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Incidence and Predictors of Mortality among Severe Acute Malnourished Under Five Children Admitted to Dilla University Referal Hospital: A Retrospective Longitudinal Study

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Abstract
Background: Many developing countries continue to experience high mortality of children with severe acute malnutrition that receive treatment in inpatient set ups associated to either co-morbidity or due to poor adherence to the World Health Organization therapeutic guidelines for the management of severe acute malnutrition. **Objective:** To assess incidence and predictors of mortality among severe acute malnourished under five children admitted to Dilla university referral hospital from 2013 to 2015 **Methods**: A 36 month retrospective cohort study was conducted among 450 under five children admitted to stabilization centers in Dilla university referral hospital between 2013 and 2015. The data was collected from a randomly selected chart after getting ethical clearance from the Institutional review board of Arba Minch University by trained professionals. Data was entered and cleaned by Epi Info version 7 and analyzed by STATA version 11. Life table was used to estimate the cumulative incidence of death and Log rank tests to compare probability of hazard between variables. Bivariate and multivariate Cox proportional hazards model were used to identify predictors. Significance was considered at P-value < 0.05 in the multivariate analysis. Model was built by forward step wise procedure; compared by likely hood ratio test and Harrell's concordance and fitness checked by cox-snell residual plot.**Result:** A total of 450 children were followed for 7389 person-day of observation; during the follow up period 56(12.4) died making overall incidence density rate of 7.57 (CI=5.83-9.84) per 1000 Person day. Survival at the end of 1st, 2nd and 3rd week was 95%, 88% and 84% respectively and overall mean survival time was 47(95%CI=45-48.6) day. Presence of Altered pulse rate [AHR =5.85, 95% CI= 2.55-13.4], altered body temperature [AHR= 6.94 (95 % CI [2.94-16.4], Shock (AHR=3.15 (95 % CI [1.5-6.5]), IV infusion (AHR=3.24 (95 % CI [1.54-6.8]) and septicemia/meningitis (AHR=2.88(95 % CI [1.413-5.9]) were independent predictors of mortality. **Conclusion and recommendation:** The incidence of death and treatment outcomes was in acceptable ranges. Intervention to further reduce deaths has to focus on children with comorbidities and altered general conditions.
Key words: Severe acute malnutrition, Incidence, Under-five children, Dilla, Hospital

INTRODUCTION

Severe Acute Malnutrition (SAM) is defined as a very low weight for height (below -3z scores of the median world health organization (WHO) growth standards, or below 70% of the median of national center for health statistics standard (NCHS) and by the presence of nutritional oedema or middle upper arm circumference (MUAC) less than 11 cm for age 6-59 month (1); which is caused by the immediate, underlying and basic factors (2).

Childhood under nutrition is a major global health problem, contributing to childhood morbidity, mortality, impaired intellectual development, suboptimal adult work capacity, and increased risk of diseases it contributes to 50 - 60% of deaths in children (2-4). It affect all age groups, but is more frequent among infants and young children (4-6 years) (3). It is estimated that 19 million preschool-age children, mostly from the WHO African Region and South-East Asia Region, are suffering from severe wasting (4).

SAM remains a major cause of child morbidity and mortality worldwide. Of the 7.6 million deaths annually among children who are under 5 years of age (5), approximately 35% are due to nutrition-related factors and 4.4% of deaths have been shown to be specifically attributable to severe wasting (4). Children with SAM have a risk of death nine times higher than that of children without SAM (6), severe wasting is estimated to account for around 400 000 child deaths each year (4). In low and middle income countries an estimated 6.9

million children under the age of five still die underlying to malnutrition. It also contributes in over 50% of child deaths in developing countries (7) and for 60% of the 10.9 million deaths in east Africa (8).

It is also the commonest reason for pediatric hospital admission in many poor countries; particularly in Sub-Saharan Africa the number of children hospitalized with severe malnutrition continues to rise (9,10). However, In Africa, 1 out of 2 children with SAM dies during hospital treatment due to inappropriate care (11). It was seen for decades that the median case fatality rate was remained unchanged at 20-30%, with even higher rates (50-60%) for oedematous cases and Death commonly occurs within first 48 hours after admission (12). However it was seen that when the necessary resources are present and standard guidelines are followed the level of mortality markedly reduced (13,14)

Even though application of the standard protocol reduced mortality the expected level was not attained in many Hospitals. A likely cause of this continuing high mortality is faulty case management (12), the severity of illness at presentation for treatment, the high prevalence of HIV and tuberculosis, and socio-economic changes resulting in an increasing severity of illness at presentation, are given as the main determinants of persistently high CFRs (15, 16).

In Ethiopia it is estimated that malnutrition contributes to an estimated 270,000 deaths of under-five children each year (17). Among the principal causes of death in young children more than half cases are attributable to under-nutrition (10). Severe malnutrition also accounts for 11% of the deaths of under five year children (18). Severe acute malnutrition is the primary diagnosis in 20% of pediatric hospital admissions (19). Unfortunately, 25- 30% of children with severe malnutrition die during hospital admissions (20). Even though there is improvement from previous records the case-fatality rates at hospitals is still unacceptably high (>30 %) (21). in many health facilities also the mortality rate from SAM at present is over 20 % (22). In different studies conducted at different settings the mortality on therapeutic management ranges from 3.6% in a study conducted in SNNPR (23) to 28.67% in Sekota hospital (24).

Despite the existence of in-patient and other nutrition programs with a common protocol such high mortality in inpatient units is unacceptable. The case in stabilization centers of DURH is not expected to be different because it gives inpatient serves for many of the nutrition deficient areas of Sidama zone, Gedieo zone and Guji zone which makes the admission rate very high and in turn the care may be compromised associated with high flow of cases. However the case was not assessed before and many of the determining factors for mortality during the inpatient cares were not well addressed in previous studies which necessitated the need for further study in the area. So the purpose of this study was to assess incidence and identify predictors of mortality among under five children with severe acute malnutrition that were managed DURH.

METHODS

Study design and settings

This retrospective longitudinal study was conducted at stabilization center of DURH through chart review. DURH is the only referral hospital in Gedeo Zone providing care for 1,105,813 catchment population. The stabilization center (SC) offers services to severely malnourished children with complication and/or failed appetite test in facility setups. Severely malnourished children are directly admitted to the center from OPD or through referral and managed according to the Protocol.

Study population and sampling technique

The Source population were All children aged less than five year with severe acute malnutrition admitted to stabilization centers (SC) in DURH from 2013- 2015. Sample size was calculated based on double population proportion formula by using Epi info version 7 computer program considering the following assumptions: 95% CI, power 80%, ratio of unexposed to exposed 1:1 and parameters outcome in exposed=15.88, outcome in unexposed = 7.85 and Risk ratio =2: and found to be 510 (25). Computer generated Simple random sampling technique was used to select records from a total of 877 SAM records. On the way children with incomplete records and admissions only with laboratory test (albumin test) were excluded.

