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#### ORIGINAL RESEARCH

## Predictors of Death from Complicated Severe Acute Malnutrition in East Ethiopia: Survival Analysis

#### Abdu Oumer <sup>b</sup> Leul Mesfin<sup>1</sup> Esubalew Tesfahun <sup>2</sup> Ahmed Ale<sup>3</sup>

<sup>1</sup>Department of Public Health, College of Medicine and Health Science, Dire Dawa University, Dire Dawa, Ethiopia; <sup>2</sup>Department of Public Health, College of Medicine and Health Science, Debre Birhan, University, Debre Birhan, Ethiopia; <sup>3</sup>School of Medicine, College of Medicine and Health Science, Dire Dawa University, Dire Dawa, Ethiopia **Background:** Severe acute malnutrition (SAM) is still the leading cause of global child morbidity and mortality, with a greater burden in sub-Saharan Africa. A facility-based treatment of SAM demands critical care for improved outcomes and survival of children. However, there is a need to understand predictors for time to death among SAM children for effective interventions.

**Objective:** To assess the predictors of death from complicated severe acute malnutrition among admitted children treated in East Ethiopia.

**Methods:** A 31-month retrospective cohort study was conducted among a total of 665 under-five children admitted with complicated SAM in Dilchora hospital, eastern Ethiopia. The data was extracted from the patient register and medical charts using the kobo tool. The life table, survival, and hazard curves were plotted. Kaplan–Meier with Log rank tests was used to estimate and compare the mean survival time. The bivariable and multivariable Cox proportional hazards models were used to identify predictors of time to death. Crude and adjusted hazard ratios with 95% confidence intervals and p-values were reported.

**Results:** A total of 665 full medical charts were reviewed with a total of 60 (9%; 95% CI: 6.8–11.2%) deaths were observed, where most of the deaths occurred during the first two weeks of admission, while 74 (11%) and 449 (68%) were cured and recovered (stabilized and transferred to outpatient), respectively. Admitted children having good appetite (AHR=0.15; 95% CI: 0.64–0.33), pneumonia (AHR=2.46, 95% CI: 1.436, 4.22), diarrhea (AHR=2.16, 95% CI: 1.16, 4.06), tuberculosis (AHR=2.86, 95% CI: 1.08, 7.63) and having a nasogastric tube inserted (AHR=2.33, 95% CI: 1.15, 4.72) were significant predictors of time to death among SAM children.

**Conclusion:** There is unacceptably high under-five mortality due to SAM, which is predicted by co-morbidities (pneumonia, diarrhea, and tuberculosis), with medical complications and nasogastric tubes.

Keywords: survival pattern, predictors, time to death, severe acute malnutrition, hospitals

#### Introduction

Acute malnutrition is characterized by a recent failure to receive adequate nutrition due to episodes of diarrhea and other acute illnesses.<sup>1,2</sup> It can be classified as moderate acute malnutrition (MAM) and severe acute malnutrition (SAM) using weight for height (WFH) or mid-upper arm circumference (MUAC) cutoff points.<sup>3,4</sup> SAM is diagnosed with low MUAC (MUAC <11.5 cm) and/or a WFH Z-score (less than -3). It is the most extreme and visible form of undernutrition that is characterized by profound wasting or edema, loss of appetite, comorbidities, and complications. It requires timely and appropriate management for the child to survive.<sup>1,3,5</sup>

Correspondence: Abdu Oumer Department of Public Health, College of Medicine and Health Science, Dire Dawa University, Dire Dawa, Ethiopia Email omab2320@gmail.com

Globally, an estimated 49 million (7.3%) children had acute malnutrition, with 16 million children being victims of SAM, accounting for estimated three million child deaths. The continent of Africa bears 28% of the global malnutrition burden.<sup>6</sup> Estimated 3 million child deaths are attributable to SAM, with over 50% of child deaths occurring in developing countries attributable to undernutrition, in general.<sup>7</sup> A forecast in 2014 showed that estimated 28.8 million children were victims of SAM and projected to decrease to 21.7 million by 2030. Despite a decline in the burden, additional 8 million new cases occur in sub-Saharan Africa each year.8 In sub-Saharan Africa, SAM affects about 3% of under-five children, with more than 400,000 child deaths each year.<sup>9</sup> In addition, estimated 6.9 million child deaths are attributable to malnutrition in low- and middle-income countries.<sup>10</sup>

