THE ROLE OF MYELOID DIFFERENTIATION OF HEMATOPOIETIC STEM CELLS IN PREGNANCY IMMUNOLOGICAL TOLERANCE : A SYSTEMATIC REVIEW

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ABSTRACT

Pregnancy represents a unique immunological state where maternal immune tolerance must be established to prevent fetal rejection while maintaining protection against pathogens. The dysregulation of this delicate balance can lead to pregnancy complications including implantation failure, preterm birth, pre-eclampsia, and fetal growth retardation. Myeloid differentiation of hematopoietic stem cells plays a crucial role in establishing and maintaining this immunological tolerance during pregnancy. This study aims to critically evaluate the literature and provide an overview of current research regarding myeloid differentiation of hematopoietic stem cells in pregnancy immunological tolerance. PubMed, Scopus Biomedicine, EBSCOhost, Science direct, Embase, Cochrane Library and Web of Science were searched for Sistematic review on myeloid differentiation of hematopoietic stem cells in immune tolerance during pregnancy, myeloid differentiation of hematopoietic stem cells are a cell population involved in the regulation of immune response by means by inhibiting it in pathologies, as well as during pregnancy. The strength of the evidence was rated quality by the rating system "GRADE". We are independent with respect to the results affected. In this systematic review, we provide an overview of the current literature regarding the differentiation of hematopoietic stem cells into fibroblasts in various tissues. PubMed, Elsevier, and Web of Science (Core Collection) were systematically searched for original articles concerning fibroblast origin after hematopoietic stem cell transplantation in collaboration with a medical information specialist. Our search found 121 studies, of which 45 were analysed for full-text analysis independently, resulting in the inclusion of 10 studies. Myeloid differentiation of hematopoietic stem cells in play an essential role in the immune system during pregnancy and they have a role in maintaining healthy pregnancy. The study will help to better understand immune mechanisms at the maternal-fetal interface. Unravelling how the fetal tissue is accepted in pregnancy will provide information for the field of fertility, obstetrics, and differentiation.
Keywords : Myeloid, hematopoietic stem cells, pregnancy, immunological tolerance

INTRODUCTION

Normal pregnancy involves the development of dynamic immune tolerance in the mother, which prevents fetal rejection. At the same time, the mother's immune system must also protect the body, the embryo, and her own body from pathogens , different pathological conditions, including viral and bacterial infections. Clearly, a delicate balance of the immune system is required for a successful pregnancy Alterations in this balance can lead to a number of diseases Implantation failure, 444 Preterm birth contractions pre-eclampsia and fetal growth retardation (Negishi, 2018). The immune system is classically divided into innate immunity and adaptive immunity. The innate immune response is mediated by cell populations such as myeloid cells and natural killer (NK) cells, as well as humoral factors that are part of the complement system. HSCs achieve this through their unique capacity for both self-renewal and multipotent differentiation. As a result, genetic mutations in HSCs (inherited or somatic) manifest as different disease phenotypes, some of which directly affect the function of his HSCs, but most of which affect their differentiated progeny. Mutations in HSCs are the main cause of many inherited blood diseases, so correcting the HSC mutations that cause these diseases may provide a cure (Carsten, Ian, Adam, & and Hiromitsu, 2022).

