



## Relationship between Pregnancy and Development of Autoimmune Diseases

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### Abstract

Research has shown that autoimmune diseases have a significant prevalence within the female population, and a considerable portion of women who are mothers. According to Khashan et al., 44.3% of women who develop an autoimmune disease have onset after the first year of pregnancy. During pregnancy, the fetus develops a separate circulatory system, however the fetus's and mother's blood often mix. This fetomaternal trafficking is known as microchimerism. Fetal components, such as DNA, may remain in the mother's system for decades after childbirth, while maternal components remain in the offspring as well. There are certain conditions causing a higher percentage of blood mixing, such as hypertension or preeclampsia. The literature shows that complications during pregnancy can also progress into the development of postpartum autoimmune diseases. When the fetus's blood mixes with maternal circulation, an autoimmune response is initiated. The mother's immune system reacts to this blood as a foreign substance, releasing autoantibodies. For example; according to research, scleroderma is one of autoimmune diseases that follows this pattern of development after pregnancy. The review of literature supports a correlation of parity and the development of autoimmune disease. Recognition of this development may provide information of risk factors, development of screening tools, or lead to new evidenced based practices.

### Keywords

Autoimmune disease; Pregnancy; Microchimerism; Scleroderma; Postpartum autoimmune; Hypertension

### Introduction

Autoimmune diseases affect a large number of the population with a ratio of two-to-one in women versus men. Many autoimmune diseases lack treatments or cures, often contributing to increased morbidity and mortality. Over time, women with children have been noted to have a higher incidence of autoimmune diseases, 44.3%, compared to nulliparous women [1,2]. Many of these autoimmune diseases lack strong research showing risks, early warning signs, treatments, or curative processes. Advances in genetic testing may lead to safer pregnancies and possibly avoid the development of debilitating ailments related to autoimmune disease processes. Additional research could identify and strengthen the link between pregnancy and autoimmune diseases leading to screening tools, risk recognition, and new methods of evidenced based practices.

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### Research Method

A review of literature was performed in search of relevant and current information. A timeline of 1995 to present was used to allow for the foundation of prior research leading to current understanding. No articles prior to 1995 were used as information found was either less relevant to newer genetic research, or contradictory to more recent research. The majority of articles used are from 2008 and newer; however, with limited new research on the topic, older articles from 1998, 2001, and 2005 were also included. Database searches were completed using CINAHL, PubMed, MEDLINE plus, and The Cochrane Library. Keyword searches included: postpartum diseases, pregnancy and autoimmune diseases, women and autoimmune disease, microchimerism, and hypertension. Articles were rejected based on lack of supportive information, outdated or contradictory research, autoimmune disease processes unrelated to pregnancy, and research involving non-childbearing women. In the end twelve articles were found detailing the development of autoimmune diseases in postpartum women.

### Results

This literature review discusses the conclusions in studies including: systematic reviews, retrospective cohorts, a matched control trial, a retrospective matched case-control and a case study. Of the seven systematic reviews, the primary focus was identifying the association between autoimmune diseases and pregnancy or postpartum disease. Some of the articles focused specifically on scleroderma, preeclampsia, hypertension, Grave's disease, gestational diabetes mellitus, type I diabetes or the correlation between autoimmune disease and hormone levels, such as prolactin and estrogen.

When a woman becomes pregnant, there is an introduction of autoantibodies into the maternal system. These autoantibodies can cause hypertension and other various characteristics of preeclampsia, which has been hypothesized to be a pregnancy, induced autoimmune response. These autoantibodies can be blocked by a 7-aa peptide. This suggests areas for further studies to possibly develop treatment options, similar to how Rhogam prevents Rh immunization [3-6].

### Microchimerism and HLA compatibility

According to Van Wyk et al. [7] the hypertension associated with pregnancy may be associated with increased microchimerism or presence of fetal cells in the maternal blood stream, contributing to the autoimmune response. Additionally, microchimerism can be detected by the use of HLA compatibility. HLA cells are particularly important within the immune system, as they help to distinguish "self" from "non-self." As a result, if HLA compatibility of a mother with her child is elevated, the ability of the maternal system to determine "self" from "non-self," regarding fetal cells, is decreased [6]. Nelson et al. [6] explained that "HLA class II compatibility of a child was more common for scleroderma patients than for controls." This suggests that women who develop scleroderma have a decreased ability to differentiate their own cells from the fetal cells remaining in their system.

