ORIGINAL ARTICLE

Common Infections and Antibiotic Susceptibility among Malnourished Children: A hospital based study from Karachi.

Saba Ahmed, Unaisa Qazi

The Indus Hospital, Korangi Crossing, Karachi

Abstract

Background
The high prevalence of infections among children with severe malnutrition coupled with an atypical clinical presentation justifies the routine use of empirical antibiotic. The choice of antibiotics has to be guided by locally prevalent pathogens and their antibiotic susceptibility patterns. Susceptibilities of organisms keep on changingand require frequent monitoring to keep antibiotics regimen up to date.

Aim
This study is aimed at determining prevailing situation of infections and antimicrobial sensitivity of bacteria among malnourished children in peri-urban catchment area of Karachi.

Material and Method
This is hospital based retrospective analysis of children from one month to 12 years of age admitted for severe or moderate malnutrition in the pediatric ward of 'The Indus Hospital' from October 2010 till July 2011. Culture reports of blood, urine; stool, ear swab and gastric aspirate were analyzed. The Kirby-Bauer diffusion method was used to check isolates susceptibility. Commonly prescribed antibiotics were graded as sensitive or resistant according to standardized charts of Clinical and laboratory standard institute (CLSI) 2012 guidelines.

Results
Total of 260 severely malnourished children were enrolled in the study. Common infections included diarrhea 68% and respiratory tract infections 48%. Gram negative bacteria constituted 60% (61) of the total isolates, *Escherichia coli* was the leading gram negative organism (45%). Gram positive bacteria constituted 40% (38) of the total isolates .Coagulase negative staphylococci species (CONS species) 31% (31) were the most common gram positive organisms. In vitro sensitivity by disk diffusion showed 64% and 61% sensitivity to Amikacin and Gentamycin. Susceptibility of isolates to Ciprofloxacin, Amoxycillin, Co-trimoxazole and Ampicillin was 53%, 29%, 25% and 13% respectively.

Conclusion
Overwhelming resistance to WHO recommended antibiotics was seen in the study population. Diarrhea and respiratory tract infections were the commonest infections among the malnourished. E.coli was the leading organism. Most bacteria isolates were sensitive to Amikacin and Gentamicin. There is a need for re-evaluation of the WHO recommendations for management if infections in malnourished children.

Corresponding Author: Saba Ahmed
77/2, Khyaban-e-Roomi
Phase 8, DHA, Karachi
Email:doctsaba@yahoo.com

Introduction

According to national nutrition and health survey of Pakistan (NNHS) 2011, malnutrition status of children under 5 years has not shown much improvement since last 46 years in Pakistan, NNHS shows 17% wasting and 23.5% severe stunting in children less than five years of age.[1] The survey has also revealed alarming micronutrient deficiencies. Prevalence of vitamin A, vitamin D, zinc, iodine and iron deficiencies are estimated to be 56%, 41%, 36%, 33% and 24% respectively.[1]

The macro and micronutrient deficiencies lead to the deterioration of immune functions[2] which in turn lead to infections. This vicious cycle is responsible for major morbidity and mortality among the malnourished children.[3]

The high prevalence of infections among children with severe malnutrition coupled with an atypical clinical presentation of sepsis justifies the routine use of empirical antibiotic treatment in the initial phase of inpatient management as recommended by World Health Organization.[4] However, the choice of antibiotics has to be guided by locally prevalent pathogens and their antibiotic susceptibility patterns. Bacterial isolates and their susceptibilities keep on changing from time to time depending on drug usage practices, emerging drug resistance and changing health policies. Failure of monitoring current microbial trends and their drug susceptibility may lead to inappropriate treatment and possibility of drug resistance.

Previous studies have shown spectrum of common infections along with the drug susceptibility patterns in children[5,6] but either these studies are old or are not specific for malnourished children. To the best of our knowledge there are no recent local studies on bacterial isolates and their antibiotic sensitivity in undernourished children.

Therefore, this study is aimed at determining prevailing situation of infections and antimicrobial sensitivity of bacteria among malnourished children in peri-urban catchment area of Karachi.

Objective

This study is aimed at determining prevailing situation of infections and antimicrobial sensitivity of bacteria among malnourished children in peri-urban catchment area of Karachi.