Hematopoietic stem cells (HSCs) are the basis for maintaining an organism's entire hematopoietic system throughout life. In adults, they remain dormant and undergo asymmetric division at regular intervals to generate a series of multipotent and unipotent progenitor cells responsible for the reproduction of specialized blood cells and the immune system. With age, the heterogeneity of the pool of HSCs and multipotent progenitors gradually increases, and they tend to differentiate primarily in one direction (myeloid, or lymphoid), but maintain hematopoiesis in the long term. The pool of truly multipotent HSCs is reduced. Age-related increases in DNA repair deficiencies lead to the accumulation of mutations with epigenetic, transcriptomic, and proteomic changes, metabolic dysregulation, and disruption of HSC differentiation programs (Shevyrev, Tereshchenko, Berezina, & Rybtsov, 2023).
Hematopoietic promotes the proliferation and recruitment of hematopoietic stem cells (HSC) in extramedullary tissues, including the spleen, increasing the number of HSC and increasing hematopoiesis. Although the mechanisms that regulate HSC function under steady-state conditions have been extensively characterized, the mechanisms by which HSC respond to modulate activation Hematopoietic system have been highlighted, such as pregnancy. (Hideyuki, Jeffrey, Zhiyu, Michihisa, & Philip, 2017). The maternal immune system protects against infection by pathogens and, through several mechanisms of immune tolerance, allows normal growth of the semiallogous fetus in utero during pregnancy (Ning, Luyu, Nan, Leying, & Xu, 2020). Hematopoietic stem cells (HSC) are multipotent progenitor cells with the unique ability to regenerate themselves into all cell types and resume proliferation in the hematopoietic system (Siyuan, Yingxu, & Yumei, 2023).

METHODS

This included a partial overview of the methods used. We used the Participants, Interventions, Comparisons, and Outcomes (PICO) template to refine inclusion and exclusion criteria in our review summaries. This study was registered in the International Prospective Register for Systematic Reviews.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) Research of myeloid differentiation of hematopoietic stem cells in pregnancy; (2) Reviews comprising patients pregnancy and immunological tolerance; (3) Case-control and prospective observational studies with abstracts investigating the differentially expressed and (4) Due to limited resources, only manuscripts written in English were included.
The exclusion criteria were as follows: (1) duplicated literature; (2) reviews comprising patients with immunological tolerance by other diseases; (3) experience summary, case report, conference abstract, reviews unable to obtain full text, and other irrelevant literature; (4) Publications that did not have primary data, such as editorials, case reports, conference proceedings, and narrative review articles, were excluded.

2.2. Search Strategy

A comprehensive information search was conducted using PubMed, Scopus Biomedicine, EBSCOhost, Science direct, Embase, Cochrane Library and Web of Science to identify relevant research publications with an unlimited start date up to november 1, 2023. medical subject headings (mesh) include terms such as myeloid differentiation, hematopoietic stem cells in Pregnancy Immunological Tolerance As Keywords In The Title Or Abstract.
The search strategy included of keywords were used together with boolean operators such as "AND" and "OR" different search strategy were used for the different databases because of their peculiarities. The search terms used for journal that we use is "the role" AND "myeloid" OR "myeloid differentiation" AND "hematopoietic stem cells" OR "myeloid hematopoietic" OR "stem cells" OR "immunological tolerance" AND " pregnancy immunological tolerance" OR "pregnancy immunological tolerance in pregnancy" OR " immunological tolerance" AND "pregnancy".

Table 1. Critical Appraisal Using Specialist Unit for Review Evidence

Authors	Study design stated?	Addressed clearly focused research question?	Study setting clearly stated?	Fair selection of study participants?	Participant characteristics provided?	Appropriateness of method of assessing outcomes	Appropriateness of sampling method	Appropriateness of methods of data analysis	Information provided on participant eligibility?	Are the results well described?	Conflict of interest reported?	Did the authors identify any limitations	Total (12)	Decision
Idris et al.,	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	10	Accepted
Uphadaya et al.,	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	11	Accepted
Feyen et al.,	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12	Accepted
Oguro et al.,	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	10	Accepted
He, Suhai et al.,	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	12	Accepted
Natascha and Christian	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	No	10	Accepted
Nkemeh, Christine et al.,	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	10	Accepted
Pessach et al.,	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	11	Accepted
Chen et al.,	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11	Accepted
Shardina et al.,	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	11	Accepted

Yes is scored as 1 while No or I can't tell is scored as 0; A total score of the entire scale is 12. A score of 6 and above is considered a pass mark and accepted while a score of less than 6 is considered poor and rejected for inclusion

