

**Short Communication****Gestational Diabetes as Part of Fatty Liver Disease****Risto Kaaja***, Marja Vääräsmäki, Johan Eriksson

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Gestational diabetes is becoming more common at the same time as the obesity epidemic, both in Finland and worldwide [1]. Pregnancy, and especially in its latter half, is associated with severe insulin resistance. High levels of body fat increase insulin resistance, which disrupts glucose metabolism, especially in obese women. In Finland, one in five pregnant women is diagnosed with gestational diabetes [2]. As a result of obesity and insulin resistance, fat often accumulates outside the actual adipose tissue as ectopic fat. One target organ for such fat is the liver, often resulting in non-alcoholic fatty liver disease (NAFLD).

In Finland, fatty liver disease is diagnosed in about one in four people, and the global incidence is even higher [3]. Although gestational diabetes is most often a reversible disorder of glucose metabolism that resolves after pregnancy, the risk of developing type 2 diabetes in follow-up studies has been up to 7-10-fold over ten years compared to women with normal glucose tolerance during pregnancy [1,4,5]. Type 2 diabetes and its common precursor, the metabolic syndrome, are major risk factors for myocardial infarction and stroke in women [6]. Every effort should be made to prevent the later development of type 2 diabetes in a woman with gestational diabetes [7].

In addition to type 2 diabetes, gestational diabetes also predicts the development of fatty liver disease [8]. It is also known that up to 60-70% of diabetics have fatty liver. Fatty liver disease and metabolic syndrome share a common pathophysiology: insulin resistance, chronic mild inflammation, and enhanced

sympathetic system activity, so these two metabolic disorders often occur simultaneously in the same individual [9]. The same pathophysiological mechanisms are highlighted in hypertensive pregnancy and gestational diabetes [10,11].

The clinical spectrum of fatty liver disease during pregnancy is quite wide. Its manifestations range from asymptomatic fatty liver during pregnancy to acute fatty liver, a dangerous complication of late pregnancy [12].

Fatty liver disease has also been shown to predict the development of gestational diabetes. Fatty liver disease diagnosed in the first trimester of pregnancy predicts the development of gestational diabetes at 24–28 weeks of gestation [13,14]. A recent study by Loo et al in Singapore supports this finding [15]. It examined 382 women before the onset of pregnancy by magnetic spectroscopy (MRS). The subjects were 20-44 years old and had a mean body mass index of 23.5 kg / m². Liver fat percentage - even before the onset of pregnancy - predicted the development of gestational diabetes significantly better than body mass index, smoking, diabetic burden, or socioeconomic background [14,15]. In addition to gestational diabetes, fatty liver disease, especially more serious levels (degree of steatosis 2-3) in the first trimester of pregnancy increases the risk of large foetal size [16]. Fatty liver disease also increases the risk of other pregnancy complications, such as hypertensive pregnancy, preterm labor, and postpartum hemorrhage [17].



Figure 1: Non-alcoholic fatty liver disease (NAFLD) increases the risk of gestational diabetes and type 2 diabetes. Placental hormones cause physiological insulin resistance in late pregnancy. Leptin secreted by a fat cell in an obese woman stimulates the sympathetic nervous system in the hypothalamus, further increasing insulin resistance both directly and indirectly by increasing lipolysis and free fatty acids through hormone-sensitive lipase. Strong insulin resistance stresses the function of beta cells in the pancreas and poses a risk of developing gestational diabetes and later type 2 diabetes.

Offspring of women with gestational diabetes are at increased risk of being overweight, obese and diabetic. Obese neonates in women with gestational diabetes also have significantly higher intracellular fat levels than neonates in healthy mothers of normal weight [18]. The amount of intracellular fat in newborns correlates with the body mass index measured before pregnancy. The results of experimental animal studies suggest that intestinal microbes in the offspring of obese mothers increase the risk of inflammation and fatty liver disease [19]. The amount of fat in the liver after developing gestational diabetes is indicative of insulin resistance and associated pathological conditions [20]. Women with the highest liver fat levels also had the highest blood levels

of triglycerides and insulin, the highest blood pressure, and the lowest levels of whole-body insulin sensitivity.

Fatty liver has been shown to predispose to type 2 diabetes. Fatty liver disease is a major risk factor for gestational diabetes, especially when associated with insulin resistance. Efforts to prevent gestational diabetes have been initiated too late: little emphasis has been placed on inhibiting the development of gestational diabetes during pregnancy [21]. It is clear that the early diagnosis and prevention of fatty liver disease through lifestyle changes can prevent the development of gestational diabetes and later type 2 diabetes [8]. When a lifestyle intervention — physical activity and diet — was initiated before or at the beginning

of pregnancy, the intervention reduced the development of gestational diabetes was reduced by 20–45% [22]. However, additional research evidence on the subject is needed.

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