Caspian J Reprod Med, 2024, 10 (1): 18-22

Caspian Journal of Reproductive Medicine

Journal homepage: www.caspjrm.ir

Original article

Retrospective Analysis of Pregnancy Outcomes Complicated by Systemic Lupus Erythematosus at a Rural Tertiary Care Center in Kerala, India

Jaimie T Jacob [1, *], S Lakshmi Vinodh [1], Nisha V [1], Anamika Francis [2]

[1] Department of obstetrics & Gynecology, Government Medical College, Trivandrum, Kerala, India
[2] Department of obstetrics & Gynecology, Dr. Moopen's Medical College, Wayanad, Kerala, India

Received: 1 Jun 2024 Accepted: 28 Jun 2024

Abstract

Background: Systemic lupus erythematosus (SLE) affects women of childbearing age, leading to higher maternal and fetal morbidity and mortality. Disease flares during pregnancy complicate care. This study evaluates maternal and fetal outcomes in pregnancies complicated by SLE.

Methods: A retrospective analysis was conducted on 31 pregnancies complicated by SLE at the Department of Obstetrics and Gynaecology, TD Medical College, Alleppey, from January 2010 to December 2018. Data on maternal demographics, obstetric history, SLE manifestations, treatments, pregnancy outcomes, complications, disease flares, interventions, and delivery details were collected. Maternal complications, including gestational hypertension, pre-eclampsia/eclampsia, HELLP syndrome, diabetes, abruption, preterm birth, fetal growth restriction, lupus nephritis, and postpartum hemorrhage, were examined. Fetal outcomes were assessed based on perinatal morbidity and mortality and NICU admissions.

Results: Among the 31 pregnancies, 67% of the women were aged 20-30 years. SLE was diagnosed during the current pregnancy in 45.2% of cases, with 53.3% of these diagnoses occurring in the first trimester. Preterm birth was the most common complication, observed in 48.4% of pregnancies, with 29% live born and 19.4% stillborn. Hypertensive disorders were prevalent, with 38.7% developing pre-eclampsia/eclampsia. Antiphospholipid antibody positivity was noted in 29% of patients. Severe SLE flares occurred in 12.9% of patients, all with nephropathy in the third trimester.

Conclusion: Favorable pregnancy outcomes are more likely in women whose SLE activity is quiescent for at least six months before conception, without lupus nephritis, antiphospholipid syndrome, or superimposed preeclampsia. The findings emphasize the need for vigilant monitoring and management of pregnancies complicated by SLE.

Keywords: Female, Lupus Erythematosus, Systemic, Pregnancy, Pregnancy Complications Pregnancy Outcome

Introduction

Systemic lupus erythematosus (SLE) is a complex, multisystemic disorder that predominantly impacts women of reproductive age. The prevalence is approximately one in 700 women, with the highest incidence occurring around the age of 30 (1).

Garris et al., in their retrospective analysis, found that patients with systemic SLE are significantly more likely to seek medical attention compared to a matched population of non-SLE patients. Specifically, individuals with SLE are 2.4 times more likely to visit a physician, 2.7 times more likely to be hospitalized, and 2.1 times more likely to present to the emergency room (2). Pregnancy in women with SLE poses a significantly higher risk for adverse outcomes. Understanding these risks is crucial for effective management and care of pregnant patients with SLE to ensure better maternal and fetal health (3).

*Correspondence author: Dr Jaimie T Jacob, Department of obstetrics & Gynecology, Government Medical College, Trivandrum, Kerala, India.

Email: jaimie.jacob@gmail.com, Tel:_+91 9447520575

[DOI: 10.22088/caspjrm.10.1.5]

Another important concern is the impact of pregnancy on SLE. Aberrations in pregnancy-related maternal immune adaptations are likely contributors to this effect. Additionally, genetic, hormonal, and environmental factors play a role in the disease's progression, potentially leading to organ damage (4). Despite these challenges, recent trends indicate more favorable outcomes for pregnant women with SLE.

