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Adverse pregnancy outcomes in patients with autoimmune rheumatic diseases. A literature review

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ABSTRACT

Autoimmune rheumatic diseases are chronic disorders with increasing prevalence and frequently affecting women in their reproductive period. Inflammatory rheumatic disorders influence the risk of developing adverse pregnancy outcomes (APOs) among these patients. This review aims to summarize both maternal and fetal complications in women with different rheumatic diseases. The article analyzes the literature from the scientific databases and prioritizes the most recent meta-analyses and systematic reviews. We described the most common inflammatory rheumatic conditions, including systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), psoriatic arthritis (PA), Sjőgren's Syndrome (SS), systemic sclerosis (SSc), ankylosing spondylitis (AS), idiopathic inflammatory myopathy (IIM), and systemic vasculitides. The majority of discussed rheumatic diseases increase the risk of maternal complications such as preeclampsia, preterm delivery, cesarean delivery (CD), but also hypertensive disorders and gestational diabetes. Mothers with autoimmune diseases have an elevated risk of developing fetal complications, including small for gestational age (SGA) and low birth weight (LBW). Some APOs are associated with higher activity of the underlying disease or greater medication use. In summary, the findings of this article indicate that women with autoimmune rheumatic diseases have an increased risk of APOs. Female patients affected by inflammatory disorders require special care from health professionals, especially during the preconception period and pregnancy.

Keywords: adverse outcomes; pregnancy; rheumatic disease; autoimmune disease

1. INTRODUCTION

Autoimmune rheumatic diseases are chronic disorders of connective tissue and multiple organs, such as the kidneys or the skin. The studies estimate that inflammatory rheumatic diseases affect approximately 5% of the population, yet

their prevalence continues to increase by around 7% per year (Schirmer et al., 2012; Lerner et al., 2016). The vast majority of patients suffering from autoimmune diseases are female. Women's predisposition is primarily explained by hormonal changes and the presence of more genes, particularly immune-related genes, on the X chromosomes (Angum et al., 2020; Oliver and Silman, 2009). The most common onset age varies depending on the disease; however, it can appear at any age and often affects patients in the reproductive years (Jokar and Jokar, 2018). Furthermore, the rising prevalence of rheumatic diseases along with high incidence in young women should contribute to further analysis of obstetric prognosis in these groups of patients.

We defined pregnancy outcomes as the maternal and fetal results of fertilization. Most frequent adverse pregnancy outcomes (APOs) in the general population include hypertensive disorders, gestational diabetes (GD), preeclampsia, preterm birth, stillbirth, intrauterine growth restriction (IUGR), and newborns small for gestational age (SGA). The prevalence of respective APOs reaches up to 25% of pregnancies globally. The risk factors for developing APOs include autoimmune and renal diseases among others (Garr Barry et al., 2022; Parikh et al., 2021). Current research on pregnancy outcomes among patients at risk enables thorough pregnancy planning, suitable treatment of the underlying disease, and management of maternal and fetal complications.

This review analyzes the current research concerning APOs in patients with respective autoimmune rheumatic diseases.

