Survival Status and Predictors of Mortality among Children Aged 0-59 Months Admitted with Severe Acute Malnutrition in Dilchora Referral Hospital, Eastern Ethiopia.

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Abstract

Background: The mortality rate of children admitted to hospital with complicated severe acute malnourishment is as high as 35 %. In Ethiopia, this ranges from 6 % to 29 %, and its predictors vary contextually.

Objective: To assess the survival status and the predictors of mortality among 0-59 months children with severe and acute malnutrition and admitted to Dilchora Referral Hospital, Eastern Ethiopia.

Methods: A retrospective cohort study was conducted on children with Severe Acute Malnutrition (SAM) treated in Dilchora Referral Hospital. The data were collected from medical records from March 07 to 16, 2016. Six hundred seventeen children were randomly selected from all eligible records of 0-59 months children admitted to the center from September 2011 to August 2015. The data were collected using a pretested data extraction format and entered into EpiData software and exported to SPSS Version 20 for analysis. Survival curve was used to display the survival status among different characteristics. The Cox proportional hazard model was done to identify independent predictors of mortality. Associations were declared as statistically significant with $p<0.05$.

Results: It was found that 47 (7.6 %) study participants had died, most of whom had died within the first week of admission to hospital, 431 (69.9 %) had been cured, and the rest were defaulted and transferred out. The mean survival of the children with HIV/AIDS, pneumonia, diarrhea, dehydration, and those who took intravenous antibiotics and fluid were significantly lower than that of their counter parts. The significant predictors of the mortality of the SAM children were loss of appetite (AHR=2.75; 95%CI: 1.08, 6.99), malaria (AHR=12.69, 95%CI: 4.57, 35.27), lower Waist for Height % (WFH %) (AHR=0.95, 95%CI: 0.9, 0.99), and HIV sero-positivity (AHR=11.57, 95%CI: 2.34, 57.2). Also, not taking Formula-100 (F-100) (AHR=3.26; 95%CI: 1.32, 8.07) and Formula-75 (F-75) (AHR=2.56, 95%CI: 1.06, 6.15) significantly increased the risk of death.

Conclusion: The level of the mortality was high. Presence of co-morbidities, intravenous fluid and antibiotics intake and not supplemented with nutritional therapy significantly increased the risk of death. Therefore, an appropriate nutritional therapy and management of co-morbidities as per the national SAM management protocol is recommended.

Key words: *Survival status, Predictors, Mortality, Severe Acute Malnutrition*

Citation: Oumer, A., Mesfin, F., Demena, M. 2016. Survival Status and Predictors of Mortality among Children Aged 0-59 Months Admitted with Severe Acute Malnutrition in Dilchora Referral Hospital, Eastern Ethiopia. *East African Journal of Health and Biomedical Sciences,* Volume 1 (1): 13-22.

Introduction

Worldwide around 52 million under five children were acutely malnourished, of whom 13.2 million and 27.8 million are in sub-Saharan Africa and South Asia, respectively. It is also estimated that 25-35 million under five children are severely malnourished, and the severe form of the acute malnutrition is responsible for one million under five children deaths every year (Hobbs and Bush, 2014).

Children who are malnourished are at nine fold increased risk of death than well-nourished ones (Keane, 2013), and this is 5–20 fold for children with low weight-for-height (WFH), or mid-upper arm circumference (MUAC) (WHO, 2013). The mortality is high in sub-Sahara Africa due to the limited access to effective and timely treatment. In 2012, about 2.7 million children were admitted to hospitals for Severe Acute Malnutrition (SAM) treatment, but higher mortality and dropout rates were major problems (Hobbs and Bush, 2014). In Malawi, from 2006 to 2007, a mortality rate ranging from 2.2% to 59% was reported among children treated in

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stabilization center (Kerac *et al*., 2014; Maurya *et al.,* 2014). In Ethiopia, this ranges 6% to 29% (Tefera *et al*., 2014; Kebede, 2015).

