#### **Review Article**

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### Role of oral fluid, electrolytes and energy in various pediatric illnesses beyond diarrhea: an Indian expert panel consensus recommendation

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#### **ABSTRACT**

Dehydration in non-diarrheal illnesses often goes unnoticed and there are no consensus treatment recommendations for management of dehydration in non-diarrheal illnesses, A multi-disciplinary committee of 10 experts from India gathered on virtual platform in September 2020 to develop consensus recommendation on current treatment strategies for managing oral fluid electrolyte and energy in pediatric patients during non-diarrheal illnesses and to identify unmet needs and gaps. A pre-meeting questionnaire-based voting system was adopted to reach consensus followed by a discussion between panel members. In absence of consensus, the topic was opened for debate to arrive at an aligned recommendation. Key clinical challenges include identifying dehydration in acute illnesses and recommending appropriate quantity and type of oral fluids based on symptom severity. This consensus statement provides guidance on management of dehydration in non-diarrheal illnesses including recommendation on oral fluid, electrolytes, and appropriate energy management in pediatric population. Oral fluid, electrolyte and energy supplementation were recommended based on symptoms in acute non-diarrheal illness increased insensible losses and/or decreased intake. Oral rehydration fluids should be prescribed accurately and at the right-time for countering dehydration, ideally early in the course of illness. Prescribing pattern should be precise and like intravenous fluids. Carbonated drinks and canned juices should not be recommended. Plain water may not be optimal in replacing electrolytes especially for anorexic patients who can only tolerate fluids. These clinical practice statements provide guidance for oral fluid, electrolytes, and energy recommendations for pediatric patients with various acute illnesses beyond diarrhea.

Keywords: Dehydration, Non-diarrheal illnesses, Oral rehydration, Ready-to-drink

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#### INTRODUCTION

Dehydration is a potentially life-threatening condition observed in children wherein depletion in total body water content hampers normal functioning.<sup>1,2</sup> The prescription of fluid and electrolytes therapy is the key tool for the pediatrician in addressing dehydration. The clinical situations in children requiring such therapy are myriad and range from urgent cases of circulatory collapse to more mundane cases of mild dehydration from gastroenteritis.<sup>3</sup> Dehydration in children due to diarrhea is common and has well-established guidelines. However, other common illnesses like fever, nausea, vomiting, heat exhaustion, viral diseases, and upper respiratory tract infection (URTIs) can cause overt or subclinical dehydration leading to fluid, electrolytes and energy (FEE) deficits in children; with general weakness depicted as a common symptom.<sup>3-6</sup>

In 1957, Holliday and colleagues devised simplified equations to link average daily metabolic rate to daily fluid requirements for an ill child based on continuing/ "maintenance" needs, and past and current losses/ "deficits" was considered the gold standard to minimize complications and improve clinical outcomes.7 In children requiring rehydration, a tradition of fluid therapy grounded on so-called "deficit therapy" approach became widespread. Reassessment of this traditional approach, again spawned in large measures by Holliday's work, has come to illustrate that such elaborate maneuvers are often unnecessary. In addition, rehydration via the oral route is crucial to assessment of its adequacy and applicability. Moreover, increasing recognition that the use of oral rehydration solutions is simple, safe and efficacious alternative for most children in need of fluid and electrolyte therapy has helped reduce need of IV therapy and hospitalization for moderate/ mild dehydration cases. Similarly, children with non-diarrheal illness, also need careful assessment and prescription of fluid and electrolyte therapy.<sup>3</sup>

Most of the scientific evidence for oral FEE management for acute illnesses with dehydration has been extrapolated from diarrheal cases; even though, the requirements for non-diarrheal illnesses can be significantly different. In general, clinicians have strong awareness of the role of fluid and electrolytes in diarrhea. However, in acute non-diarrheal illnesses, the need for prevention and treatment of dehydration, as well as energy management, is often overlooked, and hence the impact on speed of recovery is also not fully understood.

