Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2025; Vol 24: Issue 8s, https://carcinogenesis.com/

Pregnancy in Systemic Lupus Erythematosus: Achieving Low Disease Activity and Improving Maternal-Fetal Prognosis

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ABSTRACT

Systemic lupus erythematosus (SLE) significantly impacts family planning for women of reproductive age, with risks of disease exacerbation and maternal-fetal complications complicating pregnancy decisions. This review synthesizes current literature on pregnancy outcomes in women with SLE, emphasizing the importance of achieving low disease activity before conception. The data reveal a nuanced landscape of pregnancy risks, including increased rates of preeclampsia, premature birth, and fetal loss, alongside varied effects of SLE medications on both maternal and fetal health. Notably, biological therapies like hydroxychloroquine show promise in reducing adverse outcomes. Despite advancements in understanding, notable gaps remain in patient beliefs and comprehensive pregnancy planning strategies for this cohort. This manuscript advocates for enhanced interdisciplinary collaboration between rheumatologists and obstetricians, highlighting regular counseling on fertility, medication management, and risk assessment to optimize maternal and newborn health outcomes. Future research should focus on real-world experiences and perceptions of women with SLE regarding pregnancy planning to inform clinical guidelines and improve patient care.

How to Cite: Anastasia V. Poznyak, Nikita Aleksandrovich Mitkin, Elizaveta Romanovna Korchagina, Olga Nikolaevna Maltseva, Aleksandra Sergeevna Utkina, Alexander N. Orekhov, (2025) Pregnancy in Systemic Lupus Erythematosus: Achieving Low Disease Activity and Improving Maternal-Fetal Prognosis, *Journal of Carcinogenesis*, *Vol.24, No.8s*, 384-395

1. INTRODUCTION

SLE frequently occurs in female patients of reproductive age and can hamper planning of having children. Risk of exacerbation of lupus and of detrimental outcomes can affect family planning decisions. Moreover, female patients with systemic lupus erythematosus are recommended to reach six months of LDA before getting pregnant which in turn elevates risks associated with ageing. Whereas ability to conceive is believed to be uninfluenced by lupus, some particular drugs applied in lupus, e.g., NSAID and cytophosphane, can affect it [1,2].

It was reported that women's views and beliefs on risks of conceiving and bearing children in the presence of chronic diseases can be different. Dutch studies in lupus subjects showed that approximately fifty percent of the subjects did not have any adverse effects during pregnancy, twenty percent had systemic lupus erythematosus flares while pregnant, and fifteen percent of the subjects had flares after childbirth [3-5]. The complications which 50% of pregnant patients with SLE are facing involve high blood pressure (18%), premature birth (pregnancy period less than 37 weeks) (33%), Intrauterine fetal demise (4%), IUGR (15%) resulting in the birth of SGA infants. It is crucial to consider all the risks when making decisions on events regarding health of the mother and newborn. Accordingly, these patients are advised to undergo regular counselling regarding ability to conceive, therapy, contraception, and risk stratification [6-8]. This will provide more

information about the risks of pregnancy in lupus patients which may help develop strategies of family planning. While exploring the views of female patients on pregnancy planning is crucial, studies on pregnancy planning in patients with systemic lupus erythematosus are still very scarce.

Disorder activity and pregnancy planning

Pregnancies in women with systemic lupus erythematosus are related to elevated risks and need to be monitored more often by obstetrics and rheumatology specialists. Pregnant patients with lupus need to be informed on the risks of the disorder exacerbation during and after pregnancy, as well as of possible detrimental outcomes for mother and for newborn [9-12]. Cross-sectional study was conducted in 2019 and explored tendencies in mother and newborn adverse outcomes in the presence of systemic lupus erythematosus. In this analysis, data from the USA from 1998 to 2015 were investigated [13]. This analysis involved female patient mortality rates, newborn mortality rates, preeclampsia, eclampsia, hospitalization without childbirth. The authors reported that advancements in pregnancy planning with regard to systemic lupus erythematosus was probably accountable for the decrease in rates of adverse outcomes as well as in mortality rates. Studies conducted in other groups also demonstrated such results [14,15].

European Alliance of Associations for Rheumatology emphasizes that pregnancy is allowed when systemic lupus erythematosus is inactive [16]. The activity of this disorder and its flares in 1-year period prior to pregnancy are a major risk factor for detrimental results for mother and for fetus [17,18]. For female patients with systemic lupus erythematosus and other rheumatic or muscular and skeletal disorders, American College of Rheumatology guidelines do not recommend pregnancy until LDA is reached [19]. These recommendations are consistent with available data from various trials.

Doctors and patients need to be mindful of potential complications associated with an active disorder around the time of conception. Evaluating both positive and negative outcomes may assist female patients with systemic lupus erythematosus in making informed decisions about planning pregnancy, e.g., to delay until conditions are more favorable. Furthermore, assisted reproductive technology (ART) is now accessible for individuals with systemic lupus erythematosus at various clinics worldwide and needs to be considered [20-22].

Systemic lupus erythematosus is a condition which implies high heterogeneity. It presents with a range of clinical symptoms and various hematological, chemical, biological and immunity aberrances, featured by progression which is difficult to predict. Evaluating the disorder status must rely on clinical data and be measured using activity index [23-26]. This evaluation must consider disorder activity and gravity, taking into account affected organs and the seriousness of function impairment. Rheumatology specialists are responsible for providing a comprehensive history of the disorder, along with a detailed physical examination. Meanwhile, obstetricians and general practitioners must be able to identify evidence of active disorder. SLE rash, serositis pain and arthritis can be recognized easily, and further medical assessment must be performed to determine the connection with active disorder [27-29]. Kidneys or blood as well as other organs and systems can be silently involved at early stages, emphasizing the necessity of such tests as urine test, complement blood test, tests for protein in urine, specific AAbs, CBC. Whereas rheumatology specialists might apply different instruments to measure disorder activity prior to pregnancy and during it, some of those instruments are assessments that are primarily used in study settings and are hereby hard to use daily [30,31]. Such evaluations might be useful to measure the disorder activity in musculo-skeletal and mucocutaneous tissues. SLEDAI2K is a verified and reliable tool designed to assess the disorder activity by evaluating 24 specific indicators in the previous thirty days. This index also has clearly defined parameters. SLEDAI2K is not difficult to use, it has calculators accessible on the Internet, and provides pretty clear prospects on the activity of the disorder. Mild SLE shows result between 4 and 6, moderate SLE shows result from 7 to 12, and severe episodes of disease show results higher than 12 [32]. Furthermore, European Alliance of Associations for Rheumatology guidelines from 2019 rely on these categories in their instruction on management of systemic lupus erythematosus. Whereas there are still debates about SLEDAI2K, there is SLEPDAI which is adapted for pregnant patients and can be used for assessment of disease activity in pregnant female patients with lupus [33]. That tool takes into account the similarities between symptoms of systemic lupus erythematosus and pregnancy, e.g., edema, melasma, head ache, protein in urine. These features of the tool help physicians in making differential diagnoses while evaluating these individuals. Systemic Lupus Erythematosus Pregnancy Disease Activity Index can assist in treating pregnant patients with systemic lupus erythematosus, while Systemic Lupus Erythematosus Disease Activity Index can be used prior to pregnancy [34].

Systemic lupus erythematosus is a complicated condition with unpredictable progression, and it is difficult to assess. There are discussions on the peculiarities of establishing disorder activity, remission, LDA and flare-ups. There are presently no generally accepted standard values for Systemic Lupus Erythematosus Disease Activity Index prior to pregnancy even though high results may indicate elevated risks. Typically, SLEDAI2K score higher than four indicates a considerable disorder activity, meaning that treatment approach needs to be altered. Related risks should hereby be discussed if conception is planned [35].