Cognizing all these, the World Health Organization (WHO) has developed a standard SAM management protocol, which is being adopted by many countries in which non-adherence results in greater mortality (WHO, 2013). Children with SAM are predisposed to serious infections like diarrhea, pneumonia, skin infection, gut bacterial overgrowth, and others. In stabilization centers, about 15% of SAM patients require enthusiastic treatment (Bhutta *et al*., 2013; FMOH, 2013), which includes an integrated management of both nutritional deficiency and co-morbidities (Hobbs and Bush, 2014).

The implementation of the protocol reduced the mortality from 55% in 2008 to below 20 % in 2013. Formula milk or Ready to Use Therapeutic Food (RUTF) has been an important tool (WHO, 2013), as it results in rapid weight gain, recovery, and short hospital stay (Kapil, 2009). In 2013, however, the rate was unacceptably high (35%) in global situation, (Bhutta *et al.,* 2013). In Africa, the mortality was above 5%, and it also reaches 34% especially for complicated SAM based on perspective writing (Heikens, 2007).

Different co-morbidities, treatment related factors, non-adherence to the management protocol, and initial anthropometric indices are some of the factors that determine mortality from SAM (Heikens, 2007). Among infections, pneumonia, TB, HIV, diarrhea and others increase mortality among children admitted with complicated SAM (Irena *et al*., 2011; Habtemu *et al*., 2015).

The effectiveness of the treatment is evaluated based on recovery and death rate, average length of stay, and weight gain. Thus the acceptable level of mortality, the recovery, and default rate are below 10%, above 75% and below 15%, respectively (Thurstans, 2011). But these parameters are not achieved in many developing countries (Bhutta *et al*., 2013).

Although some studies have assessed the mortality rate and its predictors among children with SAM admitted to hospital (Ephrem, 2010; Melaku *et al.,* 2014; Habtemu *et al*., 2015; Kebede, 2015), most of them focused on children above six months, dealt with small sample size, and hardly showed the effects of some factors clearly (Melaku *et al.,* 2014). Moreover, as the factors vary according to context, this study assessed the mortality rate and its predictors among 0-59 months children treated for SAM in Dilchora Referral Hospital from 2011 to 2015.

Methods and Materials

Study Area, Design and Period

This study was conducted in Dilchora Referral Hospital, Dire Dawa, Eastern Ethiopia. Dire Dawa is 515 km away from Addis Ababa, capital city of Ethiopia. The city administration has population of 453, 000 (227, 000 male and 226,000 female) with 100 % health service coverage (CSA, 2013). The city has two government and four private hospitals, five higher and twelve medium private clinics, and 15 health centers and 31 health posts. In Dilchora Referral Hospital, there is a stabilization center which treats children with complicated SAM. Institution based a retrospective cohort study was conducted. The data were collected from March 07 to 16, 2016.

Study Population and Sampling Technique

The source population was all the records of 0-59 months children with SAM admitted in Dilchora Referral Hospital stabilization center. All eligible records of 0-59 months children with SAM admitted to the center from September 2011 to August 2015 were the study population. Records with incomplete data on outcome variable and with heart failure secondary to congenital heart disease were excluded from study.

The total sample size to detect the association between predictors and time to death was 631. Sample size was calculated using Stata version 13 (Stata corp., STATA 13.0 for window) for comparing survival Cox model between children not supplemented with Vitamin A in reference to Vitamin A supplemented (AHR=1.53) (Kebede, 2015). It was calculated taking two sided significant level (α) of 5%, 80% power, HR=1.53, probability of event of interest as 0.29 (Kebede, 2015). Comparing for the first and second objective, the final sample size became 631. OpenEpi software version 2.3 was used to generate random numbers. First serial number or unique SAM number was retrieved from patient registry.

Data Collection Method

The data were collected from the medical records and SAM treatment registry with a structured and cross checked data abstraction format. Diploma graduate nurses collected the data. A supervisor and the principal investigator took charge of the process.

Data Quality Control

To assure data quality, the checklist was cross-checked with the registers and cards. Recruited diploma nurses were trained for one day on how to extract the data from patient registry. The data were checked daily by the

supervisor and the principal investigator for completeness and consistency. The data were also double entered.

