Implementation Outcomes of Clinical Practice Guideline for Management of Acute Diarrhea in Children

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ABSTRACT

OBJECTIVE: To compare the length of stay and total charges for children with acute watery diarrhea admitted before and after the implementation of the 2021 clinical practice guideline for acute diarrhea in children.

METHODS: This was a descriptive study. We studied healthy children aged 1 month to 15 years with acute watery diarrhea who had been admitted for inpatient treatment at the Department of Pediatrics, Faculty of Medicine, Vajira Hospital. Independent sample t-test was used.

RESULTS: There were 51 patients in each group. Median age and IQR for the pre-implementation and post-implementation groups were 22 ± 39 and 27 ± 44 months, respectively (p = 0.403). Average length of stay in the post-implementation group was reduced by 5.9 hours with no statistical significance (63.18 hours vs 69.06 hours; p = 0.232). Average total charges after the CPG implementation were reduced significantly (7,752.31 THB vs 9925.91 THB; p < 0.004) and average investigation costs were reduced (1,326.18 THB vs 2,397.98 THB; p < 0.001). There was no difference between the two groups in terms of post-admission complications and readmission proportion within 48 hours.

CONCLUSION: Using the 2021 clinical practice guideline for acute diarrhea was effectively helpful to reduce length of stay and total charges, with no difference in post-admission complications or readmission proportions.

KEYWORDS: acute diarrhea, antibiotics use, hospital charges, laboratory investigation, length of stay

INTRODUCTION

Acute diarrhea is defined as patient having loose or liquid stool 3 or more times within a 24-hour period, lasting 7 days or less[1]. A report by the US Centers for Disease Control and Prevention revealed 1.5 million pediatric out-patient visits and 220,000 admissions per year resulting from acute diarrhea[2]. In Europe, the incidence rate in children was 4-17%[3]. In 2018, the Department of Disease Control, Ministry of Public Health, Thailand[4] reported that the highest incidence rates were among children aged 0-4 years and 5-9 years (7,948.16 and 2,628.98 per 100,000 in the population, respectively).

Acute diarrhea is usually self-limited, and antimicrobial treatment is not necessary for disease recovery. Investigations to identify the etiologic agents and antibiotics are only required in some limited cases[1,5-6]. Inappropriate use of antibiotics in acute diarrhea results in drug-resistant

bacteria. Besides, more prolonged carrier state and bacterial shedding via feces can be found in patients with *Salmonella* infections who have received inappropriate antimicrobial treatment[7]. For acute diarrhea resulting from Shiga-toxin producing *E. coli* or enterohemorrhagic *E. coli,* improper antibiotic prescription increases the risk of developing hemolytic uremic syndrome[8].

From previous studies, including several conducted in Thailand, it was found that the rates of unnecessary laboratory investigation and antimicrobial treatment were as high as 70%[9-12], resulting in longer lengths of stay and unnecessarily higher expenses. The most common unnecessary tests included stool culture, blood culture, stool viral antigen, and inflammatory markers such as C-reactive protein (CRP) and procalcitonin. In Italy Albano, et al. [13] conducted a randomized controlled trial in 2009 and showed that children who had received treatment based on the 2014 European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines had significantly lower medical expenses and shorter durations of illness. In the US 2001-2006, Tieder, et al.[14] found that rational investigation and antimicrobial drug prescriptions for pediatric acute diarrhea, following the American Academy of Pediatrics-endorsed 2003 CDC recommendation, significantly reduced hospital expenses in the emergency departments and observation wards, while readmission proportion was not different between the groups.

At Vajira Hospital, the average length of stay among children with acute watery diarrhea in the 2017-2019 fiscal years was 3.43 days[15-17], which was much longer than that of other hospitals in Thailand in 2018-2019, which was only 2.3 days[16-17]. Similarly, a study by Tieder, et al. in the United States in 2009 found that the average length of stay was only 1.9 days[10] In addition, mean of hospital charges at Vajira Hospital was 9,695 Baht (THB) per case[15-17], although the reimbursement from National Health Security Office of Thailand was only 2,335 THB per case based on Diagnosis Related Groups (DRG)[17-18].

Excess unnecessary medical costs leaded to monetary problems and substantial budget losses.

