

INSTITUTE OF HEALTH

DEPARTMENT OF EPIDEMIOLOGY

ASSESSMENT OF TIME TO RECOVERY AND PREDICTORS AMONG UNDER-FIVE CHILDREN WITH SEVERE ACUTE MALNUTRITION ADMITTED AT STABILIZING CENTERS, IN METEKELE ZONE NORTHWEST ETHIOPIA: RETROSPECTIVE COHORT STUDY

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Abstract

Background: Severe acute malnutrition is defined as weight for height below minus three World health organization growth standards or middle upper arm circumference less than 115mm for a child greater than six months and/or presence of bilateral edema. It is the reason for 20% of pediatrics hospital admissions. Despite, a bilateral effort being done at outpatient and inpatient therapeutic programs, time to recovery from severe acute malnutrition remains alarming in Ethiopia. A better understanding of predictors of recovery is important to design appropriate interventions at rehabilitation centers.

Objective: To assess time to recovery and its predictors among under-five children with severe acute malnutrition admitted at rehabilitation centers in Metekele Zone, Northwest Ethiopia, 2022.

Methods: Facility-based retrospective cohort study was conducted from May 29 to June 21, 2022, among 512 under-five children with severe acute malnutrition admitted at rehabilitation centers in Metekele Zone from 2017-2021. A simple random sampling technique was used to select the samples from the registration log book. Data were collected from medical record numbers and registrations using a structured checklist. The data were entered into Epi-data and exported to STATA for analysis. A Kaplan-Meir curve was used to estimate median survival time. Cox proportional hazard regression model used to identify predictors of time to recovery.

Results: In this study, 68.38% of children recovered from severe acute malnutrition with an overall nutritional recovery rate of 6.04 per 100 children-days observation (95% CI: 5.75-7.09). The overall median time of nutritional recovery was 13days (interquartile range10-16). Children with no tuberculosis(AHR)=1.78, 95% CI:1.08-2.92), no human immunodeficiency virus (AHR= 2.98, 95% CI:1.62-5.48), absence of inpatient complication (AHR= 3.71, 95%CI:1.29-10.32), intake of F-100 (AHR= 0.37, 95% CI: 0.16-0.89), plumpy nut (AHR= 4.23, 95% CI: 1.58-11.31), and amoxicillin (AHR= 1.86 95%CI: 1.17-2.94)were significantly predictors of time to recovery.

Conclusion and recommendation: Median time of nutritional recovery was in an acceptable range, while the rate of recovery was low compared to the sphere standard. Special attention should be given to those children who had tuberculosis, HIV, inpatient complication, and did not receive (F-100, plump nut, and amoxicillin) during admission. Efforts should be strengthened to facilitate early recovery by considering the identified predictors of time to recovery.

Keywords: Northwest Ethiopia, predictor, severe acute malnutrition, time to recovery

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Acronyms and Abbreviation

AHR	Adjusted Hazard Rate
CHR	Case Fatality Rate
CI	Confidence Interval
CHR	Crude Hazard Rate
EDHS	Ethiopian Demographic Health Survey
GTP	Growth Transformation Plan
HR	Hazard Rate
HIV	Human Immunodeficiency Virus
MAM	Moderate Acute Malnutrition
MUAC	Mid-Upper Arm Circumference
HSTP	Health Sector Transformation Plan
IQR	Inter Quartile Range
NGT	Noso-Gastric Tube
NNP	National Nutritional Program
OTP	Outpatient Therapeutic Program
RUTF	Ready To Use Therapeutic Feeding
SAM	Severe Acute Malnutrition
SC	Stabilizing Center
SD	Standard Deviation
TFU	Therapeutic Feeding Unit
UNICEF	United Nation Children Emergency Fund
WFH	Weight For Height
WFL	Weight For Length
WHO	World Health Organization

CHAPTER ONE:-INTRODUCTION

1.1. Background

Malnutrition is an abnormal physiological state caused by deficiency, excess, or imbalance of individual energy and nutrient consumption(1). It includes under and over-nutrition, both of which have severe consequences on the human body structure and function with specific physical and clinical consequences (2). Childhood under nutrition is characterized by a mixture of nutritional disorders such as wasting(low weight for height), stunting(low height for age), and underweight(low weight for age) as well as micronutrient deficiency(lack of important vitamins and minerals)(3).

Based on time course under nutrition can be categorized as acute (short-term) and chronic (long-term) malnutrition. Acute malnutrition can be categorized into moderate acute malnutrition (MAM), and severe acute malnutrition (SAM) based on the severity and presence of edema. Acute malnutrition results from a recent rapid loss of weight or a failure to gain weight due to insufficient food intake, high incidence of infectious disease, inappropriate child practices, or combination(1).

