Predictors of undesirable treatment outcome of severe acute malnutrition inpatient children in Addis Ababa, Ethiopia: a retrospective cohort study

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Abstract

**Background:** Globally, in 2018, malnutrition contributed to 45% of all child deaths. These early child deaths are due to conditions that could be prevented or treated with basic interventions. Hence, this study intends to provide a quantitative example of factors associated with undesirable treatment outcomes of severe acute malnutrition (SAM).

**Methods:** We studied a retrospective cohort of 304 children aged 6-59 months with complicated SAM admitted to Yekatit 12 teaching hospital from 2013-2016. We extracted data from hospital records on nutritional status, socio-demographic factors, and medical conditions during admission. The analysis was carried out with SPSS version 20. The Kaplan-Meier estimator was employed to analyze the recovery rate of the children undergoing treatment for SAM and Cox regression was used to adjust for confounding effects of other variables.

**Result:** From overall of 304 under-five children with SAM, 133 (51.4%) were males and 126 (48.6%) were females. Marasmus was the most common type of severe acute malnutrition 132 (51%). The recovery, death, and defaulter rate were 70.4%, 12.2% and 8.2% respectively. The main predictors of undesirable outcome were found to be presence of HIV antibody (AHR = 3.208; 95% CI: [1.045-9.846]) and sepsis (AHR = 7.677, 95% CI: [2.320-25.404])

**Conclusion:** The study revealed that the overall treatment outcomes were below the SPHERE standard recommendation and the main predictors of death in children receiving in-patient treatment for SAM were HIV and sepsis. Intervention to reduce death should focus cases with comorbidities especially HIV and sepsis.

Background

The United Nations’ first Millennium Development Goal (MDGs) to “eradicate extreme poverty and hunger” is measured by assessing a set of indicators, one of which is the prevalence of underweight children under the age of five (1). Which depicts the nutrition condition of these groups as under-nourished or as commonly referred to as malnourished. The extreme case of malnutrition typically in children under the age of 5 years is referred to as Severe Acute Malnutrition (SAM). The WHO defines SAM based on three major indicators, low weight for height/length ratio (WFH), presence of nutritional edema and an upper arm circumference (MUAC) of less than 115mm (2,3). The WHO guidelines for treatment of complicated SAM, suggests the establishment of therapeutic feeding programs (TFP) for the treatment and rehabilitation of severely malnourished individuals in order to reduce the mortality rate as a result of SAM (2,3).

Worldwide, in 2018 alone, 5.3 million children under the age of 5 died – nutrition related factors contributed to about 45% of all child deaths. Children in Sub-Saharan Africa are more than 15 times likely to die before the age of 5 than children in developed regions (4). It is often the case that children with severe acute malnutrition have a higher risk of death from relatively common childhood illnesses in the world such as diarrhea, pneumonia and malaria. (4–6)

The United Nations Sustainable Development Goals (SDGs) are based on the MDGs which were adopted in 2015. While the MDGs were conceived particularly for developing countries, the SDGs are meant to address all UN member states and are considerably more comprehensive and ambitious than MDGs. The SDG goal 2.2 concentrates on ending all forms of malnutrition as it is the dominant cause of death among under five children (3). Ethiopia is one of the countries with high under five child mortality rate, even though the under-five mortality rate has been significantly reduced from earlier years it is still unacceptably high (55.2 deaths per 1,000 live births in 2018) (7). According to the Ethiopian Mini Demographic and Health Survey report 2019, 37% of under five children are stunted, 12% severely stunted, 7% wasted, 1% severely wasted 21% underweight and 6% severely underweight (8).

The minimum international standard set for management of SAM according to SPHERE standards is a cure rate
of at least 75% and death rate less than 10% (9). However, the case fatality rates in hospitals treating SAM in developing countries have remained high. A meta-analysis which was done in low and middle income settings for inpatient treatment of complicated SAM shows a case fatality rate of 14% (range 5-30%) (10,11). There has been numerous factors attributed to high case fatality in children admitted to inpatient treatment units (12,13). Hypoglycemia, infection, anemia, dehydration, hypothermia, electrolyte imbalance, HIV and TB infection, age and sex are among the factors assumed to affect high fatality rate of children with severe acute malnutrition (13).

In the case of SAM with medical complications such as Hypoglycemia, infection, anemia, dehydration, hypothermia, electrolyte imbalance, HIV and TB infection, factors and variables that affect treatment outcomes need to be considered and this requires further clinical insight and analysis. The intent of this study is to investigate determinant factors associated with the treatment outcomes of hospitalized severely malnourished children under the inpatient management scheme of SAM with medical complications.

