Original Research Article

Predictors of morbidity & mortality in children hospitalized with severe acute malnutrition – Hospital based observational study

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Abstract

Background: Severe Acute malnutrition is the major flog which needs utmost attention to bring down the under 5 mortality & morbidity significantly. Hospitalization and inpatient care of all such children is neither feasible nor cost effective intervention. Hence it is important to identify the factors which influence morbidity & mortality in children with Severe Acute Malnutrition (SAM) and utilize them as indicators to triage and targeting the interventions towards such children so as to optimally utilize the resources especially in developing countries. **Aims and objectives:** With this background the present study was planned to determine the predictors of morbidity in children with SAM. **Methods:** This hospital based observational study was conducted in Rama Medical College Hospital & Research centre. Ghaziabad, Uttar Pradesh where consecutive children between 2 months- 5 years fulfilling the WHO case definition of SAM and complications requiring hospitalization were enrolled. The sociodemographic, clinical and biochemical factors influencing the morbidity & mortality were evaluated. **Results:** Of 3704 children screened for SAM, 504 (13.6%) fulfilled the case definition but the final analysis was done on 425 children. The most common co morbidity in these children was diarrhea (63.5%) followed by pneumonia (40%), tuberculosis (5.1%) and HIV in 1% . After multivariate regression analysis, the present study observed shock, hypoglycemia, severe anemia and bacteremia as independent risk factors significantly associated with morbidity & mortality. **Conclusion:** The morbidity & mortality of children with SAM is influenced by multiple factors and it becomes imperative to identify the red flags responsible for early deaths so as to hospitalize, triage and prioritize the interventions especially in resource limited settings.

Keywords: Severe Acute Malnutrition, Children, Predictors, Outcome, Mortality, Co- morbidity

Introduction

Severe Acute Malnutrition is one of the leading cause of morbidity & mortality in children especially in developing world and a great hurdle in accomplishing the Millennium Development Goal 4 i.e. to reduce the mortality in under-fives by two third. A recent assessment showed that efforts to prevent child death need to be strengthened in order to meet the target[1]. The median under five case fatality for severe acute malnutrition typically ranges from 30-50%[2,3]. SAM can be a direct cause of death or it can act as an indirect cause by dramatically increasing the case fatality (9 times higher than in well nourished) in children suffering from common child hood illnesses like diarrhea and pneumonia.

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The WHO has developed consensus management guidelines which include stabilization phase in which life threatening problems are identified and treated, a staged introduction of milk based nutritional rehabilitation, micronutrient and vitamin supplementation and empirical use of antimicrobial and anti- helminthic treatment. The existing scientific evidence suggest that management of SAM with Medical Nutrition therapy according to WHO guidelines have reduce case fatality significantly[4,5] but still achieving the sphere standards (CFR<5%)[1] seems to be a far-fetched goal especially in resource limited settings.

Estimates suggest that the prevalence of severe acute malnutrition (SAM) in children below 5 y of age in India is about 6.4 %, accounting for nearly 8.1 million children[6]. It may not be feasible to admit all children with SAM for appropriate management due to lack of infrastructure and resources. However it is seen that majority of the deaths in children hospitalized with SAM usually occur in first 48 hours of admission[7]. Therefore it has been suggested that there is a need to identify factors associated with early demise in children with SAM so that the available manpower and resources are optimally utilized in addressing the issues in these high risk malnourished children who if left for routine management were most likely to die. There is paucity of research literature available on risk factors for mortality in severe acute malnutrition from India. Most of the studies in this context are from African subcontinent[8,9] which may not always be applicable in our setting. So with this background in mind

the present study was undertaken to determine the risk factors influencing the morbidity & mortality in children with severe acute malnutrition.

