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ORIGINAL RESEARCH ARTICLE

PROFILE OF ACUTE GASTROENTERITIS IN CHILDREN UNDER FIVE YEARS OF AGE, AND THEIR ASSOCIATION WITH BLOOD UREA NITROGEN-TO-CREATININE RATIO

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ABSTRACT

Background: Acute gastroenteritis (AGE) is a major cause of childhood morbidity and mortality, especially in developing countries. This study aimed to explore the clinical and laboratory profile in under five children with AGE. It furthermore aimed to study the association of socio-demographic and clinical parameters with blood urea nitrogen and serum creatinine ratio (BCR).

Methods: This was a cross-sectional study carried among 62 under-five children in the Pediatric Department, Nepalgunj Medical College and Teaching Hospital. Data was entered in excel and analyzed in statistical package for social sciences. Demographic and clinical data obtained from informants was presented as frequency and percentage. BCR was calculated based on baseline serum urea and creatinine values. Chi square test and logistic regression were used to study the association of clinical and demographic profiles with BCR. Adjusted odds ratio was calculated at 95% confidence interval.

Results: The mean age of participants was 26 months. Most of the children belonged to low socio-economic status (44, 70.97%). Dehydration was the commonest clinical association (51,82.25%) followed by fever (31,50%) and abdominal pain (31,50%). Multivariate logistic regression showed that children with dehydration had greater odds (Adjusted odds ratio (AOR)=5.82) of having BCR greater than 20:1 as opposed to those without dehydration.

Conclusions: AGE was commonly seen in children with low socio-economic status. Dehydration, fever and abdominal pain were common clinical associations. High BCR (20:1) was positively associated with presence of dehydration in children presenting with acute gastroenteritis.

INTRODUCTION

Acute gastroenteritis (AGE) ranks as a major cause of morbidity and mortality in children less than five years of age.[1]The burden is higher in developing countries like Nepal owing to poor sanitation and lack of availability of safe drinking water.[2]Acute kidney injury (AKI) is one of the dreaded complications of AGE. Pre-renal AKI can occur due to hypovolemia as a sequela of dehydration and is the commonest mode of renal injury in AGE.[3] Intrinsic renal failure, though less common can be a consequence of ischemia, sepsis as well as tubular damage by enterotoxin. The laboratory predictors of acute renal injury include increase in urea and creatinine. The nitrogen content of urea is expressed as blood urea nitrogen (BUN) and is nearly half (46.67 %) of blood urea. In pre-renal causes of AKI, urea is found to rise more disproportionately compared to creatinine, leading to high BUN: serum creatinine ratio (BCR). A BCR of 20:1 is considered an indicator of pre-renal AKI in adults.[4] Although there have been many studies regarding BCR as an estimate of dehydration and marker of pre-renal injury in adults, only few studies have been conducted among children. Whether or not BCR can be a sensitive tool in distinguishing patterns of renal injury in children is still a matter of controversy.[5] While presence of dehydration is a poor prognostic factor in AGE, clinical dehydration assessment can have subjective variation. BCR being a quantitative variable, it can be useful if dehydration can be correlated with BCR values. This study aimed to assess the socio-clinical and laboratory profiles of under five children and also study the association of such parameters with BCR.

METHODS

This was a cross sectional study carried out in the Pediatric Department, Nepalgunj Medical College and Teaching Hospital, Nepalgunj, Banke, Nepal. All children between six months and five years of age who were admitted in the hospital from September 2020 to February 2021were included in the study. Children with pre-existing renal conditions including nephrotic syndrome, nephritic syndrome or chronic kidney disease were not included in the study. Dehydration was assessed using WHO clinical assessment which is based on general appearance, sunkenness of eyes, thirst and skin turgor.[6] Children with dehydration from cause other than acute gastroenteritis were also excluded from the study. Likewise, children taking

antibiotics, steroids or any long-term medications were excluded from the study due to their potential effect on renal function.

Since the participants were minor, informed consent was obtained either from mother or caregiver who were present as attendant in the hospital. All children who met the inclusion and exclusion criteria and whose caregivers consented to be enrolled in the study were included in the study. Thus, during the period of six months, the total number of eligible participants size were 62.

Socio demographic and clinical data were obtained from the participants and/or informants using structured questionnaire and checklist**.** Baseline renal profile viz. BUN and serum creatinine were obtained from laboratory reports and BCR were calculated. All relevant data were coded and entered into excel after through checking. Statistical analysis was done using SPSS (Statistical Package for the Social Science) version 16.0. Socio-demographic and clinical parameters were expressed as frequency, percentages, and mean ± SD and presented in the table. Modified Kuppuswami scale was used to assess the socio-economic condition of the participants.[7] Chi square test was used to test for group differences. Odds ratio (OR) were calculated for univariable logistic regression at 95% Confidence Interval (CI). Multivariable logistic regression was used to determine independent factors associated with BCR in children with acute gastroenteritis and adjusted odds ratio (AOR) were calculated. All variables with p value less than 0.2 were retained in the multivariable model. Ethical approval for the study was obtained from Institutional Review Committee of Nepalgunj Medical College and Teaching Hospital, Kohalpur, Banke.