Method

Study design and Study Setting

A retrospective cohort study was conducted at Yekatit 12 hospital medical college, Addis Ababa. It is one of few hospitals with an established nutrition therapy unit among St Paul’s and Zewditu hospital during the time of the study. Children affected by SAM go through initial screening in regular OPD or emergency unit. Depending on the initial assessments and after cross checking their condition against admission criteria, they will be admitted to the nutritional rehabilitation center, where they receive appropriate treatment and follow up.

The Hospital uses a standardized national management protocol of severe acute malnutrition. According to the protocol, all SAM cases with co-morbidities and poor appetite shall be admitted in the SAM inpatient management section. Whereas those diagnosed for SAM without co-morbidities and with good appetite will be linked to the outpatient management section. After completing the inpatient management, those who satisfy the discharge criteria will be directed to community based feeding program for further follow up (14).

Study population and sampling technique

The study population encompasses 6-59 months old SAM affected children admitted at the Yekatit 12 hospital inpatient unit from 2013 to 2016. The following inclusion and exclusion criteria have been adopted accordingly.

Inclusion criteria: During the time of the study, Ethiopia didn’t adopt the MUAC cut off points recommended by WHO for member states to screen children with SAM; the MoH revised its MUAC cutoff point to 11.5mm after 2016 and implementation with the “new” guideline started in 2017. For this reason, MUAC cutoff point used in this study is from the 2007 Ethiopian National Guideline for Management of SAM. Accordingly, children within the age range of 6 months to 5 years that fulfill the following criteria were included in the study.

1. Weight-for-height/length ratio < 70% of median or less than – 3Z- score
2. MUAC < 110 mm with Length >65cm
3. Presence of bilateral pitting edema with complications or a fail in the appetite test (14)

Exclusion criteria: Drop out and transfer outs were excluded in this study because their outcomes couldn’t be traced.

Sample size

The sample size was calculated using EPI info version 7.2.0.1 for a cohort study design. Based on other related studies conducted in a similar context, variables which are significantly associated with undesirable treatment outcomes were identified and were used to calculate the sample size. The computation was conducted based on the following assumptions; 95% confidence level with 80% power and an allocation ratio of 1:1 as unexposed to exposed ratio. Based on these assumptions, the computed optimal sample size (taking the largest) was 152 for
each group (Table 1).

Table 1: Sample size calculation based on factors related to undesirable outcome in children admitted with SAM

| Related Factors          | CI     | Power | Ratio | Percentage Outcome in | Sample Size |
|--------------------------|--------|-------|-------|------------------------|-------------|
|                          |        |       |       | Unexposed | Exposed | Unexposed | Exposed |
| HIV                      | 95%    | 80%   | 1.1   | 13.7%      | 60%       | 18        | 18      |
| Gastroenteritis          | 95%    | 80%   | 1.1   | 11.1%      | 25.4%     | 115       | 115     |
| Hypothermia(<35°C)       | 95%    | 80%   | 1.1   | 10.8%      | 33.3%     | 54        | 54      |
| Sign of severe pneumonia| 95%    | 80%   | 1.1   | 4%         | 21%       | 60        | 60      |
| Family size              | 95%    | 80%   | 1.1   | 6.4%       | 16.7%     | 152       | 152     |
| Blood transfusion        | 95%    | 80%   | 1.1   | 5%         | 27.6%     | 42        | 42      |

Source: For the sample size calculation, the data were obtained from the study conducted in Gondar University on analysis of hospital records on treatment outcome of SAM, treatment failure and mortality amongst children with SAM presenting with cough or respiratory difficulty and radiological pneumonia in Dhaka, Bangladesh and in St. Mary’s hospital Lacor Northern Uganda on treatment outcome among children under five years hospitalized with SAM (15–17)

**Study variables**

The study variables were categorized as dependent and independent variables. The reason in doing so was to assess which independent variables significantly affect the magnitude of the dependent variable.

The dependent variable was undesirable outcome which includes death, non-respondent and failure to respond. On the other hand, socio-demographic and admission characteristics, anthropometry, type of malnutrition, comorbidities, vaccination and breast-feeding status were considered as independent variables.

**Operational definition**

For a child admitted with SAM, the management procedure consists of 3 phases (phase 1, transition and phase 2). Children were assessed based on the Ethiopian national management protocol for SAM which is in accordance with the WHO procedure for management of SAM. The ten steps of the WHO SAM management include: treat/prevent hypoglycemia, treat/prevent hypothermia and dehydration, correct electrolyte imbalance, treat/prevent infection, correct micronutrient deficiencies, start cautious feeding, achieve catch up growth, provide sensory stimulation and emotional support and prepare for follow up after recovery.

If a child either failed to regain appetite, lose edema by day 4 after admission, gain more than 5g/kg/d by day 10 after admission or failed to gain more than 5g/kg/d for 3 successive days during phase 2 while being on
treatment, he/she was termed as failure to respond. And those that had not reached the discharge criteria after 40 days in the inpatient unit were defined as non-responders.