In Ethiopia, where the under-five child mortality rate is high (57 child deaths per 1000), malnutrition is a basic underlying cause, accounting for an estimated 57% of child mortality.<sup>11</sup> Malnutrition, primarily due to SAM, costs approximately 16.5% of the national GDP.<sup>12</sup> An estimated 9–40% of children are affected by acute malnutrition.<sup>13–18</sup> SAM is the third leading cause of mortality, accounting for 8.1% of under-five deaths.<sup>19</sup> It is also estimated that 4.8 million children need emergency nutrition support in 2019, which could aggravate the situation in Ethiopia.<sup>20</sup>

Children with complicated SAM need to be treated as inpatients to manage complications and improve child survival, since severe infections including pneumonia, diarrhea, sepsis, or HIV have a higher case fatality of up to 40%. Children with complicated SAM have a high ongoing risk of mortality throughout.<sup>21</sup> The United Nations International Children's Education Fund (UNICEF) reported that in Ethiopia, there are 152,413 cases of SAM being treated from January to May 2021.<sup>22</sup> SAM could threaten the futures of millions of children worldwide.<sup>23,24</sup> In Dire Dawa, an estimated 4.2% of children are affected by SAM, which is above the national average of 3%.<sup>13</sup> In addition, being on the border with the neighboring countries in the horn, sporadic conflicts, and population displacement make the area more prone to the adverse consequences of SAM.

The current strategy for Community-based Management of Acute Malnutrition (CMAM) is a focused and holistic approach for better SAM case management. It aims to increase the capacity to manage SAM children properly for a better treatment outcome. The proper implementation of SAM management has the potential to reduce under-five mortality from 55% to under 20% in Ethiopia.<sup>1,40</sup> However, a substantial number of deaths; 29%,<sup>14</sup> 8.4%,<sup>25</sup> 14.5%<sup>26</sup> and 5.8%<sup>27</sup> have been observed in Ethiopia, which is mainly related to facility readiness, staff capacity, and inter-regional differences related to clinical characteristics and severity of malnutrition.<sup>28</sup>

Inpatient therapeutic feeding units are faced with a lot of challenges in handling cases of SAM. Some of the challenges are limited in-patient capacity, lack of enough skilled staff in the hospitals, late presentation of children, the high default rate among children, and the serious risk of cross infections for immune-suppressed children, which totally increases the mortality rate.<sup>29</sup> A mortality rate of below 10% is considered acceptable in humanitarian situations.<sup>30</sup> However, these parameters are still not achieved in many of the developing countries due to many causes.<sup>3</sup>

In Ethiopia, majorities of children with SAM present to therapeutic feeding centers, but present with many medical complications, and many children are dying anyway.<sup>31</sup> However, the major predicting factors affecting the time to death are not well understood, particularly in Dire Dawa, which needs to be understood for targeted intervention for improved child survival and treatment success.<sup>38</sup> So, the purpose of this study was to identify the predictors of time to death from complicated SAM among under-five children managed at stabilization centers in Dire Dawa.

## Materials and methods Study area and design

This retrospective cohort study was conducted in Dire Dawa city administration in Eastern Ethiopia. In the city, there were two public hospitals providing care for complicated SAM patients. However, due to the current Covid-19 pandemic, one hospital providing SAM care was changed to a Covid-19 treatment center. Thus, the current study was conducted in Dilchora Hospital's SAM unit (stabilization center), where the majority of the SAM cases are treated. Dire Dawa is one of the two city administrations in Ethiopia which is located 515 km away from Addis Ababa, the capital city. The city has an estimated total population of more than 506,936 as of 2019/20, with the majority of residents living in the rural part. There are two governmental hospitals, four private hospitals, five higher clinics, twelve medium clinics (private), 15 health centers, and 34 health posts with 100% health service coverage.<sup>32</sup>

Dilchora hospital gives inpatient management for complicated SAM children (13 beds) in a stabilization center, in accordance with the national SAM management guideline. The data was retrieved from records from July 1, 2020, to August 30, 2020.

