

## Study of Urinary Tract Infection in Severely Malnourished Hospitalized Children

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### Abstract

**Background:** Malnutrition is an important cause of morbidity and mortality in developing country like Bangladesh. Malnourished children are always prone to develop various types of infections for example- urinary tract infection (UTI), respiratory tract infection, diarrhea and tuberculosis etc. Sign symptoms of these infection remain hidden in severe malnourished children. So suspicion of UTI in severe malnourished children along with routine examination, culture and sensitivity test is important.

**Objectives:** To evaluate the prevalence, cause and clinical feature of urinary tract infection among severely malnourished hospitalized children.

**Methods:** It was a cross sectional analytical study, conducted over severely malnourished children admitted in pediatrics department of Mymensingh Medical College hospital (Case, n=80) and well nourished children (control, n=50) admitted due to other diseases. Clinical and urinary (naked eye examination, bacteriology and culture) findings were analyzed in groups and prevalence, cause and clinical feature of urinary tract infection were evaluated.

**Results:** Prevalence of UTI among severely malnourished children was 20.0% and in well-nourished controls were 4.0% with significant statistical difference ( $p < 0.05$ ). 6.56% of children with kwashiorkor, 37.50% of marasmic children and 81.82% of children with Marasmic-kwashiorkor had UTI. In 15(93.85%) of UTI patients of cases were suffered with *E. coli* and 1(6.7%) were *proteus*. Among 15 *E. coli* 13 sensitive to Ciprofloxacin, 11 to Nalidixic acid and 12 to Gentamycin and Nitrofurantoin, 9 to Ceftriaxone, 8 to Amikacin, 6 to cefradin. Only 1 sensitive to Amoxicillin and 2 to Cotrimoxazole. All malnourished children with UTI gave history of feeding mismanagement. Most presented with fever (62.5%) and cloudy urine (68.8%).

**Conclusion:** The prevalence of UTI is significantly higher among severely malnourished children.

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**Keywords:** Urinary Tract Infection, Malnourished Children

### Introduction

Protein-energy malnutrition is a syndrome resulting from interaction between poor diets and diseases, leading to anthropometric deficits and generally with deficits in micronutrients. Protein-energy malnutrition in children can be of three types by clinical classification: marasmus (wasting from malnutrition), kwashiorkor, and marasmic

kwashiorkor.<sup>1</sup> According to WHO, severe acute malnutrition (SAM) should fulfilled one or more of the following criteria: (a) Weight-for-height median (WHM)  $< 70\%$  (b) Weight-for-height Z-score  $< -3SD$  (c) Bipedal oedema (Kwashiorkor, marasmic Kwashiorkor, oedematous malnutrition). Global prevalence of stunting and wasting was 22% and 7%

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which represent 151 million stunted and 51 million wasted children in 2017. Of them, 55% of all stunted children and 69% of all wasted children lived in Asia.<sup>2</sup> According to BDHS '2014 nutritional status of under 5 children in Bangladesh- 36% children are stunted, 14% are wasted and 33% are underweight.<sup>3</sup> Prevalence of stunting, wasting and underweight among children under 5 years (0–59 months) was 41%, 16% and 36% respectively in 2011. Although the prevalence of childhood malnutrition in Bangladesh has fallen substantially the rate of decline is not sufficient.<sup>4</sup>

The interaction between infection and nutrition has been a subject to studies past few decades. Today it is widely recognized that there is definite association between malnutrition and infection.<sup>5</sup> Urinary tract infection results from presence of organism within the urinary tract and growth of which is at least  $>10^5$  colony forming unit per ml.<sup>6</sup> The prevalence of UTI varies with age. During the first years of life male: female ratio is 2.8-5.4. Beyond 1-2 year there is a striking female preponderance with a male: female ratio of 1: 10. UTI is caused mainly by colonic bacteria. *Escherichia coli* cause 54-67% of all UTIs, followed by *Klebsiella* spp., *Proteus* spp., *Enterococcus* and *Pseudomonas* etc.<sup>7</sup>