Each study reviewed shed light on the relationship between pregnancy and autoimmune disease development differently, with a correlation of childbearing women and development of an autoimmune disease.

According to Negishi et al. [8] pregnancy and postpartum intervals elicit changes in the immune system that may result in autoimmune disease development or progression. Specifically focusing on gestational diabetes mellitus (GDM), diabetes type I, and Grave's disease, Negishi et al. [8] explained that GDM occurs in two to six percent of pregnancies and can be a precursor for the development of type I diabetes and thyroid dysfunction. It is unclear if thyroid dysfunction aggravates insulin function, potentiating diabetes development.

### Role of hormones

Various hormone functions within the woman's body can also play a significant role. In the literature review written by Quintero et al. [1] the roles of androgen and estrogen in regards to autoimmune diseases were explored. The article discussed the immunostimulatory effects of estrogen and protective effects of the androgen; and therefore, suggested why more women are affected by autoimmune diseases than men. Jorgensen et al. [2] researched the relationship between the female gender and parity related to autoimmune disease prevalence, in a completed record review for a Danish cohort, with emphasis on thirty-one autoimmune diseases from 1982 to 2008. The article explained that prolactin, like estrogen, has also been noted as a hormone with an immunostimulatory effect. Dopamine, however, has been suggested for the treatment of autoimmune diseases [9].

Articles researched included the information on the method of delivery and chromosomal differences. The hope of these results is to have a better understanding of the disease processes, those at risk, and guidelines for further research. Collectively, the articles reviewed suggest that a number of factors contribute to the development of autoimmune diseases after pregnancy, including: fetomaternal trafficking (microchimerism), chromosomal differences [10] environmental factors, sex hormones, delivery method, and complications during pregnancy. The relationship between the mother and fetus, especially in the case of a male child due to Y-chromosome, has been noted similar to a host versus graft situation, striking up an immune response. Ostensen et al. [10] also reported a correlation in the relationship between microchimerism, hormones, and an immune response during pregnancies that result in autoimmune disease development.

### Delivery method

As discussed above, delivery method can impact the risk for postpartum autoimmune disease occurrence. According to the article written by Khashan et al. [3] the method of delivery has an important influence on the amount of fetomaternal trafficking. Cesarean birth has the highest risk of transferring fetal markers, due to the increased mixing of blood. Abortion is noted to have a lower risk due to "more primitive fetal stem cells." Over time, pregnancy complications, such as preeclampsia or gestational diabetes, have been noted to be warning signs for future health problems such as cardiovascular, metabolic, and/or autoimmune diseases [3].

Of the articles regarding pregnancy and autoimmune diseases, scleroderma has shown a strong correlation between pregnancy, pregnancy complications, and development of postpartum autoimmune diseases. With the information obtained from the literature review completed by Gabrielli et al. [11], there is hope for gene specific targeting for future scleroderma treatment.

### Discussion and Conclusion

The goal of this literature review is to encourage and support the need for further research in autoimmune disease development

and parity. In other respects, the research supports a thorough family and patient history review, as well as monitoring pregnant and postpartum women in the family practice setting. As reviewed, there is a significant relationship between pregnancy and postpartum autoimmune disease development; and therefore, the "study of autoimmune disease processing and links to immune function during pregnancy may lead to new understanding and treatment of immune system dysfunction" [4]. Kaaja and Greer [12] suggests that recognizing these pregnancy complications as risk factors may allow for early interventions.

Further research is needed in the field of immunity and genetics; however, it is worth investigating if current medical treatments may be adding to the prevalence or perhaps defending the woman's body. Research questions that may assist include: Is there a difference in fetal marker presentation in women that receive RhoGam versus women that do not? Could RhoGam, or a similar product, reduce the development of autoimmune disease in postpartum women? Is there a prevalence of HLA II receptors or other receptor genotypes in women that develop autoimmune disease? In the meantime, the development of evidence based practice guidelines could assist in developing screening tools. These tools could help to identify those at risk for developing autoimmune disorders based on patient history and the use of genetic screening.

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