Clinical manifestations, comorbidities and causative organisms of infections in children aged 6 months to 59 months with Severe Acute Malnutrition

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Abstract
Objective: To study the various clinical manifestations, co-morbidities and causative organisms of infections in SAM (severe acute malnutrition) in children aged 6 months to 59 months in a tertiary care hospital of odisha.

Methods: It is a hospital based prospective observational study done in a tertiary care hospital, Cuttack, Odisha during the period of November 2015 to October 2017. All children from 6 months to 59 months of age diagnosed with SAM were included and the clinical manifestations and spectrum of infections in them were evaluated.

Results: In our study population the prevalence of SAM was found to be 2.8%. Fever was the most common symptom (71%), next was vomiting (51%), loose stools (46.8%), cough 46.3 % and poor appetite and/ or weight loss (31%). Most common comorbidities found were diarrhea(46.8%), acute respiratory tract infection (46.3%), septicemia(27.4%) and urinary tract infection(26.3%). The commonest organisms encountered in blood culture in the study were Staphylococcus aureus (48.1%) followed by CONS (28.9%), Group D Streptococcus (11.5%), E.Coli (7.7%), and Klebsiella (3.8%).

Conclusion: Severe acute malnutrition is prevalent in odisha (2.8%) and leads to increased Mortality (6.8%) in children between 6 months to 59 months of age. The commonest presentation to hospital is fever(71%) with comorbid condition acute gastroenteritis(46.8%) followed by respiratory tract infections and septicemia. The most common infective organism affecting children with SAM is staphylococcus aureus(48.1%) followed by CONS (28.9%).

Keywords: SAM (severe acute malnutrition), infections, clinical manifestations, comorbidities, Odisha.

Introduction
Malnutrition is one of the most leading causes of morbidity and mortality in children all over the world. The most extreme form of undernutrition is SAM (severe acute malnutrition). Severe acute malnutrition (SAM) is defined as weight for height/length less than −3Z score of the WHO growth charts or MUAC <115 mm or the presence
of bilateral pitting edema.\(^1\) Some of the important contributory factors for SAM are lack of exclusive breastfeeding, delayed introduction of complementary feeds, feeding diluted feeds, repeated enteric and respiratory tract infections, illiteracy, and low socioeconomic status.\(^2\) As per National Family Health Survey (NFHS)-4 (2015-16) 35.7% children below five years are underweight, 38.4% are stunted and 21% are wasted in India. Stunting and underweight prevalence has decreased since 2005-06, especially for stunting, which declined from 48 percent in 2005-06 to 38 percent in 2015-16 but the prevalence of wasting has remained about the same.\(^3\) Children with malnutrition usually present with fever, loss of appetite or with comorbid conditions like gastroenteritis and respiratory tract infections followed by urinary tract infections and septicemia\(^4,5\) There is an increased severity of common infectious diseases in children with SAM, leading to increased mortality in them.

Management of infections differ in malnourished children as compared to healthy children.\(^6\) Organisms most commonly affecting malnourished children are Staphylococcus aureus, Escherichia coli, and Salmonella typhi.\(^7\) Thus malnutrition and infection can be mutually aggravating and produces more serious consequence for the patient. A good number of SAM cases are admitted to our hospital from all over Odisha with variety of infections like RTI, diarrhoea, measles, tuberculosis, UTI etc, who may or may not have signs & symptoms of overt infection. However the clinical profile and incidence of bacteremia in malnourished children has not been adequately studied in recent past in Odisha, so this study was conducted to know the spectrum of infection and causative organisms among severe acute malnutrition cases admitted to this institution.

**Materials and Methods**

This study is a prospective observational study of patients admitted with severe acute malnutrition in the department of pediatrics in a tertiary care hospital of Odisha during the period of November 2015 to October 2017.

**Inclusion Criteria:** Children from 6 months to 59 months of age with
- Weight-for-height less than -3 SD (WHO/NCHS median height) and/or
- Visible severe wasting and/or
- Mid arm circumference (MUAC) < 11.5 cm and/or
- Bilateral pedal edema

**Exclusion Criteria**
- Children < 6 month and >5 yrs
- Malnutrition due to chronic illness (secondary malnutrition) like cleft lip, cleft palate, GERD, pyloric stenosis and other surgical condition, chronic renal failure, congenital heart diseases, liver disorders, asthma, mental retardation, cerebral palsy, suspected case of inborn error of metabolism etc.

Children whose parents denied for consent were also excluded from the study.

