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Original Research Article

Maternal sepsis- an audit in a tertiary care center in South India

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ABSTRACT

Background: Objective of this study was to audit the cases of maternal sepsis and analyze their maternal and fetal outcomes.
Methods: A retrospective analysis of cases of maternal sepsis was undertaken for one year. Cases were taken as infection with fever, tachycardia, tachypnea, low oxygen saturation, high or low white blood counts and clinical or laboratory evidence of organ dysfunction and were analyzed. Demographic profile, gestational age at the time of diagnosis, organisms & their sources of infection was noted. Maternal outcomes of abortion, preterm delivery, need for intensive care unit (ICU) / high dependency unit (HDU) stay, blood and blood products, surgical interventions for the control of infection, culture-positive rate, source of organism, antibiotic usage and maternal mortality were analyzed. Fetal outcomes of early fetal demise, preterm birth, intrauterine death, stillbirth and term birth were studied.
Results: There were a total of 2327 deliveries, with 2333 live births during the study period. Twenty-two cases were diagnosed with sepsis, of which 17 survived, and five died. The incidence of maternal sepsis was 9.4/1000 live births & maternal deaths were 22.7%. Ninety percent were in the age group of 21-39 years, 68% were referred, 59% were post-delivery. Fifty nine percent of women who survived, and none of the women who died had medical co-morbidities. Respiratory tract followed by genitourinary tract were the most common source of infection, though culture was negative in 54.5% of the cases. The organisms grown were varied, with Escherichia coli (3/10) contributing to 30% of the culture positive cases. Spontaneous abortion and preterm delivery were 18% each, 36% required surgical intervention, 81% required ICU and 64.7% HDU stay. Seventy-seven had live birth.
Conclusions: Maternal sepsis is an evolving preventable health burden. Early recognition requires a high index of clinical suspicion, even in the absence of risk factors. Mortality to morbidity ratio is very high in maternal sepsis. The timing of sepsis determines the fetal outcomes.

Keywords: Maternal sepsis, Septic shock, Organ dysfunction, Maternal mortality, Sequential organ failure assessment score

INTRODUCTION

Sepsis is a growing health problem in both developed and developing countries. It is the third cause of maternal mortality worldwide.[1] The global prevalence of maternal sepsis is estimated to be 4.4% among live births. The incidence is found to be 9-49 per 100000 deliveries in high-income countries.[2] In the UK, sepsis has emerged as a direct cause of maternal death.[3] The US data states that maternal sepsis complicates 4-10 per 10000 live births.[4,5] Though the data from low and low middle-income countries are lacking, sepsis accounts for 1 in 10 maternal deaths globally.[6,7] This increasing trend in the rise of maternal sepsis cases over the past decade is a cause for

concern in terms of the morbidity, economic and financial burden associated with this highly preventable cause.[8]

Maternal sepsis is a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion, or postpartum period.[9] In 2015-2016, there was a third consensus conference held by specialists in the field, who considered sepsis a syndrome with no diagnostic test validated so far. But they proposed a criteria to analyze the organ dysfunction included in the definition objectively, the Severe organ failure assessment score (SOFA) which incorporated Glasgow Coma Scale (GCS), oxygenation, mean arterial blood pressure, platelet count, bilirubin levels, and renal measurement or the quick SOFA which includes altered mentation, respiratory rate >21 breaths/ min and or a systolic blood pressure <101 mmhg.[10] Unfortunately, these criteria have been standardized for adult sepsis, with pregnancy being an exception. The physiological changes which occur during pregnancy and puerperium make it imperative to apply certain modifications to the above-said criteria and define a new set of algorithms for pregnancy and puerperium uniquely. Further validation studies need to be done on these new set of criteria. Nevertheless, the WHO, in conjunction with the expert consultants, concluded that the criteria for identification of maternal sepsis should be based on the suspicion of or confirmed infection with signs of mild to moderate organ dysfunction like tachycardia, tachypnoea, low blood pressure, altered mental status and reduced urine output.[9] We collected the data on those pregnant and postpartum women in whom there was a high index of suspicion of infection with clinical signs as described above. Laboratory investigations of organ dysfunction with signs of infection were also included.

