

Here is the latest edition of the Sepsis Bulletin. The bulletin covers the latest information on sepsis and comes out fortnightly. Next edition is due 10 May 2019. Older editions are available as pdfs on the Keeping Up To Date library guide (http://libguides.bodleian.ox.ac.uk/Keeping_up_to_date)

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SEPSIS BULLETIN

26 April 2019

Neonatal, paediatric and maternal sepsis

[Sepsis calculator to support antibiotic stewardship in early-onset neonatal sepsis: a meta-analysis](#)

Rinawati R. et al.

Paediatrica Indonesiana, 01 December 2018, Vol.58(6), pp.286-97

Establishing a diagnosis of neonatal sepsis is difficult. As such, appropriate timing of antibiotic therapy remains the biggest challenge. As a consequence of non-definitive diagnoses, inappropriate antibiotic administration is common. Recently, a sepsis calculator to estimate risk of early-onset sepsis (EOS) based on both maternal risk factors and infants' clinical presentation was established. The new EOS risk estimation using a neonatal sepsis calculator is an easy, effective, and safe tool to improve appropriate antibiotic use and outcomes. This calculator is ready to be implemented in all levels of neonatal care units.

Adult sepsis (cont.)

[An administrative model for benchmarking hospitals on their 30-day sepsis mortality.](#)

Darby JL et al

BMC Health Serv Res. 2019 Apr 11;19(1):221.

Given the increased attention to sepsis at the population level there is a need to assess hospital performance in the care of sepsis patients using widely-available administrative data. The goal of this study was to develop an administrative risk-adjustment model suitable for profiling hospitals on their 30-day mortality rates for patients with sepsis. A novel claims-based risk-adjustment model demonstrated wide variation in risk-standardized 30-day sepsis mortality rates across hospitals. Individual hospitals' performance rankings were stable across years and after the addition of laboratory data. This model provides a robust way to rank hospitals on sepsis mortality while adjusting for patient risk.

[Early Blood Biomarkers to Improve Sepsis/Bacteremia Diagnostics in Pediatric Emergency Settings](#)

Tamelytè, E. et al

Medicina 2019

Sepsis is the leading cause of death in children worldwide. Early recognition and treatment are essential for preventing progression to lethal outcomes. CRP and Complete Blood Count (CBC) are the initial preferred tests to distinguish between bacterial and viral infections. Specific early diagnostic markers are still missing. Together with standard blood biomarkers, such as CRP, neutrophils, or platelets count, PLT/MPV is a promising biomarker for clinical practice to help discriminate between viral disease or sepsis/bacteremia in all children, especially in early onset of symptoms. NLR and MPV could support exclusion of sepsis/bacteremia in late arrival cases.

[Neonatal sepsis biomarkers: where are we now?](#)

Gilfillan M ; Bhandari V

Research and Reports in Neonatology, 01 March 2019, Vol.9, pp.9-20

Neonatal infections annually claim lives of 1.4 million neonates worldwide. Until now, there is no ideal diagnostic test for detecting sepsis and thus management of possible sepsis cases often depends on clinical algorithm leading to empirical treatment. This often results in unnecessary antibiotic use, which may lead to emergence of antibiotic resistance. Biomarkers have shown great promise in diagnosis of sepsis and guiding appropriate treatment of neonates. In this study, we conducted a literature review of existing biomarkers to analyze their status for use as a point-of-care diagnostic in developing countries. Extensive work is being performed to find the diagnostic and prognostic value of biomarkers. However, the methodologies and study design are highly variable. Despite numerous research papers on biomarkers, their use in clinical setting is limited to CRP. The methods for detection of biomarkers are far too advanced to be used at the community level where most of the babies are dying. It is important that a harmonized multi-site study is initiated to find a battery of biomarkers for diagnosis of neonatal infections.

[Quality of Life and 1-Year Survival in Patients With Early Septic Shock: Long-Term Follow-Up of the Australasian Resuscitation in Sepsis Evaluation Trial.](#)

Higgins AM, et al

Crit Care Med. 2019 Apr 8.