# IMPORTANCE AND ROLE OF ORAL FEE THERAPY IN ACUTE NON-DIARRHEAL ILLNESSES

Acute illnesses arise unexpectedly with rapidly developing symptoms within a limited duration of time, with FEE deficit being one of the key challenges. Healthy levels of fluids and electrolytes play an important role in

maintaining the health of nerves and muscles, including those of vital organs. Total body water is higher in infants (70% of total weight) and children (65%) as compared to the adults (60%).<sup>2</sup> Infants go through rapid growth and development associated with changing pharmacokinetics from birth to adulthood. Thorough understanding of these ongoing dynamic changes is essential for maintaining fluid balance, avoiding fluid and electrolyte derangements, and optimizing pharmacotherapy.<sup>1</sup>

#### INSENSIBLE LOSSES IN ACUTE ILLNESSES

Current literature reports that water losses occur from urine output and from insensible sources that consist of almost exclusively evaporative and respiratory losses. 10 Other clinical factors can have a striking impact on insensible water losses (Table 1). Fever increases insensible losses by more than 10% per degree Celsius rise in body temperature. 3 Premature babies with larger surface areas and on open warmers/ receiving phototherapy have 2-3 times greater insensible losses. Children on ventilators may have half insensible losses of a non-ventilated children. Increased activity of the reninangiotensin axis and relatively high levels of aldosterone and angiotensin result in low sodium levels in urine. 3

Table 1: Factors affecting insensible water losses.

Increased losses	Change (%)
Hyperventilation	20-30
Increased activity	5-25
Hyperthermia	12°C

Adapted from Somers M.J.G. Fluid and Electrolyte Therapy in Children. In: Avner E, Harmon W, Niaudet P, Yoshikawa N (eds). Pediatric Nephrology. Springer, Berlin, Heidelberg. 2009.

#### Fluids

Fluid therapy is divided according to maintenance, deficit and replacement requirements.<sup>8</sup> Limitations in assessing fluid and electrolyte balance in pediatric patients include underdeveloped physiological processes, onset of thermoregulation, insensible losses and adaptation to onset of autonomic renal regulation of fluids and electrolytes.<sup>11,12</sup>

#### Electrolytes

Sodium (Na and Cl ions of the extracellular fluid which influence the systems acting on blood pH explains the metabolic acid-base abnormalities associated with changes in Cl conc leading to dehydration. <sup>11,14</sup> Potassium is another major intracellular cation that correlates to lean body mass and its levels impaired if there is insufficient supply of oxygen and energy. Thus, it is important for the right amount of Na and K to be supplied to body along with drugs, minerals, and various Cl sources (normal saline, calcium and amino acids) (Table 2). <sup>11,14</sup> There's currently no definitive data on type or level of electrolyte losses during acute non-diarrheal illnesses.

Table 2: Oral electrolyte requirements by age (mg).

Age (Years)	Na	K	Age (Years)	Mg	Age (Years)	Ca	P
0-0.5	120	500	0-0.5	30	0-0.5	210	100
0.5-1	200	700	0.5-1	75	0.5-1	270	275
1-2	225	1000	1-3	80	1-3	500	460
2-5	300	1400	4-8	130	4-8	800	500
6-9	400	1600	9-13	240	≥8	1300	1250
≥10	500	2000	>13 (M)	400			
			>13 (F)	360			

Abbreviations: Ca-calcium; F-females; K-potassium; M-male, Mg-magnesium; Na-sodium; P-phosphorus; Y-years.

