ORIGINAL ARTICLE

Maternal-fetal complications in pregnant women with systemic lupus erythematosus

Daisy Carballé García[1], Enrique Martínez González[1]*, Lisbet Mesa Fernández[1], René Espinosa Machado[1], Neila Teresa Pérez Carballé[2], María Gabriela Morales Nerey[2]

[1]"Arnaldo Milián Castro" University Clinical Surgical Provincial Hospital, Santa Clara, Villa Clara, Cuba
[2]University of Medical Sciences of Villa Clara, Santa Clara, Villa Clara, Cuba

***Enrique Martínez González. enriquemtnez81@gmail.com**

Received: 09/09/2022 - Approved: 02/02/2023

ABSTRACT

Introduction: systemic lupus erythematosus is an autoimmune disease that mainly affects women of childbearing age and has been associated with increased maternal-fetal morbidity and mortality.
Objective: to describe the main maternal-fetal complications in pregnant women with systemic lupus erythematosus.
Methods: a developmental, descriptive and cross-sectional research was conducted in 137 pregnant women with a diagnosis of systemic lupus erythematosus attended at the "Mariana Grajales" and "Arnaldo Milián Castro" Hospitals between January 2015 and December 2019 with a predominance of documentary analysis.
Results: pregnant women between 20 and 24 years old, with medium-high school level, primigravidae, who attended five or more Prenatal Care Consultations and one or two Rheumatology and High Obstetric Risk Consultations during pregnancy predominated. The 94.98% were diagnosed before pregnancy and the interval of evolution was predominantly between one and four years. The main comorbidity was arterial hypertension (22.63%), followed by diabetes mellitus (18.25%). The most frequent maternal complications were preterm delivery (28.47%) and premature rupture of membranes (24.81%), while the most frequent fetal complications were prematurity (32.77%) and low birth weight (24.37%).
Conclusions: the study showed an increase in maternal-fetal complications in pregnant women with systemic lupus erythematosus.
Key words: lupus erythematosus systemic; maternal; fetal; complications

RESUMEN

Introducción: el lupus eritematoso sistémico es una enfermedad autoinmune que afecta principalmente a mujeres en edad fértil y se ha asociado con un aumento de la morbimortalidad materno-fetal.
Objetivo: describir las principales complicaciones materno-fetales en gestantes con lupus eritematoso sistémico.

Métodos: se realizó una investigación de desarrollo, descriptiva y transversal en 137 gestantes con diagnóstico de lupus eritematoso sistémico atendidas en los Hospitales "Mariana Grajales" y "Arnaldo Milián Castro" entre enero de 2015 y diciembre de 2019 con predominio del análisis documental.
Resultados: predominaron las gestantes en edades entre 20 y 24 años, con nivel escolar Medio-Superior, primigestas, que acudieron a cinco o más Consultas de Atención Prenatal y a una o dos Consultas de Reumatología y de Alto Riesgo Obstétrico durante el embarazo. El 94,98% fueron diagnosticadas antes del embarazo y predominó el intervalo de evolución entre uno y cuatro años. La principal comorbilidad fue la hipertensión arterial (22,63%), seguida de la diabetes mellitus (18,25%). Las complicaciones maternas más frecuentes fueron el parto pretérmino (28,47%) y la rotura prematura de membranas (24,81%), mientras que las complicaciones fetales que predominaron fueron la prematuridad (32,77%) y el bajo peso al nacer (24,37%).
Conclusiones: en el estudio se constató el incremento de las complicaciones materno-fetales en gestantes con lupus eritematoso sistémico.
Palabras clave: lupus eritematoso sistémico; materno; fetal; complicaciones