To examine long-term survival and quality of life of patients with early septic shock. In patients presenting to the emergency department with early septic shock, early goal-directed therapy compared with usual care did not reduce mortality nor improve health-related quality of life at either 6 or 12 months.

[Understanding Lactatemia in Human Sepsis: Potential Impact for Early Management.](#)

Gattinoni L, et al

Am J Respir Crit Care Med. 2019 Apr 15.

Hyperlactatemia in sepsis may derive from a prevalent impairment of oxygen supply/demand and/or oxygen utilization. Discriminating between these two mechanisms may be relevant for the early fluid resuscitation strategy. This study looks at understanding the relationship between central venous oxygen saturation (ScvO₂), lactate and base excess to better determine the origin of lactate. Hyperlactatemia is powerfully correlated with severity of sepsis and it is caused more frequently by impaired tissue oxygen utilization, rather than by impaired oxygen transport. Concomitant acidemia was only observed in the presence of renal dysfunction, as rapidly detected by alactic base excess. The current strategy of fluid resuscitation could be modified according to the origin of excess lactate.

[Epidemiology of qSOFA Criteria in Undifferentiated Patients and Association with Suspected Infection and Sepsis.](#)

Anand V et al

Chest. 2019 Apr 9. pii: S0012-3692(19)30821-9.

The role of Quick Sequential Organ Failure Assessment (qSOFA) criteria in sepsis screening and management is controversial, particularly as they were derived only in patients with suspected infection. We examined the epidemiology and prognostic value of qSOFA in undifferentiated patients. Only 1 in 3 patients who are

[Neutrophil extracellular traps \(NETs\) exacerbate severity of infant sepsis](#)

Colón, D.F. et al.

Critical Care, 01 April 2019, Vol.23(1), pp.1-13

Neutrophil extracellular traps (NETs) are innate defense mechanisms that are also implicated in the pathogenesis of organ dysfunction. However, the role of NETs in pediatric sepsis is unknown. This study reveals a hitherto unrecognized mechanism of pediatric sepsis susceptibility and suggests that NETs represents a potential target to improve clinical outcomes of sepsis.

[Diagnostic accuracy of interleukin-6 for early-onset sepsis in preterm neonates](#)

Chinedu, U. et al

The Journal of Maternal-Fetal & Neonatal Medicine, 09 April 2019, p.1-201

Early-onset sepsis (EOS) is a leading cause of morbidity and mortality among neonates. Yet, accurate diagnosis remains a major challenge in clinical routine. The combination of IL-6 with other perinatal factors can significantly increase specificity and sensitivity in the diagnosis of EOS. However, overall diagnostic accuracy cannot be notably improved as there is a tradeoff between sensitivity and specificity. Although these findings do not necessarily apply in clinical routine, they can be of substantial value in the assistance of individual decision making.

[Population-based study of early-onset neonatal sepsis in Canada.](#)

Sgro M. et al

Paediatr Child Health. 2019 May;24(2):e66-e73.

To determine the incidence, types of organisms and resistance patterns involved in early-onset neonatal sepsis in Canada. We identify a lower rate of early-onset neonatal sepsis than historically suggested, with differing dominant organisms based on gestational ages and other factors, as well as high rates of resistance especially among E coli cases.

qSOFA-positive on admission have suspected infection and 1 in 6 have sepsis. qSOFA also has low sensitivity for identifying suspected infection and sepsis and its prognostic significance is not specific to infection. More sensitive and specific tools for sepsis screening and risk-stratification are needed.

[Quick sepsis-related organ failure assessment score as a possible predictor for in-hospital adverse events in infective endocarditis.](#)

Tamura Y et al

Acute Med Surg. 2019 Feb 19;6(2):138-144.

Infective endocarditis (IE) can be life-threatening because of various associated adverse events. The quick Sepsis-related Organ Failure Assessment (qSOFA) score is a straightforward useful method for predicting in-hospital mortality in patients with suspected infections. However, few data exist regarding the clinical impact of the qSOFA score on predicting adverse events in IE during hospitalization. We studied the usefulness of qSOFA score for predicting in-hospital adverse events in patients with IE. These results showed that high qSOFA score was significantly associated with in-hospital adverse events in IE patients, although further prospective study is necessary to confirm our results.