Data Processing and Analysis

The dependent variable was survival status/mortality. Whereas the independent variables were demographic characteristics (Age, sex of child, place of residence), appetite, hypothermia, presence of nutritional edema and clinical form of malnutrition, co-morbidity (pneumonia, HIV sero-status, diarrhea, dehydration status, hemoglobin level, malaria), routine medication and treatment (intravenous (IV) fluid intake, IV antibiotic treatment, blood transfusion, folic acid and Vitamin A supplementation, Formula-100 (F-100) and Formula-75 (F-75) intake, and anthropometric measurements at admission (WFH and MUAC).

In this study, recovered (cured) was used when the child reached ≥85% of median WFH or WFH Z- score ≥-2 or discharged cure by hospital according to protocol or child who fulfill discharge criteria (FMOH, 2013). Whereas censored observations were defined as those SAM children who were defaulted, transferred, recovered or non-responded. Anemia and severe anemia were defined with hemoglobin level below 11gm/dl (hematocrit level less than 33%) and 4gm/dl (hematocrit level less than 12%) at admission, respectively (FMOH, 2013).

The cleaned and checked data were entered into EpiData software Version 3.02. Then the data were exported to SPSS Version 20 for analysis. Survival curve was used to display the survival (time to death) among different characteristics. The Cox proportional hazard model with both binary and multivariate analysis was done. Associations were declared as statistically significant with $p<0.05$.

Ethical Considerations

The proposal of the study was reviewed by the Institutional Health Research Ethics Review Committee (IHRERC) of Haramaya University, College of Health and Medical Sciences. Informed written and signed consent was taken from the hospital manager and the confidentiality of the patients' records was kept. To prevent loss of patients' cards during the data collection process, the cards were immediately returned to the card room after taking the necessary data.

Results

Socio-demographic and Admission Characteristics

Out of the 631 randomly selected medical records of study participants, 617 were retrieved with card retrieval rate of 97.8%. A cohort of 617 SAM children were followed retrospectively for median time of seven days with interquartile range of nine days. Three hundred forty five (55.9%) were male, and 340 (55.2%) came from urban area. Their mean age was 23.5 months, with 14.7 standard deviation (SD), and 313 (50.7 %) of them were between 12 and 36 months. Among those who had recorded appetite test, 263 (65.1 %) had failed appetite. At admission, 325 (52.8%) were with edematous malnutrition. The rest of 281 (45.5 %), 50 (8.1%), and 286 (46.4%) were with kwashiorkor, Marasmic-Kwashiorkor, and Marasmus, respectively (Table 1). The average WFH-Z score was -4.05, with 1.9 unit of SD.

Table 1. Socio-demographic and admission of children with SAM admitted to Dilchora Referral Hospital, Dire Dawa, Ethiopia, 2016.

Characteristics		Freq.	%
Sex (n=617)	Male	345	55.9
	Female	272	44.1
Age (in months)	0-6	29	4.7
(n=617)	6-11	99	16.0
	12-23	166	26.9
	24-35	147	23.8
	36-47	90	14.6
	48-59	86	13.9
Residence (n=616)	Rural	276	44.8
	Urban	340	55.2
Appetite test	Failed test	263	65.1
(n=404)	Passed test	141	34.9
Nutritional edema	Yes	325	52.8
(n=616)	No	291	47.2
WFH % (n=579)	<70 %	161	27.8
	70-79.9 %	204	35.2
	≥80 %	214	37.0
Diagnosis (n=617)	Marasmic-kwashiorkor	50	8.1
	kwashiorkor	281	45.5
	Marasmus	286	46.4

As indicated in the table, 256 (41.5%) diarrhea and 134 (21.8%) pneumonia were the commonest co-morbidities among the children. Dehydration, Tuberculosis, HIV/AIDS, and Malaria were also observed in 110 (17.8%), 19 (3.1%), 18 (2.9%) and 16 (2.6%) of children, respectively (Table 2).

With regard to routine medication and nutritional therapy, 161 (26.2%) children had taken IV antibiotics, and 182 (29.5%) had taken IV fluid therapy. Three hundred eighty seven (62.8%) and 379 (61.5%) had received folic acid and vitamin A supplementation, respectively. Five hundred nine (83.6%) had received F-75 nutritional therapy, whereas 289 (49.7%) and 100 (17.2%) had received F-100 and Plumpy'nut, respectively (Table 3).