RESULTS AND DISCUSSION

Study selection

The literature search generated a total of 159 references: 44 in PubMed, 2 in Scopus Biomedicine, 11 in EBSCOhost, 39 in Science direct, 16 in Embase, 25 in Cochrane Library and 22 in Web of Science. After removing duplicates of references that were selected from more than one database, 74 references remained. After subsequent screening rounds of titles and abstracts based on the selection criteria described above, 19 remained for full-text analysis. This analysis excluded a further 9 articles. Articles covering (n = 10) were discussed in both the human sections of the results. Under steady-state conditions, myelopoietic cells develop in close association with a highly organized three-dimensional microenvironment.

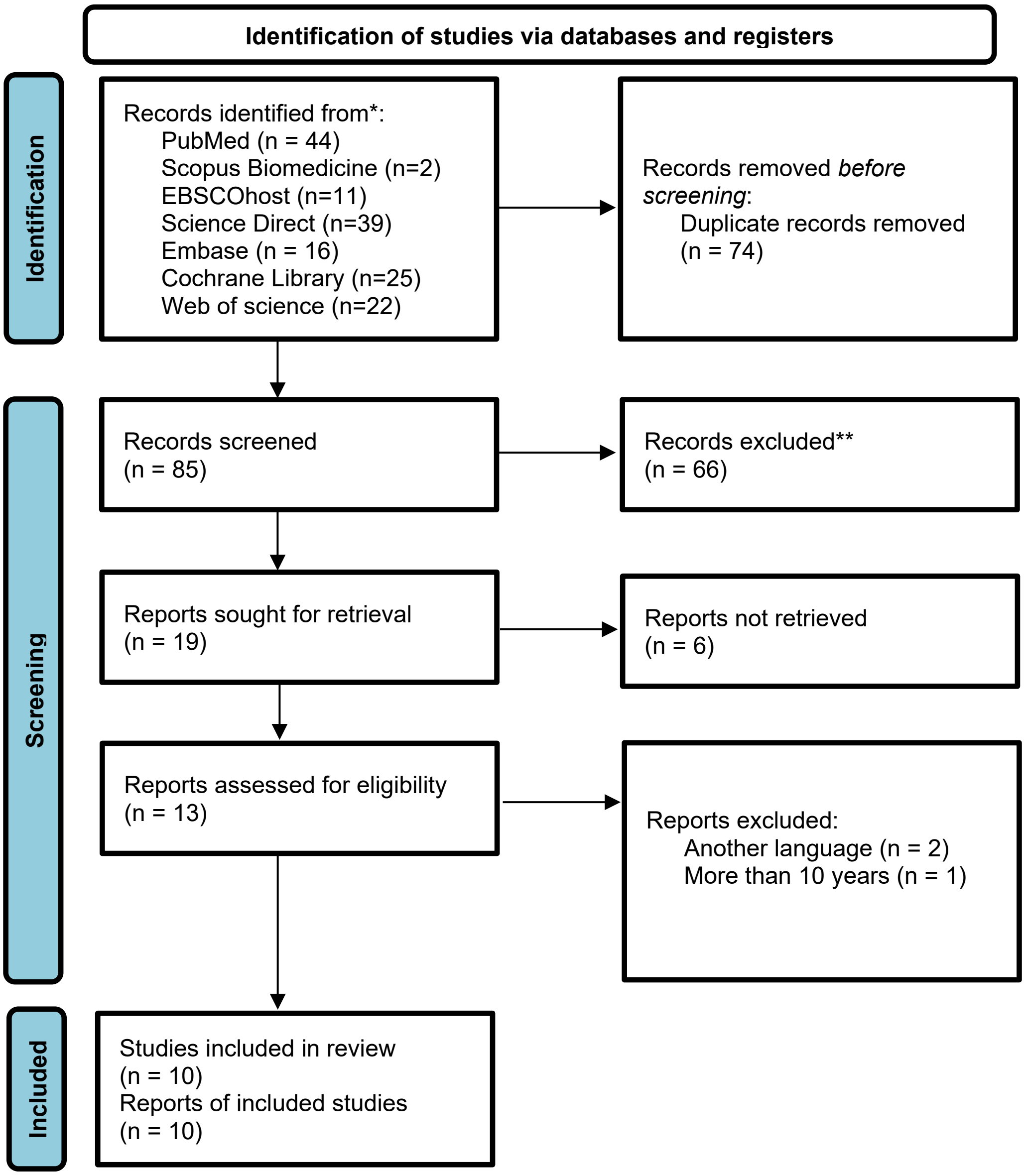

Figure 1. Flow chart of the literature search and selection process.

This structural framework is composed of many cell types, including osteoblasts and stromal cells, and their associated biosynthetic products, such as extracellular matrix components, adhesion molecules, and hematopoietic growth factors. The specific bone marrow microenvironment where hematopoiesis occurs. The presence of stem cells (HSCs) is called the stem cell niche. HSC is a subset of bone marrow cells that are capable of self-renewal and can form all types of blood cells. The hematopoietic niche plays an important role in controlling stem cell self-renewal and differentiation. Two stem niches have been characterized in bone marrow. The osteoblast niche, where osteoblasts primarily control the quiescent and asymmetric proliferation of HSC, and the vascular niche, which is primarily associated with myeloid differentiation. The hematopoietic niche regulates hematopoiesis through the release of various cytokines, which subsequently activate specific cytokine receptors or Janus kinase-dependent receptors with intrinsic kinase activity. However, recently, new families of G protein-coupled receptors and ion channels, such as the P2 receptor family activated by extracellular nucleotides, have been implicated in the regulation of hematopoiesis. It is released by endothelial and osteoblast cells 8 - 10 and may be associated with myeloid differentiation.