As a result of the aforementioned, the Department of Pediatrics, Faculty of Medicine Vajira Hospital published the 2021 clinical practice guideline for acute diarrhea in children[19], adapted from the recommendations in Europe, the United States, and Thailand[1,5-6] to standardize treatment for children, in consideration of safety and reasonable price. This study was conducted to evaluate the effectiveness of the guideline by comparing the length of stay, medical expenses, complications, and readmission proportions between patients admitted before and after the implementation of the guideline.

METHODS

This was a descriptive study. We included children aged 1 month to 15 years who were diagnosed with acute diarrhea and admitted to Vajira Hospital before and after the implementation of the 2021 clinical practice guideline for acute diarrhea in children.

The exclusion criteria comprised patients with a history of gross bloody stools or visible bloody stool at admission, including cancer patients who received last chemotherapy session less than 3 months. The exclusion criteria included all patients with immunocompromised status namely patients with or using immunosuppressive agents or systemic corticosteroid, human immunodeficiency virus (HIV) infection, asplenia, inflammatory bowel disease, congestive heart failure, chronic kidney disease, chronic liver disease, current use of diuretics, suspected of sepsis at first presentation, regardless of gastrointestinal or extra-gastrointestinal cause, systemic infections (such as meningitis) requiring antibacterial treatment, surgical abdomen, COVID-19 infection, patients admitted after the implementation of the 2021 guideline with any poor adherence to the guideline.

The 2021 guideline-adherent practice was defined as rational submission of stool culture (indicated in infants aged less than 6 months,

suspected septicemia, alteration of consciousness, or shock, fever > 38 Celsius, mucous and/or bloody stool, severe abdominal pain or present abdominal tender point, patients with HIV, cancer, current use of immunosuppressive agents, inflammatory bowel disease, stool frequency more than 10 times/day, suspected infection from *Vibrio cholera*, diarrhea not improved within 7 days, or during the disease outbreak), blood culture (indicated in infants aged less than 6 months, suspected septicemia, alteration of consciousness, or shock, mucous bloody stool with high grade fever, patients with HIV, cancer, current use of immunosuppressive agents, inflammatory bowel disease), stool for viral antigen (only indicated during the disease outbreak), and inflammatory markers such as C-reactive protein and procalcitonin (indicated in septicemia, alteration of consciousness, or shock).

According to the guideline, empirical use of antibiotics is indicated for infants aged less than 3 months with mucous bloody diarrhea, or stool white blood cell (WBC) > 5 or stool red blood cell (RBC) > 10 cells/ high power field, or patients with fever > 38 Celsius and mucous bloody diarrhea, or stool WBC > 5 or stool RBC > 10 cells/ high power field, or patients with HIV, cancer, immunosuppressive agents, inflammatory bowel disease, suspected septicemia or severe clinical presentation, or compatible with other systemic infections, such as meningitis, surgical abdomen, or suspected infection due to *Vibrio cholerae* or *Shigella* spp. The criteria for discharge with safety were sufficient hydration status, or oral intake equals or exceeds losses, regardless of stool frequency, consistency, and complete cessation of diarrhea.

Post-admission complications were defined as septicemia and/or other systemic infections, such as to the central nervous system or bones and joints, of which the signs and symptoms do not manifest at admission, or readmission with severe diarrhea within 48 hours after discharge.

The study was conducted after receiving the approval from the Institutional Review Board of the Faculty of Medicine Vajira Hospital on May 6th, 2021 (COA 081/2564). This study was divided into 2 phases. The first pre-implementation phase was performed by the retrospective method. We recruited patients before the guideline implementation collecting the adequate number of calculated sample size (N =51). The post-implementation phase consisted of a retrospective part beginning on the day of guideline implementation to the day of protocol approval, and prospective part, starting on the day of protocol approval until a total of 51 eligible patients were recruited.

In the retrospective part, we collected and reviewed the medical records. Informed consent was applied to the patients and/or their parents in the prospective part. Data recording was computerized. All procedures were performed under confidentiality.