## ENERGY REQUIREMENTS IN PEDIATRIC PATIENTS

A considerable amount of energy is required to carry out involuntary physiological functions in a human body. In children with acute illness, energy expenditure and metabolic needs can increase by more than twice the resting energy expenditure.<sup>15</sup> Energy needs are affected by several factors leading to increased risk of morbidity and mortality in infants and children. 16 The total energy requirement can be determined based on four main components 1) basal metabolic rate, 2) diet induced thermogenesis, 3) physical activity and 4) growth. 11 The recommended daily caloric requirement in children between 2 and 3 years of age is 1000 to 1400 kcal/day; this requirement increases with the age of the child. Of the various types of nutrients water is the most important of all nutrients and serves as a major substrate for metabolic reactions. There is limited evidence on the frequency of administration, route of administration or volume of oral fluid to be used in dehydrated patients which highlights the need to derive an effective fluid therapy. Further, it is also important to monitor the patient's response to therapy.8

This consensus will help us understand the oral FEE needs of pediatric patients with acute non-diarrheal illnesses, which may have an impact on overall recovery of pediatric patients, as there was a lack of similar clear guidelines.

#### Procedure

An expert panel comprising pediatricians (n=6), pediatric gastroenterologists (n=2) and nutritionists (n=2), from across the country, was formed for the purpose of formulating this consensus. The advisory-board meeting was attended by these experts virtually. The questions were prepared based on practice experiences of the panelists. The primary objective of the panel meeting was to gain insights on current treatment strategies and the role of oral fluid-electrolyte-and-energy and its impact on patient outcomes to arrive at consensus recommendation for pediatric patients with various acute common non-diarrheal illnesses.

The MEDLINE/PubMed and Cochrane databases were searched from December 2020 through June 2021. Other data sources included Google, and Google Scholar for treatment guidelines and prescribing information. Medical Subject Headings and free-text keywords were used and combined using "OR" and "AND" for "pediatrics" [MeSH Terms] OR Pediatric [Text Word]; "dehydration" [MeSH Terms] OR Dehydration [Text Word]; "Fluid Therapy" [MeSH] OR oral rehydration therapy [Text Word]. Data from published systematic reviews, meta-analyses, case reports, diagnostic studies, observational studies, review articles and epidemiological studies conducted on pediatric populations with dehydration was considered as primary evidence.

In case of inadequate evidence, recommendations were made by the expert panel. A pre-meeting questionnaire-based voting system was adopted to reach consensus. Where there was no consensus, the topic was open for debate to arrive at a conclusive statement. The general procedure followed was a brief discussion among the panelists, followed by voting to reach a consensus.

#### **CONSENSUS RECOMMENDATIONS (TABLE 3)**

Consensus recommendation 1. Adequate oral FEE supplementation is vital in recovery from common acute non-diarrheal illnesses

Based on panel members' clinical judgment, for acute non-diarrheal illnesses, clinicians should be more conscious and deliberate assessing dehydration and in recommending oral FEE to augment recovery, that aims at replacing losses of fluid and electrolytes, maintaining proper homeostasis, and preventing complications arising out of low fluid level.

#### Action statement profile

Improvement opportunity/objective: Clinicians acknowledged the strong role of fluid and electrolytes management in diarrhea; but in acute non-diarrheal illnesses, the need for prevention of dehydration as well as rehydration and energy management are often overlooked (Table 4), difference of opinion: None and value judgment: High-depends on patient profile.

Table 3: Summary of consensus statements.

