



Pediatric Malnutrition and Cholera Rehydration Review

GTFFCC Clinical Management Working
Group Meeting
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Objectives

- Review basic pathophysiology and challenges in clinical management in children with severe acute malnutrition (SAM) and cholera
- Review current guidance and previous literature/rationale
- Summarize new literature in children with SAM
 - Cardiac function
 - IV rehydration
- Discuss possible changes in current practices based on new literature and next steps

Background



Cholera and children with SAM

In 2022, over 30 countries worldwide were battling cholera outbreaks, and >85% of those countries were also reporting SAM in children <5 years

Children with SAM who present with severe purging and hypovolemic shock are at high risk of electrolyte deficits and death if not identified and rehydrated immediately

Most important issue: stabilize severely dehydrated patients with IV rehydration and then transfer for specialized care

Complications in children with SAM

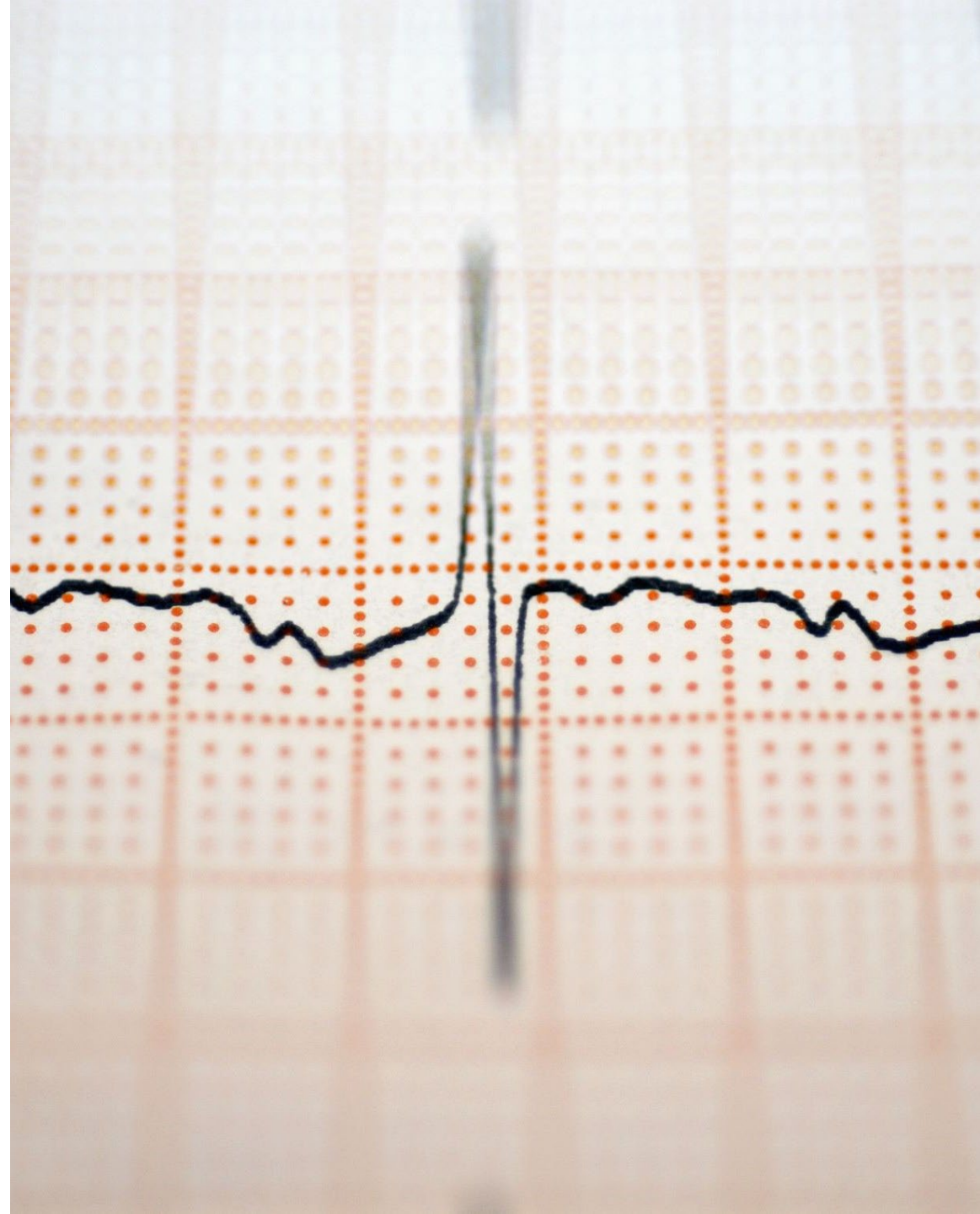
Affected Organ/System	Possible Complications
Cardiovascular	Thought to have <u>decreased cardiac output</u> and stroke volume
Liver	Higher risk for <u>hypoglycemia</u>
Circulatory	Higher risk for <u>hypothermia</u>
Metabolic	Higher risk for <u>hypoglycemia</u> , <u>hypernatremia</u> and <u>hypokalemia</u>
Immune	Higher risk for <u>infection</u>
Skin and glands	<u>Unreliable signs of dehydration</u>