Ideally, SLE should be in a quiescent state for at least six months prior to contemplating pregnancy. According to Clowse et al., active SLE at the time of conception is a significant predictor of adverse maternal and obstetric outcomes (5). Buyon et al. (2015) reported that women who experienced adverse pregnancy outcomes exhibited significantly elevated levels of disease activity at the time of conception (6).

The reported incidence of disease flare during pregnancy varies considerably, largely influenced by the level of disease activity prior to pregnancy, with estimates ranging from 25% to 65% of pregnancies (7).

Certain manifestations of SLE, such as renal flare or thrombocytopenia, may be asymptomatic, underscoring the necessity for vigilant monitoring during pregnancy. These silent flares can nonetheless elevate the risk of obstetric complications. Pregnancies in women with SLE are often complicated by increased rates of miscarriage, hypertensive disorders, thromboembolism, fetal growth restriction (FGR), premature delivery, fetal demise, neonatal lupus, and neonatal death, as documented by Barnabe et al. in their study (8).

A national study on the complications of SLE conducted by Clowse emphasized several factors that are considered to influence pregnancy outcomes. These factors include lupus activity, the presence of antiphospholipid antibodies, renal status, hypertension, and complications related to medication (5).

Women with a history of lupus nephritis are associated with a higher risk of adverse pregnancy outcomes compared to patients with SLE who do not have a history of lupus nephritis. (9).

According to the study by Andrade et al., patients with lupus nephritis have a twofold increased risk of developing pre-eclampsia and are at a higher risk for fetal loss. Additionally, individuals who experienced active disease at conception and those with significant end-organ damage are at a greater risk of disease flares during the postpartum period compared to women with inactive disease (10).

It is well-recognized that patients with SLE require close monitoring during pregnancy; however, there is limited data available to determine the optimal frequency and nature of such monitoring. Furthermore, there is a lack of comprehensive data regarding the impact of SLE on pregnancy outcomes among Keralite and Indian women. This study presents a retrospective analysis of pregnancies in SLE patients to assess maternal and fetal outcomes associated with these pregnancies.

Materials & Methods

This study is a retrospective analysis of pregnancies complicated by SLE that were managed at the Department of Obstetrics and Gynecology, TD Medical College, Alleppey, from January 2010 to December 2018. Approval was obtained from the Institutional Ethics Committee (EC24/2019 dated 12/03/2019), and permission was secured from the Medical Records Library for case record retrieval. As this is a retrospective study, informed consent was not required. All collected data was maintained with strict confidentiality.

The study analyzed the medical records of pregnant women with SLE who attended the Obstetrics and Gynaecology department during the specified period. Records with incomplete data were excluded from the analysis. A total of 31 pregnancies complicated by SLE were identified during this period. Maternal data collected included personal information, obstetric history, duration and manifestations of SLE, previous and current treatments, pregnancy outcomes, complications, disease flares, interventions, and delivery details. Maternal complications examined included gestational hypertension, pre-eclampsia/eclampsia spectrum, HELLP syndrome, presentational and gestational diabetes, abruption, preterm birth, fetal growth restriction, lupus nephritis, and postpartum hemorrhage. Fetal outcomes were assessed based on perinatal morbidity and mortality and the need for admission to the neonatal intensive care unit (NICU).

Statistical Analysis: Data were entered into an Excel spreadsheet and analyzed using appropriate statistical software. Quantitative variables were summarized using mean and standard deviation, while qualitative variables were expressed as percentages or proportions. Associations between risk factors and outcomes were analyzed using statistical tests.

Results

During the period from January 2010 to December 2018, there were 31 cases of pregnancies complicated by systemic lupus erythematosus (SLE).

Among these cases, 67% of the women were aged between 20 and 30 years, while 32% were aged between 30 and 40 years. SLE was diagnosed during the current pregnancy in 53.3% of these diagnoses occurring in the first trimester. Three cases (9.6%) were identified during a previous pregnancy, and 41.9% were diagnosed during the interpregnancy interval. Of the women with a prior diagnosis of SLE, 38.7% had experienced a quiescent period of more than six months before conception, while 19.4% conceived during an active phase of the disease. Among the pregnancies complicated by SLE, 45.2% resulted in

[DOI: 10.22088/caspjrm.10.1.5]

term delivery of a live-born infant, whereas 54.8% had adverse outcomes, as detailed in Table 1.

