### **Research achievements**

## Jhuma Sankar

MD (Pediatrics), Fellowship (Pediatric Critical Care)

# Subject of research work: Clinical research on interventions to improve mortality/ clinical outcomes in children with septic shock

Sepsis and septic shock (SS) are a major cause of mortality and morbidity in children (upto 50-70% from developing countries). As a pediatric critical care specialist and a clinical researcher, I took this up as a challenge and have been actively involved in addressing the major knowledge gaps in pediatric SS over the last one decade. I have worked on various clinical aspects of pediatric sepsis such as – fluid resuscitation, early goal directed therapy, timing of antibiotic and fluid administration and septic myocarditis to name a few. I have won several awards for my work done on these areas and have been able to publish the results in reputed national and international journals. Some of the work have been incorporated into guidelines for management of septic shock in children.

Initially (2011) I worked on use of a goal directed approach (Early Goal Directed Therapy) targeting the golden hours (1st 6 hours) in reducing mortality and found that this could be achieved with limited resources (fluids, inotropes, monitoring). For this work I received the ICMR H B Dingley award 2017. EGDT is recommended for children in septic shock based on few studies including this study.

Taking my work on EGDT further, I compared two different techniques of monitoring of superior vena caval oxygen (ScvO<sub>2</sub>) as part of EGDT therapy in children with septic shock- 'intermittent ScvO<sub>2</sub> monitoring' versus 'continuous ScvO<sub>2</sub> monitoring' and observed that when compared to the 'continuous ScvO<sub>2</sub> group' fewer children in the 'intermittent ScvO<sub>2</sub> group' achieved shock resolution within the first 6 hours.

I have recently completed a multicenter (4 centers: AIIMS Delhi, PGIMER Chandigarh, JIPMER Puducherry and St John's Hospital, Bengaluru) trial funded by the Department of Science and Technology on the 'ideal choice of fluid' for initial

resuscitation in 708 children with SS. We found lower risk of acute kidney injury (39% lower relative risk) with use of 'Balanced crystalloid solution' (BC) as compared to '0.9% saline' which is known to cause hyperchloremic metabolic acidosis. *This was the first multicenter trial in India in the field of pediatric critical care medicine*. This study may add to the choice of fluid for bolus fluid resuscitation in children with SS.

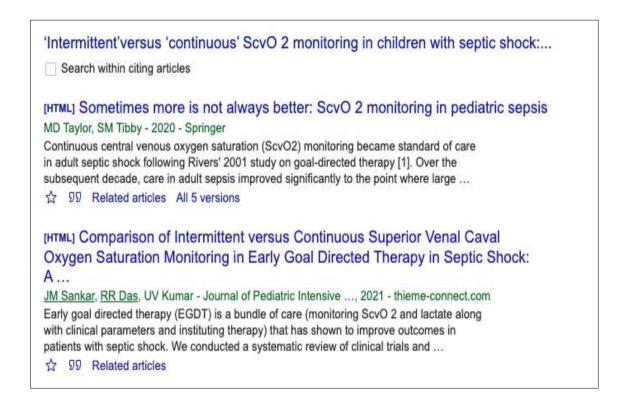
With regard to fluid therapy in SS, I have answered 2 important questions – *speed of bolus* and *choice of fluid* (above). The findings of the study on speed of boluses along with few other studies (from India and Africa) led to the change in recommendation for duration of bolus over 20-30 minutes from 5-10 minutes in SS (from 2017). I have also worked on vitamin D deficiency in SS and on pediatric Acute Respiratory Distress Syndrome.

### My most notable contributions have been -

- 1. Demonstrating early goal directed therapy is superior to standard care as it decreased the risk of mortality by 40% (received the ICMR HB Dingley award for this).
- 2. Demonstrating that 'continuous' ScvO<sub>2</sub> monitoring as part of EGDT is similar to 'intermittent' ScvO<sub>2</sub> monitoring (published in Intensive Care Medicine).
- 3. Demonstrating higher risk of respiratory failure with faster bolus (5-10 minutes) as compared to slow bolus (15-20 minutes). The septic shock guidelines recommend slow bolus now after this study and few others.
- 4. Demonstrating that balanced salt solution is associated with a lower risk of acute kidney injury as compared to 0.9% saline through the first multicenter trial in PICU in India.

