Original Research Article

Urinary tract infections in children aged 6 months to 5 years presenting with severe acute malnutrition in a tertiary care hospital

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ABSTRACT

Background: Urinary tract infections (UTI) is more common in malnourished children than in well-nourished children. Malnutrition is associated with immune deficiency which makes affected children more vulnerable to various severe infections. World Health Organization (WHO) defined severe acute malnutrition (SAM) as weight-for-height below -3 standard deviations (or Z-scores) or mid upper arm circumference <11.5 cm or visible severe wasting or bilateral pedal edema.
Methods: All eligible children were consecutively enrolled in the study. Detailed anthropometry measurements were taken and physical examination was done. Two urine specimens for routine microscopy and culture and sensitivity were sent. Antibiotic therapy was given as per standard protocol/sensitivity pattern. Statistical analysis was performed using the statistical packages for social sciences (SPSS) version 20 IBM Corporation.
Results: Prevalence of UTI in our study was 21.54% in children with SAM. UTI was more common in females than males in SAM children with maximum prevalence in less than 24 months of age. MUAC was the most prevalent diagnostic criteria. Fever was the most common presenting symptom, but 36.84% asymptomatic children with SAM had UTI. Increased frequency of micturition had 100% association with UTI. E. coli was the most common isolated bacteria. Most sensitive antibiotic was imipenem. Routinely used antibiotic like ceftriaxone showed significant percentage of resistance.
Conclusions: Given the high prevalence of UTI among children with SAM, it is suggested that urine culture should be performed in all children with SAM to diagnose UTI and to treat it on basis of antibiotic sensitivity pattern.

Keywords: Severe acute malnutrition, Urinary tract infection, Pyuria

INTRODUCTION

The World Health Organization (WHO) defines malnutrition as "The cellular imbalance between the supply of nutrients and energy and the body's demand for them to ensure growth, maintenance, and specific functions".[1] Malnutrition usually implies under-nutrition and refers to all deviations from adequate and optimal nutritional status in infants, children and in adults. In children, under-nutrition manifests as underweight and stunting (short stature), while severely undernourished children show the signs and symptoms that characterize conditions known as kwashiorkor, marasmus or marasmic-kwashiorkor.[1]

Severe acute malnutrition is a serious public-health issue that substantially increases the risk of mortality and morbidity.[2] Malnourished children are at greater risk of dying from common infections. It increases the frequency and severity of such infections and delays recovery. WHO defined severe acute malnutrition (SAM) as weight-for-height below -3 standard deviations (or Z-scores) or mid upper arm circumference <11.5 cm or visible severe wasting or bilateral pedal edema.[3]

It is known that there is synergistic interaction between malnutrition and infection- any kind of infection can worsen the nutritional status. On the other hand, even mild malnutrition, can affect the immune system and compromise body defense against infections. Severe malnutrition leads to an immunodeficiency state known as nutritionally acquired immune dysfunctions (NAIDs).

The ability of malnourished child to handle infections is lower, hence common infections from *Streptococcus pneumoniae, Klebsiella pneumoniae, Escherichia coli* and *Hemophilus influenza* are more common in them leading to pneumonia, septicemia, diarrhoea, meningitis, tuberculosis and a higher incidence of urinary tract infections (UTI) as compared to non-malnourished has been documented in severely malnourished children.[4,5]

UTI is one of the leading causes of febrile illness in pediatric age group.[6,7] In developing countries, it ranks next to gastrointestinal and respiratory tract infections as the third most common bacterial infection in children.

UTI may be asymptomatic, or may present in infants and young children with non-specific symptoms and signs, such as irritability and fever. Hence, a close suspicion is required for its correlation in children especially with SAM. Western studies consistently report that UTI accounts for 3-6% of children which are younger than 2 years of age presenting with fever without a focus (FWF), and collection and examination of urine is recognized as an important part of the investigation in young febrile child. Studies from Asia, Africa suggest that the prevalence of UTI in this group of children may be higher.[8-10]

It is well known that diagnosis of UTI is made infrequently in our setting. It is certainly easy to overlook the possibility of UTI in infants and young children.[11]

Malnourished children have impaired immune functions which include disturbance of lymphocyte response, low T-lymphocytes, depressed hypersensitivity response and decreased phagocytosis secondary to lack of complements and low secretion of immunoglobulin A.[12,13]

Most studies conducted among hospitalized children with complicated malnutrition (hypoglycemia, lethargy, hypothermia, or any other signs of illness) have reported high prevalence of UTI.[14-17]

There is paucity of data on exact prevalence of UTI in SAM. So, this study has been planned to determine the prevalence, to identify causative organisms, and to study the antibiotic sensitivity pattern of the organisms causing urinary tract infection in children suffering from severe acute malnutrition admitted in tertiary care teaching hospital. Clearly, the knowledge of the baseline risk of UTI can help clinicians to make informed diagnostic and therapeutic decisions in these children.