RESULTS

The mean age of participants was 26 months. The proportion of females was 46.77%. Majority of the participants (70.97%) belonged to lower class followed by upper and middle class (29.03%) (Table 1).

Table 1: Socio-demographic characteristics of participants

Characteristics	Frequency (%)
Age in months (Mean ± SD)	26.69 ± 17.06
Range (Minimum-Maximum)	6-60 months
≤24 months	35 (56.45)
>24 months	27 (43.55)
Gender	
Female	29 (46.77)
Male	33 (53.23)
Diet	
Vegetarian	32 (51.61)
Non-vegetarian	30 (48.39)
Socio-economic status[1]	
Middle to Upper class	18 (29.03)
Lower class	44 (70.97)

Patients were assessed clinically based on signs and symptoms. Less than one third (27.42%) of the participants presented with blood in stool. Fever and abdominal pain were seen in half of the participants (50%) each. Vomiting was present in 41.94 % of the participants. Dehydration was present in 82.26 % participants (n=51) Most of the participants (43,69.35 %) belonged to WHO some dehydration category.

Table 2: Clinical profiles of participants

Characteristics	Frequency (%)
Blood in stool	
No	45 (72.58)
Yes	17 (27.42)
Vomiting	
No	36 (58.06)
Yes	26 (41.94)
Fever	
No	31 (50.00)
Yes	31 (50.00)
Abdominal Pain	
No	31 (50.00)
Yes	31 (50.00)
Dehydration[1]	
No	11 (17.74)
Some	43 (69.35)
Severe	8 (12.90)

[1]Dehydration was classified based on WHO clinical categorization of hydration status

The mean BUN was 26.26±11.62 mg/dl and mean serum creatinine level was 1.02 ±0.38 mg/dl. Around two third of the participants (74.19%) had serum BCR more than 20:1 while one third (25.81%) had BCR less than 20:1.

Table 3: Laboratory renal profiles of participants

Characteristics	Mean ±SD (Min-Max)
S. BUN (mg/dl)	26.26 ± 11.62 (6-48 mg/dl)
S. Creatinine (mg/dl)	1.02 ± 0.38 (0.5-2.0 mg/dl)
S. BUN/S. Creatinine	26.91 ± 11.77 (7.5-72.0)
Category	Frequency (Percentage)
≤20:1	16 (25.81)
>20:1	46 (74.19)

Univariable and multivariable logistic regression was used to study the association of socio-demographic and clinical profile of participants with BCR. None of the socio-demographic factors including age, sex, socio-economic status and diet were found to be associated with BUN: creatinine ratio. Participants with blood in stool were found to have 8 times greater odds of having BCR of more than 20:1 as compared to those without blood in stool. Fever and vomiting did not show any statistically significant association with BUN: creatinine ratio. Univariate analysis showed that participants with some or severe dehydration had 8.17 odds of developing BCR greater than 20 as opposed to those with no dehydration.

Table 4: Association of socio-demographic, and presenting symptoms and signs of participants with blood urea nitrogen-to-creatinine ratio

Parameters	BUN/Creatinine ratio		Univariable model[1]		
	Low (≤20:1)	High (>20:1)	OR	95%CI	P-value
Age					0.546[2]
≤24 months	8 (22.86)	27 (77.14)	1 (Ref)		0.547
>24 months	8 (29.63)	19 (70.37)	0.70	0.23-2.21	
Gender					0.378[2]
Female	9 (31.03)	20 (68.97)	1 (Ref)		0.380
Male	7(21.21)	26 (78.79)	1.67	0.53-5.26	
Diet					0.881[2]
Vegetarian	8 (25.00)	24 (75.00)	1 (Ref)		0.881
Non-vegetarian	8 (26.67)	22 (73.33)	0.92	0.29-2.86	
Socioeconomic status					0.999[2]
MiddleToUpper	5 (27.78)	13 (72.22)	1 (Ref)		0.821
Lower	11(25.00)	33 (75.00)	1.15	0.34-3.97	
Blood in stool					**0.048*[2]**
No	15 (33.33)	30 (66.67)	1 (Ref)		0.054
Yes	01 (5.88)	16 (94.12)	8.00	0.97-66.20	
Vomiting					0.111[2]
No	12(33.33)	24 (66.67)	1 (Ref)		0.119
Yes	4 (15.38)	22 (84.62)	2.75	0.77-9.80	
Fever					0.246[2]
No	6 (19.35)	25 (80.65)	1 (Ref)		0.250
Yes	10 (32.26)	21 (67.74)	0.50	0.16-1.62	
Abdominal pain					**0.020*[2]**
No	4 (12.90)	27 (87.10)	1 (Ref)		0.026
Yes	12(38.71)	19 (61.29)	0.24	0.07-0.84	
Dehydration					**0.002*[2]**
No	7 (63.64)	4 (36.36)	1 (Ref)		0.004
Some and severe	9 (17.65)	42 (82.35)	8.17	1.97-33.92	

***Represent the statistical significance at 95% level of confidence (<0.05)**
OR=Odds Ratio and AOR=Adjusted Odds Ratio
Binary logistic regression was conducted using ENTER method
[2]P-value from Chi-square test

While univariable logistic regression showed negative association between abdominal pain and BCR, multivariable analysis showed no significant association of abdominal pain and BCR. Only dehydration seemed to correlate with BCR in multivariate analysis. The odds of having BCR more than 20:1 was 5.82 times greater in participants with dehydration (Table 5).