Data Collection Procedure and Data Quality Control

The source of data for the study was individual patient record documents including registers and monitoring cards and patient admission book. Data was collected by using structured checklist. The check list was developed from standard treatment protocol for the management of severe acute malnutrition, SAM monitoring multi chart and reviewing related literatures. The check list sought information on: Patient related data, anthropometric measurements, Co-morbidities, types of severe acute malnutrition, treatment and others.

Data collection procedure: four data collectors and one supervisor who have a bachelor degree in health science and been trained with SAM management were recruited for data collection. In addition data collectors were trained on the questioner in order to get common understanding and make aware of the context of each question in the checklist.

List of admission with SAM was obtained from admission book; which is available for SAM cases alone. Then selectively for those children who are under five and have outcome records their card number was

collected from the chart based on the check list. Lastly individual patient cardex of those listed children were obtained from card unit and necessary data was collected.

To keep data quality supervisor and data collectors were oriented on how and what information they should collect from the targeted data sources. The prepared checklist was pretested in Arbaminch hospital before actual date of data collection and necessary correction was made based on the finding. Proper categorization of the data Completeness and consistency of the collected data were checked on daily bases during data collection by supervisor and the principal investigator. Whenever there appears incompleteness and ambiguity of recording, the filled information formats was crosschecked with source data. Individual records with incomplete data were excluded. Double entry and data cleaning was also considered

Study variables and Data analysis

The Dependent variables is death; the Time variable is Time to occurrence of death measured from admission to date of event or censorship and Censoring variable coded 1=event/death ascertained by physicians, 0=censored/all outcomes other than death while the independent variables were socio-demographic, anthropometric and clinical presentations. All variables were defined according to the national SAM management protocol.

After data collection, each questionnaire was checked for completeness and consistency. Data was cleaned, edited, coded and entered into Epi-info version 7 and exported to STATA version 11 for Windows , then Exploratory data analysis carried out to check the levels of missing values, presence of influential outliers, multi-collinearity, normality and proportionality of hazards over time. HIV status was highly missing and palmar pallor and pale conjunctiva were highly collinear with anemia; all were excluded.

Bivariate analysis was done and Hazard ratio, with 95% CI and P-value was used to assess the strength of association and statistical significance. Life table was constructed to estimate probabilities of becoming death at different time intervals. Kaplan Meier survival curve together with log rank test was fitted to test for the presence of difference in incidence of death among the groups. Incidence of death with respect to person time at risk was calculated and compared for exposed and unexposed groups. Variables significant at P <0.25 level in the bivariate analysis were included in the final Cox- regression analysis, to identify independent predictors of mortality.

Model was built by forward step wise procedure and compared by likely hood ratio test and Harrell's concordance statistics test. Interactions and confounders were tested and cutoff point beta change greater than 20% used. Proportionality assumption was tested by global test based on scheonfeld residuals. Instability of parameter estimate among variables in the final fitted model was checked by using variance inflation factor (VIF) and cutoff point is the mean VIF >4. Goodness of fit of the final model was checked by Nelson Aalen cumulative hazard function against Cox Snell residual. Association was summarized by using adjusted hazard ratio and statistical significances were tested at 95% CI. Model equation was written as follows:

$$h(t, X_1, \ldots, X_k) = h_0(t)\exp(\sum_{i=1}^{k} \beta_i X_i)$$

Model equation:

$$H(t) = ho\ (t)e^{[5.85(\text{pulse rate}) + 6.94(\text{Body To}) + 3.15(\text{shock}) + 2.88(\text{Septicemia}) + 3.24(\text{IV Infusion})}$$

Where: *H (t)* =Hazard rate at time t, $h_0(t)$ =baseline hazard at time zero $X_1, \ldots, X_k$ = predictor

Ethical statement

The study used the routine existing admission and patient record data of SC. There was no direct contact with children as such, informed consent from the parents/caregivers of the children was not obtain; however, all the necessary measures were taken to maintain and assure the privacy, confidentiality and all benefits of the patients. Ethical approval was obtained from Arba Minch University, College of Medicine and Health Sciences with reference number CMHS/PG/130/08 and support letter was obtained from DURH. Consents were also obtained from respective units.

RESULTS

Description of admission characteristics

Socio-demographic characteristics and anthropometry

Out of total 510 randomly selected SAM records the data of 450(88%) was extracted with its necessary information and for the rest, the record (patient card) was not found or outcome not recorded. More than half 272(60.4%) of the children enrolled into the study were males and 303(67.3%) were under the age of two year with median age of 24 months. significant proportion 110(24.4%) of children have WFH below 70% with range of 37-125%. Moreover 253(56.2%) of children have MUAC below 11.5 cm and 285(63.3%) of the children enrolled into the study had oedematous malnutrition (*Table 1*).

Table: 1. Socio-demographic and anthropometry stratified by treatment outcome of severely malnourished under five children admitted to SC in DURH, 2013 - 2015

Admission Characteristics		**Treatment outcome**		
		Death N (%)	**Censored** N (%)	**Total N (%)**
Socio-demographic characteristics				
Age category	< 24 month	50(16.5)	253(83.5)	303(67.3)
	≥24 month	6(4.1)	141(95.9)	147(32.7)
Sex	Male	28(10.3)	244(89.7)	272(60.4)
	Female	28(15.7)	150(84.3)	178(39.6)
WT/HT	< 70%	28(25.5)	82(74.5)	110(24.4)
	≥70%	28(8.2)	312(91.8)	340(75.6)
MUAC	< 11.5	44(17.4)	209(82.6)	253(56.2)
	≥11.5	12(6.1)	185(93.9)	197(43.8)
Type of SAM	Oedematous	29(10.2)	256(89.8)	285(63.3)
	Non-edemat	27(16.4)	138(83.6)	165(36.7)

Clinical profile and Morbidity patterns

Majority (72.6%) of the children had diarrhea where 280(85.6 %) had watery diarrhea and 90 (27.5 %) children with diarrhea were dehydrated. Similarly the rate of Dehydration was 90(20%) in the total sampled children of which 49(54 %) were severely dehydrated. Significant proportion of children had deranged vital signs during admission. Altered respiration (fast breathing or respiratory failure), altered pulse rate (Brady or tachycardia) and altered body temperature (hypothermia or hyperpyrexia) was prevalent in 142(31.5%), 125(27.8%) and 78(17.3) of children respectively. While 117(26%) of children has altered level of consciousness (lethargic or comatose), 56(12.4%) has Shock with predominance of hypovolemic, septic and refractory forms. In addition it was found that 76(16.9%) children have treatment failure (primary or secondary failure) commonly due to failure to gain appetite, reduction of edema and IV line in place (*Table 2*).