Materials and Method

This hospital based observational study was conducted in Rama Hospital, Rama Medical College Hospital & Research centre, Ghaziabad, Uttar Pradesh from June 2018 to May 2020. The subjects were consecutive children of either gender, between 2 months and 5 years of age fulfilling the WHO case definition of Severe Acute Malnutrition[10] who presented to the hospital for various complaints that required hospital admission and did not fulfil exclusion criteria (detail in Figure1) were enrolled for the study. Ethical clearance was obtained from the institutional ethics committee. Written informed consent was obtained from the parents of each subject. A convenient sample of 300 was estimated on the basis of average number of malnourished children aged 2 months to 5 years likely to be admitted in the hospital during the study period. Details of the subjects on their anthropometric parameters, socio demographic profile (Age, sex, education, income, immunization, mode of feeding including breast feeding practices), clinical details and the relevant investigation conducted both routine and specific as per the clinical case were recorded in a prestructured proforma.

All admitted patients were assessed for emergency signs related to airway and breathing, circulation, coma/convulsion and severe dehydration. Digital thermometer with range 32-42^{o}C was used to measure the axillary temperature. Hypothermia was defined as axillary temperature below 35^{o}C and fever was defined as temperature above 38.5^{o}C. Blood glucose was tested with the help of glucometer using finger prick or heel prick technique and hypoglycemia was defined as blood glucose level less than 54 mg/dL. The respiratory rate was counted for full 1 minute and if it was ≥ 50 breath/min for 2-12 months and ≥ 40 breath/min for 1-5 years, it was labeled as fast breathing. Hear rate was counted for 1 minute using stethoscope and tachycardia was defined as HR > 180 beats/min and >140 beats/min for 2-12 months and 1-5 years respectively. To check for edema, the foot was grasped in hand and thumb gently pressed for 10 seconds. The child has edema if a pit remains in the foot when thumb was lifted. The assessment of diarrhea and classification of dehydration was done as per the IMNCI guidelines[11]. The children with SAM were also assessed for the presence of pneumonia, malaria, measles, throat and ear infections and anemia as per the IMNCI guidelines[11].

All the children with SAM enrolled in the study were subjected to a few investigations which were carried out in all children and others which were individualized as per the case. 1 ml blood was collected in EDTA vial for complete blood count and analyzed on Sysmex (ERBA) KX 21 analyzer. A peripheral smear was sent in all cases of anemia to look for the kind of anemia and severe anemia was defined as hemoglobin less than 7g%. 2ml blood sample was collected in plain test tube for serum electrolyte and analyzed on Eletrolyte Analyzer (Rosche 1980). The standard definition was used to define dyselectrolytemia[12]. A chest X-ray was ordered in all enrolled cases and evaluated for any opacity/infiltrates and military shadows.

Blood culture was obtained under aseptic precautions in BACTEC bottles containing universal broth and then transferred to the microbiology department for incubation and plating. Urine was also collected under aseptic precautions by suprapubic puncture or clean catch mid-stream sample in a plain sterile vial for nitrite testing by adipsticks at admission and the rest sent for routine microscopy and culture to microbiology department. Mantoux testing was done using 5 TU and the induration of more than 10 mm after 72 hours was considered positive. Fasting early morning Gastric aspirates were collected in a plain sterile vial to detect acid fast bacilli. Malaria testing was carried out using thin and thick smears and antigen detection for of Plasmodium vivax and falciparum.by 1 ml EDTA blood. Testing for HIV-1 was done in all suspected cases as per NACO guidelines. All children hospitalized with SAM were managed as per standard protocol[13,14] and the outcome recorded as discharged and improved after a followed up over a period of 6 months on OPD basis (Group I) or death (either in hospital or on 6 month of follow up on OPD basis) (Group II).

Data analysis was done by using the statistical software SPSS version 12. Data were described using standard statistics for continuous and categorical variables. Categorical variables were compared using the chi-square test. The sociodemographic, clinical and biochemical variables of enrolled subjects were evaluated in relation to the outcome using univariable analysis. Multivariate logistic regression analysis was used to identify significant risk factors for mortality. Odds ratios (ORs) and their 95% confidence intervals (CIs) are specified where applicable. A p-value of <0.05 was considered statistically significant.

Results

Out of 3704 children aged 2months -5 years who were screened for severe acute malnutrition over a period of 24 months, 504 (13.6%) fulfilled the case definition of severe acute malnutrition (SAM) (2) but the final analysis was done on 425 children as 79 got excluded in view of exclusion criteria (detailed in Figure 1).

