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ORIGINAL ARTICLE

Fetal and Neonatal Outcomes of Maternal Rheumatic diseases in a tertiary care centre of Lahore, Pakistan

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ABSTRACT

Background: Pregnancy may worsen underlying autoimmune rheumatologic illnesses. The trans-placental transmission of autoantibodies can harm the foetus or newborn.
Aim: To determine the impact of maternal rheumatological disorders on fetal and newborn outcomes.
Methods: A descriptive longitudinal study was conducted at Fatima Memorial Hospital enrolling 32 pregnant women with rheumatologic disorders by consecutive sampling. Data was collected regarding maternal demographics, diagnosis, serum markers, Fetal & neonatal outcome factors (IUGR, Fetal distress, Umbilical Doppler findings, Fetal Echo, Place of birth, Mode of delivery, discharge status, Term/pre-term birth, Gender, Low Birth Weight, Cardiac defect, NICU stay, the reason for NICU stay)
Results: The diagnosis of 50% of the subjects was SLE. 25%subjects were suffering from RA. Regarding serum markers, 50% of the mothers were Anti ds DNA positive followed by ANA with 34.4% & Lupus anticoagulant with 21.9% positivity. IUGR was recorded in 9.4%, fetal distress in 28.1%, abnormal umbilical doppler in 9.4%, and 12.5% of a newborn could not survive. Pre-term delivery was recorded in 31.3% of cases, low birth weight in 34.4%, cardiac defects in 6.3%, thrombocytopenia in 6.3%, NICU stay was required in 31.3%, EOS was reason in 12.5% and RDS in 25%.
Conclusion: Prevalence of IUGR, fetal distress, low birth weight, preterm delivery, cardiac defects and admission to NICU was high in autoimmune rheumatological pregnant females. Pre-term delivery, fetal distress and LBW were significantly associated with SLE.
Keywords: Pregnancy outcome, rheumatic disease outcome, fetus, neonate, SLE

INTRODUCTION

Autoimmune rheumatic diseases are a heterogeneous group of conditions characterized by joint involvement and a wide array of systemic symptoms. Rheumatoid arthritis (RA) and Systemic Lupus Erythematosus (SLE) are the prototypical illnesses of this group with many others. Although these reflect a wide range of clinical manifestations, they all have a shared or similar pathophysiological process[1,2].

Rheumatological illnesses have grown in prevalence and incidence over the last few decades, making them a major public health challenge. The most prevalent of these disorders are rheumatoid arthritis (RA), which has a global prevalence of 0.3-1 percent and an annual incidence of 0.02-0.05 percent[2].

Rheumatic disorders (RDs) are common in women of childbearing age. Because of earlier diagnosis and improved RD management, these women can now plan a family. Pregnancy is a sensitive time that requires specific care to control maternal sickness and avoid consequences for both the mother and the fetus. The goal of RD therapy during pregnancy should be to minimize the consequences of maternal disease on pregnancy outcomes. Active disease or flares can have a deleterious impact on fetal health and pregnancy outcome[3].

The rheumatology community has recently emphasized the reproductive health problems of the women they care for, as they are at an elevated risk for adverse pregnancy outcomes such as pre-eclampsia, protracted hospitalizations, maternal and fetal death and morbidity. Adult women with rheumatic diseases are concerned about their fertility, the possibility that their offspring will be harmed by their rheumatic disease, and the difficulties of pregnancy and motherhood[4].

RA affects women more frequently than men, and women of childbearing age are at the greatest risk[5,6,7]. Rheumatology is a relatively new field in Pakistan. There are only a few hospitals in Pakistan that have developed rheumatology clinics and qualified rheumatologists. There are no national registries that track the varied characteristics of autoimmune illnesses and how they are treated. A few local population studies have been done, providing crucial insight into the intricacies of many autoimmune illnesses, including RA[5]. Effect of RDs on pregnancy outcomes had not been studied in our ethnicity.

The objective of the study was to determine the fetal and neonatal outcomes in patients with rheumatic disorders.