A verified definition for LDA with Systemic Lupus Erythematosus Disease Activity Index lower than or equal to four is reflected by LLDAS. Lupus Low Disease Activity State takes into account the assessment of the disorder, measures the differenced compared to the last evaluation, and helps control the therapy (7.5 or less mg of prednisolone per day, maintenance dosage of immunity suppressants or biologic agents) [36,37]. Kim J.W. and colleagues performed a trial in

2021 and demonstrated that reaching Lupus Low Disease Activity State positively influences pregnancy. In this trial the authors performed a comparison of 163 pregnant patients with systemic lupus erythematosus and 596 pregnant patients without the disease [38]. The results showed that patients with systemic lupus erythematosus had elevated risks of pregnancy complications in comparison to the control group. Multi-factor analyses showed a direct correlation between detrimental outcomes and the failure to reach Lupus Low Disease Activity State prior to pregnancy. This implies that pregnancy probably needs to be delayed until Lupus Low Disease Activity State is reached [38].

Progression of systemic lupus erythematosus is also related to accumulation of damage. Certain disorders may be a contraindication to pregnancy because of an elevated risks for the mother. Failure of various organs, e.g., HF, kidney failure, high blood pressure in lungs, as well as thrombosis or IS in the past two years [39].

2. PREGNANCY OUTCOMES

Female patients with systemic lupus erythematosus are at risk of detrimental outcomes of pregnancy than general population. A trial that involved four thousand individuals with systemic lupus erythematosus demonstrated that pregnant patients with systemic lupus erythematosus were hospitalized more, had elevated blood pressure, elevated IUGR. SLE individuals had caesarean section more often, however, it can be due to personal preferences and might not represent clinical conditions [40]. Another research applied that data base as well, but explored longer period of time. The results showed that pregnant women with systemic lupus erythematosus had three times higher risk of preeclampsia (PE), twenty times more frequent mother death, and higher occurrence of thrombi and infections [41]. Newer studies have demonstrated decrease in mortality rates, which are albeit elevated in comparison to general population. Frequency of C-section and PE is still elevated in patients with systemic lupus erythematosus and did not reduce. The PROMISSE trial showed that nineteen percent of subjects had detrimental outcomes such as fetus death after twelve weeks, death of newborn, premature childbirth and SGA neonates [42]. These outcomes can be predicted by SLE anti-coagulant (odds ratio 8.32, 95% confidence interval 3.59-19.26), anti-HT drugs (odds ratio 7.05, 95% confidence interval 3.05-16.31), PGA higher than 1 (odds ratio 4.02, 95% confidence interval 1.84-8.82), low platelet count (odds ratio 1.33 per 50 K reduction, 95% confidence interval 1.09-1.63), flare-ups, elevated activity of the disorder, reduced elevation of C3 during pregnancy. MBRN studied the pregnancy outcomes in patients with systemic lupus erythematosus and found that activity of the disorder was related to elevated risk of PE (odds ratio 5.33 in comparison to healthy group, odds ratio 3.38 in comparison to not active disorder) and premature delivery (odds ratio 8.66 in comparison to healthy group, odds ratio 3.36 in comparison to not active disorder) [43]. A trial performed by Mayo clinic during thirty years showed that individuals with SLE kidney disease in active phase had elevated rates of postpartum complications in comparison to patients with inactive SLE (57% versus 11%, $p<0.001$). Female subjects with active SLE kidney disease had premature labor and fetus death more often (median thirty-four weeks versus fourty weeks $p = 0.002$, 35% versus 9%, $p = 0.031$) [44].

3. PREECLAMPSIA

In comparison to 3.4% of pregnant patients in the USA, PE may affect as much as 30% of pregnant patients with systemic lupus erythematosus, as was reported by Mehta and colleagues [45]. Cervera and colleagues conducted a study in a thousand pregnant patients with systemic lupus erythematosus and showed that PE was one of the most frequent complications. NK cells and EPC in blood may be used as biomarkers in initial stages of PE [46]. data indicate that natural killer cells can be vital in regulating proinflammatory environment in decidua in patients without SLE. And vice versa, in case of NKCs activation deficiency, remodeling of the arteries in the decidua can be impaired which elevates the PE risk [47].

PE elevates the risk of IS, kidney failure, liver failure, and maternal mortality. The associated dysfunction of the placenta elevates the risk of fetal mortality and intrauterine growth restriction. The risk of premature delivery is also increased in case of PE [48]. Premature delivery occurs in half of pregnant patients with systemic lupus erythematosus, which is three-fold higher rate than in no-lupus patients. Pre-eclampsia is the main risk factor for premature delivery in one systemic lupus erythematosus group. Among other factors there are such complications as fetal disorders and mother's disorder activity. Approximately seventy percent of those premature deliveries were for medical reasons [49].

HCQ treatment of systemic lupus erythematosus during pregnancy did not elevate the risk of birth defects, miscarriage or fetal mortality. These discoveries allowed broader application of this therapy in pregnancies. EULAR among other specialists recommend hydroxychloroquine treatment for systemic lupus erythematosus in pregnant patients [50]. Hydroxychloroquine therapy decreased the amount and severity of pregnancy complications in patients with systemic lupus erythematosus, such as SLE flare-ups, SLE syndrome in newborns, preterm delivery and IUGR, as was reported by Leroux and colleagues. Latest studies show that hydroxychloroquine therapy can reduce risk of PE as well [51].

Recent research revealed that PE is mediating approximately twenty-eight percent of the interactions between systemic lupus erythematosus and preterm deliveries. Anti-malarial drug hydroxychloroquine reduces inflammation and modulates immunity, which makes it useful for treatment of systemic lupus erythematosus [52]. Endothelium function impairment is associated with PE as well. Gómez-Guzmán and colleagues reported that hydroxychloroquine was proved to improve

functioning of the endothelium in lupus animal models. Furthermore, OS is considered an important factor in manifestation of PE and systemic lupus erythematosus [53]. Hydroxychloroquine inhibits production of ROS, thus averting tissue injuries induced by autooxidation and exerting anti-inflammation effect. Hereby, in female patients with systemic lupus erythematosus, hydroxychloroquine can decrease the risk of PE and premature birth [54].

Liu and colleagues conducted a study in 119 pregnant patients and reveled that PROM, PE, fetal distress, gestational age at birth, premature delivery, and postnatal hemorrhage risk were not elevated by hydroxychloroquine. Hydroxychloroquine therapy did not decrease PE risk considerably. Moreover, meta-analysis also showed that PE risks were not decreased notably by hydroxychloroquine (risk-reward ratio 0.61, 95% confidence interval 0.34-1.11) [55]. Although, another analysis performed by Clowse and colleagues involved seven groups, 804 female subjects and 938 pregnancies, and demonstrated that subjects receiving hydroxychloroquine therapy for systemic lupus erythematosus during pregnancy had lower disease activity and more positive pregnancy outcomes. These results suggest that pregnant individuals should continue hydroxychloroquine therapy as the medication has good safety profile and is able to decrease the systemic lupus erythematosus activity (odds ratio 0.53, 95% confidence interval 0.31-0.93) [56].

Premature delivery was found to be connected to AZA or 6-MP treatment in pregnant patients, as was reported by Nørgård and colleagues [57]. Although, adverse outcomes of pregnancies, e.g., spontaneous abortion, low birthweight (LBW) or premature delivery, were not observed. Whereas studies on the subject are scarce, there are some studies which showed that AZA has a good safety profile and few of its metabolism products are found in breast milk [58]. In addition, Gardiner and colleagues reported that while mothers were treated with AZA while breast feeding, the drug's metabolites were not found in serum of the neonates [59].

In clinical trials it is important to validate the efficacy of low-dosage glucocorticosteroids added to traditional therapy in subjects with systemic lupus erythematosus. At the same time, glucocorticosteroids in high doses significantly elevate the occurrence rates of mother and newborn morbidity, which is a contraindication for their application [60].