Regarding the presences of co-morbidities with severe acute malnutrition at admission, 159(35.3%) of the study participants had pneumonia at time of admission and 80(17.8%) were anemic. Hypoglycemia, septicemia/meningitis, malaria and disseminated TB were prevalent in 49(10.9%), 32(7.1%), 37(8.2%) and 49(10.9%) of children respectively. Of the children without co-morbidities/complications on admission, 36(8%) had developed co-morbidity/complication after admission particularly of sepsis, oral thrush and other forms of naso-cominal infection and another 1.2% developed shock (*Table 2*).

Table: 2. Clinical profile at admission stratified by treatment outcome of severely malnourished under five children admitted to SC in DURH, 2013 - 2015

Admission Characteristics		**Treatment outcome**		
		Death N (%)	**Censored** N (%)	**Total N (%)**
Clinical conditions at admissions				
Diarrhea	Yes	220(67.3)	107(32.7)	327(72.6)
	No	84(68.3)	39(31.7)	123(27.4)
Dehydration	Yes	78(86.7)	12(13.3)	90(20)
	No	226(62.8)	134(37.2)	360(80)
Respiratory rate	Altered	111(78.2)	31(21.8)	142(31.5)
	Normal	193(62.7)	115(37.3)	308(68.5)
Pulse rate	altered	52 (41.6)	73(58.4)	125(27.8)
	Normal	4(1.2)	321(98.8)	325(72.2)
Body Temperature	Altered	41(52.6)	37(47.4)	78(17.3)
	Normal	15 (4)	357(96)	372(82.7)
Level of consciousness	Normal	20(6)	313(94)	333(74)
	Altered	36(30.8)	81(69.2)	117(26)
Shock	Yes	37(66.1)	19(33.9)	56(12.4)
	No	19(4.8)	375(95.2)	394(87.6)
Treatment failure	Yes	16(21.1)	60(78.9)	76(16.9)
	No	40(10.7)	334(89.3)	374(83.1)
Pneumonia	Yes	20(12.6)	139(87.4)	159(35.3)
	No	36(12.4)	255(87.6)	291(64.7)
Anemia	Yes	40(50)	40(50)	80(17.8)
	No	16(4.3)	354(95.7)	370(82.2)
Hypoglycemia	Yes	36(73.5)	13(26.5)	49(10.9)
	No	20(5)	381(95)	401(89.1)
Tuberculosis	Yes	13(26.5)	36(73.5)	49(10.9)
	No	43(10.7)	358(89.3)	401(89.1)
Malaria	Yes	18(48.6)	19(51.4)	37(8.2)
	No	38(9.2)	375(90.8)	413(91.8)
Septicemia/ meningitis	Yes	26(81.3)	6(18.8)	32(7.1)
	No	30(7.2)	388(92.8)	418(92.9)
HAC*	Yes	18(50)	18(50)	36(8)
	No	38(9.2)	376(90.8)	414(92)

HCA= hospital acquired complication*

Routine and special medicine provision

The most common treatments provided according to the protocol were; folic acid and Vitamin A for 440(97.8%) and 395(87.8%) of children respectively. While additional 331(73.6%), 219(48.7), 86(19.1%), 38(8.4%) and 153(34%) of children required parenteral medication, ReSoMal, IV fluid, blood transfusion and NG tube insertion respectively (Table 3)

Table: 3. Routine and special medicine provision of severely malnourished under five children admitted to SC in DURH, 2013 - 2015

		Treatment outcome		
		Death N (%)	**Censored** N (%)	**Total N (%)**
Vitamin A	Yes	38(9.6)	357(90.4)	395(87.8)
	No	18(32.7)	37(67.3)	55(12.2)
Folic acid	Yes	49(11.1)	391(88.9)	440(97.8)
	No	7(70)	3(30)	10(2.2)
PO antibiotic	Yes	21(5.4)	366(94.6)	387(86)
	No	35(55.6)	28(44.4)	63(14)
Dewormed	Yes	10(2.8)	342(97.2)	352(78.2)
	No	46(46.9)	52(53.1)	98(21.8)
Parenteral atb	Yes	55(16.6)	276(83.4)	331(73.6)
	No	1(.8)	118(99.2)	119(26.4)
ReSoMal	Yes	32(14.6)	187(85.4)	219(48.7)
	No	24(10.4)	207(89.6)	231(51.3)
IV fluid	Yes	44(51.2)	42(48.8)	86(19.1)
	No	12(3.3)	352(96.7)	364(80.9)
Blood transfusion	Yes	20(52.6)	18(47.4)	38(8.4)
	No	36(8.7)	376(91.3)	412(91.6)
NG tube feed	Yes	48(31.4)	105(68.6)	153(34)
	No	8(2.7)	289(97.3)	297(66)

Incidence of mortality

A total of 450 children were followed for different periods; a minimum of 1 day and a maximum of 54 days with median follow up period of 15 days which gives 7389 person-day of observation. Based on this Incidence rate of death was calculated using Person-day of follow up as a denominator for the entire cohort and for particular groups.

Within the follow up period, 56 deaths were recorded; 17.6 % occurred in the first 48 hours, 47% in the first week and 84 % by the end of the second week. Hence, the overall incidence density rate (IDR) of death in the cohort was 7.57 (95% CI=5.83-9.84) per 1000 Person day or 2.76 per person-year and it was significantly different for Exposed and unexposed groups and for categories of predictors. within the exposed groups 37 deaths were recorded during the 2509 days of observation and 19 deaths were recorded in 4880 observation days in the unexposed groups making IDR of 14.7 and 3.89 per 1000 person-day of observation respectively and the difference was significant (p.value <0.001). The highest incidence rate of Death was observed in the first two days 8.4/1000 Person-day (4.4-16.18) when stratified in days; then decreased in the subsequent days of follow up until 21st day (last death) *(Table 4)*.

The remaining 394(87.6%) patients were censored for different reasons: discharged with cure, transferred out or lost. During the follow up period 344(76.4%) children were get cured and discharged, another 12(2.7%) were improved and have nutritional transfer, 4(0.9%) children required medical transfer, 24(5.3%) defaulted and 10(2.2%) were right censored. Of 56 deaths, 17.6 % occurred in the first 48 hours, 47% in the first week and 84 % by the end of the second week.

The cumulative probability of survival at the end of 1st, 2nd and 3rd week was 95%, 88% and 84% respectively with difference between categories of variables, while the overall mean survival time was 47(95%CI=45-48.6) day. The mean survival time was also significantly different for the exposed and unexposed groups, which was 24.6(21-27) and 37.6(35.2-40) days respectively. Children who have septicemia/meningitis, altered pulse rate, altered body temperature, shock and IV infused had markedly shorter survival time than their counter parts *(Figure 1 and Table 4)*.