[The Restrictive IV Fluid Trial in Severe Sepsis and Septic Shock \(RIFTS\): A Randomized Pilot Study.](#)

Corl KA et al

Crit Care Med. 2019 Apr 12

It is unclear if a low- or high-volume IV fluid resuscitation strategy is better for patients with severe sepsis and septic shock. This pilot study demonstrates that a restrictive resuscitation strategy can successfully reduce the amount of IV fluid administered to patients with severe sepsis and septic shock compared with usual care. Although limited by the sample size, we observed no increase in mortality, organ failure, or adverse events. These findings further support that a restrictive IV fluid strategy should be explored in a larger multicenter trial.

[Cardiovascular determinants of resuscitation from sepsis and septic shock.](#)

Guarracino F. et al

[Serum Level of Antithrombin III \(ATIII\) Could Serve as a Prognostic Biomarker in Neonatal Sepsis](#)

Samra N. et al

Fetal Pediatr Pathol. 2019 Mar 31:1-9

Neonatal sepsis syndrome continues to have a high morbidity and mortality rate despite the progress in neonatal intensive care. There is no single diagnostic test which can reliably diagnose sepsis in the newborn, beside blood culture. Antithrombin III may be one promising single marker for sepsis syndrome diagnosis and prognosis. Antithrombin III is lower in sepsis syndrome neonates and may be a useful biomarker in neonatal sepsis.

[Clinical features and antimicrobial susceptibility profiles of culture-proven neonatal sepsis in a tertiary children's hospital, 2013 to 2017.](#)

Li X. et al

Medicine (Baltimore). 2019 Mar;98(12):e14686.

Neonatal sepsis (NS) remains a major cause of morbidity and mortality in neonates, but data on the etiology and antibiotic susceptibility patterns of pathogens are limited. The aim of this study was to analyze the clinical characteristics, risk factors, and the antibiotic susceptibility patterns of pathogenic microbes associated with NS at a tertiary children's hospital in Shanghai, China. Most isolates of Gram-positive bacteria were sensitive to vancomycin, linezolid, minocycline and tigecycline, of which more than 90% were resistant to penicillin. Most isolates of Gram-negative bacteria were sensitive to amikacin and imipenem and resistant to ampicillin. Fungus was sensitive to antifungal agents. Better medical decisions, especially early detection and appropriate initial antimicrobial therapy can be made after understanding the different clinical features and pathogens of EONS and LONS.

[Immature to total neutrophil ratio as an early indicator of early neonatal sepsis.](#)

Saboohi E. et al

Pak J Med Sci. 2019 Jan-Feb;35(1):241-246.

Crit Care. 2019 Apr 15;23(1):118

We hypothesized that the cardiovascular responses to Surviving Sepsis Guidelines (SSG)-defined resuscitation are predictable based on the cardiovascular state. The cardiovascular response to SSG-based resuscitation is highly heterogeneous but predictable from pre-treatment measures of cardiovascular state.

[Implementation of guidelines for sepsis management in emergency departments: A systematic review.](#)

Sungkar Y, et al

Australas Emerg Care. 2018 Nov;21(4):111-120.

Timely, evidence-based emergency care for sepsis saves lives. The primary aim of this systematic review was to examine the effect of implementation of guidelines for the ED management of sepsis on time to antibiotic administration. Secondary aims were to examine changes in evidence-based sepsis care and patient outcomes. Implementation of local sepsis management guidelines in EDs improves the timeliness of processes of care and may improve patient outcomes.

[Knowledge and attitude towards identification of systemic inflammatory response syndrome \(SIRS\) and sepsis among emergency personnel in tertiary teaching hospital.](#)

Rahman N'A, et al

Australas Emerg Care. 2019 Mar;22(1):13-21.