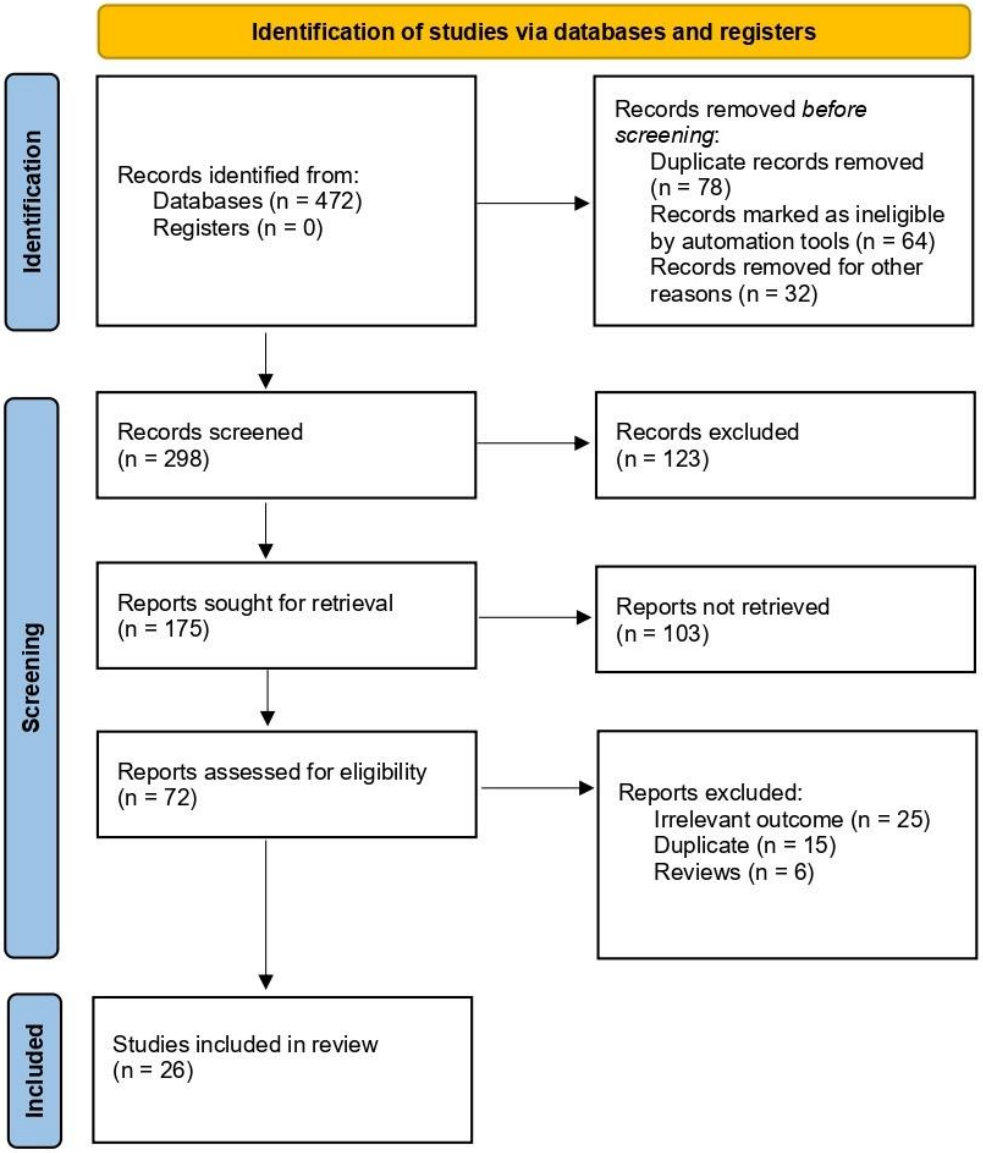

Fig. 1: PRIMA consort chart of the selected studies

2. REVIEW METHODS

This review analyzes the literature on maternal and fetal complications among pregnant women with autoimmune rheumatic diseases. We conducted the research for this review using the scientific databases PubMed and Google Scholar. During the research, we used the keywords and the Medical Subject Headings (MeSH) in combination, including ("adverse outcomes"), ("pregnancy"), ("rheumatic disease"), and ("autoimmune disease"). We prioritized the most recent systematic reviews and meta-analyses published in English, along with studies conducted on large research groups. The research team included original peer-reviewed research articles, systematic reviews, meta-analyses, randomized controlled trials, and articles published in English and published between January 2015 and April 2025. Non-English studies, case reports, and studies with poor methodology were excluded from the review. The final body of the article covers 26 studies from May 2018 to October 2024 (Fig. 1).

3. RESULTS AND DISCUSSION

Systemic Lupus Erythematosus (SLE)

Maternal and fetal complications significantly more often affect pregnant women with SLE. A meta-analysis by He and Wei (2020) published in 2017-2019 concluded that patients with SLE have a greater risk of preeclampsia/eclampsia, fetal loss, stillbirth, abortion, and cesarean delivery (CD) due to complications. Compared to the non-SLE group, the risk of IUGR and GD was similar. Mothers with SLE were significantly more likely to deliver preterm, infants who were SGA, or infants with low birth weight (LBW). They also had a greater risk of newborns hospitalized in the neonatal intensive care unit, and newborns with APGAR score <7 within 1 minute and 5 minutes. Considering GD, a systematic review and meta-analysis by Yuanyuan Dong et al. of the studies from inception to 2018 also indicated that SLE is not associated with GD. However, the article suggested that GD risk is positively associated with glucocorticoid therapy in SLE patients (Dong et al., 2019).

Women with lupus nephritis have a significantly increased risk for APOs, such as gestational hypertension, preeclampsia, lower rate of live births, higher rate of preterm births, and IUGR. A systematic review and meta-analysis by Jiayue Wu et al. of the studies published between 2000 and 2017 described that these patients are also at risk of increased use of steroids and immunosuppressants (Wu et al., 2018).

A systematic review and meta-analysis by Abheiden et al., (2024) found that articles published between 1995 and 2020 found that almost one-third of women with SLE had a preterm birth. A recent umbrella review on autoimmune diseases by Singh et al., (2024) established that patients with SLE had a greater risk of miscarriage, preeclampsia, preterm birth, SGA, and LBW. Furthermore, the authors found that the incidence of APOs is increased not only among SLE patients but also among patients who, over subsequent years, developed SLE (Muñoz et al., 2023).

