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Pregnancy and Inflammation

[*]Emmanuel Ifeanyi Obeagu[1], Solomon Matthias Gamde[2] and Getrude Uzoma Obeagu[3]

[1]Department of Medical Laboratory Science, Kampala International University, Uganda, https://orcid.org/0000-0002-4538-0161
[2]Department of Medical Laboratory Science, Faculty of Allied Health Sciences, Bingham University Karu, Nasarawa State, Nigeria, http://orcid/0000-0002-7631-8782
[2]School of Nursing Science, Kampala International University, Uganda.

ABSTRACT

The concept that pregnancy is associated with immune suppression has created a myth of pregnancy as a state of immunological weakness and, therefore, of increased susceptibility to infectious diseases. A challenging question is whether the maternal immune system is a friend or a foe of pregnancy. This paper discussed the role of the immune system during pregnancy. The challenge is to better understand the immunology of pregnancy in order to deliver the appropriate treatment to patients with pregnancy complications as well as to determine public policies for the protection of pregnant women during pandemics.

Keywords: pregnancy, inflammation, cytokines.

INTRODUCTION

The idea that pregnancy is associated with immune suppression has created a myth of pregnancy as a state of immunological weakness and, therefore, of increased susceptibility to infectious diseases [1-10]. A challenging question is whether the maternal immune system is a friend or a foe of pregnancy [11-14]. In order to discuss this, question we will first review some fundamental concepts associated with the immune system and pregnancy. A fundamental feature of the immune system is to protect the host from pathogens [15]. This function depends upon the innate immune system's capacity to coordinate cell migration for surveillance and to recognize and respond to invading microorganisms. During the first trimester, NK cells, dendritic cells, and macrophages infiltrate the decidua and accumulate around the invading trophoblast cells [16]. Interestingly, depletion of immune cells, instead of helping the pregnancy, terminates the pregnancy (Hanna J et al). Thus, deletion of macrophages, NK cells, or dendritic cells (DC) has deleterious effects on placental development, implantation, or decidual formation [17]. In elegant studies, it has been shown that in the absence of NK cells, trophoblast cells are not able to reach the endometrial vascularity leading to termination of the pregnancy [18]. These studies suggest that uNK cells are critical for trophoblast invasion in the uterus. Similarly, depletion of DCs prevented blastocyst implantation and decidual formation [19]. Indeed, this study suggests that uDC are necessary for decidual formation and may affect the angiogenic response by inhibiting blood vessel maturation. More recently, Collins et al. demonstrate that uDC association, with T cell responses to the fetal "allograft," starkly contrast with their prominent role in organ transplant rejection [20]. All of these data [19], support the idea that the fetal-maternal immune interaction is more complex than the comparison to transplant allografts. Consequently, the presence of immune cells at the implantation site is not associated with a response to the "foreign" fetus but is attracted to facilitate and protect the pregnancy.

The cytokine profile during pregnancy

The definition of pregnancy as a "Th-2" or anti-inflammatory state was enthusiastically embraced and numerous studies attempted to prove and support this hypothesis [21]. This theory postulates that pregnancy is an anti-inflammatory condition [22] and a shift in the type of cytokines produced would lead to abortion or pregnancy complications. While many studies confirmed this hypothesis, a similar number of studies argued against this notion

[23]. Implantation, placentation, and the first and early second trimester of pregnancy resemble "an open wound" that requires a strong inflammatory response. The second immunological phase of pregnancy is, in many ways, the optimal time for the mother. This is a period of rapid fetal growth and development. The mother, placenta, and fetus are symbiotic, and the predominant immunological feature is induction of an anti-inflammatory state. The woman no longer suffers from nausea and fever as she did in the first stage, in part, because the immune response is no longer the predominant endocrine feature [24].

Inflammation and immune cells during implantation

As discussed above, a high level of the proinflammatory T helper (Th)-1 and cytokines (IL-6, IL-8, TNFα) characterizes early implantation [25]. These cytokines can be secreted by the endometrial cells as well as by cells of the immune system that are recruited to the site of implantation. 65–70% are uterine-specific natural killer (NK) cells [26], and 10–20% are macrophages (Mos) and 2–4 % are dendritic cells (DCs) . NK cells in human decidua have a role in regulating trophoblast invasion by the production of IL-8 and interferon-inducible protein-10 chemokines [26]. Furthermore, decidual NK cells are potent secretors of an array of angiogenic factors that induce vascular growth that is essential for the establishment of an adequate decidua [27]. DCs are a heterogenous population of cells that initiate and coordinate the innate adaptive immune response. These cells accumulate in the pregnant uterus prior to implantation and stay in the decidua throughout pregnancy [28. Several lines of evidence point to a pivotal role of macrophages and DCs in shaping the cytokine profile at the maternal–fetal interface [29]. Furthermore, in recent studies we showed that depletion of uterine DCs (uDCs) cells resulted in a severe impairment of implantation and led to embryo resorption [30]. However, the effect observed in our study was not related to tolerance but rather to successful decidualization. In agreement with these findings, another study showed that therapy with DCs significantly decreased the spontaneous resorption rate in a mouse model [29]. These studies, both suggest that, in addition to their involvement in the immune response, uDCs also play some trophic role in regulating the process of implantation.

CONCLUSION

Immunity in pregnancyis the result of the combination of signals and responses originating from the maternal immune system and the fetal-placental immune system. The signals originated in the placenta regulates the way the maternal immune system will behave in the presence of potential dangerous signals.

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