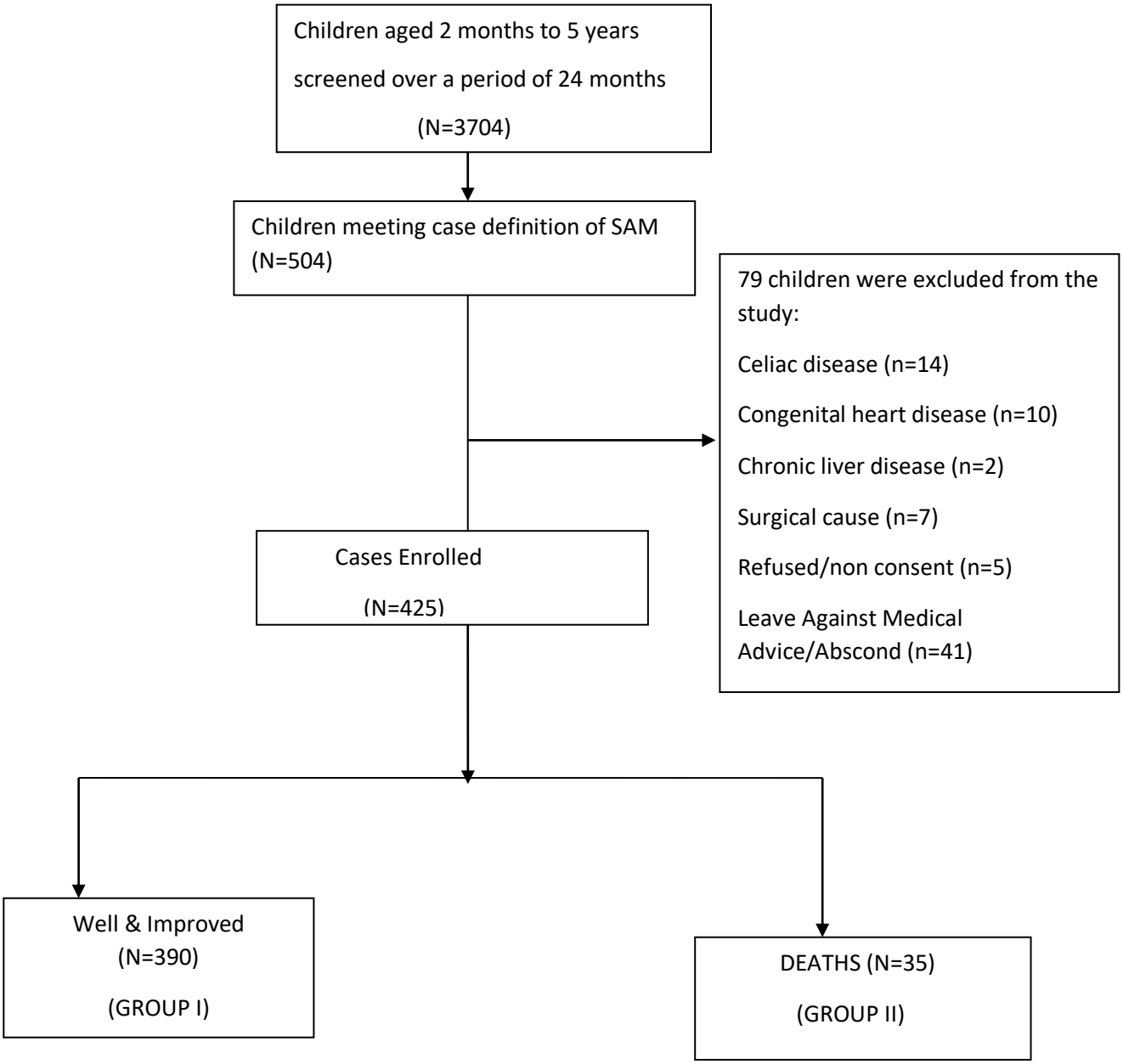

Fig 1: Flow diagram depicting flow of study subjects.

