Case Reports in Women's Health 42 (2024) e00610

Contents lists available at ScienceDirect

Case Reports in Women's Health

journal homepage: www.elsevier.com/locate/crwh

Invited Editorial

Infectious diseases in pregnancy: A continuing struggle

ARTICLE INFO

Keywords
Infection
Inflammation
Congenital anomalies
Obstetric complications
COVID-19

Humans have always grappled with pathogenic organisms that cause infections in pregnancy, whether it be bacteria, viruses, fungi, or another microorganism. Fortunately, the maternal immune system has evolved and adapted to fight these off, though with variable success. During pregnancy there are alterations to the immune system, including innate, cell-mediated and humoral, in which dysregulation in the setting of infection increases the risk of maternal, fetal and neonatal complications [1]. These immune alterations may serve to protect the pregnant person while at the same time result in adverse fetal effects.

In 1884 Robert Koch published his four postulates containing the criteria that established causality between microorganisms and disease [2]. Since then, we have learned that infections in pregnancy can directly reach and impact the wellbeing of a fetus via ascension into the uterus from the lower genital tract, through the peritoneal cavity, and through transplacental passage [3]. Thereafter, infections can illicit an exaggerated inflammatory and apoptotic innate immune response at the maternal-fetal interface leading to pregnancy complications [4]. Specifically, pathogens can activate pattern recognition receptors via pathogen-associated molecular patterns, leading to fetal rejection by the same cells that would normally promote fetal tolerance. This can lead to obstetric complications, including pregnancy loss, preterm birth, and fetal growth restriction [1].

Certain types of infections in pregnancy are now known to cause fetal anomalies and abnormal development, including limb defects, intracranial and liver calcifications, hepatosplenomegaly, chorioretinitis, fetal anemia with resultant non-immune hydrops fetalis, microcephaly, and other long-term sequelae, such as behavioral and developmental differences [1]. Of note, some infections such as listeriosis may be asymptomatic for the pregnant individual, but can still lead to poor obstetrical outcomes, including pregnancy loss, preterm labor, neonatal sepsis with meningitis, and death [5]. Concurrently, infections in pregnancy have also been linked to higher incidences of infection-related maternal morbidity and mortality compared with the general population, such as with the influenza virus [6].

However, the interaction between microorganisms and the maternal immune system can also be beneficial, including decreasing the risk of recurrent acute or even more severe related infections secondary to the humoral immune response [1]. Moreover, humans are colonized by microorganisms including bacteria that play an important role in maintaining a proper homeostasis through a symbiotic relationship known as the human microbiome. The microbiome has been shown to be protective against opportunistic infections, and studies have also shown that dysbiosis can lead to a predisposition for diabetes, allergies, inflammatory bowel disease, and other autoimmune diseases [7].

Fortunately, there are effective therapies and preventative measures for a number of different infections in pregnancy that have led to better obstetrical outcomes. These include antibiotics for tuberculosis, antivirals for influenza virus, and anti-retroviral medications for human immunodeficiency virus. Additionally, we now have vaccines to prime the immune system and prophylactic medications to prevent or reduce the risk of complications related to certain types of infections for both the pregnant person and the neonate.

Although tremendous advances in the treatment and prevention of infections in pregnancy have occurred, work remains to be done. Pregnant individuals are often excluded from research due to ethical concerns, and for fear that interventions may have severe impacts such as pregnancy loss or teratogenicity with long-term sequelae in offspring, which has happened in the past [8]. The COVID-19 pandemic is a recent example where initial clinical trials on the safety and efficacy of therapies and COVID-19 vaccination excluded pregnant individuals. This led to a delay in approval of and the recommendation for therapies and COVID-19 vaccines in pregnancy, thus leading to unnecessary harm on the pregnant population at large. Additionally, there is still physician hesitancy to offer COVID-19 vaccination in pregnancy despite the reassuring safety profile to date [9].

Importantly the number of infectious diseases has risen in recent decades due in part to ease of travel and globalization. This has also led to accelerated disease transmission, which was complicit in the COVID-

https://doi.org/10.1016/j.crwh.2024.e00610
Received 11 April 2024; Accepted 11 April 2024
Available online 16 April 2024

19 pandemic. Research on emerging infections during pregnancy is still in its infancy as little is known on the impact that many pathogens have on the pregnant individual and fetus [10].

Despite advances in our understanding of infections in pregnancy, including the pathophysiology, therapies, and prevention, there is still much to be learned. Renewed efforts, including funding for research involving pregnant individuals, are critical for us to gain further knowledge on the immunology of pregnancy, particularly as it relates to newer emerging pathogenic organisms as was highlighted by the COVID-19 pandemic. Only then will we be able to mitigate the maternal and fetal complications of these elusive pathogenic microorganisms and have better obstetrical outcomes.

Contributors

Michael J. Fassett contributed to the conception, drafting and editing of the manuscript, and literature review for the editorial.

Adrian L. Hernandez Lopez contributed to the drafting and editing of the manuscript, and literature review for the editorial.

Both authors approved the final submitted manuscript.

Funding

This editorial did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Provenance and peer review

This editorial was commissioned and not externally peer reviewed.

Conflict of interest statement

The authors declare having no conflict of interest regarding the publication of this editorial.

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