

Perception and Practice on the Management of Pediatric Diarrhea in Thailand

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Background: Various observational and survey-based studies have shown suboptimal adherence to clinic practice guidelines, on management of pediatric diarrhea in Thailand.

Objective: To define clinical practice of acute diarrhea in young children at a quaternary care teaching hospital, and to determine factors associated with the management.

Materials and Methods: The authors initially reviewed the medical records of 1,500 children aged one month to five years with a diagnosis code of acute diarrhea between January 2017 and December 2018. The authors excluded children who received treatment from other centers or had other final primary diagnosis. This resulted in 802 cases, from which the authors collected presenting symptoms, investigations, and management.

Results: The median age was 16 months (IQR 9, 29). Most children had no documentation of dehydration status (60%) and did not have mucous or blood in their stools (80%). Blood or stool tests were performed in less than 20% of the cases. Advice on lactose avoidance was noted in 16%, while antibiotics and hospital admission were noted in less than 10%. Domperidone was prescribed in 42%, while ondansetron was given in 8.7%. Multivariate logistic regression analyses showed various independent factors associated with lactose avoidance including age of less than 24 months, type of physician, vomiting, and hospital admission, antibiotic used when there was high grade fever of 39°C or higher, mucous bloody stools, performed blood culture, and stool culture, and hospital admission when there was moderate dehydration, complete blood count, and performed stool culture.

Conclusion: Recording dehydration status is suboptimal. Low rates of investigations complied with most clinical scenarios. Findings on the pediatric acute diarrhea-related management may provide future opportunities to improve education and further conduct quality improvement projects among clinicians.

Keywords: Antibiotics; Gastroenteritis; Lactose; Probiotics; Racecadotril

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Acute diarrhea is now defined as diarrhea that lasts no longer than seven days⁽¹⁾. Among the low-income countries, it accounts for 550,000 deaths per year⁽²⁾. However, a large multinational survey recently reported a 20-percent drop of diarrhea-related deaths in just one decade⁽³⁾. Children residing in the developed country also usually present with a ‘mild’ condition without septicemia or bacteremia and recover without long term complications, although the condition remains among the top three most

frequent causes of hospital visits and admissions⁽⁴⁾. Thailand, a country situated in the Southeast Asian region that became a newly industrialized country with an upper middle-income economy, have seen a shift to the trend.

Several clinical practice guidelines between 2014 and 2018 had been launched to help health care providers in the diagnosis and management of this common condition^(1,5-7). Limited investigations to find the causative agents of acute diarrhea among immunocompetent children with non-severe acute infectious diarrhea has been recommended. For example, a previous study performed in the metropolitan area of Bangkok demonstrated that among the examined 1,793 stool culture specimens, 73% grew normal flora, 10.8% had enteropathogenic *Escherichia coli*, and 2.9% had *Campylobacter jejuni*⁽⁸⁾. Therefore, antibiotics may be unlikely needed in most children. This data further reinforces that even knowing the causative agent may not change the management, especially with regards to antimicrobial agents. The current elements for the management

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of acute diarrhea are based on the following points, 1) appropriate rehydration, 2) early enteral refeeding⁽⁹⁾ while lactose avoidance may be beneficial only in some specific circumstances, and 3) if applicable and available, agents to reduce intensity and duration of symptoms such as probiotics or antisecretory agents.

Various observational and survey-based studies have shown suboptimal adherence to these guidelines^(10,11). Unnecessary investigations and management may intensify the child's pain and caregiver's anxiety, increase health care expenditure, and create an antibiotic overuse and potential medication side effects. Therefore, the authors aimed to define the practice of acute diarrhea in young immunocompetent children and to determine associated clinical factors on diarrhea-related managements at a quaternary care teaching hospital. The authors propose that these data may help to improve education of health care providers and optimize patient care.

Materials and Methods

The authors initially reviewed the medical records of 1,500 infants and children aged one month to five years coded with International Classification of Diseases (ICD)-10 for acute diarrhea or acute gastroenteritis between January 2017 and December 2018 at a teaching hospital that actively trained residents and fellows (i.e., trainees) during this period. The authors excluded cases with 1) follow-up visit cases (n=113) or received previous treatment from other medical personnel or center (n=94), 2) had other final primary diagnosis such as acute febrile illness, common cold, otitis media, occult bacteremia, constipation or anal fissure, drug reaction, or cow's milk protein allergy (n=141), 3) immunocompromised state such as patients with human immunodeficiency virus, chemotherapy use, and post-transplantation (n=16), 4) isolated vomiting (n=120), 5) chronic diarrhea (n=28), 6) known underlying diseases such as biliary atresia, asthma (n=168), and 7) limited or missing most clinical data (n=18).