Statements	
Statements	
1. Adequate oral fluid, electrolyte and energy supplementation is vital for recovery in various illnesses beyond diarrhea	Most of common acute clinical conditions in children are associated with dehydration due to decreased intake and/or increased losses. Oral fluid-electrolyte-and-energy recommendation for acute, non-diarrheal cases aims at replacing losses of fluids and electrolytes, maintaining proper homeostasis and preventing complications arising out of low fluid levels, thus, should recommended until patient recovers from underlying condition.
2. It is important to diagno	se dehydration in patients with acute non-diarrheal illness as well as monitor the need
for rehydration along with	
2.1. Diagnosis of dehydration is critical in patients with acute illness	There is no fixed set of physical signs and symptoms to assess dehydration. Acute non-diarrheal illnesses vary in presenting signs and symptoms, and may be associated with decreased oral intake and/or increased losses including insensible losses. Currently, there is no single biologic parameter for the diagnosis of dehydration. Consequently, rather than going by the primary diagnosis, the need for rehydration should be based on constellation of symptoms with the objective of preventing and managing dehydration.
2.2. Assessment of the need for rehydration is vital	Monitoring dehydration in pediatric patients with decreased oral intake and increased losses including insensible losses, even without diarrhea, is vital. It is important to monitor clinical status of the patient, oral intake, urine output, and physical signs and symptoms during oral fluid therapy.
3. Oral fluid electrolytes an	nd energy replacement should be recommended from day 1 of illness/patient visit
3.1. Recommendation for fluids should be based on patient clinical condition	Clear home-made fluids, coconut water, oral rehydration fluids, ready-to-drink with electrolytes and energy are the most recommended fluids to manage dehydration in non-diarrheal cases. Carbonated drinks, canned juices, ready-made tea, and plain water should not be recommended.
3.2. Role for scientifically formulated fluids with electrolytes and energy in recovery	Adequate fluids, electrolytes, and energy balance are vital in recovery from illnesses. Even though there are limited data, the use of low-osmolarity oral rehydration solutions (conforming to the WHO standard) in diarrheal-linked dehydration has been extended to non-diarrheal conditions. However, the WHO oral rehydration solutions may not satisfy the fluid-electrolyte-and-energy needs in non-diarrheal cases.  Panel members agreed that in patients with non-diarrheal dehydration, hyperosmolar oral rehydration solutions do not lead to diarrhea. There is a role for scientifically formulated fluids with appropriate electrolytes and energy in recovery. The ready-to-drink formats are preferable due their known quality, convenience, accuracy, and taste.
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Table 4: Therapeutic management of dehydration in diarrheal versus non-diarrheal illnesses.

Diarrheal dehydration	Non-diarrheal dehydration		
Assessing and categorizing level of dehydration (mild, moderate and severe)	Investigations are not necessary in mild to moderate dehydration, in severe dehydration, investigations required for children with electrolyte abnormalities and blood glucose level in children		
Advise mothers/caregiver on how to feed a dehydrated child (preparing and formulating homemade ORS fluids for mild to moderated dehydration)	In mild or moderate dehydration, enteral (oral) rehydration is preferable		
Give multivitamins and zinc supplement every day for around 2 weeks	In severe dehydration or in case of children who cannot tolerate enteral rehydration, IV fluid rehydration is required		
Identify and treat infections (shigella, cholera etc.)	In non-diarrheal dehydration or dehydration in other illnesses (e.g., respiratory infections, diabetic ketoacidosis, meningitis and electrolyte disturbances including hypernatremia)		
In case of gastroenteritis rapid replacement of fluids required	In cases of shock, replace remaining deficit slowly over 24-48 h		
Do not give antibiotics to children with diarrhea unless they have dysentery or severe cholera	Rate of fluid administration should adjusted according to ongoing clinical reassessment including fluid balance, if electrolytes are deranged, consider slower replacement of fluid deficit		
Monitor the child's feeding and treatments and the child's response (e.g., weight gain).  Provide rehydration via the appropriate route with close monitoring			
Adapted from Melbourne T. Clinical https://www.rch.org.au/clinicalguide/guideline_index/Dehyd	Practice Guidelines: Dehydration. 2022. Available at: dration/. Accessed on 23 August 2022, Shirreffs SM. Markers of hydration		

status. Eur J Clin Nutr. 2003;57(2):S6-9.

#### Points of discussion

#### Fever

Boutin et al demonstrated that >25% of infants presented to the pediatric emergency department (PED) for fever were dehydrated and found a good correlation between dehydration and fever. Thildren with fever may reduce fluid consumption which makes them prone to further loss of fluids and electrolytes by increased sweating. Children with a high degree of fever >40°C are at higher risk of dehydration. Hence it is most important to monitor the signs and symptoms of dehydration during fever. Fluid can be maintained by IV/orally by increasing daily fluid intake by 12% for every degree body temperature greater than 37.5°C (rectal). Guidelines recommend regular fluid intake in children with fever to prevent dehydration. In such conditions, oral rehydration solutions may help to overcome mild dehydration.

