



Obstetric outcome in patients with autoimmune connective tissue disorders - a 2 year study in a apex hospital

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OBJECTIVE(S): To study the effects of various immunological connective tissue disorders on pregnancy and the effects of pregnancy on these diseases.

METHOD(S): A total of 18 pregnant women with connective tissue disorders were studied. Of these three had scleroderma, five had rheumatoid arthritis (RA), nine had systemic lupus erythematosus (SLE), and one had SLE with antiphospholipid antibody (APLA) syndrome. These patients were followed up and outcomes analyzed.

RESULTS: No intrauterine death (IUD) or spontaneous pregnancy loss occurred in scleroderma or RA group, but in SLE group there were four preterm births, four IUDs, one spontaneous abortion, one therapeutic abortion, six preeclampsics and eight cases of flare up of the disease.

CONCLUSION(S): Connective tissue disorders in pregnancy may adversely affect both the mother and the fetus. Disease activity may be flared, but is rarely reduced. SLE patients had more unsuccessful outcomes and disease aggravation than others.

Key words: connective tissue disorders, autoimmune disorders, systemic lupus erythematosus, obstetric outcome

Introduction

Female preponderance of autoimmune connective tissue disorders had raised considerable interest regarding the outcome of pregnancies in affected women. In such patients adverse pregnancy outcomes like intrauterine growth restriction (IUGR), prematurity, recurrent pregnancy loss and stillbirth are more common. Multiple factors e.g. genetic factors, disease activity, renal involvement, previous pregnancy loss, environmental factors (sun exposure), antiphospholipid and lymphocytotoxic antibodies, drugs like sulfonamides and antibiotics, and hormones have been implicated for the adverse pregnancy outcome but precise

mechanism is still obscure. Systemic lupus erythematosus (SLE) is the prototype autoimmune connective tissue disorder, the others being rheumatoid arthritis (RA), scleroderma, Behcet's disease, and Sjogren's syndrome. In various studies a greater rate of stillbirth and spontaneous abortion is noted in patients with scleroderma but in patients with primary Sjogren's syndrome and RA contradictory outcomes are reported.

From time to time different antibodies were considered to be responsible for the pathogenesis of these diseases. Various recent studies considered the anti-Ro/SSA antibody as a possible factor for unexplained pregnancy loss. This anti-Ro/SSA antibody is directed against soluble cellular ribonucleoprotein complexes and is present in the serum of more than 10% patients of connective tissue disorders. It is strongly associated with neonatal lupus and congenital heart block - a model of passively acquired autoimmunity. We report the outcome in 18 pregnant women with autoimmune connective tissue disorders.

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Methods

Eighteen pregnant women with history of autoimmune connective tissue disorders attending the outdoor clinic were studied over the last 2 years. Detailed history was taken with special reference to duration of disease flare, present activity, medications, past obstetric outcomes, multiorgan involvement especially renal status, and present pregnancy complications like threatened abortion, preeclamptic toxemia (PET), preterm labor etc. All of them were thoroughly examined for any dermatological, skeletal, ophthalmological, neurological, gastrointestinal, and vascular manifestation. Their antibody status was assayed. Renal and liver function

tests were done. Routine obstetric investigations along with periodic ultrasonographic assessment of fetal growth and abnormality, if any, were done in all of them. Screening for all the possible antibodies in all the women was not possible due to lack of facilities and money. Skin and nerve biopsies were done in selected women. Management of these pregnant women was done in consultation with the departments of rheumatology, dermatology, and nephrology.

Results

The disease type, previous obstetric history and preexisting complications in these women are depicted in Table 1.

Table 1. Type of disease, previous obstetric history and medical complications.

Disease	Number of women	Past obstetric history	Preexisting hypertension	Preexisting renal disease
Scleroderma	3 5	1 Primigravida 2 had normal deliveries	0	0
Rheumatoid arthritis	5	2 Primigravidas 2 had normal deliveries 1 had cesarean delivery	0	0
SLE/SLE + APLA	9+1	7 Primigravidas 2 had normal deliveries 1 had two preterm still births	3	3

It is seen that previous pregnancies in women with scleroderma, RA and SLE were uneventful. The woman with SLE and APLA syndrome had two preterm stillbirths. In both these pregnancies she had developed PET. Among

another two patients with SLE who had previous live birth, in one patient the disease was diagnosed after her first child birth. None of these two patients had renal affection or hypertension.

Table 2. The events and outcomes of current pregnancy.