METHODS

A descriptive cross sectional study was conducted at Geetanjali Medical College and Hospital Udaipur, Rajasthan. All eligible children with diagnosis of severe acute malnutrition as per WHO criteria who were admitted in department of pediatrics during January 2019 to June 2020 were included in the study.

Inclusion criteria

All children between 6 months to 5 years of age with diagnosis of SAM who were admitted in department of pediatrics. SAM among children 6 months to 5 years of age is defined by any of the following: weight for height below -3 standard deviation of the median, visible severe wasting, presence of bipedal edema, and mid upper arm circumference below 11.5 cm.

Exclusion criteria

The following criteria was excluded from the study: children on antibiotic therapy, children who were known case of urinary tract malformation, and children whose parents did not give consent.

All eligible children were consecutively enrolled in the study after taking prior informed consent from the parents. Demographic profile, relevant information of individual patient was collected using well-structured proforma by interviewing the parents/attendant. At the time of enrollment, detailed evaluation and physical examination of each patient was done.

Detailed anthropometry measurements were taken with appropriate techniques. Two urine samples were collected, first urine sample was sent for routine microscopy to detect the presence of pus cells. Second sample was sent for urine culture and sensitivity. All isolates were tested for antimicrobial sensitivity and antibiotic therapy was given as per standard protocol/sensitivity pattern.

Statistical analysis was performed using the statistical packages for social sciences (SPSS) version 20 IBM Corporation. Data was entered into MS Excel software. Statistical analysis of Categorical variables was compared between patients using the chi-square test. Quantitative data was analysed using student T-test. A p value <0.05 is considered to be significant.

RESULTS

We enrolled 65 eligible children detected with severe acute malnutrition in our study. Data was collected for each subject in pre-designed proforma. Out of total 65 children whose urine culture samples were sent, 14 (21.54%) children were positive and urine culture of 51 (78.46%) children was negative. Prevalence of urinary tract infection comes out to be 21.54% in the study.

Out of the total 14 culture positive samples, *E. coli* was the most common organism, detected in 7 samples (50%) followed by *Klebsiella* in 4 samples (28.57%), *Pseudomonas* in 2 samples (14.29%) and *Acinetobacter* in 1 sample (7.14%).

Table 1 shows antibiotic sensitivity pattern in association with organisms. *E. coli* was 100% sensitive to imipenem, amikacin and nitrofurantoin followed by ceftriaxone (71.42%), while *E. coli* was 14.28% sensitive to co-amoxyclav. *Klebsiella* was 100% sensitive to imipenem, amikacin and nitrofurantoin, followed by gentamicin (75%). *Klebsiella* was 50% resistant to ceftriaxone, cefixime and co-trimoxazole respectively. *Pseudomonas* was 100% sensitive to imipenem, gentamicin, amikacin and resistant to nitrofurantoin, cefixime, ceftriaxone, co-trimoxazole. Acinetobacter was 100% sensitive to imipenem, nitrofurantoin, cotrimoxazole, while resistant to other drugs.

Table 2 shows the distribution of socio-demographic factors among children with urinary tract infection in severe acute malnutrition. Out of total 30 male children, UTI was present in 4 (13.33%) and out of total 35 female children, UTI was present in 10 (28.57%). UTI was more common in female child than male child. This difference was statistically significant with p value <0.01.

Maximum UTI positive children were in the age group 6-12 months followed by in 13-24 months. In age group 6-12 months, out of total 19 children, 5 (26.32%) were UTI positive. In age group 13-24 months, out of total 23 children, 5 (21.74%) were UTI positive. In age group 25-36 months, out of total 11 children, 2 (18.18%) were UTI positive. In age group 37-48 months, out of total 7 children, 1 (14.29%) was UTI positive and 1 (20.00%) was UTI positive out of total 5 children in age group 49-60 months.

Out of 20 children living in urban area, 5 (25%) were UTI positive and out of 45 children living in rural area, 9 (20%) were UTI positive. So, UTI was more common in urban area. However, this difference was not statistically significant (p value=0.7557). Out of total 37 children which belonged to upper lower class, 9 (24.32%) were UTI positive, out of total 13 children which belonged to middle class, 2 (15.3%) were UTI positive. In lower and upper middle class UTI positive children were 3 (27.27%) and zero respectively. Hence, UTI is more common in lower and upper lower class.