Among 425 cases, males constituted 57.6 % (245/425) of children with maximum enrollment in 7-24 months (60.7%) age group. The socio demographic and clinical profile of the children enrolled in the study is described in Table 1.

Table 1: Socio demographic and clinical profile of the children with SAM enrolled in the study

VARIABLES	2 to 6 months(N=108) (25.4%)	7 to 24 months(N= 258)(60.7%)	25 to 60 months (N=59)(13.9%)	P Value
Male	61 (56.5)	157(60.9)	27 (45.8)	0.102
Female	47 (43.5)	101 (39.1)	32 (54.2)	
Maternal Education				
Illiterate	51 (47.2)	117 (45.3)	26 (44.1)	0.086
Literate	57 (52.8)	141 (54.7)	33 (55.9)	
Weight/Height				
<-4SD	49 (45.3)	102 (39.5)	15 (25.4)	0.118
<-3SD	58 (53.7)	152 (59)	42 (71.2)	
<-2SD	1 (1)	4 (15.5)	2 (3.4)	
Pedal edema	3(2.8)	34 (13.2)	29 (49.2)	<0.001*
Mode of feeding				
Exclusive Breast	12 (11.1)	60 (23.2)	19(32.2)	0.001
Feeding	58 (53.7)	144(55.8)	35(59.3)	
Predominant/Partial	37 (34.2)	53 (20.5)	5 (8.5)	
Not Breast Fed				
Days of Hospital Stay				0.604
<3 Days	8 (7.4)	10 (3.9)	2 (3.4)	
4-7 Days	47(43.5)	112 (43.4)	24(40.7)	
>7 Days	53(49.1)	136 (52.7)	33(55.9)	
Outcome				
Discharged	96 (88.9)	240 (93)	54 (91.5)	0.422
Death	12 (11.1)	18 (7)	5 (8.5)	

Numbers in parentheses indicate percentages.

One sixth of the total admitted children had edema at admission with maximum proportion (49.2%) in the age group 25-60 months. The most common coexistent condition in hospitalized children with SAM was diarrhea (63.5%; 270/425) with around one third (34%; 92/270) having dehydration at presentation, followed by pneumonia (40%; 170/425).On studying other co morbidities of the enrolled children with SAM, tuberculosis was diagnosed in 5.1% (21/408), HIV in 1.7% (7/421), and slide positivity for malaria parasite seen in 1.6% (7/418). Emergency signs warranting admission and intervention were demonstrated in 12.5% (53/425) of children at the time of admission with 5.6% (24/425) having features of shock. The proportion of children admitted with severe anemia was 17.9% (76/425) while hypokalemia was observed in 13.9% (59/425) and hyponatremia in 6.8% (29/425).

Laboratory confirmed bacteremia occurred in 16% (65/410) of children. Staphylococcus aureus was the most common organism isolated from blood culture (n=35; 55.8%) followed by E coli (n=6; 9.2%). Other organisms isolated were Pseudomonas aeruginosa (n=3; 4.6%), Coagulase negative staphylococcus aureus (n=3; 4.6%), Enterococcus (n=3; 4.6%), Acinetobacter (n=3; 4.6%), Klebsiella (n=3; 4.6%) and Candida (n=2; 3%). Urine examination revealed a positive nitrate test by dipsticks in 32% (136/423) children, however growth was confirmed by urine culture in 18% (74/414). E coli was the most common organism isolated (n=37; 50%) followed by candida (n=12; 16.2%). Among the other isolated organisms include Enterococcus (n=4; 5.4%), Klebsiella (n=4; 5.4%), Acinetobacter (n=3; 4%) and contaminants (n=14; 19%).

The present study recorded an overall case fatality rate of 8.2% with the maximum mortality (11.1%) in 2-6 months age group. Out of total expiry, the maximum proportion of deaths occurred in children of the age group 7-24 months (51.4%). The socio demographic, clinical and biochemical parameters in relation to the outcome of children with SAM are illustrated in table 2.

Table 2 Univariable analysis of the socio demographic, clinical and biochemical characteristics of children with Severe Acute Malnutrition in relation to the outcome.

