Impact of Systematic Lupus Erythematosus (SLE) In Pregnancy

Dr. Neena Parasher

(D.G.O), Director, Department of OBS and Gynae , Shankar Medicare Centre, 1251, Sector 28, Faridabad, Haryana

DOI: 10.29322/IJSRP.12.10.2022.p13010
http://dx.doi.org/10.29322/IJSRP.12.10.2022.p13010

Paper Received Date: 20th August 2022
Paper Acceptance Date: 24th September 2022
Paper Publication Date: 6th October 2022

***Abstract*-** Systematic lupus erythematosus (SLE) is a long-term autoimmune disease (a chronic condition) that results from malfunctioning of the immune system with severity from mild to life-threatening (1). It can cause rash, arthritis, serositis, nephritis, seizures, or psychosis, which might be continuous in some cases (2). There is a high incidence of SLE in black Caribbean females (33/100000), whereas in India it is 9.9/100000 (1). The disease has a female preponderance, especially among women of childbearing age (3). In spite of the fact that SLE is the most common autoimmune rheumatic disease encountered in pregnancy, modern drug therapies and management have helped many women who are of childbearing age to conceive. SLE-suffering women have a higher fetal and material risk during pregnancy than healthy women (4). When SLE has been quiescent for six months or more before getting pregnant, the prognosis for both mother and child is best.

***Index Terms*-** Lupus, Erythematosus, Preponderance, Quiescent, Pre-Eclampsia, Lupus nephritis, Breastfeeding, Contraception

I. INTRODUCTION

Pre-Conception Evaluation

1. In order to determine whether pregnancy may pose an unacceptably high risk to either the mother or the baby, it is imperative to conduct an assessment prior to conception.
2. When a woman with SLE is undergoing a preconception evaluation, her disease activity and major organ involvement should be assessed, along with hypercoagulability or concurrent medical disorders that could impact the pregnancy.
3. The risk of lupus flare and other pregnancy complications increases when women discontinue medications used to control disease activity.
4. Pregnant women should be moved to medication compatible with pregnancy and continue to take them throughout the pregnancy.
5. A pregnant woman should have a quiescent SLE condition for at least six months before pregnancy.
6. Active SLE patients, particularly those with lupus nephritis, should be advised not to become pregnant until the disease has been well controlled for at least six months. In cases of severe cases, surrogacy or adoption may be an option.

CHARACTERSTIC	PREGNANCY-RELATED CHANGES	SLE FLARE
Mucocutaneous	Facial Flush	Photosensitive rash
	Palmar erythema	
	Postpartum hair loss	Oral or nasal ulcers
Musculoskeletal	Arthralgias	Inflammatory arthritis
	Myalgias	
Hematologic	Mild anemia	Leucopenia, lymphopenia
	Mild thrombocytopenia	Immune hemolytic anemia
		Thrombocytopenia
Renal	Physiologic proteinuria <300mg/day	Active urinary sediment
		Proteinuria >300mg/day
Immunologic	Higher complement levels	Falling complement levels
		Rising anti DNA levels
Others	Fatigue	Fever
	Mild edema	Lymphadenopathy
	Mild resting dyspnea	Pleuritis

Symptoms-Above

II. IMPACT OF LUPUS ON PREGNANCY

The prevalence of obstetric complications was also higher in women with SLE, including preterm labor, cesarean delivery, fetal growth restriction, pre-eclampsia, eclampsia, thrombosis, infection, and thrombocytopenia (15,16).

A. Maternal Complications

- **Pre-Eclampsia** –

In 16-30 percent of women with SLE, preeclampsia is one of the most common pregnancy complications (17).

- **Pre-Term Birth** –

It has been reported that preterm birth is one of the most common obstetric complications in women with SLE (19). Rates of preterm birth range from 15 to 50 percent, with an increased incidence in women with lupus nephritis or high disease activity.

- Births by cesarean section due to obstetric complications or an SLE flare-up.

B. Fetal Complications (20,21) – Pregnant women with SLE have a greater risk of miscarriage, stillbirth, growth restriction, neonatal lupus syndromes, and prematurity.

- Foetal loss – The risk of early and late pregnancy loss is higher in women with SLE. Women with active SLE, lupus nephritis and antiphospholipid syndrome (APS) are at increased risk of fetal death beyond 10 weeks.
- Foetal Growth Restriction - In women with SLE, about 10 to 30 percent of pregnancy complications are related to fetal growth restriction, and the babies are small for their gestational age. They also have lower birth weights throughout their gestation period.
- Neonatal lupus (22,23) – A passively transmitted autoimmune disease referred to as NL affects some babies who are born to mothers with specific antibodies, such as anti-Ro/SSA and anti-LA/SSB, but do not yet have SLE. In addition to cutaneous and cardiac symptoms, NL can also manifest as hematological and hepatic abnormalities.

III. SPECIAL CONSIDERATIONS

Lupus nephritis

Women with active lupus nephritis should be encouraged to delay pregnancy until the disease is inactive for at least six months to optimize maternal outcomes.