Patients and Methods

This is hospital based retrospective analysis of children from one month to 12 years of age admitted for severe or moderate malnutrition in the pediatric ward of Indus Hospital from October 2010 till July 2011.Indus is a 150 bed hospital located in Korangi, Karachi. It serves population of 2.5 million people. The main catchment areas consist of peri urban settlements and fisherman villages. It shoulders a large share of treating malnourished children along with public sector hospitals of Karachi.

Table 1: Characteristics of 250 malnourished children admitted in pediatric ward of Indus Hospital.

	Median (IQR)	
Age in years	2.36 (1.77-3.17)	
Hospital stay (days)	5 (3-7)	
	N	**%**
Gender		
Male	132	53
Female	118	47
Age groups		
<1year	7	2.8
>1 year	243	97
Acute respiratory infection (ARI)	120	48
Otitis media	7	3
Oral thrush	55	22
UTI	14	5.6
Malaria	8	3.2
Diarrhea		
Overall	169	68
Bacterial	39	23
Protozoal	6	3.5
Tuberculosis		
Overall	17	
Pulmonary	10	59
Abdominal	5	29
Nodal	2	11

Data was extracted from records of electronic information system (HMIS) of Indus Hospital. Duration of hospitalization was defined as the duration from the date of admission in hospital to the date of discharge, death or transfer to another hospital, or the date when patients left hospital against medical advice.

Inclusion and Exclusion Criteria

Children with severe acute malnutrition (SAM) and moderate acute malnutrition (MAM) were included in the study. Children who had chronic illnesses like chronic renal failure, congenital heart disease and immunodeficiency syndrome or those children who had received antibiotics prior to enrollment were not included.Study participants who did not complete the study were excluded.

Methods

A predesigned proforma was used to collect relevant information. The information included demographic and nutritional details of malnourished children. The laboratory information included microscopic/ culture reports of blood, urine, stool, ear swab and gastric aspirate. Results of imaging studies and drug sensitivity analysis of isolated organisms were also included.

Approval from the ethical review board of the hospital was taken prior to starting the study. Confidentiality of subjects and privacy of data was maintained throughout the study. Data was stored on Microsoft Excel sheets. Each study participant was allotted a study number which was not linked to any of the participants' personal identifiers. At the end of data collection, remaining identifiers, like names, addresses, medical registration numbers, lab or radiology report numbers, were permanently deleted from the data sheets. The data files were password protected and were only available to study investigators. There is no known conflict of interest in this study.

Moderate acute malnutrition (MAM) and severe acute malnutrition (SAM) were categorized according to WHO guidelines.[4] SAM was classified if mid upper arm circumference (MUAC) is less than 11.5cms or there is bilateral pedal edema or weight for height ratio is <3 z-scores of the WHO child growth standard, MAM included children having MUAC between 11.5–12.5 cms or weight-for-height between –3 and –2 z-scores of the World Health Organization.

Laboratory Evaluation

All the lab specimens used in the study were collected under aseptic conditions using standard procedures. For blood culture 1-3 milliliters of blood was drawn from a peripheral vein under aseptic conditions.The skin was cleaned with chlorhexidine and povidone iodine solution before drawing blood. Each blood sample was then inoculated into BACTEC Paeds plus F culture vials containing Soybean-Casein digest broth with resins, the sample was incubated at 37°C for 24 hours in the automated system, after which bottles were observed for turbidity. From

Tables 2: Bacterial isolates and their site of infection.

	Site of infections N (%)				
Bacteria	**Blood**	**Urine**	**Stool**	**Ear**	**Total**
Gram +ve organisms: 38 (38)					
CONS	31	-			31 (81)
MRSA	4	-		2	6 (11)
Streptococcus	3	-			3 (8)
Gram –ve organisms: 61 (62)					
E.coli	3	4	39		46 (75)
Pseudomonas	1	1		2	4 (7)
Salmonella	3	-			3 (5)
Klebsiella	-	5		1	6 (10)
Proteus	-	-		2	2 (3)
Total	45	10	39	7	101

Table 3: Susceptibility pattern of Gram negative bacterial isolates to commonly selected antibiotics