Ours is a tertiary care setup that caters to 21 districts with a daily outpatient strength of 3000 patients for various specialties with an average of 200 inpatient admissions. In our obstetrics and gynecology unit, we have an average of 2500 deliveries per year, the majority being in high-risk populations. However, both high risk and low-risk pregnancies are managed in the setup. We have intensive care units, high dependency units, and blood bank facilities at our disposal. We have a completely dedicated high dependency unit. High risk and complicated referrals are managed daily. As we get a significant part of referral from in and around areas and have the facilities to manage them, we have audited maternal sepsis cases for one year.

Aims and objectives

Aim and objective of this study was to to audit the cases of maternal sepsis and analyze their maternal and fetal outcomes.

METHODS

All the cases from June 1st, 2015 to May 30th, 2016, were collected in the department of Obstetrics and Gynecology, Kasturba Medical College, Manipal. Maternal sepsis included all antenatal, postnatal and post abortal women diagnosed with sepsis. The identification of cases was made retrospectively. All the cases of infection with fever, tachycardia, tachypnea, low oxygen saturation, high or low white blood counts and clinical or laboratory evidence of organ dysfunction were analyzed. Abnormal lab parameters like raising levels of urea and creatinine, abnormal liver function test, and the persistence of poor saturation despite oxygenation and therefore requiring ventilation, poor mentation was considered signs of organ dysfunction. The presence of hypotension with any of these parameters was taken that the patient was in septic shock and managed according to the standard protocol. Both booked and referred cases were analyzed. The cases were considered to be booked under us if they had three or more antenatal visits at our hospital.[11]

In the identified cases, booking status, demographic details like age, parity index, gestational age at the time of diagnosis, body mass index (BMI), medical co-morbidities, obstetric risk factors, organisms and their sources of infection, culture-positive rate and commonly used antibiotics was noted. Maternal outcomes of abortion, preterm delivery, need for ICU/ HDU stay, blood and blood products, surgical intervention for the control of infection, or any other interventions and maternal mortality were analyzed. Fetal outcomes of early fetal demise, preterm birth, intrauterine death, stillbirth & term birth were studied.

RESULTS

There were a total of 2327 deliveries, with 2333 live births during the study period. Twenty-two cases were diagnosed with sepsis, of which 17 survived, and five died during the study period. (Table 1) shows the demographic profile of women with sepsis.

Table 1: Demographic profile of women with maternal sepsis.

Demographic characteristics	Survived (n=17)	Dead (n=5)
	N (%)	N (%)
Age in years		
<20	01 (5.8)	0
21-39	15 (88.4)	05 (100)
>40	01 (5.8)	0

Continued.

Demographic characteristics	Survived (n=17)	Dead (n=5)
	N (%)	N (%)
Parity		
Primipara	10 (58.8)	04 (80)
Multipara	07 (41.2)	01 (20)
Booking status		
Referred	10 (58.8)	05 (100)
Booked	07 (41.2)	00
BMI		
Underweight	01 (5.8)	00
Normal	15 (88.4)	00
Obese	01 (5.8)	00
Medical Co-morbidities		
None	08 (47.2)	05(100)
Anemia	04 (23.5)	00
Diabetes	02 (11.7)	00
Hypertension	03 (17.6)	00
Obstetric risk factors		
Conception by artificial reproductive techniques	02 (11.7)	00
Multiple gestations	03 (17.6)	00
PPROM/PROM	02 (11.7)	01 (20)
Timing of diagnosis of sepsis		
Antenatal	09 (52.9)	00
1st trimester	5.8	00
2nd trimester	41.1	
3rd trimester	41.1	
Post-abortion	01 (5.8)	1 (20)
Postpartum	07 (41.3)	4 (80)
Range of total duration of hospital stay (in days)	5-30	1-30

Table 2: Organisms isolated with the source of infection in cases of maternal sepsis.

