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RESEARCH ARTICLE
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FREQUENCY OF SYSTEMIC LUPUS ERYTHEMATOSUS AMONG PREGNANT WOMEN IN TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is an idiopathic autoimmune condition which has multi-organ involvement. The risk of obstetric complications in pregnant SLE patients is significant, with an increased risk of spontaneous abortion, intrauterine fetal death, preeclampsia (PE), intrauterine growth restriction (IUGR), and preterm birth. In addition, pregnancy may be associated with disease flares requiring immunosuppressive therapy. Therefore, pregnancies in SLE patients are considered a high risk condition.

Objective: To determine the frequency of systemic lupus erythematosus among pregnant women in tertiary care hospital.

Materials and Methods: The study was conducted in the Department of Gynecology and Obstetrics at Lady Reading Hospital, Peshawar in collaboration with technical help of Karachi Metropolitan University from July 30, 2020, to January 31, 2021. This cross-sectional study included a total of 234 pregnant women who were selected consecutively. These women were then assessed for the presence of Systemic Lupus Erythematosus (SLE), aiming to determine its prevalence and potential impact on pregnancy outcomes. Comprehensive evaluations were carried out to identify SLE-related symptoms and complications, ensuring a thorough understanding of the condition within the studied population.

Results: The mean age and standard deviation of the sample was 31.1 $\pm$ 5.8 years. The mean parity was 2.2 $\pm$ 1.5 and the mean BMI of the sample was 26.1 $\pm$ 3.6kg/m^2. Family history of SLE was recorded in 32.5% of women and current SLE during pregnancy was observed in 15% of women.

Conclusion: SLE during pregnancy is fairly common in our population particularly among women who have family history of SLE. More observational studies are recommended to determine the risk

factors of SLE during pregnancy and follow up longitudinal studies to determine its effect on pregnancy outcome before recommending future directions for its prevention and control

Key Words: Systemic lupus erythematosus, body mass index, parity, pregnancy

INTRODUCTION

Systemic lupus erythematosus (SLE) is an idiopathic autoimmune condition which has multi-organ involvement[1]. SLE can affect any area of the human body, including dermatologic, neurologic, renal, cardiologic, hematologic, and other systems[2]. Some common symptoms of SLE are fatigue, arthralgia, arthritis, fever, skin rashes, anemia, edema, pleurisy, facial rash, photosensitivity, alopecia, Raynaud's phenomenon, seizures, and mouth or nose ulcers. The requirements for diagnosis are assessed through patient history, hematologic tests including complete blood counts and autoantibodies as well as physical examination[3].

The risk of obstetric complications in pregnant SLE patients is significant, with an increased risk of spontaneous abortion, intrauterine fetal death, preeclampsia (PE), intrauterine growth restriction (IUGR), and preterm birth [4]. In addition, pregnancy may be associated with disease flares requiring immunosuppressive therapy. Therefore, pregnancies in SLE patients are considered a high risk condition. Maternal health and fetal development should be monitored frequently during pregnancy. If possible, delivery should occur in a controlled setting. An obstetrician with experience in high-risk pregnancies should follow pregnant women with SLE, including a multidisciplinary approach with rheumatologic and neonatal team. Fortunately, due to medical advances the number of SLE patients who become pregnant has increased worldwide and most pregnancies are successful[5]. Recent studies have analyzed novel markers of poor pregnancy outcomes and new approaches to the management of SLE during pregnancy and SLE activity during pregnancy remains an ongoing problem, since major organ involvement can negatively affect outcomes[6].

The recognition of lupus exacerbation is sometimes difficult because the clinical symptoms may mimic those related to pregnancy. Moreover, the prompt management of lupus in the mother and at the same time appropriate maintenance of normal fetal development poses a great challenge to clinicians[78]. In the 2013 catastrophic antiphospholipid syndrome (CAPS) study, 54% of the women during pregnancy had primary antiphospholipid syndrome and 47% had SLE[9]. In another study, SLE during pregnancy was diagnosed in 5.8%[10]

The present study is designed to determine the frequency of SLE among pregnant women presenting to our OPD. The idea behind doing this study came into our mind but reading the literature and finding that 90% of the SLE population are females. Moreover, we also read that SLE can remain silent and it flares up during pregnancy and this can lead to adverse maternal and fetal outcome. In the meantime, we did not find any local literature on the burden of SLE in our local pregnant population. As SLE in pregnancy can vary from one population to another therefore, we designed this study to report the local burden and magnitude of the problem and report it to higher authorities. The results of this study can also help us to identify gaps in knowledge and practice and we can devise future research recommendations to reduce the morbidity associated with SLE during pregnancy.