Antimicrobials	**Drug susceptibility of bacterial isolates** Susceptibility/Total (%)				
	E. coli (46)	**Salmonella** (3)	**Klebsiella** (6)	**Proteus** (2)	**Pseudomonas** (4)
Amikin	25/29(86)	3/3(100)	5/6(83)	½ (50)	¾ (75)
Amoxcillin	8/43(18.6)	3/3(100)	2/3(66)	N/D	All strains resistant
Ampicillin	3/45(6.6)	1/3(33)	N/D	N/D	All strains resistant
Ceftazidime	2/38(5.2)	3/3(100)	2/3(66)	½ (50)	All strains resistant
Ciprofloxacin	22/45(48.8)	3/3(100)	4/6(66)	½ (50)	N/D
Co-trimoxazole	12/45(26.6)	2/3(66)	¾ (75)	N/D	All strains resistant
Vancomycin	N/D	N/D	N/D	N/D	N/D
Gentamycin	29/44(66)	3/3(100)	3/3(100)	1/1(100)	4/4(100)
Nitrofurantoin	5/11(45)	N/D	1/1(100)	N/D	N/D
Tobramycin	N/D	N/D	N/D	N/D	¾ (75)

E.coli= Escherichia coli, MRSA= Methicillin resistant Staphylococcus Aureus, CONS= Coagulase negative staphylococci, Salmon=Salmonella Typhimurium, Strep=Streptococcus pneumonia, Klebs= Klebsiella pneumonia, Proteus=Proteus mirabilis, Pseudomonas= Pseudomonas aeruginosa.

bottles showing turbidity, Gram's stain was done and further inoculations were made on blood, chocolate, MacConkey and Sabourand-dextrose agar respectively. The plates were then incubated at 37°C for 18 – 24 hours. Culture bottles that did not show turbidity were further incubated for up to 10 days. Identification of Staphylococcus aureus was done by Coagulase test.

The Kirby-Bauer diffusion method was used to test the susceptibility to the isolates on Muller-Hinton Agar according to Clinical and laboratory standard institute (CLSI) 2012 guidelines.[7] Commonly prescribed antibiotics were tested and graded as sensitive or resistant according to zone sizes which

Table 4: Susceptibility pattern of Gram positive bacterial isolates to commonly selected antibiotics

Antimicrobials	Drug susceptibility of bacterial isolates Susceptibility/Total (%)		
	CONS(31)	**MRSA**(6)	**Streptococcus**(3)
Amikin	26/27(96)	N/D	2/2(100)
Amoxcillin	10/28(35.7)	4/6(66)	2/2(100)
Ampicillin	6/22(27)	2/6(33)	1/3(33)
Ceftazidime	N/D	N/D	N/D
Ciprofloxacin	18/25(72)	4/6(66)	2/3(66)
Co-trimoxazole	5/23(21.7)	2/6(33)	1/3(33)
Vancomycin	27/27(100)	3/3(100)	N/D
Gentamycin	16/26(61.5)	4/5(80)	2/3(66)
Nitrofurantoin	N/D	1/1(100)	N/D
Tobramycin	3/5(60)	N/D	N/D

E.coli= Escherichia coli, MRSA= Methicillin resistant Staphylococcus Aureus, CONS= Coagulase negative staphylococci, Salmon=Salmonella Typhimurium, Strep=Streptococcus pneumonia, Klebs= Klebsiella pneumonia, Proteus=Proteus mirabilis, Pseudomonas= Pseudomonas aeruginosa.

are interpreted according to standardized charts of CLSI-2012. Clean-voided midstream or catheterized urine specimens were taken for urine analysis. Urine microscopy and culture was done according to standard procedures at 24 and 48 h. Growth was categorized as negative when colony count of bacteria was $<10^4$ CFU/ml and positive when colony count was $>10^5$ CFU/ml. Organisms species identification was done by standard biochemical tests.

Diagnosis of Malaria was made by microscopic examination of thick and thin film of Giemsa stained blood films. Thick film was used for estimation of parasite load and thin film was done for species identification.

Stool sample analysis consisted of direct microscopy and Iodine staining for parasites, stool cultures was done on MacConkey and Salmonella-Shigella (SS) agar. Where clinically suspected, Thiosulphate-Citrate-Bile-Sucrose (TCBS) agar was done for vibriocholera.

Gastric aspirates were used for isolation of Mycobacterium Tuberculosis. Cultures for tuberculosis consisted of both solid and liquid mediums. 7H9 broth constituted the liquid medium while Lowenstin Jenson medium was used as solid agar. Drug sensitivity testing for first line anti-tuberculous drugs was also done on Mycobacterium growth indicator (MGIT).