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MATERIAL AND METHODS

A descriptive longitudinal study was conducted for a one-year duration (from January 2021 to December 2021) at Fatima Memorial Hospital (FMH). All (32) pregnant women at any stage of pregnancy with rheumatologic disorders following up in the obstetric unit and rheumatology clinics at FMH were included in the study by non-probability consecutive sampling. Women with rheumatic disease unconfirmed by a specialist rheumatology review were excluded from the study. This study was approved by the Institutional Review Board of FMH IRB No FMH-10-2021-IRB-964-M dated 24 December 2021. Informed consent was obtained from all the participants.

Participants were enrolled at the time of follow-up at the rheumatology clinic or prenatal care clinics FMH. Data was collected by a Paediatric postgraduate trainee or Neonatology Fellow. Data was collected on a pre-designed, study proforma that included maternal demographics, diagnosis, serum markers, Fetal & neonatal outcome factors (IUGR, Fetal distress, Umbilical doppler findings, Fetal Echo, Place of birth, Mode of delivery, discharge status, Term/preterm birth, gender, Low Birth Weight, Cardiac defect, NICU stay, the reason for NICU stay, lupus rash, follow up for rash and any other abnormality at 6 weeks). Babies born to these women were followed up till 6 weeks after birth. If a baby was delivered at a facility other than FMH, close follow-up was maintained through telephonic and electronic means. Neonate is defined as a newborn who is less than 4 weeks old. Full-term is defined as a baby born between 37 to 42 weeks. Preterm is defined as any baby born before 37 completed weeks of pregnancy. Extremely preterm is defined as a baby born before 28 weeks. Inborn is a baby born within the study site hospital. Outborn

is a baby born outside the hospital. Data was entered and analyzed using IBM SPSS statistics software for Windows, version 26.0. The data were represented as the mean and standard deviation for quantitative variables. Frequencies and percentages were reported for the qualitative variables. Chi-square/ Fischer exact test was applied to compare SLE and non-SLE groups. A p-value less than 0.05 was considered significant.

RESULTS

A total of 32 pregnant females diagnosed with any of the autoimmune rheumatological disorders were enrolled in the study. Maternal age was 30.87±4.66. The mean age at the time of diagnosis of rheumatic disorder was 27.09±4.32. Frequency and percentages of Maternal Disease (Antiphospholipid syndrome, SLE, Rheumatoid arthritis, Seronegative arthritis, Takayasu arteritis), Maternal serum markers (RA factor positive, ANA positive, Anti ds DNA positive, Lupus anticoagulant positive), Use of medicine pre-pregnancy and during pregnancy are presented in Table 1.

Table 1: Frequency and percentage of maternal factors (n=32)

Maternal Factors	Subcategories	Frequenc
Maternal Disease	Antiphospholipid syndrome	6 (18.8%)
	SLE	16(50.0)
	Rheumatoid arthritis	8(25.0)
	Seronegative arthritis	1(3.1)
	Takayasu arteritis	1(3.1)
Maternal serum markers	RA factor positive	7(21.9)
	ANA positive	11(34.4)
	Anti ds DNA positive	16(50.0)
	Lupus anticoagulant positive	7(21.9)
Pre-Pregnancy on medicine	No	9(28.1)
	Yes	23(71.9)
During pregnancy on medicine	No	6(18.8)
	Yes	26(81.3)

Table 2: Frequency and percentage of Fetal & neonatal factors (n=32)

Fetal & Neonatal factors	Subcategories	Frequency	%age
IUGR	No	29	90.6
	Yes	3	9.4
Fetal distress	No	23	71.9
	Yes	9	28.1
Umbilical Doppler	Normal	29	90.6
	absent diastolic flow	2	6.3
	reversed diastolic flow	1	3.1
Fetal monitoring	No	5	15.6
	Yes	27	84.4
Fetal Echo	Done	15	46.9
	not done	17	53.1
Place of birth	FMH	29	90.6
	Outborn	3	9.4
Mode of delivery	LSCS	15	46.9
	SVD	17	53.1
Discharged or not	discharged	28	87.5
	expired	3	9.4
	stillbirth	1	3.1
Term/preterm	extremely preterm	4	12.5
	preterm	6	18.8
	full term	22	68.8
Gender	female	15	46.9
	Male	17	53.1
Low Birth Weight	No	21	65.6
	Yes	11	34.4
Cardiac defect	No	29	90.6
	not known	1	3.1
	PDA	2	6.3
NICU stay	No	22	68.8
	Yes	10	31.3
Thrombocytopenia	thrombocytopenia	2	6.3
Reason for NICU stay	Early onset sepsis	4	12.5
	Respiratory Distress syndrome	8	25.0
Rash at birth	No	31	96.9
	not known	1	3.1