The parents of the children who satisfied the inclusion criteria were informed and a written consent was taken from them. This study was approved by the Ethics and Research Committee of our hospital.

**Demographic Details and Clinical Information**

A detailed history of all cases with reference to nutritional history, SES, contact with TB, history of diarrhea and other infectious diseases. Birth history, family order, duration of breastfeeding, immunization, weaning and duration of illness were taken. A thorough examination was carried out along with different anthropometric measurements expressed in standard deviation from the median of the reference population standards (NCHS). Clinical evidence of associated infections were considered. Data regarding residential area, sex, age and date of birth, socio-economic status, perinatal history, feeding practice was collected by questionnaire method. Proper history of all children suffering from
various presentations were taken and questioned and data regarding frequency, nature and duration of diarrhea and vomiting and fever along with cough and other symptoms were recorded. Other associated infections like urinary tract infection, pneumonia, septicemia, TB, malaria and HIV were assessed. History of chronic diseases such as sickle cell disease, HIV/AIDS and TB was also enquired. All the evidence and finding were recorded in predefined performa and data were analyzed statistically.

General Examination
A thorough clinical examination was done on all the enrolled patients and severe acute malnutrition was diagnosed as per WHO criteria. The measurements done were as follows:

Weight
Children < 2yrs of age were weighed using a 25 kg Salter hanging scale (CMS Weighing equipment, High Holborn, London United kingdom) and those > 2yrs of age were weighed while standing on the measuring board. Before each recording the scales were adjusted to zero. Weight was rounded off to nearest 100 grams and measured daily during morning. The reference which was applied was of WHO chart which compared weight/length or weight/height.

Length / Height
- For children <2 yrs length was measured using an infantometer in the recumbent position by two examiners. For > 2 yrs children and able to walk, height was measured while standing using a stadiometer.
- Weight for height/length and Z score of less than -3SD were included in the study.

Mid-Upper Arm Circumference (MUAC)
For measurement of MUAC a midpoint between acromion process and olecranon process was chosen on the left arm. The reading was recorded to the nearest 0.1cm. MUAC< 11.5cm were considered as severe acute malnutrition. MUAC can be measured above 6 months of age.

Specimen Collection and Laboratory Procedures
Investigations which were done at SCB Medical College and SVPPGIP main laboratory were CBC, CPS, ESR, Blood slide for malaria parasite, serum total protein and albumin, serum electrolytes, x-ray chest, urine and stool examination, test for HIV. Culture and sensitivity testing of blood, urine, stool and pus were done. Random blood glucose estimation was done in the ward.

Data Analysis
Data were entered into a computer excel 2007 using IBM SPSS 21 and Microsoft. Data was analyzed using SPSS software. The 95% confidence interval was determined. Factors/predictors with p-value of less than 0.05 were considered significant. Data were double entered into an Access database and checked for errors.

Results
A total of 311 patients enrolled in the study between 6 month to 59 month of age during this period of 2 years (November 2015 to October 2017). Out of these 102 patients were excluded as per exclusion criteria and 19 patients left against medical advice during study period. So the remaining 190 patients constituted the study population.
Out of total 10878 patients admitted to our hospital during the 2 years of study period, 311/10878(2.8%) patients were having features of SAM. (Table No-1)
The commonest clinical symptom in the present study was fever 71%, then vomiting 51%, loose stools 46.8% ,cough 46.3 % and poor appetite/or weight loss in 31% of cases. Other presenting complaints were oedema 14.7%, distention of abdomen in 13.1%, rash 4.2%, convulsion 3.1%, ear discharge 2.1% and bleeding 1.6%. (TABLE NO-2) 52 of the blood cultures collected grew bacteria out of which 25(48.1) grew Staphylococcus aureus, 15(28.9%) grew CONS, all being Staphylococcus epidermidis, 6(11.5%) grew Group D streptococcus, 4(7.7%) E.Coli and
Klebsiella species in 2(3.8%). Gram positive organisms were more common in the above findings (Table No -3) The most common comorbidities associated with severe acute malnutrition were acute gastroenteritis in 89 /190 (46.8%), followed by acute respiratory tract infection in 88/190 (46.3%), sepsicaemia in 52/190 (27.4%) urinary tract infection in 50/190 (26.3%), malaria in 8/190 (4.2%) patients. Other associated infections were tuberculosis in 5 / 190 (2.6%), measles in 5 /190 (2.6%), meningitis 4/190 (2.1) otitis media in 4/190 (2.1%) and HIV in 1/190 (0.5%). Other infection skin infection like pyoderma, scabies, candidiasis are found in variable number of patient were 21/190 (11%), 6/190 (3.1%) and 4/190 (2.1%) respectively. (Table No 4)