Variable studied N= 425		Group I Discharge N=390 (%)	Group 2 Expired N=35 (%)	P value
Age Groups	0-6 months (n=108)	96 (88.9)	12 (11.1)	0.001
	7-24 months (n=258)	240 (93)	18 (7)	
	25-60 months (n=59)	54 (91.5)	5 (8.5)	
Residence	Urban (n=268)	259(96.6)	9(3.4)	<0.001
	Rural (n=157)	131(83.4)	26(16.6)	
Immunization Status	Unimmunized (n=168)	144(85.7)	24(14.3)	<0.001
	Partially immunized (n=167)	160(95.8)	7(4.2)	<0.001
	Immunized (n=90)	86(95.5)	4(4.5)	<0.001
Breast Feeding till 6 months	Exclusive/Predominant BF (n=92)	90(97.8)	2(2.2)	<0.0001
	Partial BF (n=238)	221(92.8)	17(7.2)	<0.0001
	Not Breast Fed (n=95)	79(83.1)	16(16.9)	<0.0001
Weight for Height	<-4SD (n=167)	140(83.8)	27(16.2)	<0.0001
	Between -3SD & -4SD (n=251)	244(97.2)	7(2.8)	
Maternal Education	Illiterate(n=169)	146(86.3%)	23(13.7)	0.030
	Literate ((n=256)	244(95.3%)	12(4.7)	

Emergency Signs	Present (n=54)	26 (48.1)	28 (51.9)	<0.0001
	Absent (n=371)	364 (98.1)	7 (1.9)	
Edema (N=425)	Present (n=106)	90 (84.9)	16(15.1)	0.005
	Absent (n=319)	300(93.7)	19 (6.3)	
Shock (N=425)	Present (n=24)	12 (50)	12 (50)	0.017
	Absent (n=401)	378 (94.2)	23 (5.8)	
Signs of Dehydration (N=425)	Present (n=93)	76 (81.7)	17 (18.3)	<0.0001
	Absent (n=332)	314 (94.5)	18 (5.5)	
Temperature in ^{0}C (N=425)	Hypothermia <35^0 C (n=21)	15/21 (71.4)	6/21 (28.6)	0.006
	>35^0 C-<38^0 C (n=355)	329/355 (92.7)	26/355 (7.3)	
	Pyrexia >38^0 C (n=49)	46/49 (93.8)	3/49 (6.2)	<0.0001
Blood Dextrose (N=425)	Hypoglycemia <54 mg/dL (n=33)	25(75.7)	8(24.3)	<0.0001
	Normoglycemia ≥54 mg/dL (n=392)	365 (93.1)	27(6.9)	
Pneumonia (N=425)	Present (n=169)	148 (87.6)	21 (12.4)	0.007
	Not Present (n=256)	242(94.5)	14(5.5)	
Diarrhea (N=425)	Present (n=220)	195(88.6)	25(11.4)	0.026
	Absent (n=205)	195 (95.1)	10 (4.9)	
Persistent Diarrhea	Present (n=114)	100(87.7)	14(12.3)	0.039
	Not Present (n=311)	289 (92.9)	22 (7.1)	
HIV Status	Negative (n=416)	383(93)	33(7)	<0.0001
	Positive (n=5)	4(80)	1(20)	0.09
Children with tuberculosis	Mantoux Test Positive (n=46/408)	38/387 (9.8)	8/21 (38)	<0.0001
	GA for AFB Positive (n=4/408)	2/392 (0.5)	2/16 (12.5)	0.002
	Miliary shadow on X Ray (n=11/425)	9/390 (2.3)	2/35 (5.7)	0.241
Hemoglobin (gm/dL) (N=425)	<7gm.dl (n=76)	61(80.2)	15(19.8)	<0.0001
	≥7gm/dl (n=349)	329 (94.3)	20 (5.7)	
Sodium (meq/L) (N=425)	<130 (n=29)	23 (79.3)	6(20.7)	<0.0001
	130-150 (n=291)	278 (95.5)	13 (4.5)	
	>150 (n=105)	89 (84.8)	16(15.2)	<0.0001
Potassium (meq/L) (N=425)	<3 (n=59)	49 (83)	10 (17)	
	3-5.5 (n=289)	271 (93.8)	18 (6.2)	
	>5.5 (n=77)	70 (91)	7(9)	<0.0001
Blood Culture (N=410)	Sterile (n=345)	329 (95.4)	16 (4.6)	<0.0001
	Growth (n=65)	50(76.9)	15 (23.1)	
Urine Culture (N=414)	Sterile (n=340)	321(94.4)	19(5.6)	<0.0001
	Growth (n=74)	67(90.5)	7(9.5)	

