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ORIGINAL ARTICLE

Impact of maternal rheumatic diseases on fetal and neonatal outcomes delivering in a Tertiary Care Hospital.

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ABSTRACT… Objective: To determine the impact of rheumatic diseases on fetal and neonatal outcomes. **Study Design:** Prospective, Observational study. **Setting:** Department of Obstetrics and Gynecology, Neonatology, and Rheumatology, Fatima Memorial Hospital, Lahore, Pakistan. **Period:** January 2023 to January 2024. **Methods:** A total of 61 pregnant women aged 20-40 years, with rheumatological illnesses, and having gestational age of 12 weeks or more were analyzed. Maternal demographics, clinical characteristics, and gestational age at time of study entry were documented. The neonatal outcomes such as birth weight, gestational age, NICU stay, and mortality were documented. Data analysis was performed using IBM-SPSS Statistics, version 26.0. With the significance level set at $p < 0.05$, the chi-square test or Fisher's exact test were utilized to evaluate associations between categorical data. **Results:** In a total of 61 females, the mean age, gestational age, and duration of rheumatic illness at the time of enrollment were 30.13 ± 4.50 years, 25.45±9.19 weeks, and 25.48±5.29 years, respectively. The most common rheumatic disease were systemic lupus erythematosus (SLE), rheumatoid arthritis, and syndrome of antiphospholipids, found in 24 (39.3%), 11 (18.0%), and 8 (13.1%) females, respectively. The mean birth weight was 2492.13±820.0 grams while, 20 (32.8%) newborns had low birth weight. Live-birth was reported in 55 (90.2%) cases. **Conclusion:** Systemic lupus erythematosus, rheumatoid arthritis, and syndrome of antiphospholipids were the most common rheumatic diseases among pregnant females. The risk of adverse outcomes in pregnant females with rheumatic diseases seems high.

Key words: Gestational Age, Low Birth Weight, Neonate, Rheumatic Diseases, Thrombocytopenia.

INTRODUCTION

Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are two rheumatic conditions that are especially difficult to treat during pregnancy since they are systemic diseases that affect the fetus as well as the mother.[1,2] Several authors have identified low birth weight, fetal discomfort, and preterm delivery as negative pregnancy outcomes. Preterm delivery, low birth weight, and fetal distress are among the adverse pregnancy outcomes mentioned by a number of writers. These autoimmune illnesses are frequently observed in women who are of reproductive age.[3]

One such issue, RA, may really be disease-related in the case of a current illness. Women with untreated RA during pregnancy have increased rates of neonatal intensive care unit (NICU) admissions, preterm delivery risk factors, and the necessity of a cesarean section or other assisted birth method.[4] Similarly, if SLE is active during pregnancy, it is mostly linked to higher increased incidence of intrauterine growth retardation (IUGR) incarceration and infant death. Another common form of rheumatic disease is SLE.[5]

The influence of disorders on the health of the fetus and newborn is still a concern, even with the advancements in therapy that have improved the outcome for mothers. Congenital heart defects, thrombocytopenia, and neonatal respiratory distress are possible consequences of untreated rheumatic diseases.[6] Despite international study efforts, there is still a dearth of data addressing these repercussions in resource-poor countries

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like Pakistan.[7] The current study was planned to determine the impact of rheumatic diseases on fetal and neonatal outcomes. It is anticipated that the results would give crucial information on the risks of these illnesses and guide interdisciplinary management options to improve maternal and newborn outcomes.