#### Nausea, vomiting

Nausea and vomiting are common in the pediatric population and is a frequent symptom associated with viral infection.<sup>4</sup> Vomiting is associated with loss of fluids and electrolytes (Na, K, Cl) leading to increased risk of dehydration.<sup>20-22</sup> For vomiting in formula fed infants, one-half to one ounce of oral rehydration salts every 15 minutes for 2-3 hours is recommended. As per the opinion of the expert panel, oral rehydration salts can be given in small sips as tolerated, even for vomiting not related to diarrhea.<sup>4</sup>

#### Heat-related illness (HRI)

HRI is a clinical spectrum of disorders that results from exposure to extreme environmental heat and the body's inability to efficiently regulate heat.<sup>23</sup> Untreated dehydration can lead to three different types of HRI, including heat cramps, heat exhaustion, and heat stroke.<sup>24,25</sup> The choice of oral rehydration therapy (ORT) in children depends on the degree of dehydration.<sup>26</sup> Rehydration is the first step to manage dehydration by recognizing and understanding the symptoms in HRI.<sup>27</sup> Children with dehydration should be rehydrated with cool fluid containing sugar and salt.<sup>24,28</sup> There is a lack of evidence for the management of dehydration caused by HRI in children.

#### Viral illness

The symptoms of viral illnesses like dengue, varicella infection, and hand, foot, and mouth disease (HFMD) are considerably inter-related and may lead to late diagnosis or misdiagnosis.<sup>29</sup> All these viral infectious diseases, typically, have dehydration as one of the key symptoms and fluid management is preferred.

Often, URTIs are accompanied by fever that results in loss of fluids through excessive sweating. However, no

significant evidence is found on dehydration being one of key symptoms of URTIs.<sup>30</sup> Maintaining hydration is important part of care of infants with bronchiolitis. Tachypnea and fever increase fluid loss, potentially worsening dehydration.<sup>31</sup> Panel believed abnormal respiratory pattern should not used as sign of dehydration as it is not specific and could have many underlying possibilities. Infants should given enough fluids to avoid dehydration and restore fluid loss. Amounts of fluids should not cross 100% of daily fluid requirements, normally set to 100 ml/kg for infants<10 kg.<sup>31</sup>

Consensus recommendation 2. It is important to diagnose dehydration in patients with acute non-diarrheal illnesses as well as monitor the need for rehydration along with energy needs

Currently, there is no single biologic parameter for the diagnosis of dehydration. Consequently, rather than going by the primary diagnosis, the need for rehydration should be based on the constellation of signs and symptoms with the objective of preventing and managing dehydration.

Diagnosis of dehydration is critical in patients with acute illnesses.

#### Action statement profile

Improvement opportunity/objective: Organizing fluid needs in a pediatric patient into maintenance, deficit, replacement, and even preventative or anticipatory fluid therapy can provide an orderly, rational, real-world approach to determining appropriate fluid therapy. By paying closer attention to the FEE needs of pediatric patients, the healthcare professionals (HCP) can have a more positive impact on the overall recovery of the child

Difference of opinion: Minor difference of opinion, with two panelist raising reservations on the utility of weight and urine color monitoring

Value judgment: High-depends on patient profile

#### Points of discussion

As per literature, children with mild dehydration will have minimal clinical signs and only a modest decline in urine output. In estimating the severity of dehydration, a change in weight from baseline is the most objective measure.<sup>3,32</sup> As rehydration proceeds, following weights on a serial basis becomes an important adjunct in assessing the efficacy of fluid repletion. If no baseline weight is known, the clinician should rely on other clinical parameters.

In a review of pre-school children with dehydration, the best clinical indicators of volume depletion decreased skin turgor, poor peripheral perfusion, and kussmaul breathing accompanied more significant dehydration, underscoring the difficulty with which mild degrees of dehydration may be estimated by the clinician without access to prior weights.<sup>3,33</sup>

The group agreed abnormal skin turgor, dryness of the tongue and eyes, capillary refill time, frequency of passing urine, and tachycardia as reliable indicators of dehydration. The signs to consider for monitoring clinical status were oral intake, urine output, urine color, and weight changes during oral fluid therapy.

