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Pregnancy Outcomes in Autoimmune Diseases

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Abstract:-
Background: Autoimmune diseases are common in reproductive age group. Pregnancy is known to alter the disease course in many patients with autoimmune diseases.The aim of this study is to assess the impact of autoimmune connective tissue disorders and its treatment on the outcomes of pregnancy. Methods: 15 antenatal patients with autoimmune connective tissue diseases, comprising of Systemic Lupus Erythematosus (SLE), antiphospholipid antibody syndrome (APS), Undifferentiated Connective Tissue Diseases (UCTD), Rheumatoid Arthritis(RA),Sjogren's syndrome, systemic sclerosis were analyzed with respect to their parity, obstetric history, course during the pregnancy and maternal and fetal outcomes.
Results. The primary autoimmune disease was Systemic lupus erythematosus in 5 patients, 3 patients had Rheumatoid arthritis, 2 patients had Systemic sclerosis, 3 patients had Undifferentiated connective tissue disease and 1 patient each had sjogren's syndrome and Primary Antiphospholipid antibody syndrome. : 6 patients had active underlying disease at the time of pregnancy. 2 patients had bad obstetric history. 2 had preterm induced vaginal deliveries and 1had preterm LSCS.
Maternal complications of pre-eclampsia, eclampsia was observed in 2 patients with SLE and APS Fetal growth restriction was observed in 3 patients. Intrauterine death was reported in 2 patients. 1 patient with severe Systemic lupus erythematosus with Anti phospholipid antibody syndrome expired at 26 weeks of gestation.
Conclusions: Patients with active underlying disease had more adverse outcomes like maternal mortality, FGR, Preterm delivery and still birth. Well controlled underlying autoimmune disease improves the maternal and fetal outcomes.

Keywords:- *Autoimmune Diseases in Pregnancy, SLE In Pregnancy, Antiphospholipid Antibody Syndrome, Rheumatoid Arthritis In Pregnancy, Recurrent Pregnancy Loss.*

I. INTRODUCTION

Autoimmune diseases are chronic multi-system disorders, mainly affecting reproductive age group. The improvements in diagnostic and treatment modalities have made a positive impact on the survival and quality of life of these patients. Hence, pregnancy is becoming common in patients with autoimmune disorders. The physiological changes associated with pregnancy produce immunological variations in the course of the disease and vice versa.

Certain conditions like rheumatoid arthritis improve during pregnancy while others remain relatively unchanged or may worsen during pregnancy. There is a long lasting impact of these disorders on both the mother and fetus which needs due consideration as well. Multi-organ involvement and the presence of auto-antibodies affect the pregnancy outcomes. Therefore, pregnancy in autoimmune diseases was considered as a taboo in the past. With early diagnosis of autoimmune diseases and better treatment options, pregnancy is no longer forbidden in patients with autoimmune diseases. Preconception counseling, regular follow up and interdisciplinary care involving obstetrician and rheumatologist improve the perinatal outcome[1].

The aim of the present study was to assess the impact of autoimmune connective tissue disorders and its treatment on maternal and fetal outcomes.

II. METHODS

We performed an observational analysis of 15 antenatal patients with autoimmune connective tissue diseases, who were followed during their pregnancies at the department of Obstetrics and Gynaecology and Rheumatology.

Patients with Systemic Lupus Erythematosus (SLE),Rheumatoid arthritis,(RA) antiphospholipid antibody syndrome (APS), Sjogren's syndrome, Undifferentiated Connective Tissue Diseases (UCTD) and scleroderma were analyzed. Patient's demographic parameters, obstetric history, disease activity status, parity, disease course during pregnancy, complications, obstetric and fetal outcomes were assessed.

III. RESULTS

Fifteen patients with autoimmune diseases were studied.

The demographic profile of the patients is depicted in Table 1. Mean age of patient at the time of pregnancy was 27 years. 6 patients had active underlying disease at the time of pregnancy. Out of 15 patients, 10 patients were multigravida. 2 patients had bad obstetric history. Table 2.

The primary autoimmune disease was Systemic lupus erythematosus in 5 patients, 3 patients had Rheumatoid arthritis, 2 patients had Systemic sclerosis, 3 patients had Undifferentiated connective tissue disease and 1 patient each had sjogren's syndrome and Primary Antiphospholipid antibody syndrome.