STATISTICAL ANALYSIS

We determined the sample size for comparing two independent means with the following equation:

$$n_1 = \frac{(z_{1-\frac{\alpha}{2}} + z_{1-\beta})^2 \left[\sigma_1^2 + \frac{\sigma_2^2}{r}\right]}{\Delta^2}$$
$$r = \frac{n_2}{n_1}, \Delta = \mu_1 - \mu_2$$

where α (type I error) was 5%, ß (type II error) was 10%, μ_1 was the average length of stay in Vajira Hospital (3.43 days), μ_2 was the average length of stay in Thailand (2.3 days), and σ was 1.76 (standard deviation for length of stay among children with acute diarrhea admitted to Vajira Hospital during the 2017-2019 fiscal years). Ultimately, the sample size was 51 patients in each group.

Data were analysed using SPSS Version 28.0. Numerical data such as age, duration of diarrhea before admission, stool frequency, length of stay, and medical expenses were presented as mean with standard deviation, or median with interquartile range. These data were compared using the Mann–Whitney U test and independent samples t-test. Categorical data such as

sex, underlying diseases, gross stool appearance, and dehydration status were presented as frequency and percent. The Chi-square test or Fisher's exact test were used to compare these parameters. A p-value < 0.05 was considered statistically significant.

RESULTS

We eventually recruited eligible pre- and post-implementation groups, each of which consisted of 51 patients. The pre-implementation period was from February 4th, 2020 through January 24th, 2021, while the post-implementation period was from January 25th, 2021 through August 7th, 2022. Details about the inclusion and exclusion processes are shown in Figure 1.

Post-implementation participants were more predominantly male compared to the pre-implementation group with statistical significance (66.7% VS 47.1%, respectively). The post-implementation group had significantly more patients with mild dehydration than those of the pre-implementation group (62.7% VS 33.3%, respectively). We found no significant difference in age, underlying diseases, duration of diarrhea before admission, gross stool appearance, stool frequency, body temperature at admission or ward types between the two groups (table 1).

Pre-implementation and post-implementation participants who received guideline-adherent treatment were 2 out of 51 (3.9%) and 51 out of 51 participants (100%), respectively.

Investigation of the post-implementation participants showed significant decreases including in stool culture, blood culture, C-reactive protein and procalcitonin (table 2). When excluding pre-admission costs for COVID-19 screening during the pandemic in post-implementation participants, adherence to the guideline could significantly decrease the investigation cost with a mean decrease of 1,071.08 THB; and when adjusted with Thailand's medical care consumer price index[20] year 2020-2021, the adjusted mean decrease was 1,071.80 THB (p-value < 0.001).

Guideline-adherent practice could reduce the rate of empirical antibiotic use by 13.7%, despite having no statistical significance (p-value = 0.154), as shown in Table 2. The guideline insignificantly lowered total charges with a mean decrease of 304.78 THB (p-value = 0.693) and an adjusted mean decrease of 363.98 THB (p-value = 0.639). However, when excluding costs spent on COVID-19 preventive measures such as pre-admission COVID-19 screening, isolation ward, and personal protective equipment, adherence to the guideline could significantly cut down on total charges with a mean reduction of 2,114.39 THB (p-value < 0.004) and adjusted mean reduction of 2,173.59 THB (p-value < 0.004).
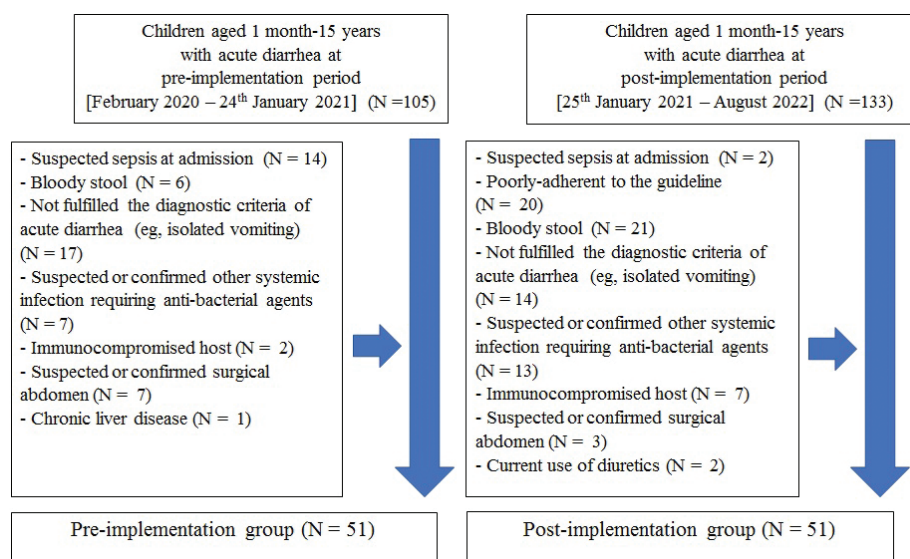