#### Study population and eligibility criteria

The results of this study are applicable to all children aged 0– 59 months with complicated SAM admitted to the Dilchora Hospital stabilization center. All eligible records of 0–59 months' children with SAM admitted to the center from September 2017 to March 2020 were from the study population (as this may show the most recent burden of the problem). Records of SAM children with missing treatment outcomes, admission, and discharge date were not included in the study as these are the primary outcomes of the study to be addressed.

#### Sample size determination

The minimum sample size for detecting the predictors of time to death from complicated SAM was calculated using Stata version 14 (Stata Corp., STATA 14.0 for window) for sample, and power calculation module. The sample size for comparing the survival Cox model and comparing slope to the reference was used. In addition, samples were calculated for each predictor, and the maximum calculated sample was taken. By taking anemia as a predictor of time to death (AHR = 1.36), the ratio of exposed to non-exposed as 1, the probability of death (0.29),<sup>31</sup> a significance level (0.05), and power (80%), the minimum sample size to identify predictors of time to death among SAM children became 666.

### Sampling technique

Simple random sampling using the serial numbers of SAM children in the SAM registry was used to generate a table of random numbers. Then, the unique medical record number corresponding to the selected random serial number is identified. Then, using the unique medical record number, the medical charts of randomly selected children were retrieved from the card room, and data was collected.

### Data collection method

A cross-checked data abstraction format prepared in line with the SAM registry and the medical charts of children was used to collect data. The data was collected from the medical records and the SAM treatment registry through cross-validation. Graduate nurses and health officers were used for collecting the data.

### Data quality control

To assure data quality, the checklist was cross-checked with the SAM register and medical charts. Data collectors were trained for one day, on how to extract the data from the patient registry. During training, data collectors exercised the data collection on at least five medical charts of children with the supervision of the researchers. Daily checkups and feedback were given by the investigators and supervisors on the appropriateness, completeness, and consistency of the collected data by taking a random sample of the collected data. The data was entered into the Kobo tool for controlled and quality data collection.

#### Variables of the study

The dependent variable was time to death from SAM among children. Meanwhile, the independent variables were demographic characteristics (age, sex of the child, place of residence), clinical conditions (vomiting, dehydration, loss of appetite, and hypothermia), presence of nutritional edema, co-morbidities (pneumonia, HIV status, diarrhea, anemia, malaria, tuberculosis, and hypothermia), routine medication intake (intravenous (IV) fluid intake, IV antibiotic treatment, blood transfusion, folic acid, vitamin A supplementation, deworming, and presence of nasogastric tube), and level of anthropometric deficits at admission.

### **Operational definitions**

In this study, cure from SAM was achieved when the SAM child reached the discharge criteria; weight-forheight/length is  $\geq -2$  Z-scores and they have had no edema for at least 2 weeks, or MUAC is  $\geq 12.5$  cm, and they have had no edema for at least 2 weeks without any acute medical complications. However, recovered (stabilized) is defined as when the child is treated for acute medical complications at a stabilization center and transferred to OTP (not cured yet) for continuous SAM treatment.<sup>30,33</sup> Censored observations were defined as those SAM children who were defaulted, transferred, disappeared, recovered, or non-responded in which the primary outcome of interest (death) was not observed. Anemia was defined with a hemoglobin level below 11 gm/dl (hematocrit level less than 33%) at admission,<sup>33</sup> while hypothermia is defined as when the body temperature is below 35.5°C.

