Doppler studies in maternal diabetes mellitus

Based on Doppler in Obstetrics: by K Nicolaides, G Rizzo, K Hecher

PATHOPHYSIOLOGY

Maternal diabetes mellitus is associated with a high risk of fetal death. In the past, before the introduction of insulin, the main cause of death was in association with maternal keto-acidosis, but now most fetal deaths are non-keto-acidotic and occur in association with fetal macrosomia.

The major source of glucose in the fetus is the mother and there is a good correlation between maternal and fetal blood glucose concentrations.[1] In pregnancies complicated by diabetes mellitus, the maternal hyperglycemia causes fetal hyperglycemia and hyperinsulinemia.[2] Furthermore, the fetal insulin to glucose ratio is increased because hyperglycemia and/or the other metabolic derangements associated with maternal diabetes mellitus act on the fetal pancreas to cause ß-cell hyperplasia and precocious pancreatic maturation.[2] Fetal hyperinsulinemia causes macrosomia, either directly through its anabolic effect on nutrient uptake and utilization, or indirectly through related peptides such as insulin-like growth factors.

Although good diabetic control in the third trimester of pregnancy reduces the incidence of macrosomia, the latter is not always preventable. In pregnant women with diabetes mellitus, despite stringent maternal glycemic control, the fluctuation in maternal glucose concentration is greater than in non-diabetics and it is possible that, during short-lived episodes of hyperglycemia, an already hyperplastic fetal pancreas will respond with a disproportionately high release of insulin.

In diabetic pregnancies, analysis of blood samples obtained by cordocentesis has demonstrated significant acidemia and hyperlacticemia in the absence of hypoxemia.[3-5] Fetal acidemia, which may offer an explanation for the unexplained stillbirths of diabetic pregnancies, is likely to be the consequence of increased metabolic rate. Salvesen et al. performed cordocentesis in diabetic pregnancies and reported a significant association between fetal plasma insulin concentration and the degree of fetal academia.[2] In pregnant sheep, chronic hyperglycemia results in increased aerobic and anaerobic glucose metabolism, with consequent increased oxygen consumption, lactate production and fall in pH and pO2.[6-8] Glucose oxidation and oxygen consumption are also increased by hyperinsulinemia, and this effect is independent of that caused by hyperglycemia.[8] Hyperlacticemia occurs because the fetus has a reduced capacity for oxidative metabolism and low pyruvate dehydrogenase activity. Severe hyperglycemia is characterized by acidemia and hypoxemia, but minor degrees of hyperglycemia are associated with acidemia in the absence of hypoxemia.[6] However, in the presence of mild fetal hypoxemia, minor degrees of fetal hyperglycemia do result in severe acidosis and even fetal death.[9]

The alternative explanation for fetal acidemia in maternal diabetes mellitus is impaired placental perfusion. Histological studies have reported decreased villous surface area, villous edema and thickening of the basement membrane.[10] However, the finding that acidemia is not accompanied by

hypoxemia suggests that the acidemia is unlikely to be due to impaired placental function; in pregnancies complicated by fetal growth restriction due to uteroplacental insufficiency, acidemia is accompanied by hypoxemia.

DOPPLER STUDIES

In maternal diabetes mellitus:

- Impedance to flow in the uterine arteries is normal, even in patients with nephropathy and vasculopathy.[11,12] Impedance to flow is not related to either short-term or long-term maternal glycemic control. However, increased impedance, as in non-diabetic pregnancies, identifies a group at high risk for subsequent development of PE and / or FGR.

- Increased impedance to flow in the umbilical arteries is associated with the development of PE and / or FGR. Impedance to flow is not related to either short-term or long-term maternal glycemic control.[11,13,14] There is contradictory evidence concerning a possible increase in impedance in pregnancies with maternal vasculopathy.[11,13,14]

- There is no evidence of redistribution in the fetal circulation with decreased PI in the middle cerebral artery and increased PI in the descending thoracic aorta.[11,15,16] In diabetes, unlike FGR due to impaired placentation, metabolic derangements in the fetus may lead to acidemia without hypoxemia. Therefore, the classic redistribution seen in fetal hypoxemia due to impaired placentation may not occur even in severely compromised fetuses, and it is therefore important not to be misled by apparently normal fetal Doppler results.

