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Original Research Paper

Nephrology

FETAL AND MATERNAL OUTCOMES OF PREGNANCY IN SEVERE LUPUS NEPHRITIS.

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ABSTRACT

Objective. To evaluate the fetal and maternal outcomes of pregnancy in severe lupus nephritis.

Methods. Records of all women with severe lupus nephritis who had pregnancy during regular clinic follow-up were analysed. Fetal outcome studied were stillbirth, abortions (spontaneous/therapeutic), live birth, fetal distress, preterm birth, low birth weight, neonatal death, and congenital malformations. Preeclampsia, gestational hypertension, peripatum haemorrhage, gestational diabetes and maternal infections were evaluated along with renal flare related to pregnancy. Outcomes were compared between planned and unplanned pregnancies.

Results. Of 174 women screened, 36 pregnancies occurred in 26 women. 22(61%) resulted in live births, 7(19.4%) underwent therapeutic termination, 5(13.8%) spontaneous abortions and 2(5.5%) stillbirths. 21 (58.4%) were planned pregnancies and they had significantly more live births than unplanned pregnancies (p = 0.0001). 8(22.2%) pregnancies were complicated with renal flare.

Conclusion. Although there is significant risk of adverse maternal and fetal outcomes in pregnancy with severe lupus nephritis, planned pregnancies can be successful with close monitoring and continuous therapy. Preconception counselling discussing the same will be beneficial.

KEYWORDS : Lupus Nephritis, Pregnancy

INTRODUCTION

Patients with systemic lupus erythematosus (SLE) have a higher risk of adverse maternal and fetal outcomes in pregnancy as compared to the general population.1 However, recent evidence suggests favourable outcomes with mild or quiescent disease.2 Studies evaluating the relationship between nephritis(not restricting to severe nephritis) and pregnancy have shown conflicting evidence2-6. Gladman et al have reported that lupus nephritis in pregnancy does not lead to worsened pregnancy or fetal outcomes; and the changes in kidney disease activity during pregnancy are similar to those in the nonpregnant state.5 As the existing data from India is scare, we investigated the fetal and maternal outcomes of pregnancy with severe lupus nephritis from western India.

Participants & methods

The study was carried out in accordance with Good Clinical Practice Guidelines (October 2013) after permission from Institutional Ethics Committee with a consent waiver.

Participants selection

For this retrospective analysis, we screened the records of all the women who had presented to the lupus nephritis clinic in a tertiary referral center in Mumbai. Patients with severe lupus nephritis who had a pregnancy during regular clinic follow-up were included. We used a definition of severe lupus nephritis stated by the Consensus Conference of the International Study of Kidney Disease in Children(Paris, 1980: endorsed by the World Health Organization).7 It includes histologic class III, IV, and V with superimposed severe segmental or diffuse proliferative nephritis. Patients with incomplete follow up records were excluded. All patients were treated in accordance to KDIGO guidelines for glomerulonephritis.10 As per the clinic protocol all patients were followed up every month in the first trimester, fortnightly in second trimester and weekly thereafter.

METHODS

We analysed the records of all patients for demographic and clinical details. Patients were divided into those who had planned versus unplanned pregnancy. Planned pregnancy was defined as patients who were allowed to conceive when [1] stable inactive disease for last six months; [2] oral prednisone ≤10 mg per day; [3] urine protein < 0.5 g/24 hours; (4) absence of any major organ dysfunction; (5) discontinuation of immunosuppressants like cyclophosphamide, methotrexate, and mycophenolate mofetil (MMF) for last six months.

Outcome measures

Fetal outcomes: [1]Stillbirth: death of a fetus in utero > 20 weeks' gestation; [2]Spontaneous abortion: termination of pregnancy < 20 weeks' gestation caused by natural factors; [3]Therapeutic abortion: artificial termination of pregnancy for medical indication; [4] Fetal distress: fetus hypoxia and acidosis, endangering its health [5] Preterm birth: birth < 37 weeks of gestation; [6]Low birth weight: weight below 10th percentile sex and gestational age(< 10th percentile for); [7] Neonatal death: death within 28 days of birth; [8]Congenital malformations.

Maternal outcomes: Preeclampsia and gestational hypertension were defined as per ACOG guidelines(2013).8 Other outcomes were peripartum hemorrhage, gestational diabetes, maternal infection, surgical interventions. Renal flares were defined as per International consensus for a definition of disease flare in lupus.9 Active lupus nephritis: active urinary sediment [>3 RBC/high-power field (HPF), or >5 WBC/HPF, or cellular casts), proteinuria 500mg/day, or eGFR <60 ml/min/1.73 m2 with active urinary sediment.

Statistical analysis

Each pregnancy episode was considered as a separate observation. Quantitative variables (age, time interval) were reported as mean, SD and range. Frequencies and percentages were used for categorical variables (fetal and maternal outcomes) and these were compared using chi-square test. P < 0.05 was statistically significant.

RESULTS

Patient characteristics

Records of 174 women following regularly at lupus clinic were screened. Of these, 26 patients had 36 pregnancy episodes. Demographic details are listed in Table 1. 6 (16.6%) pregnancies were the first presentation of SLE, 21 (58.4%) were planned pregnancies with inactive disease and 9 (25%) were unplannned. Most of the patients (36%) were on maintenance with azathioprine and steroids at conception. MMF and cyclophosphamide at least 6 months prior to planned pregnancy. Barring 6 newly diagnosed SLE, rest all the patients were on 5-7.5mg/day of prednisolone and hydroxychloroquine during pregnancy.

