Placental pathology after assisted reproduction: impact on the outcome of pregnancy

Sacha et al. (1) provided a detailed comparison of the placental pathology of >500 term singleton live births conceived with fresh embryo transfer and the placental pathology of those conceived without assisted reproductive technology (ART). The investigators concluded that fresh in vitro fertilization or intracytoplasmic sperm injection (ICSI) is associated with increased anatomic and vascular placental pathologies in term singleton live births compared with that in births conceived without ART. These findings were driven primarily by the significantly higher odds of anatomic and vascular pathologies observed in ICSI pregnancies. There was no significant difference in the placental weight between the 2 groups. There is no clear explanation why ICSI pregnancies are associated with a higher incidence of placental abnormalities. It is important to investigate how fertility interventions may lead to specific obstetric problems. The investigators performed a subgroup analysis to compare pregnancies conceived using ICSI for nonmale factor infertility with non-ART pregnancies. An altered anatomic pathology in addition to a significantly smaller placenta was observed in patients who underwent ICSI for nonmale factor infertility. Are these placental abnormalities due to the injection of abnormal sperms, or is it due to the manipulation of gametes? The investigators tried to explain the underlying possible reason for the increased incidence of abnormal placentas in ICSI pregnancies by suggesting that it is caused by more abnormalities in histone modifications and, possibly, abnormal epigenetic signaling.

This was a retrospective study with limited power to assess all the categories of placental pathology. The study did not include frozen embryo transfers, and a separate study is needed for that. There was a significant difference in the demographic characteristics between the 2 groups, including age, race, parity, and the incidence of preeclampsia. However, the investigators adjusted for these confounding factors, including maternal age, race, body mass index, parity, and gestational age at delivery, but they could not adjust for potentially confounding factors such as pre-existing maternal conditions or previous pregnancy history.

Although this was a retrospective study, to our knowledge, this is the first study to compare the anatomy and pathology of placentas in ART pregnancies with those of placentas in non-ART pregnancies. The association of anatomic and vascular placental pathologies with large placentas in deliveries of lower-birth-weight babies is a finding that suggests that these placentas have less efficient nutrient transfer from the placenta to the fetus. It should be taken into consideration that a study of placental pathology in term pregnancies in non-ART women showed an array of inflammatory and vascular placental lesions that occurred after uncomplicated pregnancies and deliveries. Because our knowledge of the human placenta is limited owing to the lack of a functional experimental model, it is suggested that the vascular and anatomic changes in the placenta are possibly the cause for this higher incidence of fetal complications in ART pregnancies.

It would be of great interest to diagnose these placental abnormities during pregnancy and study their possible effects on the fetus. Unfortunately, studies on ultrasonography and magnetic resonance imaging of the placenta during pregnancy were directed mainly at abnormally invasive and low-lying placentas. Few studies have evaluated the morphology, pathology, and vascular abnormalities of the placenta. Placental pathology identification and description require a pathologist with experience in this field. A point of strength of the study by Sacha et al. (1) is that only 1 pathologist with special expertise in the pathology of the placenta examined almost all cases in the study, thus minimizing interobserver variability in interpretation.

A methodologic sonographic evaluation of the placenta should include the location of; visual estimation of the size, thickness, morphology, site, and anatomy of; and a search for abnormalities (2). Increased placental echogenicity can be due to an associated placental hemorrhage or hypoxia, and premature calcification may reflect vascular insufficiency and may be associated with adverse outcome (3). Adverse obstetric outcomes have been linked to abnormal placentation, namely, abnormally invasive and low-lying placentas. Little has been linked to the anatomic vascular or pathologic abnormalities of the placenta.

The vascular pathology of the placenta in non-ART pregnancies is very common. It was reported to be 51.2% in the study by Sacha et al. (1). This should be into consideration while comparing the incidence with that of the vascular pathology in ART pregnancies.

The appropriate vascularization of the placental bed is of vital importance because the failure of physiologic transformation is considered to be the anatomic basis for reduced perfusion to the intervillous space in women with preeclampsia, fetal growth retardation, and premature labor (4). These vessels have unique importance. In a prospective observational study, it was found that the placental flow index and vascularization flow index were significantly lower in the small-for-gestational-age group than in normal babies. Additionally, a significantly smaller placental volume was found in the small-for-gestational-age group (5).

The important question that remains is how much these anatomic and vascular changes in the placenta are reflected on its function and the outcome of pregnancy. The other question is to what extent these ultrasound, anatomic, and vascular changes in the placenta represent the actual findings during its examination after delivery. To answer these questions, we propose a prospective study to assess the various ultrasound features of the placenta. Then, these should be compared with the anatomic and pathologic examinations of the placenta after delivery. Finally, the Doppler evaluation of placental vascular indices should be compared with the status of the fetus after delivery.

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