- The fetus is at increased risk of hypertrophic cardiomyopathy. This disease is characterized by a thickening of the interventricular septum and right and left ventricular walls (Figure 1), as well as abnormal development of cardiac function - decrease in the ratio between early and active ventricular filling at the level of both the mitral and tricuspid valves (Figure 2).[17,18] The cardiomegaly and cardiac dysfunction may be evident from as early as 20 weeks' gestation. The lower ratio between early and active ventricular filling at the level of the atrioventricular valves in fetuses of diabetic mothers may be due to impaired development of ventricular compliance, possibly secondary to cardiac wall thickening. In addition, the ratio may be influenced by reduced preload, as a consequence of the polycythemia, and therefore increased blood viscosity in fetuses of diabetic mothers. The cardiac hypertrophy of fetuses of diabetic mothers resolves during the first year of postnatal life. However, it is possible that the cardiac hypertrophy and dysfunction observed in intrauterine life may affect cardiac function in adult life.

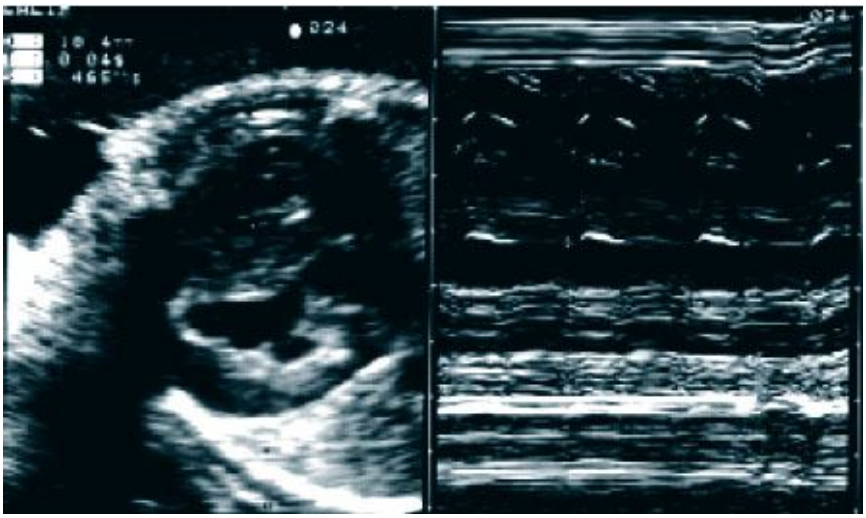

Figure 1: Real-time and M-mode tracing of a fetus of an insulin-dependent diabetic mother at 36 weeks' gestation. The interventricular wall septal thickness is increased (10 mm compared to the expected mean of 5 mm for this gestation).

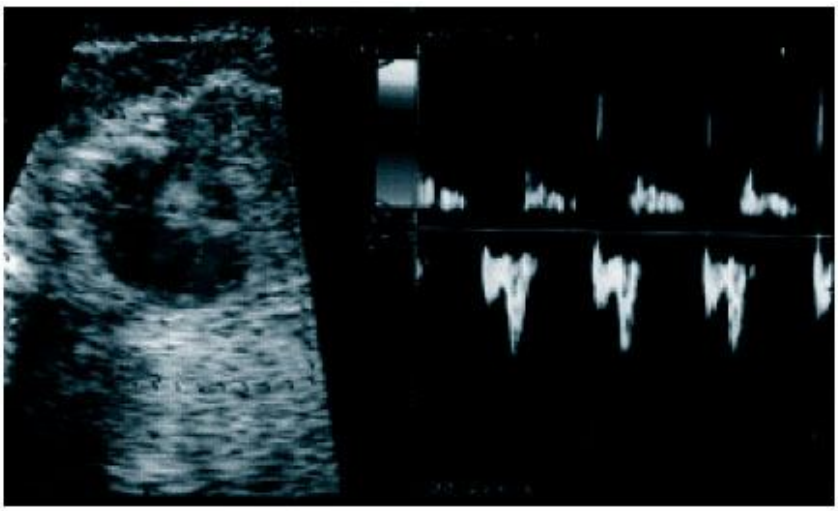

Figure 2: Flow velocity waveforms across the tricuspid valve in a fetus of an insulin-dependent diabetic mother at 32 weeks' gestation. The E/A ratio is decreased (0.48 compared to expected mean of 0.77 for this gestation).

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