UTI tended to be remaining hidden in malnourished children due to reductive adaptation. UTI is an important occult infection in malnourished children and must be specifically looked for in SAM patients.<sup>8</sup>

Malnourished children particularly those with fever are at increased risk of UTI. Urine analysis is useful for screening of UTI of these patients. Urine culture should be performed those patients showing an abnormal urine analysis.<sup>9</sup>

Infected urine stimulates an immunological and inflammatory response leading to renal injury and scarring, ultimately leading to end stage renal

failure.<sup>7</sup> In a subtropical country like ours; there is a temporal relationship in the antibiotic sensitivity pattern of UTI. Hence frequent large scale studies are required from time to time to note the changes in sensitivity and resistance. Complicated UTI and subsequent renal failure still continues to be one of the major causes of mortality in children in this part of Asia.<sup>7,10</sup> From the global reports reviewed, UTI prevalence rates in SAM patients range from as low as 6% to as high as 37% in developing countries, while the most common bacterial isolates from urine cultures are Gram-negative coliform organisms such as *Escherichia coli* and *Klebsiella* species.<sup>9</sup> Another study showed that among 300 SAM children tested, a urinary tract infection (UTI) was detected in 48 (16%). *E. coli* represented more than three-quarters of the microorganisms isolated, followed by *K. pneumoniae*, *Proteus mirabilis*, *P. penneri* and *E. faecium*.<sup>11</sup>

The current study was carried out to evaluate urinary tract infection among severely malnourished hospitalized children in Bangladesh.

## Methods

### Study design

It is across sectional analytical study done in paediatric department of Mymensingh Medical College Hospital from July 2012 to June 2013. Severely malnourished children admitted in pediatrics department of Mymensingh Medical College Hospital were taken as case. Well nourished children admitted for other reason were taken as control. All cases and control met the inclusion and exclusion criteria were included in the study. 80 children with severe acute malnutrition (SAM) aged 1 to 5 years were taken as case. 50 well nourished children aged from 1 to 5 years suffering from disease other than SAM were taken as control. SAM was diagnosed by WHO criteria for diagnosis of SAM in children under 5

years. Inclusion criteria for control was Weight-for-height median (WHM) > 80% and weight-for-height Z-score (WHZ) < -1SD. Children who received antibiotic at least 72 hours before and after admission to the hospital were excluded from the study. Patients with edema due to other disease like congestive cardiac failure, nephrotic syndrome were excluded from the study. Detailed history and clinical examination including anthropometry were done in both cases and control.

#### Laboratory investigation

In severely malnourished children below 3 years, urine was collected by suprapubic aspiration. In older and well nourished children urine were collected after cleansing the external genitalia with soap solution and sterile water. Then clean catch mid stream sample of urine were collected in sterilized test tube. Physical characters of urine sample were noted. Within one hour of collection, the urine sample was send to laboratory for microscopic examination and culture. Pus cells more than 10 HPF of centrifuged urine were considered as a criterion for significant pyuria. Urine cultures were done on blood agar media and Macconkeys agar

media. Colony counts were done by loop method. Bacterial isolates were tested for microbial sensitivity by disk impregnation method. A colony count of  $10^5$  colony forming unit per ml or more was taken as a case of UTI. In addition to routine and culture sensitivity examination of urine, following investigations were done in some selected cases to exclude the causes of edema due to other than SAM. These were (1) urine for albumin (2) chest x-ray P/A view (3) complete blood count (4) X-Ray KUB (5) USG of KUB.

#### Ethical consideration

Prior to the commencement of this study, the research protocol was approved by the Ethical Committee of Mymensingh Medical College & Hospital. The aims and objectives of the study were explained to the patients guardian in easily understandable local language and written consent were taken.