Severe acute malnutrition (SAM) is defined as very low weight for length/height below minus three World Health Organization (WHO) growth standards or middle upper arm circumference, less than 115mm for a child greater than six months, or presence of bilateral pitting edema(4), which is caused by immediate, basic and underlying factors(1). SAM children who have a clinical feature of infection, metabolic disturbance, and/or failed appetite are known as complicated SAM, they require inpatient treatment initially with low-protein milk-based feeds and are discharged to continue nutritional management as an outpatient(5).

Complicated SAM children are managed at SC in three consecutive phases; the first phase (phase I), the transition phase, and phase II. In phase I, admitted SAM children were resuscitated, treated for infections, restored electrolyte balance, and prevented hypoglycemia and hypothermia on the indication. F75 milk therapeutic food is used during phase I treatment. In phase II treatment, F100 was used as much as the children could take and an additional diet is recommended until they achieved weight for height >85% and no edema for 10 consecutive days. Additionally, routine medicines of vitamin-A, folic acid, iron, antibiotics, antimalarial, measles, and deworming are used in the treatment of SAM children(4).

1.2. Statement of the problem

Globally, severe acute malnutrition(SAM) is still a serious public health problem and the leading cause of morbidity and mortality among under-five years of children(6). According to the united nation international child emergence Fund (UNICEF), WHO, and the World Bank of 2021 report revealed that globally an estimated, 149.2 million (22%), 45.4 million (6.7%), and 38.9 million(5.6%) under-five children were living with stunting, wasting, and overweight respectively, and 1.3 million (3%) were severely wasted. About, more than two-thirds and one-quarter of wasted children live in Asia and Africa respectively(7).

Ethiopian min demographic health surveys (EMDHS) of 2019 revealed that 7% of under-five children were wasted and 1% of them were severely wasted. In the Benshangule_ Gumuz region, the prevalence of stunting, wasting, and underweight were 41%, 6.1%, and 31% respectively which is higher than the national figure (8). Globally, malnutrition contributes to 50-60% of the total under-five mortality(9), with severe wasting alone accounting for 4.4% of death(10,11). The risk of death among SAM is twelve times higher than in well-nourished children (12). Every year, it is predicted that 3 million children under the age of five die as a result of SAM in the world(13), the majority of them living in South Asia and sub-Saharan Africa(14).

SAM is the major public health concern, accounting for more than half of all infant and child mortality(15), as well as the third-highest cause of under-five child mortality, with more than one-fourth of deaths, occurring during inpatient treatment (16,17). Every month, 25 000 under-five children with SAM were admitted to hospitals in Ethiopia (16), and the reason for 20% of pediatric hospital admission(18). According to sphere standards, under-five children with SAM treated in SC should be less than four weeks to recover, and alarming if it is greater than six weeks(19). However, the time of recovery from SAM among under-five children with SAM admitted to TFC is still alarming in the world. For instance, an institution-based study done in India indicates the recovery rate and median time of recovery were 46% and six weeks respectively(20). In Malawi median time of recovery from SAM was 49 days(21). A systematic review and meta-analysis study conducted in Sub-Saharan African countries indicate that the pooled recovery rate from SAM was 71.2% (22).

Even though, the Sphere standard recommended short recovery times, most studies done in Ethiopia found that the median time to recovery was high ranging from 11 days to 8.7 weeks(23,24). Likewise, institutional retrospective cohort studies have been conducted in Ethiopia reported that there were inconsistencies in the rate of recovery which range from 25.6% to 82.4% at TFCs (25,26). This indicates, that the prognosis for SAM management continues to be challenging(4) and better outcomes of inpatient intervention remain low due to co-morbidities, poor adherence to treatment guidelines, and mismanagement of the cases(27,28).

Evidence indicates that age(22) sex(29), residence(30), vaccination status(31), breastfeeding status(32), types of malnutrition(29), baseline anthropometric measurement(22), co-morbidities like HIV, pneumonia, and TB(28,29), diarrhea, malaria, anemia, shock clinical features like vomiting hypothermia, palmar pallor(33), dehydration, routine medication, special medication feeding status(26) and stabilizing centers(34) were some of the predictors for time to recovery among under-five children admitted with SAM.