Patients who were discharged after reaching the discharge criteria (weight for height/length > 85% of median on more than one occasion or no edema for 10 days and a target weight gain reached for two consecutive measurements, if the child is admitted with MUAC) were considered as cured. Whereas those who discontinued treatment or disappeared from nutritional rehabilitation ward before completing treatment were defined as dropouts. Patients whose treatment results are unknown due to transfer to another health facility were defined as transfer outs. And those patients who died from any cause during the course of treatment were defined as dead.

In this study, undesirable outcomes were considered to be: death, non-responder and failure to respond (drop out and transfer outs were excluded in this study because their outcomes couldn’t be traced).

Certain prominent comorbidities were selected under the assumption that it is highly probable that they might be correlated to SAM. This assumptions are based on findings on other studies. The comorbidities considered are the presence of shock, anemia, pneumonia and HIV.

Data collection procedure and data quality assurance

Inpatient register book of the Yekatit 12 Hospital which contained the admission, patient history and discharge information was used as the main data source. Children diagnosed with SAM within the study time frame were selected. Then, each patient record was examined based on the inclusion and exclusion criteria. Records which were complete and that fulfilled the inclusion criteria were included in the study. The data examination and selection producer was carried out by the principal investigator based on checklist adopted from the world health organization guideline for inpatient treatment of SAM 2003 manual.

Testing of the checklist for its completeness and clarity was done before the actual data collection took place and modifications were applied as needed.

Data management and analysis

Following the completion of data collection, the data were categorized and coded. Then, the collected data were entered into a computer using EPI-Info software program. The data entry and cleaning were done using EPI-Info 7.1.3.10 version which was later on exported to SPSS version 20.0 statistical software packages for analysis.

In this study, the dependent variable was undesirable outcome (which incorporates the variables, death, non-responder and failure to respond). Children with undesirable outcome were considered as event and all other outcomes were censored. Finally, the outcome of each subject was dichotomized into censored or undesirable outcome.

Descriptive statistics was used to summarize and describe the data. Regarding survival analysis, Life table analysis was used to estimate the cumulative proportion of survival among children with SAM at different time point. Kaplan Meier survival curve together with log-rank test was fitted to test for the presence of difference in undesirable outcome among groups; the time variable was assumed to be the time to the occurrence of undesirable outcome measured from admission to date of an event. Variables at P-value of <0.25 in the bivariate analysis were included in the final Cox regression analysis to identify the independent predictors of undesirable outcome. In addition, Crude and adjusted hazard ratio with their 95% Confidence Interval (CI) were estimated and summarized. The study result was also compared with the minimum standard presented by the “Sphere” project.

Result

A total of 677 children with SAM were admitted at Yekatit 12 hospital from 2013-2016, 373 were excluded from the study and 304 were eligible for the study. From the eligible cases, 25 were dropouts and 20 were transferred
out to other institutions; both were excluded from the analysis because their outcomes couldn’t be traced. There were no significant statistical difference between background characteristics of the 45 excluded children when compared with children in the study. Thus, the total number of the study subjects in the study is 259 (Fig.1).

Figure 1: Schematic representing the sampling procedure of the study. The chart shows the process of how study subjects were selected. Undesirable outcome includes death, non-respondent and failure to respond

Socio-demographic characteristics, anthropometry and type of malnutrition

From the 259 subjects studied, 133 (51.4%) were males, and 214 (82.6%) were aged below 24 months with the median age of 17.5 (interquartile range: 12-24) months. Majority of the study population (80.7%) belong to family size of less than 3 children.

With regards to the nutritional status of the children, 206 (79.5%) had a WFH ≥ 70 % of median, and 160 (61.8%) had MUAC of <11cm and 132 (51%) children in the study had marasmus (Table 2).

From those with undesirable outcome, 26 (20.6%) were females, 9 (18%) lived in a household with number of children greater than 3. Regarding the nutritional status, 12 (22.6%) have WFH <70% of median and 30 (18.8%) had MUAC of <11cm. (Table 2)

Table 2: Socio-demographic and anthropometry of children with SAM admitted to Yekatit 12 hospital, 2013 - 2016