4. HYPOTHYROIDISM

Spontaneous abortion and preterm delivery were connected to sub-clinical underactive thyroid and positive testing for thyroid Abs in female patients with euthyroidism. Benhadi and colleagues performed a study which demonstrated that TSH concentrations were elevated within normal limits, elevating risk of adverse outcomes of pregnancy, such as spontaneous abortion and fetal or newborn death [61]. Small alterations in thyroid gland functioning were related to breech presentation, elevated rates of C-section. A study was performed which demonstrated that L-thyroxine therapy in pregnant female patients with TPOAb positivity in the 1st trimester with thyroid-stimulating hormone higher than 2.5 mU/l had reduced detrimental pregnancy outcomes in comparison to female patients who did not receive this therapy in RCT in an iodine deficit region [62]. Moreover, postnatal thyroiditis (PPT) occurs in from five to ten percent of all females and from twenty to twenty-five percent of females with T1DM. Disruption of thyroid gland functioning occurs in approximately five percent of all pregnant females, e.g., underactive thyroid or overactive thyroid [63]. Spontaneous abortion and primary thyroid disorders are more frequent in female patients with systemic lupus erythematosus, particularly if the disorder is active and in presence of APLAs. It was reported that neonates of female patients with systemic lupus erythematosus tend to have heart block (HB) and often need to be admitted to NICU [64]. It was revealed that rates of mortality are elevated in pregnant patients with systemic lupus erythematosus. Underactive thyroid and AITD, a condition where thyroid Abs are present, occur more often in female subjects with systemic lupus erythematosus. Disrupted thyroid function was observed in twenty-one percent of female subjects with systemic lupus erythematosus and in ten percent of the control subjects, as was revealed in a case-control study with application of a questionary ($p=0.02$). Although it was reported that it is unclear how often underactive thyroid and autoimmune thyroid disease occur in pregnant patients with systemic lupus erythematosus [65].

5. STROKE

SLE may induce multiple complications which influence the CNS. Hereby, it is unlikely that there is only one pathologic mechanism which is responsible for all neurologic abnormalities associated with the disease. It was suggested that anti-PL, anti-neuronal, antiP, antiendothelial and other AAbs and by-products of inflammation can be implicated in those mechanisms. Thrombi in blood vessels are mostly associated with anti-PL Abs [66]. Bloodflow in cerebral arteries is frequently the region of the thrombi which cause transient ischemic attack (TIA) or ischemic stroke (IS). IS and transient ischemic attacks are rarely induced by systemic lupus erythematosus. Hereby, the role of anti-PL Abs in central nervous system systemic lupus erythematosus is small in case there are no other impacts of anti-PL Abs on the brain. Whereas anti-PL Abs can only slightly affect central nervous system systemic lupus erythematosus, they give AAbs greater "credibility" in the pathology of the disease [67]. Effect of anti-PL Abs can be simply shown in vitro. Importantly, there are emerging data from trials in animal models that such AAbs play a huge role in thrombus formation and spontaneous abortion. Central nervous system symptoms of systemic lupus erythematosus can vary, among them are head ache and MCI as well as serious symptoms such as seizure, amnesia and IS. For some CNS symptoms of systemic lupus erythematosus, especially associated with coagulopathy, validated therapeutic approaches have been developed [68]. Although, mechanisms of its

cognitive and emotional onset are completely unexplored. Its pathogenesis was connected to some immune effectors, such as brain-reactive AAbs, inflammatory processes, cytokines. Other CNS factors notably contribute to it, e.g., microglial processes and BBB. Although, CNS symptoms of systemic lupus erythematosus are believed to be induced by a variety of factors, as no complex model was yet defined. This variety hinders the investigation since it was usually based on empiric conclusions to choose therapeutic approaches for patients with neuropsychiatric systemic lupus erythematosus. More approaches for this disease could be engineered provided further elucidation of that systemic lupus erythematosus symptom [69].

Moreover, female patients with systemic lupus erythematosus have more severe complications associated with pregnancy in comparison to healthy controls. In comparison to patients without systemic lupus erythematosus, risk of mother's death was about twenty times higher (325/100000 live births). Rates of mortality among all pregnant patients with systemic lupus erythematosus were 0.32%, that is equivalent to approximately eleven maternal deaths per year in the United States. This risk was still notably higher in patients with systemic lupus erythematosus after adjustment for mother age (odds rate 17.8, confidence interval 7.2-44) [70].

6. INFECTION

Systemic lupus erythematosus is featured by chronic inflammation which poses danger to multiple organs and can cause cutaneous, renal, CNS, blood, joint and serosa disorders. The chronic inflammatory processes are induced by acquired immunity regulation impairments and the excessive production of different AAbs. Infections induced by fungi, parasites, viruses and bacteria can lead to anomalies of the immunity processes in genetically sensitive patients [71]. Whereas patient's genome elevates the risk of this disorder, it can be not related to the development of systemic lupus erythematosus. Numerous trials indicate that autoimmune mechanisms can lead to different outcomes depending on different genomic or viral factors. Although, this theory requires more research in order to elucidate the interplay of genes and infections [72]. The discrepancy in disease rates among mono-zygotic twins elevates the probability that environment factors have a role in the progression of auto-immune disorders. Systemic lupus erythematosus is a condition which implies immunity deficiency, whereas pregnancy also implies attenuation of immune system, hereby it can be concluded that the risk of infections in pregnant patients with systemic lupus erythematosus is greatly elevated [73].

7. FETAL OUTCOMES

Fetal Loss

Rates on fetus death in pregnant patients with systemic lupus erythematosus used to be approximately 43%, which has reduced to 17% in the year 2002. A study which involved 356 pregnancies in patients with systemic lupus erythematosus demonstrated that systemic lupus erythematosus elevated rates of fetal loss more than 2 times [1]. Another research involved 148 patients with systemic lupus erythematosus and pregnancy and 78905 pregnant patients without systemic lupus erythematosus. The results showed that risk of miscarriage was elevated in patients with systemic lupus erythematosus (odds ratio 4.84, confidence interval 1.72-11.08) and was linked to the disorder gravity [74]. Such factors as anti-PL Abs, SLE kidney disease, kidney failure, and high SLE activity during six months prior to pregnancy or in pregnancy were major risk factors for miscarriage [75].

Fetal complications

Research conducted in Taiwan involved 2059 systemic lupus erythematosus pregnancies. The results showed that these patients had elevated occurrence of IUGR, premature delivery and still birth [76]. Consistently, Italian researchers demonstrated that risk of premature birth and SGA newborns was elevated in the systemic lupus erythematosus group. The authors also detected that systemic lupus erythematosus pregnancies were at risk of premature labor, especially for individuals with a history of SLE kidney disease and HT. IUGR was linked to HT, SLE flare-ups and Raynaud syndrome [77].

Neonatal SLE

About 33% of female patient with systemic lupus erythematosus have Anti-SSA/Ro autoantibodies and Anti-SSB/La autoantibodies. In ten percent of pregnancies of patients who have such Abs, there is a risk of neonatal SLE. Newborn SLE can involve skin and heart disorders. In the skin neonatal SLE, the newborn exhibits a rash sensitive to light, and also may exhibit higher hepatic function parameters [78]. After half a year these manifestations pass. CCHB is found in newborns in rare cases (from one to two percent) of maternal of antiRo and antiLa Abs present. These rates are elevated to 17% when the previous offspring of this female patient had this condition. CCHB might result in fetus loss in 17.5% which usually happens before the thirtieth week of the pregnancy. There are currently no recommendations for management of the progression of CCHB, although specialists advise to undergo serial fetal echo-cardiography (FE) at sixteen to twenty-six weeks of pregnancy. Available evidence indicates that hydroxychloroquine therapy in pregnant patients with antiRo and antiLa antibodies may decrease the incidence of congenital complete heart block [79].

Long–term outcomes

Results of research on long-term consequences for neonates of female SLE patients are contradicting. Whereas some authors discovered elevated need for special education for offspring of women with systemic lupus erythematosus and APLAs, other authors reported that even though systemic lupus erythematosus elevates risk of premature delivery, it does not increase the risk of CNS disorders in the newborns [80].