Table: 4: Incidence density rate of death stratified by predictor variables among severely malnourished under five children admitted to SC in DURH, 2013 - 2015

variables		Frequency	Person-day	Death	IDR*	P-value
Overall		450	7389	56	7.57	
Comorbidity	Yes	303(67.3)	2509	37	14.7	<.001
	No	147(32.7)	4880	19	3.89	
Pulse rate	Altered	125(27.8)	2371	52	22	<.001
	Normal	325(72.2)	5018	4	0.8	
Body Temp	Altered	78(17.3)	1451	41	28.25	<.001
	Normal	372(82.7)	5938	15	2.5	
Shock	Yes	56(12.4)	1117	37	33	<.001
	No	394(87.6)	6272	19	3	
Transfusion	Yes	86(19.1)	1598	44	27.5	<.001
	No	364(80.9)	5791	12	2	
NG-tube	Yes	153(34)	2672	48	18	<.001
	No	297(66)	4717	8	8	
Anemia	Yes	80(17.8)	1470	40	27.2	<.001
	No	370(82.2)	5919	16	7.7	
Malaria	Yes	37(8.2)	656	8	12.2	<.001
	No	413(91.8)	6733	48	7	
Hypo-glycemia	Yes	49(10.9)	879	36	41	<.001
	No	401(89.1)	6570	20	3	
Septicemia/meningitis	Yes	32(7.1)	579	26	45	<.001
	No	418(92.9)	6810	30	4.4	
HAC	Yes	36(8)	610	18	29.5	<.001
	No	414(92)	6779	38	5.6	

** IDR-Incidence density rate per 1000 person-day* *HAC*= hospital acquired complication

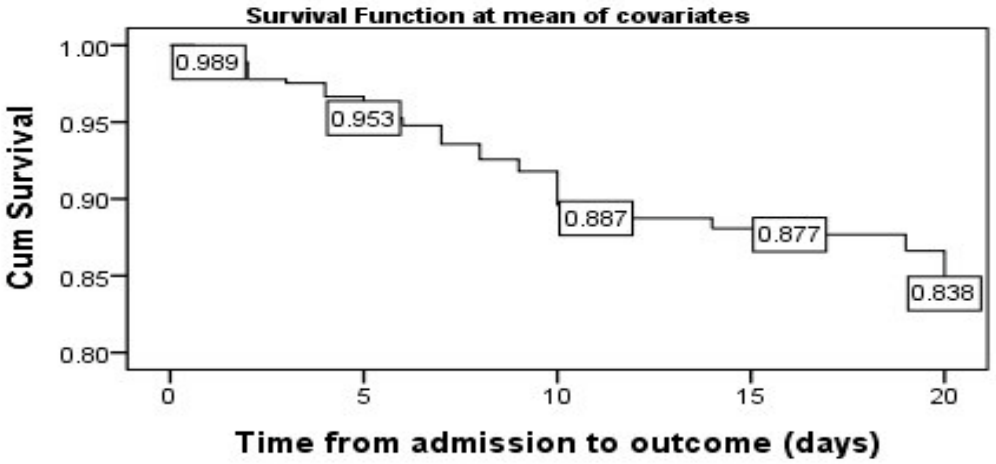


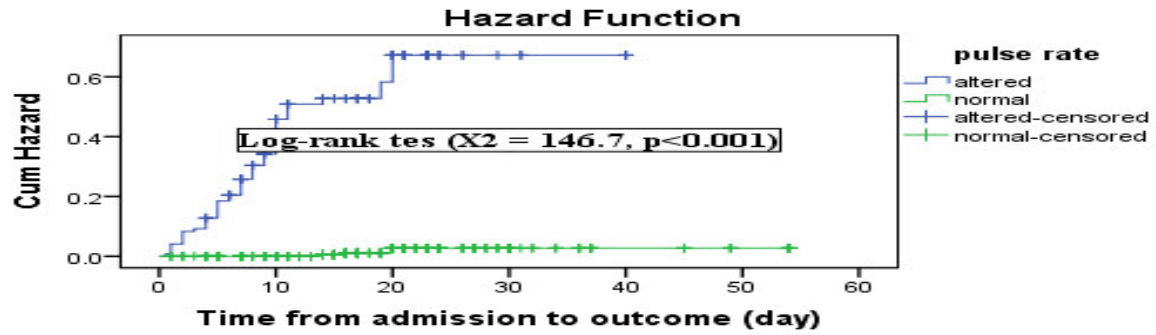
Figure: 1. Kaplan-Meier Survival estimate among severely malnourished under five children admitted to SC in DURH, 2013 - 2015

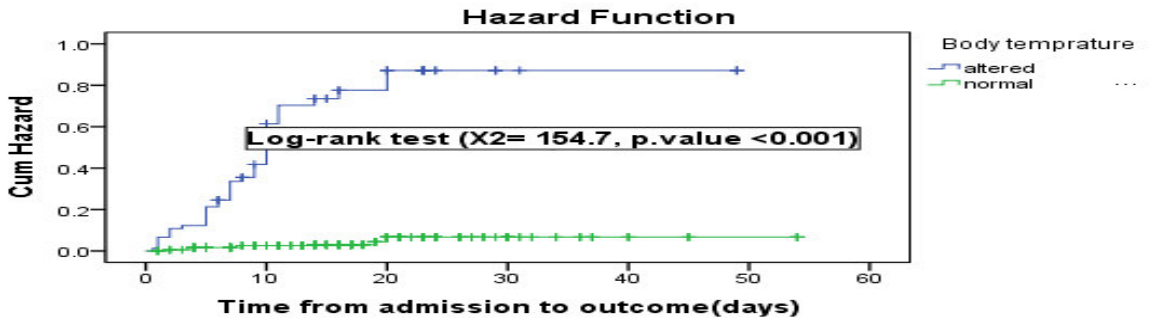
Predictors of mortality

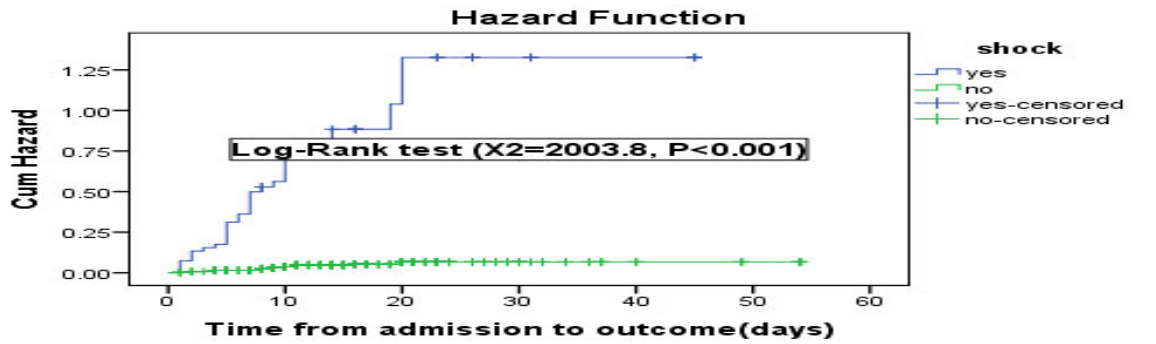
To show the hazard of death during the course of intervention period, Kaplan Meier survival curves were used over different factors. To test the significance of the observed difference in survival time curves between each factor, the log-rank test was used. There is a significantly different survival time among exposed and unexposed children (X^2=17, P<0.001). It also varies between children with altered vital condition and normal children, among transfused, NG-tube fade, with comorbid conditions and Anemic children (Table 5 and figure 2).