INTRODUCTION

Systemic lupus erythematosus (SLE) is one of the most widely studied diseases in medicine and is considered the prototype of systemic autoimmune disease, producing chronic and recurrent activation of the immune system leading to inflammation and tissue damage.[1]
It is estimated that at least five million people worldwide have lupus and that more than 100,000 new cases are diagnosed each year. The prevalence and incidence of SLE vary widely in the medical literature. The published prevalence ranges from 20 to 240 per 100 thousand persons and the incidence from 1 to 10 per 100 thousand person-years, with a female-to-male ratio of 9:1.[2,3]
Maternal-fetal complications in pregnant women with lupus can be diverse. These include higher rates of preterm delivery, fetal death, intrauterine growth restriction, low birth weight, preeclampsia, HELLP syndrome (hemolysis, elevated liver enzymes, low platelet count), and obstetric hemorrhage, among others.[4,5]
Although the coexistence of SLE and pregnancy has been associated with increased morbimortality, different therapeutic interventions have led to improved rates of successful pregnancies in recent years, with an approach that starts from the preconception stage, and should involve the performance of a multidisciplinary team headed by the Rheumatology and Obstetrics Specialist.[6]
This research aimed to describe the behavior of the most common maternal-fetal complications in lupus pregnant women attended at the "Mariana Grajales" and "Arnaldo Milián Castro" Hospitals between January 2015 and December 2019.

METHODS

A developmental, descriptive and cross-sectional research was carried out.
The study population consisted of the total number of pregnant patients with SLE diagnosis (137) attended at the "Mariana Grajales" Gynecological and

Obstetric Teaching University Hospital and at the "Arnaldo Milián Castro" Clinical-Surgical University Hospital in the city of Santa Clara, Villa Clara Province, from January 2015 to December 2019.
Since we worked with the total population, no sampling technique was applied.
A documentary review of the clinical histories filed in the Statistics Department of both hospitals was carried out and the data obtained were collected in an observation guide created with the variables of interest.
The information obtained was processed through a database using the Excel 2010 program of the Office 2010 package and the statistical processing software SPSS version 15.0 for Windows and the program for epidemiological analysis with tabulated data EPIDAT version 3.1.
The database was initially cleaned to detect aberrant observations and then scanned to identify missing values and outliers. Subsequently, the descriptive analysis of the sample was performed, for which the information was organized in frequency and contingency tables using absolute frequencies (number of cases) and relative frequencies (per hundreds). The data were represented graphically according to the type of information.
For quantitative variables, the appropriate statisticians were calculated. The Chi-square test was used to identify significant differences between categories and to evaluate the possible association between qualitative variables.
The change detected was quantified using a 95% confidence interval and a statistical significance level of 5%.
If $0.01 < p < 0.05$ significant differences.
Ethical considerations: the study was governed by the ethical principles of biomedical research established in the Declaration of Helsinki and with that established by the World Health Organization in the version corresponding to the 52nd General Assembly in Edinburgh, in October 2000. In addition, it was governed by the state regulations of the Ministry of Public Health of the Republic of Cuba and prior approval was obtained from the Ethics Committees of the institutions involved.

RESULTS

There was a predominance of 20 to 24 year-olds (32.85%), followed by 25 to 29 year-olds (24.82%), medium-higher education level (42.33%) -Table 1- and primigravidae (52.55%) -Table 2-.

Table 1. Distribution of pregnant women with systemic lupus erythematosus according to age groups and schooling

Age group (years)	Schooling						Total	
	High School		Senior School		University			
	No.	%	No.	%	No.	%	No.	%
15 - 19	5	3.65	11	8.03	0	0.00	16	11.68
20 - 24	24	17.52	16	11.68	5	3.65	45	32.85
25 - 29	12	8.76	14	10.22	8	5.84	34	24.82
30 - 34	6	4.38	9	6.56	8	5.84	23	16.78
35 - 39	6	4.38	7	5.11	4	2.92	17	12.41
40 - 44	1	0.73	1	0.73	0	0.00	2	1.46
Total	**54**	**39.42**	**58**	**42.33**	**25**	**18.25**	**137**	**100.0**

Source: medical records

Table 2. Distribution of pregnant women with systemic lupus erythematosus by age and number of pregnancies

Age group (years)	Number of pregnancies				Total	
	Primigestas		Multigestas			
	No.	%	No.	%	No.	%
15 - 19	8	5.84	8	5.84	16	11.68
20 - 24	29	21.17	16	11.68	45	32.85
25 - 29	19	13.87	15	10.95	34	24.82
30 - 34	9	6.56	14	10.22	23	16.78
35 - 39	6	4.38	11	8.03	17	12.41
40 - 44	1	0.73	1	0.73	2	1.46
Total	**72**	**52.55**	**65**	**47.45**	**137**	**100.0**

Source: medical records

Statistically significant differences were found in the attendance at the visits. In Prenatal Care, there was a predominance of pregnant women who attended five or more visits (87.59%). The behavior of the attendance at the Rheumatology and High Obstetric Risk consultations was different because both were dominated by pregnant women who received only one or two consultations during pregnancy and who represented 59.12% and 72.26%, respectively. It should be noted that 21.17% of the patients did not attend the Rheumatology Consultation, while 13.87% did not attend the High Obstetric Risk Consultation during pregnancy (Table 3).