#### Data analysis

Collected data were compiled, checked. Data processing and analysis were done with the help of computer using SPSS (Statistical Package for Social Science) version 12.

### Results

57.5% of cases and 58.0% of controls were from the age group of <3 years and 42.5% of cases and 42.0% of controls were from the age group of >3 years, there was no significant difference between two groups ( $p > 0.05$ ).

Table I: Age distribution of study subjects (n=130)

Study group	Age group (years)		Total No. (%)
	<3 No. (%)	3+ No. (%)	
Case	46 (57.5)	34 (42.5)	80 (100.0)
Control	29 (58.0)	21 (42.0)	50 (100.0)
Total	75 (57.7)	55 (42.3)	130 (100.0)

\*Chi-square test was done to measure the level of significance.

Figure with parentheses indicates in percentage.  $\chi^2 = 0.003$ ,  $df = 1$ ,  $p = 0.955$

Table II: Sex distribution of study subjects (n=130)

Study group	Age group (years)		Total No. (%)
	Male	Female	
	No. (%)	No. (%)	
Case	44 (55.0)	36 (45.0)	80 (100.0)
Control	29 (58.0)	21 (42.0)	50 (100.0)
Total	73 (56.2)	57 (43.8)	130 (100.0)

\*Chi-square test was done to measure the level of significance.

Figure with parentheses indicates in percentage.

$\chi^2 = 0.112$ ,  $df = 1$ ,  $p = 0.737$

Among cases 55.0% were male and 45.0% were female and among controls 58.0% were male and 42.0% were female with no significant statistical difference ( $p > 0.05$ ).

Table III: Prevalence of UTI in well-nourished (Control) and malnourished (Case) children

Study group	Age Group (Years)		Total No. (%)
	UTI present	UTI absent	
	No. (%)	No. (%)	
Case	16 (20.0)	64 (80.0)	80 (100.0)
Control	2 (4.0)	48 (96.0)	50 (100.0)
Total	18 (13.8)	112 (86.2)	130 (100.0)

\*Chi-square test was done to measure the level of significance.

Figure with parentheses indicates in percentage.

$\chi^2 = 6.603$ ,  $p = 0.010$

Prevalence of UTI among cases were 20.0% and controls were 4.0% with significant statistical difference ( $p < 0.05$ ).

Table IV: Age-wise prevalence of UTI in malnourished children (n=80)

Age group (years)	UTI present	UTI absent	Total
<3	10 (21.7)	36 (78.3)	46 (100.0)
3+	6 (17.6)	28 (82.4)	34 (100.0)
Total	16 (20.0)	64 (80.0)	80 (100.0)

\*Chi-square test was done to measure the level of significance.

Figure with parentheses indicates in percentage.

$\chi^2 = 0.205$ ,  $p = 0.651$

10 (21.7%) of malnourished children aged <3 years and 6(17.6%) of malnourished children aged >3 years had UTI with no significant statistical difference between age groups ( $p > 0.05$ ).

Table V: Sex-wise prevalence of UTI in malnourished children (n=80)

Sex	UTI present	UTI absent	Total
Male	8 (18.2)	36 (81.8)	44 (100.0)
Female	8 (22.2)	28 (77.8)	36 (100.0)
Total	16 (20.0)	64 (80.0)	80 (100.0)

\*Chi-square test was done to measure the level of significance.

Figure with parentheses indicates in percentage.

$\chi^2 = 0.202$ ,  $df = 1$ ,  $p = 0.653$

Among malnourished children 8(18.2%) of male and 8(22.2%) of female had UTI with no significant sex difference ( $p>0.05$ ).