Statistical analysis

Data was entered and analyzed using SPSS 21. Descriptive analysis was done. Median (IQR) was calculated for age of patient (years) and hospital stay (days). Frequency and percentage was computed for baseline characteristics of malnourished children gender, pneumonia, malaria, otitis media, UTI, diarrhea, TB and oral thrush. Rate of susceptibility was computed for commonly selected antibiotics of bacterial isolates.

Results

Total of 260 severe and moderate malnourished children were enrolled in the study, 10 participants were excluded from the final analysis due to incomplete data. Fifty three percent children were males while 47% were females. The median age was 2.36 years (IQR 1.77-3.17). Majority of the children (97%) were above one year of age. Un-vaccinated, partially and completely vaccinated children were 16% (19/118), 21% (25/118) and 63% (74/118) respectively. Commonly diagnosed infections included diarrhea 68% (based on clinical exam and positive cultures) and respiratory tract infections 48% (positive x-ray findings). Seventeen children were suffering from tuberculosis out of which 10 (58%) had pulmonary tuberculosis and 7 (41%) had extra pulmonary tuberculosis (EPTB). Abdominal and nodal T.B was present in 5/7 (29%) and 2/7 (11%) children. The common laboratory findings among the tuberculosis children were hilar lymphadenopathy (13/17) and chest cavities (8/17). Manteaux test was positive in 4 out of 17 tuberculous children, 2 out of 17 samples of gastric aspirate grew Mycobacterium Tuberculosis. Three out of five children with abdominal T.B had ascites, matted abdominal loops and abdominal lymphadenopathy. Eight children had malaria out of which 6 had plasmodium Vivax and 2 had plasmodium Falciparum infections.

One hundred and one (40%) of the 250 specimens cultured, grew bacterial isolates. Gram negative bacteria constituted 60% (61) of the total isolates, *Escherichia coli* was the leading gram negative organism (45%) followed by Klebsiella (6%) and Pseudomonas Aerouginosa (4%) species.Gram positive bacteria constituted 40% (38) of the total isolates. Coagulase negative staphylococci species (CONS species) 31% (31) were the most common gram positive organisms followed by Methicillin resistant staphylococcus aureus (MRSA) 6% (6) and streptococcus 3% (3).

In vitro sensitivity by disk diffusion showed that 64% organisms were sensitive to Amikin, 61% organisms were sensitive to Gentamycin. Susceptibility of isolates to Ciprofloxacin, Amoxycillin, Co-trimoxazole and Ampicillin was 53%, 29%, 25% and 13% respectively. All the strains of MRSA and CNS species were resistant to Cloxacillin.

Discussion

Relation between malnutrition and infection is bidirectional ending up in a vicious cycle. Infections cause hyper metabolism in malnourished children which leads to further weight loss due to reduced food intake and increased excretion of nitrogen.[8,9]

The common infections observed in nutritionally deprived

children are gastrointestinal and respiratory infections. The first line of defense against these types of infection is the innate immune system, particularly epithelial barriers and the mucosal immune response. Mucous production is significantly reduced in intestinal and respiratory tracts of malnourished children resulting in loss of protective mucus blanket which normally sweeps away bacteria[10] Secretory IgA another important component of the mucosal response is also reduced making malnourished children more prone to develop diarrhea and respiratory tract infections.[11]

In our study predominant infection was diarrhea (68%) followed by respiratory infections (48%).This is consistent with other studies.[12,13,14] Excessive diarrhea can be explained by presence of atrophied and permeable gut mucosa, poor hygienic conditions and Zinc and vitamin A deficiencies among malnourished children. Excessive gut colonization with bacteria and yeast can also be a contributing factor.[15] All cases of diarrhea were caused by *Escherichia coli* (*E.coli*) in our study which is similar to another study done in a tertiary hospital of Karachi in 2010.[16] This could be due to contamination of food and water and unsatisfactory hygienic conditions. A study from Bangladesh found contamination of food and water with *E.coli*.[16] Education of mothers in food safety measures and improving water supply and sanitation can reduce bacterial diarrhea to a great extent in malnourished children.

Bacterial pathogens were isolated from 12 out of 120 cases of pneumonia; *Methicillin resistant staphylococcus aureus* (MRSA), *Streptococcus pneumonia* and *Klebsiella* were responsible for 6, 3 and 3 cases respectively. Other studies have reported *Streptococcus pneumonia and Haemophilus influenzae* as main causative agents of pneumonia in malnourished children.[17] Lack of similar finding in our study could be due to increased use of pneumococcal and *H. influenzae*type b vaccines in Pakistan.

