Assessment of risk factors concerning of systemic lupus erythamatosus on women and outcome of pregnancy at Karbala city

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Abstract— **Background:** Systemic lupus erythematosus (SLE) is a systemic inflammation autoimmune disease which can effect multiple systems of the human body. The underlying cause of SLE is not fully known, however, genetics, heredity, and environmental features are associated with the severity and outcome of the disease. SLE is a chronic disease that is more frequent in women of reproductive age. The relationship between lupus and pregnancy is problematic: maternal and fetal outcomes are worse than in the general population, and the management of flare-ups is difficult during this period. **Objectives:** The aim of the present work was ANA and anti-dsDNA to determine the prevalence of autoimmune in a cohort of Iraqi SLE woman patients and to describe their sites and relation to clinical characteristics, laboratory features and disease activity in pregnant women. **Patients and Methods:** A total of 30 patients with SLE (all patients were females) with ages ranged between (20 – 40) years were taken from (Al – Hassein Medical city/Karbala). Control group consisted of 20 healthy females who were free from signs and symptoms of SLE, with ANA tested by Immunofluorescence technique, also anti – dsDNA antibody was measured by enzyme linked immunosorbent assays kit supplied by (Euroimmune, Germany). C3 and C4 were measured using turbidimetry technique, their kits were supplied by(Vital Diagnostics , Italy). **Results:** In the present study the ANA antibodies were positive in 100% of the cases. The mean value of anti – dsDNA (300.4±201.44) which shown in highly significance. In addition results showed that serum levels of C3 and C4 were low significantly in pregnant women of SLE in coparsion with those healthy in significant negative correlation between C3 and C4 levels in lupus. **Conclusion:** The effect of systemic lupus erythematosus on pregnant women are associated with high risk on pregnant itself and her baby in compeer with healthy pregnant women.

Index Terms— Systemic lupus erythematosus, Antinuclear antibodies, Lupus pregnancy.

1 INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoantibody mediated multisystem autoimmune disease, with substantial female predominance. The common disease beginning is in the third to fourth decades of life, during the reproductive time[1]. Its pathogenesis involves aberrant apoptotic mechanisms combined with dysregulated immune responses leading to loss of self-tolerance against nuclear antigens and to autoantibody production .The result is an immune complex disease with inflammation of various organs and tissues[2]. Pregnant women with SLE is still a high risk state with increased maternal and fetal morbidity and mortality. Increase in SLE disease action is expected during pregnancy because of the rising levels of estrogen, progesterone, prolactin and T-helper cells. Therefore, close collaboration of a maternal-fetal medicine specialist and a rheumatologist in a high risk clinic is essential to productively manage those pregnant women with SLE[3].

Even if the presence of autoantibodies in SLE has been known, for more than 60 years, still today a great attempt is being made to understand the pathogenetic, diagnostic, and prognostic meaning of such autoantibodies[4]. Women with SLE are at higher risk for exacerbations of the disease through pregnancy, spontaneous abortions, intrauterine fetal death, pre eclampsia and eclampsia, preterm delivery and intrauterine growth retardation[5]. Historically, fetal and maternal well being of patients with SLE seemed to be compromised to the extent that the medical community recommended against pregnancy in SLE patients. It was difficult to assess whether superimposing pregnancy was detrimental as the clinical outcome of non-patients was poor[6].

In SLE, the body's immune system produces antibodies against itself, particularly against protein in the cell nucleus .SLE is triggered by environmental factors that are unknown. These stimuli begin a reaction that leads to destruction of other cells in the body and exposure of their DNA, histones, and other proteins (particularly parts of the cell nucleus). The body's sensitized B-lymphocyte cells will now produce antibodies against these nuclear-related proteins. Antinuclear antibodies (ANA) are most characteristic and present in more than 95% of patients. Anti-double stranded DNA (ds-DNA) and Anti smith antibodies (anti-Sm antibodies) are unique to patients with SLE[7].

Patients and methods:

During the period from 1/January /2013 to 1/April /2015, thirty patients with Systemic lupus erythymatosus (All patients were a females) with ages ranged between (20-40) years were

taken from (Al-Hussein Medical City/Karbala). Control group consisted of 20 healthy females who were free from signs and symptoms of systemic lupus erythmatosus who matched in age with patients, and had no history for any lupus problems. The important questioner were collected from pregnant females with SLE and pregnant healthy females. ANA tested by Immunoflorescence technique and anti ds-DNA antibody was measured by enzyme linked immunosorbent assays kit supplied by (Euroimmune, Germany), according to manufacturer instructions, values up to 100 IU/ml were considered positive. C3 & C4 were measured using turbidimetry technique; their kits were supplied by(Vital Diagnostics , Italy) according to the manufacturer's protocol.

TABLE 1
GENERAL INFORMATION OF PREGNANT WOMEN WITH SLE .