Table VI: Prevalence of UTI in various categories of malnourished children

Categories of malnourished	UTI present	Total No.	Prevalence (%)
1. Kwashiorkor	4	61	6.56
2. Marasmus	3	8	37.50
3. Marasmic-kwashiorkor	9	11	81.82

Z-test:

1 vs 2 :  $z = 1.78$ ,  $p = 0.075$

2 vs 3 :  $z = 2.14$ ,  $p = 0.032$

6 (6.56%) of total 61 children with kwashiorkor had UTI, 3 (37.50%) of total 8 marasmic children had UTI and 9(81.82%) total 11 children with Marasmic-kwashiorkor had UTI.

Table VII: Relationship between the naked eye appearances with the culture findings of urine

Groups	Naked eye appearance of urine	UTI present	UTI absent	Total	p value*
Case	Cloudy	11 (78.6)	3 (21.4)	14 (100.0)	0.001
	Clear	5 (7.6)	61 (92.4)	66 (100.0)	
	Total	16 (20.0)	64 (80.0)	80 (100.0)	
Control	Cloudy	1 (100.0)	0 (.0)	1 (100.0)	0.018
	Clear	1 (2.0)	48 (98.0)	49 (100.0)	
	Total	2 (4.0)	48 (96.0)	50 (100.0)	

\*Chi-square test with Yates correction was done to measure the level of significance.

Figure with parentheses indicates in percentage.

Among malnourished cases necked eye appearance (cloudy/clear) of urine was significantly different between UTI positive and UTI negative cases ( $p<0.05$ ) and among well-nourished controls necked eye appearance (cloudy/clear) of urine was significantly different between UTI positive and UTI negative cases ( $p<0.05$ ).

Table VIII: Relationship between the naked-eye appearance with the culture findings of urine

Groups	Naked-eye appearance of urine	UTI present	UTI absent	Total	p value*
Case	Pyuria	14 (93.3)	1 (6.7)	15 (100.0)	0.001
	Apyuria	2 (3.1)	63 (96.9)	65 (100.0)	
	Total	16 (20.0)	64 (80.0)	80 (100.0)	
Control	Pyuria	2 (100.0)	0 (.0)	2 (100.0)	0.001
	Apyuria	0 (.0)	48 (100.0)	48 (100.0)	
	Total	2 (4.0)	48 (96.0)	50 (100.0)	

\*Chi-square test with Yates correction was done to measure the level of significance.

Figure with parentheses indicates in percentage.

Among malnourished cases necked eye appearance (Pyuria/apyuria) of urine was significantly different between UTI positive and UTI negative cases ( $p=0.01$ ) and among well-nourished controls necked eye appearance (pyuria/apyuria) of urine was significantly different between UTI positive and UTI negative cases ( $p=0.01$ ).

Table IX: Pathogens causing UTI and their antibiotic sensitivity

Organism	Number (%) of pathogens	Number of pathogens sensitive									
		AMO	CIP	NAL	AMI	GEN	COT	NIT	CEF	AMO	CEP
Case											
<i>E. coli</i>	15	1	13	11	8	12	2	12	6	6	9
<i>Proteus</i>	1	0	1	1	1	1	0	1	0	0	1
Control											
<i>E. coli</i>	2	0	2	1	1	2	1	2	0	1	2

In 15(93.85%) of UTI patients of cases were suffered with *E. coli* and 1(6.7%) were *proteus*. Organisms in all of controls were *E. coli*. Among 15 *E. coli* 13 sensitive to Ciprofloxacin, 11 to Nalidixic acid and 12 to Gentamycin and Nitrofurantoin, 9 to Ceftriaxone, 8 to Amikacin, 6 to cefradin. Only 1 sensitive to Amoxicillin and 2 to Cotrimoxazole.

Table X: Presenting symptoms in malnourished children associated with UTI (n=16)

Presenting symptoms	Frequency	Percent
Fever	10	62.5
Irritability	4	25.0
Vomiting	4	25.0
Frequency of micturation	4	25.0
Loose motion	3	18.8
Cloudy urine	11	68.8
Dysuria	2	12.5
Dribbling	1	6.3
Screaming at urination	2	12.5
Narrow stream	3	18.8
Malodorous urine	6	37.5
Feeding mismanagement	16	100.0
Immunization history	8	50.0

All malnourished children with UTI gave history of feeding mismanagement. Most presented with fever (62.5%) and cloudy urine (68.8%). Other associated features were irritability, vomiting, frequency of micturation, malodorous urine, loose motion, dysuria, dribbling and narrow stream.

