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Measurement of Fetomaternal Outcome in Pregnant Patients with Sepsis

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ABSTRACT

Sepsis during pregnancy is a severe condition associated with significant maternal and fetal morbidity and mortality. It necessitates early identification and intervention to mitigate adverse outcomes. **Objective:** The study was aimed to evaluate and compare feto-maternal outcomes in pregnant patients with sepsis versus those without sepsis. **Methods:** This comparative cross-sectional study was conducted at Social Security Teaching Hospital, Lahore, from July 2023 to January 2024. A total of 240 pregnant women were included, with 120 diagnosed with sepsis and 120 without sepsis (control group). Obstetrically modified qSOFA and SOFA scores, were used for sepsis diagnosis. Data on vital signs, laboratory investigations, and fetal monitoring were collected and analyzed using SPSS version 24.0. Multivariate analysis was employed to adjust for potential confounders, and p-values of ≤ 0.05 were considered statistically significant. **Results:** The sepsis group exhibited significantly worse outcomes compared to the control group. The mean age was 27.8 ± 9.4 years, and mean Body mass index (BMI) was 25.3 ± 5.6. Maternal outcomes included 8.3 % oligohydramnios, 46.67% cesarean sections for non-reassuring fetal profiles, and 15 % preterm premature rupture of membranes. Maternal Intensive Care Unit ICU admission was necessary for 8.3% of patients, with a maternal mortality rate of 1.67%. Fetal outcomes included 5% intrauterine fetal growth restriction, 28.33% small for gestational age, 3.3% stillbirth, and 53.33% neonatal ICU admissions. **Conclusions:** Sepsis in pregnancy significantly increases the risk of adverse feto-maternal outcomes, including preterm birth, fetal distress, intrauterine growth restriction, and neonatal complications. Early detection and aggressive management are crucial to improving outcomes.

INTRODUCTION

Sepsis during pregnancy is a serious condition that can lead to significant maternal and fetal morbidity and mortality. It is the third leading cause of maternal death worldwide and treated as medical emergency [1]. The physical changes that occur during pregnancy could hide the symptoms of sepsis; thus, making it hard to diagnose. The main factors that cause sepsis at this stage include; dengue fever at 24.3%, while 14.4% have hepatitis E, another 12.2% suffer from Urinary Tract Infections (UTIs) [2]. Sepsis increases risks for multiple organ dysfunctions like Acute Respiratory Distress Syndrome (ARDS), Acute Renal Failure (ARF), and Disseminated Intravascular Coagulation (DIC) among pregnant women. This condition can also lead to preeclampsia and eclampsia thus worsening the overall health conditions of expectant mothers [3]. Diagnosis of sepsis in pregnant women is complicated by the physiological changes of pregnancy that can obscure typical sepsis indicators. The adaptation of the Sepsis-3 criteria to the obstetric population is still under debate. Key indicators include maternal tachycardia, fever, elevated white blood cell count, and hypotension, though these signs must be interpreted cautiously in the

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context of pregnancy [4]. Maternal sepsis is associated with an almost threefold risk of preterm delivery leading to complications for the newborn, including respiratory distress and developmental challenges. Studies have also shown a six- to eightfold increased risk of perinatal mortality in pregnancies complicated by maternal sepsis [5]. Maternal sepsis can affect placental function, leading to fetal growth restriction and babies born small for their gestational age [6]. Sepsis-related complications may necessitate cesarean delivery due to non-reassuring fetal status or intolerance of labor. Surgical delivery can have implications for both mother and baby. The combination of prematurity, low birth weight and potential neonatal sepsis contributes to this increased risk. Studies indicate neonatal mortality rates can be as high as 43.8% in cases of severe maternal sepsis [7]. Signs show that surviving infants may exhibit long-term neurodevelopmental problems following maternal sepsis. These could be among other things; -mental retardation, muscle weakness or even conduct issues. The causes are usually several hence assumed to be caused by, the baby's brain being infected directly and causing inflammation or even delivery before term [8]. The timing and mode of delivery in septic pregnancies are critical decisions influenced by gestational age, maternal condition, and fetal well-being. In cases of severe sepsis or septic shock, early delivery may be necessary to improve maternal outcomes, even if it results in preterm birth. The mode of delivery should be individualized, with cesarean delivery considered in cases of maternal instability or fetal distress [9]. Prompt administration of broad-spectrum antibiotics is critical in the management of sepsis in pregnancy. Empirical antibiotic therapy should be initiated within the first hour of recognition of sepsis, followed by adjustment based on culture results. Commonly used antibiotics include ceftriaxone, ampicillin, and metronidazole, tailored to cover common pathogens like Group B Streptococcus, Escherichia coli, and anaerobes. Intensive supportive care is essential for managing sepsis in pregnant women [10]. This includes fluid resuscitation, vasopressors for hemodynamic support, and oxygen therapy to maintain adequate oxygenation). Early involvement of a multidisciplinary team, including obstetricians, intensivists, and neonatologists, is crucial for optimal outcomes. Although there have been many studies on sepsis among overall populations, research focused on pregnancy is scanty when considering mother's and baby's fate as well as childbirth. There is insufficiently detailed data in literature about how the beginning of sepsis at different times during gestation can lead to different results, and how severe sepsis could be delivered [11]. Very little research has been conducted on preventive sepsis strategies in pregnancy. It is important to have studies that concentrate on the detection of threats as well as methods of prevention like immunization, preventive antibiotics and community based programs. Ethnic and economic factors' role in the rate and consequences of sepsis during pregnancy is still not clear [12].