Table 1. Pregnancy outcomes in patients with systemic lupus erythematosus at a rural tertiary care center in Kerala, India (n = 31)

	(Number)	%
First trimester abortion	1	3.2
Second trimester abortion	1	3.2
Term live birth	14	45.2
Preterm live birth	9	29
Term stillborn	0	0
Preterm stillborn	6	19.4

All pregnancies with SLE were associated with various complications, with preterm birth being the most common (Table 2.

Table 2. Pregnancy complications in patients with systemic lupus erythematosus at a rural tertiary care center in Kerala, India (n = 31)

	Number	%
Gestational Hypertension	2	6.5
Pre-eclampsia	9	29
Eclampsia	3	9.7
Chronic hypertension	7	22.6
HELLP syndrome	2	6.5
Gestational diabetes mellitus	2	6.5
Pre-gestational diabetes	3	9.7
Abruption	4	12.9
Preterm birth	16	51.6
Fetal growth restriction	8	25.8
APLA Antibodies	9	29.0
Lupus Nephritis	9	29.0
Postpartum haemorrhage	2	6.5

Mode of delivery and fetal outcome were assessed by recording miscarriage, live birth, still birth, term birth, preterm birth, small gestational age (SGA), NICU admission, neonatal death, neonatal lupus, congenital heart block, as shown in Table 3. The miscarriage rate was 6.5%, indicating that the majority of pregnancies resulted in live births. A significant proportion of deliveries were via caesarean section (58.1%), while vaginal deliveries accounted for 35.4% of cases. The live birth rate was notably high at 74.1%, with 23 out of 31 pregnancies resulting in live births. The stillbirth rate was recorded at 19.4%, reflecting some of the risks associated with SLE during pregnancy. Approximately 45.2% of the births were term deliveries, while nearly half (48.4%) were preterm, highlighting the potential for premature labor in this population. A significant proportion of infants (55.8%) were classified as SGA, which can be a concern for fetal development.

Table 3. Mode of delivery and fetal outcomes in patients with systemic lupus erythematosus at a rural tertiary care center in Kerala, India (n = 31)

Outcome	Number	%
Miscarriage	2	6.5
Vaginal delivery	11	35.4
Caesarean delivery	18	58.1
Miscarriage	2	6.5
Live birth	23	74.1
Still birth	6	19.4
Term birth	14	45.2
Preterm birth	15	48.4
SGA*	17	55.8
NICU admission	10	32.2
Neonatal death	0	0.0
Neonatal lupus	0	0.0
Congenital heart block	0	0.0

*SGA: Small for Gestational Age

Discussion

The findings of our study reveal that a significant majority (67%) of patients were between the ages of 20 and 30 years. Among the 31 patients analyzed, systemic lupus erythematosus (SLE) was diagnosed during the current pregnancy in 45.2% of cases, with 53.3% of these diagnoses made in the first trimester. This high rate of early detection may be attributed to the investigation of recurrent pregnancy loss, a common concern among many of the patients in our cohort.

Optimal pregnancy outcomes are generally observed in women who meet the following criteria: (1) lupus activity has been quiescent for at least six months before conception; (2) there is no lupus nephritis, indicated by proteinuria or renal dysfunction; (3) antiphospholipid syndrome or lupus anticoagulant is absent; and (4) superimposed preeclampsia does not develop. In our study, among the previously diagnosed SLE patients, 38.7% had a quiescent period of more than six months before conception, while 19.4% conceived during an active phase. Additionally, 29% of

[DOI: 10.22088/caspjrm.10.1.5]

the pregnant women with SLE had a diagnosis of lupus nephritis.