| Admission characteristics | Outcome | Improved (%) | Undesirable outcome (%) |
|---------------------------|---------|--------------|-------------------------|
|                           |         |              |                         |
| Socio-demographic characteristics |         |              |                         |
| Sex                       |         |              |                         |
| Male                      |         | 114(85.7)    | 19(14.3)                |
| Female                    |         | 100(79.4)    | 26(20.6)                |
| Age                       |         |              |                         |
| <24 month                 |         | 177(82.7)    | 37(17.3)                |
| ≥24 month                 |         | 37(82.2)     | 8(17.8)                 |
| Family size               |         |              |                         |
| <3 children               |         | 173(82.8)    | 36(17.2)                |
| ≥3 children               |         | 41(82)       | 9(18)                   |
| Anthropometry and type of malnutrition |         |              |                         |
| WT/HT or L                |         |              |                         |
| <70 % of median           |         | 41(77.4)     | 12(22.6)                |
| ≥70% of median            |         | 173(84)      | 33(16)                  |
| MUAC                      |         |              |                         |
| <11 cm                    |         | 130(81.2)    | 30(18.8)                |
| ≥11 cm                    |         | 84(84.8)     | 15(15.2)                |
| Type of malnutrition      |         |              |                         |
| Non-edematous             |         | 109(82.6)    | 23(17.4)                |
| Edematous                 |         | 105(82.7)    | 22(17.3)                |
Abbreviations: SAM, severe acute malnutrition; WT/HT, weight/height or length in percent; MUAC, mid upper arm circumference

**Clinical profile and morbidity patterns**

More than half (55.5%) of children had diarrhea and a significant proportion of children (39.6%) had pneumonia at the time of admission. Anemia, Sepsis, skin lesion (dermatitis of kwashiorkor), Tuberculosis and shock were prevalent in 67(29.5%), 19(8.4%), 20(8.8%), 18(7.9%) and 7(3.1%) children respectively. HIV test was also carried out for 190(73.4%) children of which, 11(5.8%) were tested to be positive (Table 3).

Table 3: Clinical profile of children with SAM at admission at Yekatit 12 hospital, 2013 - 2016

| Admission characteristics | Outcome               | Improved (%) | Undesirable outcome (%) |
|---------------------------|-----------------------|--------------|-------------------------|
| Anemia Yes                |                       | 55(82.1)     | 12(17.9)                |
| Pneumonia Yes             |                       | 69(76.7)     | 21(23.3)                |
| Diarrheal disease Yes     |                       | 102(81)      | 24(19)                  |
| Sepsis Yes                |                       | 10(52.6)     | 9(47.4)                 |
| Skin lesion Yes           |                       | 14(70)       | 6(30)                   |
| Tuberculosis Yes          |                       | 14(77.8)     | 4(22.1)                 |
| Shock Yes                 |                       | 3(42.9)      | 4(57.1)                 |
| HIV Antibody Positive     |                       | 7(63.6)      | 4(36.4)                 |
| Others Yes                |                       | 19(73.1)     | 7(26.9)                 |

Others: include Urinary tract infection, Electrolyte imbalance, Bacterial conjunctivitis and Otitis Media

**Treatment outcome**

During the study period, 214(70.4%) children were cured and linked to outpatient therapy which is below the minimum recovery rate recommended in the SPHERE standard which is 75%. On the other hand, 37 (12.2%) had died during treatment which is also higher than the SPHERE standard recommendation of 10% mortality rate. Moreover 64.9% of the deaths had occurred in the first 7 days of admission. On the other hand, 25(8.2%) cases were registered as dropouts, 8(2.6%) as non-respondents and 20(6.6%) as transfers. The average (± SD) length of stay in the hospital was 16 days (±10.7), and the average weight gain during the inpatient treatment phase was 8.13g/kg/day for non-edematous malnutrition (Table 4).

Table 4: Comparison of treatment outcomes with SPHERE standard indicators
| Indicators                  | Results       | SPHERE standards |
|----------------------------|---------------|------------------|
|                            |               | Acceptable       | Alarming        |
| Cure rate (%)              | 70.4 %        | >75%             | <50             |
| Death rate (%)             | 12.2 %        | <10%             | >15             |
| Default rate (%)           | 8.2 %         | <15%             | >25             |
| Rate of weight gain (g/kg/day) | 8.13g/kg/day | ≥ 8 | <8 |
| Average length of stay (days) | 16 days      | < 30 days        |                 |

**Abbreviations:** SPHERE, Social and Public Health Economics Research Group

**Survival analysis**

A total of 304 children were followed for different periods with a minimum of 1 day and a maximum of 63 days with a median follow-up period of 14 days (Fig.2). The median nutritional recovery time of the entire cohort using Kaplan Meier survival analysis is 17 days (95% CI: 15.615-18.385). The greatest number and proportion of terminal events occur for the first 7 days (Table 5).