Table 3. Distribution of pregnant women with systemic lupus erythematosus according to attendance at medical visits

Consultation assistance	Medical visits					
	Prenatals		Rheumatology		High Risk Obstetrics	
	No.	%	No.	%	No.	%
None	4	2.92	29	21.17	19	13.87
One or two	6	4.38	81	59.12	99	72.26
Three or four	7	5.11	19	13.87	16	11.68
Five or more	120	87.59	8	5.84	3	2.19
Total	**137**	**100.0**	**137**	**100.0**	**137**	**100.0**

X^2=304,46; p=0,000
Source: medical records

In 94.89% of the patients, the diagnosis of SLE was established prior to pregnancy. The most frequent time of evolution of the disease was between one and four years (30.66%), followed by five to nine years (27.74%) -Table 4-.

Table 4. Distribution of pregnant women according to the time of evolution of systemic lupus erythematosus

Time of evolution (years)	Diagnosis of systemic lupus erythematosus	
	No.	%
< 1	8	5.84
1 - 4	42	30.66
5 - 9	38	27.74
10 - 14	28	20.44
≥ 15	21	15.32
Total	**137**	**100.0**

Source: medical records

The study of the comorbidities associated with SLE (Figure 1) showed that the most frequent was chronic arterial hypertension (22.63%), followed by diabetes mellitus (18.25%) and bronchial asthma (10.95%). In the specific case of antiphospholipid syndrome secondary to SLE, the prevalence was 5.84%.

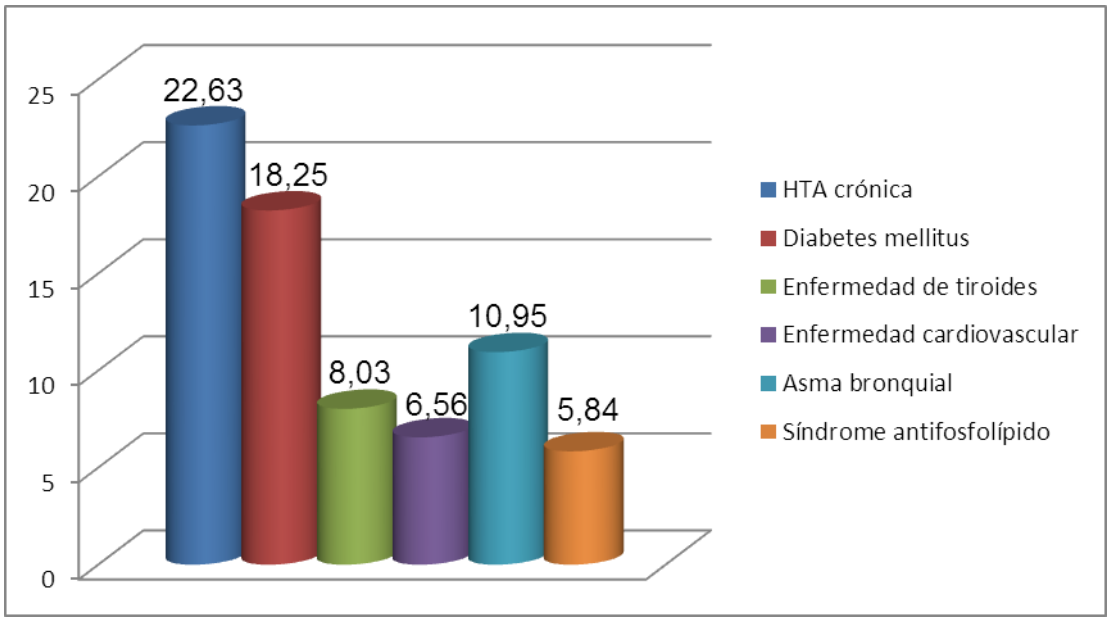

Figure 1. Distribution of pregnant women according to comorbidities associated with systemic lupus erythematosus
Source: medical records

In the behavior of maternal complications in pregnant women with lupus, the most frequent were preterm delivery (28.47%), premature rupture of membranes (24.81%) and gestational hypertension (15.33%). Two maternal deaths were recorded, representing a case fatality rate of 1.46% (Table 5).

