International Guidelines 2020 for the Management of Septic Shock in Children

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The recent version of pediatric septic shock guidelines, 2020 have addressed practical issues pertaining to pediatric septic shock management, which can be applicable to resource-limited setting as well. Supportive aspects in management of septic shock such as ventilation, antibiotic stewardship, and nutrition are addressed compared to previous guidelines that concentrated more on first-hour management. The current guideline needs to be adapted to local clinical practice cautiously in the light of experience, clinical acumen and judgement.

Keywords: *Fluid resuscitation, Golden hour, MODS, PARDS*.

Recently the society of critical care medicine (SCCM) has published evidence-based guideline of management of pediatric septic shock and multi-organ dysfunction in children [1]. This guideline is an update to the previously published version in the year 2017 [2] and the scope of guideline includes all term neonates (>37 wks) till end of childhood up to 18 year. Due to complex and different pathophysiology of shock in preterms, the guideline has not particularly looked for evidence pertaining to shock in preterm neonates. In general, the words 'suggested for' or 'suggested against' have been used to denote 'a weak recommendation' emerging from very 'low to low-quality evidence' for or against certain practice, respectively; while the words 'recommended for' or 'recommended against' have been used to denote 'strong recommendation' for or against certain practice arising from 'moderate to high quality evidence'. However, some of the recommendations in all the above mentioned categories have also emerged as best practice statement, based on the consensus opinion of experts when adequate evidence is not available.

KEY CHANGES

As compared to previously published guideline the current guideline is more extensive and detailed which covers supportive and ancillary management of pediatric septic shock which were henceforth not covered in the previous version. These include details of evidence-based recommendation on antimicrobial therapy, source control of infection, nutrition, ventilation, prophylaxis against bedsore, deep vein thrombosis and ulcer. As compared to previous guidelines, the current guideline has de-emphasized the role of lactate in hemodynamic monitoring. Similarly, it promotes restrictive fluid up to 40 mL/kg (previously up to 60 mL/kg) and each bolus of 10-20 mL/kg (previously 20 mL/kg) during resuscitation in settings where there is no support of intensive care facility to avoid fluid overload. As is the case in many health care facilities in lower-middle income countries, where prevalence of malnutrition in children is very high, unsupervised administration of high volume of fluid can actually increase mortality. Hence the current guideline has been more conservative in these scenario. Further, it has set a time frame of 3 hour for initiation of antibiotics in children with sepsis but without septic shock. In light of recent emerging evidence the guideline has replaced epinephrine or nor-epinephrine in place of dopamine as first choice inotrope. However, its applicability in resource-limited setting may remain an issue where these two drugs are not easily available and dopamine may have to be used as first line drug in these situations. As the recent guideline has not mentioned exact cut-off of blood pressure for hypotension, normal range of blood glucose or hemoglobin level cutoff for transfusion in unstable children, for point of care issues related to these topics, the readers still have to either refer the previous version or other published guideline. The summary of 2020 surviving sepsis campaign guideline in contrast with 2017 guideline has been provided in ***Table* I.**

THE WAY FORWARD

The current version addressed practical issues pertaining to pediatric septic shock management, which can be applicable to resource-limited setting as well. Supportive aspects in management of septic shock such as ventilation, antibiotic stewardship, and nutrition are addressed compared to previous guidelines that concentrated more on first hour management. Like with any other International guidelines, the current guideline also needs to be adapted to local clinical practice cautiously in the light of experience, clinical acumen and judgment for its maximum benefit/utilization.

Table I Comparison of the 2020 Surviving Sepsis Campaign Guideline With 2017 Guideline for the Management of Children With Septic Shock or Sepsis Associated Organ Dysfunction

Steps	*2020 Recommendation [1]*	*2017 Guideline [2]*	*Implications for resource-limited setting*
Screening, diagnosis and management	Suggested for		
	• Systematic screening for timely detection	Same	• In our setup, thorough and repetitive clinical examination should be done to identify children with septic shock in time.
	Recommended		
	• Protocol/guideline-based management	Same	
	• Obtaining blood culture before initiation of antimicrobial therapy	Same	• Facility for blood lactate estimation is not easily available in majority health facilities in India
	No recommendation		
	• Blood lactate values for categorizing children	Did not mention	
Antimicrobial therapy	*Recommended*		
	• In children with septic shock, give antibiotics in the first hour of shock recognition	Same	• In our setup, strict hospital driven antimicrobial stewardship program along with written antibiotic policy needs to be implemented for timely de-escalation of antimicrobials
	• Give empiric broad-spectrum antibiotics while awaiting culture report and narrow down or stop subsequently as per culture and sensitivity	No mention	
	• Use pharmacokinetic/ pharmaco-dynamic based antimicrobial dosing	No mention	• Every attempt should be made to obtain blood culture before initiation of antibiotics where ever possible.
	• Daily assessment for timely de-escalation of antimicrobials	No mention	
	• Duration of antimicrobials as per site, etiology, treatment response and control of source	No mention	• Due to serious risk of misuse, multiple antibiotics therapy solely based on immunocompetent status should be discouraged.
	Suggested for		
	• In children without septic shock but with other organ dysfunction starting antimicrobials within 3 hr	No mention	• Decision for continuation, de-escalation, or stoppage should be made on clinical basis taking consideration of site of infection, agent, host risk factors
	• In immunosuppressed or high-risk children use of multiple empiric anti-biotics to expand coverage, evade resistance or achieve synergy	No mention	
	Suggested against		
	• In immunocompetent children routine use of empiric multidrug therapy	No mention	
Source control	*Recommended for*		
	• Implementation of source control strategy for prevention of infection as early as possible • Removal of intravascular line which are confirmed source of infection after establishing alternative vascular access	No mention	In Indian setting where aseptic maintenance of central lines is an issue, the emphasis should be on timely removal as soon as possible (when they are no more required)
Fluid therapy	*Suggested*		