Table 5: Median nutritional recovery time of SAM at admission in Yekatit 12 hospital, 2013-2016
| Characteristics   | Number | Median recovery time | Log rank X² -value |
|------------------|--------|----------------------|--------------------|
|                  |        | Estimate | 95%CI               |                    |
| **Sex**          |        |           |                    |                    |
| Male             | 16     | 14.162-17.838 | 1.857              |
| Female           | 18     | 16.043-19.957 |                    |
| **Age categorical** |      |           |                    |                    |
| <24 month        | 17     | 15.443-18.557 | 0.977              |
| ≥24 month        | 18     | 14.994-21.006 |                    |
| **Family size**  |        |           |                    |                    |
| <3 children      | 17     | 15.535-18.465 | 3.443              |
| ≥3 children      | 21     | 16.111-25.889 |                    |
| **WT/HT or L**   |        |           |                    |                    |
| <70% of median   | 17     | 12.150-21.850 | 0.00               |
| ≥70% of median   | 17     | 15.612-18.388 |                    |
| **MUAC**         |        |           |                    |                    |
| <11 cm           | 18     | 16.264-19.736 | 4.336              |
| ≥11 cm           | 15     | 13.063-16.937 |                    |
| **Type of malnutrition** |   |           |                    |                    |
| Edematous        | 18     | 16.443-19.557 | 0.308              |
| Non - edematous  | 16     | 13.626-18.374 |                    |
| **EBF**          | YES    | 17        | 15.588-18.412      | 3.893              |
| Comorbidities    | Yes    | 17        | 15.411-18.713      | 0.007              |
| Anemia           | Yes    | 17        | 14.800-19.200      | 0.320              |
| Pneumonia        | Yes    | 18        | 15.746-20.254      | 0.258              |
| Diarrheal disease| Yes    | 18        | 15.935-20.065      | 0.205              |
| Sepsis           | Yes    | 18        | 9.361-26.639       | 0.160              |
| Skin lesion      | Yes    | 20        | 16.561-23.439      | 1.790              |
| Shock            | Yes    | 28        | 24.799-31.201      | 2.146              |
| TB               | Yes    | 30        | 23.802-36.198      | 8.094              |
| HIV antibody     | Positive | 18      | 7.698-28.302       | 0.165              |
| Vaccination      | Yes    | 17        | 15.348-18.652      | 0.193              |

Figure 2: Kaplan -Meier Survival estimate among children with SAM admitted to Yekatit 12 hospital, 2013-2016

**Cox regression analysis**

**Bivariate analysis**

Using Cox regression, bivariate analysis was performed for the independent variables. In the bivariate analysis, a significant difference was observed between potential predictors; WT/HT or L <70% of median, pneumonia,
sepsis, shock and HIV antibody positive children were associated with undesirable outcome (Table 6).

**Multivariate Cox regression**

HIV antibody positive children and children with Sepsis were found to be independent predictors of undesirable outcome in severely malnourished children admitted to Yekatit 12 hospital. However, WT/HT or L <70% of median, pneumonia shock was not independent predictor of undesirable outcome (Table 6).

Table 6: Bivariate analysis and multiple cox regression of factors associated with undesirable outcome (death, no responder and failure to respond) with SAM admitted to Yekatit 12 hospital 2013-2016

| Variables          | Crude hazard ratio (CHR) | P-value | Adjusted hazard ratio (AHR) | P-value |
|--------------------|--------------------------|---------|----------------------------|---------|
| WT/HT or L         |                          |         |                            |         |
| <70% of median     | 1.513(0.779-2.940)       | 0.222   | 1.812(0.769-4.267)         | 0.1     |
| ≥70% of median     | 1                        |         | 1                           |         |
| Pneumonia          |                          |         |                            |         |
| Yes                | 1.471(0.809-2.675)       | 0.206   | 2.224(0.898-5.506)         | 0.0     |
| No                 | 1                        |         | 1                           |         |
| Sepsis             |                          |         |                            |         |
| Yes                | 4.091(1.950-8.581)       | 0.000*  | 7.677(2.320-25.404)        | 0.0     |
| No                 | 1                        |         | 1                           |         |
| Shock              |                          |         |                            |         |
| Yes                | 3.715(1.314-10.507)      | 0.013   | 0.799(0.141-4.532)         | 0.8     |
| No                 | 1                        |         | 1                           |         |
| HIV antibody       |                          |         |                            |         |
| Positive           | 3.446(1.177-10.087)      | 0.024*  | 3.208(1.045-9.846)         | 0.0     |
| Negative           | 1                        |         | 1                           |         |

*Significant at P-value <0.25

**Discussion**

This study was conducted on 304 severely malnourished children 6-59 months old with complicated SAM admitted to Yekatit 12 teaching hospital from 2013-2016 and it shows that the cure, death and defaulter rate were 70.4%, 12.2% and 8.2% respectively. The rate of weight gain was 8.13g/kg/day and 16 days was the average length of hospital stay. The median nutritional recovery time of the entire cohort was found out to be 17 days (95% CI: 15.615-18.385). The greatest number and proportion of terminal events occur within the first 7 days. Sepsis and HIV antibody positive cases were also found out to be independent predictors of undesirable outcome significantly, diminishing the survival probability of children with SAM. Such a similar effect was also identified in other studies (11,18).