Table 5: Association of BCR value with all parameters with P < 0.20 in univariable model

Parameters	Multivariable model[1]		
	AOR	95% CI	P-value
Blood in stool			
No	1 (Ref)		0.204
Yes	4.18	0.46-37.93	
Abdominal pain			
No	1 (Ref)		0.061
Yes	0.26	0.07-1.07	
Dehydration			
No	1 (Ref)		**0.025***
Yes	5.82	1.25-27.20	

[1]Adjusted for blood in stool, abdominal pain and dehydration.
***Represent the statistical significance at 95% level of confidence (<0.05)**

DISCUSSION

In our study, acute gastroenteritis was seen in more in children less than two years of age as compared to those above two years of age; however, the difference is not marked. Reviews of previous studies show that the morbidity and mortality due to diarrhea is highest in children less than 2 years of age.[8]Studies show that rotavirus and adenovirus diarrhea is more common in children less than 2 years of age while norovirus and astrovirus diarrhea is more common in children above 2 years of age. [9] In our study, the prevalence of diarrhea was almost common among males and females. Although some studies show greater incidence in males[8] and some in females[10]; the variation is not significant in any of the studies. Most cases of AGE was seen in children with low socio-economic status. This could be attributed to poor sanitation and hygiene, lack of access to safe drinking water and inadequate access to antidiarrheal medicines including oral rehydration therapy. In our study, blood in stool was seen in 27.12 % children with AGE. According to International Encyclopedia of public health, 2017; bloody diarrhea accounts for 10 % of diarrheal episodes in children under five years of age.[11] While watery diarrhea due to rota virus is the commonest cause of diarrhea amongst children, bloody diarrhea could be due to *Shigella, Salmonella, Entaemoeba histolytica, E. coli, Campylobacter*.[12] Bloody diarrhea coupled with renal impairment and thrombocytopenia could also be the manifestation of hemolytic uremic syndrome which is a common pathology in children.[13] Dehydration was categorized into no, some and severe dehydration based on WHO classification that incorporates general appearance, sunkenness of eyes, thirst and skin turgor. While no dehydration corresponds to a fluid deficit of less than 5 % of body weight, severe dehydration corresponds to fluid loss of more than 10 % of body weight.[6]

Pediatric reference values for BUN and creatinine is not as clearly demarcated in the literature as for adults. Despite the subtle differences in various literature, the reference value for serum creatinine level in children less than five years of age is usually below 0.5-0.7 mg/dl.[14,15]In this context, the mean serum creatinine level was markedly high in our study, the mean value being 1.02 mg/dl. Although BUN is supposedly less affected by muscle mass and weight like serum creatinine, a serum analyte of around 2000 children of age 3-6 years showed that the mean BUN was 13.19±2.91mg/dl suggesting that the average BUN values in children is markedly lower than that of adults.[15] Likewise, another small single center retrospective review showed that the mean BUN value for children less than 2 years of age was 20.1 ±1.91 mg/dl and 2-5 years of age was 16.5±14.0 mg/dl.[5] Nevertheless, the average BUN in ours study was found to be quite high. In adults, a BCR of 20:1 is generally considered a marker for differentiation of pre-renal AKI from other causes of renal injury. BUN: creatinine ratio is less clearly defined in children. A study shows than BCR is greater than in younger children as compared to old children. It is thus important to have age specific criteria for estimating normal BCR levels.[5] Our study, however did not show significant association of age with BCR. However, the sample size in our study was small; thus, the effect of age on BCR could have been masked. There was no association between gender and BCR in our study. Studies in adult show that BCR is higher in males than females which could be higher due to greater muscle mass in males.[16] The gender specific difference in BMI or muscle mass is less evident in children under five years of age. Our study showed that blood in stool was significantly associated with BCR with the ratio being greater in cases of gastrointestinal (GI) bleed. A BCR ratio of more than 30:1 is used to differentiate upper GI bleed from lower GI bleed in children.[17,18]This is because the transit time is higher in upper GI bleed, allowing more time for absorption and catabolism.[19] BCR was found to be significantly associated with severity of dehydration. This is obvious considering that dehydration correlates with renal ischemia and subsequent increased absorption of urea.

One of the major limitations of this study was the sample size which was relatively small, thus the findings may not be generalizable to the population. Likewise, we have not taken into account weight or BMI of the children, which indeed might affect serum creatinine levels. This, being a cross sectional study, only the baseline renal profile was studied. The eventual progression of dehydration could therefore not be correlated with its impact on renal parameters.

CONCLUSION

Acute gastroenteritis was more prevalent in children with low socio-economic status. Common associated symptoms include dehydration, fever and abdominal pain. High BCR (20:1) was positively associated with presence of dehydration in children presenting with acute gastroenteritis.

CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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