## Data processing and analysis

The collected data through the Kobo tool was exported to SPSS statistical software version 20 for data cleaning and analysis. The data were cleaned and checked for outliers and inconsistencies ahead of the statistical analysis. Frequency, percentage, mean, median, and standard deviation were used to present the data. The Kolmogorov-Smirnov test was done to check the distribution of ratio scale variables. Graphs and tables were presented. The life tables and survival curve were used to display the cumulative survival and survival function with different patient characteristics. The Kaplan-Meier test with a Log rank test was used to compare the mean or median survival time among different categories. The Coxproportional hazard assumption was checked in Stata/SE 14.0 both graphically and statistically. After checking the Cox proportional hazard assumption, both bivariable and multivariable Cox proportional hazard regression analysis with crude and adjusted hazard ratio (CHR and AHR) and 95% Confidence interval (95% CI) were reported. The Cox proportional hazard assumption was tested using a global test in Stata Version 14.0. To test the proportional hazard estimate over time, both graphical (survival and Kaplan-Meier by categorical variables) and statistical (global test) methods were used. Predictor variables with a p-value below 0.2 in bivariable Cox regression were candidates for the multivariable Cox regression analysis. Predictor variables with a P-value below 5% was used to declare as statistically significant predictors of time to death from SAM.

## Ethical considerations

An ethical support letter was obtained from the Dire Dawa University, College of Medicine and Health Science research and ethics review committee. The support letters were subsequently taken to the city administration health bureau and the hospital. Written informed consent was taken from the hospital administration on behalf of the clients that the information collected would be kept confidential and be used only for the proposed study. Specific personal identifiers of children were not collected to maintain the client's private health issues like HIV status.

## Results

## Socio-demographic characteristics of SAM children

In this study, a total of 665 full medical records of children were reviewed, where, more than half, 363 (54.6%) were males. A total of 210 (31.6%) SAM children were aged

below twelve months, and a mean age of 20 months ( $\pm 15$  months). Regarding residence, the majority of SAM children treated in the SAM unit, 385 (57.9%), were from rural areas.

## Medical characteristics of admitted children

Concerning the admission history of children, about 426 (64.1%) and 217 (32.6%) were diagnosed with marasmus and kwashiorkor, respectively, being the common clinical forms of SAM, while only 22 (3.3%) of SAM children had Marasmic-Kwashiorkor at admission. About 417 (62.7%), 401 (60.3%), and 310 (46.6%) children were affected by vomiting, diarrhea, and dehydration, respectively. On the other hand, only 10 (1.5%) and 7 (1.1%) were victims of hyperthermia and hypothermia, respectively. About 651 (97.9%), 110 (16.5%), and 148 (22.3%) of admitted SAM children were given an intravenous antibiotic, a nasogastric tube (NG tube), and intravenous infusions, respectively. Meanwhile, a total of 91 (13.7%) of children received a blood transfusion during their hospital stay for treatment of anemia (Table 1).

## Survival patterns of SAM children

Concerning the treatment outcomes of SAM children, the majority of children (67.5%) were recovered. Also, about 11.1%, 2%, and 10.4% of SAM children were cured, self-discharged without clinical improvement, and defaulted in the course of SAM treatment. A total of 60 (9%: 95% CI: 6.8–11.2%) deaths were observed among SAM children during treatment at a stabilization center within the hospital (Figure 1). The overall cumulative incidence density for mortality was found to be 0.022.

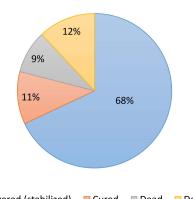
A life table, survival chart, and Kaplan Meier tests were done to explore and understand the survival patterns of SAM children. A total of 60 (9%; 95% CI: 6.8%–11.2%) deaths were observed among admitted SAM children in the hospital. The vast majority of them, 78.3% of children, died within ten days of being admitted to a hospital where medical complications and mismanagement are common (Table 2 and Figure 2). The median survival time of SAM children was 10 days, with a minimum and maximum hospital stay of 1 and 47 days, respectively. The survival patterns of children showed a significant decline and increased hazard of death during the early first weeks of admissions. Regarding the duration of the hospital stay, the average