Among the remaining 802 cases, the authors systematically collected demographic data, physicians (staffs versus trainees), clinical symptoms, degree of dehydration, diarrhea-related investigations such as stool examination, stool culture, complete blood count, electrolytes, or blood culture, and treatment such as route of fluid management being intravenous, nasogastric, or oral route, lactose avoidance, antibiotics, antiemetic agents, probiotics, or antisecretory agent, and hospital admission. The

Table 1. Baseline characteristics of the 802 young children with acute diarrhea

Characteristics	Results; n (%)
Age (months); median (IQR)	16 (9, 29)
1 to 12 months	307 (38)
≥12 months	495 (62)
Male	435 (54)
Duration of diarrhea (hour), median (IQR)	24 (24, 72)
Body temperature ≥39°C	73 (9)
Vomiting	370 (46)
Stool	
Non-mucous non-bloody	647 (81)
Mucous (non-bloody)	83 (10)
Blood/mucous bloody	72 (9)
Documented degree of dehydration status	
Not recorded	482 (60)
Without dehydration	67 (8)
Mild	159 (20)
Moderate	94 (12)
Severe or shock	0 (0)

IQR=interquartile range

Institutional Review Board at the institution approved the study (IRB No. 2019/54). Informed consent was waived due to its nature of retrospective chart review.

All analyses were done by IBM SPSS Statistics software, version 21.0 (IBM Corp., Armonk, NY, USA). Data were expressed as number (percent), median (interquartile range [IQR]), and proportions (with 95% confidence interval [CI]). Comparisons of discrete variables across different groups were assessed using chi-square test or Fisher's exact test, if applicable; Mann-Whitney U test was used for non-normal distribution continuous variables. Univariate and multivariate logistic regression analyses were performed to define the factors associated management. A p-value of less than 0.05 was considered statistically significant.

Results

The authors reviewed 802 cases of which 77% were treated in the outpatient department with 48% managed by staff and 52% by trainees, and 23% in the emergency department mainly managed by the trainees. The demographic and baseline data of these young children with acute diarrhea are shown in Table 1. The median age was 16 months (IQR 9, 29) with a median duration of diarrhea prior to the hospital visit of 24 hours. Almost half had documented

Table 2. Investigations and management in young children with acute diarrhea

Characteristics	Total (n=802); n (%)	Staffs (n=299); n (%)	Trainees (n=503); n (%)	p-value
Stool investigations				
Stool examination	156 (19.5)	49 (16.4)	107 (21.3)	0.10
Stool culture	151 (18.8)	46 (15.4)	105 (20.9)	0.06
Blood investigations				
Complete blood count	150 (18.7)	44 (14.7)	106 (21.1)	0.03
Electrolytes	129 (16.1)	35 (11.7)	94 (18.7)	0.01
Blood culture	70 (8.7)	21 (7.0)	49 (9.7)	0.20
Managements				
Lactose avoidance	129 (16.1)	72 (24.1)	57 (11.3)	<0.01
Antibiotics	67 (8.4)	31 (10.4)	36 (7.2)	0.12
Intravenous ondansetron	70 (8.7)	24 (8.0)	46 (9.1)	0.61
Oral domperidone	337 (42.0)	120 (40.1)	217 (43.1)	0.42
Probiotics	84 (10.5)	68 (22.7)	16 (3.2)	<0.01
Racecadotril	162 (20.2)	120 (40.1)	42 (8.3)	<0.01
Hospital admission	73 (9.1)	33 (11.0)	40 (8.0)	0.17

Table 3. Multivariable logistic regression analyses on the managements of acute diarrhea in children