The complexity of this microenvironmental regulation becomes particularly evident during pregnancy, where the hematopoietic system undergoes significant adaptations to meet increased physiological demands. The included studies demonstrated that pregnancy-induced changes in the bone marrow niche involve alterations in both cellular composition and molecular signaling pathways. These modifications are essential for supporting extramedullary hematopoiesis and ensuring adequate immune cell production to maintain maternal-fetal tolerance. During gestation, the osteoblast niche undergoes dynamic remodeling, with increased expression of key regulatory molecules that promote HSC activation and mobilization. The vascular niche simultaneously expands to accommodate enhanced myeloid differentiation requirements. This coordinated response involves the upregulation of specific growth factors and cytokines that create gradients within the bone marrow environment, directing HSC fate decisions toward myeloid lineage commitment.

The extracellular matrix components within the hematopoietic niche also play crucial roles in pregnancy-related adaptations. Proteoglycans, collagens, and fibronectin create a three-dimensional scaffold that not only provides structural support but also serves as a reservoir for bioactive molecules. These matrix proteins undergo pregnancy-specific modifications that influence HSC adhesion, migration, and differentiation patterns. The interaction between HSCs and matrix components is mediated through integrin receptors, which transmit mechanical and chemical signals that regulate cell behavior.

Adhesion molecules represent another critical component of the niche architecture that is dynamically regulated during pregnancy. Cell adhesion molecules such as VCAM-1, ICAM-1, and selectins facilitate HSC-niche interactions and control HSC retention versus mobilization. The studies revealed that pregnancy hormones, particularly estrogen and progesterone, modulate the expression of these adhesion molecules, thereby influencing HSC trafficking and extramedullary hematopoiesis.

The biosynthetic products of niche cells create a complex molecular environment that changes throughout pregnancy progression. Osteoblasts and stromal cells increase their production of hematopoietic growth factors, including stem cell factor (SCF), thrombopoietin (TPO), and Flt3 ligand, which are essential for HSC maintenance and expansion. These factors work synergistically with pregnancy-specific hormones to promote the myeloid differentiation program necessary for immune system adaptation.