Type of disease	Ante-natal complication	Spontaneous abortion	Pregnancy outcome			IUD	Disease (flare/diminish/same)	Fetal /neonatal complication
			Induced abortion	Preterm delivery	Live birth			
Sclerodema	0	0	1 (drug)	0	2 (nd)	0	same	none
RA	0	0	1 (drug)	0	4 (2 cs) (2nd)	0	4 same 1 diminished	none
SLE /SLE+ APLA	PIH-6 GDM-1	1	1 (flare)	4 (1-live birth) (3-IUD)	4 (1-term) (1-preterm) (2-cs)	4 (3-preterm) (1-term)	2 same 8 flare	1-jaundice 2-IUGR

PIH - pregnancy induced hypertension
cs - cesarean section

GDM - gestational diabetes mellitus
IUD - intrauterine death

nd - normal delivery
IUGR - intrauterine growth restriction

Table 2 gives the outcomes of pregnancy. It was noted that 6 among 10 patients with SLE developed pregnancy induced hypertension (PIH) and one patient suffering from SLE + APLA developed gestational diabetes mellitus. As an effect

of pregnancy, activities were diminished in one patient with RA but flare was observed in eight patients with SLE. In one patient due to severe flare therapeutic abortion was performed. Therapeutic abortion was also performed in one

patient each with scleroderma and in one with RA as both of them were on methotrexate when they conceived. No adverse obstetric outcome was noted in patients with scleroderma and RA. Two cesarean sections were performed in patients with RA for obstetric indications. On the contrary, in patients with SLE one had spontaneous abortion, four had intrauterine fetal death (three preterm and one term) and four had live births (one preterm birth who developed jaundice in neonatal period, two cesarean section for uncontrolled PIH and one for IUGR, and one term normal delivery). One of the 10 SLE affected patients was positive for anti Ro/SS-A and anti La/SS-B antibodies. Therapeutic abortion was performed in this patient for severe flare. There was no significant affection of the baby except that the preterm live born baby developed jaundice which subsided subsequently.

Discussion

Autoimmune disorders in pregnancy carry risks to mother (especially miscarriage, preeclampsia and thromboembolism) and fetus (especially IUGR and IUD). The newborn can also show residual effects of transplacental maternal antibody passage.

Detection of flare during pregnancy is hampered by the fact that many of the signs and symptoms associated with flare can mimic normal manifestations of pregnancy more so with preeclampsia. Ruiz-Irastorza et al¹ found that 65% of patients with SLE experienced exacerbation at a rate of 0.082 per patient-month. Derksen et al² reported fewer than 20% exacerbations in women with sustained remission prior to pregnancy. In our study eight among 10 patients showed some features of flare, though six of them had features of PET. As commonly found in most of the cases, flare was mild. Hench³, Ostensen⁴ and others have reported a protective effect of pregnancy on RA, though a quarter of them had no improvement and some had even worsened. In our study, disease activity improved in one of five patients suffering from RA with no change in others.

The exact incidence of pregnancy related hypertension associated with connective tissue disorders especially SLE is not known but it appears from different studies⁵⁻⁸ that the incidence is 20-30% and more if associated with chronic hypertension, lupus nephritis, secondary APLA, and chronic steroid use. Given the microvascular nature of involvement of scleroderma the incidence of IUGR and PET is expectedly more in such patients, but this view is not supported by large numbers of case studies. In our study six among 10 patients of SLE developed preeclampsia and two had IUGR.

Women with SLE are more likely to have unsuccessful pregnancy outcome than general obstetric population. In

most retrospective studies the rate of pregnancy loss ranges between 8% and 41% with a median of 22%^{7,8}. Control of disease activity, preexisting renal disease and presence of antiphospholipid antibody affect the pregnancy outcome. Unlike SLE, RA has little effect on pregnancy outcome; only 15-25% of pregnancies with RA end in miscarriages⁹, a figure that may or may not be slightly higher than in normal women. Seventy five percent or more pregnancies complicated with scleroderma also end in either term or preterm live birth¹⁰. In our study fruitful pregnancies with SLE were only 50%, whereas with RA and with scleroderma they were 80% and 66% respectively.

The 15% newborns of SLE affected mothers were ultimately affected with neonatal lupus and were serologically positive for anti-Ro/SS-A antibodies^{11,12}. But unfortunately the only one pregnancy in our study that was serologically positive for anti-Ro/SS-A antibodies had to be terminated due to severe flare the disease.

Conclusion

Obstetricians must keep in mind the commoner immunological connective tissue disorders, how they influence pregnancy and are influenced by pregnancy, and the risks and management of the mother and her conceptus.

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