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Previous literature on cardiac function in children with SAM

- Several studies identified reduced heart size in children with SAM, but findings regarding heart function has been conflicting
 - Some studies found impaired heart function, but this was in proportion to total body surface area (BSA) and metabolic demand
 - Other studies found decreased heart function in patients disproportional to BSA and metabolic needs



Rationale for current GTFCC guidance on treatment of children with cholera and SAM

Limited and conflicting data regarding cardiac function and IV fluid administration

Guidance was developed on available literature and expert opinion



Current guidelines

Current GTFCC guidelines – rehydration in children with severe dehydration

SAM	Non-SAM		
<u>15 mL/kg IV fluids over 1 hr</u> If improves, repeat 15 mL/kg over next 1 hr	<1 yr	30mL/kg RL over 1 hr, then 70 mL/kg over 5 hrs	Total: <u>100 mL/kg over 6 hrs</u>
	≥1 yr	30 mL/kg RL in 30 min, then 70 mL/kg over 2.5 hrs	Total: <u>100 mL/kg over 3 hrs</u>
Recommended IV fluids: • RL with with 5% dextrose • Half-strength Darrow's solution with 5% dextrose • 0.45% NS with 5% dextrose			

Current MSF cholera guidelines – rehydration in patients <5 years with severe dehydration

SAM	Non-SAM
20 ml/kg of RL over <u>30 minutes</u>	20 mL/kg RL <u>over 15 minutes</u>
<i>If danger signs still present, repeat the bolus up to 2 times</i>	
70 mL/kg of RL <u>over 6 hours</u>	70 mL/kg of RL <u>over 3 hours</u>



New literature

Heart function in children with SAM

- Two recent publications have challenged the belief that children with SAM are at greater risk of cardiac dysfunction when compared to those without SAM
 - The Appropriate Fluid Resuscitation In Malnutrition (AFRIM study, 2017)
 - The Cardiac Physiology in Malnutrition (CAPMAL study, 2019)

