# Obstetric Sepsis: Changing Trends in the Management, Controversies and the Way Forward

**Hiralal Konar**

Maternal sepsis is a life threatening condition. It often ends with an organ dysfunction resulting from infection during pregnancy, child birth, post abortion or post partum period. Globally sepsis is the lead cause of maternal morbidity and mortality. Worldwide 25-40% of maternal deaths and 50% of perinatal deaths are due to sepsis.[1,2] Maternal mortality survey in India (2013), revealed, sepsis is the third important cause of maternal deaths.[3]

Sepsis has a complex pathophysiology. Physiological changes in pregnancy mimic the changes of sepsis, with this often there is delay in the diagnosis and initiation of management. Physiological changes in pregnancy affects almost all the body system mainly the cardiovascular, respiratory, renal, coagulation and the metabolic systems. These adaptations are designed to support the growth of the fetus. However these changes impair maternal defense capacity to respond against sepsis. There is upregulation of prostaglandins (PGE2) and Nitric Oxide (NO) due to high levels of estradiol in pregnancy. This causes abrupt development of maternal hypotension and organ dysfunction.[4]

Author's experience in the management of obstetric sepsis, started sincethe work at NRS Medical College hospital, Calcutta as the registrar. This institute has the very long term study over the years, in the management of septic abortion cases. One such study5from this Medical college Hospital (1993) revealed significant maternal deaths (15.6%) in cases with septic abortion. Visceral injury was present in 25% of cases.[2] Selective and timely surgical intervention, could bring down the death rate from 25% (1976) to 6.2%[6] (1990). All the cases of septic abortion were associated with severe type of polymicrobial infection. Presence of visceral injury made the control of sepsis very difficult. Initial management was the medical and surgical management was considered only at the late phase. Finally, it was changed to combinedapproach of medical and aggressive surgical as on priority. This change in practice established a significant improvement in survivaloutcome in such cases. This institute was pioneer to start the management of anaerobic organisms by metronidazole (Flagyl) rectally, as IV preparations were not available those days.[7]

Global Maternal Sepsis Study (GLOSS) WHO 2017, has developed strategies for prevention, early detection and effective management for women with sepsis in low and middle income countries (LMIC) and high income countries (HICS).[8] Sequential Organ Failure Assessment (SOFA) or Obstetrically modified qSOFA score allowed a rapid clinical assessment. Such a score > 2 is associated with high risk of mortality.[9] Other scoring system, modified early warning scores (MEWS) is also used as an important tool to identify an ill patient. Use of prophylactic antibiotic for prevention of sepsis (NICE) is introduced in most of the institutes.[10] Antibiotic resistance is a global problem. Overall, 10 million deaths are estimated globally by 2050 due to antibiotic resistance.11Identification of pathogen is commonly done by blood culture. It is positive in 20-40% of cases with severe sepsis. Moreover it is time consuming. Currently DNA sequencing of multiple pathogens and identification

Corresponding author : Hiralal Konar

of resistance genes from blood samples are possible. Matrix-assisted laser desorption / ionization (MALDI) to identify wide spectrum organism could be one. Different biomarkers of sepsis are used for assessment of severity of pathology. Commonly used parameters are: procalcitonin, serum lactate, C-reactive protein and others. Levels of serum lactate > 4 mm mol/L is associated with higher mortality (46%). Raised serum lactate indicates tissue hypoperfusion and hypoxia. Pathophysiology of sepsis is a complex one. Activation of pro inflammatory cytokines (IL-1,6.8.12.TNF) complement systems, coagulation system is evident. Release of biomediators like NO, CD4, cytotoxic cells, generation of immunological response and production of antibodies make the situation more complex.[12]

Control of sepsis with appropriate antimicrobial agents are essential. Clinicians need to think beyond the traditional concept of pathogens. Based on the current understanding therapy with immunoglobulin (IV Igs) are made as an adjuvant to antibiotics. IV Igs therapy found to improve the survival outcome of patients with sepsis. It improves endothelial dysfunction, hypotension and inhibits the pro inflammatory cytokines. Overall morbidity and mortality are reduced.

Incorporation of extracorporeal membrane oxygenation (ECMO) is found to improve the survival rate significantly (80%) in cases with septic shock associated with respiratory failure.[13] Levosimendan a new pressor drug has been observed to improve the hemodynamic profile and organ dysfunction. Vasopressors are needed for patients admitted in intensive care unit with severe shock. Commonly used drug is noradrenaline. Currently Levosimendan, has been found to improve the hemodynamic profile and organ function. It is found to be a noble inotropic drug with vasodilatory properties. Additionally it has anti inflammatory and anti oxidative properties against anerobic oxidative metabolism.