The study revealed that 12.2% children died during the follow up period which is higher than the SPHERE standard recommendation of 10% mortality rate (9). On the other hand it was significantly less as compared to findings of a similar study conducted in Zambia with 46% mortality rate(19). The result can also be compared to exemplary studies conducted in a relatively similar context. A study carried out at Hawassa university referral hospital(Ethiopia) depicts a 15.2% death rate which is again above the value revealed in this study (20). In contrast a couple of similar studies carried out in Gedo zone in southern Ethiopia and in Jimma town depict an observed mortality rate of 9.3% and 12.6% respectively (18,21). This study reported a higher mortality rate than that of the case of Gedo and Jimma.

The recovery rate of SAM children cases admitted at Yekatit 12 hospital (70.4%) is below the minimum recovery
rate recommended in the SPHERE standard which is 75%. This could be due to issues of institutional capacity or for the fact that the hospital is a referral health institution and cases arrive at a later stage of the illness which in turn results in a greater proportion of terminal events to occur within the first 7 days of admission. Some institutional factors which are likely to contribute to diminished recovery rate include high staff turnover, unbalanced case load, lack of training, lack of quality assurance procedures, availability of medical supplies and incomplete ward setup (for example, lack of isolated rooms for malnourished children) (22,23).

In this study, the defaulter rate was 8.2%. This is consistent with the minimum international standard set for management of severe acute malnutrition which is <15%. This is also consistent with other similar studies in Ethiopia (21,24)

The average length of hospital stay was found out to be 16 days which is consistent with the minimum international standard set for management of severe acute malnutrition (SPHERE standard). The standard recommends an average length of stay of less than 30 days (9). The finding of the study in this regard is also in line with other analogous studies conducted in Ethiopia (11,18,21).

An average weight gain of 8.13g/kg/day for children with non-edematous malnutrition was computed for the study sample. This value is in line with the SPHERE standard, which is 8g/kg/day(9). The average weight gain computed in this study is similar to other studies as well (18,21,25). Average weight gain for edematous malnutrition cases was difficult to compute for the reason that there was no documentation regarding when the edema was lost and when weight gain was noticed.

In the study sepsis and HIV antibody positive cases were found to be independent predictors of undesirable outcomes (death, non-responder and failure to respond). Adjusting other variables, children with sepsis were 7.7(CI 2.320-25.404) times more likely to have undesirable outcome than children admitted without sepsis. This was in agreement with other reports (19,26,27). Although sepsis was less common in this study (only 8.4%), compared to other comorbidities, it was found to be an independent predictor of undesirable outcome.

Malnutrition and infection/sepsis have a synergistic relationship, through which malnutrition inhibits immune response and infectious diseases can exacerbate malnutrition which in turn increases the severity, duration and frequency of infection (28). In addition to this, the diagnosis of infection in malnourished children is difficult because clinical manifestations of infection such as fever may not be apparent (14). The intertwined effects of malnutrition and infection eventually lead to higher risk of mortality. Similarly, the risk of undesirable outcome in children with SAM that are HIV antibody positive was 3.2 (C.I 1.045-9.846) times higher than those cases that are HIV antibody negative. Other similar studies also found out that HIV antibody positive children were 3 times more likely to die (3,10,11).

We compared the excluded group of children with that of children included in this study and found no significant differences in their ages or sex (for those with available information) or admission characteristics (mean MUAC, mean WHZ, type of comorbidity) and household characteristics (family size) of the children. Thus, selection bias was less likely to occur.

**Strength And Limitation Of The Study**

A major strength of the study was that all the data collection and screening was carried out by the principal investigator which eliminates problems that might arise from lack of scientific judgment. Records have been thoroughly evaluated and only those deemed fit have been included in the study. Regarding the methodology adopted, the process of finding out comorbidities with significant influence on treatment outcomes involved two levels of investigation. First, all the recorded comorbidities were independently run in bivariate cox regression and those with P-value <0.25 were used for the multivariate regression at a later stage.

On the contrary, since the study is retrospective in nature, it completely relied on secondary data source in the form of medical records. Such data source could have incomplete records and missing information. Another drawback common to survival analysis in general is the situation where the treatment outcomes of defaulters and those referred to another institution could not be traced. These groups were simply left out from the analysis.
Conclusions And Recommendations

Conclusion

The study was conducted to investigate predictors of undesirable treatment outcomes and identify factors associated with undesirable treatment outcomes for children admitted with SAM at Yekatit 12 hospital within a time frame of 4 years (2013 – 2016). Accordingly, the study found out that the main predictors of undesirable outcome for SAM cases admitted to Yekatit 12 hospital in the specified time frame were HIV and sepsis.

The study also revealed that the overall treatment outcomes were not in line with the SPHERE standard recommendation. The observed mortality rate was higher than what is recommended in the standard and the cure rate was also well below the minimum rate recommended by the SPHERE standard.