Rheumatoid Arthritis (RA)

The research concludes that patients with RA have a significantly increased APOs risk. Tian et al., (2023a) reported an increased risk of developing SGA in offspring from mothers with RA. Furthermore, Muñoz et al., (2022) pointed out the increased risk of gestational hypertension, preeclampsia, IUGR, premature delivery, CD, and an extended hospital stay among patients with RA. Tian et al., (2023b) also conducted a meta-analysis of the 2006-2018 studies. They established a strong association between RA and preeclampsia.

Likewise, Lv et al., (2023) in their systematic review and meta-analysis found a higher incidence of APOs in women with RA. Their results concerned a significantly increased risk of maternal complications (preeclampsia, GD, spontaneous abortions, CD) as well as fetal complications (stillbirth, SGA, LBW, congenital abnormalities, type 1 diabetes, and asthma developing in children from RA mothers). Furthermore, the authors established the association between higher RA activity and an increased risk of premature delivery and CD.

Psoriatic Arthritis (PA)

A meta-analysis by Xie et al., (2021) of the studies from inception to 2020 found that patients with PA have a significantly increased risk of developing adverse maternal outcomes, including CD, preterm birth, preeclampsia/eclampsia, GD, and gestational hypertension. However, the risk for neonatal outcomes, such as SGA, LBW, congenital malformations, APGAR score <7, neonatal mortality, and stillbirth, was not elevated compared to the general population. Most of these findings are consistent with a systematic review by Meissner et al., (2021). The authors found no significant risk of adverse neonatal outcomes, nor was there an increased risk of GD.

Considering CD, a Norwegian population-based study from 2023 revealed that women with PA have a significantly greater risk for emergency CD, especially among patients with more active disease, but not for elective CD (Skorpen et al., 2023).

In a Danish nationwide case-control study, Johansen et al., (2022) found that women with PA have a doubled risk of ectopic pregnancy compared to women without the diagnosis.

Sjőgren's Syndrome

Patients with primary Sjőgren's Syndrome (pSS) have a significantly elevated risk of APOs such as spontaneous abortion, preterm delivery, LBW, and congenital malformations, as concluded in a meta-analysis by Baoqing Geng et al. focusing on the studies from 2005-2021 (Geng et al., 2022). Some conclusions are consistent with a recent retrospective analysis by Tan et al., (2024). According to their findings, women with pSS statistically more often experience miscarriage, both natural and therapeutic, and natural miscarriages happen at an earlier stage of pregnancy compared to the control group. They also found a greater prevalence of placental abnormalities, CD, and fetal abnormalities (particularly cardiac abnormalities) among patients with pSS; however, no elevated risk of preterm birth and LBW.

Chan et al., (2023) in an Asian population study noted a higher incidence of preeclampsia/eclampsia, shock, and preterm delivery among women with Sjőgren's Syndrome. They also found an increased risk of adverse fetal outcomes, including unexplained stillbirth, SGA, and poor outcomes regarding APGAR score within 1 minute.

Systemic Sclerosis (SSc)

Research on APOs in populations with SSc remains limited, primarily due to the use of small samples. In a Spanish retrospective single-center study from 2022, the risk of miscarriages, preeclampsia, premature deliveries, and SGA was elevated among patients with SSc compared to healthy controls (Barilaro et al., 2022). An extensive nationwide cohort study from the United States analyzing data between 2000 and 2017 concluded that women with SSc are still at a greater risk of developing APOs. They are at a significantly greater risk of hypertensive disorders, premature birth, CD, and longer hospital length of stay, but also statistically more often have fetal complications, including fetal death and IUGR (Kawano et al., 2023).

Ankylosing Spondylitis (AS)

The number of studies regarding pregnancy in women with AS is also narrow. The American retrospective cohort study analyzed a database of almost 10 million women to compare pregnancy outcomes between patients with AS and patients without the diagnosis. They found that women with AS had a statistically greater prevalence of GD, placenta previa, and CD, but also SGA and intrauterine fetal death (Amikam et al., 2024).

Another cohort study from Korea also confirmed the risk of CD in patients with AS to be significantly increased. However, the other maternal and fetal outcomes analyzed in the study were similar to the control group (Park et al., 2021).

Idiopathic inflammatory myopathy (IIM)

Dermatomyositis (DM) and polymyositis (PM) are the most common forms of IIM, and few studies are focusing on their influence on pregnancy outcomes. A systematic review by Tang et al., (2022) found that DM/PM elevated the risk of preterm birth and fetal death among patients with active disease during pregnancy. A study based on a Swedish population by Che et al., (2019) drew a similar conclusion - the risk of preterm birth was increased three times in patients after IIM diagnosis. These women also had a 6-fold risk of delivering a child with LBW and a 2-fold risk of CD.