Table 5. Distribution of maternal complications in pregnant women with systemic lupus erythematosus

Complications	No.	%
Premature rupture of membranes	34	24.81
Gestational hypertension	21	15.33
Preterm labor	39	28.47
Miscarriage	11	8.03
Maternal death	2	1.46
Other	16	16.68

Fuente: historias clínicas

Table 6. Distribution of perinatal complications in pregnant women with systemic lupus erythematosus

Perinatal complications	No.	%
Prematurity	39	32.77
Low birth weight	29	24.37
Early connatal sepsis	8	6.72
Fetal abortion	7	5.88
Neonatal lupus	2	1.68

Fuente: historias clínicas

During the period studied there were 119 births in pregnant women with SLE. The most frequent perinatal complications were prematurity (32.77%) and low birth weight (24.37%) and there were seven fetal deaths (5.88%). Neonatal lupus was present in 1.68% of the births (Table 6).

DISCUSSION

The predominance of the age groups 20 to 24 years and 25 to 29 years corresponds with the statement that the disease can appear at any age, but in most of the patients it begins between 15 and 40 years of age.[4,6,7,8,9] As for the predominance observed in patients with medium-high schooling level, this result differs from that reported by other authors who report a greater frequency in patients with secondary schooling level.[8]

The finding of a higher percentage of primigravidae coincides with the results obtained in recent studies carried out in the northwestern region of Colombia in which 55% of the pregnant women with SLE studied were primigravidae.[9]

There was a high rate of attendance to Prenatal Care Consultations, but not to specialized Rheumatology and High Obstetric Risk Consultations.

It has been recommended that pregnant women with lupus should be evaluated by the Rheumatology Specialist every month or more frequently in case of crisis. On the other hand, the Obstetrics Specialist will evaluate her every month until the 28th week, then every two weeks until the 36th week and weekly thereafter. Specialized follow-up during pregnancy can be considered essential considering that approximately 50% of women with SLE have some degree of lupus activity during pregnancy and the risk of moderate or severe exacerbation of disease activity is around 15 to 30%.[6,10]

The observed predominance of lupus diagnosis before pregnancy can be considered a positive contributing factor to the preconception follow-up of the disease and, consequently, to improve the maternal-fetal prognosis.

In the preconception stage, from the first consultation with a patient of reproductive age with a diagnosis of SLE, the issue of family planning should be addressed in order to determine the appropriate time to become pregnant (disease remission of at least six months before pregnancy), as well as the compatible treatment for the control of lupus during pregnancy. It should be noted that women with SLE have the same fertility rates compared to healthy women, with the exception of patients with significant renal function compromise, active disease or amenorrhea induced by cytotoxic therapy.[10,11]

The time of evolution of SLE may be another factor to take into account. In patients with long-standing disease, prolonged treatments, especially with glucocorticoids, may contribute to the appearance of complications such as myopathy, osteoporosis, arterial hypertension, diabetes, atherosclerotic vascular disease and infections, among others.[12]

In the present study, arterial hypertension and diabetes mellitus predominated as the most frequent comorbidities associated with SLE. It is considered that this may be related to the high incidence and prevalence of these chronic diseases in the Cuban population in general. Colombian authors have reported that thyroid disease is the most frequent comorbidity.[9]

In the specific case of antiphospholipid syndrome there is an increased risk of both maternal complications in the form of disease activity flares and

thrombosis and fetal complications in the form of early and late pregnancy loss, intrauterine growth retardation and hypertensive disorders of pregnancy. It is therefore essential, first and foremost, to assess both preconceptionally and during pregnancy and puerperium.[13]

Preterm delivery (28.47%), premature rupture of membranes (24.81%) and gestational hypertension (15.33%) predominated as maternal complications. Other authors obtained different results because both reported a predominance of preeclampsia: one 25.6%[9] and the other 22.5%.[14]