Numbers in parentheses indicate percentages
P value <0.05 - significant
However, after multivariate logistic regression analysis, presence of shock, anemia , hypoglycemia and bacteremia were implicated as significant predictors of mortality as enlisted in Table 3.

Table 3: Factors determining mortality of children with Severe Acute Malnutrition using Multivariate Logistic Regression Analysis

Variables	P values	Adjusted OR	95% CI
Hemoglobin (<7gm/dL)	0.001	1.8	(1.3 - 2.5)
Positive Blood culture	0.002	13.1	(2.7 - 64.5)
Abnormal Chest X Ray	<0.001	28.1	(5.2 – 151.0)
Reactive HIV status	0.036	20.6	(1.3 - 344.8)
Positive Gastric Aspirate for Acid Fast Bacilli	0.013	79.2	(2.5 - 2525.8)
Presence of Shock	0.003	41.1	(3.5-490.4)
Hypoglycemia	0.020	1.0	(1.0-1.1)

OR- Odds Ratio
CI- Confidence Interval
P value < 0.05 significant
With each gram fall in hemoglobin below 7gm/dL, the risk of mortality rises by 1.8 times. Similarly with every 1mg/dL fall in blood glucose below 54mg/dL would increase a unit time risk of death in children with severe acute malnutrition.

Discussion

The case management of children with SAM hospitalized with complications was extremely challenging and the outcome was determined by multiple factors. The study achieved case fatality rate of 8.2% which however failed to meet the acceptable level of care against the sphere standards (death rate<5%)[1]. The outcome of the present study is comparable to the CFR of 10.8% reported from Bangladesh[15] but far less than from other African studies[8,9,16,17]. Apart from the case management as per the Standardized WHO guidelines,[13,14] the other critical steps which

promoted favorable outcome were triaging the patients, identification and prompt management of the emergency signs, screening and management of co morbid conditions, availability and optimal utilization of resources (locally prepared therapeutic diet) for adequate care and individualized round the clock good quality care by doctors and nursing staff.

A higher proportion of male children enrolled in our study and similar pattern reported elsewhere[8,9] reflects male preference in health seeking behavior particularly in developing countries. Around two third of the study group were 7-24 months age signifying the most vulnerable population to develop malnutrition particularly during the transition phase from breast feeding to the introduction of complementary foods. This is also the critical period to intervene and implement correct Infant and Young Child Feeding (IYCF) practices so as to optimize the child's genetic potential. Among the socio demographic parameters, the factors significantly associated with mortality in children with SAM were rural background, maternal illiteracy, absence of breast feeding and immunization. Often these factors are interrelated. Approximately 50% of the mothers were illiterate and unaware of the optimal feeding, child rearing practices and the need for age appropriate immunization. Least mortality was observed in exclusively breast fed children which confirms the protective effects of the breast milk. The above factors have also been implicated as risk factors of SAM in a case control study[18]. Around 40% of children enrolled in the study had weight for height SD score <- 4SD thereby predisposing them to a higher mortality. Hence it becomes important to strengthen growth monitoring and actively screen the children at peripheral health centers for the presence of SAM and start intervention at a much earlier stage to prevent the setting in of complications and further progression to such a debilitating state. The most common co morbid conditions associated with children admitted with SAM in the present study were diarrhea followed by pneumonia and tuberculosis. In another crossectional study from India to assess the co morbidities associated with SAM, 54% had diarrhea while 27.9% of children suffered acute respiratory tract infections[19]. A Columbian study[20] reported diarrhea in 68.4% of malnourished children and a similar high incidence also seen in two other African studies[21,22] Another study from Africa[16] found HIV (29.2%) and malaria (21%) to be major co morbidities associated with SAM children and a comparable incidence of respiratory illness and tuberculosis (18 % each). In the current study, case fatality in association with co morbid states like diarrhea (9.3%) became higher than in association with dehydration to 19.4% but still remained lower than the reported literature figures of 22% and 26.6%[8,9] It merits the rational use of intravenous fluids in severely malnourished children with diarrhea in accordance with WHO protocol. This reiterates that diarrhea and pneumonia continue to be the main co morbidities in hospitalized children with SAM and are responsible for around one third of under 5 mortality worldwide. There is a need to intensify and judiciously implement interventions like introduction of pentavalent and rotavirus vaccine and stepping up measles immunization to fight against these biggest killers of developing countries. Although our study had smaller proportion of children with underlying HIV infection and TB but the observed death rate was quiet high, 28.6% and 38% respectively in parallel to reported studies[8,9,23] It is important to actively screen and manage co morbidities like TB and HIV at specialized DOTS and ART center respectively to reduce their burden and mortality.