Table 2. Major co-morbidities among severely acute malnourished children in Dilchora Referral Hospital, Dire Dawa, Ethiopia, 2016

Characteristics		Freq.	%
HIVsero-status	Positive	18	2.9
(n=617)	Negative	416	67.4
	Unknown	183	29.7
TB (n=616)	Yes	19	3.1
	No	597	96.9
Pneumonia	Yes	134	21.8
(n=616)	No	482	78.2
Diarrhea	Yes	256	41.5
(n=617)	No	361	58.5
Dehydration	Yes	110	17.8
(n=617)	No	507	82.2
Malaria	Yes	16	2.6
(n=617)	No	306	49.6
	Unknown	295	47.8

Table 3. Patterns of routine medication and nutritional therapy intake among severely acute malnourished children admitted in Dilchora Referral Hospital, Dire Dawa, Ethiopia, 2016.

Variables		Freq.	%
IV antibiotics (n=615)	Yes	161	26.2
	No	454	73.8
Blood transfusion	Yes	34	5.5
(n=616)	No	582	94.5
IV fluid (n=616)	Yes	182	29.5
	No	434	70.5
Folic acid	Yes	387	62.8
supplementation(n=616)	No	229	37.2
Vitamin A	Yes	379	61.5
Supplementation (n=616)	No	237	38.5
F-100 intake (n=581)	Yes	289	49.7
	No	292	50.3
F-75 intake (n=609)	Yes	509	83.6
	No	100	16.4
Plumpy'nut intake	Yes	100	17.2
(n=580)	No	480	82.8

Mortality and Survival of SAM Children

With regard to the treatment outcome of the children, 47 (7.6%) died, 431 (69.9%) were cured and discharged, 47 (7.6%) were transferred out, and 88 (14.3%) were defaulters. The person time at risk for the children was 6267 days, with cumulative incidence of 0.0075 deaths per person days (7.5 deaths/1000 person days). The median of waiting time in the hospital was 7 days, with minimum and maximum hospital stay of 1 and 81 days (Inter Quartile Range (IQR) =9 days), respectively. The Survival patterns of children were dropped early in the first weeks. Most of the deaths (85%) occurred within the first ten days of the admission (Figure 1). The average length of stay in the hospital was 10 days (SD±10.4). The average rate of weight gain was 15.6g/kg/day, with lower rate of 3.4g/kg/day and higher rate of 30g/kg/day for edematous and non-edematous malnutrition, respectively. The mean survival time for the cohort was 69.28 days with median survival time of 80 days.

Those with failed appetite had lower mean survival time (57.43 days) than those with passed appetite (72.54 days) (p-value of log rank = 0.105). Additionally, the SAM children with HIV/AIDS had significantly shorter survival time than the sero-negative ones. Children with co-morbidities (HIV/AIDS, pneumonia, diarrhea and dehydration) had significantly shorter mean survival time than their counter parts.

Predictors of Mortality among SAM Children

Bivariate analysis showed that edematous malnutrition was associated with a non-significant decrease in the risk of death from SAM, one centimeter increase in WFH% index was associated with 5% significant decrease in the risk (CHR=0.95, 95%CI:0.92, 0.98). HIV sero-positivity (CHR=3.39, 95%CI: 1.22, 9.44) and pneumonia (CHR=2.43, 95%CI: 1.36, 4.35) were significantly associated with risk of death in time from SAM. Additionally, IV antibiotic medication intake also significantly increased the risk of death (CHR=2.39, 95%CI: 1.35, 4.25) (Table 4). Those who did not get F-75 had twice increased risk of death from SAM at time than those who took it (CHR=2.10, 95%CI: 1.09, 4.07).