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Maternal complications of pre eclampsia, eclampsia was observed in 2 patients with SLE and APS. Table 3.

11 patients delivered vaginally and 4 underwent LSCS.Out of the 11 vaginally delivered patients, 2 had preterm induced vaginal deliveries. Amongst the 4 patients who underwent LSCS, 1had preterm LSCS.

Mean baby birth weight in successful pregnancies was 2.4 kg. Fetal growth restriction was observed in 3 patients. Intrauterine death was reported in 2 patients.

1 patient with severe Systemic lupus erythematosus with Anti phospholipid antibody syndrome expired at 26 weeks of gestation. Table 5 shows the disease status and perinatal outcome.

Table 1: Age of the patient

Age of patient	No.of patients
<19 yrs	0
20-25 yrs	4
26-30yrs	8
31-35yrs	3

Table 2: Parity status

Parity	No. of patients
primigravida	5
multigravida	8
Multigravida with BOH	2

Table 3: Incidence of complications

Complication	No. of patients
Pre-eclampsia	1
Eclampsia	1
FGR	3
Preterm delivery	3
Maternal death	1
Hypothyroidism	2
Still birth	2

The maternal mortality was in the case of diagnosed Active Lupus with APS. She was on treatment with azathioprine, Prednisone 10mg Once a day and Hydroxychloroquine. She presented with eclampsia at 26 weeks and landed up in hypertensive encephalopathy postnatally.

Table-4: Outcome of pregnancy

Outcome	Number of patients
Vaginal delivery	11
LSCS	4

Table-5 Disease status and perinatal outcome

Patient Number	Diagnosis	Disease activity	Complications	Outcome	Baby Weight (kg)
1	SLE	Remission	Fetal growth Retardation, Hypothyroidism	Elective LSCS	2.3
2	SLE	Active	Ecclampsia, Thrombocytopenia, Maternal Mortality	PTVD	0.85 FSB
3	SLE	Remission	No	FTVD	2.5
4	SLE, APS	Active	Infertility, OI, IUGR, Preeclampsia, Premature delivery	LSCS, Placenta accreta, Hysterectomy	1.8
5	SLE	Remission	Nil	LSCS	2.7
6	Rheumatoid arthritis	Active	Anemia	FTND	2.6
7	Rheumatoid arthritis	Remission	No	FTND	3.2
8	Rheumatoid arthritis	Remission	No	FTND	2.9
9	Systemic sclerosis	Remission	Primary infertility, ovulation induction used	Emergency LSCS	3.1
10	Systemic sclerosis	Active	FGR	FTND	2
11	Sjogren's syndrome	Remission	No	FTND	3.2
12	Undifferentiated CTD	Remission	FGR	PTVD	1.7
13	Undifferentiated CTD	Remission	Hypothyroidism	PT LSCS	1.5
14	Undifferentiated CTD	Active	Fetal CHB	Fetal demise 24 weeks	NA
15	Antiphospholipid antibody syndrome	Active	PE, NND	LSCS, Post dated	NA

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IV. DISCUSSION

Autoimmune disorders in pregnancy are challenging to manage. These conditions not only predispose patients to poor obstetric outcomes but also increases the risk of maternal mortality in perinatal period. Diagnosis of autoimmune conditions or their flare during pregnancy is difficult due to overlapping symptoms. Generalized fatigue, weakness, skin changes, anemia are common symptoms seen in pregnancy and autoimmune conditions. Raised ESR and higher complement levels in normal pregnancy adds to the existing confusion.

In SLE patients, pregnancy predisposes for high rates of SLE flare, hypertension, nephritis and preeclampsia[2]. About 25% of all pregnancies in lupus are unsuccessful. The premature birth rate is 39%. Pregnancy outcomes are particularly adverse, if there is presence of active lupus nephritis flare or APA antibodies. The adverse outcomes seen are hypertension, premature birth, abortions. In our study, out of 5 patients 2 had active disease at the time of conception and had LBW babies. One patient had eclampsia and succumbed to death. She had active disease despite of treatment with steroids, Azathioprine and hydroxychloroquine. We observed that those who were in remission were able to continue the pregnancy till term and had uneventful perinatal outcome.

