy with high refractive error in offspring: a nationwide population-based cohort study. *Diabetologia*. 2021;64(11):2466–2477. doi:10.1007/s00125-021-05526-z
73. Guo Y, Lu J, Zhu L, Hao X, Huang K. Association between hyperglycemia during pregnancy and offspring's refractive error: a focused review. *Eur J Ophthalmol*. 2025;35(1):60–68. doi:10.1177/11206721241238389
74. Damm P. Gestational diabetes mellitus and subsequent development of overt diabetes mellitus. *Dan Med Bull*. 1998;45(5):495–509.
75. Allen VM, Armson BA, Wilson RD, et al. Retired: teratogenicity associated with pre-existing and gestational diabete. *J Obstet Gynaecol Canada*. 2007;29(11):927–934. doi:10.1016/S1701-2163(16)32653-6