Organisms isolated	Source of infectivity	Survived (n=17)	Dead (n=5)
Culture sterile	-	8	4
Candida	Blood	0	1
E. Coli	In urine/blood through urinary tract/GIT/ gluteal abscess	3	0
Enterococcus fecalis	Stool & endocervical swab/urine & blood	2	0
Streptococcus pneumonia	Sputum (Respiratory tract)	1	0
Acinetobacter* and *Streptococcus	Endotracheal tube (Respiratory tract) & blood	1	0
Tuberculosis	Lung, causing empyema	1	0
Dengue	Blood	1	0

Among the maternal sepsis cases, one was following abortion, two aborted after antenatal diagnosis of sepsis in them. Though 13 cases had none of the medical co-morbidities, when analyzed further, we found that many of them had obstetric risk factors like multiple pregnancies, use of artificial reproductive techniques, preterm premature rupture of membranes, and also the process of abortion itself. Here the classification of BMI by WHO was considered.[12]

(Table 2) depicts the organism isolated & the possible sources for infectivity. Each case could have multiple sources of infection at the time of diagnosis as some were

in multiple organ dysfunction with septic shock, so had disseminated infection.

(Table 3) shows the maternal outcomes in women with sepsis. An important fact worth noting is that sepsis has contributed to 22.7% of maternal mortality.

Table 3: Maternal outcomes in women with sepsis.

Maternal outcomes (n)	Survived (n=17)	Dead (n=5)
	N (%)	N (%)
Spontaneous abortion	03 (17.6)	1 (20)
Preterm delivery	04 (23.5)	0
Needing surgical intervention (re-laparotomy debridement/evacuation)	05 (17.6)	03(60)
HDU stay	11 (64.7)	0
ICU stay	13 (76.4)	5 (100)
Mode of delivery		
Vaginal delivery	05	1 (20)
Instrumental delivery	-	1 (20)
Cesarean delivery	10	2 (40)

Table 4: Fetal outcomes in women with sepsis.

Fetal outcomes	Survived (n=17)	Dead (n=5)
	N (%)	N (%)
Live born, term	08 (47.2)	04(80)
Live born, preterm	05 (29.4)	0
Abortion	03 (17.6)	1(20)
Stillbirth	01 (5.8)	0

(Table 4) shows the fetal outcomes in mothers with maternal sepsis. The majority of the babies had good neonatal outcome as the timing of sepsis in 11 women was postpartum. Two of the patients had an abortion following sepsis, and one had sepsis following an abortion.

DISCUSSION

Currently, though sepsis has been identified as a growing health problem with high mortality, lack of data on the incidence, epidemiology, and outcomes in the pregnant population, especially in the lower-income and lower-middle-income countries, makes comparison and estimation of the burden difficult. Moreover, this lack of data makes it imperative to research this subject to build a foundation for further studies. So, a one-year data on maternal sepsis was collected and analyzed.

In this study, the demographic profile of the women who survived and those who died of sepsis, show that primiparous postpartum women were at a higher risk similar to the literature available.[8] Nevertheless, one study showed a higher predisposition in multiparous women.[13] Though extremities of age, BMI>30, medical co-morbidities like anemia & diabetes increase the risk of sepsis, in our study, the numbers were too small and there is a need of greater sample to prove the association. In the group of patients who died, BMI could not be calculated as they were very sick on arrival, but all looked to be either normal or in the lower category. Similarly, to establish an association of obstetric risk factors like conception by artificial reproductive techniques, multiple pregnancies, preterm prelabor rupture of membranes & induction of labor, a more extensive data is needed though an association has been observed.[14,15] In our study, there were other contributory factors like placenta previa, multiple gestations, which increased the risk.

The culture was negative in (12/22) that is 54.5%, and there was no specific source identified in them, which was more than found in the literature in which states no source was identified in 30% of the cases.[16] The reason for this might be due to the high number of referrals who were already on antibiotics which might have contributed to the high culture sterile rate. The sources are commonly nonpelvic in the antenatal period & usually pelvic in the postnatal period similar to our study.[17] Respiratory tract was the most common source in the antenatal period and genitourinary in the postnatal period. Escherichia coli was the more common organism grown, along with many organisms that varied and were inconsistent with the studies shown so far.[18-20] There was one case of dengue and tuberculosis, which could be infections exacerbated by the physiological changes in pregnancy or incidental infections in pregnancy.[7]