An emergency department (ED) is often the first point of medical contact for sepsis patient, which plays an important role in early identification and management of high-risk septic patients. The present study was aim to evaluate emergency personnel's knowledge and attitude toward identification and management of systemic inflammatory response syndrome (SIRS) and sepsis. The emergency personnel demonstrated a moderate knowledge and neutral attitude toward identification and management of SIRS and sepsis. Therefore, the awareness and knowledge of SIRS and sepsis should be enhanced among emergency personnel in order to improve outcome.

[Targeting the Blood-Brain Barrier to Prevent Sepsis-Associated Cognitive Impairment.](#)

Neonatal septicemia is responsible for 1.5 to 2.0 million deaths/year in the under developed countries of the world. Pakistan is number three among these countries and accounts for 7% of global neonatal deaths. The objective of the study was to determine the role of simple hematological parameter, immature to total neutrophil ratio (I/T ratio) in diagnosing early onset neonatal bacterial infection. I/T ratio is a useful tool for early onset sepsis (EOS) with reasonable specificity but cannot be relied upon as sole indicator. Combination of normal immature to total neutrophil Ratio with negative CRP values in neonates with presumed sepsis is an indicator of non-infected neonate which comprised 78.8% of our study population.

[\[Late onset neonatal sepsis in an intensive care neonatal unit: etiological agents and most frequent location\]](#). Spanish

Samudio G.C. et al.

Rev Chilena Infectol. 2018;35(5):547-552

Nosocomial neonatal sepsis (NNS) is a frequent entity in intensive care units, causing great morbidity and mortality. The most frequent site is blood, followed by lungs and urine. The most frequent infection was bacteremia, mainly by staphylococci resistant to methicillin. CNS involvement was elevated, as well as mortality.

[C23, an oligopeptide derived from cold-inducible RNA-binding protein, suppresses inflammation and reduces lung injury in neonatal sepsis.](#)

Denning NL, et al

J Pediatr Surg. 2019 Jan 4. pii: S0022-3468(18)30885-6.

Neonatal sepsis remains a leading cause of infant mortality. Cold-inducible RNA binding protein (CIRP) is an inflammatory mediator that induces TNF- α production in macrophages. C23 is a CIRP-derived peptide that blocks CIRP from binding its receptor. We therefore hypothesized that treatment with C23 reduces systemic inflammation and protects the lungs in neonatal sepsis. Inhibition of CIRP with C23 treatment is protective in septic neonatal mice as demonstrated by reduced inflammatory markers systemically and in the lung. Therefore, C23 has

Nwafor DC et al

J Cent Nerv Syst Dis. 2019 Apr 9;11:1179573519840652.

Sepsis is a systemic inflammatory disease resulting from an infection. This disorder affects 750 000 people annually in the United States and has a 62% rehospitalization rate. Septic symptoms range from typical flu-like symptoms (eg, headache, fever) to a multifactorial syndrome known as sepsis-associated encephalopathy (SAE). Patients with SAE exhibit an acute altered mental status and often have higher mortality and morbidity. In addition, many sepsis survivors are also burdened with long-term cognitive impairment. The mechanisms through which sepsis initiates SAE and promotes long-term cognitive impairment in septic survivors are poorly understood. Due to its unique role as an interface between the brain and the periphery, numerous studies support a regulatory role for the blood-brain barrier (BBB) in the progression of acute and chronic brain dysfunction. In this review, we discuss the current body of literature which supports the BBB as a nexus which integrates signals from the brain and the periphery in sepsis.

[Diagnostic value of procalcitonin and presepsin for sepsis in critically ill adult patients: a systematic review and meta-analysis.](#)

Kondo Y, et al

J Intensive Care. 2019 Apr 15;7:22.

Early and accurate diagnosis of sepsis is challenging. Although procalcitonin and presepsin have been identified as potential biomarkers to differentiate between sepsis and other non-infectious causes of systemic inflammation, the diagnostic accuracy of these biomarkers remains controversial. Herein, we performed a comprehensive meta-analysis to assess the overall diagnostic value of procalcitonin and presepsin for the diagnosis of sepsis. Our meta-analysis provided evidence that the diagnostic accuracy of procalcitonin and presepsin in detecting infection was similar and that both are useful for early diagnosis of sepsis and subsequent reduction of mortality in critically ill adult patients.