The study was aimed to assess the impact of maternal sepsis on fetal health and development, as well as to determine the prevalence of adverse fetal outcomes associated with maternal sepsis. Additionally, the study seeks to identify potential risk factors that contribute to poor fetal outcomes in pregnancies complicated by sepsis. This research will provide valuable insights into the consequences of sepsis during pregnancy and help inform strategies for early detection, intervention, and management to improve both maternal and fetal outcomes.

METHODS

This was a comparative cross-sectional analysis conducted at Social Security Teaching Hospital, Lahore, from July 2023 to January 2024, following approval from the ethical review committee (Ref: 07/23). The primary objective was to evaluate and compare feto-maternal outcomes in pregnant patients diagnosed with sepsis from those without sepsis.

The sample size was determined using the following formula for comparing two proportions:

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 \times [p1(1-p1) + p2(1-p2)]}{(p1-p2)^2}$$

- Where:
- n = required sample size for each group
- $Z_{\alpha/2}$= Z value (the critical value) corresponding to a significance level of 0.05 (1.96 for a two-tailed test)
- Zβ= Z value corresponding to a power of 80 % (0.84)
- p1= expected proportion in the sepsis group (e.g., prevalence of sepsis-related outcomes)
- p2= expected proportion in the control group
- p1–p2= expected effect size or difference between the two groups

Assuming a prevalence of sepsis of 10% in the target population and an anticipated effect size (p1 – p2 p_ 1 – p _ 2p1– p2) of 0.2 for key maternal and fetal outcomes, the formula was applied to calculate the required sample size. The calculations were performed using standard statistical software, resulting in a need for 120 patients in each group to ensure adequate power. A multistage sampling technique was employed to select participants. Initially, all pregnant women (either singleton or multiple gestations) admitted to the Department of Obstetrics and Gynecology during the study period were screened for eligibility based on predefined inclusion and exclusion criteria. The sepsis group was composed of patients diagnosed with sepsis based on obstetrically modified quick Sequential Organ

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Failure Assessment (qSOFA) and Sequential Organ Failure Assessment (SOFA) scores, validated for use in the target population. The control group included pregnant women without any sepsis diagnosis, matched by age, parity, and gestational age. This approach ensured that the control group was comparable to the sepsis group in terms of key baseline characteristics, reducing potential confounding factors. The sample size was calculated 240 participants, with 120 patients in each group. A power analysis was conducted to detect significant differences in maternal and fetal outcomes between groups, with a 95% confidence interval and 80% power. A multistage sampling technique was employed. Participants included in the sepsis group were those diagnosed with sepsis during pregnancy, confirmed by obstetrically modified qSOFA and SOFA scores, and laboratory investigations. Exclusion criteria for both groups included pre-existing medical conditions known to affect fetal outcomes (e.g., hypertension, diabetes mellitus), gestational trophoblastic diseases, other rare pregnancy complications unrelated to sepsis, elective termination of pregnancy, or intrauterine fetal demise before the diagnosis of sepsis. Informed consent was obtained from all willing participants before enrollment. Baseline demographics, including age, gestational age, parity, medical history, and obstetric history, were recorded. Clinical parameters, including vital signs, complete blood count, blood culture results, and fetal monitoring data such as fetal heart rate, were documented for both groups. The obstetrically modified qSOFA and SOFA scores were used to diagnose sepsis, incorporating specific parameters adjusted for pregnancy. These scores have been validated in the target population through a prior pilot study to ensure accuracy and reliability in this cohort. Primary outcomes included fetal growth restriction, oligohydramnios, hypertensive disorders of pregnancy, cesarean delivery for non-reassuring fetal status or labor intolerance, infants born small for gestational age, and stillbirth. Secondary outcomes encompassed individual components of placental dysfunction, as well as other maternal and neonatal complications. To address potential confounders, multivariate analysis techniques were applied, adjusting for variables such as maternal age, parity, pre-existing medical conditions, and gestational age at diagnosis. Data were entered and analyzed using SPSS version 24.0. Descriptive statistics, including means, standard deviations, and percentages, were calculated. Inferential statistics, including chi-square tests, t-tests, and multivariate logistic regression, were used to assess associations between sepsis and maternal and fetal outcomes, comparing the sepsis group with the control group. p-values of ≤0.05 were considered statistically significant.