WHO developed SAM management guidelines, for complicated SAM as a part of clinical guidelines in 1999 and updated in 2013, and strict adherence to these steps by health care providers can reduce CFR by 10% in an inpatient setting(4). In Ethiopia, the outpatient therapeutic feeding program (OTP) was piloted in a specific area in 2004; currently, it has been expanded to every health facility and health post in the country. With this program, services are expanded from hospital-based health care to the community-based therapeutic care (CTC) strategy, which includes community outreach, (OTP), targeted supplementary feeding programs (TSF), and inpatient treatment(35). Besides, this huge problem of under nutrition, the Ethiopian government launched the "Seqota declaration as one of the nutritional agendas to end under nutrition by 2030"(36).

Despite, a bilateral effort for the management of SAM both at OTPs and TFCs being done in the corner of the country, a hospital-based study done in Ethiopia revealed an alarming low recovery, and a high mortality rate was reported 46% and 29% respectively(37). As one of the emerging and pastoralist regions, Benshangul Gumuze bears a high proportion of malnutrition in Ethiopia. So far, studies have been undertaken to assess the time of recovery and predictors among hospitalized SAM children(30,31,38,39). However, the majority of

these studies were limited to children above the age of six months and single stabilizing centers.

Furthermore, since the endorsement of TFCs at Metekele Zone health institutions, time to recovery and major predicting factors for time to recovery is not well addressed. In addition, most of the previous studies used a logistic regression model to identify factors associated with recovery rate from SAM, which lack the survival time and censored observations. Generating local evidence for time to recovery is highly important to meet the goal of therapeutic feeding centers.

Additionally, evaluating and auditing the recovery rates of malnourished children at a therapeutic center are very useful for countries to identify the gaps and measure the effectiveness of center-based management of SAM to develop the best interventional strategy in the future. Therefore, this study aims to assess time to recovery and its predictors among under-five children admitted with SAM in SCs at public health facilities in Metekele Zone, Northwest Ethiopia.

1.3. Significance of the study

The finding of this study will help the health centers, hospitals, Zonal and regional health officials for planning health strategies, and interventions for child health. It will help health care providers to recognize main predictors, prioritize intervention areas and implement key interventions, and improve care for continual reduction of morbidity and mortality among under-five children. Moreover, the result of this study will also offer input for a non-governmental organization working in this area and for the researcher to conduct further research on the related subject.

CHAPTER TWO: LITERATURE REVIEW

2.1. Magnitude of recovery rate among under-five children with SAM

According to the international sphere standard, providing the overall therapeutic feeding program for severe acute malnutrition mortality should not exceed 10%, the default should be less than 15%, and over 75% of children should be discharged with recovery and less than four weeks to recover (19).

The finding of the study done in India indicated that the recovery rate among under-five children with SAM admitted to SC was 46.4% with the median time of recovery was six weeks (20). A study carried out in Malawi suggested that the overall median time to recovery was 49 days(21). A retrospective cohort study done on predictors of recovery from complicated SAM among under-five children admitted at Mbale Hospital, Uganda indicated that the overall recovery rate and time to recovery from SAM were 76% and 27 days respectively(40).

A systematic review and meta-analysis study conducted in Sub-Saharan African countries indicate that the pooled recovery rate from SAM was 71.2%(22). A retrospective cohort study conducted in Ghana revealed that the overall recovery rate among Hospitalized SAM children was 33.6%(41). A multicenter retrospective follow-up study in Amhara region, Northwest Ethiopia indicated that the overall recovery rate and median time of recovery among underfive children admitted with SAM were 62.13% and 16 days respectively(22). A study carried out at Felege-Hiowt Referral Hospital shows that the recovery rate of under-five children with SAM admitted in SC was 58.4% with a mean recovery of 18 days(28). A similar study done at North Shoa Zone revealed that the overall recovery rate and median time of recovery from SAM were 55.9% and 16 days(34).

Another finding of a study done in Bahir Dar city, the recovery rate and median recovery times were 51.9% and 16 days, respectively(39). A similar retrospective cohort study done in Gondar Referral Hospital reported that the overall recovery rate and median recovery rate of under-five children from SAM were 69.2% and 11 days, respectively(27). The finding of a retrospective cohort study done in Hawassa General Hospital showed that the recovery rate was 69.3% and the median time of recovery from SAM among under-five children admitted in SC was 17 days(42). A prospective cohort study conducted in Jimma Specialized Medical

Center revealed that the overall recovery rate among hospitalized SAM children was 25.6% with a median time of recovery was 26 days(25). Moreover, a retrospective cohort study conducted in Assossa General Hospital showed that the overall recovery rate among hospitalized SAM children was 65.4% with a median time of recovery was 15 days(43).