METHODS

This prospective observational study was conducted at the department of obstetrics and gynecology, neonatology, and rheumatology, Fatima Memorial Hospital, Lahore, Pakistan during January 2023 to January 2024. The study was approved by Institutional Review Board (IRB#: FMH-24/09/2024-IRB-1487). A sample size of 61 was calculated using online OpenEPI sample size calculator taking the proportion of newborns to rheumatic disease mothers requiring NICU admission as 13.2%[8], with 95% confidence level, and 8.5% margin of error. Clinical diagnosis of mother's rheumatic illness status was validated by the Department of obstetrics and rheumatology during the prenatal visits. The study's inclusion criteria were pregnant women aged 20-40 years, with rheumatological illnesses, and having gestational age of 12 weeks or more. Each research participant provided proper written and informed consent, and only those mothers were included who ensured regular follow up and evaluation till pregnancy outcomes. Females with chronic renal failure, dialysis, any kinds of malignancy, HIV, or liver failure were excluded.

During the usual prenatal treatment, pregnant women were enrolled from the obstetric and rheumatology OPD, who assured proper follow-up and interdisciplinary coordination. Maternal demographics, clinical characteristics, and gestational age at time of study entry were documented. Echocardiography, Doppler investigations, and ultrasound were used to evaluate the fetus well being. The neonatal outcomes such as birth weight, gestational age, NICU stay, and mortality were documented. Neonates were evaluated for a period of 6-8 weeks after delivery to ascertain consequences. A special proforma was designed to record all study information.

Data analysis was performed using IBM-SPSS Statistics, version 26.0. Frequencies and percentages were represented for categorical data, while mean amd standard deviation (SD) were calculated for continuous data. With the significance level set at $p < 0.05$, the chi-square test or Fisher's exact test were utilized to evaluate the association between categorical data.

RESULTS

In a total of 61 females, the mean age, gestational age, and duration of rheumatic illness at the time of enrollment were 30.13 ± 4.50 years, 25.45±9.19 weeks, and 25.48±5.29 years, respectively. The most common rheumatic disease among pregnant females were found to be SLE, rheumatoid arthritis, and syndrome of antiphospholipids, found in 24 (39.3%), 11 (18.0%), and 8 (13.1%) females, respectively. Figure-1 is showing the frequency of various rheumatic diseases among pregnant females.

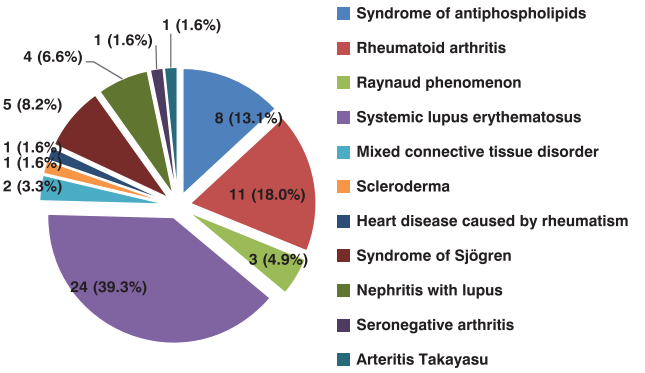

Figure-1. Rhematic diseases in pregnant females (n=61)

The mean gestational age at the time of delivery was 35.45±4.35 weeks, while 19 (31.1%) babies were born as pre-term. The mean birth weight was 2492.13±820.0 grams while, 20 (32.8%) newborns had low birth weight (<2500 grams). There was need for NICU admission in 18 (29.5%) newborns. Live-birth was reported in 55 (90.2%) cases. Table-I is showing details about the fetal and neonatal outcomes among females with rheumatic diseases.

Comparison of neonatal and fetal outcomes among females with and without SLE showed that fetal distress (33.3% vs. 8.3%, p=0.031), and

low birth weight (50.0% vs. 22.2%, p=0.048) were significantly more prevalent among females with SLE, while all other outcomes were statistically insignificant, and the details are shown in Table-II.