RESULTS

In this cross-sectional study, 240 pregnant patients were evaluated, with 120 diagnosed with sepsis (sepsis group) and 120 without sepsis (control group) to measure and compare maternal and fetal outcomes. The clinical parameters, including vital signs, laboratory investigations, and fetal monitoring data, were thoroughly documented and analyzed. The mean age of the participants in the sepsis group was 27.8 ± 9.4 years, while in the control group, it was 28.1 ± 8.9 years (p = 0.71). The mean Body Mass Index (BMI) was 25.3 ± 5.6 in the sepsis group and 24.8 ± 5.4 in the control group (p = 0.43). The mean gestational age at presentation was 33.2 ± 4.2 weeks in the sepsis group and 34.1 ± 3.8 weeks in the control group (p = 0.12) (Table 1).

Table 1: Characteristics of Study Population

Variables	Sepsis Group (n = 120)	Control Group (n = 120)	p - value
Age (Mean ± SD) (Years)	27.8 ± 9.42	28.1 ± 8.9	0.71
BMI	5.3 ± 5.6	24.8 ± 5.4	0.43
Gestational Age at Presentation (Mean ± SD) (Weeks)	33.2 ± 4.2	34.1 ± 3.8	0.12
Gestational Diabetes	18 (15%)	10 (8.3%)	0.09
Pregnancy-Induced Hypertension	24 (20%)	16 (13.3%)	0.13

The average heart rate in the sepsis group was 105 ± 15 beats per minute, the mean systolic blood pressure was 112 ± 10 mmHg, and the average temperature was 38.5°C ± 0.8°C. In the control group, the average heart rate was 80 ± 10 beats per minute, the mean systolic blood pressure was 120 ± 8 mmHg, and the average temperature was 36.8°C ± 0.5°C. Laboratory investigations revealed that the mean white blood cell count was significantly elevated in the sepsis group at 15,000 ± 5,000/mm^3 compared to 8,000 ± 3,000/mm^3 in the control group (p < 0.01). Hemoglobin levels were slightly lower in the sepsis group (10.5 ± 1.2 g/dL) compared to the control group (11.8 ± 1.0 g/dL) (p = 0.02). Positive blood cultures were found in 30 % (n = 36) of the sepsis group, while no positive cultures were observed in the control group. Elevated C-reactive Protein (CRP) levels were observed in 65 % (n = 78) of the sepsis group compared to 10 % (n = 12) in the control group (p < 0.01). Abnormal fetal heart rate patterns were observed in 45% (n = 54) of the sepsis group, compared to 12% (n = 14) in the control group (p < 0.01). Reduced fetal movements were reported in 25 % (n = 30) of the sepsis group, compared to 5% (n = 6) in the control group (p < 0.01) (Table 2).

Table 2: Baseline Characteristics and Clinical Parameters

Parameter	Sepsis Group Mean ± SD / n (%)	Control Group Mean ± SD / n (%)	p - value
Age (years)	27.8 ± 9.42	28.1 ± 8.9	0.71
BMI	5.3 ± 5.63	24.8 ± 5.4	0.43
Gestational Age at Presentation (weeks)	3.2 ± 4.2	34.1 ± 3.8	0.12
Heart Rate (bpm)	105 ± 15	80 ± 10	<0.01
Systolic Blood Pressure (mmHg)	112 ± 10	120 ± 8	<0.01

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Temperature (°C)	38.5 ± 0.8	36.8 ± 0.5	<0.01
WBC Count (x10^3/mm^3)	15,000 ± 5,000	8,000 ± 3,000	<0.01
Hemoglobin (g/dL)	10.5 ± 1.2	11.8 ± 1.0	0.02
Positive Blood Culture	36 (30%)	0 (0%)	N/A
Elevated CRP	78 (65%)	12 (10%)	<0.01
Abnormal Fetal Heart Rate	54 (45%)	14 (12%)	<0.01
Reduced Fetal Movements	30 (25%)	6 (5%)	<0.01