Clinical condition	Frequency Percen			
Vomiting	Yes	417	62.7%	
	No	248	37.3%	
	Total	665	100%	
Dehydration	Yes	310	46.6%	
	No	355	53.4%	
Appetite test	Pass	504	75.8%	
	Fail	161	24.2%	
Grade of edema	+	43	6.5%	
	++	83	12.5%	
	+++	113	17%	
	Non edematous (0)	426	64.1%	
Pneumonia	Yes	286	43%	
	No	379	57%	
	Total	665	100%	
HIV status	Positive	5	0.8%	
	Negative	51	7.7%	
	Unknown	609	91.6%	
Diarrhea	Yes No	401 264 665	60.3% 39.7% 100%	
Anemia	Yes	304	45.7%	
	No	361	54.3%	
Malaria	Yes No		0.3% 99.7%	
ТВ	Yes	23	3.5%	
	No	642	96.5%	
Hyperthermia	Yes	10	l.5%	
	No	655	98.5%	
Hypothermia	Yes	7	1.1%	
	No	658	98.9%	
IV fluid intake	Yes	148	22.3%	
	No	517	77.7%	
IV antibiotic	Yes	651	97.9%	
treatment	No	14	2.1%	
Naso-gastric tube	Yes	110	16.5%	
	No	555	83.5%	
Blood transfusion	Yes	91	3.7%	
	No	574	86.3%	

Table ICo-Morbidity and Medical Conditions of ChildrenAdmitted to Stabilization Center in Dire Dawa, from 2017 to2020 (n = 665)

**Notes:** + - refers to pedal edema, ++ - edema of the leg, and +++ - generalized body edema.

Treatment outcomes of SAM patients treated in stabilization center



Recovered (stabilized) Cured Dead Defaulted

 $\ensuremath{\textit{Figure I}}$  Treatment outcomes of SAM children treated in stabilization center, Eastern Ethiopia.

length of stay in the hospital was 12 days (SD  $\pm$  7.35 days).

Those SAM children with a failed appetite at admission had a significantly lower mean survival time (26.9 days) as compared to those with a passed appetite test (43.6 days) (p-value of log-rank = 0.0001). In addition, children with the diagnosis of tuberculosis had a significantly lower mean survival time as compared to their counterparts. Children with pneumonia and diarrhea at admission had a significantly shorter mean survival time than the others. Children who received routine medications (deworming and NG tube) had significantly shorter mean survival times than their counterparts.

## Predictors of time to death among under-five children with SAM

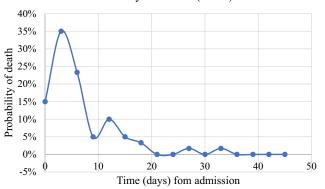
Bivariable Cox proportional hazard regression was done to identify the potential predictors of time to death from complicated SAM among children. The risks of death were found to be lower among those over the age of two, males, and children of city dwellers. Those SAM children who were diagnosed with dehydration (CHR=2.0; 95% CI: 1.18–3.38) and pneumonia (CHR=2.68: 95% CI: 1.58–4.56) had a significantly increased risk of death from SAM. In addition, children with TB in the course of SAM treatment (CHR=2.85; 95% CI: 1.14–7.14) and those on IV fluid treatment (CHR=3.23; 95% CI: 1.94–5.36) had a significantly

Interval Start Time (in Days)	Subjects Entered	Subjects Censored	Subjects Exposed to Risk	Number of Terminal Events	Probability of Events (Death)
0	665	13	658.5	9	15%
3	643	73	606.5	21	35%
6	549	123	487.5	14	23.3%
9	412	135	344.5	3	5%
12	274	101	223.5	6	10%
15	167	51	141.5	3	5%
18	113	33	96.5	2	3.3%
21	78	31	62.5	0	0%
24	47	16	39	0	0%
27	31	10	26	1	1.7%
30	20	5	17.5	0	0%
33	15	4	13	1	1.7%
36	10	5	7.5	0	0%
39	5	1	4.5	0	0%
42	4	2	3	0	0%
45	2	2	1	0	0%
Total	3035	605	2732.5	60	100%

 Table 2 Life Table Showing the Survival and Hazards of SAM Children Treated in Stabilization Center, in Dire Dawa from 2017 to 2020, Ethiopia

three-fold increased hazard of death. Children who were unable to swallow food and those who had the NGT implanted had a 13-fold increased risk of death (CHR=13.02; 95% CI: 7.54–22.48). Meanwhile, children who got vitamin supplements, deworming, and IV antibiotics had a lower hazard of death (Table 3).