General information		Pregnant with SLE N(%)	Pregnant without SLE N(%)
Number of patients		30	20
Age	Rang (years)	20-44	21-45
	Mean (years)	24.6±6.4	23.3±2.4
	Of a women at conception (years)	22±3	23±5
Previous pregnancies		2.6±0.6	3.6±42
Previous deliveries		2.2±1.2	2.8±1.4
Disease duration before conception(years)		5.7±3.8	
Know about effect of pregnancy on SLE		6(20)	
Know about effect of SLE on Pregnancy		6(20)	
Butterfly rash		12((40)	
Photosensitivity		7(23.3)	
SLE flare at conception		8(30)	
Education		13 (43.3)	
Medication during pregnancy		27(90)	

Table 2
Laboratory investigation of pregnant women with SLE .

Laboratory investigation	*Pregnant women with SLE*	*Pregnant women without SLE*	*P .value*
ANA	Positive	Negative	
Anti-dsDNA (Iu/ml)	300.4±201.44	22.35±7.477	0.001
C3 (mg/dl)	46.45±20.15	125.3±27.428	0.001
C4 (mg/dl)	9.22±4.17	25.951±9.333	0.001
Anti Ro/ SS-A 52 (ku/l)	13.401±21	0.23±43	0.046
Anti SS-B(ku/l)	8.56±43	0.21±54	0.061

Table 3
Types of delivery and perinatal outcome of pregnant women with SLE .

Types of delivery	***pregnant women with SLE***
Cesarean delivery	22(73.3%)
Vaginal delivery	8(26.6%)
Pregnancy loss	6(20%)
Abortion	4(13.3%)
Still birth	1(3.3%)
Dead baby	1(3.3%)
Live birth	21(70)
Congenital anomaly	2(6.6%)
Birth weight(kg)	2.4±0.75

Discussion

These lupus – like symptoms include palmar erythema (reddening of the palms), temporary facial blush, increase in protein in urine due to an increase in glomerular filtration rate, and postpartum alopecia (hair loss)[8]. However, some of the conditions mentioned above, specially postpartum hair loss is common in all pregnancies; therefore, it is difficult to determine whether or not certain SLE – associated conditions are truly exacerbated by pregnancy. It has been suggested that different measures to evaluate SLE symptoms are needed to decipher between pregnancy and SLE – associated symptoms[9]. Among woman with lupus, the interaction between the physiological changes to the immune system brought about by pregnancy and the pathological changes caused by the disease alter the normal course of the reproductive process[10]. Antibodies to DNA are highly specific for SLE and were reported to be found in 40 – 70% of the SLE patients in one study[11] and in 50 – 70% in another[12]. The relation between anti – dsDNA with lupus nephritis is documented in many studies[12,13,14]. The fetuses born to mothers with SLE may appear major complications. These complications range from spontaneous abortion to stillbirths. Although certain studies suggest that SLE-associated flares increase during pregnancy, other studies show no change in the number of disease flares during pregnancy. These differences likely occur because of a discrepancy in the definition of lupus flares and how disease activity is assessed within each study .Common characteristics exhibited during pregnancy may be misread as lupus flares(Mok and Wong 2001)[15]. SLE pregnancies are considered high risk because there is an increased risk of spontaneous miscarriage, pre-eclampsia, fetal death, and pre-term delivery (Khamashta 2006)[16]. The frequency of dead baby 3.3% ,which is higher than in the general population [17]. In another study, the authors reported a increase in the risk of stillbirth in lupus patients. In our study, the live birth was 70% of lupus pregnancies and this is in accordance with other studies that showed a live birth rate of 72.9 –89.7% [18,19].

Different auto-antibodies have been associated with SLE in the past, most notably anti-nuclear antibodies (ANA) and anti-double-stranded DNA (anti-dsDNA) antibodies, the most relevant tests in diagnosing SLE. Patients with SLE have been shown to have elevated antibody levels in 50 – 80% of cases, correlating with disease activity[20]. In the present study the ANA antibodies were positive in 100% of the cases. The mean value of anti-dsDNA(300.4±201.44)which shown in highly significance. In other studies on Egyptian SLE patients, the ANA was positive in 93–

100% [21,22,23] while the anti-dsDNA was positive in 64–67% [21,22]. Our results showed that serum levels of C3& C4 were significantly low in pregnant women with SLE as compared with those with healthy one with significant negative correlation between C3 and C4 levels in lupus. This results agreement with[24]. Others,[25,26] concluded in their studies that changes in anti-dsDNA and complement concentrations were reported predominately to accompany flare up of lupus.

Conclusion: The effect of systemic lupus erythematosus on pregnant women are associated with high risk on pregnant itself and her baby in compeer with healthy pregnant women. Also elevated level of anti – dsDNA, but low levels of C3 and C4 during pregnancy progression as much as in healthy pregnant women.