Table: 5. Mean survival time and log-rank test for survival difference between variables among severely malnourished under five children admitted to SC in DURH, 2013 - 2015

variables		Mean survival(95% CI)	Log-Rank test
comorbidity	Present	24.6(21-27)	X^2=17, P<0.001
	Absent	37.6(35.2-40)	
Body Temp	Altered	25.4(20.3-30)	X^2=154.7, P<0.001
	Normal	51.4(50-52.7)	
Pulse rate	Altered	24.7(21.6-27.8)	X^2=146.7, P<0.001
	Normal	53(52-54)	
Shock	Yes	18.5(13.8-23.3)	X^2=203.8, P<0.001
	No	51.2(50-52.4)	
Transfused	Yes	18(15.5-20.76)	X^2=158, P<0.001
	No	52.2(51.2-53.3)	
NG-tube	Yes	37.3(33.5-41.2)	X^2=73.5, P<0.001
	No	52.5(51.5-53.5)	
Anemia	Yes	21.6(17.8-25.5)	X^2=144.2, P<0.001
	No	51.6(50.6-52.8)	
Hypo-glycemia	Yes	16.7(12-21.5)	X^2=234, P<0.001
	No	51(49.6-52.3)	
Septicemia/meningitis	Yes	9.3(6.2-12.4)	X^2=263, P<0.001
	No	49.7(48-51.2)	
HAC	Yes	30.7(23-38.3)	X^2=46, P<0.001
	No	48.6(47-50.3)	
Tuberculosis	Positive	31(27-35.2)	X^2=6.83, P=.009
	Negative	47.8(46-49.6)	



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Cum Hazard
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0.00
Log-Rank test (X2=2003.8, P<0.001)
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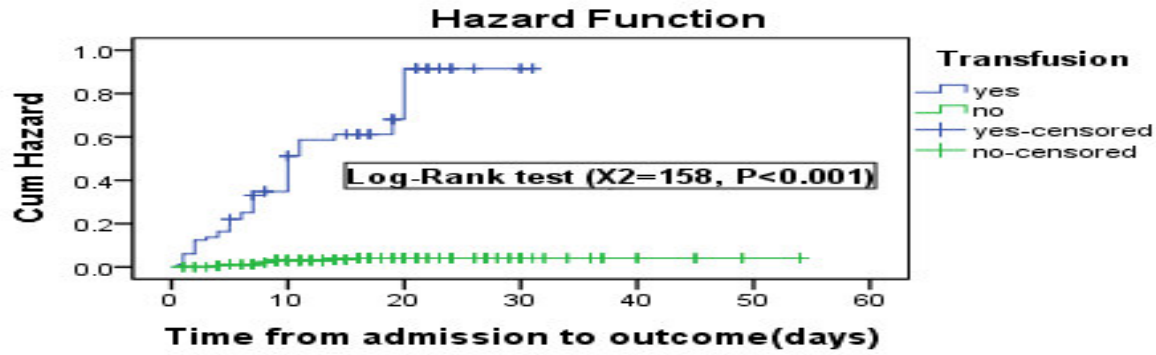
30
40
50
60
Time from admission to outcome(days)
shock
yes
no
yes-censored
no-censored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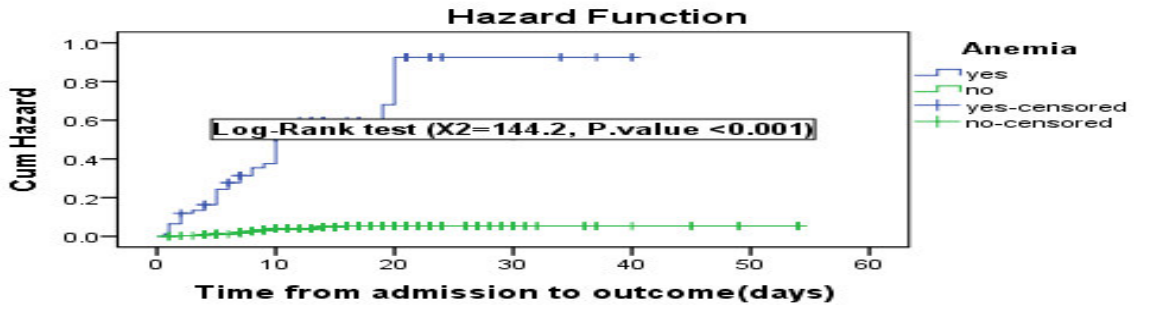
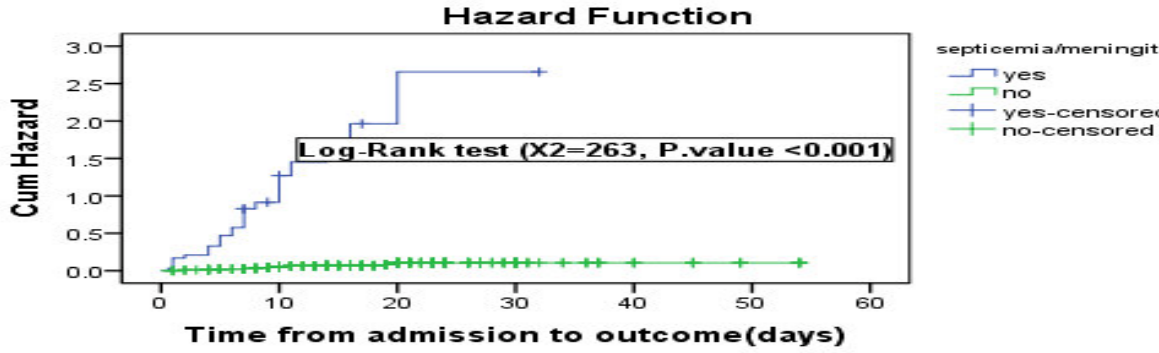
0.2
0.0
Log-Rank test (X2=158, P<0.001)
0
10
20
30
40
50
60
Time from admission to outcome(days)
Transfusion
yes
no
yes-censored
no-censored


Hazard Function
Cum Hazard
1.0
0.8
0.6
0.4
0.2
0.0
Log-Rank test (X2=144.2, P.value <0.001)
0
10
20
30
40
50
60
Time from admission to outcome(days)
Anemia
yes
no
yes-censored
no-censored