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Gynecology and Obstetrics at Lady Reading Hospital, Peshawar in collaboration with technical help of Karachi Metropolitan University, over a six-month period from July 30, 2020, to January 31, 2021. The sample size of 234 was calculated based on a 5.8% proportion of SLE during pregnancy, with a 95% confidence level and 3% absolute precision. Non-probability consecutive sampling was used to select participants. Inclusion criteria were women aged 20-45 years, presenting in their first trimester according to the date of their last menstrual period (LMP), regardless of gravidity or parity. Exclusion criteria included pregnancies complicated by hypothyroidism, diabetes, other major medical or metabolic disorders, obesity, severe anemia (Hb less than 6 gm%), or severe malnutrition.

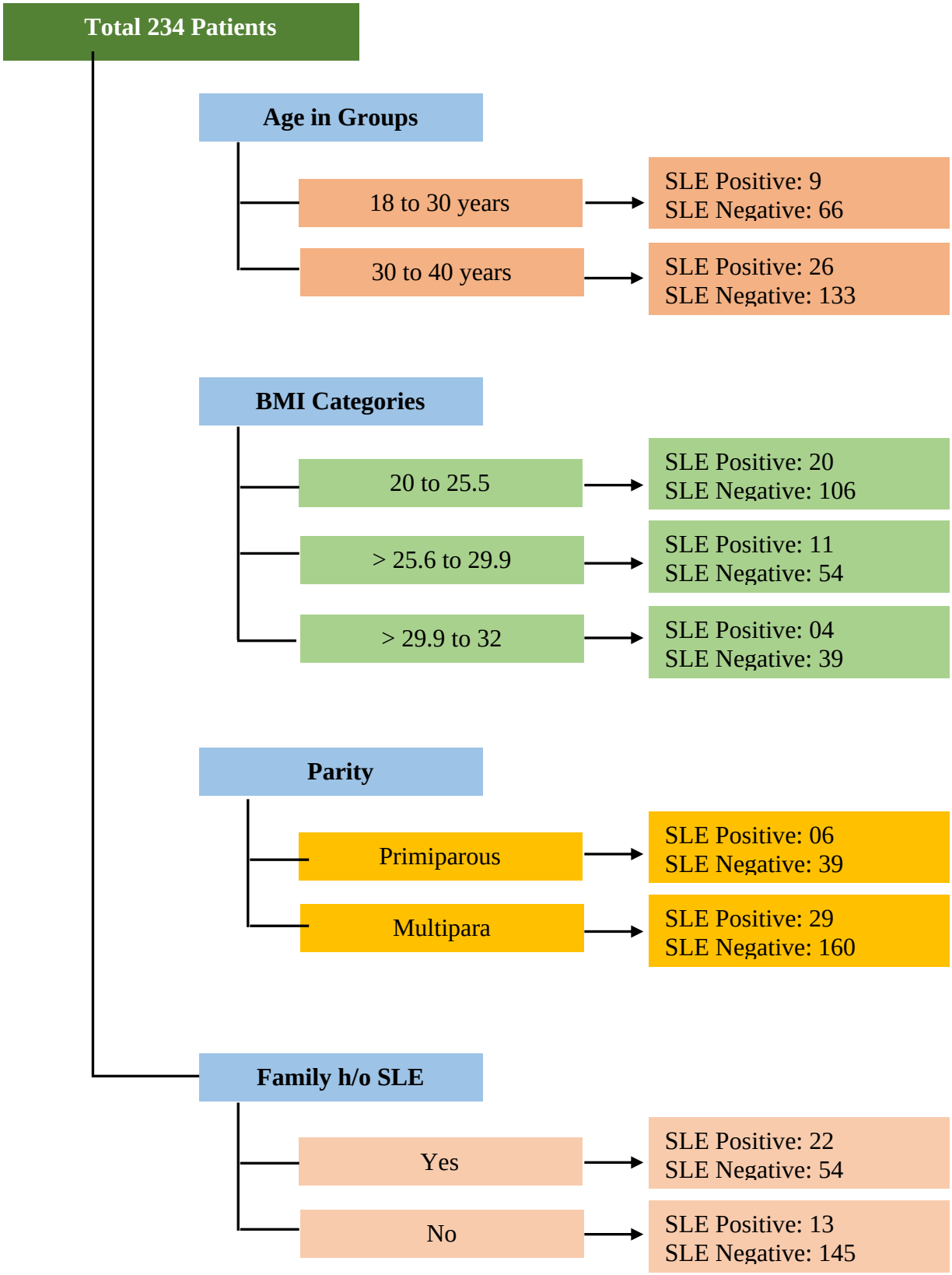
Data Collection Procedure

The study was conducted after approval is obtained from research board of CPSP and ethical board of the hospital. All pregnant women in their first trimester was invited to participate in the study through OPD. The purpose and benefits of the study was explained to all women, they were assured that study is done purely for research and data publication, risk and benefits was explained to all women and if agreed upon, an informed written consent was obtained. All women were subjected to detailed history and clinical examination. All women were assessed on the basis of American College of Rheumatology classification criteria for systemic lupus erythematosus criteria for the detection of SLE. All women were managed as per international guidelines laid down for the management of SLE during pregnancy. All this data was recorded on a specially designed proforma. Confounding factors and bias was controlled by strictly following exclusion criteria.

Data Anlaysis Procedure

Data was stored and analyzed in SPSS version 23. Mean + SD was calculated for numerical variables like age, BMI, gravidy, parity. Frequencies and percentages was calculated for categorical variables like SLE. SLE was stratified with regards to age, BMI, gravidy, parity and family history of SLE using chi square test with p value of < 0.05 kept as significant to see the effect modification. All results were presented in the form of tables and graphs.