#### Utility and use of biomarkers

The adequacy of children's fluid intake could be measured with urinary biomarkers of hydration such as urine osmolality, urine specific gravity, and urine color.<sup>34,35</sup> As per the literature, urine color may be used for self-assessment of hydration since it can reliably be self-assessed by children above eight years of age.<sup>17,36</sup> However, as per the expert panel, urine color may not be a reliable guide, due to lack of awareness of ideal urine color, amongst parents.

There are no widely accepted specific threshold values for urine concentration to define adequate hydration in children. Apart from this, a marker like serum/plasma osmolality (POSM) is considered as the gold standard for determining dehydration.<sup>37,38</sup> Fluid deficit leads to elevated osmolality levels in both intracellular fluid (ICF) and extracellular fluid, the rise is especially observed in ICF. Thus, in significant electrolyte loss or gain, POSM can be used as a marker indicating dehydration or fluid overload.<sup>38</sup>

The timely and accurate diagnosis of dehydration remains a challenge in the pediatric emergency department and research is ongoing to create a non-invasive tool or validated scale to measure dehydration. A comparison trial designed to validate a Friedman clinical dehydration scale (CDS) tool, showed urine sodium and serum bicarbonate were considered to be the best biomarkers that indicate dehydration. The study also found that CDS score was closely associated with serum bicarbonate levels. Therefore, such non-invasive scales/tools may also play an important role in determining dehydration in critically ill patients. S

Assessment of the need for rehydration is vital

#### Action statement profile

*Improvement opportunity/objective:* By paying closer attention to the FEE needs of pediatric patients, the HCP can have a more positive impact on the overall recovery of the child.

Difference of opinion: Minor difference of opinion, with two panelist raising doubts on the utility of weight and urine color monitoring.

*Value judgment:* High – depends on patient profile.

There should be a methodical approach to determine the fluid therapy based on the severity of dehydration. Management of fluid and electrolyte is recommended for supportive care in the acutely ill child and in children in the operative setting. Taking into consideration all the above possibilities, the line of treatment needs to be framed carefully. It should encompass suitable fluid treatment and target the recovery of the deficits by a suitable replacement therapy to avoid complications and co-morbidities during the growth years.

This highlights that the assessment of rehydration should be based on symptom severity rather than the primary diagnosis.

In addition, most of the doctors agreed that the need for fluids is not the same for all patients with a particular illness and depends on the severity of the condition. Infants and young children present minimal or no clinical findings except for reduced urine output. However, children with moderate dehydration demonstrate decreased skin turgor, dry mucous membranes, abnormal respiratory pattern, and tachycardia with a prolonged capillary refill.<sup>39</sup> Oral fluid replacement is preferred in children with mild to moderate dehydration unless any contraindication exists.

Consensus statement 3. Oral fluid electrolytes and energy replacement should be recommended early in the course of illness (at patient visit / day 1 of illness)

Recommendation for fluids should be based on overall patient clinical condition

Action statement profile

Improvement opportunity/objective: Improve clarity in recommending appropriate fluids with electrolytes and energy

Difference of opinion: Moderate difference of opinion across topics.

Value judgment: High-depends on patient profile.

#### Points of discussion

The recognition of each child's individual clinical situation and each situation's goal with respect to hydration and energy needs is crucial for the provision of the appropriate oral FEE, at the earliest time, including clear recommendation on duration.<sup>3</sup>

The panel discussion also highlighted the importance of ideal energy requirements, for reviving fluid deficits, maintaining proper fluid and electrolyte homeostasis, and preventing complications arising out of low fluid level. All except one panel member agreed that intake of energy supplements is important to protect against breakdown of muscles for energy.