Rheumatoid arthritis poses significant challenges for conception. In a Dutch study, Pregnancy-induced Amelioration of Rheumatoid arthritis (PARA), 42% of patients with Rheumatoid arthritis had longer time to pregnancy (TTP) which was significantly higher than the national average of 3.5-24.2% depending on the geographic area[3]. The factors associated with reduced fertility are high disease activity, use of NSAIDs and prednisone > 7.5 mg per day. Hence, in RA patients, it is desirable to achieve low disease activity or remission before planning for conception.

In the same study it was shown that half of the patients showed decrease in RA disease activity in the third trimester and 27% of the patients were in remission in the third trimester. While other studies showed around 40-90% improvement during pregnancy. These numbers are better during recent years as compared to older studies probably due to availability of effective medication during preconception period. During postpartum period there is RA flare in around 66-90% patients[4]. The rate of miscarriage is not increased in RA patients as compared to general population.[5] Whereas the probability of preeclampsia is slightly raised than the general population. There is increased risk of preterm delivery more so in patients with high to moderate disease activity (20% vs 12% in mild disease)[6] Rheumatoid arthritis patients with high disease activity have more chances of having small for gestational age (SGA) infants. There are some reports of increased incidence of Cesarean section in patients with RA, however this finding was not supported in other studies. All the 3 RA patients in our study delivered vaginally at term though 1 patient had active disease status.

In patients with Sjogren's syndrome, there is risk of Atrioventicular conduction block in fetus as well as increased incidence of spontaneous abortion, preterm delivery and cesarean section. In a series of 34 patients with primary Sjogren's syndrome, there were 2 cases with intrauterine Atrioventricular block in fetus. There is also higher percentage of low-birth-weight babies in patients with Sjogren's syndrome. Out our 15 patients 1 had AV conduction block diagnosed at anomaly scan and subsequently validated by fetal 2D ECHO. Patients with late diffuse systemic sclerosis especially with end organ damage have more frequency of miscarriage than general population (42% vs 13% for all other groups)[7]. However, in early and mild disease it is comparable to the normal population. Preeclampsia, abruptio placentae, premature rupture of membranes, placenta praevia, excessive bleeding is reported obstetric complications in patients with systemic sclerosis[8]. The incidence of preterm birth (29% vs 5%) and Fetal growth restriction is higher in patients with systemic sclerosis[7]. In the prospective study by Steen, there is no significant change in disease activity in patients with systemic sclerosis due to pregnancy[7]. Recent studies found lower incidences of renal crisis in patients with Systemic sclerosis as compared to previous studies. Diagnosis of renal crisis is challenging as symptoms of preeclampsia and renal crisis are overlapping. Progressive daily increase of serum creatinine value and microangiopathic hemolytic anemia is typical of renal crisis whereas in preeclampsia there is higher rise in transaminase levels and serum uric acid levels. In patients with Pulmonary arterial hypertension and history of renal crisis who required ACE inhibitors, it is advisable to avoid the conception.

One patient of systemic sclerosis in our study had primary infertility and conceived with ovulation induction.

All patients with AIRD (Autoimmune rheumatic diseases) should be screened for presence of anti- Ro/SSA antibodies as these are associated with risk of congenital complete heart block in 1-2% patients. In such pregnancies, the obstetric sonograms and fetal echocardiograms should be done every 2 weeks starting from 16th week of gestation.

Treatment of patients with autoimmune diseases is a difficult task. The pharmacokinetics of drugs are altered in pregnancy causing unpredictable drug effects. Immunosuppressants like Methotrexate, Mycophenolatemofetil[9] are contraindicated in pregnancy due to their teratogenic potential. The use of steroids should be minimal to avoid maternal hypertension, diabetes and possible fetal growth restriction. Use of Azathioprine, Calcineurine Inhibitors, Sulfasalazine, Hydroxychloroquine is permissible in pregnancy. More and more data is available for the safety of Anti TNF drugs in pregnancy and they are recommended to be used in pregnancy. There is inadequate data to support the use of other biologics in pregnancy.

There was Intrauterine fetal death in 1 patient at 24 weeks.

This study is a retrospective analysis of small number of patients. Though the number of patients is less , the follow up and joint interdisciplinary management has definitely improved the perinatal outcome.

V. CONCLUSIONS

Autoimmune diseases in pregnancy needs special care for optimum outcomes. Patients with active underlying disease had more adverse outcomes like maternal mortality, Intrauterine growth retardation, preterm delivery and still birth. Well controlled underlying autoimmune disease improves the maternal and fetal outcomes.

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