Lactose avoidance	Adjusted OR (95% CI)	Antibiotic use	Adjusted OR (95% CI)	Hospital admission	Adjusted OR (95% CI)
Age ≤24 months	4.6 (2.5 to 8.5)	Fever ≥39°C	2.8 (1.3 to 6.0)	Moderate dehydration	6.3 (2.6 to 15.3)
Staffs vs. trainees	2.7 (1.8 to 4.0)	Mucous bloody stool	4.9 (2.6 to 9.4)	Complete blood count	8.2 (3.0 to 22.0)
Vomiting	0.6 (0.4 to 0.9)	Performed stool culture	2.8 (1.4 to 5.9)	Performed stool culture	2.5 (1.1 to 5.7)
Hospital admission	2.1 (1.1 to 3.7)	Performed blood culture	3.0 (1.4 to 6.5)		

OR=odds ratio; CI=confidence interval

vomiting and most did not have mucous or blood in the stools (81%). Interestingly, there was no documentation of dehydration status in 60% of the patient records. Among the 320 cases that recorded dehydration status, none had severe dehydration or shock. All except nine (85/94; 90%) children with moderate dehydration received intravenous fluid. None received fluid via nasogastric tube during the study period.

Physicians ordered diarrhea-related tests such as stool examination or culture, complete blood count, and electrolytes in less than 20% of cases. The trainees performed complete blood count and electrolytes more common than the staffs as shown in Table 2. With regards to the management, advice on lactose avoidance was given in 16%. Antibiotics were given in a small percentage of children. Intravenous ondansetron was given only in 8.7%, whereas oral domperidone was prescribed in 42%. Physicians decided to hospitalize 9% of children.

The authors conducted multiple logistic

regression analyses to define independent factors on the diarrhea-related management as shown in Table 3. The advice on lactose avoidance was independently associated with being young infants aged less than 24 months, type of physicians such as staffs or trainees, vomiting, and hospital admission. Antibiotic use was associated with high grade fever of 39°C or higher, mucous bloody stools, performed blood culture, and stool culture. Finally, hospital admission was associated with documented moderate dehydration, performed complete blood count, and stool culture. No effect modifier was noted among these independent factors.

Discussion

The authors reported a study conducting at a quaternary care teaching hospital located in a newly industrialized country to define practice on the management of young children presented with acute diarrhea. Acute diarrhea was primarily managed by the trainees such as residents or fellows in 63%. The

present study children were mostly older than one year old, visited the hospital early, presented with non-mucous non-bloody diarrhea, being non-toxic, and non-severe dehydration.

The dehydration status was however inadequately documented in 60% of the reviewed charts. However, the authors postulated that those cases without a proper documentation of dehydration status were not moderately or severely dehydrated as they did not receive intravenous fluid or being admitted to the hospital (data not shown). A limited number of children with recorded of dehydration status, 90% of them with moderate dehydration received intravenous fluid, and no children received fluid via nasogastric tube. The current guideline recommends rehydration therapy via oral or nasogastric route as the initial fluid replacement for moderate dehydration, unless the child cannot appropriately drink fluid by mouth or has significant vomiting or alteration of consciousness⁽¹⁾. Previous studies had shown that 66% to 74% of children with acute gastroenteritis received intravenous fluid at the initial setting^(10,11), though a systematic review reported no significant difference in the duration of hospitalization between children receiving intravenous hydration and those receiving initial oral rehydration therapy⁽¹²⁾. Intravenous fluid therapy is a common practice in children with moderate dehydration in the present study country. This could be due to physician and parental preferences and beliefs, as well as the lack of convincing local data. Survey-based studies on the preferred route of initial fluid management and clinical outcome should be further conducted.

In compliance with the established guidelines^(1,5), most diarrhea-related tests were performed only in small percentages of less than 20% of children as shown in Table 2. Electrolytes were more commonly performed by the trainees. Trainees at the present study hospital provided patient care both in the outpatient setting (319/503; 63.4%) and the emergency department (184/503; 36.6%). They may perceive that the children seen in the emergency department would more likely require additional investigations than the children in the general outpatient setting. Serum electrolytes should be mainly measured in children who have severe dehydration or require intravenous fluid therapy because these children may need adjustment of the IV fluid according to their serum sodium level⁽¹⁾. However, the authors did not have all the subjective data such as ability to drink fluid, degree of vomiting, and conscious level, to properly define the appropriateness of clinical practice on fluid

management and testing for serum electrolytes during the first few hours of initial patient visit.