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Steps	*2020 Recommendation [1]*	*2017 Guideline [2]*	*Implications for resource-limited setting*
	• Using 40-60mL/kg of fluid (10-20 mL/kg per bolus) in first hour with appropriate clinical titration • Fluid bolus up to 40mL/kg may be given in first hour in case of hypotension in health facility without support of intensive care • Use of crystalloids as compared to colloids in first hour fluid resuscitation • Use of balanced/buffered crystalloids rather 0.9% saline	• Fluid volume up to 60 mL/kg (each bolus of 20mL/kg) in first hour resuscitation • Either crystalloid or colloids can be used for fluid resuscitation	In Indian set-up where pediatric intensive care facilities are not widely available, aggressive fluid resuscitation (more than 40mL/kg) needs to be avoided especially in absence of hypotension as per age
	Recommended against • Bolus fluid in the absence of hypotension in a health facility without support of intensive care • Use of starch/gelatin for resuscitation	• No mention • No mention	
Hemodynamic monitoring	*Suggested for* • Use of advanced hemodynamic variables (*e.g* cardiac output/ cardiac index, central venous oxygen saturation, systemic vascular resistance) where ever available in addition to clinical parameters • Use of serial trends of lactate rather single isolated value *Suggested against* • Isolated use of clinical signs in categorising warm or cold shock *No recommendation for or against* • Whether to target a MAP 5th centile or 50th centile for hemodynamic stability	• Frequent re-evaluation of hemodynamic parameters for choosing the appropriate vasoactive/ inotropic drug • Provided a range of normal heart rate as per age as well as mean arterial pressure(50th centile) as per age • Provided age wise targets for perfusion pressure (MAP-CVP)	• Interpretation of advanced clinical condition of the child, hemodynamic parameters should be in context with not just numbers. • Though serial blood lactate value provides idea about microcirculation during resuscitation, it may remain elevated even after correction of microcirculation if associated with hepaticor renal dysfunction. Hence in these situation, lactate levels should be interpreted cautiously • There is no consensus whether to target 5th centile, 10th centile or 50th centile MAP for critically ill children during resuscitation. MAP-CVP target provided by previous guideline may be used
Vasoactive medications	Suggested for • Epinephrine or norepinephrine in place of dopamine as first-line • Dopamine may be substituted as first line when epinephrine or norepinephrine are not available • May add vasopressin or titrate catecholaminesby clinician to achieve target *No recommendation for or against* • Use of vasoactive agents in peripheral line • Specific first-line vasoactive agent one above the other • Adding inodilator in children with cardiac dysfunction despite addition of vasopressors	• Dopamine, dobutamine, or epinephrine can be used as first-line inotropic support. • Low-dose epinephrine as the first-line choice for cold hypotensiveshock • Vasopressin as rescue therapy • Epinephrine may be infused through a peripheral IV route or through an intraosseous needle while attaining central venous access • Milrinone is first-line	• It is reasonable to initiate vasoactive agent after a fluid resuscitation of 40-60mL/kg and first line vasoactive agents may be administered by a peripheral venous route till the time central venous line is inserted • Usual recommended doses (IV/IO) of commonly used vasoactive drugs (as infusion)(3) 1. Epinephrine 0.1 to 1 mcg/kg/min (higher doses may be considered in case to case basis) Norepinephrine 0.1 to 1 mcg/kg/min 2. Dopamine up to 10 mcg/kg/min infusion 3. Dobutamine up to 10 mcg/kg/min infusion