In the sepsis care bundle, initiation of broad-spectrum antibiotics within one hour of sepsis's suspicion of sepsis reduced the morbidity & mortality of sepsis.[21] As half of the cases were postnatal women who would have already received cephalosporins for cesarean delivery or amoxicillin for vaginal delivery as prophylaxis, according to the local protocol, the piperacillin-tazobactam combination was initiated, unless there was a suspicion of a specific organism perse. This antibiotic regimen was de-escalated, depending on culture and sensitivity reports. This is following the reviews of sepsis done so far.[22] A combination of piperacillin-tazobactam was chosen because of its broad range of activity and the fact that many of these women would have received antibiotic prophylaxis during the time of delivery, including third-generation cephalosporins /amoxicillin.[23,24] If the culture came negative, but the patient showed visible clinical improvement, then the same antibiotics were continued. If the patient continued to worsen, then clindamycin was started, and multiple attempts to get culture from a different source was made. There were two cases were colistin had to be used due to unresponsiveness/antibiotic resistance.

In our study, we had an incidence of 9.4 per 1000 live births of maternal sepsis, which contributed to 22.7% of

maternal mortality. This mortality rate is slightly higher than the data available, which states that genito-urinary tract sepsis contributes to 11% of maternal mortality.[1] If other infection sources are considered, which includes both genital and extragenital causes of sepsis, as we did here, then its contribution may be as high as 25-40% of maternal deaths worldwide.[25] This is a cause of concern as in many developing countries, the numbers are not caught in the data, and the true incidence might be still higher.

One more concern is the associated morbidity in the survivors, both for the mother and the fetus. In the mother, there is an increased risk of abortion, preterm labor (2.81fold increased risk), need for surgical interventions for either evacuation of products of conception following an abortion or abortion following sepsis or laparotomy for removal of the source of sepsis, admission in the high dependency/ intensive care unit, prolonged hospital admission and repeated admissions.[15,20] Besides, the fetus is at higher risk of miscarriage, stillbirth & premature birth. Studies quote a combined stillbirth rate of 25-50% in both the high income & lower-middle-income countries. However, in this study, there was only 1 stillbirth, which accounted for a 5% rate. This low rate is probably because the timings of sepsis were in the third trimester only in 7 patients. However, if we consider 1 of these seven women to have a stillbirth, this accounts to ~ 28%, which is similar to the numbers in the studies done.[26] As can be seen, there was a twofold risk in the incidence of cesarean delivery when sepsis was diagnosed antenatally. Also, cesarean delivery increased the risk of puerperal sepsis. This is similar to a study done by Kankuri et al which states that the risk of cesarean delivery increases by 2.6-fold in antepartum sepsis and the risk of sepsis is 3.2 times higher in postpartum women who have delivered by cesarean delivery.[27]

Though it is a preventable cause, major deterrents have stood in the pathway of appropriate management of sepsis. However, the recent advancement of a uniform definition of sepsis in adults has laid a foundation for a definition by WHO on maternal sepsis, which has paved a pathway for advanced research on maternal sepsis in a standardized way comparable between countries. There is a need to validate the SOFA criteria in pregnant women and the reliability of procalcitonin and other inflammatory markers in pregnancy and puerperium. Early recognition of sepsis with a high index of clinical suspicion, early initiation of sepsis care bundle that includes administration of appropriate broad-spectrum antibiotics, de-escalation of antibiotics on the availability of culture and sensitivity report are the ways we can tackle sepsis successfully & prevent antibiotic resistance.[28-30] Awareness among clinicians of sepsis might lead to early diagnosis and effective management of sepsis.[6,31] A long road lies ahead in this battle against maternal sepsis due to the ever-evolving and new data available. Antibiotic stewardship can help in the judicious use of antibiotics and combat antibiotic resistance.

The primary limitations are the retrospective nature of the study and the small sample size. Collection of information like the women's socioeconomic status, the timing of initiation of antibiotics/ intravenous fluids was not possible in most cases.

CONCLUSION

Maternal sepsis is a growing preventable health burden on which further research needs to be done by more pros pective studies. The WHO definition and identification of maternal sepsis is a valid, practical, and standardized way for further research. Early recognition requires a high index of clinical suspicion, even in the absence of risk factors. Mortality to morbidity ratio is very high in maternal sepsis. The timing of sepsis determines the fetal outcomes.

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