The predictors of time to death from SAM were assessed using multivariable Cox proportional hazard regression. Failed appetite, comorbidities (diarrhea, pneumonia and tuberculosis), not taking deworming, and the presence of an NG tube were important predictors of time to death among admitted complicated SAM children. Children who had a good appetite (AHR=0.15; 95% CI:



Probability of events (death)

Figure 2 Hazard (I-survival) curve for admitted SAM children in stabilization center: from admission to outcome (death).

0.64–0.34) and those who took deworming tablets (AHR=0.36; 95% CI: 0.20–0.64) had lower risks of death due to SAM. While children with pneumonia (AHR=2.43; 95% CI: 1.42–4.16) and diarrhea (AHR=1.96; 95% CI: 1.08–3.56), respectively, had a 2.4-and 2-fold increased risk of death from SAM, respectively. Furthermore, children with tuberculosis (AHR=2.86; 95% CI: 1.08–7.63) and those with nasogastric tubes inserted (AHR=2.32; 95% CI: 0.15–4.72) had a higher risk of death than their peers (Table 4).

#### Discussions

The purpose of this study was to identify the predictors of time to death from SAM among children treated in a stabilization center within the hospital, in Ethiopia. The findings of this study showed that a significantly higher number of deaths (9%: 95% CI: 6.8%–11.2%) were observed among admitted children. Despite the fact that Ethiopia is implementing a standard management protocol for complicated SAM management for children, the mortality is found to be high. Other similar studies also reported 7.6% in eastern Ethiopia,<sup>34</sup> and the Wolaita Zone (8.8%),<sup>35</sup> while it was higher than the result from North Ethiopia (3.8%).<sup>36</sup> However, a higher mortality rate was observed in Yaoundé, Cameroon (15%),<sup>5</sup> Zambia (46%),<sup>37</sup> northern Ethiopia (29%) and southwest Ethiopia (14.5).<sup>26</sup>

#### Table 3 Bivariable Cox Proportional Hazard Regression Model for Predictors of Death from SAM in Eastern Ethiopia

Predictor Variables		Outcome		CHR (95% CI)
		Dead	Censored	
Age in months	≤ 24 months	39 (65%)	482 (79.7%)	l
	>24 months	21 (35%)	123 (20.3%)	0.80(0.61–1.05)
Sex	Male	25 (6.9%)	338 (93.1%)	0.57 (0.34–0.96) *
	Female	35 (11.6%)	267 (88.4%)	I
Resident	Urban	24 (8.6%)	256 (91.4%)	0.93 (0.56–1.56)
	Rural	36 (9.4%)	349 (90.6%)	I
Clinical form of malnutrition	Marasmus	38 (9%)	384 (91%)	I
	Kwashiorkor	19 (8.7%)	200 (91.3%)	0.86 (0.27–2.81)
	Marasmic-Kwashiorkor	3 (12.5%)	21 (87.5%)	0.73 (0.22–2.49)
Vomiting	Yes	42 (10.1%)	375 (89.9%)	I.42 (0.82–2.47)
	No	18 (7.3%)	230 (92.7%)	I
Dehydration	Yes	38 (12.3%)	272 (87.7%)	2.00 (1.18–3.38) *
	No	22 (6.2%)	333 (93.8%)	I
Appetite test	Pass	II (2.2%)	493 (97.8%)	0.06(0.03–0.12) *
	Fail	49 (30.4%)	112 (69.6%)	I
Pneumonia	Yes	39 (13.6%)	247 (86.4%)	2.68 (1.58–4.56) *
	No	21 (5.5%)	358 (94.5%)	I
Diarrhea	Yes	45 (11.2%)	356 (88.8%)	2.16 (1.16–4.06) *
	No	15 (5.7%)	249 (94.3%)	I
Anemia	Yes	29 (9.5%)	275 (90.5%)	I.08 (0.65–I.79)
	No	31 (8.6%)	330 (91.4%)	I
Tuberculosis	Yes	5 (21.7%)	18 (78.3%)	2.85 (1.14–7.14) *
	No	55 (8.6%)	587 (91.4%)	I
Hypothermia	Yes	2 (28.6%)	5 (71.4%)	3.65 (0.89–14.97)
	No	58 (8.8%)	600 (91.2%)	I
IV fluid	Yes	28 (18.9%)	120 (81.1%)	3.23 (1.94–5.36) *
	No	32 (6.2%)	485 (93.8%)	I
IV antibiotics	Yes	59 (9.1%)	592 (90.9%)	0.88 (0.12–6.41)
	No	I (7.1%)	13 (92.9%)	I
Blood transfusion	Yes	10 (11%)	81 (89%)	I.18 (0.60–2.35)
	No	50 (8.7%)	524 (91.3%)	I
Folic acid and Vitamin A	Yes	39 (7.6%)	474 (92.4%)	0.56 (0.33–0.95) *
	No	21 (21%)	131 (86.2%)	I
Deworming	Yes	18 (4.5%)	389 (95.5%)	0.27 (0.16–0.48) *
	No	42 (16.2%)	217 (83.8%)	I
NG tube	Yes No	41 (37.3%) 19 (3.4%)	69 (62.7%) 536 (96.6%)	I 3.02 (7.54–22.48)