Data Flowchart of the results



RESULTS

A total of 234 cases of pregnant women were included in the study. The mean age and standard deviation of the sample was 31.1 + 5.8 years. Age distribution showed that 32.1% (75 individuals) were between 18-30 years, while 67.9% (159 individuals) were over 30-40 years. Regarding parity, 19.2% (45 individuals) were primiparous, and 80.0% (189 individuals) were multiparous. The BMI classification revealed that 53.8% (126 individuals) had a BMI of 20-25.5 kg/m², 27.8% (65 individuals) had a BMI of >25.5-29.9 kg/m², and 18.4% (43 individuals) had a BMI of >29.9-32

kg/m². In terms of family history of Systemic Lupus Erythematosus (SLE), 32.5% (76 individuals) had a family history, while 67.5% (158 individuals) did not. Finally, 15.0% (35 individuals) had SLE, whereas 85.0% (199 individuals) did not. **Table 1.**

In this study comparing individuals with and without systemic lupus erythematosus (SLE), the distribution of participants across different variables showed notable differences. In the age group 18-30 years, 12.0% of SLE patients fell into this category compared to 16.4% of non-SLE individuals (P=0.384). For the BMI categories, 15.9% of SLE patients had a BMI of 20-25.5, 16.9% had a BMI of 25.5-29.9, and 9.3% had a BMI of 29.9-32, whereas 84.1%, 83.1%, and 90.7% of non-SLE individuals fell into these respective categories (P=0.506). Regarding parity, 13.3% of SLE patients were primiparous compared to 15.3% of non-SLE individuals, with 86.7% of SLE patients and 84.7% of non-SLE individuals being multiparous (P=0.734). The most significant difference was observed in the family history of SLE, where 28.9% of SLE patients reported a family history of the disease compared to only 8.2% of non-SLE individuals (P<0.001). **Table 2.**

Table 1. Baseline and clinical characteristics of the study participants (n = 234)

Parameters	**Number**	**%**
Age in groups		
18-30 years	75	32.1
> 30-40 years	159	67.9
Parity		
Primiparous	45	19.2
Multipara	189	80.0
BMI (kg/m)		
20-25.5	126	53.8
> 25.5-29.9	65	27.8
> 29.9-32	43	18.4
Family history of SLE		
Yes	76	32.5
No	158	67.5
Systemic Lupus Erythematosus (SLE)		
Yes	35	15.0
No	199	85.0