#### Brief citations on the research works described above

1. **Sankar J,** Singh M, Kumar K, Sankar MJ, Kabra SK, Lodha R. 'Intermittent' versus 'continuous' ScvO2 monitoring in children with septic shock: a randomised, non-inferiority trial. Intensive Care Med. 2020 Jan;46(1):82-92.



2. **Sankar J,** Sankar MJ, Suresh CP, Dubey NK, Singh A. Early goal-directed therapy in pediatric septic shock: comparison of outcomes "with" and "without" intermittent superior venacaval oxygen saturation monitoring: a prospective cohort study\*. Pediatr Crit Care Med. 2014 May;15(4):e157-67.

Early goal-directed therapy in pediatric septic shock: comparison of outcomes "with"	
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[HTML] Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children  SL Weiss, MJ Peters, W Alhazzani, MSD Agus Intensive care, 2020 - Springer  Objectives To develop evidence-based recommendations for clinicians caring for children (including infants, school-aged children, and adolescents) with septic shock and other sepsis-associated organ dysfunction. Design A panel of 49 international experts  \$\frac{1}{2}\$ To Cited by 324 Related articles All 35 versions	[HTML] springer.com
American College of Critical Care Medicine clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock  AL Davis, JA Carcillo, RK Aneja Critical care, 2017 - ingentaconnect.com  Objectives: The American College of Critical Care Medicine provided 2002 and 2007  guidelines for hemodynamic support of newborn and pediatric septic shock. Provide the 2014 update of the 2007 American College of Critical Care Medicine "Clinical Guidelines for  TO Cited by 514 Related articles All 35 versions	[HTML] Iww.com
Global case-fatality rates in pediatric severe sepsis and septic shock: a systematic review and meta-analysis  B Tan, JJM Wong, R Sultana, JCJW Koh, M Jit JAMA, 2019 - jamanetwork.com  Importance The global patterns and distribution of case-fatality rates (CFRs) in pediatric severe sepsis and septic shock remain poorly described. Objective We performed a systematic review and meta-analysis of studies of children with severe sepsis and septic  \$\frac{1}{12}\$ \$\square\$ Cited by 56 Related articles All 7 versions	[HTML] jamanetwork.com
T Kawasaki - Journal of intensive care, 2017 - Springer Sepsis is one of the leading causes of mortality among children worldwide. Unfortunately, however, reliable evidence was insufficient in pediatric sepsis and many aspects in clinical practice actually depend on expert consensus and some evidence in adult sepsis. More	[HTML] springer.com

3. Fluid Bolus Over 15-20 Versus 5-10 Minutes Each in the First Hour of Resuscitation in Children With Septic Shock: A Randomized Controlled Trial. Jhuma Sankar, MD1; Javed Ismail, MD1; M. Jeeva Sankar, MD; Suresh C.P., Rameshwar S. Meena, MD. Pediatr Crit Care Med. 2017;18(10): e435-e445.