[The cost impact of PCT-guided antibiotic stewardship versus usual care for hospitalised patients with suspected sepsis or lower respiratory tract infections in the US: A health economic model analysis.](#)

promising therapeutic potential in treatment of neonatal sepsis.

[The utility of systemic inflammatory response syndrome \(SIRS\) for diagnosing sepsis in the immediate postpartum period.](#)

Shafik S et al

J Infect Public Health. 2019 Apr 19. pii: S1876-0341(19)30136-4.

The systemic inflammatory response syndrome (SIRS) and sepsis definitions were developed to improve the ability for early detection of infection and sepsis. We studied the incidence of immediate postpartum SIRS and sepsis. We further studied immediate postpartum SIRS as a potential predictor for immediate postpartum sepsis. Our findings suggest that immediate postpartum SIRS is not useful for the identification of immediate postpartum sepsis. Furthermore, SIRS does not appear to be a useful screening tool for infection and sepsis in the immediate postpartum period.

[Drugs for the Prevention and Treatment of Sepsis in the Newborn.](#)

Mukhopadhyay S, et al.

Clin Perinatol. 2019 Jun;46(2):327-347

Antimicrobial medications are the most commonly used medications in the neonatal intensive care unit. Antibiotics are used for infection prophylaxis, empiric treatment, and definitive treatment of confirmed infection. The choice of medication should be informed by the epidemiology and microbiology of infection in specific clinical scenarios and by the clinical condition of the infant. Understanding evolving pathogen susceptibility to antimicrobials and key pharmacotherapy determinants in neonates can inform optimal antibiotic use.

[Major Adverse Kidney Events in Pediatric Sepsis.](#)

Weiss SL et al

Clin J Am Soc Nephrol. 2019 Apr 18. pii: CJN.12201018.

Mewes JC et al

PLoS One. 2019 Apr 23;14(4):e0214222.

Procalcitonin is a biomarker that supports clinical decision-making on when to initiate and discontinue antibiotic therapy. Several cost (-effectiveness) analyses have been conducted on Procalcitonin-guided antibiotic stewardship, but none mainly based on US originated data. Using a Procalcitonin-algorithm to guide antibiotic use in sepsis and hospitalised lower respiratory tract infection patients is expected to generate cost-savings to the hospital and lower rates of antibiotic resistance and C.difficile infections.

[A probable case of catastrophic antiphospholipid syndrome: Should high-dose steroids be given in the setting of polymicrobial sepsis?](#)

Tucker, S.A. et al.

SAGE Open Medical Case Reports, 2019, Vol.7

In this clinical vignette, we present a case of a 59-year-old woman with catastrophic antiphospholipid syndrome likely triggered by polymicrobial sepsis. The diagnostic criteria and clinical manifestations of catastrophic antiphospholipid syndrome are reviewed. We also compare diagnostic criteria and clinical manifestations with other clinical entities in the differential diagnosis, including thrombotic thrombocytopenic purpura-hemolytic-uremic syndrome, disseminated intravascular coagulation, sepsis, and inflammatory bowel disease. Catastrophic antiphospholipid syndrome is a rare, but lethal condition, and treatment recommendations are based on expert consensus and analyses of the international Catastrophic Antiphospholipid Syndrome Registry. Current management guidelines recommend triple therapy, with anticoagulation, glucocorticoids, and plasma exchange or intravenous immunoglobulins. This case brings this rare clinical entity to the attention of clinicians and emphasizes the need for more research to understand the best management. It also raises the question of whether high-dose steroids should be continued for treatment of catastrophic antiphospholipid syndrome in the setting of a severe sepsis.

[Flagellin attenuates experimental sepsis in a macrophage-dependent manner](#)

Yang, X. et al

Major adverse kidney events, a composite of death, new kidney replacement therapy, or persistent kidney dysfunction, is a potential patient-centered outcome for clinical trials in sepsis-associated kidney injury. We sought to determine the incidence of major adverse kidney events within 30 days and validate this end point in pediatric sepsis. In children with sepsis, major adverse kidney events within 30 days are common, feasible to measure, and a promising end point for future clinical trials.