Among maternal outcomes, 8.3% (n = 10) in the sepsis group experienced oligohydramnios compared to 3.3% (n = 4) in the control group (p = 0.07). Cesarean sections due to non-reassuring fetal profiles were more common in the sepsis group (46.67%, n = 56) compared to the control group (28.33%, n = 34) (p = 0.01). Preterm premature rupture of membranes occurred in 15% (n = 18) of cases in the sepsis group compared to 8.3% (n = 10) in the control group (p = 0.11). Intra-amniotic infections were reported in 11.67% (n = 14) of patients in the sepsis group, while none were observed in the control group (p<0.01). Additionally, postpartum hemorrhage was more common in the sepsis group (35%, n = 42) compared to the control group (13.3%, n = 16) (p < 0.01), and postpartum infections occurred in 3.3% (n = 4) of patients in the sepsis group compared to none in the control group (p=0.04). Maternal ICU admission at delivery was necessary for 8.3% (n = 10) of patients in the sepsis group compared to 1.67% (n = 2) in the control group (p = 0.02), and maternal mortality was reported in 1.67% (n = 2) of cases in the sepsis group, with no cases in the control group (p=0.15). Significant differences in maternal and fetal outcomes were observed between the two groups (Table 3).

Table 3: Maternal and Fetal Outcomes in Sepsis During Pregnancy

Variables	Sepsis Group (n = 120)	Control Group (n = 120)	p - value
Maternal Outcomes			
Oligohydramnios	10 (8.3%)	4 (3.3%)	0.07
Cesarean Section Due to Non-Reassuring Fetal Profile	56 (46.67%)	34 (28.33%)	0.01
Preterm Premature Rupture of Membranes	18 (15%)	10 (8.3%)	0.11
Intra-Amniotic Infections	14 (11.67%)	0 (0%)	<0.01
Postpartum Hemorrhage	42 (35%)	16 (13.3%)	<0.01
Postpartum Infections	4 (3.3%)	0 (0%)	0.04
Maternal ICU Admission at Delivery	10 (8.3%)	2 (1.67%)	0.02
Maternal Mortality	2 (1.67%)	0 (0%)	0.15
Fetal Outcomes			
Intrauterine Fetal Growth Restriction	6 (5%)	2 (1.67%)	0.14
Small for Gestational Age	34 (28.33%)	20 (16.67%)	0.04
Stillbirth	4 (3.3%)	2 (1.67%)	0.41
Preterm Birth			
<34 Weeks	32 (26.67%)	20 (16.67%)	0.02
34-37 Weeks	22 (18.33%)	10 (8.3%)	0.05
Neonatal ICU Admissions	64 (53.33%)	32 (26.67%)	<0.01
5 Min Apgar Score <7	18 (15%)	10 (8.3%)	0.12
Fetal Mortality	4 (3.3%)	2 (1.67%)	0.41

Intrauterine fetal growth restriction was observed in 5% (n = 6) of cases in the sepsis group compared to 1.67% (n = 2) in the control group (p = 0.14). Infants small for gestational age were more common in the sepsis group (28.33%, n = 34) compared to the control group (16.67%, n = 20) (p = 0.04). The stillbirth rate was 3.3% (n = 4) in the sepsis group and 1.67% (n = 2) in the control group (p = 0.41). Preterm birth occurred more frequently in the sepsis group, with 26.67% (n = 32) before 34 weeks (p = 0.02) and 18.33% (n = 22) between 34 and 37 weeks (p = 0.05), compared to 16.67% (n = 20) and 8.3% (n = 10) in the control group, respectively. Neonatal ICU admissions were required for 53.33% (n = 64) of newborns in the sepsis group compared to 26.67% (n = 32) in the control group (p < 0.01) and 15% (n = 18) had a 5-minute Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) score of less than 7 in the sepsis group compared to 8.3% (n = 10) in the control group (p = 0.12). Fetal mortality was 3.3% (n = 4) in the sepsis group and 1.67% (n = 2) in the control group (p = 0.41) (Table 4).

Table 4: Organ System Involvement and Severity of Infection

Variables	Sepsis Group (n = 120)
Organ System Involved	
Kidney	52 (43.33%)
Pulmonary	46 (38.33%)
Gastrointestinal	10 (8.3%)
Genital tract	14 (11.67%)
CNS	4 (3.3%)
Severity of Infection	
Antepartum ICU Admission	14 (11.67%)
qSOFA Score > 2	38 (31.67%)
Gestational Age at Sepsis	
0-24 Weeks	54 (45%)
>24 Weeks	66 (55%)

These findings highlight the significant maternal and fetal risks associated with sepsis during pregnancy and emphasize the importance of monitoring clinical parameters and comparing outcomes with those of non-septic pregnancies to better understand the impact of sepsis.