2.2. Predictors of time to recovery among under-five children admitted with SAM

2.2.1. Socio-demographic related predictors

A retrospective study conducted in Bangladeshi indicated that being female sex was increase the time to recovery from SAM(44). A study conducted and Bahir Dar revealed that being female increase the probability of getting recovery from SAM(28). Another retrospective cohort study conducted at a multicenter Hospital in Amhara region reported that being female sex was decrease the time to recovery from SAM(29). Similarly, a finding of a retrospective study conducted at Afar Referral Hospital indicated that sex was a statistical predictor of time to recovery from SAM(30).

According to retrospective studies carried out at Afar Referral Hospital, Debre-Markos, and Finote-Selam Waghimra Zone Northeast Ethiopia, and Yekatit 12 Hospital suggested that age was increase the time to recovery from SAM(30,45–47). The finding of a retrospective study conducted at Afar Referral Hospital indicated that being an urban resident decrease the chance of time to recovery from SAM(30). The finding of a retrospective cohort study conducted in the North Wollo Zone of Amhara region showed that SAM children with new admission were increased time to recovery compared to readmission of SAM children(48).

2.2.2. Clinical presentation-related predictors

A retrospective cohort study done at Addis Ababa indicated that SAM children with pale conjunctiva during admission was decrease the time to nutritional recovery rate(49). The finding of a retrospective cohort study conducted at the public Hospital of Aksum Ethiopia indicated that palmar pallor decreases the time to recovery from SAM with a medina nutritional recovery of 17 days(33). A retrospective cohort study carried out at Waghimra Zone indicated that vomiting during admission was decrease the time to recovery from SAM with a median nutritional recovery time of 16days(46). The result of a study carried out in West Ethiopia indicated that hypothermia decreased the time to recovery from SAM (50). The

finding of a retrospective cohort study done on time to recovery rate and its predictors among under-five children with SAM in SC of Gondar Referral Hospital indicates that altered temperature, at admission, and having Kawash-dermatitis were increase time to recovery from SAM(27). A study conducted at Jimma Specialized Medical Center reveled that SAM children present in shock at admission was a longer nutritional recovery time(31). Another study carried out at Tigray revealed that loss of appetite was assonated with decreased recovery rate from SAM(51).

2.2.3. Underling comorbidity-related predictors

The finding of a retrospective cohort study conducted at the Sanglah Denpasar General Hospital Indonesia indicated that under-five children with co-morbidity were significant predictors of time to recovery from SAM(52). The finding of a study conducted in Niger and Amazon suggested that under-five children with malaria at admission increased the time to recovery from SAM(53,54). Similarly, a retrospective cohort study done at Jimma Specialized Medical Center indicated that under-five children who presented with malaria at admission were delayed time of recovery from SAM(31). A similar study was done in Zambia and reported that pneumonia decreases the time to recovery from SAM(55).

A multicenter retrospective follow-up study done in selected health facilities in Amhara region, Northwest Ethiopia indicated that under-five children with pneumonia, tuberculosis, anemia, and HIV/ADIS were delayed time to recovery from SAM with a median time of recovery of 16 days(29). In addition, the findings of a retrospective cohort study conducted at Debre-Markos and Finote-Selam Hospitals showed that HIV/ADIS decreases the probability of getting recovery from SAM(45). A prospective cohort study carried out at North Gondar Zone indicated that diarrhea was delayed the time to recovery from SAM(56). The finding of a retrospective cohort study conducted at St. Paul's Hospital Millennium Medical College, Gondar Referral Hospital, and Ayder Hospital indicated that SAM children with tuberculosis and anemia were a decrease nutritional recovery rate(27,30,42).

The retrospective cohort study done on time to recovery and its predictors among under-five children with SAM conducted in Bahir-Dar indicated that children who had HIV infection was decreased recovery rate from SAM(28). The finding of a study carried out in therapeutic feeding centers, in Southern Ethiopia showed that having complications during inpatient

treatment was increase the time to recovery from SAM with a median recovery time of 33 days(26).