Controversies in management remain in many areas such as selection of antibiotics, initiation of intensive care management and optimum glycemic status. Pregnancy is a state of abnormal glycemic control with insulin resistance. Most intensivists consider a level of <180 mg/dl is optimum. Use of corticosteroids in the management of septic shock is a long term debate. Forty two such randomized control trials favored its use and reduction of maternal mortality. Many reviews stated that the quality of evidence was low. RCOG guidelines do not consider its use in sepsis.[14] Use of corticosteroids for fetal lung maturity, for women with asthma or connective tissue disorder need to be maintained with caution. Recent studies did not reveal any adverse effects on fetal outcome on repeated doses of corticosteroids.

Benefits of steroids as shown with several RCT. Corticosteroids have been used as an anti inflammatory agent for patients with systemic inflammatory response syndrome (SIRS) or with adrenal insufficiency. Other proposed advantages of corticosteroids are:

(a) stabilization of lysosomal membranes (b) Counteracts the anerobicoxidative metabolism (c) improves regional blood flow (micro circulation) (d) positive inotropic effect to the myocardium and as a vasopressor agent.

Current research opens the new horizon. Universal detection of genes (genomics), mRNA (transcriptomics), proteins (proteomics), and metabolites (metabolomics) in biological specimens (blood, urine, amniotic fluid, cervico vaginal fluid) is possible through 'Omic' technologies. It is being studied extensively in the present days.[15] Currently there is a shift to an individualized approach clinical care.It is done by studying the individual's biological response to the pathogens.[16]

Otherwise precision medicine is the way forward. Transnational research and clinical trials are expected to help the understanding of the pathogenesis of sepsis in pregnancy, labor and puerperium. Personalized medicine is the future health care.

## REFERENCE


1. Global Maternal Sepsis Study. Stop Sepsis Campaign. [https://srhr.org/sepsis/2019/01/08/2nd-world-sepsis-congress-maternal-and-neonatal-sepsissession/].
2. Goldenberg RL, McClure E, Saleem S, Reddy U. Infection-related stillbirths. Lancet 2010;375:1482–1490.
3. Konar Hiralal, Chakraborty AB. Maternal Mortality : A FOGSI study: 63(2):88:2013.
4. Antonucci E, Fiaccadori E, Donadello K, Taccone FS, Franchi F, Scoletta S. Myocardial depression in sepsis: from pathogenesis to clinical manifestations and treatment. J Crit Care 2014;29:500–511.
5. Konar Hiralal. Changing Trends in Septic Abortion: Jr. Obst. Gynec. India 43: 288: 1993.
6. Chakravorty B N, Gun KM, Das N. Jr. Obst. Gynec. India:26: 481:1976.
7. Dutta D C, Roy TK. Jr. Obst. Gynec. India 31: 738:1981.
8. Bonet M, Oladapo OT, Khan DN, Mathai M, Gulmezoglu AM. New WHO guidance on prevention and treatment of maternal peripartum infections. Lancet Glob Health 2015;3:e667–668.
9. Bowyer L, Robinson HL, Barrett H, et al. SOMANZ guidelines for the investigation and management sepsis in pregnancy. Aust NZ J ObstetGynaecol 2017;57:540–551.
10. National Institute for Health and Care Excellence. Sepsis: recognition, diagnosis and early management. NICE guideline 51. London: NICE; 2016 [https://www.nice.org.uk/guidance/ng51/resources/sepsis-recognition-diagnosis-and-early-management-1837508256709].
11. Cecconi M, Evans L, Levy M, Rhodes A. Sepsis and septic shock. Lancet 2018;392:75–87. 51 Knowles SJ, O'Sullivan NP, Meenan AM, Hanniffy R, Robson M. Maternal sepsis incidence, aetiology and outcome for mother and fetus: a prospective study. BJOG 2015;122:663–671.
12. Schulte W, Bernhagen J, Bucala R. Cytokines in sepsis: potent immunoregulators and potential therapeutic targets–an updated view. Mediators Inflflamm2013;2013:165974.
13. Sharma NS, Wille KM, Bellot SC, Diaz-Guzman E. Modern use of extracorporeal life support in pregnancy and postpartum. ASAIO J 2015;61:110–114.
14. Royal College of Obstetricians and Gynaecologists. Bacterial Sepsis following Pregnancy. Green-top Guideline No.64b. London: RCOG; 2012 [https:// www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg64b/].
15. Horgan RP, Kenny LC. 'Omic' technologies: genomics, transcriptomics, proteomics and metabolomics. The Obstetrician &Gynaecologist2011;13:189–195.
16. Hill S. Personalised Medicine Strategy. NHS England Blog 2015 [https:// www.england.nhs.uk/blog/sue-hill/].