Medications

When prescribing medications in gestation, any possible risk to the developing fetus should be considered. HCQ is believed to be safe to use in pregnant patients. Trials of newborns of mothers who received HCQ therapy during pregnancy demonstrated that this drug has a good safety profile and does not affect the newborns' QT interval. Recent research showed elevated risk of fetus abnormalities in those who were exposed to HCQ during gestation. Although, these results were not adjusted to such risk factors as tobacco use, alcohol consumption, drugs usage etc [81]. It is noteworthy that no specific patters were detected, the latter is the principle of proving teratogenic properties. Numerous trials showed that HCQ therapy in pregnant patients reduces the SLE flare-ups and decreases PE risk. Although, claims information shows that total of 16.1% of female SLE patients receive the medications during gestation. Mildly elevated numbers were detected in Sweden, where 36% of female patients with lupus received the medication during gestation. In this context, we underline to the individuals with SLE that continuation of HCQ during gestation is vital. HCQ can be used in nursing period as well [82].

NSAID can regulate arthralgia and arthritis in subjects with systemic lupus erythematosus. The FDA has announced that NSAID can induce severe renal problems in the fetus which may result in deficiency of amniotic fluid and fetal loss after twenty weeks of pregnancy. After thirty weeks, NSAID may induce preterm fetal closure of the arterial duct. Individuals with SLE are advised to discontinue the use of NSAID at the twentieth week of pregnancy. Aspirin at low dosage is the allowed medication during gestation. NSAID drugs can be used during nursing period [83].

Early evidence indicated that glucocorticosteroids elevated risk of development of cleft palate. Although, a trial conducted in Denmark demonstrated that incidence of lip/palate clefts was not elevated in 51973 newborns who were exposed to glucocorticosteroids during gestation [84,85]. However, glucocorticosteroids are able to facilitate gestational DM and HT, PROM, and SGA newborns. Presently available guidelines advise to use low dosage of prednisone in gestation. If a female patient receives prednisone at a dose higher than 20 mg/d, it is recommended to discard breast milk for 4 hours after taking the drug [86].

Sulfasalazine therapy can be applied to regulate arthritis in individuals with systemic lupus erythematosus. Evidence from the IBD literature verifies its efficacy in gestation. A case of diarrhoea was documented in a newborn whose mother received this therapy. Hereby, nursing patients are advised to stop taking this drug if the newborn has diarrhoea [87].

Subjects with considerably affected organs might need immunity suppressants during gestation. Cytophosphane, MTX and leflunomide have shown teratogenicity and cannot be used in pregnancy and during planning of pregnancy. Leflunomide's elimination half-life is particularly long, patients hereby must go through a preconception drug withdrawal procedure with cholestyramine. Metabolite concentrations in blood lower than 0.03μg/mL are considered safe for conception and gestation. Methotrexate (MTX) must be discontinued 1-3 months before conceiving. Cytophosphane therapy must be stopped 3 months before conceiving [88].

Mycophenolate mofetil and mycophenolic acid currently are widely used for SLE kidney disease. This treatment shows high teratogenicity and elevates risk of miscarriage in early pregnancy. An analysis of available data on the use of this treatment demonstrated 22% incidence of malformation and 45% incidence of miscarriage. Suppression of mycophenolic acid purine production is considered to be the reason of the genotoxic properties. This therapy must be discontinued 6 weeks before conceiving [89].

Ciclosporin, tacrolimus and AZA were proved to be safe to use in gestation, and also can be a replacement to the abovementioned teratogenic drugs. Abatacept, rituximab and belimumab were found to not penetrate placenta for the first fourteen weeks of pregnancy. Hereby, these drugs may be used prior to pregnancy. For individuals who need those medications for SLE management, discussion of their advantages and disadvantages is recommended before deciding to use this therapy in gestation [90,91].

The FDA has issued an approval of the drug voclosporin as a therapy for systemic lupus erythematosus kidney disease. Presently available guidelines do not recommend using this drug in gestation and in nursing period [92].

8. CONCLUSION

In conclusion, navigating pregnancy in women with systemic lupus erythematosus (SLE) presents unique challenges that necessitate careful planning and multidisciplinary management. This review underscores the critical importance of achieving low disease activity prior to conception to minimize risks for both the mother and fetus. Evidence suggests that timely intervention and appropriate medication management, particularly with hydroxychloroquine, can lead to improved pregnancy outcomes. However, substantial gaps remain in understanding patients' perspectives and the psychosocial factors

influencing their family planning decisions.

Future research should prioritize qualitative studies to explore women's experiences and beliefs regarding pregnancy in the context of SLE. By focusing on patient-centered approaches, healthcare providers can better tailor counseling and support, ensuring informed decision-making. Enhanced communication between rheumatologists, obstetricians, and patients is essential to develop comprehensive care strategies that address both clinical and emotional needs. Ultimately, fostering a supportive environment will empower women with SLE to make informed choices about their reproductive health, leading to safer pregnancies and healthier outcomes for both mothers and their children.

REFERENCES

[1] Dao KH, Bermas BL. Systemic Lupus Erythematosus Management in Pregnancy. Int J Womens Health. 2022 Feb 15;14:199-211. doi: 10.2147/IJWH.S282604. PMID: 35210867; PMCID: PMC8859727.

[2] Lu, J., Xu, D., Wan, Q. et al. Pregnancy outcomes and risk factors analysis in patients with systemic lupus erythematous. BMC Pregnancy Childbirth 24, 495 (2024). https://doi.org/10.1186/s12884-024-06701-x

[3] Blomjous BS, Johanna I P V, Zijlstra E, Cramer K, Voskuyl AE, Bultink AIEM. Desire to have children and preferences regarding to pre-pregnancy counselling in women with SLE. Rheumatology (Oxford). 2021 Jun 18;60(6):2706-2713. doi: 10.1093/rheumatology/keaa684. PMID: 33241288; PMCID: PMC8489423.

[4] Kidney Disease: Improving Global Outcomes (KDIGO) Lupus Nephritis Work Group. KDIGO 2024 Clinical Practice Guideline for the management of LUPUS NEPHRITIS. Kidney Int. 2024 Jan;105(1S):S1-S69. doi: 10.1016/j.kint.2023.09.002. PMID: 38182286.

[5] Marder W, Littlejohn EA, Somers EC. Pregnancy and autoimmune connective tissue diseases. Best Pract Res Clin Rheumatol. 2016 Feb;30(1):63-80. doi: 10.1016/j.berh.2016.05.002. Epub 2016 Jun 25. Erratum in: Best Pract Res Clin Rheumatol. 2020 Dec;34(6):101490. doi: 10.1016/j.berh.2020.101490. PMID: 27421217; PMCID: PMC4947513.

[6] de Jesus GR, Mendoza-Pinto C, de Jesus NR, Dos Santos FC, Klumb EM, Carrasco MG, Levy RA. Understanding and Managing Pregnancy in Patients with Lupus. Autoimmune Dis. 2015;2015:943490. doi: 10.1155/2015/943490. Epub 2015 Jul 12. PMID: 26246905; PMCID: PMC4515284.

[7] Vela-Casasempere P, Caño Alameda R, Gómez Sabater S, Cortell Aznar S, Pérez Pascual E. Considering belimumab during pregnancy: A more viable option over time. Lupus. 2024 Jun;33(7):700-715. doi: 10.1177/09612033241245549. Epub 2024 Apr 9. PMID: 38594808; PMCID: PMC11193323.

[8] Rose HL, Ho WK. Management of very high risk pregnancy with secondary anti-phospholipid syndrome and triple positivity to the anti-phospholipid antibodies. J Thromb Thrombolysis. 2014 Nov;38(4):453-6. doi: 10.1007/s11239-014-1080-7. PMID: 24777280.

[9] Rosta K, Heinzl F, Kuczwara V, Schindler S, Falcone V, Catic A, Riedmann M, Leitner H, Simader E, Ritschl V, Stamm T, Szlatinay A, Mandl P, Mazzucato-Puchner A. Pregnancy outcomes in patients with systemic lupus erythematosus compared to a high-risk tertiary cohort and to standard population from the Austrian birth registry. Acta Obstet Gynecol Scand. 2024 Sep;103(9):1820-1828. doi: 10.1111/aogs.14880. Epub 2024 Jun 28. PMID: 38943224; PMCID: PMC11324932.