Method of fluid administration is mostly dependent on the severity of dehydration. Table 5 represents the recommended oral fluid management in treatment of electrolyte loss and revival of fluid and electrolyte deficit.<sup>1</sup>

Table 5: Overview of electrolytes and management of deficiencies.

Electrolytes	Normal daily requirements	Treatment of deficit (Oral)
Na	2-5 mEq/kg/day	2-5 mEq/kg/day in divided doses
K	Neonate: 2-6 mEq/kg/day Children: 2-3 mEq/kg/day	2-5 mEq/kg/day in divided doses, not to exceed 1-2 mEq/kg/dose
Mg	0.3-0.5 mEq/kg/, day (1 mEq = ~12 mg of elemental Mg)	10-20 mg elemental /kg/dose up to four times per day (oral replacement is challenging because of GI intolerance)
Ca	Neonates: 200 mg/day (elemental), children: 700- 1300 mg/day	(Dose expressed as elemental Ca) 50- 150 mg/kg/day in four to six divided doses
P	1-2 mmol/kg/day	0.08-0.32 mmol/kg/day

Abbreviations: Ca, calcium; GI, gastrointestinal; K, potassium; Mg, magnesium; Na, sodium; P, phosphorus.

Maintenance fluids compensate for insensible losses and are required for all patients. They are administered intravenously or orally. 8.40 Pediatric patients in an outpatient department setting may all have elevated maintenance fluid requirements. In fever, there is 12% increase in maintenance fluid requirements with every degree rise in body temperature. 18 The expert panel was also in complete agreement that it is important to monitor hydration in pediatric patients with decreased oral intake and increased losses including insensible losses and fluid output. Furthermore, the panel also agreed that oral fluids should be recommended for the inpatient department (IPD) setting.

Role for scientifically formulated fluids with electrolytes and energy in recovery

#### Action statement profile:

Improvement opportunity/ objective: Improve clarity in recommending (low-osmolarity) WHO-oral rehydration salts (ORS) and-non-WHO ORS formulations, difference of opinion:

Moderate difference of opinion across topics and value judgment: High-depends on patient profile.

#### Points of discussion

ORS is the non-proprietary name for a balanced glucoseelectrolyte mixture. It was first used in 1969 and approved, recommended, and distributed by the United Nations International Children's Emergency Fund (UNICEF) and the WHO as a drug for the treatment of clinical dehydration throughout the world. The WHO and the UNICEF have recommended a single formulation of ORS to prevent or treat dehydration irrespective of the cause or age group affected.<sup>41</sup>

Low osmolarity ORS solution (75 mEq/L sodium concentration, 75 mmol/l glucose concentration, and osmolarity is 245 mOsm/L) has shown efficacy for the management of dehydration in children, and 33% reduction in unscheduled supplemental intravenous therapy. The 245 mOsm/L solutions were also demonstrated to be safe and efficacious for children with dehydration, and therefore the WHO and the UNICEF now recommend that countries use and manufacture it, for dehydration in different modes of therapy. 41,42 In a combined analysis of various studies with other reduced osmolarity ORS solutions (osmolarity 210-268 mOsm/l, Na 50-75 mEq/l) stool output was reduced by about 20% and incidence of vomiting by about 30%. During panel discussion, two panelists believed that some ready-todrink (RTD) ORS products in the market are not WHO compliant, due to difference in composition between different manufacturers and osmolality may also differ from the WHO recommended range.

#### ORS vs homemade fluids vs premixed /(RTD)

Complications occur when infants/children are given liquids such as juice, sports beverages, and milk (excluding breast feeding infants) for rehydration due to their inappropriate glucose and electrolyte composition. These types of fluid do not have the right mix of sugar and electrolytes, which may affect the degree of dehydration and do not meet the needs of dehydrated patients.<sup>3</sup> However, children who are breastfed should continue to breastfeed.<sup>8</sup> A study has shown that the electrolytes in the beverages are less (especially potassium), osmolarity was very high (693 mOsm/L) and pH was more acidic.<sup>43</sup>