Our assessment of various complications and outcomes in pregnant women with SLE aligns with previous studies on adverse pregnancy outcomes in SLE patients (3,5,9). The most common complication reported was hypertensive disorders, with 38.7% of patients developing pre-eclampsia/eclampsia. Antiphospholipid antibody (APLA) positivity was observed in 29% of our patients, compared to 21.28% in a case-control study on lupus pregnancy outcomes (3). Preterm birth was recorded in 48.4% of patients, of which 29% were liveborn and 19.4% were stillborn. Abruptio placentae occurred in 12.9% of our patients (11).

Severe SLE flares were noted in 12.9% of patients, all of whom had nephropathy in the third trimester, which is higher than the rates reported in a multicentric prospective cohort study (12). The complications were more frequent when patients conceived during the active phase of the disease. Consistent with a multicentric cohort study by Buyon et al., our findings indicate that pregnancy outcomes are more favorable in patients with inactive or stable mild/moderate SLE (11).

Our findings indicate that pregnancy outcomes are more favorable in patients with inactive or stable mild/moderate SLE.

Previous studies have reported significantly elevated rates of adverse perinatal outcomes in pregnancies complicated by SLE, including preterm delivery, fetal growth restriction, stillbirth, and neonatal lupus syndrome (13). Our study similarly showed 55.8% of babies were small for gestational age, 48.4% were born preterm, and the stillbirth rate was 19.4%. There were 10 NICU admissions, primarily due to prematurity and related complications, and no cases of neonatal lupus were observed.

A preconception assessment is essential to determine whether pregnancy poses an unacceptably high risk to maternal or fetal health, to initiate interventions to optimize disease activity, and to adjust medications to minimize harm to the fetus.

The study's limitations, including its retrospective nature, small sample size, incomplete renal biopsy data, and lack of detailed medication histories, highlight the need for further research. Future studies should aim for larger, prospective cohorts with comprehensive data collection to better understand and mitigate the risks associated with SLE in pregnancy.

Conclusion

In conclusion, the study emphasizes that favorable pregnancy outcomes are more likely in women whose lupus activity is quiescent for at least six months before conception, without lupus nephritis, antiphospholipid syndrome, or superimposed preeclampsia. Despite these findings, the study identified a high rate of complications, including hypertensive disorders, preterm births, and stillbirths. The prevalence of severe SLE flares, particularly in the third trimester among women with nephropathy, underscores the need for vigilant monitoring and management.

Our findings highlight the importance of preconception assessment and ongoing monitoring to manage SLE activity and minimize risks, thereby improving maternal and fetal outcomes in pregnancies complicated by SLE.

Acknowledgements

We would like to express our sincere gratitude to Department of obstetrics & Gynecology for their support and resources that made this research possible. Their expertise and encouragement were instrumental in the successful completion of this work.

Conflicts of Interest

No declared conflicts of interest.

References

1. Mackens S, Santos-Ribeiro S, Van De Vijver A, Racca A, Van Landuyt L, Tournaye H, et al. Frozen embryo transfer: a review on the optimal endometrial preparation and timing. Human Reproduction. 2017; 32(11): 2234-42.
2. Ghobara T, Gelbaya TA, Ayeleke RO. Cycle regimens for frozen-thawed embryo transfer. Cochrane Database Syst Rev 2017; 7(7): CD003414.
3. Doody KJ. Cryopreservation and delayed embryo transfer–assisted reproductive technology registry and reporting implications. Fertil Steril 2014; 102(1): 27-31.
4. de Ziegler D, Pirtea P, Andersen CY, et al. Role of gonadotropin-releasing hormone agonists, human chorionic gonadotropin (hCG), progesterone, and

[DOI: 10.22088/caspjrm.10.1.5]