Hazard Function
Cum Hazard
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Log-Rank test (X2=263, P.value <0.001)
0
10
20
30
40
50
60
Time from admission to outcome(days)
septicemia/meningitis
yes
no
yes-censored
no-censored

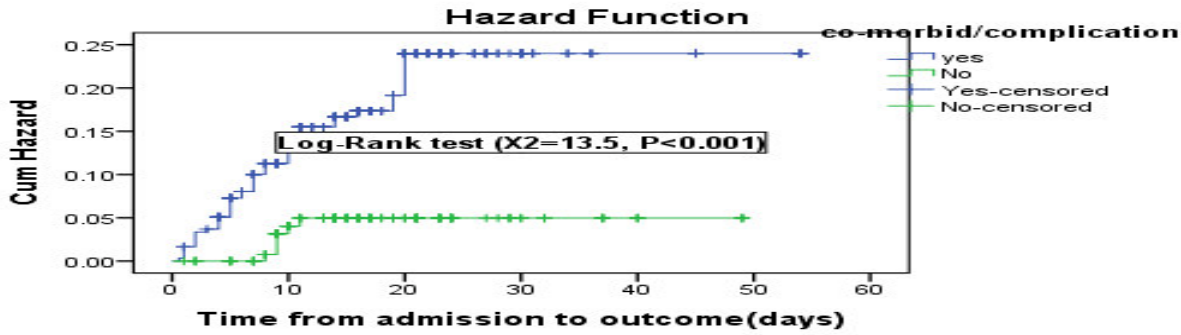


Figure: 2. Difference in hazard of death between variables among SAM children admitted to stabilization centers in DURH, 2013 - 2015

Cox-regression analysis

Bivariate analysis: using Cox regression bivariate analysis was performed for the independent variables. During regression, death was considered as failure and all other outcomes considered as censored. In bivariate analysis, a significant difference was observed between predictors; dehydration, altered respiration, pulse rate, shock, special antibiotic, IV fluid, blood transfusion, NG tube, anemia, malaria, hypoglycemia, tuberculosis, septicemia/meningitis and hospital acquired complication were associated with mortality (Table 6).

Table: 6. Bivariate analysis (Cox regression) of factors associated with death in severely malnourished children admitted to SC in DURH, 2013 - 2015

Predictor variable		Frequency	CHR	95 % CI	p.value
Sex	Male	272(60.4)	.861	.654-1.134	.288
	Female	178(39.6)	1		
Age category	≤24 month	303(67.3)	1.5	.848-2.641	.264
	> 24 month	147(32.7)	1		
WT/HT	< 70%	110(24.4)	1.2	.64-1.602	.253
	≥70%	340(75.6)	1		
MUAC	< 11.5	253(56.2)	1.4	.73-1.64	.253
	≥11.5	197(43.8)	1		
Type of SAM	Oedemat	285(63.3)	.74	.22-1.3	.251
	Non-edemat	165(36.7)	1		
Diarrhea	Yes	327(72.6)	.84	.47- 1.49	.552
	No	123(27.4)	1		
Dehydration	Yes	90(20)	3	1.7-5	<.001*
	No	360(80)	1		
Respiratory rate	Altered	142(31.5)	2	1.6-2.75	<.001*
	Normal	308(68.5)	1		
Pulse rate	Altered	125(27.8)	6	3.8-10.7	<.001*
	Normal	325(72.2)	1		
Body Temperature	Altered	78(17.3)	4	2.9-5.4	<.001*
	Normal	372(82.7)	1		
Level of consciousness	Normal	333(74)	1		
	Altered	117(26)	1.6	1.5-1.7	<.001*
Shock	Yes	56(12.4)	4.3	3.24-5.6	<.001*
	No	394(87.6)	1		
Vitamin A	Yes	395(87.8)	.78	.46- 1.5	.33
	No	55(12.2)	1		
Folic Acid	Yes	440(97.8)	.86	.55-1.32	.273
	No	10(2.2)	1		

Table: 6. Bivariate analysis (Cox regression) of factors associated with death in severely malnourished children admitted to SC in DURH, 2013 - 2015 (*continued*)

Predictor variable		Frequency	CHR	95 % CI	p.value
Amoxicillin	Yes	387(86)	.63	.33-1.2	.261
	No	63(14)	1		
Dewormed	Yes	352(78.2)	.802	.49-1.23	.27
	No	98(21.8)	1		
Parenteral antibiotic	Yes	331(73.6)	4.3	1.6-6.5	<.001*
	No	119(26.4)	1		
Resomal	Yes	219(48.7)	1. 17	0.8-1.5	..251
	No	231(51.3)	1		
IV-fluid	Yes	86(19.1)	4.3	3-6	<.001*
	No	364(80.9)	1		
Blood	Yes	38(8.4)	2.7	2-3.6	<.001*
	No	412(91.6)	**1**		
NG-tube	Yes	153(34)	3.5	2.4-5.2	<.001*
	No	297(66)	1		
Anemia	Yes	80(17.8	3.8	2.8-5	<.001*
	No	370(82.2)	1		
Malaria	Yes	37(8.2)	2.2	1.7-2.9	<.001*
	No	413(91.8)	1		
Hypo-glycaemia	Yes	49(10.9)	4.5	3.4-6	<.001*
	No	401(89.1)	1		
Tuberculosis	Positive	49(10.9)	2.3	1.3-4.2	.011*
	Negative	401(89.1)	1		
Pneumonia	Present	159(35.3)	1.05	.0.6-1.8	.86
	Absent	291(64.7)	1		
Sept/meningitis	Present	32(7.1)	4.8	3.6-6.3	<.001*
	Absent	418(92.9)	1		
HAC	Present	36(8)	2.3	1.7-3.11	<.001*
	Absent	414(92)	1		

** significant at p-value< .05 CHR=crude hazard ratio*

Multiple Cox regression: By using variables which have p.value of < .25 in the bivariate analysis Multiple Cox regression (forward stepwise) was performed. Altered body temperature (axillary To ≤ 35 &≥39°C), altered pulse rate (brady/tachycardia), shock, septicemia/meningitis and parenteral fluid administration were found to be independent predictors of death in severely malnourished children admitted to SC in DURH. However, type of malnutrition, dehydration, respiratory rate, level of consciousness, special antibiotic, malaria, Tuberculosis and MUAC were not independent predictors of death (Table 7).