Table 2. Comparison of Demographic and Clinical Characteristics in Patients with Systemic Lupus Erythematosus (SLE) (n = 234)

Variables	**SYSTEMIC LUPUS ERYTHEMATOSUS**		**P-values**
	Yes (n = 35)	**No (n = 199)**	
Age groups			
18-30 years	9(12.0%)	66 (88.0%)	0.384
> 30-40 years	26(16.4%)	133(83.6%)	
BMI Categories			
20-25.5	20(15.9%)	106 (84.1%)	0.506
> 25.5-29.9	11(16.9%)	54 (83.1%)	
> 29.9-32	4(9.3%)	39 (90.7%)	
Parity			
Primiparous	06(13.3%)	39 (86.7%)	0.734
Multipara	29(15.3%)	160 (84.7%)	
Family History of SLE			
Yes	22(28.9%)	54 (71.1%)	< 0.001*

No	13(8.2%)	145 (91.8%)	

* P-value is statistically significant calculated by Fisher's exact test of chi-square

DISCUSSION

Systemic lupus erythematosus (SLE) is an autoimmune disease with an annual incidence of 4–35 cases per 100,000 people, which predominantly find in females of child-bearing age[11]. Disease relapse can occur in throughout the entire pregnancy and often immediately after termination of pregnancy. Several studies reported the SLE relapse during pregnancy and considered an important role for estrogen in causing disease[11]. Although the majority of studies showed an increased SLE relapse during pregnancy, but some believe that the frequency of flares during pregnancy is similar to non-pregnancy[12–14]. In a study conducted by Urowits et al., disease activity at the onset of pregnancy did not predict the risk of exacerbation during pregnancy. They reported that patients with inactive SLE less likely to experience a flare of disease[15]. However, methodological differences and the use of different sample sizes may be the cause of discrepancies in the obtained results. A lupus flare during pregnancy is dependent on disease's activity at the time of fertilization. The frequency of flare has been reported 7–33% in women who were in remission for at least 6 months before conception, while 61– 67% of patients with active SLE at the onset of pregnancy have been a disease flare. However, there is no consensus among researchers that increased lupus activity is due to pregnancy or spontaneous fluctuation of disease[16–18]

Some pregnancy adverse outcomes can be related to SLE, including pre-eclampsia, abortion, preterm birth, stillbirth, and fetal growth restriction. A recent meta-analysis study showed that the SLE had a high impact on maternal and fetal outcomes following pregnancy. Pre-eclampsia and hypertension had significantly higher rates among women with SLE (relative risk (RR): 1.85 1.91, 95% confidence interval (CI) 1.44–2.53; P = 0.00001) and (RR: 1.99, 95% CI 1.54–
2.56; P = 0.00001) respectively. In addition, thromboembolic disease and abortion were also significantly higher in the SLE patients[19]. Nevertheless, several studies have shown SLE to have unfavorable pregnancy outcomes, the factors associated with such complications seem to be varied from region to region[20].

There is some debate as to whether the rate of flare in SLE is increased during pregnancy. This is partially because many features such as alopecia, palmar erythema, fatigue and facial erythema, which may indicate active disease, can be normal features of pregnancy. The [15,21,22]. These flares are usually mild, with cutaneous and joint disease being the most common manifestations. Such flares present little risk to mother or child but ought to be treated in case they herald a more serious episode. The flare rate is greater and overall risk greater for women with active disease within six months of conception. Thus, ideally, pregnancy should only be advised when the woman's disease has been in remission for at least six months. While women may have new organ involvement during pregnancy, the type of flare can, to some extent, be predicted by previous disease patterns and immunology, as described above. Whenever possible, women should be assessed pre-conceptually. This gives them the opportunity to make an informed decision based on their individual risks prior to proceeding with a pregnancy. It enables appropriate adjustments to drug regimens to be made prior to conception