Table 3 shows distribution of clinico-epidemiological factors among children with urinary tract infection in severe acute malnutrition. Among children with incomplete immunization, 8 (21.62%) were UTI positive and with complete immunization, 6 (21.43%) were UTI positive. So, occurrence of UTI is not affected by immunization status in our study with p value=0.9899.

In children who stayed at hospital for ≥6 days, 11 (30.55%) children were UTI positive. Out of 29 children who stayed at hospital for <6 days, 3 (10.34%) children were UTI positive. Maximum number of children which were UTI positive had a prolonged stay in hospital with p value <0.0001.

Out of 62 children in which mid upper arm circumference was <11.5 cm, UTI was detected in 14 (22.58%) and out of 60 children in which weight for height was <-3SD, UTI was detected in 11 (18.33%). Out of 4 children with edema positivity, UTI was detected in 0% and out of 4 children with severe wasting, UTI was present in 1 (25%).

All 3 children with presenting complaint of increased frequency of micturition had UTI. It shows that increased frequency of micturition was 100% associated with UTI. Among asymptomatic children 36.84% had UTI.

Urine culture was positive in 3 samples (5.88%) out of total 48 samples with pus cell count <5/Hpf and urine culture was positive in 11 samples (78.57%) out of total 14 samples containing pus cell count ≥5/Hpf. There was statistically significant difference between urine pus cell and presence of UTI as p value is <0.05.

Outcome of the children enrolled in the study showed that out of total 65, 50 (76.92%) recovered and 15 (23.08%) were discharged on oral antibiotics. There was no mortality in the study population during duration of the study.

Table 1: Antibiotic sensitivity pattern in association with organisms.

Drugs	E.coli (7) %	Klebsiella (4) %	Pseudomonas (2) %	Acinetobacter (1) %	Total (n=14)
Imipenem	7 (100)	4 (100)	2 (100)	1 (100)	14
Nitrofurantoin	7 (100)	4 (100)	-	1 (100)	12
Co-trimoxazole	2 (28.57)	2 (50)	-	1 (100)	5
Co-amoxyclav	1 (14.28)	1 (25)	1 (50)	-	3
Cefixime	4 (57.14)	2 (50)	-	-	6
Ceftriaxone	5 (71.42)	2 (50)	-	-	7
Gentamicin	7 (100)	3 (75)	2 (100)	-	12
Amikacin	7 (100)	4 (100)	2 (100)	-	13

Table 2: Distribution of socio-demographic factors among children with urinary tract infection in severe acute malnutrition.

Socio-demographic factors	UTI present Number (%)	UTI absent Number (%)	Total
Gender			
Male	4 (13.33)	26 (86.67)	30
Female	10 (28.57)	25 (71.43)	35
Total	14	51	65
P value	< 0.01		
Age in months			
6–12	5 (26.32)	14 (73.68)	19
13-24	5 (21.74)	18 (78.26)	23
25-36	2 (18.18)	9 (81.81)	11
37-48	1 (14.29)	6 (85.71)	7
49-60	1 (20.00)	4 (80.00)	5
Total	14 (21.54)	51 (78.46)	65
Residence			
Urban	5 (25)	15 (75)	20
Rural	9 (20)	36 (80)	45
Total	14 (21.53)	51 (78.46)	65
P value	0.7557		
Socioeconomic class			
Upper middle	0 (0)	4 (100)	4
Middle	2 (15.3)	11 (84.6)	13
Upper lower	9 (24.32)	28 (75.67)	37
Lower	3 (27.27)	8 (72.72)	11
Total	14 (21.53)	51 (78.46)	65

Table 3: Distribution of clinico-epidemiological factors among children with urinary tract infection in severe acute malnutrition.

Clinico-epidemiological factors	UTI present Number (%)	UTI absent Number (%)	Total
Immunization			
Incomplete	8 (21.62)	29 (78.37)	37
Complete	6 (21.42)	22 (78.57)	28
Total	14 (21.53)	51 (78.46)	65
P value	0.9899		
Duration of hospital stay (days)			
<6	3 (10.34)	26 (89.66)	29
≥6	11 (30.55)	25 (69.45)	36
Total	14	51	65
P value	<0.0001		
Criteria of SAM in children with UTI			
MAUC <11.5 cm	14 (22.58)	48 (77.42)	62
Weight for height <-3SD	11 (18.33)	49 (81.67)	60
Edema positive	0 (0)	4 (100)	4
Visible severe wasting	1 (25)	3 (75)	4
Presenting complaints			
Cough	3 (15.78)	16 (84.22)	19
Fever	3 (13.63)	19 (86.37)	22
Increased frequency of micturition	3 (100)	0	3
Loose stools	2 (18.18)	9 (81.82)	11
Pain in abdomen	1 (16.67)	5 (83.33)	6
Vomiting	0 (0)	7 (00)	7

Continued.