Table No 1: Prevalence of SAM in the Study Population

| Total No of Patients | No. of Sam Patients (%) | Others (%) |
|----------------------|-------------------------|------------|
| 10878                | 311 (2.8)               | 10,567 (97.2) |

Table No 2: Distribution of the Study Population as Per Major Present Complaint (n=190)

| S. NO. | Complaints                        | Frequency | Percentage (%) |
|--------|-----------------------------------|-----------|----------------|
| 1.     | Fever                             | 135       | 71             |
| 2.     | Vomiting                          | 97        | 51             |
| 3.     | Loose Motion                      | 89        | 46.8           |
| 4.     | Cough                             | 88        | 46.3           |
| 5.     | Loss of Appetite/ (Weight Loss)   | 59        | 31             |
| 6.     | Edema                             | 28        | 14.7           |
| 7.     | Abdominal Distension              | 25        | 13.1           |
| 8.     | Rash                              | 8         | 4.2            |
| 9.     | Convulsion                        | 6         | 3.1            |
| 10.    | Ear Discharge                     | 4         | 2.1            |
| 11.    | Bleeding                          | 3         | 1.6            |

Table No 3: Type and Proportion of Bacteria Isolated From Blood Culture (n=52)

| Organism                | Frequency | Percentage (%) |
|-------------------------|-----------|----------------|
| Staph.Aureus            | 25        | 48.1           |
| CONS                    | 15        | 28.9           |
| GDS                     | 6         | 11.5           |
| E.Coli                  | 4         | 7.7            |
| Klebsiella Species      | 2         | 3.8            |
| Total                   | 52        |                |

Table No 4: Associated Co-Morbidities in the Study Population (n=190)

| Type of Diseases        | Frequency | Percentage (%) |
|-------------------------|-----------|----------------|
| Acute Gastroenteritis   | 89        | 46.8           |
| ARI                     | 88        | 46.3           |
| Sepsis                  | 52        | 27.4           |
| UTI                     | 50        | 26.3           |
| Malaria                 | 8         | 4.2            |
| Measles                 | 5         | 2.6            |
| TB                      | 5         | 2.6            |
| Meningitis              | 4         | 2.1            |
| Otitis Media            | 4         | 2.1            |
| HIV                     | 1         | 0.5            |
| Skin Infections         |           |                |
| Pyoderma                | 21        | 11             |
| Candidiasis             | 6         | 3.1            |
| Scabies                 | 4         | 2.1            |

Discussion

The prevalence of severe acute malnutrition in our study population was 2.8%(311/10878).According to NFHS-4 (2015-2016) data the overall prevalence of severe acute malnutrition in odisha is around 6.4% which is much more than our results which may be due to poor referral, ignorance and lack of access to health services in some parts of the state. Mahgoub et al found prevalence of SAM to be 27.3%in a study done in Sudan which is significantly high which may be due to geographical and racial variation among study population.(Table No 1)

In our study, the most common clinical symptom was fever (71%) followed by vomiting (51%), loose stools (46.8%), cough(46.3%) and poor appetite and /or weight loss(31%) .Other features were edema(14.7%), abdominal distension (13.1%), rash (4.2%), convulsion(3.1%),ear discharge (2.1%), and bleeding(1.6%).

In 2008 Bernal et al conducted a study on treatment of SAM in children by implementing the WHO Guidelines in which fever (26.3%) was the most common symptom in 26.3% cases and most common comorbid condition was diarrhea (68.4%) and it was significantly higher in children with severe acute malnutrition (P = 0.003).