Evidence has shown ORS to be simpler and effective when compared to the recommended home fluids in preventing dehydration.<sup>44</sup> Oral rehydration powders are easy to store, less expensive, and have an extended shelflife, but these powders should be mixed accurately to alterations in glucose prevent and electrolyte concentrations.<sup>45</sup> An incorrect amount of water for dilution can hamper the concentration of electrolytes. 45,46 In a consumer behavior study from India it was found that reconstitution variations led to a deviation in the resulting osmolality of the ORS solution from the recommended value of 245 mOsmol/kg.47 Therefore, premixed ORS is recommended compared to homemade powdered alternative. 45 It is also essential to counsel the parents and care givers on the correct method of reconstituting ORS powder and the potential adverse effect of incorrect concentration of ORS, if not prepared as per the labeled instructions. 47 The European Society of Pediatric Gastroenterology and Nutrition recommends a premixed ORS which has predefined concentration consisting of 60 mmol/L of Na with osmolarity between 200 mOsm/L and 250 mOsm/L, for children in developed countries. 48,49 The American Academy of Pediatrics also recommended that an ORS of predefined concentration consists of 45 mmol/L to 50 mmol/L of Na and can be used for rehydration and maintenance in healthy children who are mildly or moderately dehydrated. 45,50

#### Specific to non-diarrheal illnesses

The panel opined that a holistic approach including all nutrients is important to achieve desired results. The panel was of an opinion that clear homemade fluids like dal water, herbal tea, soup made with proper care and instructions could be given. Dal (pulses) water, homemade chicken broth or vegetable juice with natural vegetables as well as herbal teas with ginger, honey, curcumin, and pepper can help soothe the child and provide hydration. However, parents sometimes give homemade solutions that are not appropriate and vary from parent to parent leading to errors and inadequate rehydration. There were other experts who thought that fresh fruit juices may provide more sugar and fewer electrolytes whereas one expert was of an opinion that the composition of coconut water is unreliable as an appropriate rehydration fluid. Since the evidence is limited, consensus was reached mainly based on clinician's experience that scientifically formulated fluids with electrolytes and energy have a role in patient recovery. Apart from the convenience benefit, the panel was also of the opinion that RTD formats are preferable due to their quality standard with known concentration of electrolytes, energy contents as compared to variable home-made preparations. Other advantages of RTD formats includes hygienic packaging and better palatability with increased compliance in children versus highly variable salt and glucose intake with inherent potential for errors in dilution.<sup>45</sup> Panel members agreed that, in patients with non-diarrhea related dehydration, hyperosmolar oral rehydration solutions do not lead to diarrhea.

A consensus was reached that carbonated drinks and canned juices, should not be recommended especially for those with diarrhea. Plain water is not optimal in replacing electrolytes especially for those with anorexia who can mostly tolerate fluids only. Patients should be advised to take frequent small sips of fluids every few minutes (5-10 minutes) if not able to drink large volumes.

#### Challenges and evidence gaps

The timely and accurate diagnosis of dehydration remains a challenge in the pediatric population. There are some markers like, body mass changes, blood and urine indices and bioelectrical impedance analysis which have been the most widely investigated markers for determining the ideal level of hydration. Most of the scientific evidence for fluid management for out-patient cases with dehydration have been extrapolated from diarrheal cases. More 'real-world' evidence is needed to determine the severity, incidence, and character/type of dehydration in various acute illnesses beyond diarrhea and generate data for definitive recommendations on how oral FEE management impacts recovery from acute non-diarrheal illnesses. Real world evidence is also required on role of various fluids, including ready-to-drink hydration and electrolyte drinks for addressing dehydration.

#### **CONCLUSIONS**

Physicians should recommend and monitor dehydration treatments in every patient with the same intensity as that with diarrheal conditions. The appropriate management of FEE balance from early in the course of illness is essential for recovery in every patient with acute illnesses, whether diarrheal or non-diarrheal. Further research is required to address the evidence gaps in the management of dehydration in pediatric patients with various acute non-diarrheal illness for improved outcomes.

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