Clinico-epidemiological factors	UTI present Number (%)	UTI absent Number (%)	Total
Asymptomatic	7 (36.84)	12 (63.16)	19
Urine pus cells			
<5 pyruria-	3 (5.88)	48 (94.12)	51
≥5 pyruria+	11 (78.57)	3 (21.43)	14
P value	< 0.001		

DISCUSSION

In the present study, total 65 children with severe acute malnutrition between the age group 6 months to 5 years were enrolled to study the prevalence of urinary tract infection. Urinary tract infection was found in 14 (21.54%) out of total 65 children with SAM enrolled in our study. This was in accordance with the previously done study by Sharma et al in severe acute malnourished children where they found the prevalence of UTI to be 22.4%.[17] Previous studies have reported UTI prevalence ranging from 4% to 32.7%.[2,15-19] Prevalence of UTI in our study is slightly higher than that of a similar studies done on severe malnourished children by Page et al and Singh et al where they reported prevalence of UTI to be 16% and 14% respectively.[20,21]

In our study, total number of males was 30 (46.15%) and females were 35 (53.85%). There was female predominance in our study. Difference in distribution among both genders was statistically not significant (p value >0.05). It was different from the studies done by Girish and Page et al in which male children were more than female children.[20,22] While in the study done by Kumar et al and by Muhsin et al in which female children were more than male children.[2,23] In our study 4 male children (13.33%) and 10 female children (28.57%) had UTI. It was similar with the study done by Ibrahim et al and Muhsin et al where they found UTI predominance in females than males.[23,24]

In our study, maximum number of children were in the age group between 13-24 months (35.38%), followed by 6-12 months (29.23%). The mean age of children was 26.61±14.96 months as compared to 27.04 months found in study of Sharma et al in which majority of cases were in age group 13-36 months.[17] Similar facts were observed by Kumar et al in which majority of cases were in age group between 13-24 months.[25] Dangi et al also observed that majority of cases (35%) were in the age group between 1-2 years.[9] UTI in SAM children was observed to be higher among the age group of 6-12 months (26.32%) and 13-24 months (21.74%). So, in our study more number of children with UTI was seen in less than 2 years of age. Similar results were seen in study done by Ibrahim et al in which maximum number of the cases of UTI occurred in the age group of less than 2 years.[24]

In current study, out of 65 children, 45 (69.23%) belonged to rural area and 20 (30.77%) belonged to urban area. These results were similar to studies done by Nagar et al and Prasad et al where mostly children belonged to rural area.[4,26] Out of 20 children belonging to urban area, UTI was present in 5 (25%) children and out of 45 children belonging to rural area, UTI was present in 9 (20%) children. Although more children which belong to urban area had UTI but this difference is statistically not significant. So area of residence does not affect the incidence of UTI among children with SAM.

In our study, maximum number of children 37 (56.92%) belonged to upper lower class. Results were comparable in study done by Kumar et al and in study done by Kumar et al where 94.7% and 67% of the study group belong to lower socio-economic class respectively.[2,18] Out of total 37 children which belonged to upper lower class, 9 (24.32%) had UTI. In lower class 3 (27.27%) had UTI, in middle class 2 (15.3%) had UTI. No UTI was seen among upper middle class. This shows that UTI was more common in lower and upper lower socioeconomic classes in our study which might attribute to poor hygienic conditions among these groups.

In our study, UTI was present in 8 (21.62%) children out of 37 in which immunization was incomplete and in 6 (21.42%) children out of 28 in which immunization was complete. This difference was statistically not significant. This shows that UTI is not associated with the status of immunization. Previous study done by Arya et al showed 52% children were completely immunized, indicating slightly higher coverage of vaccination among their study population.[18]

Among the different diagnostic criteria of SAM in our study, 62 (95.38%) children out of total 65 were having MUAC <11.5 cm, followed by 60 (92.30%) having weight for height/length <-3 SD. It indicates that MUAC is most prevalent diagnostic criteria among children with SAM followed by weight for height. Study done by Girish and Premalatha also found to have MUAC <11.5 cm in most of their study population.[22] Results were different in the study done by Sharma et al where most common criteria was weight for height in 85.9% followed by 47.1% having MUAC <11.5 cm, 32.9% with visible severe wasting and 16.5% having edema positivity.[17]

Difference in their results might be due to more number of cases with edema which altered the mid upper arm circumference. In our study, UTI was positive in 14 (22.5%) children having MUAC <11.5 cm, 11 (18.33%) children with weight for height <-3 SD and 1 (25%) with severe wasting.