Table: 7. Multiple Cox regression analysis of factors associated with death in severely malnourished children admitted to SC in DURH, 2013 - 2015

Predictors		CHR(95%CI)	AHR(95%CI)	p.value
pulse rate				
	Altered	6 [3.8-10.7]	5.85(2.55-13.4)	0.003
	Normal	1	1	
Body T0				
	Altered	4 [2.9-5.4]	6.94(2.94-16.4)	<0.001
	Normal	1	1	
Shock				
	Present	4.3 [3.24-5.6]	3.15(1.5-6.5)	<0.001
	Absent	1	1	
Septicemia/meningitis				
	Present	4.8 [3.6-6.3]	2.88(1.413-5.9)	0.01
	Absent	1	1	
IV Infusion				
	Yes	4.3 [3-6]	3.24(1.54-6.8)	0.004
	No	1	1	

DISCUSSION

This study assessed incidence and predictors of mortality among severe acute malnourished under five children admitted to Dilla university referral hospital. A total of 450 children were followed for 7389 person-day of observation; during the follow up period 56(12.4%) died making overall incidence density rate of 7.57 (95% CI=5.83-9.84) per 1000 Person day or 2.76 per person-year and it was significantly different for Exposed and unexposed groups. Survivals at the end of 1st, 2nd and 3rd week was 95%, 88% and 84% respectively and overall mean survival time was 47(95%CI=45-48.6) day. Presence of septicemia/meningitis, shock, altered body temperature, altered pulse rate and IV infusion were independent predictors of mortality.

From this study, the overall incidence density rate (IDR) of death in the cohort was 7.57 (95% CI=5.83-9.84) per 1000 Person day or 2.76 per person-year of observation. This incidence rate of death was much lower than the finding of a research conducted in Zambia (26) in which case the incidence density rate of death was 20.4 per person-year. This difference could be due to clinical profile and quality of care; in Zambia 32% of children admitted were HIV reactive and it was a significant predictor of death, 46% of children were died with 93% within two days which indicates poor quality of care.

The highest incidence rate of death was observed in the first two days 8.4/1000 Person-day (4.4-16.18) when stratified in days; then decreased in the subsequent days and week of enrolment. This is supported by other studies (24-26). The peak incidence of death shortly after admission may have several explanations; since the risk of early death is associated with complications such as hypoglycemia, hypothermia, dehydration, septicemia, etc are prevalent at admission and unless children were managed promptly they are fatal.

The cumulative probability of survival at the end of 1st, 2nd and 3rd week was 95%, 88% and 84% respectively, while the mean survival time was 47(95%CI=45-48.6) day. The survival time of exposed children was significantly shorter than unexposed children; 24.6(21-27) and 37.6(35.2-40) days respectively. Also Children who have septicemia/meningitis, hypoglycemia, shock and IV Infusion had markedly shorter survival time than their counter parts. Since exposed children have comorbidities/complications which are fatal they spend shorter in the hospital and their survival as well is short (24-26).

Altered body temperature (hypothermia and hyperpyrexia) was significantly associated with an increased risk of mortality among severely malnourished children in the present study. The Risk of earlier death was 6.94 (95 % CI [2.94-16.4] times higher for children who have altered body temperature than children who have normal body temperature. Hypothermia increased the hazard of mortality by three fold (AHR =3.0, 95%CI= 1.4–6.6) in another study (25), in contrast to these findings a study conducted in South Africa showed no association (27). Since, Hypothermia and hyperpyrexia affects biochemical reaction of the body; and they are indicators of altered metabolism, sepsis and serious infections the mortality ascribed to such alteration is high (22,28).

The risk of death in children who have altered pulse rate was six times (AHR =5.85, 95%CI= 2.55-13.4) higher than those who have normal pulse rate. A study found that the presence of low pulse rate (<90) or imperceptible pulse led to the increased risk of death in children by 3.9 times (29). Furthermore the development of shock significantly increased the hazard of mortality in our study (AHR=3.15 (95 % CI [1.5-6.5]). Altered pulse rate is a primary indicator of presence of shock, serious infections, severe dehydration and fluid and electrolyte imbalance which are highly killers in SAM management (9); when the case aggravates to the extent of shock which include septic, hypovolemic and refractory forms are highly fatal for children and the common feared complications in SAM management (1,10,11).

Accordingly, the hazard of mortality was higher (AHR=3.24 (95 % CI [1.54-6.8]) among children who required IV infusions (fluid or blood) than their counter parts. This finding compares well with the previous studies, which could be due to the fact that the use of IV transfusion serve as markers of severity of malnutrition and secondary complications like; fluid overload and infection could contributing to mortality. For that matter, fluid restriction is recommended by the WHO and other SAM management protocols (24, 28).

Similarly, the presence of septicemia/meningitis which is measured clinically and with laboratory test significantly increased mortality of SAM children in the hospital; those children who had septicemia were three times more likely to die than children without infection (AHR=2.88(95 % CI [1.413-5.9]). high risk of mortality in the presence of septicemia was also reported by other studies (29) This could be explained by the fact that sepsis is a serious infection and side effects associated with the management leads to high mortality.

Other predictors such as tuberculosis and malaria were not predicted mortality in our study. This was in contrast to other studies (24) in which case the risk of death in TB was three times (HR = 2.88, 95% CI = 1.72, 4.65) and malaria ascribed a risk of 2.13(95%CI = 1.12, 7.35). This may be due to the severity of the disease that majority of malaria cases were mild. In the same way type of malnutrition (edematous/non-edematous), dehydration and Anthropometry measurements were not independently predicted hazard of mortality.

STRENGTH AND LIMITATION OF THE STUDY

The data was collected and crosschecked through different records (SC record, patient registry, patient card,

SAM multi-chart and cardex/progress charts). Since the outcome is death it is easy to establish temporal relationship with predictor variables which are documented at time of admission. Also data regarding predictors were collected at admission, before the discharge outcome was known guaranteeing that the measurement of predictor variables was not biased by knowledge of the subjects' outcomes.

The findings of this study might suffer from the fact that it is retrospective study and based on records; availability of data for all variables is difficult and those with incomplete information are excluded from analysis. Some variables were missing while the others were not recordable. More over the reliability of the recorded data couldn't be ascertained and potential bias associated with excluded records and unknown status of absconds were there.

CONCLUSION AND RECOMMENDATIONS

In this study the overall incidence density rate (IDR) of death in the cohort was by far lower than other studies. However, incidence of death was still higher at the first few days of admission. The cumulative probability of survival at the end of 1st, 2nd and 3rd weak was 95.3%, 90% and 85% respectively and overall mean survival time was 47(95%CI=45-48.6) day. The main predictors of hospital deaths for severely malnourished children admitted to SC of DURH were having altered body temperature (hypothermia/ hyperpyrexia), altered pulse rate (brady/ tachycardia), having comorbidities like shock, septicemia/meningitis and transfused children. However, anemia, type of SAM, dehydration and need for parenteral medication were not found to be independent predictors of death.

Therefore appropriate diagnosis and management of cases in SC according to the national protocol is needed with special attention to be paid for those with altered vital conditions and for those children with shock and acute complications like septicemia/meningitis. More over care during transfusion and prevention of secondary complications seek due attention. Further organization of ICU is crucial. The finding of this research may provide necessary information in areas of improvement; however further research is needed to give policy level recommendation.