Recent advances in understanding the role of metabolic factors in niche function have revealed that pregnancy-induced metabolic changes significantly impact HSC behavior. The increased metabolic demands during pregnancy alter the local microenvironment, affecting oxygen tension, nutrient availability, and metabolite concentrations within the bone marrow niche. These metabolic shifts influence HSC metabolism and differentiation decisions, favoring myeloid lineage commitment to support immune tolerance mechanisms.

The temporal dynamics of niche modifications during pregnancy follow a carefully orchestrated pattern that correlates with gestational age and fetal development milestones. Early pregnancy involves initial niche activation and HSC priming, while mid-gestation is characterized by maximal extramedullary hematopoiesis and immune system expansion. Late pregnancy shows continued adaptation to prepare for parturition and postpartum immune challenges.

The studies also revealed that the hematopoietic niche during pregnancy exhibits enhanced plasticity, allowing for rapid responses to changing physiological demands. This adaptability is crucial for maintaining immune homeostasis while accommodating fetal development. The niche can quickly adjust its cellular composition and molecular output in response to maternal stress, infection, or other pregnancy complications. Furthermore, the interaction between sympathetic nervous system innervation and the hematopoietic niche represents an important regulatory mechanism that is modulated during pregnancy. Neuronal signals influence niche cell behavior and HSC function through the release of neurotransmitters and neuropeptides. Pregnancy-related changes in sympathetic tone affect this neuro-hematopoietic axis, contributing to the overall adaptation of the hematopoietic system

Table 2. Overview of the articles selected in this systematic review.

Author	Years	Journal	Study	Samples	Outcome
Idris et al.,	2021	Frontiers in Medicine	Experimental design	80	These results relation studies on cytokines such as osteopontin and other growth factors and correlation with neonatal outcomes (i.e., birth weight, apgar score, Hb concentration, haematocrit)
Uphadaya et al.,	2018	Journal of experimental medicine	Experimental design	22	These studies provided fundamental insights into HSC/progenitor differentiation by analyzing long-term outcomes and/or static composition of progenitor populations. In contrast, little is known about lineage sequence, development, and emergence of progenitor populations from HSCs in real time. However, such kinetic information is crucial for understanding adult hematopoiesis and its hierarchical structure.
Feyen et al.,	2022	Nature Comunication Journal	Experimental design	18	These data suggest that myeloid cells are involved in hematopoietic dysfunction, which is associated with activation of interferon signaling through a putative neutrophil-NK cell axis . Therefore, innate immunity may be achieved at the expense of system deterioration due to increased chronic inflammatory signals to stem cells and their niche.
Oguro et al.,	2017	The Journal of Clinical Investigation	Randomized Experimental	40	Extramedullary hematopoiesis (EMH) is induced during pregnancy to support the rapid increase in maternal blood volume. Activation of the EMH requires proliferation and recruitment of hematopoietic stem cells (HSCs), a process that is dependent on estrogen receptor alpha (ERα) in HSCs.
He, Suhai et al.,	2023	Elsevier Journal	Experimental design	24	Granulocyte/macrophage colony stimulating factor was added to the above culture system to construct a culture system for inducing myeloid cell differentiation.

Natascha and Christian	2020	Frotiers in immunology	Case control	83	During pregnancy, the immune systems of mother and offspring are challenged by their close adjacency to balance tolerance and rejection. After birth the neonate has to continue this balance towards its new environment by tolerating commensals while rejecting pathogens and towards its developing tissues to avoid inflammatory damage while overcoming immunosuppression
Nkemeh, Christine et al.,	2023	American Journal of obstetric and gynecology	Observational prospective	54	Increased HSC mobilization during pregnancy is positively correlated with gestational age. We speculate that this response may be due to signaling pathways that may expand with advancing gestational age. We plan to investigate the mechanisms that induce her HSC mobilization during pregnancy and the association between HSC mobilization and adverse pregnancy outcomes.
Pessach et al.,	2013	Human Reproduction Update	Cohhort study	46	Administration of women during the second and third trimesters appears to be safe based on available data but the clinical experience is rather limited.
Chen et al.,	2018	Nature communication Journal	Observational dan experimental design	40	Our results identify Med23 as a gatekeeper of HSC myeloid potential and provide unique insights into the relationship between Med23-mediated transcriptional regulation, HSC myeloid potential, and HSC activation.
Shardina et al.,	2022	Cell and tissue biology journal		71	MDSCs are powerful regulators of critical immunological processes during pregnancy, as well as in the neonatal period. It becomes obvious that the search For new targets that have the ability to regulate MDSC and create tolerance Between mother and child will have great potential for their use in pregnancy