Most of the infections were caused by gram negative bacteria (61%). The most common organism was *Escherichia coli* (45%) followed by Klebsiella 6%) and Pseudomonas Aerouginosa (4%). Reduced function of complement system, diminished chemotactic and phagocytic abilities of leucocytes could be the reasons of predominant gram negative infections.[18,19]

Gram positive bacteria constituted 40% (38) of the total isolates. Coagulase negative staphylococci species (CoNS species) 31% (31) were the most common gram positive organisms followed by Methicillin resistant staphylococcus aureus (MRSA) 6% (6). Presence of CoNs has been reported in other studies as well.[5,20]

CONS form part of the normal skin flora, and are frequent contaminants of blood cultures but rarely cause significant infections in immune-competent hosts. To differentiate between CoNS-positive blood cultures due to skin contamination from a true blood stream infection is difficult. Clinicians often rely on presence of systemic signs of bacteremia along with a positive culture for treatment. Such assessments have not been reported for malnourished children. Currently CONS is regarded as contaminant in malnourished children. In our study both Chlorhexidine and povidone iodine solutions were used to disinfect the skin prior to blood sampling in order to minimize risk of skin contamination. We gave antibiotics to children who had clinical signs of bacteremia along with CONS positive blood culture due to the reason that many children had skin ulcers making them prone to invasive CONS infections. Also it was clinically difficult to differentiate true infections from refeeding syndromes and silent aspirations. In our opinion judging clinical significance of CONS among malnourished children is vital as it will have profound impact on future treatment guidelines. We strongly believe that more studies in this regarded are needed.

In our study sensitivity to Amikacin was 64%, sixty one percent of organisms were sensitive to Gentamycin while 53% Susceptibility of organisms to Ciprofloxacin was noted. Deceased susceptibility was documented to commonly used antibiotics, such as Amoxicillin, Co-trimoxazole and Ampicillin. Similar resistance to WHO recommended antibiotics have been noted in other studies also.[21,22]

WHO recommends ampicillin parenterally for 2 days followed by enteral amoxicillin/ampicillin for a further 5 days and gentamicin parenterally for 7 days.[23] WHO guidelines also do not differentiate antibiotic treatment for hospitalized severe acute malnutrition children (SAM) with those who have danger signs such as sepsis, cyanosis, grunting, convulsion and inability to drink. Furthermore there is a lack of studies addressing toxicity of Gentamicin in terms of renal function and otoxicity in SAM children.

Keeping in mind that microbial resistance profiles vary widely with time and also introduction of pneumococcal and *Haemophilus influenzae* type b vaccines in Pakistan is expected to change spectrum of pathogens we recommend that clinicians should choose initial antibiotics according to current local microbial profile and susceptibility patterns until a change is warranted based on culture sensitivity report or clinical deterioration of the patient. No recent efforts have been made to audit current situation of antibiotic sensitivity and the magnitude of bacteremia in malnourished children and a recent survey in this regard is urgently needed.

Limitation

We were unable to evaluate children for HIV status and repeat blood cultures for CoNspositive cases to rule out contaminants from true bacteremia. This could affect the outcomes.

The WHO recommendations for management of infections in malnourished children is followed in many regions, however,

this study has only evaluated results from a single center in one country.

Conclusion

Overwhelming resistance to WHO recommended antibiotics was seen in the study population. Diarrhea and respiratory tract infections were the commonest infections among the malnourished.Gram negative infections were predominant and E.coli was the leading organism. Most bacteria isolates were sensitive to Amikacin and Gentamicin. There is a need for re-evaluation of the WHO recommendations for management if infections in malnourished children.

