New research shows that increasing number of lost pregnancies is linked to higher risk of developing type 2 diabetes

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New research published in *Diabetologia* shows that the higher the number of pregnancy losses a woman has, the higher her risk of

developing type 2 diabetes. The study is by Dr. Pia Egerup, Copenhagen University Hospital, Denmark, and colleagues.

Pregnancy loss is a common event, and previous research has linked it with later development of cardiovascular disease and heart failure. In this study, the authors investigated if pregnancy loss was associated with later development of type 2 <u>diabetes</u>.

Using a Danish nationwide cohort, the authors identified all <u>women</u> born from 1957 to 1997 with a diagnosis of type 2 diabetes during the period 1977 to 2017. Each <u>woman</u> with diabetes was matched by birth year and educational level with 10 control women without diabetes in the general Danish population. Statistical modelling was then used to calculate the odds of developing type 2 diabetes with different numbers of pregnancy losses.

The study identified 24,774 women with type 2 diabetes and selected 247,740 controls without diabetes. Women who had experienced 1, 2 or 3 pregnancy losses had an 18%, 38% and 71% higher risk, respectively, of developing type 2 diabetes as compared to ever-pregnant women with no pregnancy losses. Women who had never been pregnant had a 56% increased risk of developing type 2 diabetes compared to women who had been pregnant with any number of losses from zero upwards. Similar results were found after adjustment for obesity and gestational diabetes.

The authors say: "We cannot rule out that the psychological distress related to pregnancy loss can initiate <u>lifestyle changes</u> that increase BMI and thereby the risk of type 2 diabetes. We only had information about BMI for 12% of cases and 17% of controls as this information was first recorded in pregnant women from 2004. However, our subgroup analysis in which we adjusted for obesity still showed a significant association between pregnancy loss and type 2 diabetes, with more losses leading to a higher risk. This <u>subgroup analysis</u> indicated that the higher risk for

type 2 diabetes in women with pregnancy losses cannot be explained by obesity alone."

The authors state that the association between pregnancy loss and type 2 diabetes could principally be due to shared immunological and/or metabolic components. They say: "Perhaps the same genetic background could predispose to an <u>increased risk</u> for both pregnancy losses and type 2 diabetes. Also, pregnancy loss could initiate an immunological cascade that also could lead to later type 2 diabetes. Additionally, it is possible that prediabetic metabolic conditions—present before the diagnosis of diabetes—could influence the association."

The association was strongest in women with a high likelihood of pregnancy losses involving chromosomally normal foetuses (euploid losses) and losses with an immunological background (e.g. recurrent pregnancy loss without prior live birth and stillbirth). The authors say this supports the theory that the association could be influenced by immunological or metabolic factors.

They suggest that women with three or more pregnancy losses could have their blood sugar profile more frequently monitored so that lifestyle advice can be offered to lower their risk and interventions can be applied early if diabetes develops.

They conclude: "We found a significant and consistent association between pregnancy loss and later type 2 diabetes that increased with increasing number of losses. Thus, <u>pregnancy</u> loss and recurrent <u>pregnancy loss</u> are significant risk factors for later type 2 diabetes. Future studies should explore whether this association is due to common background factors or prediabetic metabolic conditions."

More information: Pia Egerup et al. Pregnancy loss is associated with type 2 diabetes: a nationwide case—control study, *Diabetologia* (2020).

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