Presence of antiphospholipid antibodies

aPLs are present in about a quarter to a half of patients with SLE; however, few patients develop thrombotic or obstetric complications related to APS.

Pregnant women with SLE with have an obstetric history suggestive of APS (fetal death after 10 weeks or more consecutive miscarriages, or premature birth <34 weeks due to preeclampsia or placental insufficiency) or unexplained venous or arterial thrombotic event, should be tested for the presence of aPLs (i.e. lupus anticoagulant [LA], immunoglobulin G [IgG] and IgM anticardiolipin [aCL] antibodies; and IgG and IgM anti-beta2-glycoprotein [GP] I)

IV. Presence of anti-Ro and anti-La antibodies

As mentioned above, a fetus exposed to anti-Ro/SSA and/or anti-La/SSB antibodies is at an increased risk of developing congenital complete heart block or NL.

Management of SLE in pregnancy

1. During pregnancy, a rheumatologist and an obstetrician who is experienced in caring for high-risk members should collaborate closely to manage pregnant women with SLE.
2. Monitoring SLE activity – Initial evaluation at the time of diagnosis
   a. Physical examination, including blood pressure
   b. Renal function (creatinine, urinalysis, spot urine protein/creatinine ratio).
   c. CBC
   d. Liver function tests
   e. Anti-Ro/SSA or anti-LA/SSB antibodies
   f. Lupus anticoagulant (LA) and anticardiolipin antibody (ACL) assays
   g. Anti-double stranded DNA (dsDNA) antibodies
   h. Complement (CH50, or C3 and C4)
   i. Serum uric acid
3. Monitor by repeat testing, including CBC, Creatinine, Urinalysis with an examination of urinary sediment, urine protein/creatinine ratio or 24-hour urine collection, Complement (CH50, or C3 and C4), Anti-double-stranded DNA antibodies (dsDNA).
4. Maternal-fetal monitoring – During pregnancy, a recommended schedule for monitoring maternal and fetal health should be followed. Over and above routine T1 and T2 anomaly scans,
   a. First-trimester ultrasound evaluation to know the date of delivery.
   b. Monitoring fetal growth and placental insufficiency with ultrasound in the third trimester. The frequency of monitoring will depend on fetal and maternal well-being, but around four weeks will normally be recommended.
   c. The final four to six weeks of pregnancy are an ideal time to conduct nonstress tests and/or biophysical profiles for women with lupus.
   d. Patients with positive anti-Ro/SSA or anti-LA/SSB antibodies should be closely monitored for congenital heart block.
5. Postpartum laboratory testing – There is a possibility that some women with SLE might experience an exacerbation of the disease during the postpartum period. Women with active disease at conception or those with significant organ damage should be aware that they are at a greater risk of disease flares during this timeframe than women with inactive disease. Recommended tests include:
   a. Urinalysis, urine protein/creatinine ratio
   b. Renal function if the urinalysis is abnormal
   c. CBC

A woman who develops active SLE after delivery is treated as a non-pregnant woman; however, some medications used to treat active SLE may not be compatible with breastfeeding; It is, therefore, important to discuss with their clinicians the risks and benefits of various treatment options with breastfeeding women.

V. MEDICATIONS

A. **Recommended During Pregnancy**

- Hydroxychloroquine –

HCQ is generally considered safe when administered to pregnant women with SLE (6,7) unless contraindications are present. Several studies have demonstrated that patients who continued their HCQ during pregnancy had fewer disease flares and better outcomes, and they did not suffer adverse congenital malformations.

- Low dose Aspirin –

Regardless of the presence of antiphospholipid antibodies, this treatment can be given after 12 weeks of pregnancy to reduce the risk of preeclampsia (8) and its sequelae.

B. **Selectively Used During Pregnancy**

- NSAID's –

However, conflicting evidence suggests an increase in spontaneous abortion in the first trimester (9+) despite its use not being associated with congenital anomalies. NSAIDs are safe to use after the first trimester of pregnancy and should be avoided after 30 weeks. They may cause premature closure of the ductus arteriosus and other complications.

- Glucocorticoids –

Prednisolone should be started with the lowest dose possible. If possible, it should not exceed 10mg. Use of steroids =in 1st trimester might cause cleft lip, cleft palate, etc.

- Azathioprine –

(10) The dose cannot exceed 2 mg per day during pregnancy.

- Cycloserine –

(11) In pregnancy, this drug can be used, but the maternal benefits must outweigh the risks to the fetus.

- Tacrolimus –

(12) If lupus nephritis flares severely during pregnancy, it should only be considered.

Contra Indication

- Cyclophosphamide
- Methotrexate
- Mycophenolate mofetil
- Leflunomide (13,14)

Breastfeeding

Most women with systemic lupus erythematosus (SLE) are encouraged to breastfeed. The safety of medications in lactation varies. Hydroxychloroquine (HCQ), prednisone, cyclosporine, azathioprine, and tacrolimus are considered safe during breastfeeding. Breastfeeding is not comparable with methotrexate, mycophenolate, cyclophosphamide, leflunomide, and small molecules such as facitinib.