Parameter		Frequency (%)
Fetal echocardiography	Fetal echocardiography	
	Normal	44 (72.1%)
	Not finished	16 (26.2%)
	Pericardial effusion with fetal bradycardia	1 (1.6%)
Doppler scan findings	Normal	55 (91.7%)
	Intrauterine growth restriction	11 (18.0%)
	Fetal stomach enlargement	1 (1.6%)
	Increased diastolic pressure	1 (1.6%)
	Absent diastolic flow	2 (3.3%)
	Reversed diastolic flow	2 (3.3%)
	Fetal distress	11 (18.0%)
Delivery mode	Vaginal delivery	19 (31.1%)
	Cesarean section	41 (67.2%)
Birthplace	Out born	17 (27.9%)
	Inborn	44 (72.1%)
Gender	Male	35 (57.4%)
	Female	25 (41.0%)
Clinical findings	Pulmonary hypertension	3 (4.9%)
	Patent ductus arteriosus	2 (3.3%)
	Tricuspid regurgitation	1 (1.6%)
	Thrombocytopenia	4 (6.6%)
Final outcome	Stillbirth	1 (1.6%)
	Expired	4 (6.6%)
	Alive (discharged)	55 (90.2%)

Table-I. Fetal and neonatal outcomes in women with rheumatic diseases (total n=61)

One pregnancy was miscarriage

Outcomes	Present SLE (n = 24)	SLE Outcome (n = 36)	P-Value
Fetal distress	8 (33.3%)	3 (8.3%)	0.031
Intrauterine growth restriction	5 (20.8%)	6 (16.7%)	0.655
Low birth weight	12 (50.0%)	8 (22.2%)	0.048
Thrombocytopenia	2 (8.3%)	2 (5.6%)	0.702
Admission in NICU	10 (41.7%)	8 (22.2%)	0.174
Premature Birth	10 (41.7%)	9 (25.0%)	0.238
heart disease	1 (4.2%)	2 (5.6%)	0.712
Stillbirth	1 (4.2%)	-	0.146
Expired	3 (12.5%)	1 (2.8%)	
Alive (Discharged)	20 (83.3%)	35 (97.2%)	

Table-II. Neonatal and fetal outcomes in women with and without Systemic lupus erythematosus (total n = 60)

DISCUSSION

Rheumatic illnesses are a major problem during pregnancy since they impact the outcomes for both the mother and the fetus. Systemic lupus erythematosus (SLE) accounted for 39.3% of the 61 pregnant patients with rheumatic disorders in our study; rheumatoid arthritis (34.4%) and antiphospholipid syndrome (APS) were the other most common diagnoses. These results highlight the variety of maternal rheumatic diseases and how they affect the newborn's health in different ways. Poor neonatal outcomes have been widely associated with systemic lupus erythematosus, mostly because of inflammatory pathways and placental anomalies. Our study found a high correlation ($p < 0.05$) between SLE and low birth weight and fetal distress, which is consistent with previous recent studies.[9] These challenges are often mediated by placental insufficiency, a feature of pregnancies associated with SLE.

Unlike previous research that identified a strong association between SLE and infant mortality, our study found no correlation. Variations in disease activity levels, sample sizes, or hospital environments may be the cause of this discrepancy. Additionally, advancements in disease management, like the use of biologics and early therapy, may have lessened some of the risks that have previously been associated with pregnancies with SLE.[10] SLE and NICU hospitalization do not significantly correlate in our study highlights the potential benefits of early illness control and comprehensive prenatal care. Despite these developments, there are still serious risks associated with SLE, necessitating continued care and individualized therapy.[11]

Rheumatoid arthritis was diagnosed in 34.4% of the women in our sample, which is a significant proportion of maternal diagnoses. Pregnancy complications associated with RA include preterm delivery, an increase in NICU admissions and low birth weight. Preterm delivery happened in 32.2% of instances and low birth weight in 33.9% of cases in our study. These findings are in line with past research demonstrating the detrimental effects of untreated RA during pregnancy.[12] Immunomodulatory changes during pregnancy frequently lead to a decrease in RA disease activity; nonetheless, postpartum flare-ups are frequent, with up to 40% of women reporting increased disease activity following childbirth.[13] These flares highlight the importance of continued monitoring and treatment following the peripartum period.[14]