estrogen in luteal phase support after hCG triggering, and when in pregnancy hormonal support can be stopped. Fertil Steril 2018; 109(5): 749-55.
5. Seikkula J, Ahinko K, Polo-Kantola P, et al. Mid-luteal phase gonadotropin-releasing hormone agonist support in frozen-thawed embryo transfers during artificial cycles: a prospective interventional pilot study. J Gynecol Obstet Hum Reprod 2018; 47(8): 391-5.
6. Chegini N, Rong H, Bennett B, et al. Molecular Analysis of Intraperitoneal Environment and Its Relationship to Adhesion Formation and Endometriosis. J Soc Gynecol Investig 1998; 11001(5): 112A.
7. Khan KN, Kitajima M, Hiraki K, et al. Cell proliferation effect of GnRH agonist on pathological lesions of women with endometriosis, adenomyosis and uterine myoma. Hum Reprod 2010; 25(11): 2878-90.
8. Salehpour S, Nazari L, Hosseini S, et al. Efficacy of daily GnRH agonist for luteal phase support following GnRH agonist triggered ICSI cycles versus conventional strategy: A Randomized controlled trial. JBRA Assist Reprod 2021; 25(3): 368.
9. Maghraby H, Abdelbadie AS, Aboali A, et al. GnRH agonist as a luteal support in IVF cycle: mini-review—is there a role? Middle East Fertil Soc J 2022; 27(1): 1-4.
10. Fusi FM, Brigante CM, Zanga L, et al. GnRH agonists to sustain the luteal phase in antagonist IVF cycles: a randomized prospective trial. Reprod Biol Endocrinol 2019; 17(1): 1-6.
11. Steiner N, Shrem G, Tannus S, et al. Effect of GnRH agonist and letrozole treatment in women with recurrent implantation failure. Fertility and Sterility. 2019; 112(1): 98-104.
12. Chang W-S, Lin P-H, Li C-J, et al. Additional single dose GnRH agonist during luteal phase support may improve live birth rate in GnRHa-HRT frozen–thawed embryo transfer cycle: a retrospective cohort study. BMC Pregnancy Childbirth 2023; 23(1): 174.
13. Zhao J, Hao J, Li Y. Individualized luteal phase support after fresh embryo transfer: unanswered questions, a review. Reprod Health 2022; 19(1): 1-9.
14. Qian Y, Wan Q, Bu X-Q, et al. Pregnancy outcomes of four different cycle protocols for frozen embryo transfer: a large retrospective cohort study. Repro Dev Med 2023; 7(03): 135-41.
15. Fanchin R, Ayoubi J-M, Olivennes F, Righini C, de Ziegler D, Frydman R. Hormonal influence on the uterine contractility during ovarian stimulation. Hum Repro 2000; 15(suppl_1): 90-100.
16. Tesarik J, Hazout A, Mendoza-Tesarik R, et al. Beneficial effect of luteal-phase GnRH agonist administration on embryo implantation after ICSI in both GnRH agonist-and antagonist-treated ovarian stimulation cycles. Hum Repro 2006; 21(10): 2572-9.
17. Aboulghar M. Luteal support in reproduction: when, what and how? Curr Opin Obstet Gynecol 2009; 21(3): 279-84.
18. Fatemi H, Popovic-Todorovic B, Papanikolaou E, Donoso P, Devroey P. An update of luteal phase support in stimulated IVF cycles. Hum Repro Update 2007; 13(6): 581-90.
19. Pirard C, Donnez J, Loumaye E. GnRH. agonist as luteal phase support in assisted reproduction technique cycles: results of a pilot study. Hum Repro 2006; 21(7): 1894-900.
20. Murdoch WJ. Immunolocalization of a gonadotropin-releasing hormone receptor site in murine endometrium that mediates apoptosis. Cell Tissue Res 1995; 282: 527-9.
21. Reshef E, Lei Z, Rao CV, et al. The presence of gonadotropin receptors in nonpregnant human uterus, human placenta, fetal membranes, and decidua. J Clin Endocrinol Metab 1990; 70(2): 421-30.
22. Razieh DF, Maryam AR, Nasim T. Beneficial effect of luteal-phase gonadotropin-releasing hormone agonist administration on implantation rate afterintracytoplasmic sperm injection. Taiwan J Obstet Gynecol 2009; 48(3): 245-8.
23. Nakhuda GS, Chu MC, Wang JG, et al. Elevated serum müllerian-inhibiting substance may be a marker for ovarian hyperstimulation syndrome in normal women undergoing in vitro fertilization. Fertil steril 2006; 85(5): 1541-3.

[DOI: 10.22088/caspjrm.10.1.5]