2.2.4. Anthropometric related predictors

The finding of a study conducted in India indicated that a better WHZ at enrolment was significantly increased the recovery rate from SAM(57). The finding of a study done in therapeutic feeding centers, in Southern Ethiopia showed that an increased MUAC and weight during admission were increased nutritional recovery rate with a median recovery time of 24 days (26). The study carried out in Yekatit 12 Hospital revealed that daily weight gain increased the recovery rate and median recovery rate of 11 days(47). The finding of the study conducted at Bahir-Dar indicated that nutritional edema was significantly associated with recovery(22)

2.2.5. Types of SAM diagnosed related predictors

The finding of research conducted in India indicated that Kwashiorkor was a significant predictor of time to recovery among under-five children admitted with SAM(53). Similarly, retrospective follow-up studies done in Amhara Region indicated that Kwashiorkor was decrease the recovery rate from SAM(22). The study carried out in Felege-Hiowt, Wolidiy, and North Shoa reported that children presented with edematous malnutrition were significantly associated with time to recovery(28,34,58). A retrospective follow-up studies done at Southern Ethiopia and Waghimra Zone indicated that marasmus was decrease nutritional recovery rate and median time to recovery of 29 days and 15 days respectively(26,46). The finding of a study conducted in Pawe Hospital on predictors of cure rate among under-five children with SAM indicated that being marasmus increase the recovery rate from SAM(38). The result of the study done in west Ethiopia shows that marasmic-Kwashiorkor increased the recovery rate from SAM(50).

2.2.6. Medication-related predictors

A retrospective cohort study done on predictors of recovery from complicated SAM among under-five children admitted at Mbale Hospital, Uganda indicated that deworming was increase the nutritional recovery rate(40). The study carried out in Yekatit 12 Hospital revealed that being not dewormed during admission decreased the recovery rate and the median time of recovery was 23 days(47).

The finding of a retrospective cohort study conducted at St. Paul's Hospital Millennium Medical College, Ayder Hospital, and Southern Ethiopia indicated that SAM children who received F100 milk were an increased recovery rate from SAM (30,42,59). The finding of a study done at SPMMC and Amhara Region showed that children who did not have a history of bottle feeding and no IV fluid infusion increased the rate of recovery from SAM(22,30).

The result of a study conducted in South Wollo Zone, Amhara Region, Ethiopia indicated that under-five children with breastfeeding status at admission were a short time of recovery from SAM(32). A retrospective cohort study conducted at a stabilization center in Southern Ethiopia reported that children who did not received special medication (IV fluid, IV antibiotic, and blood transfusion) at admission were decreased recovery rate and the median time of recovery was 24 days(42). The finding of a study done at Felege-Hiowt Referral Hospital suggested that children who took vaccinated and routine vitamin-A supplementation were an increased nutritional recovery rate(28).

Similar studies done in Aksum and Bahri-Dar city indicated that receiving a Plumpy nut during admission decreased the time to recovery from SAM with a median recovery time of 14 days(33,39). The study conducted at Pawe General Hospital indicated that feeding through nasogastric decreased the recovery rate from SAM(38). The finding of a retrospective cohort study conducted at Debre-Markos and Finote-Selam Hospitals showed that folic acid supplementation was an independent decreased the time to recovery from SAM (45). The result of a retrospective cohort study done at JUMC indicated that intake of amoxicillin increased the speed of time to recovery from SAM(31).

2.2.7. Health facility-related predictors

A systematic review and meta-analysis of observational studies conducted in Sub-Saharan Africa indicated that being treated in Health Center was independently associated with time to recovery from SAM (48). A Multicenter Prospective Cohort Study conducted in East Amhara Hospitals reported that being admitted to Referral Hospital decreased the time to recovery compared to a General Hospital(60). The finding of a study done in therapeutic feeding centers, in Southern Ethiopia indicated that stabilizing centers also decreased the time to recovery from SAM with a median time of recovery 27 days (66).

2.3. Conceptual Framework

The following conceptual framework was developed after a review of pertinent literature. In the literature review, different characteristics were mentioned as factors for time to recovery among under-five children admitted with severe acute malnutrition. The factors were categorized as socio-demographic, anthropometric, types of SAM diagnosed, clinical condition, comorbidity, medication, and health facility-related variables in the conceptual framework. Each of the factors with its constructs is linked with time to recovery as well some of them are related to each other as seen by the direction of linkage.



Key _____ Direct association between dependent and independent variables -----> Indirect association among predictors variables

Figure 1:-Schematic presentation of a conceptual framework to assess time to recovery and its predictors among U-5 children with SAM admitted at retaliation centers, in Metekele Zone, NW Ethiopia, 2022.

Source: Adapted from different literatures(27–29,31,39,42,46,47,49,52).

CHAPTER THREE: OBJECTIVES

3.1. General objective

To assess time to recovery and its predictors among under-five children with severe acute malnutrition admitted at rehabilitation centers from January 1st, 2017, to December 30, 2021, in Metekele Zone, Northwest Ethiopia, 2022.