It is suggested that pregnant women with SLE have a 20-fold increase in the risk of death and a two to eight-fold increase in the risk of complications such as preeclampsia, arterial hypertension, peripartum hemorrhage and infections.[6]

As for fetal complications, several authors highlight prematurity and intrauterine growth restriction. Fetal morbidities depend on the lupus activity of the mother before and during pregnancy and on the possible teratogenicity of the treatment used.[15,16]

In the specific case of neonatal lupus, a complication that occurs in one to 2% of neonates born to lupus mothers, it is caused by the presence of passively transferred anti-Ro and anti-La antibodies of maternal origin. The clinical manifestations of this disease are complex and varied, among them atrioventricular block of varying degree, permanent and irreversible, which is reported in up to 50% of the cases and requires pacemaker in 66%.[16,17]

CONCLUSIONS

The predominant age range was between 20 and 24 years, with medium-high schooling level, primigravidae, with a time of SLE evolution of one to four years and with the diagnosis of the disease established before pregnancy.

There was a high rate of attendance to Prenatal Care Consultations and an opposite behavior for Rheumatology and High Obstetric Risk Consultations. Among the comorbidities, arterial hypertension and diabetes mellitus had a higher incidence. The most frequent maternal-perinatal complications were preterm delivery, premature rupture of membranes, prematurity and low birth weight.

SLE contributes to the increased risk of maternal-fetal complications and requires appropriate management, both in preconception and prenatal care.

BIBLIOGRAPHIC REFERENCES

1. Mercado Crow MK. Etiología y patogenia del lupus eritematoso sistémico. In: Firestein GS, Budd RC, Gabriel SE, McInnes IB, O´Dell JR. Kelley y Firestein. Tratado de reumatología. 10ma ed. Barcelona: Elsevier; 2018. p. 1329-1344.
2. Bermúdez Marrero WM, Vizcaíno Luna Y, Bermúdez Marrero WA. Lupus eritematoso sistémico. Acta Méd Centro [Internet]. 2017 [cited 11/21/2022];11(1):82-95. Available at: http://www.revactamedicacentro.sld.cu/index.php/amc/article/view/795/980
3. Dall'Era M, Wofsy D. Manifestaciones clínicas del lupus eritematoso sistémico. In: Firestein GS, Budd RC, Gabriel SE, McInnes IB, O´Dell JR. Kelley y Firestein. Tratado de reumatología. 10ma ed. Barcelona: Elsevier; 2018. p. 1345-1367.