					Pathologies

This systematic review investigated to what extent cells from a hematopoietic stem cells in pregnancy immunological tolerance. we present the results of this systematic review based on categorisation by the investigated tissue types and species. Although there is significant heterogeneity in the results reported by various studies, there is clear evidence pointing to the presence of a small but non-negligible number of fibroblasts of hematopoietic lineage in non-hematopoietic tissues. This number of cells seems to increase when tissue damage occurs.

Hematopoietic stem cells give rise to all blood cells in a differentiation process that involves widespread epigenome remodeling. Here we present genome-wide reference maps of the associated DNA methylation dynamics. Maternal EMH during pregnancy requires increased proliferation of HSCs in the bone marrow, recruitment to the spleen and splenic erythropoiesis, processes that depend on ERα function in HSCs (Kostlin, 2014). Sex hormones such as E2 are not the only endogenous ligands for estrogen receptors. The oxysterol 27-hydroxycholesterol (27HC) also binds to estrogen receptors and modulates their function. Extramedullary hematopoiesis (EMH) is induced during pregnancy to support the rapid increase in maternal blood volume. Activation of the EMH requires proliferation and recruitment of hematopoietic stem cells (HSCs), and this process is dependent on the estrogen receptor α (ERα) within the HSCs. Here we show that treating mice with estradiol to model the increase in estradiol during pregnancy induces HSC proliferation in the bone marrow but not HSC mobilization. Treatment with 27-hydroxycholesterol (27HC), an alternative ERα ligand, induced ERα-dependent HSC recruitment and EMH, but not HSC division in bone marrow. During pregnancy, 27HC levels in hematopoietic stem/progenitor cells were increased by CYP27A1, a type of cholesterol hydroxylase. In Cyp27a1-deficient mice, 27HC levels, HSC recruitment and EMH were significantly reduced during pregnancy, but myelopoiesis and EMH were normal in response to hemorrhage or G-CSF treatment. Therefore, specific hematopoietic stress induces EMH through different mechanisms. Two different ERα ligands, estradiol and 27HC, act together to promote EMH during pregnancy. This indicates the interplay of physiological functions of 27HC as well as hormonal and metabolic mechanisms in normal. Oxysterols are metabolites of cholesterol, and 27HC is the most abundant oxysterol (Hideyuki, Jeffrey, Zhiyu, Michihisa, & Philip, 2017)

Maternal extramedullary hematopoiesis (EMH) during pregnancy requires increased proliferation of HSC in the bone marrow, recruitment to the spleen and splenic erythropoiesis, processes that depend on ERα function in HSC (Nakada, 2014). Hematopoietic stem cells (HSC) are essential to sustaining the life of living organisms. However, the mechanism of HSC control is complex. Studies have shown that there are various factors, either intrinsic or extrinsic, that shape the profile of HSCs. (Siyuan, Yingxu, & Yumei, 2023). Hematopoietic stem cells (HSCs) are multipotent progenitor cells with the unique ability to self-renew and regenerate into all cell types and resume proliferation in the hematopoietic system. In particular, scientists discovered that many stem cells exhibited hematopoietic function when injected intravenously into normal adult mice that had received lethal doses of radiation (Yin, et al., 2022). The transplanted cells differentiated well into lymphoid and myeloid cells to sustain life and demonstrated the ability to restore the destroyed hematopoietic system. The cellular potential of hematopoietic stem cells (HSC) is traditionally pretreated by lethal doses of radiation, thus transferring donor cells (or single cells) to recipients lacking a functional endogenous hematopoietic system. Defined by the transplantation of This assay has long been the gold standard for functional HSCs (Hui & Zhaofeng, 2020).