[Use of an Early Onset-Sepsis Calculator to Decrease Unnecessary NICU Admissions and Increase Exclusive Breastfeeding.](#)

Bridges M. et al

J Obstet Gynecol Neonatal Nurs. 2019 Apr 8.

To evaluate the effects of use of the Kaiser Neonatal Early-Onset Sepsis Calculator (NEOSC) on NICU admissions, laboratory testing, antibiotic exposure, and exclusive breastfeeding (EBF) rates in full-term neonates exposed to chorioamnionitis. Most neonates exposed to chorioamnionitis appeared well and did not require NICU admission, laboratory testing, or antibiotic therapy. Rates of EBF improved after use of NEOSC was implemented. The practice change helped prevent adverse consequences, such as painful interventions and separation of the mother and neonate. No neonates were readmitted for sepsis.

Adult sepsis

[Vitamin C, Hydrocortisone, and Thiamine for the Treatment of Severe Sepsis and Septic Shock: A Retrospective Analysis of Real-World Application](#)

Litwak, J.J. et al.

Journal of Clinical Medicine 2019 | MDPI AG

A recent study suggested mortality benefits using vitamin C, hydrocortisone, and thiamine combination therapy (triple therapy) in addition to standard care in patients with severe sepsis and septic shock. In order to further evaluate the effects of triple therapy

Critical Care, 01 April 2019, Vol.23(1), pp.1-14

Sepsis is the leading cause of death among critically ill patients, and no specific therapeutic agent is currently approved for the treatment of sepsis. These novel findings not only established the potential value of application of flagellin as an immunoadjuvant in treating sepsis, but also provided new insights into targeted therapeutic strategy on the basis of monocyte TLR5 expression in septic patients.

[An administrative model for benchmarking hospitals on their 30-day sepsis mortality](#)

Darby, J.L. et al.

BMC Health Services Research 2019

Given the increased attention to sepsis at the population level there is a need to assess hospital performance in the care of sepsis patients using widely-available administrative data. The goal of this study was to develop an administrative risk-adjustment model suitable for profiling hospitals on their 30-day mortality rates for patients with sepsis. A novel claims-based risk-adjustment model demonstrated wide variation in risk-standardized 30-day sepsis mortality rates across hospitals. Individual hospitals' performance rankings were stable across years and after the addition of laboratory data. This model provides a robust way to rank hospitals on sepsis mortality while adjusting for patient risk.

[Quick Sepsis-related Organ Failure Assessment score is not sensitive enough to predict 28-day mortality in emergency department patients with sepsis: a retrospective review.](#)

Kim KS et al

Clin Exp Emerg Med. 2019 Mar;6(1):77-83

To test the hypothesis that the quick Sepsis-related Organ Failure Assessment (qSOFA) score, derived from vital signs taken during triage and recommended by current sepsis guidelines for screening patients with infections for organ dysfunction, is not sensitive enough to predict the risk of mortality in emergency department (ED) sepsis patients. The current clinical criteria of the qSOFA are less sensitive than the SIRS assessment and SOFA to predict 28-day mortality in ED patients with sepsis.

in real-world clinical practice, we conducted a retrospective observational cohort study at an academic tertiary care hospital. When compared to standard care, triple therapy did not improve hospital or ICU mortality in patients with septic shock. A randomized controlled trial evaluating the effects of triple therapy is necessary prior to implementing vitamin C, hydrocortisone, and thiamine combination therapy as a standard of care in patients with septic shock.

[Comparison of long-term mortality in patients with acute myocardial infarction associated with or without sepsis](#)

Liu, E.S. et al.

International Journal of Infectious Diseases, 01 February 2019, Vol.79, pp.169-178

Although the association between systemic infection and cardiovascular events has been identified, uncertainty remains regarding the incidence and prognosis of sepsis in acute myocardial infarction (AMI). The purpose of this research was to assess the impact of sepsis on survival after first AMI. In conclusion, sepsis significantly increased the mortality risk of patients after first AMI. PCI may improve the long-term survival of patients in comparison to those managed conservatively.

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