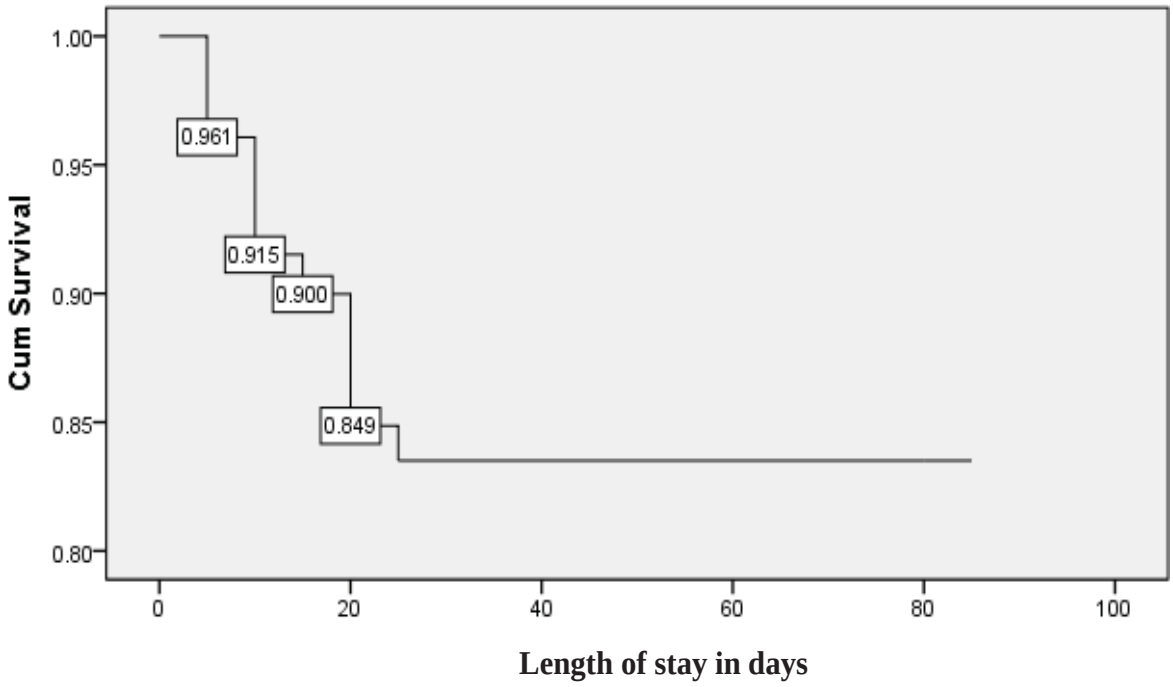

Figure 1. Survival functions of admitted SAM children from admission to death or other outcomes in Dilchora Referral Hospital, Eastern Ethiopia, 2016.

Table 4. Binary Cox proportional hazard Model for predictors of mortality from SAM among children admitted in Dilchora Referral Hospital, Dire Dawa, Ethiopia, 2016.