Frequency and percentages of Fetal & neonatal factors (IUGR, presence of Fetal distress, Umbilical doppler findings, Fetal monitoring, Fetal Echo, Place of birth, Mode of delivery, Discharged or not, Term/pre-term birth, Gender, Low Birth Weight, Cardiac defect, NICU stay, the reason for NICU stay, thrombocytopenia,) are presented in table 2.

On the follow-up visit at 6 weeks, no rash or any other abnormality was observed in the study subjects. Two children did not return for follow-up.`In the present study, 16 enrolled subjects were diagnosed with SLE. All the SLE-positive subjects were Anti-ds-DNA positive. For further analysis, 2 groups were made and the Mode of delivery, Discharge status, Term/pre-term delivery status, presence of fetal distress and LBW were compared in both groups. Fetal distress, pre-term delivery and LBW were significantly higher in the SLE group with p value<0.05) (Table 3).

Table 3: Cross-tabulation of SLE with fetal/neonatal factors (n=32)

Variables	Sub-category	Non-SLE	SLE	Fischer exact/chi-square value	P value
Mode of delivery	LSCS	7	8	.125	.723
	SVD	9	8		
Outcome	Discharged	16	12	4.571	0.102
	Expired	0	3		
	Stillbirth	0	1		
Gestation at delivery	extremely preterm	0	4	9.576	.008*
	Preterm	1	5		
	full term	15	7		
Fetal distress	No	15	8	7.575	.008*
	Yes	1	8		
LBW	No	15	6	11.221	.001*
	Yes	1	10		

DISCUSSION

The main findings of the present study were: half of the enrolled subjects were diagnosed with cases of SLE, one fourth were of RA. Regarding serum markers, half of the mothers were Anti ds DNA positive (all the SLE cases), ANA was positive in one-third & Lupus anticoagulant is one-fourth. IUGR, fetal distress, Preterm delivery, low birth weight, and NICU stay due to RDS or EOS had very high frequency. abnormal umbilical doppler, death of newborn or stillbirth, cardiac defects & thrombocytopenia had moderately high frequency. Fetal distress and LBW were significantly associated with SLE. We could not find any study to compare with our ethnicity. Following international studies compare with our findings.

According to a study conducted on RD in Japan, SLE had the highest prevalence, followed by APS, RA, and other disorders. Compared to the general obstetric population GOP, pregnancies with RDs tended to have a greater incidence of emergency caesarean sections and preterm deliveries. The birthweight of infants born to mothers with SLE and APS was significantly lower than that of infants born to GOP, and the presence of anti-DNA antibodies was significantly associated with an increased risk of prenatal complications[8]. Findings were similar to the present study except for LSCS. In our study SVD prevalence was a little higher than SVD and we did not compare it with GOP.

In large-scale comparative research of RD conducted in California, the lack of an increase in congenital malformations was a source of solace. It was determined, however, that women with RDs had an increased risk of preterm birth and having a small-for-gestational-age infant[6]. This is consistent with our investigation, but for congenital abnormalities, we identified PDA despite not comparing it to healthy controls.

Rheumatoid arthritis (RA) was the most prevalent diagnosis in a Mexican study, followed by systemic erythematosus lupus (SLE) and antiphospholipid syndrome (APS). Compared to pregnancies with GOP, pregnancies with RD appeared to have more emergency caesarean sections, premature births, and LBW infants[9]. In our analysis, SLE was the most prevalent diagnosis, followed by RA and APS.

There was a drop in live births, an increase in preterm deliveries and an increase in caesarean sections among female Iraqi RA patients. Insufficient knowledge exists regarding the significance of contraceptive technique efficacy with teratogenic drugs (methotrexate, and leflunomide)[10].