REFERENCES

1. Lateef, A. and Petri, M. "Management of pregnancy in systemic lupus erythematosus" Rev Rheumatol. (2012);8:710-8.
2. Lech, M. and Anders, HJ. "The pathogenesis of lupus nephritis" J. Am. Soc. Nephrol. (2013);24(9):1357-66.
3. G. Ruiz-Irastorza, F.; Lima, J.; Alves, *et al.* "Increased rate of lupus flare during pregnancyand the puerperium": a prospective study of 78 pregnancies Br. J. Rheumatol. 35 (2) (1996), pp. 133–138.
4. E. Cozzani, M.; Drosera, G.; Gasparini, A. and Parodi, "Serology of lupus erythematosus: correlation between immunopathological features and clinical aspects Autoimmune Disease" (2014), p. 321-359.
5. Vyas, V.; Shukla, D.; Patil, S. and Mohite, S. "Caesarean section in a case of systemic lupus erythematosus" Indian J. Anaesth (2014);58:193-5.
6. Donaldson, LB. and De Alvarez, RR. "Further observations on lupus erythematosus associated with pregnancy" Am. J. Obstet. Gynecol. (1962);83:1461–73.
7. Anisur, R. and David A, *et al.* "Mechanisms of Disease Systemic Lupus Erythematosus" N. Engl. J. Med. (2008); 358:929-39.
8. Buyon, J. P. "Updates on lupus and pregnancy." Bull NYU Hosp Jt Dis (2009). **67**(3): 271-275.
9. Smyth, A. and V. D. Garovic "Systemic lupus erythematosus and pregnancy." Minerva Urol. Nefrol. (2009). **61**(4): 457-474.
10. Kiss, E.; Bhattoa, HP.; Bettembuk, P.; Balogh, A. and Szegedi, G. "Pregnancy in women with systemic lupus erythematosus" Eur. J. Obstet. Gynecol. Reprod. Biol. (2002);101(2):129-34.
11. Bootsma, H.; Spronk, PE.; Ter Borg, EJ. *et al.* "The predictive value of fluctuations in IgM and IgG class anti-dsDNA antibodies for relapses in systemic lupus erythematosus A prospective long term observation" Ann. Rheum. Dis. (1997) Nov;56(11):661–6.
12. Rahman, A. "Autoantibodies, lupus and the science of sabotage" Rheumatology (Oxford) (2004);43(11):1326–36 [Epub 2004 Aug 24].
13. Yee, CS.; Hussein, H. Skan, J. *et al.* Association of damage with autoantibody profile, age, race, sex and disease duration in systemic lupus erythematosus. Rheumatology (Oxford) 2003; 42(2):276–9.
14. Gilliam, BE.; Ombrello, AK.; Burlingame, RW. *et al.* "Measurement of autoantibodies in pediatric-onset systemic lupus erythematosus and their relationship with disease-associated manifestations" Semin Arthritis Rheum (2012);41(6):840–8 [Epub 2011 Dec 15].
15. Mok, C. C. and R. W. Wong, "Pregnancy in systemic lupus erythematosus." Postgrad Med. J. (2001).77(905): 157-165.
16. Khamashta, M. A. "Systemic lupus erythematosus and pregnancy." Best Pract Res Clin Rheumatol. (2006).20(4): 685-694.
17. Petri, M. and Allbritton, J. "Fetal outcome of lupus pregnancy: a retrospective
case-control study of the Hopkins Lupus Cohort" J. Rheumatol. (1993); 20 (4): 650-6.
18. C.L. The, J.S. Wong,; N.K.N. Ngeh, and W.L.H. Loh, "Systemic lupus erythematosus pregnancies": a case series from a tertiary east Malaysian hospital Lupus 18 (2009), pp. 278–282.
19. D.A. Whitelaw,; D. Hall, and T. Kotze, "Pregnancy in systemic lupus erythematosus": a retrospective study from a developing community Clin Rheumatol, 27 (2008), pp. 577–580.
20. J.A. Simon,; J. Cabiedes,; E. Ortiz,; J. Alcocer-Varela, J. and Sanchez-Guerrero "Anti-nucleosome antibodies in patients with systemic lupus erythematosus of recent onset. Potential utility as a diagnostic tool and disease activity marker Rheumatology (Oxford), 43 (2) (2004), pp. 220–224.
21. T.A. Gheita,; G.S. Azkalany,; H.S. El-Fishawy, and AM. Nour Eldin "Shrinking lung syndrome in systemic lupus erythematosus patients"; clinical characteristics, disease activity and damage Int J Rheum Dis, 14 (4) (2011), pp. 361–368.
22. T.A. Gheita,; I.H. Bassyouni, and R.H. Bassyouni "Plasma concentrations of growth arrest specific protein 6 and the soluble form of its tyrosine kinase receptor Axl in patients with systemic lupus erythematosus and Behçets disease" J. Clin. Immunol. 32 (2012), pp. 1279–1286.
23. A. Rizk, T.A.; Gheita, S.; Nassef, A. Abdallah "The impact of obesity in systemic lupus erythematosus on disease parameters, quality of life, functional capacity and the risk of atherosclerosis" Int J Rheum Dis, 15 (2012), pp. 261–267.
24. Nashwa Noreldin , Samah elshweek, .Mohamed M. Attia "Biomarkers assay for identification and prediction of

flare in patients with Systemic lupus Erythematosus". Journal of American Science 2014;10:(10) 105-111.

25. Hussain, N.; Jaffery, G. S. Hasnain. "Serum Complement C3 and C4 levels in relation to diagnosis of lupus nephritis". Tropical Journal of 6Pharmaceutical Research 2008;7: 1117-21.