Variables		Outcome		CHR (95%CI)	AHR (95%CI)
		Dead Freq. (%)	Censored Freq. (%)		
Age	<12 months	9 (7.0)	119 (93.0)	1	
	≥12 months	38 (7.8)	451 (92.2)	1.04 (0.50 - 2.14)	
Sex	Male	27 (7.8)	318 (92.2)	1.12 (0.63 - 2.00)	
	Female	20 (7.4)	252 (92.6)	1	
Family residence	Rural	17 (6.2)	259 (95.8)	0.72 (0.40 - 1.30)	
	Urban	30 (8.8)	310 (91.2)	1	
Appetite test	Failed appetite	22 (8.4)	241 (91.6)	1.99 (0.85 - 4.67)*	2.75 (1.08 -6.99)*
	Passed appetite	7 (4.0)	134 (96.0)	1	1
MUAC	Per 1 cm increase			0.88 (0.72 - 1.09)	
WFH %	Per 1 % increase			0.95 (0.92 - 0.98)*	0.95 (0.90 -0.99)*
Edema	Yes	23 (7.1)	302 (92.9)	0.73 (0.41 - 1.30)	
	No	24 (8.2)	267 (91.8)	1	
Diagnosis	Marasmic-Kwashiorkor	5 (10.0)	45 (90.0)	0.93 (0.35 - 2.42)	
	Kwashiorkor	17 (6.0)	264 (94.0)	0.61 (0.33 - 1.13)	
	Marasmus	25 (8.7)	261 (91.3)	1	
HIV sero-status	Yes	4 (22.2)	14 (77.8)	3.39 (1.22 - 9.44)*	11.57 (2.34-57.22)*
	No	43 (7.2)	556 (92.8)	1	1
Tuberculosis	Yes	1 (5.3)	18 (94.7)	0.84 (0.12 - 6.07)	
	No	46 (7.7)	551 (92.3)	1	
Pneumonia	Yes	19 (14.2)	115 (85.8)	2.43 (1.36 - 4.35)*	
	No	28 (5.8)	454 (94.2)	1	
Diarrhea	Yes	29 (11.3)	227 (88.7)	2.38 (1.32 - 4.28)*	2.52 (0.93 - 6.83)
	No	18 (5.0)	343 (95.0)	1	1
Dehydration	Yes	17 (15.5)	93 (84.5)	3.07 (1.69 - 5.60)*	
	No	30 (5.9)	477 (94.1)	1	
Malaria	Yes	7 (43.8)	9 (56.3)	6.10 (2.73 - 13.66)*	12.7 (4.57 - 35.27)*
	No	40 (6.7)	561(93.3)	1	1
Anemia (Hgb <11g/dl)	Anemic	17 (10.2)	150 (89.8)	1.28 (0.38 - 4.39)	
	Non anemic	3 (8.6)	32 (91.4)	1	
IV antibiotics	Yes	22 (13.7)	139 (86.3)	2.39 (1.35 - 4.25)*	
	No	25 (5.5)	429 (94.5)	1	
Blood transfusion	Yes	5 (14.7)	29 (85.3)	2.06 (0.81 - 5.20)	
	No	42 (7.2)	540 (92.8)	1	
IV fluid intake	Yes	19 (8.1)	163 (83.6)	1.48 (0.82-2.65)	
	No	28 (6.5)	406 (93.5)	1	
Folic acid supplementation	Yes	24 (6.2)	363 (93.8)	1	
	No	22 (9.6)	207 (90.4)	1.56 (0.87 - 2.78)	
Vitamin A	Yes	27 (7.1)	352 (92.9)	1	
	No	19 (8.0)	218 (92.0)	1.10 (0.61 - 1.98)	
F-100 intake	Yes	19 (6.6)	270 (93.4)	1	1
	No	27 (9.2)	265 (90.8)	1.79 (0.99 - 3.22)*	3.26 (1.32 - 8.07)*
F-75 intake	Yes	34 (6.7)	475 (93.3)	1	1
	No	12 (12.0)	88 (88.0)	2.10 (1.09 - 4.07)*	2.56 (1.06 - 6.15)*
Plumpy'nut intake	Yes	5 (5)	95 (95.0)	1	
	No	39 (8.1)	441 (91.9)	1.92 (0.76 - 4.88)	

*Note: * p<0.05*

After adjusting for confounders through step wise backward Cox regression method, the children with failed appetite had 2.7 times increased risk of death from SAM after admission (AHR=2.75, 95%CI: 1.08, 6.99). Sero-positivity for HIV significantly increased the risk of death from SAM by 11 fold than non-reactive for HIV test (AHR=11.57, 95%CI: 2.34, 57.22). Those infected with malaria were twelve times more likely to die than those without malaria (AHR=12.70, 95%CI: 4.57, 35.27). Those who were not treated with F-100 (AHR=3.26, 95%CI: 1.32, 8.07) and F-75 (AHR=2.56, 95%CI: 1.06, 6.15) were more likely to die than their counterparts ($p< 0.05$) (Table 4).

Discussion

This study revealed that 7.6% had died, 69.9% had been cured, 14.3% had been defaulters and 8.2% had been transferred out and non-responders from treatment in therapeutic feeding center. The mean survival time for the cohort of SAM children was 69.28 days, with median survival time of 80 days. The level of mortality and the measure of the effectiveness of other treatments are acceptable, except the slightly lower cure rate (Thurstans, 2011). The mortality rate is a bit higher than the one reported from Jimma (6%) (Habtemu *et al.,* 2015), but lower than the ones found in Tigray (12%) (Melaku *et al.,* 2014) and in Sekota (29%) (Kebede, 2015). The humanitarian charter standards set the mortality rate below 10%, cure rate above 75%, and default rate below 15% (Thurstans, 2011). In this study, the result showed acceptably short length of hospital stay and acceptable rate of weight gain.