Note: \*Refers to statistically significant predictors of time to death at 5% significant level.

The SPHERE minimum standard for humanitarian response states that the death rate should be below 10% as a target.<sup>30</sup> However, as the situation is not in an

emergency setting, but in a relatively stable setting, a higher mortality incidence that needs due attention is found. This may be related to the frequent occurrence of

Variables		Outcome	Outcome		P-value
		Dead Freq. (%)	Censored Freq. (%)		
Appetite test	Pass Fail	(2.2%) 49 (30.4%)	493 (97.8%) 112 (69.6%)	0.15(0.64–0.34) I	0.001*
Pneumonia	Yes No	39 (13.6%) 21 (5.5%)	247 (86.4%) 358 (94.5%)	2.43(1.42–4.16) I	0.012*
Diarrhea	Yes No	45 (11.2%) 15 (5.7%)	356 (88.8%) 249 (94.3%)	I.96(I.08–3.56) I	0.001*
Tuberculosis	Yes No	5 (21.7%) 55 (8.6%)	18 (78.3%) 587 (91.4%)	2.86(1.08–7.63)	0.087
Deworming	Yes No	18 (4.4%) 42 (16.2%)	388 (95.5%) 217 (83.8%)	0.36(0.20–0.64)	0.0001*
NG tube	Yes No	41 (37.3%) 19 (3.4%)	69 (62.7%) 536 (96.6%)	2.32 (0.15–4.72)	0.017*

Table 4 Multivariable Cox-Proportional Hazard Regression Model for Predictors of Death from SAM

Note: \*Shows a statistically significant predictors at p-value below 0.05.

medical complications, such as diarrhea,<sup>38</sup> pneumonia, and others impairing nutritional recovery,<sup>3,39</sup> and prolong hospitalization, which negatively affects nutrient intake. In addition, since the cure is expected at outpatient therapeutic feeding, where children are transferred from hospitals, the current mortality rate may be increased. That means a significant number of children are dying in the early phase of hospital admission, which should be addressed for improved health care and effective treatment.<sup>40</sup>

In this study, the mean survival time was 40.43 days with most of the deaths occurring within the first two weeks of admission to the hospital. This might be due to the fact that children in the early stages of treatment are more prone to fatal medical complications and some mismanagement that may potentially increase the risk of death.<sup>41–44</sup> In addition, the presence of respiratory complications that are commonly observed in children, like pneumonia, TB, and loss of appetite, accompanied by comorbidities, decreases child survival and shortens the mean survival time.<sup>33,45</sup> This warrants careful identification, diagnosis, and management of such medical comorbidities in accordance with the national protocol.

A number of factors were found to be important predictors of child survival. A 2.4-fold increased hazard of death was observed among children with a diagnosis of pneumonia. In addition, a fourfold increased risk of death was also reported for pneumonia.<sup>46</sup> Other studies conducted in Northwest and Northern Ethiopia showed that children with pneumonia have a 29% and 56% lower likelihood of recovering from SAM and have an increased risk of death, respectively.<sup>47,48,51</sup> Furthermore, TB has the potential to increase the risk of death by three-fold (AHR=2.86; 1.08–7.63). Similarly, a study conducted at Sekota Hospital, northern Ethiopia (HR=2.88)<sup>49</sup> and (AHR: 1.6)<sup>50</sup> showed an increased risk of death by three and two folds. Frequent infections, particularly respiratory diseases, have the potential to limit dietary intake and child oxygenation, which may potentially increase the risk of early death.