MYELOID DIFFERENTIATION IN PREGNANCY IMMUNOLOGICAL TOLERANCE

Immune tolerance the fetus was thought to be largely 'separated' from the mother, but now there is significant transport of fetal material across the placenta into the maternal circulation and vice versa throughout pregnancy. In fact, this is the basis for the development of non-invasive prenatal tests. Therefore, alloantigens of trophoblast cells are secreted into the maternal circulation daily during the third trimester of pregnancy, which is implicated in the prevalence of PE. Therefore, both the concept and issue of immune tolerance are certainly real and important. In any case, the immunobiology of the fetus is theoretically treated similarly to the treatment of primarily implanted His grafts, and in some cases uteroplacental insufficiency [PET and intrauterine growth restriction (IUGR)] is taken into account.

Following the recognition of maternal immunotolerance, a chief discovery was the choice of HLA-G, a gene with few alleles, for the antigens used at the placental interface. Thus, the idea that placental HLA-G proteins facilitate semiallogeneic pregnancy by inhibiting maternal immune responses to foreign

(paternal) antigens via these actions on immune cells is now well established. It is also well established that regulatory T cells (Tregs) play an indispensable role in maintaining immunological unresponsiveness to self-antigens and in suppressing excessive immune responses deleterious to the host. Much of present thinking seems to involve a crucial role for Tregs in maintaining immunological tolerance during pregnancy with the result that effector T cells cannot accumulate within the decidua (the specialized stromal tissue encapsulating the fetus and placenta). In an excellent review, Williams et al remark "Regulatory T cells (Tregs) are a subset of inhibitory CD4+ helper T cells that function to curb the immune response to infection, inflammation, and autoimmunity." "There are two developmental pathways of Tregs: thymic (tTreg) and extrathymic or peripheral (pTreg). tTregs appear to suppress autoimmunity, whereas pTregs may restrain immune responses to foreign antigens, such as those from diet, commensal bacteria, and allergens." Their differential production is controlled by a transcription factor called Foxp3. Further, "a Foxp3 enhancer, conserved noncoding sequence1 (CNS1), essential for pTreg but dispensable for tTreg cell generation, is present only in placental mammals. It is suggested that during evolution, a CNS1-dependent mechanism of extrathymic differentiation of Treg cells emerged in placental animals to enforce maternal–fetal tolerance". Williams et al. conclude that "These findings indicate that maternal–fetal tolerance to paternal alloantigens is an active process in which pTregs specifically respond to paternal antigens to induce tolerance. Thus, therapies should aim not to suppress the maternal immune system but rather to enhance tolerance. These findings are consistent with an increase in the percentage of Tregs during pregnancy and with no such increase in women with recurrent pregnancy loss. Maternal tolerance is based on exposure to the paternal alloantigens, although mechanisms such as the haem oxygenase detoxification of haem from degrading erythrocytes are also important. Note too that pregnancy loss is often caused by automimmune activity
Additionally, Treg cells have several important roles in the control of infection, include moderating the otherwise potentially dangerous response to infection and being exploited by certain parasites to induce immunotolerance. Finally, here, it is also recognized that the placenta does allow maternal IgG antibodies to pass to the fetus to protect it against infections. Also, foreign fetal cells persist in the maternal circulation. One cause of PE is clearly an abnormal immune response toward the placenta. There is substantial evidence for exposure to partner's semen as prevention for PE, largely due to the absorption of several immune modulating factors present in seminal fluid (William, 2012)

