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Immunological causes of fetal rejection in premature delivery

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Abstract

Premature delivery is the leading cause of neonatal mortality worldwide. Risks for respiratory distress, sepsis, necrotizing enterocolitis, and intraventricular hemorrhage all increase significantly with premature birth. Approximately 1 in 10 deliveries are preterm in the United States, and preliminary data from the recent National Center for Health Statistics suggest an ongoing rise in preterm delivery. Preterm birth can be either spontaneous or iatrogenic, with ~75% occurring spontaneously. The pathogenesis of spontaneous preterm birth remains poorly understood and accumulating evidence suggests that it is a complex syndrome in which there are multiple attributable causes. The fetus may have very mild symptoms of premature birth or more serious health problems. Not all premature babies have health complications. But being born too early can cause short-term and long-term medical problems. In general, the earlier a baby is born, the higher the risk of complications. Birth weight plays a key role too. The initial laboratory evaluation should include measurement of complete blood count, Renal function test, Liver function test, Rh and Blood grouping, Random blood sugar. Prevention By preterm birth therapeutics (tocolytics). Tocolytics are drugs used to delay preterm delivery by relaxing uterine myometrial contractions. They are used to prolong pregnancy to provide time to administer antenatal corticosteroids to accelerate fetal lung maturation and transfer patients to a specialized neonatal unit.

Keywords: PTB, CBC, Premature delivery, Neonatal mortality, Birth.

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1. Introduction

Preterm birth continues to be a clinical problem of vast significance all over the world. The complexities of the biology of preterm birth suggest a syndrome with multiple mechanisms leading to uterine contraction, cervical dilation and rupture of membranes. Multiple genetic, environmental, and basic biological factors are associated with preterm birth [1]. Preterm birth continues to constitute one of the biggest problems in obstetrics. It is defined as a birth taking place before completion of 37 weeks gestation. Preterm births account for 75% of perinatal mortality and for 35% of neonatal mortality, as well as for 16% of deaths in children younger than 5 years [2]. A preterm birth means a baby is born too early. The birth takes place before the 37th week of pregnancy. A typical pregnancy lasts about 40 weeks [3]. The WHO recently reported that preterm birth (delivery before 37 completed weeks of pregnancy) is on the rise in most countries, and now constitutes the second leading cause of death globally for children under five [4]. Trophoblast cells originate from a blastocyst and seem to appear four days after fertilization in humans. Its function is to supply nutrients to the embryo and develop into a key part of the placenta. Trophoblast cells regulate immune response at the maternal-fetal interface, to promote tolerogenic phenotype. It can sense and respond to receptors presence on microorganisms [5]. Vulnerability to infection may compromise the immune system around maternal-fetal interface resulting in pregnancy problems including chorioamnionitis and premature delivery. In 40% of preterm delivery cases, bacterial infections have been diagnosed, while 80% of premature births occur before the 30th week of pregnancy, suggesting evidence of infection [6]. Bacterial infections can enter the maternal-fetal interface via three different routes: ascending, descending, and maternal blood circulation. After penetration in placental and fetal tissues, the bacterial infection is considered a risk to pregnancy and fetus. It triggers an immune response against a pathogen that may promote inflammation destroying fetal and placental cellular constituents. It has been documented that trophoblast and immune cells can improve fetal acceptability; however, overactive response of these cells to bacteria resulting to fetal rejection [7]. Animal studies have demonstrated that bacterial components contribute to preterm birth and in the presence of placental infection and inflammation. Similar studies have been conducted in clinics, and evidence shows that preterm delivery linked to placental infection and inflammation [8]. Fetal rejection may caused by

anti-maternal HLA antibodies called PRA (panel reactive antibodies). A panel-reactive antibody (PRA) is a group of antibodies in a test serum that are reactive against any of several known specific antigens in a panel of test leukocytes or purified HLA antigens from cells. It is an immunologic metric routinely performed by clinical laboratories on the blood of people awaiting organ transplantation [9]. Principally, the major histocompatibility complex (MHC) molecules are held responsible for such graft rejection. MHC molecules that present antigen in humans are also called human leukocyte antigen molecules. The antibodies forming against human leukocyte antigens are called anti-human leukocyte antigen (anti-HLA) antibodies [10]. Hitherto, three types of events have proved to trigger HLA sensitization: blood transfusions, pregnancies and transplants. However, only pregnancy is a natural source of HLA immunization. Pregnant women may develop a humoral response against paternal antigens during pregnancy due to immune maternal cells and fetal trophoblasts interaction . In fact, HLA antibodies may be identified in a variable proportion of 10–75 % previous pregnant women, depending on the series, the method used to identify and characterize these antibodies and the number of pregnancies [11]. Most of the published studies focus on the appearance of HLA antibodies after delivery and suggest that the sensitization ratio correlates with the number of previous pregnancies, so that after a third pregnancy from the same father, HLA sensitization evaluated with sensitive single-antigen beads on Luminex may be detectable in up to 75 % of women following birth [12]. Nowadays, there is increased evidence that the presence of other non-HLA antibodies, like auto-antibodies against angiotensin II type 1 receptor (AT_1R antibodies) may also induce humoral responses after solid organ transplantation (SOT) [13]. Recurrent pregnancy loss (RPL) is commonly defined as ≥2 consecutive intrauterine pregnancy losses prior to a gestational age (GA) 20−24 weeks. Primary RPL occurs in the absence of previous live birth, while secondary RPL occurs after a previous pregnancy is carried ≥24 GA [14]. Recurrent pregnancy loss and premature labour affects up to 3% of reproductive age couples. RPL is a stressor that negatively affects the psychological wellbeing of patients. Multiple causative factors contribute to premature labour. Genetic abnormalities of the fetus, especially aneuploidy, are one of the main causes of RPL and are associated with advancing female age. All societies agree on the importance of evaluating antiphospholipid syndrome in RPL. However, there is great debate and controversy regarding other possible immunological workup of RPL, including thyroid autoimmunity, cytokines, natural killer cells, antisperm antibodies, antinuclear antibodies, anti-human leukocyte adhesion (HLA) antibodies, and HLA. ASRM states there is inconsistent data to support testing of these other factors and a lack of effective immunomodulatory treatments for RPL [15].

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