Recommendation

Accordingly, rigorous HIV screening should be carried out for every severely malnourished child to be admitted at the ward.

Since the presence of HIV and sepsis are found out to be the greatest contributors towards undesirable treatment outcomes, appropriate diagnosis and management should be put in place with special attention to those diagnosed with sepsis.

It should be noted that additional resources and special attention should be dedicated to SAM cases within the first 7 days of admission for the reason that the mortality rate is observed to be higher in this time period.

Abbreviations

CI, Confidence Interval; EDHS, Ethiopian Demographic Health survey; HIV, Human immunodeficiency Virus; HR, Hazard ratio; MAM, Moderate acute malnutrition; MUAC, mid upper arm circumference; SAM, severe acute malnutrition; SDG, sustainable development goal; SPHERE, Social and Public Health Economics Research Group; TFP, therapeutic feeding program; WFH or L, weight for height or length; WHO, World health organization

Declarations

Ethics approval and consent to participate

Ethical clearance and approval were obtained from Institutional Review Board of Addis Continental Institute of Public Health and Yekatit 12 hospital for retrieving patients’ medical cards. The study is a retrospective chart review and uses secondary data sources, therefore there was no direct contact with patients and the data were used anonymously by using unique identity numbers instead of names in order to protect patient privacy.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.
Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors have made substantial intellectual contribution to the conception and design of the study and also in the acquisition, analysis and interpretation of data. Moreover, the authors have been involved in drafting the manuscript, and agree to be accountable for all aspect of the work. All authors have read and approved the manuscript.

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References

1. UN Millennium Project | Goals, targets & indicators [Internet]. Millennium Project. 2006 [cited 2016 Oct 16]. Available from: http://www.unmillenniumproject.org/goals/gti.htm
2. Isanaka S, Villamor E, Shepherd S, Grais RF. Assessing the impact of the introduction of the WHO Growth Standards and weight-for-height Z score criterion on the response to treatment of severe acute malnutrition in children: secondary data analysis. Pediatrics. 2009 Jan;123(1):e54–9.
3. WHO/UNICEF. WHO 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 | ENN [Internet]. 2009 [cited 2016 Jul 12]. Available from: http://www.ennonline.net/whogrowthstandardssam
4. WHO | Children: reducing mortality [Internet]. WHO. 2019 [cited 2019 Sept 19]. Available from: http://www.who.int/mediacentre/factsheets/fs178/en/
5. Ahmed MM, Hokororo A, Kideny BR, Kabyemera R, Kamugisha E. Prevalence of undernutrition and risk factors of severe undernutrition among children admitted to Bugando Medical Centre in Mwanza, Tanzania. BMC Nutr. 2016;2:49.
6. Kanan SOH, Swar MO. Prevalence and outcome of severe malnutrition in children less than five-year-old in Omdurman Paediatric Hospital, Sudan. Sudan J Paediatr. 2016;16(1):23–30.
7. Bohn JA, Kassaye BM, Record D, Chou BC, Kraft IL, Purdy JC, et al. Demographic and mortality analysis of hospitalized children at a referral hospital in Addis Ababa, Ethiopia. BMC Pediatr [Internet]. 2016 Oct 21 [cited 2016 Nov 1];16. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5073447/
8. Ethiopia Mini Demographic and Health Survey [Internet]. Central statistical Agency Addis Ababa, Ethiopia; 2019 [cited 2019 Jul 26]. Available from: https://www.google.com/?gfe_rd=cr&ei=OyOXV5qgeFjLb8AY75qQA&gws_rd=ssl&cr&fg=1#q=mini+EDHS+2019
9. The Sphere Handbook | Management of acute malnutrition and micronutrient deficiencies standard 2: Severe acute malnutrition [Internet]. [cited 2016 Oct 16]. Available from: http://www.spherehandbook.org/en/management-of-acute-malnutrition-and-micronutrient-deficiencies-standard-2-severe-acute-malnutrition/
10. Lenters LM, Wazny K, Webb P, Ahmed T, Bhatta ZA. Treatment of severe and moderate acute malnutrition in low- and middle-income settings: a systematic review, meta-analysis and Delphi process. BMC Public Health. 2013 Sep 17;13(Suppl 3):S23.
11. Gebremichael DY. Predictors of nutritional recovery time and survival status among children with severe acute malnutrition who have been managed in therapeutic feeding centers, Southern Ethiopia: retrospective cohort study. BMC Public Health [Internet]. 2015 Dec 21 [cited 2016 Nov 1];15. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4687080/

12. Bernal C, Velasquez C, Alcaraz G, Botero J. Treatment of Severe Malnutrition in Children: Experience in... : Journal of Pediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr. 2008;46:322-8.