Thirteen percent of females had antiphospholipid syndrome, which has been connected to pregnancy problems such intrauterine growth restriction (IUGR), premature birth, and recurrent pregnancy loss. The role placental thrombosis plays in mediating these effects, are consistent with our study's link between APS and IUGR.[15] Early identification and preventative usage of anticoagulants, such as low-dose aspirin and heparin, have been shown to significantly reduce pregnancy loss rates.[16] Early initiation of these medications is necessary to improve outcomes in pregnancies associated with APS. Our findings demonstrate the importance of routine fetal monitoring in pregnancies complicated by rheumatic disease. This study was able to put early interventions into place by utilizing Doppler tests to detect issues like nonexistent 3.3% for diastolic flow, 3.3% for reversed diastolic flow, and enhanced diastolic flow by 1%. Despite the significant associations observed in this study, it is important to recognize that outcomes vary depending on the kind and severity of rheumatism in mothers. The relatively low prevalence of these disorders in our sample highlights the requirement for more extensive, multicenter research to look at how they affect the health of mothers and newborns. Researchers have shown that achieving remission of sickness prior to conception significantly improves pregnancy outcomes in rheumatic disorders.[17] Preconception counseling is a crucial component of this approach, allowing physicians to talk with patients about medication safety, disease activity control, and regular monitoring schedules.

Future research should focus on assessing the long-term infants effects born to moms who have rheumatic illnesses. The impact of treatment exposure and maternal disease activity on the newborn's growth, neurodevelopment,

and immune system must be considered in care planning. Emerging medications such as JAK inhibitors and novel biologics provide intriguing therapeutic alternatives, but a detailed evaluation of their safety profiles during pregnancy is necessary.[18] Research on the cost-effectiveness of models of interdisciplinary care may give healthcare policymakers valuable information, especially in resource-constrained contexts. Posing with SLE, risk among the illnesses examined, this study shows the substantial impact of rheumatic conditions in mothers on the outcomes of newborns. Even though improvements in maternity care have reduced some hazards, the results highlight the significance of early detection, close observation, and interdisciplinary management in maximizing results.

These findings are particularly relevant in low-resource settings where disparities in healthcare access may exacerbate risks. By addressing these concerns, healthcare providers can improve outcomes for mothers and babies in this high-risk population. Enhancing medical professionals' education and training programs is necessary to improve the management of rheumatic disorders during pregnancy. Prioritizing patient education, prompt intervention access, and comprehensive follow-up protocols can further enhance outcomes for mothers and newborns. Future advancements in customized medicine may offer new strategies for effectively coping with the challenges posed by these high-risk pregnancies.

Even though the study's findings provide useful information regarding how rheumatic illnesses impact fetal and neonatal outcomes, there are some limitations. The comparatively limited sample size could restrict the outcomes' generalizability, particularly for less common rheumatic diseases. The observational study design precludes any inferences regarding causality, underscoring the need for randomized controlled trials to evaluate the efficacy of specific therapies. Variability in participant disease activity and treatment compliance may potentially have affected the outcomes, underscoring the importance of standard care practices.

CONCLUSION

Systemic lupus erythematosus, rheumatoid arthritis, and syndrome of antiphospholipids were the most common rheumatic diseases among pregnant females. The risk of adverse outcomes in pregnant females with rheumatic diseases seems high.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1	**Fahad Iqbal:** Data collection, drafting, responsible for data's integrity, proof reading, approved for publication.
2	**Faiza Yasin:** Study concept and design, proof reading, critical revisions, approved for publication.
3	**Saadat Ullah:** Study concept and design, proof reading, critical revisions, approved for publication.
4	**Muhammad Haroon:** Literature review, data analysis, proof reading, approved for publication.
5	**Zahid Anwar:** Study concept and design, proof reading, critical revisions, approved for publication.
6	**Saqib Aslam:** Data collection, data analysis, proof reading, approved for publication.