

Pregnancy Outcomes in Patients with Systemic Lupus Erythematosus

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ABSTRACT

Background & aim: Pregnant women with systemic lupus erythematosus (SLE) are considered to be at higher risk in terms of fetal complications and adverse outcomes. The aim of this study was to investigate the fetal outcomes in pregnant women with SLE

Methods: This retrospective medical record review study was conducted on 125 patients with the SLE referred to the Clinic and Department of Rheumatology of Imam Reza Hospital in Mashhad, Iran from January 1997 to December 2017. The patients were classified according to the criteria of the Systemic Lupus International Collaborating Clinics classification for the SLE. The data including age, personal characteristics, pregnancy outcome and data related to the patients' discharge were extracted from the medical records.

Results: There were 217 pregnancies in 125 patients with the SLE. The mean age of the subjects was 27.25±5.08 years at pregnancy time. Among all, 86 (36.9%) pregnancies were reported as full-term deliveries. The incidence of fetal wastage in the patients was observed as 49.3%. Abortion, prematurity, and stillbirth were seen in 114 (52.5%), 12 (5.5%), and 5 (2.3%) pregnancies, respectively. Neonatal death was noticed in 8 (3.6%) pregnancies and neonatal lupus was reported in 3 neonates (1.3% of the pregnancies).

Conclusion: The risk of fetal complications and adverse outcomes were high in the patients with SLE. In geographical region under study, the subjects with the SLE continued to have high-risk pregnancies so that consultation with their doctors in preconception period and during pregnancy should be considered.

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune multi-system disease that is mainly observed in the women of childbearing age (1). Almost every organ can be involved in lupus, leading to a wide variety of clinical manifestations and symptomatology (2). Lupus is a serious disease with significant rates of morbidity and mortality. The patients suffering from lupus experience several incidents of hospitalizations and need multidisciplinary care.

Moreover, end organ damage and treatment-related side effects result in considerable disability (3). Lupus-infected women often worry about becoming pregnant and their ability to fulfill maternal responsibilities. There

is a high risk of complications and detrimental fetal outcomes in pregnant women with lupus. In addition, pregnancy can trigger lupus disease activity, which requires maternal immunosuppressive intervention (4).

The risk of adverse fetal outcomes has been proven to increase in pregnancies complicated by lupus. There are a number of fetal and neonatal problems, which are associated with lupus. The frequency of fetal loss in the SLE pregnancies has been reported in the past to reach as high as 50%, including stillbirth, prematurity, and spontaneous abortion (miscarriage) (5-14). The results of a recent study carried out on the analysis of long-term data over the past 40 years showed a

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decrease in spontaneous abortion rate from 50% to less than 20% (14). With this background in mind, the aim of this study was to investigate the pregnancy outcomes in the patients with the SLE.

Table 1. Definitions of adverse pregnancy outcomes

Pregnancy outcome	Definition
Abortion	To end pregnancy prior to 20 th week of gestation
Spontaneous abortion (Miscarriage)	Natural fetal death before end of 20 th week of gestation
Therapeutic abortion	Abortion following a diagnosis of medical necessity
Recurrent abortions or recurrent miscarriages	≥3 Spontaneous abortions
Stillbirth	Fetal death after 20 th week of pregnancy
Fetal wastage	Sum of spontaneous abortions and stillbirths
Preterm birth or prematurity	Neonate birth between 20 th and 37 th weeks of gestation
Full-term deliveries	Neonate birth after 37 th week of gestation
Live birth	Birth of a live neonate
Neonatal death	Death of neonate in first 28 days after birth
Perinatal death	Sum of stillbirths and neonatal deaths

Materials and Methods

In this retrospective medical record review study, the medical records of all patients diagnosed with the SLE at the Clinic and Department of Rheumatology of Imam Reza Hospital in Mashhad, Iran from January 1 in 1997 to December 31 in 2017 were reviewed. The subjects were classified according to the criteria of the Systemic Lupus International Collaborating Clinics classification for the SLE (15). All the data, including age, personal background, and pregnancy outcomes were obtained from medical records and discharge reports of the subjects.

The first trimester, second trimester, third trimester, and puerperium were defined as from conception to the end of the 12th week, the 13th week to 27th week, from the 28th week until delivery, and 4 weeks post-partum or after abortion, respectively. Furthermore, fetal outcomes are defined in table 1. Prior to pregnancy, disease activity was assessed using the SLE activity index (SLEDAI). The disease was considered active if the SLEDAI>4. The

pregnancies were divided into two groups, including (A) the patients with active disease and (B) the subjects with inactive disease.