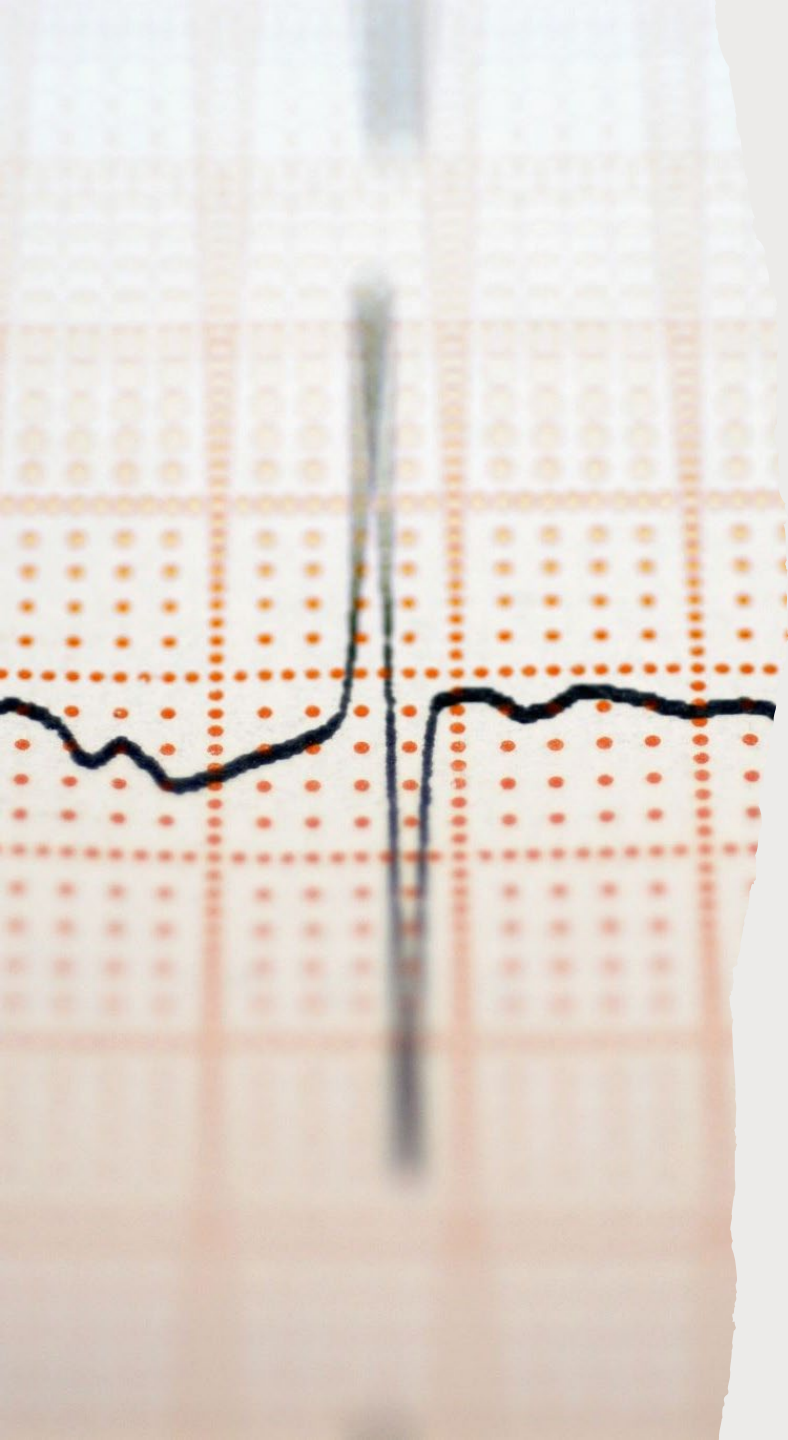
Heart function in children with SAM

AFRIM Study,
2017

Assessed cardiac response to IV fluid rehydration utilizing echo in children with SAM and hypovolemic shock from gastroenteritis before and after rehydration

Maximum IV rehydration given was up to two IV RL boluses of 15 ml/kg/hr

Findings: No compromised cardiac function or signs of fluid overload at baseline or following IV rehydration

An ECG strip on orange grid paper is visible on the left side of the slide. It shows a single lead with a P wave, a sharp QRS complex, and a T wave. The paper has a vertical line and horizontal lines forming a grid.

Heart function in children with SAM CAPMAL study, 2019

- Assessed cardiac function in children with SAM utilizing echo and ECG following IV rehydration
- Children with SAM and hypovolemic shock from gastroenteritis received 20 mL/kg/hr IV RL boluses (could be repeated twice)
- Findings: No significant cardiac dysfunction, fluid overload, or fatal arrhythmias were observed

Rehydration in children with SAM and gastroenteritis

- As a result of limited cholera and SAM studies, the review was broadened to rehydration of children with SAM and diarrheal disease
 - Houston KA et al. 'Intravenous rehydration of malnourished children with acute gastroenteritis and severe dehydration' (2018) was used as a starting point to assess intravenous rehydration of malnourished children with gastroenteritis and severe dehydration
 - Literature published between 2018–2023 utilizing the previous methodology was also included
 - Five studies total met the review criteria
- **No evidence of fluid overload or other fluid-related adverse events including children managed on more liberal rehydration protocols**

Children with SAM and cholera

- After screening and analysis, only one study met criteria for assessment of children with SAM infected with cholera
 - Alam et. al. *'Safety of rapid intravenous rehydration and comparative efficacy of 3 oral rehydration solutions in the treatment of severely malnourished children with dehydrating cholera'*
- **Objectives:** Assess safety of rapid IV rehydration in SAM patients and compare efficacy of 3 different ORS solutions

Evaluating Safety of IV Rehydration of SAM Patients with Cholera Study

Results:

- 149 (85%) presented with severe dehydration requiring IV rehydration
- ~103 mL/kg IV fluid administered over 6 hours
 - Initial fluid resuscitation was 30 ml/kg over 30 min and then 70 ml/kg over next 5.5 hrs
- All patients were successfully rehydrated within 6 hours
- No patients developed notable electrolyte derangements
- No patients died, developed signs of fluid overload or heart failure

Potential next steps

- Perform further multicenter trials across various countries to continue addressing these questions/challenges
- Create algorithms to simplify management of SAM patient with cholera for any medical center with focus on stabilization and then transfer to TFC
- Perform SAM screening for all patients ≤ 5 years for malnutrition in CTCs
- Work on improved surveillance to help identify these patients; discuss methods for improved sharing of data with partners/stakeholders

Thank You!