[10] Society for Maternal-Fetal Medicine (SMFM). Electronic address: pubs@smfm.org; Silver R, Craigo S, Porter F, Osmundson SS, Kuller JA, Norton ME. Society for Maternal-Fetal Medicine Consult Series #64: Systemic lupus erythematosus in pregnancy. Am J Obstet Gynecol. 2023 Mar;228(3):B41-B60. doi: 10.1016/j.ajog.2022.09.001. Epub 2022 Sep 6. PMID: 36084704.

[11] Hwang YM, Wei Q, Piekos SN, Vemuri B, Molani S, Mease P, Hood L, Hadlock J. Maternal-fetal outcomes in patients with immune-mediated inflammatory diseases, with consideration of comorbidities: a retrospective cohort study in a large U.S. healthcare system. EClinicalMedicine. 2024 Feb 1;68:102435. doi: 10.1016/j.eclinm.2024.102435. PMID: 38586478; PMCID: PMC10994966.

[12] Makarm, W.K., Zaghlol, R.S. & Kotb, L.I. Risk assessment score for adverse pregnancy outcome in systemic lupus erythematosus patients. Egypt Rheumatol Rehabil 49, 33 (2022). https://doi.org/10.1186/s43166-022-00131-3

[13] Barnado A, Hubbard J, Green S, Camai A, Wheless L, Osmundson S. Systemic Lupus Erythematosus Delivery Outcomes Are Unchanged Across Three Decades. ACR Open Rheumatol. 2022 Aug;4(8):711-720. doi: 10.1002/acr2.11447. Epub 2022 Jun 6. PMID: 35670028; PMCID: PMC9374054.

[14] Gamba A, Zen M, Depascale R, Calligaro A, Gatto M, Iaccarino L, Doria A. Modern Management of Pregnancy in Systemic Lupus Erythematosus: From Prenatal Counseling to Postpartum Support. J Clin Med. 2024 Jun 13;13(12):3454. doi: 10.3390/jcm13123454. PMID: 38929983; PMCID: PMC11204490.

[15] Castellanos Gutierrez AS, Figueras F, Morales-Prieto DM, Schleußner E, Espinosa G, Baños N. Placental

damage in pregnancies with systemic lupus erythematosus: A narrative review. Front Immunol. 2022 Aug 17;13:941586. doi: 10.3389/fimmu.2022.941586. PMID: 36059466; PMCID: PMC9428442.

[16] Fanouriakis A, Kostopoulou M, Andersen J, Aringer M, Arnaud L, Bae SC, Boletis J, Bruce IN, Cervera R, Doria A, Dörner T, Furie RA, Gladman DD, Houssiau FA, Inês LS, Jayne D, Kouloumas M, Kovács L, Mok CC, Morand EF, Moroni G, Mosca M, Mucke J, Mukhtyar CB, Nagy G, Navarra S, Parodis I, Pego-Reigosa JM, Petri M, Pons-Estel BA, Schneider M, Smolen JS, Svenungsson E, Tanaka Y, Tektonidou MG, Teng YO, Tincani A, Vital EM, van Vollenhoven RF, Wincup C, Bertsias G, Boumpas DT. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. Ann Rheum Dis. 2024 Jan 2;83(1):15-29. doi: 10.1136/ard-2023-224762. PMID: 37827694.

[17] Lockshin MD. Assisted reproductive technologies for women with rheumatic AID. Best Pract Res Clin Obstet Gynaecol. 2020 Apr;64:85-96. doi: 10.1016/j.bpobgyn.2019.10.002. Epub 2019 Oct 23. PMID: 31791669.

[18] Eudy AM, Siega-Riz AM, Engel SM, Franceschini N, Howard AG, Clowse MEB, Petri M. Effect of pregnancy on disease flares in patients with systemic lupus erythematosus. Ann Rheum Dis. 2018 Jun;77(6):855-860. doi: 10.1136/annrheumdis-2017-212535. Epub 2018 Feb 20. PMID: 29463519; PMCID: PMC6037310.

[19] Sammaritano LR, Bermas BL, Chakravarty EE, Chambers C, Clowse MEB, Lockshin MD, Marder W, Guyatt G, Branch DW, Buyon J, Christopher-Stine L, Crow-Hercher R, Cush J, Druzin M, Kavanaugh A, Laskin CA, Plante L, Salmon J, Simard J, Somers EC, Steen V, Tedeschi SK, Vinet E, White CW, Yazdany J, Barbhaiya M, Bettendorf B, Eudy A, Jayatilleke A, Shah AA, Sullivan N, Tarter LL, Birru Talabi M, Turgunbaev M, Turner A, D'Anci KE. 2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases. Arthritis Care Res (Hoboken). 2020 Apr;72(4):461-488. doi: 10.1002/acr.24130. Epub 2020 Feb 26. PMID: 32090466.

[20] Tan B, So PN, Krishnan A, Carriazo S, Bahamonde JR, Lamech TM, Hassanein M, Lerma E, Wiegley N; GlomCon Editorial Team. Approach to Pregnancy in Patients With Lupus Nephritis. Kidney Med. 2023 Sep 17;5(11):100724. doi: 10.1016/j.xkme.2023.100724. PMID: 37915962; PMCID: PMC10616386.

[21] Stojan G, Baer AN. Flares of systemic lupus erythematosus during pregnancy and the puerperium: prevention, diagnosis and management. Expert Rev Clin Immunol. 2012 Jul;8(5):439-53. doi: 10.1586/eci.12.36. PMID: 22882219.

[22] Sims, C., Clowse, M.E.B. A comprehensive guide for managing the reproductive health of patients with vasculitis. Nat Rev Rheumatol 18, 711–723 (2022). https://doi.org/10.1038/s41584-022-00842-z

[23] Justiz Vaillant AA, Goyal A, Varacallo M. Systemic Lupus Erythematosus. [Updated 2023 Aug 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535405/

[24] Yu H, Nagafuchi Y, Fujio K. Clinical and Immunological Biomarkers for Systemic Lupus Erythematosus. Biomolecules. 2021 Jun 22;11(7):928. doi: 10.3390/biom11070928. PMID: 34206696; PMCID: PMC8301935.

[25] Fava A, Petri M. Systemic lupus erythematosus: Diagnosis and clinical management. J Autoimmun. 2019 Jan;96:1-13. doi: 10.1016/j.jaut.2018.11.001. Epub 2018 Nov 16. PMID: 30448290; PMCID: PMC6310637.

[26] Poznyak AV, Orekhova VA, Sukhorukov VN, Khotina VA, Popov MA, Orekhov AN. Atheroprotective Aspects of Heat Shock Proteins. Int J Mol Sci. 2023 Jul 21;24(14):11750. doi: 10.3390/ijms241411750. PMID: 37511509; PMCID: PMC10380699.

[27] Alharbi L, Almoallim H. History-Taking Skills in Rheumatology. 2021 Jan 6. In: Almoallim H, Cheikh M, editors. Skills in Rheumatology [Internet]. Singapore: Springer; 2021. Chapter 1. Available from: https://www.ncbi.nlm.nih.gov/books/NBK585764/doi: 10.1007/978-981-15-8323-0_1

[28] Hassan R, Faruqui H, Alquraa R, et al. Classification Criteria and Clinical Practice Guidelines for Rheumatic Diseases. 2021 Jan 6. In: Almoallim H, Cheikh M, editors. Skills in Rheumatology [Internet]. Singapore: Springer; 2021. Chapter 25. Available from: https://www.ncbi.nlm.nih.gov/books/NBK585758/doi: 10.1007/978-981-15-8323-0_25

[29] Rana S, Lemoine E, Granger JP, Karumanchi SA. Preeclampsia: Pathophysiology, Challenges, and Perspectives. Circ Res. 2019 Mar 29;124(7):1094-1112. doi: 10.1161/CIRCRESAHA.118.313276. Erratum in: Circ Res. 2020 Jan 3;126(1):e8. doi: 10.1161/RES.0000000000000315. PMID: 30920918.