Contraception

- Since few drug interactions are seen with SLE drugs, oral contraceptives should be avoided.
- POP is a better option
- These patients should consider IUCDs as the best contraceptive method.

REFERENCES

1. Rees F, Doherty M, Grainge M, Davenport G, Lanyon P, Zhang W. The incidence and prevalence of systemic lupus erythematosus in the UK, 1999-2012. Ann Rheum Dis. 2016;75(1):136-141. 2. Dall'Era M. Chapter 21. Systemic lupus erythematosus. In Imboden JB, Stone JH,m o, eos. Current reumatology diagnosis & treatment. 3ed. USA: McGraw-Hill, 2013 3. Petri M. Epidemiology of systemic lupus erythematosus. Best Pract Res ClinRheumatol. 2002;16(5):847-858 4. Buyon JP, Kim MY, Guerra MM, et al. Predictors of Pregnancy Outcomes in onents with Lupust A Cohort Study Ann Intern Med 2015; 163:153. 5.Kwok LW, Tom LS, Zhu T, et al. Predictors of maternal and fetal outcomes in pregnancies of patients with systemic lupus erythematosus. Lupus 2011; 20:829. 6. Clowse ME, Magder , Witter. Petr coquine in lupus pregnancy. Arthritis Rheum 2006; 54:3640 7. Parke AL, Rothfield NF. Antimalarial drugs in pregnancy--the North American experience. Lupus 1996; 5 Suppl 1:567 B.LeFevre ML, U.S. Preventive Services Task Force. low-dose aspirin use for the prevention of lity from preeclampsia: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2014; 161.819 9. stensen M. Khamashta M. Lockshin M et al. Anti-inflammatory and immunosuppressive drugs and reproduction. Arthritis Rether 2018 2024 Seppola M. Immunosuppression during pregnancy: transmission of ozathioprine and its metabolites from the mother to the fetus. Am J Obstet Gynecol 1973; 115:1100, 11. Ostensen M, Lockshin M, Doria A, Valesini G, Meroni P, Gordon Brucato A, Tincani A. Update on pregnancy of biological agents and some immunosuppressive anti-rheumatic drugs. Rheumatology (Oxford) 2008;47(3):28-31. 12. Webster P, Wardle A, Bramhom K, et al. Tacrolimus is an effective treatment for lupus nephritis in pregnancy. Lupus 2014, 23:1182.13Robinson L, Braddock S, XU R, Lopez Jimenez J, Mirrosoul N, Salas E, Luo Y, Jones K, et al. Pregnancy outcome in women exposed to leflunomide before or during pregnancy. Arthritis Rheum. 2012 14. 50. Chambers CD. Johnson DL, Robinson K, Braddock SK, X Cassina M, Johnson D. Robinson L, Braddock S, XU R, Lopez Jimenez, Sovi, Salast, Luo YJ, Jin S, et al. Birth outcomes in women who have taken leflunomide during pregnancy. Arthritis Rheum. 2010;62(5):1494-1503. 15. Smyth A Oliveira GH, Lahr BD, et al. A systematic review and meta-analysis of pregnancy outcomes in patient Frymematosus and lupus nephritis. Clin J Am SocNephrol 2010, 5.2060. 16. Petri M. Prospective study of systemic lupus erythematosus pregnancies. Lupus 2004; 13:688. 17. Chakravorty EF, Colón I, Longen ES, et al. Factors that predict prematurity and preeclampu cored by systemic lupus erythematosus. Am J Obstet Gynecol 2005; 192.1897. 18. Gibbins KI, Ware Branch D. Pre-eclampsia as a manifestation of antiphospholipid syndrome: assessing the current status. Lupus 2014, 23:1229. 19. Saavedra e v eze pregnancies that are complicated by systemic lupus erythematosus. Am Reed D, et al. Maternal and foetal outcomes in pregnant patients with active lupus nephritis lupus 2009, 1013 .21 of previous lupus nephritis on maternal and fetal outcomes during pregnancy. Clin Rheumatol 2012, 31.813. 20. Wagner S), Craid Vero-Lastra O, et al. Impact of previous lupus nephritis on maternare », et al. Pregnancy and systemic lupus erythematosust review of clinical features and outcome of 51 pregnancies at a single institution. Clin Rev Allergy Immunol 2010; 38:302. 22. Brucato A Frassi M, Franceschini F, et al. Risk of congenital comprese Carvalheiros G.VitaP.MartaS, et al. Pregnancy and systemic lupus ery anti-ko/SSA antibodies detected by counterimmunoelectrophoresis: a prospective study of 100 women. Arthritis Rheum 2001; 44:1832. 23. Buyon JP, Hiebert R, Copel J, et al. Autoimmune associated congenital heart blocka demographic, more block in newborns of mothers with anti-Ro/SSA antibodies detected by morbidity and recurrence rates obtained from a national neonatal lupus registry. J Am Coll Cardiol 1997 m . (51)

AUTHORS

First Author – Dr. Neena Parasher, D.G.O, Parashar_neena@yahoo.com