13. Bachou, Hanifa. The challenge of improving the management of hospitalised children with severe acute malnutrition in Uganda. Univ Bergen [Internet]. 2008 Jun 3 [cited 2016 Sep 28]; Available from: http://bora.uib.no/handle/1956/3062

14. Protocol For The Management Of Severe Acute Malnutrition [Internet]. Ethiopia - Federal Ministry Of Health; 2007 [cited 2016 Oct 16]. Available from: https://www.google.com.et/?gws_rd=cr&sei=FkkDWOXPJeLX6QS_z4DADQ#q=sam+guideline+ethiopia

15. Abeje AT, Gudayu TW, Beftu YDM and BB. Analysis of Hospital Records on Treatment Outcome of Severe Acute Malnutrition: The Case of Gonder University Tertiary Hospital. Pediatr Ther [Internet]. 2016 Mar 31 [cited 2016 Aug 23];2016. Available from: http://www.omicsonline.org/pediatrics-therapeutics-abstract.php?abstract_id=70302

16. Nyeko R, Calbi V, Ssegujja BO, Ayot GF. Treatment outcome among children under-five years hospitalized with severe acute malnutrition in St. Mary’s hospital Lacor, Northern Uganda. BMC Nutr. 2016;2:19.

17. Chisti MJ, Salam MA, Bardhan PK, Faruque ASG, Shahid ASMSB, Shahunja KM, et al. Treatment Failure and Mortality amongst Children with Severe Acute Malnutrition Presenting with Cough or Respiratory Difficulty and Radiological Pneumonia. PloS ONE [Internet]. 2015 Oct 9 [cited 2016 Nov 1];10(10). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4599910/

18. Girum T, Kote M, Tariku B, Bekele H. Survival status and predictors of mortality among severely acute malnourished children <5 years of age admitted to stabilization centers in Gedeo Zone: a retrospective cohort study. Ther Clin Risk Manag. 2017 Jan 23;13:101-10.

19. Munthali T, Jacobs C, Sitali L, Dambe R, Micheo 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). Arch Public Health [Internet]. 2015 May 1 [cited 2017 Apr 28];73(1). Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4416273/

20. Treatment Outcome and Predictors of Severe Acute Malnutrition using the WHO Guideline at a Referral Hospital in Southern Ethiopia (PDF Download Available). ResearchGate [Internet]. [cited 2017 Feb 13]; Available from: https://www.researchgate.net/publication/298792662_Treatment_Outcome_and_Predictors_of_Severe_Acute_Malnutrition_using_the_WHO_Guideline_at_a_Referral_Hospital_in_Southern_Ethiopia

21. Jarso H, Workicho A, Alemsiged 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 Pediatr [Internet]. 2015 Jul 15 [cited 2017 Apr 28];15. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4502938/

22. Khatri RB, Mishra SR, Khanal V, Choulagai B. Factors Associated with Underweight among Children of Former-Kamaiyais in Nepal. Front Public Health [Internet]. 2015 Jan 29 [cited 2017 May 1];3. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4310217/

23. Ashworth A, Chopra M, McCoy D, Sanders D, Jackson D, Karaolis N, et al. WHO guidelines for management of severe malnutrition in rural South African hospitals: effect on case fatality and the influence of operational factors. Lancet Lond Engl. 2004 Apr 3;363(9415):1110–5.

24. Hassen SL, Astatkie A, Mekonnen TC, Bogale GG. Survival Status and Its Determinants among Under-Five Children with Severe Acute Malnutrition Admitted to Inpatient Therapeutic Feeding Centers in South Wollo Zone, Amhara Region, Ethiopia. J Nutr Metab. 2019 Mar 31;2019:1–9.

25. 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 [Internet]. 2010 Jan 1 [cited 2016 Jul 25];24(3). Available from: http://www.ajol.info/index.php/ejhd/article/view/68392

26. Talbert A, Thuo N, Karisa J, Chesaro C, Ohuma E, Ignas J, et al. Diarrhoea complicating severe acute malnutrition in Kenyan children: a prospective descriptive study of risk factors and outcome. PloS One. 2012;7(6):e38321.

27. Page A-L, Rekeneire N de, Sayadi S, Aberrane S, Janssens A-C, Rieux C, et al. Infections in Children
Admitted with Complicated Severe Acute Malnutrition in Niger. PLOS ONE. 2013 Jul 17;8(7):e68699.
28. medanth - Malnutrition-Infection Complex [Internet]. [cited 2017 Apr 29]. Available from: https://medanth.wikispaces.com/Malnutrition-Infection+Complex
Figure 1

Schematic representing the sampling procedure of the study. The chart shows the process of how study subjects were selected. Undesirable outcome includes death, non-respondent and failure to respond.
Figure 2
Kaplan–Meier Survival estimate among children with SAM admitted to Yekatit 12 hospital, 2013-2016