Table 1: Patients characteristics

Number of patients /Number of pregnancies	26/36
Age at Presentation, years	24.86 ± 3.75 (16 - 35)
Age at Pregnancy, years	27.56 ± 4.08 (19 - 37)
Interval between SLE diagnosis and Pregnancy, years	3.2 ± 2.38 (0.5 - 10)
Hypertension, n(%)	9/26 (34.61%)
Antiphospholipid antibody, n(%)	8/26 (30.7%)
Histology (n = 25, one not biopsied) Class III Class IV Class V or IV + V	2 (12%) 11 (44%) 12 (48%)
Immunosuppression 6 months pre-pregnancy Azathioprine + steroids Mycophenolate + steroids Cyclophosphamide + Steroids Mycophenolate + tacrolimus + steroids Steroids Nil	12/36 (33.3%) 6/36 (16.7%) 2/36 (5.5%) 1/36 (2.7%) 8/36 (22.2%) 7/36 (19.4%)
Immunosuppression during pregnancy Azathioprine + steroids Mycophenolate + steroids Cyclophosphamide + Steroids Tacrolimus + steroids Steroids Nil	13/36 (36.1%) 3/36 (8.3%) 2/36 (5.5%) 1/36 (2.7%) 11/36 (30.5%) 6/36 (16.6%)

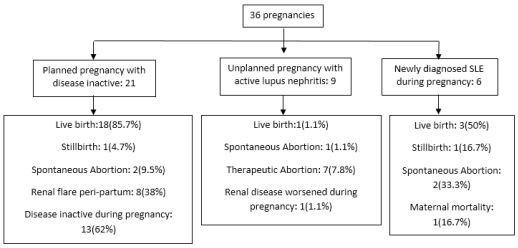
Fetal outcomes

Of the 36 pregnancies, 22(61%) resulted in live births. 7 (19.4%) had to be terminated therapeutically as patients were on teratogenic drugs at conception. There were 5 (13.8%) spontaneous abortions and 2 (5.5%) stillbirths. As compared to unplanned pregnancies, planned pregnancies had significantly higher chances of live births, 1.1% vs 85.7% ($\chi 2 = 15.09$, $p = 0.0001$). Of the 22 live births, 5 (22.7%) were preterm deliveries [3: fetal distress, 1: oligohydramnios and premature rupture of membranes, 1: severe preeclampsia]. 9 (41%) of the 22 live births were by LSCS, rest delivered vaginally. Average birth weight was 2.2kg ±0.5kg (1.3-3.75kg) and 2 (9%) babies had low birth weight. 1 neonatal death occurred on Day 11 in a preterm low birth weight baby due to respiratory distress. 1 neonate had cleft lip, cleft palate with microtia. It was an unplanned pregnancy while the mother was on MMF which was stopped in the 7th week of gestation.

Maternal outcome

One (2.7%) mother developed severe preeclampsia and 2(5.5%) pregnancies were complicated by gestational hypertension. 1 (2.7%) patient had severe sepsis. There were no episodes of peripartum haemorrhage or gestational diabetes. Of the 13(59%) vaginal deliveries, 1 was assisted with forceps. 8 (22.2%) pregnancies were complicated with renal flare [figure 1] and 1 had worsening of active nephritis. 1 (2.7%) patient presented with rapidly progressive glomerulonephritis in the 5th month of gestation (first presentation of SLE), had a spontaneous abortion, remained on hemodialysis for 2 weeks and succumbed to sepsis and respiratory distress.

Figure 1: Renal status of pregnancies



DISCUSSION

In this cohort of 36 pregnancies, we report a high rate of fetal loss (39%). This includes therapeutic abortions (19.4%), spontaneous abortions (13.8%) and stillbirths (5.5%). This rate is higher than that reported in prior prospective studies3,11,12. 7 (19.4%) pregnancies had to be terminated as patients were on teratogens (Cyclophosphamide: 2, MMF: 3, methotrexate: 1 and losartan: 1). This emphasizes the unmet need of patient awareness and efficacy of contraceptive methods. As SLE is most prevalent in women in reproductively active age group, it is imperative to levy practices to prevent such conceptions. In our cohort, 1 patient who conceived on MMF developed congenital malformations despite discontinuation in 7th week of gestation. Thus, fetal screening for malformations is imperative in all pregnancies when the mother has had exposure to teratogens.

As expected the outcomes were significantly better in planned pregnancies. Recent study13 on planned pregnancies have reported a fetal loss of 4.9% and lesser incidence of preterm births. In our cohort the outcome of preterm births was favourable. 8(38%) flares occurred in the peripartum period, of which 2 were treated with MMF and rest all were treated with steroids and had favourable outcomes. 1 patient with worsening of disease during unplanned pregnancy, only partially responded to the treatment and suffered permanent loss of GFR. Our study is in accordance with Rahman et al5 who found that quiescent nephritis and normal kidney function at conception were the only predictors of a favourable maternal outcome. This underscores the need for close monitoring of lupus activity at the conception and throughout the pregnancy.

Due to the retrospective nature of this study, the completeness of data is difficult to ascertain. Also, the small sample size makes it difficult to draw comparisons between planned and unplanned pregnancies. Larger prospective studies are needed in Indian patients with severe lupus nephritis.

In Conclusion, our findings suggest that although pregnancy is not contraindicated in patients with lupus nephritis; they are at significant risk of adverse maternal and fetal outcomes. Planned pregnancies can be successful in most women with close monitoring and continuous therapy. Renal flares can occur even with patients with inactive nephritis at the beginning of pregnancy. There is a need for adequate preconception counselling involving all the risks, which can guide women to have shared decision in the planning of future pregnancies.

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