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Steps	*2020 Recommendation [1]*	*2017 Guideline [2]*	*Implications for resource-limited setting*
		inodilator in patients with epinephrine-resistant shock with normal blood pressure.	4. Milrinoneup 0.75mcg/kg/ min. 5. Vasopressin up to 0.002 units/kg/ min
Ventilation	*Suggested for* • A trial of NIV over invasive ventilation in children with PARDS • High PEEP in sepsisinduced PARDS • Trial of prone positioning in PARDS • Use of iNO as rescue therapy • Use of neuromuscular blockade *Suggested against* • Use of etomidate for intubation • Routine use of iNO *No recommendation for or against* •Intubation of children with fluid refractory, vasopressor resistant shock • HFO over conventional ventilation • Recruitment maneuvers	• High-flow nasal cannula /non-invasive respiratory support can be given to selected patients • Etomidate to be avoided • Those with persistent or worsening shock should be considered as high risk for deterioration and should receive ventilatory support	Although the current guideline has not mentioned exact value for defining high PEEP in PARDS, the readers may go through pediatric acute lung injury consensus conference group (4) (Generally a PEEP up to 10-15 cmH2O may be needed in severe PARDS and occasionally upto >15 15 cmH2O)
Steroids	*Suggested against* • Use of IV hydrocortisone for treating children with septic shock who are stabilized by adequate fluid resuscitation and vasopressor therapy *Suggested for* • Use of hydrocortisone in treating septic shock children where hemodynamic stability is not achieved with fluid resuscitation and vasopressors	In a child at risk of adrenal insufficiency with shock even after epinephrine or norepinephrine infusion, injection hydrocortisone should be given after obtaining sample for serum cortisol level	• Serum cortisol level may not be available at all facilities. • IV hydrocortisone can be considered at dose of 100 mg/ m^2 stat dose followed by100mg/m^2 /d in 4 divided doses in children who remain hypotensive despite adequate fluid resuscitation and vasopressor
Endocrine and metabolic	*Recommended against* • Routine insulin therapy to achieve normoglycemia (< 140 mg/dL) *No recommendation* • Range of blood sugar levels as target, but suggested to target <180 mg/dL as consensus • Whether to target normal calcium levels *Suggested against* • Routine use of levothyroxine *Suggested for* • Either antipyretic therapy or permissive approach for fever control	• Maintaining glucose range of 80-150 mg/dL by appropriate titration of glucose/ insulin infusion and avoiding use of lesser glucose (5% D or lower volume of 10% D) in hyperglycemic patient • Thyroxine in catecholamine resistant shock with underlying thyroid insufficiency • Maintenance of normal ionized calcium level by calcium replacement	As calcium is required for cardiac contractility, targeting normal ionic calcium levels for these children as per previous guideline seems rational in current scenario.
Nutrition	*Suggested against* • Withholding enteral feeding solely based on ionotropic support • Supplementing with specialised lipid emulsion • Routine measurement of gastric	No mention in previous version	Early trophic feeds are to considered and may increase feeds further provided no increment in vasoactive support or decreasing the vasoactive drug support

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Steps	*2020 Recommendation [1]*	*2017 Guideline [2]*	*Implications for resource-limited setting*
	residual volume routine prokinetic agent • Use of micronutrient selenium, glutamine, arginine, zinc, thiamine, vitamin D as immunomodulators *Suggested for* • Enteral nutrition as preferred to parenteral nutrition and withholding parenteral nutrition till 7 days of PICU admission • Orogastric feed as compared post pyloric feed *No recommendation* •Early trophic/hypocaloric feed vs full early enteral feed		
Blood products	*Suggested against* • Transfusion of PRBC with Hb ≥7g/dL for stabilized children •Prophylactic platelet transfusion (based on platelet levels) or plasma transfusion in nonbleeding cases *No recommendation* •Hb transfusion threshold for unstable children	Transfuse to maintain Hb ≥7 g/dL for stable children and ≥10 g/dL for children with septic shock	During resuscitation phase of shock one may target Hb ≥10 g/dL
Extracorporeal therapy	*Suggested against* • Routine plasma exchange • Routine high-volume hemofiltration over standard hemofiltration *Suggested for* • Early renal replacement therapy for prevention and treatment of fluid overload • VV ECMO (VA in case VV fails) in PARDS and refractory hypoxemia	Individualized approach while using extracorporeal therapies such as ECMO, CRRT, and blood purification (hemofiltration, hemoperfusion, and therapeutic plasma exchange [TPE]) in pediatric septic shock	
Routine IVIG	*Suggested against**	No mention	
Routine prophylaxis for critically ill children	*Suggested against** • Routine stress ulcer prophylaxis • Routine deep vein prophylaxis	No mention	

*Information extracted from Weiss, et al. [1] and Davis, et al. [2]; MAP: Mean arterial pressure; NIV: Non-invasive blood pressure; VV: Venovenous; VA: Venoarterial; PARDS: Pediatrics acute respiratory distress syndrome; *Selected cases may be benefitted on a case-to-case basis; HFO: High frequency oscillation; iNO: Inhaled nitric oxide.*

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