The children included in our study were presented with cluster of symptoms. Maximum children presented with fever 22 (33.84%). The percentage of increased frequency of micturition was 4.62% only, and 19 (29.23%) children were asymptomatic. Fever was the most common presenting complaint in our study. Similar observations were noticed in study done by Prasad et al and study done by Sharma et al where they found fever as the most common presentation.[17,26] Girish and Premalatha found vomiting in 69.3% cases as most common presenting complaint.[22] Out of 22 children presented with fever, 3 (13.6%) had UTI. Out of 19 children who were asymptomatic, 7 (36.84%) had UTI. All 3 children which presented with increased frequency of micturition were 100% associated with UTI. This can be explained by the fact that most cases of UTI in children with SAM are asymptomatic.

In our study, out of the 51 samples containing pus cells count <5/Hpf (pyuria negative), culture was positive in 3 (4.61%) samples and out of 14 samples containing pus cells count ≥5/Hpf (pyuria positive), culture was positive in 11 (78.57%).[12] So, samples with pus cells ≥5/Hpf had more incidence of positive urine culture according to our study and this difference was statistically significant (p value <0.05). These results were comparable with the study done by Sharma et al where all the samples with pus cells ≥5/Hpf were culture positive.[17]

In our study, 14 urine samples were culture positive. Out of the total 14 culture positive cases, *E. coli* was found in 7 cases (50%) followed by *Klebsiella* in 4 cases (28.75%), *Pseudomonas* in 2 cases (14.29%) and *Acinetobacter* in 1 (7.14%). *E. coli* was found to be the most common bacteria causing UTI in children with SAM. These observations were similar to several other previous studies.[15,17,21,23,25] In the present study, the second most common isolated bacteria was *Klebsiella*.

In current study, out of 14 urine culture positive samples, 100% isolates were sensitive to imipenem, 92.86% to amikacin, 85.71% to nitrofurantoin, 85.71% to gentamicin, 50% to ceftriaxone, 42.85% to cefixime, 35.71% to co-trimoxazole, 21.43% to co-amoxyclav. Results were comparable with the study conducted by Sharma et al.[17]

In our study, *E. coli* which was the principle bacteria isolated, showed 100% sensitivity to imipenem, nitrofurantoin, amikacin and gentamicin followed by ceftriaxone (71.42%), cefixime (57.14%) and low sensitivity to co-trimoxazole (28.57%) and co-amoxyclav (14.28%).

In present study, *E. coli* was 100% sensitive to amikacin which was similar to the observations noticed by Kumar.[25] In our study, all *E. coli* were sensitive to gentamicin which was similar to study done by Ibrahim et al.[24] In our study *Klebsiella* was found 100% sensitive to imipenem, amikacin and nitrofurantoin, followed by gentamicin

(75%). Pseudomonas was 100% sensitive to imipenem, gentamicin, amikacin and resistant to nitrofurantoin, cefixime, ceftriaxone, co-trimoxazole. *Acinetobacter* was 100% sensitive to imipenem, nitrofurantoin, cotrimoxazole, while resistant to other drugs. These results were comparable with several previous studies.[15,17,21,23-28]

In our study, out of total 36 children who stayed in hospital for ≥6 days, 11 (30.55%) children had UTI as compared to 3 (10.34%) out of 29 children who stayed <6 days in hospital. Maximum number of children with UTI had prolonged hospital stay and this difference was statistically significant. This can be due to the reason that additional burden of UTI among children with SAM delayed the recovery. Out of total 65 children enrolled, 50 (76.92%) were recovered and 15 (23.08%) were discharged on oral antibiotics. There was no mortality in the study population during the study period.

In our study, prevalence of UTI in SAM children was 21.54%. Presence of UTI in SAM requires specific antibiotic treatment and prolonged hospital stay. So, UTI in children with SAM needs to be evaluated to reduce the burden of co-morbidities in children with SAM. Small sample size is the only limitation in our study. Larger sample size could have been better to establish a better correlation which could be beneficial for the community.

CONCLUSION

UTI is an important occult infection in malnourished children which delays the recovery and increases the duration of hospital stay. It is often missed as a large number of children are asymptomatic. Given the high prevalence of UTI among children with SAM, it is suggested that urine culture should be performed in all severely acute malnourished children to diagnose UTI and to treat it on basis of antibiotic sensitivity pattern. Thus, it is an important step toward strengthening the therapeutic management in these children.

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