3.2. Specific objectives

- To estimate time to recovery from SAM among under-five children with severe acute malnutrition admitted at rehabilitation centers from January 1st, 2017 to December 30, 2021, in Metekele Zone, Northwest Ethiopia, 2022.
- To identify predictors of time to recovery among under-five children with severe acute malnutrition admitted at rehabilitation centers from January 1st, 2017 to December 30, 2021, in Metekele Zone, Northwest Ethiopia, 2022.

CHAPTER FOUR: METHODS AND MATERIALS

4.1. Study area and period

The study was conducted at Metekele Zone public health facilities Benshagul-Gumuz Region, which is located 540 km from Addis Ababa, the capital city of Ethiopia. According to the census 2007 population projection, Metekele Zone has an estimated total population of 485,118 in June 2022. Of those, 78, 330 were children under the age of five years. According to Metekele Zone Department annual report, there were eight rehabilitation and 168 OTP centers in the Zone. The pediatric ward has an isolated room for therapeutic feeding of severe acute malnutrition. Both the SCs and OTP centers use standard management protocols for treating children with severe acute malnutrition. All SAM cases with comorbidities and poor appetite were admitted to TFC for in-patient management, whereas those diagnosed with SAM without co-morbidities and having good appetite were linked to outpatient management. After inpatient management, those who fulfilled discharge criteria were linked to a community-based feeding program for follow-up. Data were collected from May 29/2022 up to June 19/2022.



Figure 2:-Map of the study area Metekele Zone, Northwest Ethiopia, 2022.

4.2. Study design

Facility-based retrospective cohort study design was employed.

4.3. Population

4.3.1. Source population

All under-five children with severe acute malnutrition admitted at rehabilitation centers at public health facilities, in Metekele Zone from January 1st, 2017, to December 30, 2021.

4.3.2. Study population

All eligible randomly selected under-five children with SAM admitted at rehabilitation centers for care at selected public health facilities, in Metekele Zone from January 1st, 2017, to December 30, 2021.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

All under-five children with SAM treated at rehabilitation centers from 2017-2021 at selected public health facilities diagnosed; by WFH/L <-3 Z score or MUAC <115 mm with length > 65 cm for children greater than six months or presence of bilateral pitting edema and have a complication. Under-five children diagnosed with severe acute malnutrition and failed appetite test were also included in the study.

4.4.2. Exclusion criteria

Under-five children with SAM who were admitted at rehabilitation centers, but whose records were incomplete such as (admission and discharge date, anthropometric data, and treatment outcomes). Similarly, those SAM children whose cards were lost at the time of data collection.

4.5. Sample size determination, sampling technique, and procedures

4.5.1. Sample size determination

The sample size was determined by using the Schoenfeld formula for survival analysis in STATA Version 15 by considering the following assumptions:-

Parameters

- I. Significance level α (two-sided) =0.05, Z(α /2)=1.96
- II. Power = 80%; β =0.2, Z(β)=0.842

- III. HR = Hazard ratio for the predictors variable from previous studies.
- IV. E = Number of an event (recovery) from previous studies
- V. P = Proportion of variability among covariates (for 1:1 allocation) = 0.5
- VI. Finally, 10% non-response rate (NRR) for an incomplete chart was added.

Sample size
$$=\frac{\text{Event}}{\text{Probablity of event}}$$
 (61)

Event =
$$\frac{(Z\alpha/2 + Z\beta)^2}{(\ln(HR))^2 P(1 - P)}$$

Table1:-Sample size was calculated by using STATA version 15 for predictors of time to recovery among U-5 children with SAM treated at rehabilitation centers, in Metekele Zone, NW Ethiopia, 2022.

No	Predictor variables	Parameters			Sample	NRR	Final sample	Referen	
		Ζα	Ζβ	AHR	R	size	(10%)	size	ce
1	Anemia(yes/no)	95%	80%	1.36	0.692	480	48	528	(27)
2	Tuberculosis(yes/no)	95%	80%	1.38	0.693	439	44	483	(42)
3	Use of amoxicillin(yes/no)	95%	80%	1.54	0.73	231	23	254	(31)
4	Breastfeeding status at	95%	80%	1.42	0.754	339	34	373	(32)
	admission(yes/no)								

4.5.2. Sampling Technique and Procedures

The data were abstracted from one General Hospital and three selected Health Centers. Initially, the General Hospital was selected purposively and three Health Centers were selected by using a lottery method. The sample was allocated proportionally for the randomly selected stabilizing centers. The sample was allocated by using the formula

$$ni = \left(\frac{n}{N}\right)Ni$$

Where ni = Sample size from each of four public health facilities

n = Total sample size that is selected for the study

Ni= Total registered SAM children in each health facility during the study period

N= Total SAM children admitted to SCs in four public health facilities.