DISCUSSION

Severe immunological reaction to an infection that causes systemic inflammation throughout the body is a major health risk known as sepsis. This illness is frequently referred to as an infection-induced systemic inflammatory response syndrome (SIRS) [13]. Pneumonia is the most common infection in pregnant women that precedes sepsis, with diseases of the reproductive system coming in close second. Lung inflammation incidents seem to be more common during childbirth, but infections related to vaginal delivery or medical treatments frequently become more apparent in the postoperative period [14]. Septic shock usually develops from Streptococcus species infections more quickly than from infections caused by

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other bacteria [15]. Thus, in order to reduce sepsis-related maternal mortality, it is critical to quickly diagnose and treat group A streptococcal infection. Particularly after giving birth, postpartum individuals show a noticeably higher risk of contracting these diseases than do non-pregnant individuals [16, 17]. The study elucidates the significant impact of sepsis on both maternal and fetal outcomes in pregnancy, with multiple organ systems being affected, high severity of infection, and critical timing of onset. The study further demonstrates significant maternal outcomes associated with sepsis. Oligohydramnios was observed in 8.3% of cases, and cesarean sections due to non-reassuring fetal profiles were performed in 46.67% of patients. Preterm premature rupture of membranes occurred in 15% of cases, intra-amniotic infections in 11.67%, post-partum hemorrhage in 35%, and post-partum infections in 3.3%. Additionally, 8.3% of patients required maternal ICU admission at delivery, and maternal mortality was reported in 1.67% of cases. In 12% of obstetric patients, sepsis results in respiratory failure that necessitates intubation [18]. 17 Pregnancy-related complications associated with this infection include atrial fibrillation, pneumothorax, and pericardial tamponade (4%) [19]. These findings underscore the severe impact of sepsis on maternal health, leading to complications that necessitate advanced medical interventions and increase the risk of mortality [20]. Fetal outcomes are equally concerning, with intrauterine fetal growth restriction observed in 5% of cases, and 28.33% of newborns being small for gestational age. The stillbirth rate was 3.3%, and preterm birth occurred in 26.67% of cases before 34 weeks and in 18.33% between 34 and 37 weeks. Neonatal ICU admissions were required for 53.33% of newborns, and 15% had a 5-minute APGAR score of less than 7. Fetal mortality was 3.3%. These statistics indicate a high burden of adverse fetal outcomes in pregnancies complicated by sepsis, highlighting the need for vigilant prenatal care and early intervention to mitigate risks and consistent with the findings of previous work [21]. These perinatal correlates with the findings of another study that stated 11.9% small for gestational age births, 5.1% cases of preterm premature rupture of membranes, 33.9% cesarean deliveries and 23.7% cases of post-partum hemorrhages due to sepsis in pregnancy [22]. The dysregulated host response to maternal infection during sepsis significantly impacts placental development and function, resulting in poor perinatal outcomes. In case a pregnant woman gets sepsis, this results from a broken mechanism of the body that fights immunity against attacks and leads to SIRS. The volatility of inflammatory cytokines like TNF-alpha, IL-1, and IL-6 during sepsis might cause inflammation in the placenta. Sepsis also causes malfunctioning endothelial cells and abnormal blood clotting thus interfering with normal blood flow within the placental blood vessels [23]. When inflammation and reduced blood circulation are combined, placental hypoxia and oxidative stress can occur, which further damage its tissues and impair its functionality, thus leading to adverse fetal outcomes. The results of this paper could support the development of local-driven clinical guidelines on the management of sepsis in pregnancy which can help healthcare policymakers formulate policies aimed at minimizing the occurrence as well as enhancing management of sepsis in pregnancy [24]. Current knowledge and practice gaps were identified in the study, thus creating more scope for researching innovative diagnostic tools as well as management techniques on how to treat sepsis during pregnancies. Differences in the management of sepsis and pregnancy care can introduce variability that affects outcomes.

CONCLUSIONS

This study underscores the severity of sepsis as a significant risk factor for adverse fetal outcomes, including preterm birth, fetal distress, intrauterine growth restriction, and neonatal complications. These findings emphasize the importance of early recognition and prompt management of sepsis in pregnant women to mitigate the potential adverse effects on fetal well-being.

Authors Contribution

Conceptualization: ZEH, AJ, SJ, MA, UA, NS
Methodology: DC
Formal analysis: CR, DC
Writing-review and editing: ME

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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