The high incidence of severe anemia in our study is consistent with previous reports[19,24] mainly due to nutritional factors as well as incident helminthic and parasitic infections. The proportion of children with laboratory confirmed bacteremia (16%) is analogous to other reported studies[8,25] but the spectrum of organisms isolated in the two studies was different from each other as well as from our study. Maitland et al[8] from Kenya have reported streptococcus pneumoniae in 35% of their cases followed by E coli in 12% and non typhoidal salmonella in 10%. In Uganda, Bachou et al[25] have reported S typhimurium in 27.4%, followed by Staphylococcus aureus in 26.3%, streptococcus pneumoniae in 13.2% and S enteridis in 11.8%. When screened for infections, the present study recorded mortality rate of 23.1% and 9.5% in blood and urine culture proven patients respectively. Analogous figures have been reported from studies elsewhere in literature[8,25,26]. The wide spectrum of organisms responsible for bacteremia encourages the use of broad spectrum antibiotics to include organisms and modification in accordance with the culture sensitivity report as infections continue to be the major cause of mortality in children with SAM. So it becomes extremely important to isolate the organisms using blood and urine cultures to rationalize the antibiotic usage in this group.

The clinical parameters associated with adverse outcome in our study were the presence of emergency signs at admission i.e. shock, dehydration, hypothermia and edema. Biochemical indicators which predispose to increased mortality in current study include hypoglycemia, dyselectrolytemic states like hypokalemia and hyponatremia and evidence of blood culture proven sepsis. Maitland et al[6] has also reported consistent results and proposed a Triage System for identification of high risk groups of children with severe malnutrition for optimal utilization of health care in resource-limited settings. He identified a high risk group with features of shock, impaired consciousness, bradycardia and hypoglycemia associated with immediate risk of early death and greatest requirement for intervention and close monitoring. In resource limited setting like ours and in other developing countries hospitalizing all children with SAM is neither feasible nor cost effective approach to prevent morbidity and mortality. This will indeed prevent us from delivering optimal care to the most desired subset that if left untreated or intervened late are at highest risk of mortality. After multivariate logistic regression, the current study identified shock, hypoglycemia, severe anemia and bacteremia as significant independent risk factors associated with mortality. It is important for the treating doctor to screen and identify these red flags and hospitalize these children to intervene early .This will help us to optimally utilize the available resources and manpower and deliver early targeted interventions which could modify their outcome.

Conclusion

This study has attempted to identify a subset of children with SAM with clinically discernible signs and biochemical markers of mortality as early intervention can optimize the resources and improve the outcome. Also an active search for co morbid conditions like Tuberculosis, HIV and underlying septicemia is mandatory as they are significantly implicated for decease. There is a need for studies with large sample size for formal assessment of the risk factors attributing to death to rationalize the utilization of resources and improve outcome towards the management of children with severe acute malnutrition.

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