Women with RA or SLE and their infants reported negative outcomes, especially infants of SLE-affected mothers. The frequency of maternal/infant re-hospitalization increased and was most pronounced in the early postpartum months. During these intervals, close monitoring was essential for minimizing harmful effects. The infants of women with SLE were more susceptible to abnormalities and death[11].

At least six months before conception, optimal regulation of RD activity must be achieved. Maternal-placental syndrome, which manifests as preeclampsia, eclampsia, fetal growth restriction, and preterm, is frequently associated with high-risk pregnancies. Rheumatic illness flares and obstetric difficulties can coexist, making differentiated diagnosis challenging. Before and throughout pregnancy, only medications that do not increase the risk of fetal problems should be administered. Teratogenic medicines (such as methotrexate, leflunomide, and cyclophosphamide) must be discontinued before conception[12].

Factors that may be used to predict the likelihood of PTB in RA patients include the disease activity and severity of rheumatoid arthritis (RA), laboratory parameters (cytokines and immune cell population), and sociodemographic characteristics such as race, smoking, alcohol consumption, and level of education[13].

As SLE typically manifests in young adults, pregnancy is common and generally successful. Nevertheless, pregnancy is considered high-risk due to a combination of maternal (lupus flare, diabetes, pre-eclampsia) and fetal (miscarriage, intrauterine fetal mortality, preterm birth, intrauterine growth restriction, and congenital heart block) hazards. Pregnancy should be scheduled for a time when SLE is under good management (on allowable medications)[14]. In SLE patients, high CRP, APA positivity, anti-dsDNA positivity, and kidney involvement were indicators of unfavourable pregnancy outcomes[15]. Active illness was a predictor of SLE flare and fetal death in Malaysian women, while SLE flare was the primary predictor of preterm delivery[16].

In women with APS, the risks of fetal loss, abortion, thrombosis, and premature birth were also dramatically increased. The risk of neonatal mortality, infants short for gestational age, preterm infants, and infants admitted to the neonatal critical care unit was also considerably increased in mothers with APS[17]. The number of APS-diagnosed individuals in our sample was so little that exceptional results cannot be stated.

Research conducted in Sweden found that despite the intensive monitoring, the majority of pregnancies resulted in at least one abnormal pregnancy outcome (APO), but only a handful was severe. Lupus nephritis as the primary risk factor for APO in SLE patients[18].

The study was conducted at a single centre and a limited number of patients visited this setting so only a smaller sample was enrolled. The wide majority in our sample is represented by SLE whereas the overall prevalence of RA is higher[2]. For the rest of the RD, the sample size was very small for further analysis. A broad study with large sample size, multicenter and enrolling maximum subtypes of rheumatological disorders is recommended in our ethnicity as well a comparison with healthy adults is also recommended. pre-gestational counselling and a multi-disciplinary approach could result in positive pregnancy outcomes[19].

CONCLUSION

Prevalence of IUGR, fetal distress, low birth weight, preterm delivery, cardiac defects and admission to NICU was high in autoimmune rheumatological pregnant females. Pre-term delivery, fetal distress and LBW were significantly associated with SLE. Therefore, multidisciplinary care should be provided from pre conception period till the neonatal period.