A study by Kolstad et al., (2018) analyzed 15 years of data from an American dataset. It concluded that women with IIM have an increased risk of gestational hypertensive disorders.

Systemic Vasculitides

A French nationwide population-based cohort study from 2023 analyzed pregnancy complications in women with systemic vasculitides. Mettler et al., (2023) concluded that these patients have not only a higher rate of hypertensive disorders, but also an induced preterm birth. Large vessel vasculitis, antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, and immune complex-mediated small vessel vasculitis were the vasculitis subtypes primarily associated with this risk.

Maternal complications in pregnant patients with Takayasu arteritis, including hypertension, miscarriage, and preeclampsia, were found in a systematic review and meta-analysis by Partalidou et al., (2023). However, a recent systematic review on the connection between ANCA-associated vasculitis and APOs established that the occurrence of both maternal and fetal complications was similar to the control group (Ashok et al., 2023). Current research suggests that the majority of rheumatic diseases are associated with a greater risk of both maternal and fetal complications (Table 1).

Table 1: Main findings of the included studies

Autoimmune rheumatic disease	**APOs with increased risk**	**Article**
SLE	preeclampsia/eclampsia, fetal loss, stillbirth, abortion, CD, preterm delivery, SGA, LBW, APGAR <7	He and Wei, 2020
	preterm delivery	Abheiden et al., 2024
	miscarriage, preeclampsia, preterm birth, SGA, LBW	Singh et al., 2024
Lupus Nephritis	gestational hypertension, preeclampsia, lower rate of live births, preterm delivery, IUGR	Wu et al., 2018
RA	SGA	Tian et al., 2023a
	gestational hypertension, preeclampsia, IUGR, premature delivery, CD, extended hospital stay	Muñoz et al., 2022
	preeclampsia	Tian et al., 2023b
	preeclampsia, GD, spontaneous abortions, CD, stillbirth, SGA, LBW, congenital abnormalities, type 1 diabetes, asthma developing in children from RA mothers	Jiamin et al., 2023
PA	CD, preterm birth, preeclampsia/eclampsia, GD, gestational hypertension, SGA, LBW, congenital malformations, APGAR <7, neonatal mortality, stillbirth	Xie et al., 2021
	CD, preterm birth, preeclampsia/eclampsia, gestational hypertension	Meissner et al., 2021
	emergency CD	Skorpen et al., 2023
	ectopic pregnancy	Johansen et al., 2022
Sjőgren's Syndrome	spontaneous abortion, preterm delivery, LBW, congenital malformations	Geng et al., 2022
	miscarriage, placental abnormalities, CD, fetal abnormalities	Tan et al., 2024
	preeclampsia/eclampsia, shock, preterm delivery, stillbirth, SGA, poor APGAR outcome	Chan et al., 2023
SSc	miscarriage, preeclampsia, premature delivery, SGA	Barilaro et al., 2022
	hypertensive disorders, premature birth, CD, longer hospital length of stay, fetal death, IUGR	Kawano et al., 2023
AS	GD, placenta previa, CD, SGA, intrauterine fetal death	Amikam et al., 2024
	CD	Park et al., 2021
IIM	preterm delivery, fetal death	Tang et al, 2022
	preterm delivery, CD, LBW	Che et al., 2019
	gestational hypertensive disorders	Kolstad et al., 2018
Systemic Vasculitides	hypertensive disorders, induced preterm birth	Mettler et al., 2023
	hypertension, miscarriage, preeclampsia	Partalidou et al., 2023

5. CONCLUSION

The review examines the current evidence regarding APOs in patients with various autoimmune rheumatic diseases. The leading associations concern the higher prevalence of preeclampsia, preterm delivery, CD, but also hypertensive disorders, and gestational diabetes. Intensified immunosuppressive therapy and higher activity of the underlying disorder may affect the development of some APOs. Furthermore, offspring from mothers with diagnosed autoimmune diseases have a greater risk of fetal complications such as SGA and LBW. Therefore, it remains crucial for health professionals to provide exceptional care to patients with inflammatory rheumatic disorders during the preconception period and pregnancy. The cooperation among specialists in the fields of gynecology, rheumatology, and neonatology enables a reasonable prognosis for the pregnancy.

Author's Contributions

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Formal analysis: Marika Gutowska, Aleksandra Przybylska, Adrianna Perzanowska
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Writing - review and editing: Julia Ciechanowicz, Aleksandra Przybylska
Visualization: Piotr Kupidłowski, Agata Nowacka
Supervision: Julia Ciechanowicz, Adrianna Perzanowska
Project administration: Stanisław Ciechanowicz, Marika Gutowska

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Informed consent

Not applicable

Ethical approval

Not applicable

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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