For Mandura HC: n=66/810*528=43

Manbuk HC:	n=84/810*528=55
Bullen HC:	n=98/810*528=64
PGH:	n=562/810*528=366

The sampling frame was prepared to form each selected rehabilitation center by identifying the eligible children with SAM from the registration logbook. Then a computer-generated simple random sampling technique was used to select SAM children from the charts. Finally, by using patient medical record number from the therapeutic feeding registration book, an individual card was retrieved from the card room.



(Key: HC: health center, GHP: general hospital, PPA: population proportion allocation, SRS: simple random sample, SCs: stabilizing centers, SAM: severe acute malnutrition)

Figure 3:-Schematic diagram of sampling procedures to assess time to recovery and its predictors among U-5 children with SAM admitted at rehabilitation centers in Metekele Zone, NW Ethiopia, 2022.

4.6. Data Collection Procedures

Data were collected by using structured data extraction tools, which were adapted from standard treatment protocol for the management of severe acute malnutrition(4), SAM registration logbook, SAM monitoring multi-chart, and reviewing different kinds of literature. The data extraction checklist was prepared based on routine data registration protocol using the standardized entry. The checklist format consists of socio-demographic-related data, admission categories, and anthropometric measurements, types of SAM, clinical and co-morbidities, types of feeding, medication-related data, and health facility-related variables.

Four data collectors and two supervisors who had training and experience on SAM were recruited for data collection and supervision. The data was extracted from randomly selected under-five children with SAM medical records and registers documented from January 1, 2017, to December 30, 2021. The starting point for retrospective follow-up was the time from the first under-five children with SAM admission date and the endpoint was the date of time to recovery or censored (death, defaulted, medical transfer, and non-responded).

4.7. Study Variables

4.7.1. Dependent Variable

The dependent variable in this study was time to recover from severe acute malnutrition.

4.7.2. Independent Variables

The independent variables of the study were; socio-demographic (age, sex, and residence), admission categories (new and readmission), clinical characteristics (vomiting, dehydration, shock, hypothermia, palmar pallor, and dermatitis), types of SAM diagnoses(marasmus, kwashiorkor, and marasmus-kwashiorkor), anthropometric measurement(weight, height, MUAC, and edema), co-morbidities(HIV, TB, malaria, diarrhea, pneumonia, and anemia), types of medication(F-75, F-100, breastfeeding, NGT feeding, routine antibiotic (amoxicillin, vitamin A, folic acid, deworming, antimalarial, and vaccination status), special antibiotic (IV antibiotic, IV fluid, and blood transfusion) and Health facility related variables(hospital and health centers).

4.8. Operational Definition

Time to recovery: Defined as the length of time from the start of treatment to the time a child was discharged with recovery(29).

Recovery: A child older than 6 months is declared recovery when children free from medical complications, edema and achieved sufficient weight gain (WFH \geq -3Z score and MUAC \geq 125mm. A cure is declared for infants less than 6 months old when it is clear that he/she is gaining weight on breast milk alone after the supplemented suckling technique has been used, there is no medical problem(4).

Survival time: defined as the measured follow-up of time from the first admission up to occurrences of the event(29).

Censored: defined as those SAM children, who died, defaulted, medical transferred to another treatment center or did not respond to treatment(29).

SAM: defined as a weight for height below -3 z scores of the median WHO growth standards or presence of bilateral pitting edema or mid-upper arm circumference < 115 mm for a child \geq 6 months age(4).

Defaulted: defined as children that are absent for two consecutive weighings (two days in inpatient)(4).

Non-responded: A patient who could not meet the discharge criteria after 42 days of inpatient management(24).

Stabilization Center: is a place where children with SAM along with medical complications and poor appetite are treated(39).

Incomplete record: under-five children with SAM admitted to stabilizing centers with not complete records, such as; age, admission and discharge date SAM type, and treatment outcomes (46).

Length of stay: The number of days the child stayed in the SCs from admission until the child develops an event of interest (recovery) or censored(46).

Co-morbidity/complication at admission – co-existence of other diseases (s) with severe malnutrition when the patient is admitted to the SCs or manifestation of the new disease(s) on the underlying severe malnutrition during the first 24hrs of patient's admission to the hospital(4).

Co-morbidity/complication after admission – the manifestation of the new disease(s) on the underlying severe malnutrition after the first 24hrs of the patient's admission to the hospital(4).

New admission: Patients that are directly admitted to in-patient care to start the nutritional treatment (5).