References

1. National Nutrition Survey- Pakistan- 2001-02 available on www.gjms.com.pk. Accessed on 10-9-2012.
2. Leonor R, Cervantes E, Ortiz R. Malnutrition and Gastrointestinal and Respiratory Infections in Children: A Public Health Problem. *Int J Environ Res Public Health* 2011 April; 8(4): 1174–1205.
3. Black R.E, Allen HL, Bhutta Z.A, Caulfield L.E, *e tal*. Maternal and child under nutrition: global and regional exposures and health consequences. www.the lancet.com, Published online Jan17, 2008 DOI: 10.1016/50140-6736(07)61690-0 Accessed 25 Feb 2010.
4. Shoham J and Duffield A. Proceedings of the World Health rganization/UNICEF/World Food Programme/United Nations High Commissioner for Refugees Consultation on the Management of Moderate Malnutrition in Children under 5 Years of age. www.who.int/.../moderate_malnutrition/FNBv30n3_suppl_report.pdf. Accessed on 20-9-12
5. Panezai.A, Rafeeq.M, Bajwa.M.A, etal.Infections of Children Associated with Malnutrition in Quetta, Pakistan. Pjmhs 2011; 5(3).Website: www.pjmhsonline.com
6. Ejaz MS, Rasheed I, Zehra H. Clinical pattern of infections in malnourished children. *Medical channel* 2010; 16(3):352-556.
7. Clinical and laboratory standard institute guidelines, 2012.www.clsi.org. Accessed on 20-9-12.
8. Powanda MC, Beisel WR. Metabolic effects of infection on protein and energy status *J. Nutr* 2003**;** *133(1):* 322S-327S.
9. Phillips RS., Enwonwu CO, OkoloS,Hassan A. Metabolic effects of acute measles in chronically malnourished Nigerian children. *J. Nutr. Biochem* 2004; *15(5):* 281-288.
10. Beisel, W.R. Nutrition in pediatric HIV infection: Setting the research agenda. Nutrition and immune function: Overview. *J Nutr* 1996; *126*:2611S-2615S
11. França TGD, Ishikawa LLW, Zorzella-Pezavento SFG, Chiuso-Minicucci F, da Cunha MLRS, Sartori A. Impact of malnutrition on immunity and infection . J. Venom. Anim. Toxins incl. Trop 2009; online version issue 1678-9199.
12. IfraS, Khemchand.M Morbidity Patterns Of Severely Malnourished Children At Tertiary Care Hospital..Pak Pediatr J 2014; 38(1): 3-8.
13. Bernal C, Velásquez C, Alcaraz G, Botero J. Treatment of severe malnutrition in children: experience in implementing the World Health Organization guidelines in Turbo, Colombia. *J Pediatr Gastroenterol Nutr* 2008; 46(3):322-8. doi: 10.1097/MPG.0b013e318156c2c3
14. Sunguya BF, Koola JI, Atkinson S. Infections associated with severe malnutrition among hospitalised children in East Africa. *Tanzan Health Res Bull* 2006; 8: 189-92 pmid:
15. Maren JHR, Lilian K, Henrik AB. Vibeke BC.The Immune System in Children with Malnutrition—A Systematic Review. PLoS ONE 2014; 9(8): e105017.
16. Black RE, Brown KH, Becker S, Alim AR and Merson MH. Contamination of weaning foods and transmission of enterotoxigenic *Escherichia coli* diarrhoea in children in rural Bangladesh. *Transactions Royal Soc Tropical Med Hyg* 192;): 259-264.
17. Singh V. The burden of pneumonia in children: an Asian perspective. *Paediatric Respr Rev* 2005;:88–93
18. Vásquez-Garibay E, Campollo-Rivas O, Romero-Velarde E, Méndez Estrada C, García-Iglesias T, *et al*. Effect of renutrition on natural and cell-mediated immune response in infants with severe malnutrition. *J Pediatr Gastroenterol Nutr* 2002; 34(3): 296–301.
19. Janeway CA Jr, Medzhitov R. Innate immune recognition. *Ann Rev Immunol* 2002; *20*: 197-216.
20. Okomo UA, Garba D, Fombah AE, Secka O, Ikumapayi UN, Udo JJ, Ota MO. Bacterial isolates and antibiotic sensitivity among Gambian children with severe acute malnutrition.*Int J Pediatr* 2011:825123.
21. Hanifa Bachou**,** Thorkild Tylleskär**,** Deogratias H Kaddu-Mulindwa and James K Tumwine. Bacteraemia among severely malnourished children infected and uninfected with the human immunodeficiency virus-1 in Kampala, Uganda. *BMC Infectious diseases* 2006, 6:160 doi: 10.1186/1471-2334-6-160.
22. H. Çaksen,Y. Cesur, A. Üner, S. Arslan, S. Sar, V. ÇelebiM. Kuru. Urinary tract infection and antibiotic susceptibility in malnourished children. *International Urology and Nephrology* 2000; 32 (2): 245-247.
23. Lazzerini M and Tickell D. Antibiotics in severely malnourished children: systematic review of efficacy, safety and pharmacokinetics. *Bulletin of the World Health Organization* 2011; 89:594-607. doi: 10.2471/BLT.10.084715.