The data were analyzed using SPSS software (version 20). The numerical variables were described by mean score and standard deviation. The clinical and laboratory findings were compared between the two groups using the Fisher's exact test for qualitative variables and Student's t-test or the Mann-Whitney U test for quantitative variables (according to the nature or distribution of the variables). P-value less than 0.05 was statistically considered significant.

Results

There were 217 pregnancies in 125 patients. The mean age of the subjects was reported as 27.25 ±5.08 years at pregnancy time. The fetal outcomes of the patients are summarized in table 2. Table 3 tabulates the comparison between the demographic characteristics, laboratory features, and medications between the two groups. No neonate was noticed with

Table 2. Pregnancy outcomes in studied patients

Pregnancy outcome	Number (%)
Live birth	95 (43.8)
Full-term deliveries	86 (36.9)
Total	12 (5.5)
Prematurity	9 (75)
Spontaneous	3 (25)
Therapeutic	
Total	114 (52.5)
Abortion	102 (47.0)
Spontaneous abortion	12 (5.5)
Therapeutic abortion	

Stillbirth	5 (2.3)
Neonatal death	8 (3.6)
Fetal wastage	107 (49.3)
Perinatal death	13 (5.9)

Table 3. Comparison of baseline variables between group A (active disease) and group B (inactive disease)

Variable	Total n=217	Group A (Active disease) n=153	Group B (Inactive disease) n=64	P-value
Mean age (year)	27.25±5.08	28.85±5.34	26.62±4.79	0.004 Independent t-test
Number of pregnancies	217	64	153	-
Antiphospholipid syndrome	115 (52.9)	74 (48.3)	36 (56.25)	0.452 Fisher's exact test
Prednisolone (mg/day) (before pregnancy)	5.48±9.47	9.75±13.53	3.5±6.22	0.002 Independent t-test
Hydroxychloroquine (before pregnancy)	167 (76.9%)	130 (84.9)	37 (57.8)	0.000 Fisher's exact test
Azathioprine (before pregnancy)	26 (12.6)	15 (23.4)	11 (7.2)	0.000 Fisher's exact test
Complicated pregnancy	131 (60.3)	43 (67.2)	88 (57.5)	0.002 Fisher's exact test

malformation. Neonatal lupus was observed in 3 neonates (all the newborns had complete heart block).

Discussion

The frequency of adverse pregnancy outcomes is higher in patients with the SLE, compared to subjects with any other rheumatic diseases. Despite the dramatic improvements in pregnancy outcomes in patients with SLE during the last several decades, the SLE is still regarded as a risk of potentially serious maternal and fetal complications. According to the literature, poor pregnancy outcome was reported in patients with the SLE (10-20). The frequency of fetal failure in pregnant women with the SLE has been reported in the past to be as high as 50%. The incidence of abortion and stillbirth in pregnant women with lupus ranges from 6%–35% and 0%–22%, respectively, which is higher than the rate among normal population (21, 22). The findings of a recent analysis of long-term data investigating last 40 years revealed a drop in spontaneous abortion rate from 50% to less than 20% (19).

In the present study, the incidence rates of fetal wastage and abortion in the patients were 54.8% and 52.5%, which were higher than those in most of the previous studies. The prevalence of spontaneous abortions in the subjects of this study was reported as 47%, which was a higher

rate, compared to that in most of the studies. Perinatal death is attributed to both stillbirth (intrauterine fetal demise) and neonatal death, approximately 10 cases per 1000 in general population. The prevalence rate of perinatal death was estimated as 4.7% in the SLE patients. In the present study, the incidence of perinatal death was higher than that in most of the studies (6.4%) (23).

Neonatal death is common in pregnant women with the SLE, some of which were due to extreme prematurity or congenital heart block. During 2000 to 2005, there were 21 neonatal deaths among 1859 pregnancies that were 1.13% more than twice the general population rate (18). The rate of neonatal death was reported as 3.6% in the present study. Pregnancy loss (fetal wastage) is the combination of both spontaneous abortions and perinatal deaths. With the exclusion of elective (induced, therapeutic) abortions, the prevalence rate of pregnancy loss in patients with lupus in the last 5 years significantly decreased under 20%, compared to that in most of the studies (14). In this study, the pregnancy loss continued to remain high (49.3%).

The rate of fetal complications among the study population was very high. Two factors may be responsible for this high prevalence rate. The first one is that in Iran, children are considered very important for families and some divorces

are due to not having a child; therefore, many patients become pregnant during the active phase of the disease. The second one is that some patients stop their treatment due to the fear of side effects on the fetus.

Conclusion

In the geographical region under study, the risk of complications and adverse fetal outcomes in pregnant women with the SLE is still very high and it is suggested that the patients should consult with their doctors before pregnancy.

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Conflicts of interest

The authors declare no conflicts of interest.

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