[30] Kesarwani V, Bukhari MH, Kahlenberg JM, Wang S. Urinary complement biomarkers in immune-mediated kidney diseases. Front Immunol. 2024 Jun 3;15:1357869. doi: 10.3389/fimmu.2024.1357869. PMID: 38895123; PMCID: PMC11184941.

[31] Xu Y, Li Y, Zhang Y, Li G. Urine complement analysis implies complement activation is involved in

membranous nephropathy. Front Med (Lausanne). 2025 Feb 13;12:1515928. doi: 10.3389/fmed.2025.1515928. PMID: 40018357; PMCID: PMC11865186.

[32] Koo M, Lu MC. Performance of a New Instrument for the Measurement of Systemic Lupus Erythematosus Disease Activity: The SLE-DAS. Medicina (Kaunas). 2023 Nov 29;59(12):2097. doi: 10.3390/medicina59122097. PMID: 38138199; PMCID: PMC10744780.

[33] Fanouriakis A, Kostopoulou M, Cheema K, Anders HJ, Aringer M, Bajema I, Boletis J, Frangou E, Houssiau FA, Hollis J, Karras A, Marchiori F, Marks SD, Moroni G, Mosca M, Parodis I, Praga M, Schneider M, Smolen JS, Tesar V, Trachana M, van Vollenhoven RF, Voskuyl AE, Teng YKO, van Leew B, Bertsias G, Jayne D, Boumpas DT. 2019 Update of the Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of lupus nephritis. Ann Rheum Dis. 2020 Jun;79(6):713-723. doi: 10.1136/annrheumdis-2020-216924. Epub 2020 Mar 27. PMID: 32220834.

[34] Louthrenoo W, Trongkamolthum T, Kasitanon N, Wongthanee A. Pregnancy outcomes between pregnant systemic lupus erythematosus patients with clinical remission and those with low disease activity: A comparative study. Arch Rheumatol. 2021 Dec 24;37(3):361-374. doi: 10.46497/ArchRheumatol.2022.9140. PMID: 36589601; PMCID: PMC9791546.

[35] Piga M, Arnaud L. The Main Challenges in Systemic Lupus Erythematosus: Where Do We Stand? J Clin Med. 2021 Jan 11;10(2):243. doi: 10.3390/jcm10020243. PMID: 33440874; PMCID: PMC7827672.

[36] Assunção H, Jesus D, Larosa M, Henriques C, Matos A, Le Guern V, Rubiño F, da Silva JAP, Rua-Figueroa I, Costedoat-Chalumeau N, Doria A, Inês LS. Definition of low disease activity state based on the SLE-DAS: derivation and validation in a multicentre real-life cohort. Rheumatology (Oxford). 2022 Aug 3;61(8):3309-3316. doi: 10.1093/rheumatology/keab895. PMID: 34864894.

[37] Hunnicutt J, Georgiou ME, Richards A, Quasny H, Magder L, Goldman D, Petri MA. Patients achieving low lupus disease activity state, systemic lupus erythematosus disease control or remission showed lower rates of organ damage during longitudinal follow-up: analysis of the Hopkins Lupus Cohort. Lupus Sci Med. 2024 Dec 11;11(2):e001206. doi: 10.1136/lupus-2024-001206. PMID: 39663154; PMCID: PMC11647352.

[38] Kim JW, Jung JY, Kim HA, Yang JI, Kwak DW, Suh CH. Lupus Low Disease Activity State Achievement Is Important for Reducing Adverse Outcomes in Pregnant Patients With Systemic Lupus Erythematosus. J Rheumatol. 2021 May;48(5):707-716. doi: 10.3899/jrheum.200802. Epub 2020 Oct 15. PMID: 33060317.

[39] Dao KH, Bermas BL. Systemic Lupus Erythematosus Management in Pregnancy. Int J Womens Health. 2022 Feb 15;14:199-211. doi: 10.2147/IJWH.S282604. PMID: 35210867; PMCID: PMC8859727.

[40] Al Rayes H, AlOudah N, Alsolaimani R, Alharthi A, Attar M, Daghasi H, Albeity A, Afifi AM, AlQahtani A, Alkaff A, Alkhamesi SM, Elnady B. Adverse Impact of Systemic Lupus Erythematosus on Pregnancy Outcomes: A Saudi Arabia Retrospective Multi-Center Study. Open Access Rheumatol. 2024 Feb 1;16:31-41. doi: 10.2147/OARRR.S448186. PMID: 38322608; PMCID: PMC10844007.

[41] Clowse ME, Jamison M, Myers E, James AH. A national study of the complications of lupus in pregnancy. Am J Obstet Gynecol. 2008 Aug;199(2):127.e1-6. doi: 10.1016/j.ajog.2008.03.012. Epub 2008 May 5. PMID: 18456233; PMCID: PMC2542836.

[42] Salmon JE. PROMISSE: progress in understanding pregnancy complications in patients with SLE. Arthritis Res Ther. 2012;14(Suppl 3):A39. doi: 10.1186/ar3973. Epub 2012 Sep 27. PMCID: PMC3467516.

[43] Skorpen CG, Lydersen S, Gilboe IM, Skomsvoll JF, Salvesen KÅ, Palm Ø, Svean Koksvik HS, Jakobsen B, Wallenius M. Influence of disease activity and medications on offspring birth weight, pre-eclampsia and preterm birth in systemic lupus erythematosus: a population-based study. Ann Rheum Dis. 2018 Feb;77(2):264-269. doi: 10.1136/annrheumdis-2017-211641. Epub 2017 Nov 1. PMID: 29092851.

[44] Smyth A, Oliveira GH, Lahr BD, Bailey KR, Norby SM, Garovic VD. A systematic review and meta-analysis of pregnancy outcomes in patients with systemic lupus erythematosus and lupus nephritis. Clin J Am Soc Nephrol. 2010 Nov;5(11):2060-8. doi: 10.2215/CJN.00240110. Epub 2010 Aug 5. PMID: 20688887; PMCID: PMC3001786.

[45] Mehta B, Luo Y, Xu J, Sammaritano L, Salmon J, Lockshin M, Goodman S, Ibrahim S. Trends in Maternal and Fetal Outcomes Among Pregnant Women With Systemic Lupus Erythematosus in the United States: A Cross-sectional Analysis. Ann Intern Med. 2019 Aug 6;171(3):164-171. doi: 10.7326/M19-0120. Epub 2019 Jul 9. Erratum in: Ann Intern Med. 2023 Mar;176(3):432. doi: 10.7326/L23-0008. PMID: 31284305.

[46] Cervera R, Font J, Carmona F, Balasch J. Pregnancy outcome in systemic lupus erythematosus: good news for the new millennium. Autoimmun Rev. 2002 Dec;1(6):354-9. doi: 10.1016/s1568-9972(02)00082-4. PMID: 12848991.

[47] Yue S, Meng J. Role of Decidual Natural Killer Cells in the Pathogenesis of Preeclampsia. Am J Reprod Immunol. 2025 Jan;93(1):e70033. doi: 10.1111/aji.70033. PMID: 39739937.

[48] Wang X, Shields CA, Ekperikpe U, Amaral LM, Williams JM, Cornelius DC. VASCULAR AND RENAL MECHANISMS OF PREECLAMPSIA. Curr Opin Physiol. 2023 Jun;33:100655. doi: 10.1016/j.cophys.2023.100655. Epub 2023 Mar 2. PMID: 37009057; PMCID: PMC10062189.

[49] Lu J, Xu D, Wan Q, Chen H. Pregnancy outcomes and risk factors analysis in patients with systemic lupus erythematous. BMC Pregnancy Childbirth. 2024 Jul 22;24(1):495. doi: 10.1186/s12884-024-06701-x. PMID: 39039448; PMCID: PMC11265087.