The authors also demonstrated that most children did not receive adjunctive management for acute diarrhea. Dietary lactose avoidance has always been a common advice during the past two decades that physicians provide to the caregiver of diarrheal children. A Cochrane review reported that lactose-free products were associated with a reduction in the duration of diarrhea in hospitalized children by approximately 18 hours⁽¹³⁾. However, the routine use of lactose-free milks or lactose avoidance is not recommended especially within the first few days of the onset. Avoidance of lactose may therefore be advised in the inpatient settings or children with diarrhea continuing for longer than seven days⁽¹⁾. In the present study, children were advised to avoid lactose-containing products in 16.1%, which is lower than the South Korean and Italian studies at 27.3% and 27.6%, respectively^(10,11). Associated factors with lactose avoidance were younger children of less than 24 months, types of doctors, vomiting, and hospital admission (Table 3). Infants and young toddlers may still consume substantial amount of milk; therefore, physicians may consider lactose avoidance as a therapeutic option in this age group. Negative association of vomiting is difficult to explain as children with vomiting were less likely to receive advice on lactose avoidance. Physicians more commonly provided advice on avoiding lactose in the hospitalized children as these children may have more severe diarrhea symptoms. Findings on antibiotic use seemed rational as the independent factors were clinically linked to the pattern of invasive diarrhea. Hospital admission was associated with moderate dehydration, performed complete blood count, and stool culture. Reasonably, physicians may consider sending additional blood and stool tests in the hospitalized children.

Regarding the antiemetic and adjunctive agents, ondansetron is effective in alleviating vomiting related to acute gastroenteritis⁽⁷⁾. While domperidone was prescribed in 42% of children, which the proportion was comparable between the staffs and trainees as shown in Table 2, it is not supported by the guideline or recent review⁽¹⁴⁾. Domperidone is associated with cardiac arrhythmia such as prolonged QT interval⁽¹⁵⁾; therefore, the use of domperidone should be used judiciously. Probiotics use in young children is not a common practice (10.5%), even when most children were likely suffering from acute viral diarrhea or gastroenteritis as noted that 81% of the children

presented with non-mucous non-bloody diarrhea. The position paper supported probiotics in acute gastroenteritis especially *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*^(1,16). *S. boulardii* is available, but it does not belong to the national essential drug list as does racecadotril, the efficacious antisecretory agent for acute diarrhea with minimal side effects⁽¹⁷⁾. Self-payment is required for the non-national drug list items. A study from Thailand also demonstrated that the cost-benefit of probiotics *Lactobacillus acidophilus* with *Bifidobacterium bifidum* in 106 hospitalized children with acute diarrhea were not significantly different when compared to the ones who received standard of care⁽¹⁸⁾. Furthermore, two recent high-quality studies also reported non-significant differences in the various outcomes on pediatric acute diarrhea when compared probiotics and placebo^(19,20). Therefore, the local data on the efficacy and cost-benefit analysis of proposed probiotics may be required before implementing certain agents into the national drug list.

The authors are aware of the nature of the present study that the association cannot fully define the “causality” of clinical symptoms especially the disease characteristics and severity with the performed investigations, prescribed managements, or outcomes. The authors also did not have access to all the laboratory results. The study in the large teaching hospital may limit generalizability to all settings. Nevertheless, the present study data would provide insights for health care providers on the current practice on the management of this common condition at comparable academic institutions.

Conclusion

From the data of many young children with acute diarrhea at a teaching hospital, the record on dehydration status is suboptimal. Low rates of investigations are noted, which act in accordance with the current guidelines. Findings on the diarrhea-related management, especially on the route of given fluid, and on the antiemetic and adjunctive agents may provide future opportunities to improve education and further conduct quality improvement projects among pediatric health care providers.

What is already known on this topic?

Several clinical practice guidelines in childhood acute diarrhea have been launched, but studies have shown that clinicians may not adhere to those recommendations.

What this study adds?

In a single tertiary care teaching hospital, low rates of investigations were complied with most clinical scenarios. However, some findings on the management may provide future opportunities to conduct quality improvement and education projects among clinicians.

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Ethical approval

All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional research committee (the Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine Ramathibodi Hospital, Mahidol University) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was waived due to a retrospective nature of study.

Availability of data and materials

The datasets generated or analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

Authors' contributions

Sukyotin S drafted the initial manuscript and analyzed the data. Tanpowpong P and Treepongkaruna S read, critically reviewed, and finalized the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflicts of interest

The authors declare that they have no conflict of interest.

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