4. Nares Torices MA, Hernández Pacheco JA, Estrada Altamirano A, Mendoza-Calderón A, Cervera-Buenfil CI, Villalva-Hernández LD, et al. Lupus eritematoso sistémico activo durante el embarazo. Curso clínico y pronóstico en una Unidad de Cuidados Intensivos. Perinatol Reprod Hum [Internet]. 2012 [cited 11/21/2022];26(2):96-105. Available at: https://www.scielo.org.mx/scielo.php?script=sci_arttext&pid=S0187-53372012000200004
5. Bundhun PK, Soogund MZ, Huang F. Impact of systemic lupus erythematosus on maternal and fetal outcomes following pregnancy: a meta-analysis of studies published between years 2001-2016. J Autoimmun [Internet]. 2017 [cited 11/21/2022];79:17-27. Available at: https://pubmed.ncbi.nlm.nih.gov/28256367/. https://doi.org/10.1016/j.jaut.2017.02.009
6. García Posada R, Ospina AT. Lupus eritematoso sistémico y embarazo: una visión desde la medicina materno fetal. XXVI Curso de Actualización en Ginecología y Obstetricia [Internet]. 2018 [cited 11/21/2022];26:13-20. Available at: https://revistas.udea.edu.co/index.php/ginecologia_y_obstetricia/article/view/346809
7. Sociedad Española de Reumatología. Manual SER de enfermedades reumáticas. 6ta Ed. Barcelona: Elsevier España; 2014. p. 335-347.
8. Rivas-López R, García Figueroa RB, Romero Cabello R. Lupus eritematoso sistémico y embarazo. Ginecol Obstet Mex [Internet]. 2003 [cited 11/21/2022];71(8):400-408. Available at: https://www.imbiomed.com.mx/articulo.php?id=24482
9. Ocampo Ramirez SM, Hoyos Patiño S, Lambertino Montaño JR, Gutiérrez-Marín JH, Campo-Campo MN, Sanín-Blair JE. Caracterización de mujeres embarazadas con lupus eritematoso sistémico y resultados materno-fetales en el noroeste de Colombia. Estudio descriptivo. Iatreia [Internet]. 2019 [cited 11/21/2022];32(4):266-275. Available at: http://www.scielo.org.co/pdf/iat/v32n4/0121-0793-iat-32-04-00266.pdf
10. Stuht López D, Santoyo Haro S, Lara Barragán I. Lupus eritematoso sistémico en el embarazo. Acta Méd Grupo Ángeles [Internet]. 2018 [cited 11/21/2022];16(4):331-338. Available at: https://www.scielo.org.mx/pdf/amga/v16n4/1870-7203-amga-16-04-331.pdf
11. Doria A, Iaccarino L, Arienti S, Ghirardello A, Zampieri S, Rampudda ME, et al. Th2 immune deviation induced by pregnancy: the two faces of autoimmune rheumatic diseases. Reprod Toxicol [Internet]. 2006 [cited 11/21/2022];22(2):234-241. Available at: https://pubmed.ncbi.nlm.nih.gov/16704920/. https://doi.org/10.1016/j.reprotox.2006.04.001
12. Vilardell Tarrés M, Ordi Ros J. Lupus eritematoso sistémico. In: Rozman BorstnarC, Cardellach López F. Farreras-Rozman Medicina Interna. 17a ed. Barcelona: Elsevier; 2012. p. 1017-1022.
13. Espinosa G, Galindo Izquierdo M, Marcos Puig B, Casellas Caro M, Delgado Beltrán P, Martínez López JA, et al. Control del embarazo en pacientes con lupus eritematoso sistémico y síndrome antifosfolípido. Parte 1: Infertilidad, preservación ovárica y valoración preconcepcional. Documento de consenso de la Sociedad Española de Ginecología y Obstetricia (SEGO), Sociedad Española de Medicina Interna (SEMI) y Sociedad Española de Reumatología (SER). Reumatol Clin [Internet]. 2021 [cited 11/21/2022];17(2):61-66. Available at: https://www.sciencedirect.com/science/article/abs/pii/S1699258X19301305. https://doi.org/10.1016/j.reuma.2019.09.002
14. Clowse ME, Jamison M, Myers E, James AH. A national study of the complications of lupus in pregnancy. Am J Obstet Gynecol [Internet]. 2008 [cited

11/21/2022];199(2):127.e1–127.e6. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2542836/. https://doi.org/10.1016/j.ajog.2008.03.012
15. Larburu Zavala S. Influencia mutua entre lupus eritematoso sistémico y embarazo [thesis]. Leioa: Universidad del País Vasco; 2017 [cited 11/21/2022]. Available at: https://addi.ehu.es/bitstream/handle/10810/31041/TFG_Larburu_Zavala_Rev.pdf
16. Mesa Abad P, Tovar Muñoz L, Serrano Navarro I, Ventura Puertos P. Berlango Jiménez J. El embarazo en mujeres con lupus eritematoso sistémico: una revisión integrativa. Enferm Nefrol [Internet]. 2020 [cited 11/21/2022];23(1):11-21. Available at: https://scielo.isciii.es/scielo.php?script=sci_arttext&pid=S2254-28842020000100002. https://dx.doi.org/10.37551/s2254-28842020002
17. González Arenas E, Aceves Barrios CA, Reyes Gómez U, Yalaupari Mejía JP. Endocarditis infecciosa asociada a cables de marcapaso en lactante menor con lupus neonatal. Enf Infec Microbiol [Internet]. 2022 [cited 11/21/2022];42(2):82-90. Available at: https://www.medigraphic.com/pdfs/micro/ei-2022/ei222g.pdf

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

CONTRIBUTION OF THE AUTHORS

DCG: conceptualization, data curation, formal analysis, research, methodology, validation, writing the original draft, writing (review and editing).
EMG: formal analysis, methodology, validation, visualization, writing the original draft, writing (review and editing).
LMF, REM: data curation, validation.