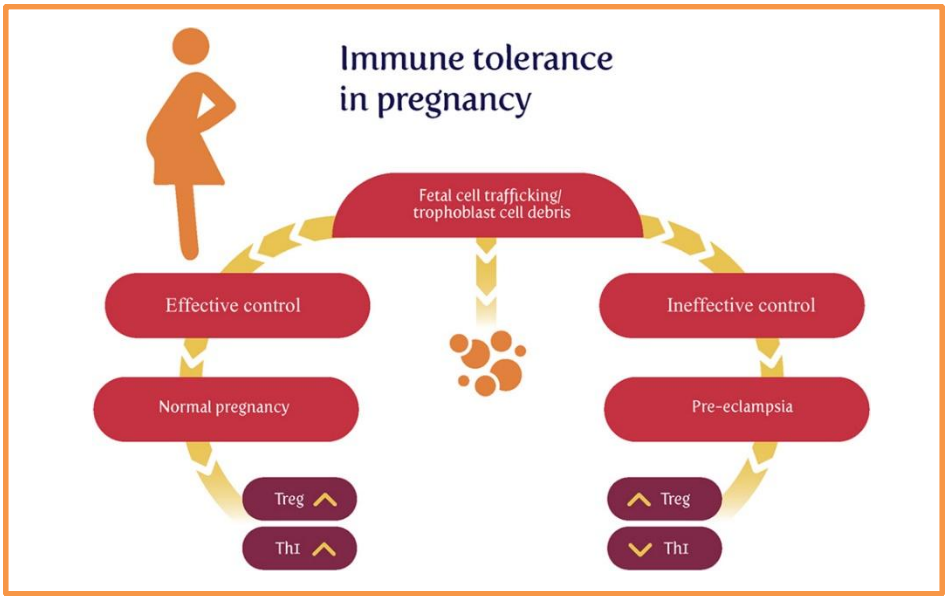

Figure 2. Immune Tolerance in pregnancy

HEMATOPOIETIC STEM CELLS IN PREGNANCY IMMUNOLOGICAL TOLERANCE

Cell therapy, by definition, is the administration of living cells to 4,444 patients to replace or repair damaged or malfunctioning organs or tissues. Cells can be derived from the patient himself (autologous) or from a human leukocyte antigen (HLA) matched or mismatched donor (allogeneic). Cells used for therapy have different potentials and can be unstimulated or differentiated in vitro. Cells can be administered intravenously or applied directly to damaged organs or tissues. Recent studies have shown that the main mechanism of action of stem cell therapy is through transplantation of donor cells and subsequent differentiation and replacement of damaged tissue, or secondly through trophic effects through the secretion of soluble factors such as cytokines and growth factors. (Asa & Lilian, 2020)
Hematopoietic stem cells (HSCs) are multipotent primitive cells that can develop into all types of blood cells, including myeloid-lineage and lymphoid-lineage cells (1). HSCs can be found in several organs, such as peripheral blood (PB), bone marrow (BM), and umbilical cord blood (UCB). All blood cell lineages are produced via functional maturation of a rare population of multipotent HSCs that can proliferate by self-renewal and differentiation. Thus, understanding the molecular mechanisms regulating the self-renewal and cell fate determination of HSCs/progenitor cells is important for the development of clinical applications based on disease type and severity. Only a small population of HSCs is required to initiate the entire hematopoietic process (Yoon & Seok, 2020)

Strength of the study

This review was clear, with predefined inclusion/exclusion criteria for patient population, intervention, comparator, outcome, and study design.

Limitation of research

We are aware of some limitations of our study. Tthe study was performed on a limited sample size because limited by chriteria inclusion so can make a risk bias.

CONCLUSION

Currently, there is a fairly large amount of research aimed at studying the role myeloid differentiation of hematopoietic stem cells in immune tolerance during pregnancy in pathological processes.
It is known that, in addition to the negative impact in pathologies, Myloid differentiation are powerful regulators of critical immunological processes during pregnancy,

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