Table XI: Presenting signs in malnourished children associated with UTI (n=16)

Presenting signs	Frequency	Percent
Raised temperature	10	62.5
Abnormal Genitalia	1	6.3
Tight prepuce	3	18.8
Palpable bladder	7	43.8
Lower abdomen tenderness	2	12.5
Oedema	13	81.3

## Discussion

In the present study 57.5% of cases of severely malnourished children (SAM) and 58.05% of well nourished controls were from the age group of <3 years and 42.5% of cases and 42.0% of controls were from the age group of >3 years were enrolled in the study. There was no significant difference between two age groups ( $p>0.05$ ) (Table-I). There were 44 male and 36 female children in SAM cases, whereas 29 male and 21 female children in well nourished group. There was also no significant sex difference between two groups ( $p>0.05$ ) (Table-II).

In our study prevalence of UTI among severely malnourished children was 20.0% and controls were 4.0% with significant statistical difference ( $p<0.05$ ) (Table-III). The prevalence of UTI among severely malnourished children in different previous studies showed significant disparity. *Dey et al*<sup>12</sup> in their study found prevalence of UTI in SAM patient was 16.67%. *Kumar et al*<sup>13</sup> in their study showed the prevalence of UTI in SAM patients was 15%. *Uwaezouke et al*<sup>9</sup> in his narrative review found prevalence of UTI in SAM patients in the developing countries as low as 6% to as high as 37%. The wide variation in prevalence rates could be explained by the use of different study methods, as well as consideration or noconsideration of study confounders.

In female first UTI usually occurs by the age of 5 years with peak during infancy and toilet training. After the first UTI 60%-80% of girls develop a second UTI within 18 month. In boys most UTI occurs during the first years of life. The prevalence of UTI varies with age. During the first years of life male: female ratio is 2.8-5.4. Beyond 1-2 year there is a striking female preponderance with a male: female ratio of 1: 10.<sup>7</sup> In current study, 21.7% of malnourished children aged <3 years and 17.6% aged >3 years had UTI and 18.2% of male and 22.2%

of female malnourished children had UTI with no significant age and sex difference ( $p>0.05$ ) (Table IV) (Table V).

Our study found 37.50% of children marasmus, 81.82% of children with marasmic-kwashiorkor, 6.56% of children with kwashiorkor had UTI (Table-VI). *Ibrahim et al*<sup>14</sup> in a study found prevalence of urinary tract infection was 19.5% in marasmus, 14.8% in marasmic kwashiorkor and 33.3% in kwashiorkor. *Kabbin et al*<sup>15</sup> observed 46% marasmic, 23% marasmic-kwashiorkor and 2.3% kwashiorkor children had UTI in their study. These studies shows different prevalence of UTI in different types of SAM and more common in marasmus and marasmic-kwashiorkor.

Among malnourished cases and well nourished control naked eye appearance (cloudy/clear) of urine was significantly different between UTI positive and UTI negative cases ( $p<0.05$ ) (Table-VII). Among malnourished cases and well nourished control naked eye appearance (Pyuria/apyuria) of urine was significantly different between UTI positive and UTI negative cases ( $p=0.01$ ) (Table-VIII).

In the current study 14 cases and 1 control had cloudy urine ( $p<0.05$ ) (Table-VII). We found 15 cases and 2 control had pyuria ( $p=0.01$ ) (Table-VIII). Both cloudy appearance and pyuria were significantly higher in culture positive samples ( $p<0.05$ ). *Rabasa and Sattima et al*<sup>16</sup> found pyuria in 62.5% of malnourished children with UTI, fourteen of cases and only one of controls had cloudy appearance and fifteen cases and two controls had pyuria. Both cloudy appearance and pyuria were significantly higher in culture positive samples ( $p<0.05$ ).