[50] Berman A, Kenet G, Lubetsky A, Agmon-Levin N, Soffer S, Barg AA, Levy-Mendelovich S, Cohen O, Waldman-Radinsky L, Lalezari S, Klang E, Efros O. Hydroxychloroquine and pregnancy outcomes in patients with anti-phospholipid syndrome: a systematic review and meta-analysis. RMD Open. 2025 Aug 27;11(3):e005825. doi: 10.1136/rmdopen-2025-005825. PMID: 40866107; PMCID: PMC12410631.

[51] Leroux M, Desveaux C, Parcevaux M, Julliac B, Gouyon JB, Dallay D, Pellegrin JL, Boukerrou M, Blanco P, Lazaro E. Impact of hydroxychloroquine on preterm delivery and intrauterine growth restriction in pregnant women with systemic lupus erythematosus: a descriptive cohort study. Lupus. 2015 Nov;24(13):1384-91. doi: 10.1177/0961203315591027. Epub 2015 Jun 16. PMID: 26082465.

[52] Gajić M, Schröder-Heurich B, Mayer-Pickel K. Deciphering the immunological interactions: targeting preeclampsia with Hydroxychloroquine's biological mechanisms. Front Pharmacol. 2024 Feb 5;15:1298928. doi: 10.3389/fphar.2024.1298928. PMID: 38375029; PMCID: PMC10875033.

[53] Gómez-Guzmán M, Jiménez R, Romero M, Sánchez M, Zarzuelo MJ, Gómez-Morales M, O'Valle F, López-Farré AJ, Algieri F, Gálvez J, Pérez-Vizcaino F, Sabio JM, Duarte J. Chronic hydroxychloroquine improves endothelial dysfunction and protects kidney in a mouse model of systemic lupus erythematosus. Hypertension. 2014 Aug;64(2):330-7. doi: 10.1161/HYPERTENSIONAHA.114.03587. Epub 2014 May 19. PMID: 24842914.

[54] Qiu W, Han X, Yu T, Jiang L, Wang X, Feng R, Duan X, Teng Y, Yin H, Bokarewa MI, Deng GM. Inhibitory effect of hydroxychloroquine on glucocorticoid-induced osteoporosis in lupus therapy. Clin Transl Immunology. 2024 Oct 14;13(10):e70010. doi: 10.1002/cti2.70010. PMID: 39416769; PMCID: PMC11480648.

[55] Liu Y, Zhang Y, Wei Y, Yang H. Effect of hydroxychloroquine on preeclampsia in lupus pregnancies: a propensity score-matched analysis and meta-analysis. Arch Gynecol Obstet. 2021 Feb;303(2):435-441. doi: 10.1007/s00404-020-05762-5. Epub 2020 Sep 3. PMID: 32880707.

[56] Clowse MEB, Eudy AM, Balevic S, Sanders-Schmidler G, Kosinski A, Fischer-Betz R, Gladman DD, Molad Y, Nalli C, Mokbel A, Tincani A, Urowitz M, Bay C, van Noord M, Petri M. Hydroxychloroquine in the pregnancies of women with lupus: a meta-analysis of individual participant data. Lupus Sci Med. 2022 Mar;9(1):e000651. doi: 10.1136/lupus-2021-000651. PMID: 35318256; PMCID: PMC8935175.

[57] Nørgård BM. Birth outcome in women with ulcerative colitis and Crohn's disease, and pharmacoepidemiological aspects of anti-inflammatory drug therapy. Dan Med Bull. 2011 Dec;58(12):B4360. PMID: 22142578.

[58] Sun H, Mao J, Su X, Du Q. Impact of spontaneous abortion history and induced abortion history on perinatal outcomes of singleton pregnancies. BMC Public Health. 2023 Nov 29;23(1):2360. doi: 10.1186/s12889-023-17264-5. PMID: 38031055; PMCID: PMC10685546.

[59] Singh M, Qualie J, Currie A, Howarth ES, Khare MM. Is breastfeeding safe with azathioprine? Obstet Med. 2011 Sep;4(3):104-7. doi: 10.1258/om.2011.110013. Epub 2011 Aug 23. PMID: 27579102; PMCID: PMC4989605.

[60] Martin-Iglesias D, Paredes-Ruiz D, Ruiz-Irastorza G. Use of Glucocorticoids in SLE: A Clinical Approach. Mediterr J Rheumatol. 2024 Jun 30;35(Suppl 2):342-353. doi: 10.31138/mjr.230124.uos. PMID: 39193186; PMCID: PMC11345604.

[61] Benhadi N, Wiersinga WM, Reitsma JB, Vrijkotte TG, Bonsel GJ. Higher maternal TSH levels in pregnancy are associated with increased risk for miscarriage, fetal or neonatal death. Eur J Endocrinol. 2009 Jun;160(6):985-91. doi: 10.1530/EJE-08-0953. Epub 2009 Mar 9. PMID: 19273570.

[62] Lazarus J. Thyroid Regulation and Dysfunction in the Pregnant Patient. [Updated 2016 Jul 21]. In: Feingold KR, Ahmed SF, Anawalt B, et al., editors. Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279059/

[63] Naji Rad S, Deluxe L. Postpartum Thyroiditis. [Updated 2023 Jun 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from:

https://www.ncbi.nlm.nih.gov/books/NBK557646/

[64] Smyth A, Garovic VD. Systemic lupus erythematosus and pregnancy. Minerva Urol Nefrol. 2009 Dec;61(4):457-74. PMID: 19816395.

[65] Peng M, Luo T, Weng X, Dong Y, Xie Y, Huang S, Liang N, Wen S, Zhai Y, Xie Y, Chen Y. A retrospective analysis on maternal and neonatal outcomes in pSS/AITD pregnancies. Sci Rep. 2025 Jan 27;15(1):3437. doi: 10.1038/s41598-024-83937-9. PMID: 39870646; PMCID: PMC11772809.

[66] McGlasson S, Wiseman S, Wardlaw J, Dhaun N, Hunt DPJ. Neurological Disease in Lupus: Toward a Personalized Medicine Approach. Front Immunol. 2018 Jun 6;9:1146. doi: 10.3389/fimmu.2018.01146. PMID: 29928273; PMCID: PMC5997834.

[67] Leal Rato M, Bandeira M, Romão VC, Aguiar de Sousa D. Neurologic Manifestations of the Antiphospholipid Syndrome - an Update. Curr Neurol Neurosci Rep. 2021 Jun 14;21(8):41. doi: 10.1007/s11910-021-01124-z. PMID: 34125304; PMCID: PMC8200381.

[68] Schwartz N, Stock AD, Putterman C. Neuropsychiatric lupus: new mechanistic insights and future treatment directions. Nat Rev Rheumatol. 2019 Mar;15(3):137-152. doi: 10.1038/s41584-018-0156-8. PMID: 30659245; PMCID: PMC8023338.

[69] Kölliker-Frers R, Udovin L, Otero-Losada M, Kobiec T, Herrera MI, Palacios J, Razzitte G, Capani F. Neuroinflammation: An Integrating Overview of Reactive-Neuroimmune Cell Interactions in Health and Disease. Mediators Inflamm. 2021 May 31;2021:9999146. doi: 10.1155/2021/9999146. PMID: 34158806; PMCID: PMC8187052.

[70] Knight CL, Nelson-Piercy C. Management of systemic lupus erythematosus during pregnancy: challenges and solutions. Open Access Rheumatol. 2017 Mar 10;9:37-53. doi: 10.2147/OARRR.S87828. PMID: 28331377; PMCID: PMC5354538.

[71] Ameer MA, Chaudhry H, Mushtaq J, Khan OS, Babar M, Hashim T, Zeb S, Tariq MA, Patlolla SR, Ali J, Hashim SN, Hashim S. An Overview of Systemic Lupus Erythematosus (SLE) Pathogenesis, Classification, and Management. Cureus. 2022 Oct 15;14(10):e30330. doi: 10.7759/cureus.30330. PMID: 36407159; PMCID: PMC9662848.