It is known that reduced metabolic adaptation in SAM children usually makes the typical symptoms of comorbidities absent. This might lead to atypical presentations of children despite the fact that they have medical complications, but not clinically evident. But children may come up with a loss of appetite, an important clinical indicator of inherent medical complications. This study also found that children with loss of appetite had higher hazards of death. One study found that it increases the risk of death by almost threefold (AHR=2.7).<sup>34</sup> Thus, clinicians need to be careful about the possibility of hiding a serious infection and should routinely give presumptive antibiotics as per the guideline.<sup>33,41</sup>

In addition, diarrhea was shown to increase the risk of death by 2.16 folds (AHR: 2.16; 1.16–4.06) compared to those who did not have diarrhea. Previous studies also pointed out that it increased the risk of death by 2.52.<sup>34</sup> Furthermore, taking a deworming medication can reduce the risk of death by 64% when compared to those who did

not take a deworming medication (AHR: 0.36, 0.21–0.66). Also, altered pulse rate due to various clinical conditions, including diarrhea, significantly increased the risk of death (AHR = 2.44, p-value <0.001).<sup>26</sup> The presence of a nasogastric tube indicates that the child is unable to feed himself or herself consciously. Those children with NG tubes are more likely to be victims of medical complications and infections that warrant serious medical follow-up for a better clinical outcome. In addition, NG tube feeding in the presence of other complications increase child's risk of death by 26%.<sup>48</sup>

This study indicated that a higher number of child deaths are observed, with important factors that determine child survival being identified. However, the findings of this study should be thought of in the light of some inherent limitations. Since the nature of the data is secondary data, the information for some children is lost and may be related to the outcome in that the current estimate may be underestimated. On the other hand, this study pinpoints important predictors for high mortality using appropriate statistical methods. This evidence will inform the hospital and others to focus on the most important areas to focus on for improved child survival. Further, there should be evidence on the facility readiness and quality of care for children that may contribute to increased risk of mortality, in addition to the clinical presentation of SAM children.

### **Conclusions and recommendations**

In general, a higher child mortality rate and lower child survival were found among admitted SAM children in the hospital. In addition, loss of appetite at admission, the presence of medical complications (pneumonia, TB, and diarrhea), not getting deworming tablets, and being on NG tube feeding were important predictors of early death among SAM children. Implementation research on the level of implementation, quality of care, health professional's readiness, skills, and other infrastructures should be thought about for a better understanding of the causes of higher mortality, besides medical conditions of the child. In addition, there should be an enhanced outreach program for malnutrition screening to identify SAM and acute malnutrition earlier before medical complications happen, reducing late presentations. There should be a targeted intervention in accordance with the national protocol for the management of SAM within hospitals.

## **Abbreviations**

CI, confidence interval; HR, hazard ratio; MAM, moderate acute malnutrition; MUAC, mid-upper arm circumference; NG, nasogastric tube; SAM, severe acute malnutrition; TB, tuberculosis; UNICEF, United Nation International Children Education Fund; WFH, weight for height; WHO, World Health Organization.

## **Data Sharing Statement**

All data generated or analyzed during this study are included in this published article.

# Ethics Approval and Consent to Participate

The research was reviewed and ethically adopted by Dire Dawa University, College of Medicine and Health Science research and ethics review committee. Then, a written informed consent to collect data was obtained from the hospital manager on behalf of the SAM children's record. All possible ethical cares were respected throughout the conduct of the research project. All relevant ethical principles under the Helsinki declaration were followed and respected.

## Acknowledgments

The authors would like to acknowledge Dire Dawa University for giving this opportunity to conduct this study. We would like to thank our data collectors, card retrievers, and staff of the Dilchora hospital for their valuable help and support for the accomplishment of this research.

## **Author Contributions**

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

## Funding

No specific funding was obtained.

#### Disclosure

All the authors declare that they have no conflicts of interest in this work.

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