Another study done by Bagga et al in 2003 also found fever and diarrhea as the most common presentations. Other studies which showed
similar results were by Ashraf et al in 2001 which reported diarrhea (25.8%) and fever/vomiting (30.9%) as the common presenting symptoms in malnourished children\(^9\).(Table No-2) Out of 52 blood culture samples which grew bacteria 25(48.1%) were Staphylococcus aureus, 15(28.9%) grew CONS, all being Staphylococcus epidermidis, 6(11.5%) grew group D streptococcus, 4 (7.7%) were E.Coli and 2(3.8%) were Klebsiella species. Gram+ve aerobes were the most common isolates accounting for 88.5% (46/52) followed by the Gram –ve aerobes 11.5% (6/52). Umma Abdullahi Idris et al (2018) in his study found that Staphylococcus aureus (41.5%), Escherichia coli (17.1%), and Salmonella typhi (12.2%) were the most frequent isolates in the individuals with severe malnutrition\(^7\). S.aureus predominance in this study may be due to the fact that it reflected the community predominant organism as most children were from community. There has been variable associations between malnutrition and risk of bacteremia. Previous studies from kenya have suggested an increased likelihood of Gram negative bacteraemia in children with malnutrition\(^10\). Vitamin A deficiency may be a predisposing factor to Staphylococcus aureus infections through phagocyte dysfunction and decreased complement activity\(^11\). Other risk factor that could have contributed to the high prevalence of Staphylococcus aureus includes prior hospitalization as majority of the study participants were referred from peripheral hospital. Coagulase Negative Staphylococcus (CONS) was the second leading cause of bacteremia in this study. Studies from Africa and Jamaica have found CONS as the predominant organism ranging between 26.7 to 40 %\(^{12,13}\). In our study the proportion of CONS isolates was 32.5%, which may have been due to the use of 70% alcohol alone to clean the skin prior to venepuncture, rather than using it in combination with 10% povidone iodine as in other studies \(^{4,13,14}\). CONS are common commensals of skin and can enter the bloodstream if there is breech in barrier as in malnutrition\(^{12}\). CONS are recognized as important cause of sepsis among critically ill and immunocompromised children. \(^{12,13}\). This makes judging the clinical significance of CONS very important before considering them as contaminants. Group D Streptococcus bacteria were another Gram – positive blood bacterial isolates in this study. It accounted for 11.5% of all isolates. Group D Streptococcus are normal commensals of the gastrointestinal tract of humans. In malnourished children there occurs damage to the gastrointestinal mucosa and impaired immune response which leads to infection with these bacteria. E.coli and klebsiella species were the Gram – negative isolates that were demonstrated by this study. They accounted for 7.7% and 3.8% of all isolates respectively. Alem et al (2011) in Ethiopia\(^{15}\) and Christie et al (1992) \(^{12}\) in Jamaica also reported similar results.(Table No-3) The most common comorbidities associated with SAM were AGE (46.8%), followed ARI (46.3%), septicemia (27.4%), UTI (26.3%), malaria (4.2%) and other associated co-infection were tuberculosis (2.6%) measles (2.6%), otitis media (2.1%), HIV (0.5%) and skin infection like pyoderma, candidiasis and scabies. Prasanth et al (2018) reported pneumonia as the major co - morbid condition in 43% of cases. Their study reported diarrhea in 21% of cases\(^{16}\). Our study had similar as done by Sharma et al\(^{17}\) and Bernal et al\(^{5}\) who reported diarrheas as the major comorbid condition in malnourished children. (Table No-4) Summary
- The overall prevalence of SAM in our study population was 2.8%.
- Fever was the most common clinical feature associated with SAM.
- Commonest comorbidities associated with SAM are diarrhoea followed by ARI, septicaemia and UTI.
- Commonest complications encountered in the study are dehydration, followed sepsis,
hypothermia and hypoglycemia.

- 27.4% of SAM children showed positive blood culture.
- The organisms isolated from blood cultures are Staphylococcus aureus followed by CONS, GDS, E.coli. and klebsiella

**Study Limitations**

1. This is a hospital based observational study and the true prevalence of SAM in the community could not be ascertained from it.
2. Many patients had already taken one or two of the commonly used antibiotics prior to recruitment. This may have lowered the detection rate of blood bacterial isolates and sensitive pattern.

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Abbreviations
SAM Severe Acute Malnutrition
MUAC Mid Upper Arm Circumference
NFHS National Family Health Survey
NCHS National centre for health statistics
RTI Respiratory Tract Infection
UTI Urinary Tract Infection
GERD Gastroesophageal reflux disease
AGE Acute gastroenteritis
SES Socioeconomic status
CONS Coagulase negative staphylococcus
HIV Human Immunodeficiency Virus
AIDS Acquired immunodeficiency syndrome
TB Tuberculosis
CBC Complete blood count
CPS Comment peripheral smear
E.COLI Escherichia coli
ESR Erythrocyte sedimentation rate
GDS Group D streptococcus
SD Standard deviation
SCBMCH Sriram Chandra Bhanja Medical College & Hospital
SVPPGIP Sardar Vallabhbhai Patel Postgraduate Institute of Paediatrics