In the present study the causative organism of UTI in all cases and controls were gram negatives. Out of total 16 cases of UTI, in

15(93.85%) cases organism were *E. coli* and 1(6.7%) case was *proteus*. Organisms in all of controls were *E. coli* (Table-IX). Okomoet *al*<sup>17</sup> showed out of total 17 urinary isolates *E. coli* accounted for 55.6% of the isolates; one child had polymicrobial bacteriuria (*Proteus mirabilis* and *Providentia alcalifaciens*). Sharmaet *al*<sup>18</sup> in a study observed, out of the total 19 culture positive cases, *E. coli* was commonest organism in 13 patients (68.4%) followed by *Citrobacter* in 2 cases (10.5%), *Pseudomonas* in 2 cases (10.5.5%) and *Acinetobacter* and *Klebsiella* 1-1 each (4.8%). These two studies support the present study.

In the present study among 15 cases of UTI caused by *E. coli*, 13 sensitive to Ciprofloxacin, 11 to Nalidaxic acid and 12 to Gentamycin and Nitrofurantoin, 9 to Ceftriaxone, 8 to Amikacin, 6 to cefradin. Only 1 sensitive to Amoxicillin 2 to Cotrimoxazole (Table-IX). It is observed that organisms were mostly sensitive to Quinolone groups and Aminoglycoside group. Ibrahimet *al* in their study found all the urinary isolates were sensitive to Gentamycin, Ceftazidime, and Ciprofloxacin.<sup>15</sup> Pageet *al* found most enterobacteriaceae isolated in their study were resistant to amoxicillin and Cotrimoxazole but susceptible to Ceftazidime/Ceftriaxone, Gentamicin and Quinolones. Among the organisms isolated from urine (*E. coli* and *K. pneumoniae*), almost 20% were resistant to Gentamicin and almost half to Cefalotine.<sup>19</sup> Çaksen H *et al* found the most common isolated microorganism from urine cultures was *Escherichia coli* (54.8%). Most strains of *Escherichia coli* were resistant to Cotrimoxazole (82.3%), Ceftriaxone (17.6%), Cefotaxime (17.6%), and Ciprofloxacin (17.6%), but none of them were resistant to Gentamicin.<sup>20</sup> In conclusion, they would like to emphasize that UTI predominantly by gram negative microorganisms are frequent in the infants with malnutrition, and these microorganisms are mostly resistant to Cotrimoxazole which is used commonly in

practical medicine and prophylaxis.<sup>20</sup> So all the above studies shows different sensitivity pattern of the causative organism of SAM with UTI. But all studies showed more susceptibility to Aminoglycoside and Quinolone groups.

All malnourished children with UTI gave history of feeding mismanagement. Most presented with fever (62.5%) and cloudy urine (68.8%). Other associated features were irritability, vomiting, frequency of micturition, malodorous urine, loose motion, dysuria, dribbling and narrow stream (Table-X). Choudhary *et al*<sup>21</sup> in India found fever to be the most common presenting symptom in children with SAM accounting for (70.7%), followed by vomiting (52%), loose motion (46.7%), cough (46.7%), and loss of appetite (30.7%). In Casken *et al*<sup>20</sup> found the main symptoms were fever, vomiting, diarrhea, cough, and seizures. These two studies support the current study.

### Conclusion

In the light of the current study it can be clearly postulated that UTI is significantly more prevalent among severely malnourished children. Sensitivity of drugs to causative organism of UTI also changes from time to time. So children with severe malnutrition should be routinely screened for UTI, culture and sensitivity should be also done in selected cases. Further long term prospective study should be carried out to observe the complication of UTI on children with severe malnutrition.

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