[72] Harley ITW, Sawalha AH. Systemic lupus erythematosus as a genetic disease. Clin Immunol. 2022 Mar;236:108953. doi: 10.1016/j.clim.2022.108953. Epub 2022 Feb 9. PMID: 35149194; PMCID: PMC9167620.

[73] Ulff-Møller CJ, Svendsen AJ, Viemose LN, Jacobsen S. Concordance of autoimmune disease in a nationwide Danish systemic lupus erythematosus twin cohort. Semin Arthritis Rheum. 2018 Feb;47(4):538-544. doi: 10.1016/j.semarthrit.2017.06.007. Epub 2017 Jun 23. PMID: 28755788.

[74] Halberg P, Alsbjørn B, Balslev JT, Lorenzen I, Gerstoft J, Ullman S, Wiik A. Systemic lupus erythematosus. Follow-up study of 148 patients. II: Predictive factors of importance for course and outcome. Clin Rheumatol. 1987 Mar;6(1):22-6. doi: 10.1007/BF02200996. PMID: 3581695.

[75] Moyer A, Edens C. Impact of Systemic Lupus Erythematosus on Conception: Insights into Infertility, Fertility Preservation, Assisted Reproductive Technology, and Pregnancy Outcomes. Semin Reprod Med. 2024 Sep;42(3):209-227. doi: 10.1055/s-0044-1793827. Epub 2024 Dec 12. PMID: 39667369; PMCID: PMC12094854.

[76] Chen YJ, Chang JC, Lai EL, Liao TL, Chen HH, Hung WT, Hsieh TY, Huang WN, Chen YH, Lin CH, Chen YM. Maternal and perinatal outcomes of pregnancies in systemic lupus erythematosus: A nationwide population-based study. Semin Arthritis Rheum. 2020 Jun;50(3):451-457. doi: 10.1016/j.semarthrit.2020.01.014. Epub 2020 Feb 4. PMID: 32115237.

[77] Mohan P, Chengappa KG, Sharma J, Gupta A, Adhisivam B, Negi VS, Keepanasseril A. Pregnancy Outcomes in Women With Systemic Lupus Erythematosus (SLE): A Matched-Observational Study From India. Int J Rheum Dis. 2025 Jun;28(6):e70328. doi: 10.1111/1756-185X.70328. PMID: 40522124.

[78] Brucato A, Cimaz R, Caporali R, Ramoni V, Buyon J. Pregnancy outcomes in patients with autoimmune diseases and anti-Ro/SSA antibodies. Clin Rev Allergy Immunol. 2011 Feb;40(1):27-41. doi: 10.1007/s12016-009-8190-6. PMID: 20012231; PMCID: PMC3558034.

[79] Popescu MR, Dudu A, Jurcut C, Ciobanu AM, Zagrean AM, Panaitescu AM. A Broader Perspective on Anti-Ro Antibodies and Their Fetal Consequences-A Case Report and Literature Review. Diagnostics (Basel). 2020 Jul 14;10(7):478. doi: 10.3390/diagnostics10070478. PMID: 32674462; PMCID: PMC7399931.

[80] Marder W, Romero VC, Ganser MA, Hyzy MA, Gordon C, McCune WJ, Somers EC. Increased usage of special educational services by children born to mothers with systemic lupus erythematosus and

antiphospholipid antibodies. Lupus Sci Med. 2014 Jul 15;1(1):e000034. doi: 10.1136/lupus-2014-000034. PMID: 25379194; PMCID: PMC4213825.

[81] Huybrechts KF, Bateman BT, Zhu Y, Straub L, Mogun H, Kim SC, Desai RJ, Hernandez-Diaz S. Hydroxychloroquine early in pregnancy and risk of birth defects. Am J Obstet Gynecol. 2021 Mar;224(3):290.e1-290.e22. doi: 10.1016/j.ajog.2020.09.007. Epub 2020 Sep 19. PMID: 32961123; PMCID: PMC7501839.

[82] Clowse MEB, Eudy AM, Balevic S, Sanders-Schmidler G, Kosinski A, Fischer-Betz R, Gladman DD, Molad Y, Nalli C, Mokbel A, Tincani A, Urowitz M, Bay C, van Noord M, Petri M. Hydroxychloroquine in the pregnancies of women with lupus: a meta-analysis of individual participant data. Lupus Sci Med. 2022 Mar;9(1):e000651. doi: 10.1136/lupus-2021-000651. PMID: 35318256; PMCID: PMC8935175.

[83] Dathe K, Frank J, Padberg S, Hultzsch S, Beck E, Schaefer C. Fetal adverse effects following NSAID or metamizole exposure in the 2nd and 3rd trimester: an evaluation of the German Embryotox cohort. BMC Pregnancy Childbirth. 2022 Aug 26;22(1):666. doi: 10.1186/s12884-022-04986-4. PMID: 36028798; PMCID: PMC9413886.

[84] Bay Bjørn AM, Ehrenstein V, Hundborg HH, Nohr EA, Sørensen HT, Nørgaard M. Use of corticosteroids in early pregnancy is not associated with risk of oral clefts and other congenital malformations in offspring. Am J Ther. 2014 Mar-Apr;21(2):73-80. doi: 10.1097/MJT.0b013e3182491e02. PMID: 23011170.

[85] Hviid A, Mølgaard-Nielsen D. Corticosteroid use during pregnancy and risk of orofacial clefts. CMAJ. 2011 Apr 19;183(7):796-804. doi: 10.1503/cmaj.101063. Epub 2011 Apr 11. PMID: 21482652; PMCID: PMC3080529.

[86] Pofi R, Tomlinson JW. Glucocorticoids in pregnancy. Obstet Med. 2020 Jun;13(2):62-69. doi: 10.1177/1753495X19847832. Epub 2019 Jun 9. PMID: 32714437; PMCID: PMC7359660.

[87] Carr-Locke DL. Sulfasalazine-induced lupus syndrome in a patient with Crohn's disease. Am J Gastroenterol. 1982 Sep;77(9):614-6. PMID: 6126117.

[88] Abadie RB, Keller CL, Jones NT, Mayeux EL, Klapper RJ, Anderson L, Kaye AM, Ahmadzadeh S, Varrassi G, Shekoohi S, Kaye AD. Review of Teratogenic Effects of Leflunomide, Accutane, Thalidomide, Warfarin, Tetracycline, and Angiotensin-Converting Enzyme Inhibitors. Cureus. 2023 Dec 13;15(12):e50465. doi: 10.7759/cureus.50465. PMID: 38222129; PMCID: PMC10786328.

[89] Coscia LA, Armenti DP, King RW, Sifontis NM, Constantinescu S, Moritz MJ. Update on the Teratogenicity of Maternal Mycophenolate Mofetil. J Pediatr Genet. 2015 Jun;4(2):42-55. doi: 10.1055/s-0035-1556743. PMID: 27617117; PMCID: PMC4944211.

[90] Nakai T, Honda N, Soga E, Fukui S, Kitada A, Yokogawa N, Okada M. A retrospective analysis of the safety of tacrolimus use and its optimal cut-off concentration during pregnancy in women with systemic lupus erythematosus: study from two Japanese tertiary referral centers. Arthritis Res Ther. 2024 Jan 4;26(1):15. doi: 10.1186/s13075-023-03256-8. PMID: 38178242; PMCID: PMC10765865.

[91] Ponticelli C, Moroni G. Fetal Toxicity of Immunosuppressive Drugs in Pregnancy. J Clin Med. 2018 Dec 15;7(12):552. doi: 10.3390/jcm7120552. PMID: 30558290; PMCID: PMC6306731.

[92] Heo YA. Voclosporin: First Approval. Drugs. 2021 Apr;81(5):605-610. doi: 10.1007/s40265-021-01488-z. PMID: 33788181; PMCID: PMC8010786.

Author Contributions: writing—original draft preparation, A.V.P.; writing—review and editing, A.A.V, E.R.K., O.N.M., A.S.U., A.N.O.

Funding: This research was funded by Russian Science Foundation, grant number 25-75-10012

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.