(including commencement of folic acid) and optimal timing of pregnancy. Baseline investigations should be taken as part of the evaluation and should include dsDNA, Ro, La, Smith and cardiolipin antibodies, lupus anticoagulant, full blood count and renal function. In women with known renal disease or an abnormal urinalysis, this should include a 24 urinary protein and creatinine clearance. Our findings of 15% frequency of SLE are similar to those reported in previous studies, with flare rates ranging widely between 25% and 65%[23]. In addition, shorter times since SLE diagnosis were associated with a higher incidence of disease activity during pregnancy. This can be explained because the disease stabilization process is still ongoing, with the best therapy up till then under implementation, which increases the risk of exacerbations. A recent study with data obtained from the Hopkins Lupus Cohort (1987–2015) showed that, when compared with nonpregnant women with SLE, pregnant women did appear to flare more frequently. In addition, women taking HCQ did not appear to have an increased risk of lupus flare during pregnancy or the postpartum period, and prednisone administration contributed to a decrease in disease activity during pregnancy[24]. Rate of disease activation during pregnancy at the lower thresholds of available evidence, with most women taking immunosuppressive therapy during pregnancy, mainly prednisone and chloroquine. Whereas in prior decades many women with lupus were expected to flare during or after pregnancy, more recent data suggest that a large proportion of women have minimal disease activity throughout gestation[144]. Indeed, over the years, we have observed a marked reduction in SLE activity rates in our institution's high-risk prenatal outpatient clinic. A previous study[25] conducted between 1995 and 2005 has shown a rate of 85.3%. More recently, another study[10] conducted between 2002 and 2012 demonstrated a rate of 39.2%, ultimately reaching a rate a little more than 25% of our current sample. This improvement was largely based on specialized care, with the adoption of institutional protocols specifically aimed at the obstetric follow-up of women with SLE.

Several studies have demonstrated the safety and efficacy of HCQ during gestation. Discontinuation of this drug leads to increased disease activity. A previous cohort study and a randomized, controlled trial recognized reduced SLE activity and improved outcomes among women who continued HCQ therapy during pregnancy, with no association with adverse events or congenital malformations[12] A retrospective study by the US Truven Health MarketScan administrative health care claims database (2006–2012) evaluated drug and resource use in pregnant women with lupus. It concluded that pregnancies in these women were associated with a higher risk of complications and higher health care costs, but fewer prescribed medications, including immunosuppressant.

Therefore, the increased risk of complications and decreased immunosuppressant use suggest that patients require additional guidance to enable a safer pregnancy and maintain SLE in remission. Additionally, despite the well-known increased pregnancy complications related to active lupus, women with SLE had fewer rheumatology visits during pregnancy This illustrates the need for coordinated care among obstetricians and rheumatologists[26]. A meta-analysis performed in 2018 of 16 studies (which included 1760 pregnant patients with SLE) reported that gestational hypertension, preeclampsia, SLE flare, proteinuria and hypocomplementemia were significantly associated with pregnant women with lupus nephritis (LN). The women presented with a significant decrease in live births and a significant increase in preterm births and FGR[27]. Another report showed that women with LN have an increased risk of renal a[28] and nonrenal flares during pregnancy compared with women without renal involvement. A recent study found that SLE patients with especially proliferative nephritis (classes III and IV) presented with a higher frequency of adverse maternal outcomes, such as disease flares, hospitalization directly or not related to SLE, cesarean delivery and preeclampsia[29]. Our data revealed that, although nearly half the sample had some kind of renal impairment, our perinatal results were satisfactory. Several indices have been created to systematize the criteria to define lupus activity. The specific literature provides scales that aim to measure SLE activity taking into account particular situations related to pregnancy, such as the SLEPDAI and the Lupus Activity Index in Pregnancy. Nonetheless, these indices are used widely as research tools[30]. However, we consider that disease activity should be systematically evaluated by the SLEPDA[31] because its score is presented as an important factor that guides adjustment or change in medication[32]. In the prospective PROMISSE study of 385 pregnant SLE patients, unfavorable outcomes happened at a

higher rate of 43.8% (CI: 29.5–58.8) in women with aPL compared with 15.4% in those without aPL. In addition, patients with APS have an increased risk of diverse pregnancy complications such as FGR, SGA and premature newborns, pregnancy loss with recurrent early miscarriages, or isolated late miscarriages, preeclampsia, eclampsia and HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome[33].

CONCLUSION

SLE during pregnancy is fairly common in our population particularly among women who have family history of SLE. More observational studies are recommended to determine the risk factors of SLE during pregnancy and follow up longitudinal studies to determine its effect on pregnancy outcome before recommending future directions for its prevention and control.

Conflict of Interest:

There is no any conflict of interest

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