The mean survival time was higher than the mean reported from Sekota (10 days) (Kebede, 2015). This difference might be due to the higher number of actual death and lower censored cases which decreased the mean of survival time. Like similar findings in Uganda (Bachou *et al.,* 2006) and in Mekele (Melaku *et al.,* 2014), in this study most of the deaths occurred within the first week of admission to Therapeutic Feeding Unit (TFU).

In the current study, SAM children with pneumonia, HIV/AIDS, diarrhea, and dehydration had significantly shorter mean survival time than their counterparts. HIV/AIDS is associated with increased risk of other acute and chronic opportunistic infections which aggravate the risk of death. Not taking F-100 and F-75 was associated with significantly shorter survival time. This result is supported by the fact that the nutritional therapies are particularly suited for SAM children for reduced metabolic state (WHO, 2013).

This study also showed that failed appetite, HIV/AIDS, malaria, and not taking F-75 were significant predictors of mortality from SAM in the hospital. Loss of appetite (FMOH, 2013) is a manifestation of disease in SAM and associated with other co-morbidities which increase the severity of SAM patient's condition. But IV fluid, IV antibiotics intake, diarrhea and dehydration have not reached statistical significance level. However, other studies showed that Diarrhea, IV antibiotics and IV fluid intake were significantly associated with the risk of the death. (Munthali *et al.,* 2015; Bachou *et al.,* 2006; Melaku *et al.,* 2014; Habtemu *et al.,* 2015)

In contrast, unlike results from Kebede (2015), in the current study, routine medical therapy increased the risk of death from SAM. In our study, for each increase in anthropometric indices (WFH % and MUAC) there was a decrease in mortality from SAM which is similar with findings from Malawi, although the effect is higher in the latter (Kerac *et al*., 2014). It is probably because as the child's nutritional status deteriorates, there is an increase in co-morbidity and other physiological stresses which increase mortality (Kapil and Sachdev, 2010).

Additionally this study showed that those who did not take F-75 intake are at higher risks of death than who took F-75. It is associated with the fact that F-75, which decreases the risks of fluid overload and other related abnormalities, is best suited for the reduced physiological capacity of SAM children and reduces the mortality rate (Bhutta *et al*., 2013; FMOH, 2013). Appropriate nutritional therapy in conjunction with the national SAM management protocol promotes early recovery and decreases the risk of death.

Missed data, like bottle feeding and breast feeding histories and inconsistency of patient medical records, together with the absence of the actual outcome of defaulters, were some of the limitations of the present study.

Conclusion and Recommendations

In this study there was substantial level of mortality among the children admitted with SAM. Dehydration and malaria were the common medical complications affecting SAM children. Malaria, HIV status, failed appetite, not taking F-100 and F-75 were identified as the independent predictors of the death due to SAM.

This study showed substantial level of mortality, and also identified some treatment and morbidity related factors for increased risk of deaths among SAM children. Thus Dilchora Referral Hospital, in collaboration with

other NGOs and concerned bodies, should put an effort to improve the outcome in terms of mortality, recovery rate and default rate. There should be strengthened efforts to decrease mortality as a result of SAM from current level to below 5%.

Further researches should be conducted on the level of the implementation of the national protocol with especial focus on using the new WHO growth standard, as it will identify SAM children early in order to enhance child survival below the current level. In addition, the adherence level of patients to the application of the treatment protocol should be studied.

Acknowledgment

The authors would like to acknowledge Haramaya University and Wolkite University for the financial support of this study. We would also like to acknowledge officials of Dilchora Referral Hospital, data collectors, card retrievers, Dr. Habtamu and Sr. Etnesh for their kindness and support.

Conflict of Interests

The authors declare that there is no conflict of interest.

Authors' Contributions

AO participated from inception of idea, proposal development, data collection, analysis and final write up. FM and MD has participated in the amendment of proposal and the write up of final result. All authors approved the final manuscript.

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