Fluid bolus over 15–20 versus 5–10 minutes each in the first hour of resuscitation in	
[HTML] Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children SL Weiss, MJ Peters, W Alhazzani, MSD Agus Intensive care, 2020 - Springer Objectives To develop evidence-based recommendations for clinicians caring for children (including infants, school-aged children, and adolescents) with septic shock and other sepsis-associated organ dysfunction. Design A panel of 49 international experts	[HTML] springer.com
[HTML] Part III: minimum quality threshold in preclinical sepsis studies (MQTiPSS) for fluid resuscitation and antimicrobial therapy endpoints  J Hellman, S Bahrami, M Boros, IH Chaudry, G Fritsch Shock, 2019 - journals.lww.com  As outlined in the "International Guidelines for Management of Sepsis and Septic Shock: 2016," initial fluid resuscitation and administration of antibiotics are key steps in the early management of sepsis and septic shock. However, such clear guidelines do not exist for  \$\frac{1}{12}\$ \$\sqrt{13}\$ Cited by 28 Related articles All 11 versions	[HTML] lww.com
Suspecting hyperferritinemic sepsis in iron-deficient population: do we need a lower plasma ferritin threshold?  S Ghosh, AK Baranwal, P Bhatia Pediatric Critical Care, 2018 - cdn.journals.lww.com Objectives: Hyperferritinemia is being suggested to identify patients with sepsis-induced macrophage activation syndrome for early intervention. However, data among iron-deficient children are scarce. This study was planned to explore the biological behavior of plasma  \$\frac{1}{12}\$ To Cited by 15 Related articles All 7 versions	[HTML] lww.com
[HTML] COVID-19 PICU guidelines: for high-and limited-resource settings S Kache, MJ Chisti, F Gumbo, E Mupere, X Zhi Pediatric, 2020 - nature.com Background Fewer children than adults have been affected by the COVID-19 pandemic, and the clinical manifestations are distinct from those of adults. Some children particularly those with acute or chronic co-morbidities are likely to develop critical illness. Recently, a	[HTML] nature.com
Part 1: Executive summary: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care  RM Merchant, AA Topjian, AR Panchal, A Cheng Circulation, 2020 - Am Heart Assoc  The 2020 American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care provides a comprehensive review of evidence-based recommendations for resuscitation and emergency cardiovascular care. The initial  \$\frac{1}{12}\$ To Cited by 45 Related articles All 4 versions	[PDF] ahajournals.org Full View
[HTML] Part 4: pediatric basic and advanced life support: 2020 American Heart Association guidelines for cardiopulmonary resuscitation and emergency  AA Topjian, TT Raymond, D Atkins, M Chan, JP Duff Circulation, 2020 - Am Heart Assoc These guidelines contain recommendations for pediatric basic and advanced life support, excluding the newborn period, and are based on the best available resuscitation science.	[нтмь] ahajournals.org Full View

Apart from the above major achievements/ awards I have been successful in completing several research projects related to sepsis and septic shock and have been able to publish the findings of all completed projects till date. The following table highlights the outstanding research contributions, awards won and publications during the period 2008-2018.

Table: Important projects undertaken and completed, awards won and papers published from 2010-2020

C	published from 2010-2020					
S.	Project completed	Name of Award	Awarding Agency	Year		
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1.	Early goal directed therapy in pediatric septic shock	ICMR HB Dingley Memorial award	ICMR	September, 2017		
2.	Decreasing the Time to Administration of First Dose of Antibiotics in Children with Severe Sepsis	Student received ICMR CNMC  - STS excellence award 2019 for the STS scholarship project (2016) (Chief guide)	ICMR	December 2020		
3.	Honey vs. Standard care in pressure ulcers in children	WFPICCS HARD grant manufacturing award in Pediatric Critical Care	WFPICCS- HARD manufacturing	June, 2017		
4.	Association of fluid overload with mortality in critically ill mechanically ventilated children	V.V Balagopal Raju Award (second prize) for oral paper	Indian Academy of Pediatrics (PEDICON 2016)	January, 2016		
5.	High dose versus low dose snake antivenom- a systematic review	Best paper Indian Journal of Critical Care Medicine	Indian Society of Critical Care Medicine - CRITICARE 2016, Agra	February, 2016		
6.	Fluid bolus over 15-20 minutes versus 5-10 minutes in children with septic shock	Best oral paper award	17th National Congress of Pediatric Critical Care, Jaipur	November, 2015		
7.	Effect of peer counselling by mother support groups on infant and young child feeding practices	James Flett Endowment award for paper on social pediatrics	Indian Academy of Pediatrics (PEDICON 2014)	January, 2014		
8.	PIM and PIM 2 scores at different time points in a developing country	Best oral paper award	14th National Congress of Pediatric Critical Care, Mangalore	November, 2012		
9.	Medication errors in CPR	Best paper award for paper	3rd National Assembly of Pediatric Emergency Medicine, Guwahati,	March, 2012		
10.	Outcome of acute fulminant myocarditis in children	Received Best Poster award (Critical Care)	49th Annual conference of the Indian Academy of Pediatrics held at Gurgaon	January, 2012		
11.	Early Goal Directed Therapy in Pediatric Septic shock- a prospective cohort study	Best oral paper award	13th National Congress of Pediatric Critical Care, Hyderabad	November, 2011		