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REFERENCES

1. Uddin Z, Khan A, Haroon M, Faiq M, Rabbani S, Lashari NA. Spectrum Of Ocular Manifestations Of Rheumatic Autoimmune Diseases: A Tertiary Care Experience In Pakistan. J Ayub Med Coll Abbottabad. 2021 Oct-Dec;33(4):612-616.
2. Egalini F, Parasiliti Caprino M, Gaggero G, Cappiello V, Giannelli J, Rossetto Giaccherino R,et al. Endocrine Disorders in Autoimmune Rheumatological Diseases: A Focus on Thyroid Autoimmune Diseases and on the Effects of Chronic Glucocorticoid Treatment. Endocrines. 2021 Jul 1;2(3):171-84.
3. Andreoli L, Gerardi MC, Fernandes M, Bortoluzzi A, Bellando-Randone S, Brucato A, et al. Disease activity assessment of rheumatic diseases during pregnancy: a comprehensive review of indices used in clinical studies. Autoimmun Rev. 2019 Feb;18(2):164-176. doi: 10.1016/j.autrev.2018.08.008.
4. Carandang K, Mruk V, Ardoin SP, Huynh B, Clowse ME, Berlan ED, et al. Reproductive health needs of adolescent and young adult women with pediatric rheumatic diseases. Pediatric Rheumatology. 2020 Dec;18(1):1-1.
5. Khaliq T, Khan A, Malik IA. Clinical profile and treatment outcomes of patients with rheumatoid arthritis at a tertiary care hospital of Pakistan. Age. 2020 Jul 1;43:13-03.
6. Strouse J, Donovan BM, Fatima M, Fernandez-Ruiz R, Baer RJ, Nidey N, et al. Impact of autoimmune rheumatic diseases on birth outcomes: A population-based study. RMD Open. 2019;5(1):1–10.
7. Hills F. Connective tissue and dermatological conditions in pregnancy. Obstetrics, Gynaecology & Reproductive Medicine. 2021 Jun 1;31(6):162-9.
8. Sugawara E, Kato M, Fujieda Y, Oku K, Bohgaki T, Yasuda S, et al. Pregnancy outcomes in women with rheumatic diseases: a real-world observational study in Japan. Lupus. 2019 Oct;28(12):1407-1416. doi: 10.1177/0961203319877258
9. Hernández F, Negrete AL, Taylor CS, Barbosa LP, Barriga-Maldonado E, Chavez RR,et al. AB0843 OBSTETRIC AND PERINATAL OUTCOMES IN MEXICAN WOMEN WITH RHEUMATIC DISEASES. (2021): 1445-1446.
10. Salih LB, Jasim NA. Pregnancy Outcumes and Contraceptive Use in Women with Rheumatoid Arthritis: A Comparative Study. Современная ревматология. 2022 Dec 17;16(6):38-42.
11. Singh N, Sabo J, Crane DA, Doody DR, Schiff MA, Mueller BA. Birth outcomes and re-hospitalizations among pregnant women with rheumatoid arthritis and systemic lupus erythematosus and their offspring. Arthritis Care Res (Hoboken). 2023 Jan 10. doi: 10.1002/acr.25087.
12. Grygiel-Gorniak B, Masiero E, Nevaneeth BC, Jojy MM. Rheumatic Diseases in Reproductive Age—the Possibilities and the Risks. Reproductive Sciences. 2022 Mar 31:1-13.
13. Falcon RM, Alcazar RM, Mondragon AV, Penserga EG, Tantengco OA. Rheumatoid arthritis and the risk of preterm birth. American Journal of Reproductive Immunology. 2022 Nov 30.
14. Petri M. Pregnancy and systemic lupus erythematosus. Best Practice & Research Clinical Obstetrics & Gynaecology. 2020 Apr 1;64:24-30.
15. Zamani B, Shayestehpour M, Esfahanian F, Akbari H. The study of factors associated with pregnancy outcomes in patients with systemic lupus erythematosus. BMC Research Notes. 2020 Dec;13(1):1-6.
16. Kalok A, Cader RA, Indirayani I, Karim AK, Shah SA, Ismail NA, et al. Pregnancy outcomes in systemic lupus erythematosus (SLE) women. Hormone Molecular Biology and Clinical Investigation. 2019 Dec 1;40(3).
17. Liu L, Sun D. Pregnancy outcomes in patients with primary antiphospholipid syndrome: A systematic review and meta-analysis. Medicine. 2019 May;98(20).
18. Saleh M, Sjöwall C, Strevens H, Jönsen A, Bengtsson AA, Compagno M. Adverse pregnancy outcomes after multi-professional follow-up of women with systemic lupus erythematosus: an observational study from a single centre in Sweden. Journal of Clinical Medicine. 2020 Aug 11;9(8):2598.
19. Ceccarelli F, Pirone C, Perricone C, Selntigia A, Orefice V, Pacucci VA, et al. Pregnancy outcome in systemic lupus erythematosus patients: A monocentric cohort analysis. Rheumatology. 2021 Apr;60(4):1747-54.