New study reveals that children of mothers with diabetes during pregnancy have an increased risk of eye problems

August 18 2021

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A new study published in *Diabetologia* (the journal of the European Association for the Study of Diabetes [EASD]) finds that mothers who

have diabetes before or during their pregnancy are more likely to have children who go on to develop eye problems.

The research is by Dr. Jiangbo Du, State Key Laboratory of Reproductive Medicine, Nanjing Medical University, Nanjing, China, and Dr. Jiong Li, Aarhus University, Aarhus, Denmark, and colleagues. It analysed the associations between maternal diabetes before or during pregnancy and the risk of high refractive error (RE): conditions in which there is a failure of the eye to properly focus images on the retina.

RE is one of the most common forms of visual impairment and includes both long and short-sightedness as well as astigmatism. Collectively these conditions are the second most common form of disability globally, and while low-degree REs can be corrected optically using spectacles or contact lenses, more serious high-degree REs can develop into severe and irreversible visual impairment that can reduce an individual's quality of life.

In recent decades there has been a rapid increase in the prevalence of RE, indicating that non-genetic factors may play an important role in its development. An increased tendency to perform close-up work such as using computers for long periods, as well as a lack of outdoor activity has been established as the main acquired risk factors for low and moderate RE development in school-age children and young adults. The causes of high RE defects, however, are still not fully understood.

Earlier research has shown that individuals with severe RE may have congenital eye defects before birth, suggesting that the conditions to which the foetus is exposed in the uterus may play a role in the development of more serious RE in later life. Maternal hyperglycaemia (high blood sugar) during pregnancy may lead to elevated foetal blood glucose levels, which can damage the retina and optic nerve and may lead to changes in the shape of the eyes that ultimately cause RE.

The authors believed that exposure to the effects of maternal diabetes while in the uterus could negatively affect the development of the foetus and lead to high RE in later life. They also anticipated that the most pronounced associations would be observed among mothers with diabetic complications since they usually represent more severe cases of the disease.

The team conducted a population-based cohort study using several Danish national medical registers and incorporated the details of all live births in Denmark from 1977 to 2016. Follow-up began at birth and continued until the first high RE diagnosis (where applicable), the death of the subject, their emigration, their 25th birthday, or the end of the study period on 31 December 2016, whichever came first. Mothers were considered to have diabetes if they were diagnosed with the disease either before or during pregnancy, and those with pre-gestational diabetes who had developed problems relating to their condition were grouped according to whether they had one or multiple complications.

The authors analysed both the occurrence of high RE in offspring and the specific type of eye problem. Out of 2,470,580 live births included in the study, 56,419 (2.3%) were exposed to maternal diabetes with 0.9% and 0.3% being type 1 and type 2 pre-gestational diabetes respectively (meaning diabetes already present before pregnancy), and 1.1% involving gestational diabetes.

The proportion of births to mothers with diabetes increased over the study period from 0.4% in 1977 to 6.5% in 2016 and diabetes was associated with the mother being older, more educated, having had more pregnancies, and being more likely to live alone.

During the follow-up period, high RE was diagnosed in 533 offspring of mothers with diabetes, and 19,695 offspring of those without the disease. Exposure to maternal diabetes was associated with a 39%

greater risk of high RE compared to unexposed offspring.

The researchers observed a difference in RE risk between type 1 and type 2 forms of diabetes with rates of high RE compared to unexposed individuals being 32% and 68% higher respectively. In addition, children of mothers with complications arising from diabetes were twice as likely to have eye problems, compared to an 18% increase in high RE risk in children of mothers who had no complications from the disease.

The authors say: "It was interesting to observe that hypermetropia (long-sightedness) occurred more frequently in childhood and myopia (short-sightedness) was more frequent in adolescence and young adulthood."

They suggest that the difference might be due to the natural process of emmetropisation in which the eye changes shape during early childhood to achieve normal vision by becoming less long-sighted, and which could correct most hyperopia in early infancy over time. In addition, they point out that the increasing number of years and intensity of school education could increase the risk of myopia from early childhood to young adulthood.

The strengths of this study are that it used high-quality data covering the whole Danish population over a long follow-up period, thus minimising the possibility of selection bias and recall bias. Availability of sociodemographic and medical information enabled the team to adjust for a wide range of factors which could influence the studied medical outcomes, and the large sample size allowed them to investigate details such as the specific types of RE involved.

The authors say: "In this nationwide population-based cohort study, we observed that children born to mothers with either pre-gestational or gestational diabetes were at an increased risk of developing high RE in general, as well as specific types of high RE, persisting from the

neonatal period to early adulthood. Children born to mothers with diabetic complications had the highest risk of high RE."

The researchers suggest: "As many REs in young children are treatable, early identification and intervention can have a lifelong positive impact. Although the 39% increased risk is a relatively low effect size, from a public health perspective, considering the high global prevalence of REs, any tiny improvement in this low-risk preventable factor will contribute to a huge reduction in absolute numbers of these eye conditions."

They advise that early screening for eye disorders in the children of mothers with diabetes may play an important role in maintaining good eyesight health.

More information: Jiangbo Du et al, Association of maternal diabetes during pregnancy with high refractive error in offspring: a nationwide population-based cohort study, *Diabetologia* (2021). DOI: 10.1007/s00125-021-05526-z

Provided by Diabetologia