Figure 1   Inclusion and exclusion process

Table 1 Demographic data and baseline clinical characteristics of the participants

Factors	Pre-implementation group (N = 51)	Post-implementation group (N = 51)	P-value
Age (months)			
Median (IQR)	22 (12-51)	27 (14-57)	0.403
Sex			
Male, N (%)	24 (47.1)	34 (66.7)	0.046*
Underlying diseases			
Present, N (%)	7 (13.7)	13 (25.5)	0.135
Duration of diarrhea before admission (days)			
Median (IQR)	1 (1-2)	1 (1-2)	0.283
Gross stool appearance			
Watery, non-mucous stool, N (%)	39 (76.5)	37 (72.5)	0.650
Body temperature at admission			
Temperature > 38˚c, N (%)	30 (58.8)	32 (62.7)	0.685
Degree of dehydration, N (%)			
Mild dehydration	17 (33.3)	32 (62.7)	0.005*
Moderate dehydration	33 (64.7)	19 (37.3)	
Severe dehydration	1 (2)	0 (0)	
Ward type, N (%)			
General ward	32 (62.7)	40 (78.4)	0.082
Private ward	19 (37.3)	11 (21.6)	

Abbreviation: IQR, interquartile range

Table 2 Comparison of the laboratory investigation and empirical antibiotics use between two groups

Factors	Pre-implementation group (N = 51)	Post-implementation group (N = 51)	Difference of proportion (95% CI)	P-value
Stool culture (%)	42 (82.4)	28 (54.9)	-0.275 (-0.435, -0.094)	0.003*
Blood culture (%)	49 (96)	23 (45.1)	-0.51 (-0.638, -0.343)	< 0.001*
C-reactive protein and/ or procalcitonin (%)	15 (29.4)	6 (11.8)	-0.176 (-0.323, -0.016)	0.028*
Empirical antibiotics use (%)	23 (45.1)	16 (31.4)	-0.137 (-0.316, 0.052)	0.154

Abbreviation: CI, confident interval

In spite of having no statistical significance, the post-implementation group had a shorter average length of stay compared to that of the pre-implementation group with a mean reduction of 5.9 hours (p-value = 0.232). We found that none of the participants from either group developed post-admission complications, such as central nervous system infection, bone and joint infection or septicemia. Similarly, no participants were readmitted with more severe diarrhea within 48 hours after discharge (table 3). Rates of positive stool culture in the pre- and post-implementation groups were 9.5% and 17.8%, respectively. All the identified causative organisms in stool were *Salmonella* spp. None of the blood culture specimens from the two groups were found to have pathogenic bacteria.

DISCUSSION

The post-CPG implementation group had a shorter length of stay by 5.9 hours compared to that of the pre-CPG implementation group, but without statistical significance. The 2021 clinical practice guideline for acute diarrhea in children by the Department of Pediatrics, Faculty of Medicine Vajira Hospital helped lessen unnecessary tests, such as for stool culture and blood culture, which previously prolonged the length of stay to wait for the results to become negative. The 2021 guideline, as well as the 2014 ESPGHAN guidelines, recommends the criteria for timely but safe discharge from hospital, such as when sufficient rehydration is achieved, and oral intake equals or exceeds losses, regardless of complete cessation of diarrhea.