ABBREVIATIONS

AHR: Adjusted Hazard Ratio, DURH: Dilla University Referal Hospital**, EDHS:** Ethiopian Demographic and Health Surveys, **IMCI:** Integrated Management of Childhood Illness, **MUAC:** Mid Upper Arm Circumference, **PEM:** Protein Energy Malnutrition, **ReSoMal:** Oral REhydration SOlution for severely MALnourished patients, **SAM:** Severe Acute Malnutrition (wasting and/or nutritional oedema), **SC:** Stabilization Center, **UNICEF:** United Nations Children's Fund, **WHO**: World Health Organization

AUTHORS' CONTRIBUTIONS

TG has made substantial intellectual contributions to conception, design, and acquisition of data, analysis and interpretation of data to this study. He also has been involved in drafting the manuscript and revising it critically for important intellectual contents. MK and BT has made substantial contributions to conception, design, analysis and interpretation of data and participated in the critical review and editing of all the manuscript drafts for scientific merit and depth. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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REFERENCE

1. Sheila R, Camille EK, Abebe A, Habtamu F, Meselech R. Evaluation of Community Management of Acute Malnutrition (CMAM): Ethiopia Country Case Study. New York: United Nations Children's Fund (UNICEF); 2012.
2. UNICEF. An assessment of the causes of severe malnutrition in Ethiopia. Washington D, USA: 2005.
3. Berger SG, de Pee S, Bloem MW, Halati S, Semba RD. Malnutrition and morbidity are higher in children who are missed by periodic vitamin A capsule distribution for child survival in rural Indonesia. J Nutr. 2007;137(5):1328-1333.
4. Black R. Maternal and child undernutrition and overweight in low-income and middle income countries. Lancet. 2013; 382:427–51.11.
5. United Nations Interagency Group for Child Mortality Estimation. Levels and trends in child mortality Report. New York UNCsF, 2012.

6. WHO child growth standards and the identification of severe acute malnutrition in infants and children. A joint statement by the World Health Organization and the United Nations Children's Fund. Geneva: World Health Organization; 2009
7. Chopra M ME BJ, Campbell H, Rudan I. Ending of preventable deaths from pneumonia and diarrhea: An achievable goal. The Lancet. 2013.
8. G Y. Malnutrition among children in Southern Ethiopia: levels and risk factors. Ethiop J Health Dev. 2000;14(3):283-92.
9. Bachou H TJ, Mwadime RK, Tylleskär T. Risk factors in hospital deaths in severely malnourished children in Kampala, Uganda. BMC Pediatr. 2006;6(1):7.
10. Caulfield LE DM, Blössner M, Black RE. Undernutrition as an underlying cause of child deaths associated with diarrhea, pneumonia, malaria, and measles. Am J Clin Nutr. 2004.
11. Collins S, Dent N, Binns P, Bahwere P, Sadler K. Management of severe acute malnutrition in children. The Lancet 368: 1992-2000. 2006.
12. Schofield C, Ashworth A. Why have mortality rates for severe malnutrition remained so high? Reviews/Analysis. Bull WHO 1996; 74 (2): 223- 29.
13. Ahmed T, Ali M, Ullah MM, Choudhury IA, Haque ME, Salam MA, et al. Mortality in severely malnourished children with diarrhoea and use of a standardized management protocol. Lancet. 1999; 353:1919-22.
14. WHO informal consultation. Informal consultation to review current literature on severe malnutrition. Geneva: WHO; 2004.
15. Kessler L, Daley H, Malenga G, Graham S. The impact of the human immunodeficiency virus type 1 on the management of severe malnutrition in Malawi. Ann Trop Paediatr. 2000; 20(1):50-56.
16. 22.Maitland K, Berkley JA, Shebbe M, Peshu N, English M, Newton CR. Children with severe malnutrition: can those at highest risk of death be identified with the WHO protocol?. PLoS Med. 2006; 3(12):e500.
17. Abuye C. Nutrition Baseline Survey Report for the National Nutrition Program of Ethiopia. Addis Ababa, Ethiopia: Ethiopian Health and Nutrition Research Institute; 2009/10: 98
18. 24.Gudina E, Yemane B, Alemayehu W. Seasonal variation in the prevalence of acute under nutrition among children under five years of age in east rural Ethiopia: a longitudinal study. Journal of Bio Medical Central Public Health. 2013; 13(864):1-8.
19. D.M.Gordon, S. Frenning, H.R. Draper, M. Kokeb. "Prevalence and burden of diseases presenting to a general pediatrics ward in Gondar, Ethiopia". Journal of Tropical Pediatrics. 2013; 59(5): 350–357.
20. WHO, UNICEF, WFP. Community-based management of severe acute malnutrition. Geneva, Switzerland; 2007.
21. Gernaat HB, Dechering WH, Voorhoeve HW. Mortality in severe protein-energy malnutrition at Nchelenge, Zambia. J Trop Pediatr. 1998;44(4):211–7.
22. Michael G, Yvonne G. In: Sylvie C. Protocol for the Management of Severe Acute Malnutrition. 2nd ed. Addis Ababa: Ethiopian Federal Ministry of Health; 2007.
23. Teferi E, Lera M, Sita S, Bogale Z, Datiko DG, Yassin MA. Treatment outcome of children with severe acute malnutrition admitted to therapeutic feeding centers in Southern Region of Ethiopia. Ethiop J Health Dev. 2010;24(3).
24. 29.Desta KS. A Survival Status and Predictors of Mortality among Children Aged 0-59 Months with Severe Acute Malnutrition Admitted to Stabilization Center at Sekota Hospital Waghemra Zone. J Nutr Disorders Ther. 2015; 5: 160.
25. Jarso H. Workicho A, Alemseged F. Survival status and predictors of mortality in severely malnourished children admitted to Jimma University Specialized Hospital from 2010 to 2012, Jimma, Ethiopia: a retrospective longitudinal study. BMC Pediatrics. 2015; 15:76.
26. Munthali T, Jacobs C, Sitali L, Dambe R, Michelo C. Mortality and morbidity patterns in under-five children with severe acute malnutrition (SAM) in Zambia: a five-year retrospective review of hospital-based records (2009–2013). Archives of Public Health. 2015; 73:23.
27. De Maayer T, Saloojee H. Clinical outcomes of severe malnutrition in a high tuberculosis and HIV setting. Arch Dis Child. 2011;96(6):560–4.
28. FMOH. Training manual on the management of severe acute malnutrition. 2nd ed. AA: Federal Ministry of health Ethiopia; 2013.
29. VD JM, Roy SK, Khan WA, Ara G, Chakraborty B, Islam S. Risk factors for mortality due to shigellosis among SAM children in Bangladesh. *J Health Popul Nutr* 2005;23:259-65.