Acknowledgments

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Ben Allen

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GTFCC

Kate Alberty

Kirrily De Polnay

Iza Ciglenecki

Potential Next Steps

- Discuss increasing IV fluid hydration protocols in children with SAM and cholera presenting in hypovolemic shock based on new literature
- Aim to perform multicenter trials across various countries
- Systematically screen all children <5 years for malnutrition admitted to CTCs
- Work on improved surveillance to help identify these vulnerable patients and discuss methods for improved sharing of data with partners/stakeholders

Trials Underway

Efficacy of dopamine, epinephrine and blood transfusion for treatment of fluid refractory shock in children with severe acute malnutrition or severe underweight and cholera or other dehydrating diarrhoeas: protocol for a randomised controlled clinical trial

Monira Sarmin¹, Nusrat Jahan Shaly¹, Tania Sultana¹, Md Tariqujjaman¹,
Shamima Sharmin Shikha¹, Nafisa Mariam¹, Didarul Haque George¹, Mosharrat Tabassum¹,
Baitun Nahar¹, Farzana Afroze¹, Lubaba Shahrin¹, Md Iqbal Hossain¹, Baharul Alam¹,
Abu Syed Golam Faruque¹, M Munirul Islam¹, Din-E-Mujahid Mohammad Faruque Osmany²,
Chaudhury Meshkat Ahmed², Karim Manji³, Niranjana Kissoon⁴, Mohammad Jobayer Chisti⁵,
Tahmeed Ahmed¹

Trials Underway

STUDY PROTOCOL 

Gastroenteritis Rehydration Of children with Severe Acute Malnutrition (GASTROSAM): A Phase II Randomised Controlled trial: Trial Protocol [version 1; peer review: 2 approved]

Peter Olupot-Olupot , Florence Aloroker, Ayub Mpoya, Hellen Mnjalla, George Passi , Margaret Nakuya, Kirsty Houston
Nchafatso Obonyo , Mainga Hamaluba , Jennifer A Evans, Roisin Connon , Elizabeth C George, Diana M Gibb,
Kathryn Maitland  

Trials Underway

- 2 trials currently underway assessing safety of rehydration in children with SAM and dehydrating gastroenteritis

Extra Slides

Assessment of Dehydration

Clinical Presentation	Dehydration Level	Treatment Plan
<u>Two of the following signs:</u> -Lethargic or unconscious -Sunken eyes -Not able to drink or drinking poorly -Skin pinch goes back very slowly	Severe Dehydration	Plan C IV rehydration
<u>Two of the following signs:</u> -Restless, irritable -Sunken eyes -Drinks eagerly, thirsty -Skin pinch goes back slowly	Some Dehydration	Oral Rehydration
Not enough signs to classify as some or severe dehydration	Severe Dehydration	Discharge home with close return precautions

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Electrolyte Composition of Diarrhea Caused by Different Organisms and Oral Rehydration Solutions

Organism	Electrolytes mMol/L				<u>mOsm/L</u>
	<u>Na</u>	<u>K</u>	<u>Cl</u>	<u>HCO3</u>	<u>Osmolarity</u>
Cholera	88	30	86	32	300
Rotavirus	37	38	86	6	300
ETEC	53	37	24	18	300

ORS	Electrolytes mMol/L					<u>mOsm/L</u>
	<u>Na</u>	<u>K</u>	<u>Cl</u>	<u>HCO3</u>	<u>Glucose</u>	<u>Osmolarity</u>
Resomal	45	40	70	7	125	300
Standard ORS	90	20	80	10	111	311
Low Omol ORS	75	20	65	10	75	245

Molla AM, Rahman M, Sarker SA, Sack DA, Molla A. Stool electrolyte content and purging rates in diarrhea caused by rotavirus, enterotoxigenic *E. coli*, and *V. cholerae* in children.

Research Strategy

- Literature review included the various types of sources (including peer-reviewed and grey literature, guidance, expert opinions, and other relevant evidence). Utilized Cochrane Review procedure
- Comprehensive database search of the following databases was conducted:
 - PubMed/Medline
 - Cochrane Library
 - Scopus
 - ClinicalTrials.gov
 - WHO, UNICEF and Ministry of Health Websites
 - Google search