Table 3 Comparison of investigation costs, hospital charges, length of stay, and complications between two groups

Factors	Pre-implementation group (N = 51)	Post-implementation group (N = 51)	Mean difference (95% CI)	P-value
Investigation costs, excluding pre-admission COVID-19 screening [THB, mean (SD)]	2,397.25 (1,434.44)	1,326.18 (764.34)	-1,071.08 (-1,522.63, -619.53)	< 0.001*
Adjusted investigation costs, excluding pre-admission COVID-19 screening [THB, mean (SD)]	2,397.98 (1,434.87)	1,326.18 (764.34)	-1,071.80 (-1,523.45, -620.15)	< 0.001*
Total charges [THB, mean (SD)]	9,866.71 (3,794.53)	9,561.92 (3,983.80)	-304.78 (-1,833.23, 1,223.66)	0.693
Adjusted total charges [THB, mean (SD)]	9,925.91 (3,817.29)	9,561.92 (3,983.80)	-363.98 (-1,896.80, 1,168.83)	0.639
Total charges, excluding costs for COVID-19 preventive measures [THB, mean (SD)]	9,866.71 (3,794.53)	7,752.31 (3,521.99)	-2,114.39 (-3,552.66, -676.12)	< 0.004*
Adjusted total charges, excluding costs for COVID-19 preventive measures [THB, mean (SD)]	9,925.91 (3,817.29)	7,752.31 (3,521.99)	-2,173.59 (-3,616.51, -730.68)	< 0.004*
Length of stay [hours, mean (SD)]	69.06 (26.04)	63.16 (23.42)	- 5.90 (-15.63, 3.83)	0.232
Post-admission complications (%)	0 (0)	0 (0)	N/A **	N/A **
Readmission with acute diarrhea within 48 hours (%)	0 (0)	0 (0)	N/A **	N/A **

Abbreviations: CI, confidence interval; THB, Thai baht

** Calculated by difference of proportion

Meanwhile, the reason behind statistical insignificance could be the COVID-19 pandemic. The post-implementation period in this study occurred simultaneously with the delta and omicron variant era. During that chaotic period, all patients with signs and symptoms compatible with COVID-19, including fever, loose stool, and vomiting, would be sent to isolation wards to wait for pre-admission COVID-19 screening results, of which the running time lasted for 8-24 hours. When it became negative, a patient could be transferred to a general ward or private ward. These additional processes required in the post-implementation period could also potentially prolong the length of stay.

After the implementation of the guideline, when the expenses spent on COVID-19 preventive measures were excluded, adjusted total costs and investigation costs were reduced significantly, consistent with the study by Tieder, et al.[14] due to a decrease in unnecessary testing and use of

antimicrobial drugs, especially injections which usually necessitate other medical equipment in the process.

Since the difference in degree of dehydration between two groups could be the potential confounder to the results of our study, subgroup analysis was done on patients with mild dehydration in both phases. We found that any improvement in terms of length of stay, investigation costs and total charges in the post-implementation group were similar to findings in primary analysis.

Post-admission complications and readmission proportion between the two groups were not different, similar to the study by Tieder, et al.[14] The most common cause was virus, especially in immunocompetent children. Despite high mortality rates in young children without treatment, the clinical course was usually benign and self-limited with proper management. With thorough history-taking and physical examination to identify high-risk patients, it is safe to limit investigation

and antibiotic use as necessary according to the guideline for otherwise healthy children with acute watery diarrhea.

A strength of our study was that there have been very few studies[13-14] demonstrating the association between guideline-adherent laboratory investigation and empirical antibiotics prescription in pediatric acute diarrhea and the length of stay and medical expenses. In addition, we analysed the adjusted hospital charges, using Thailand's consumer price index, published by the Ministry of Commerce, which made our findings more reliable and consistent with economic principles.

This study had some limitations. We gathered pre-CPG implementation group information in a retrospective manner using data collected from past medical records. Thus, some of the data may be incomplete or have information inaccuracies due to recording errors. The COVID-19 pandemic, during the post-implementation period, led to a substantial reduction in numbers of in-patients with acute diarrhea and could prolong the length of stay. Due to this barrier and the limited time frame for study, we could not perform random sampling to select the participants and decided to recruit the patients prospectively until a total of 51 patients were recruited.

CONCLUSION

In conclusion, the 2021 clinical practice guideline for acute diarrhea in children by the Department of Pediatrics, Faculty of Medicine Vajira Hospital helped reduce length of stay and hospital charges among previously healthy children with acute watery diarrhea, with no difference in post-admission complications or readmission proportions.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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DATA AVAILABILITY STATEMENT

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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