Vital sign classification: Categorical variables for temperature, respiratory rate, and pulse rate were created from admission measures using cut-offs defined by levels that would imply a definite need for urgent therapeutic intervention(62).

4.9. Data Processing and Analysis

Data were checked for its completeness and entered into Epi data manager version 3.1, then exported to STATA version 15 for cleaning, coding, and analysis. During the analysis, recovery was considered a failure variable, and all others were considered censored observations. Summary measures such as frequencies, percentages, rates, mean, standard deviation, incidence density, and median were calculated. The Kaplan-Meier (KM) survival method was applied to estimate the median time of recovery at a given time. Log-Rank test was used to assess for a statistically significant difference in the median time of recovery between categories of variables. Cumulative survival probability at certain time intervals was estimated using a life table.

Cox proportional hazard model was carried out to identify predictors of time to recovery among under-five -children with SAM. All variables with a p-value of less than or equal to 0.25 in the bi-variable cox regression analysis were exported to the final multivariable Cox regression analysis. A variable with a p-value less than 0.05 with a corresponding 95% CI was considered a significant predictor in this study.

The Cox proportional hazard assumption was checked by using graphical representation (loglog plot) and the Schoenfeld residuals test. A graphical presentation of categorical variables was parallel and the Schoenfeld residuals test (Global test X^2 (16) =17.1, p-value=0.38 and detailed Schoenfeld residual test met the assumption (Annex IV). Final Nelson-Aalen cumulative hazard function against Cox Snell residual plot test was used to check model adequacy (V). The predict command was used to generate the Cox-Snell residuals from the model. At the end, the Nelson-Aalen cumulative hazard function and the variable can compare the hazard function of the diagonal line. It is shown in the graph that the hazard function follows the 45-degree line closely over time. Hence, it was possible to conclude that the final model fits the data well.

4.10. Data Quality Management

Data quality was assured by careful designing of data abstraction tools, recruitment of data collectors, and supervisors who have previous experience. The data collection checklist was

pretested at Jawi hospital on 26 randomly selected records (5% of the sample size) one week before the actual study and amendments were taken to the checklist based on pretest findings. The records have also reviewed both baseline and follow-up for completeness, and then eligible SAM cards were identified by their MRN with the help of data collectors.

Two days of training were given for both data collectors and supervisors on data collection tools and data collection procedures. Strictly, follow-up and supervision were carried out during data collection by the principal investigator, and feedback was given on a daily base. After completion of the data, the principal investigator and the supervisor daily checked the completeness, accuracy, and consistency of each questionnaire. Finally, data entry validation was done by using the Epi-Data manager version 3.1 software.

4.11. Ethical Consideration

Ethical clearance was obtained from the Ethical Review Board (ERB) of Jimma University Institute of Health (JUIH). A letter of support was presented to Zonal health department and Health Facilities to get permission. Then, the objective of the study was explained to the respective bodies as well as data collectors. In ordered to ensure the confidentiality of the study participants; their names and other identifiers were not used in the data analysis. In addition, the name of patients, physicians, and other health care professionals who examined the patient would not be recorded in the data abstraction format and all the questionnaires were handled confidentially.

4.12. Dissemination Plan

The result of the study was presented and submitted to Jimma University, faculty of public health department of epidemiology as partial fulfillment of Masters of Public Health in Epidemiology. The finding will be reported to ZHD, district office, Hospital, and health centers. In addition, efforts will be made to publish the paper in an internationally reputable journal.

5. RESULTS

5.1. Socio-demographic characteristics

Among 528 randomly selected under-five children with SAM admitted at rehabilitation centers during the study period, 97 %(n=512) of the participant had a complete record. Thus, the rest of few, 3 %(n=16) with incomplete records were excluded from the analysis. Of those 16 were excluded (13 had incomplete data and three patient charts were lost during data collection).

Among the total records, above two-thirds (69.7 %, n=357) were obtained from General Hospital and the rest from health centers. Of the total, one-thirds (33.79%, n=173) of children admitted with SAM were found in the age group of 12-23 months and more than half (64.45%, n=330) of children were from rural areas. The mean age of the study subject was 21 months with a standard deviation (\pm 13.8) month (Table 2).

Table 2: Baseline socio-demographic characteristics of U-5 children with SAM admitted at rehabilitation centers in public health facilities, Metekele Zone NW Ethiopia, 2022.

Variables	Characteristics	Frequency	Percent
Gender	Male	260	50.78
	Female	252	49.22
Age	0-5 months	30	6.05
	6 -11 months	87	16.80
	12-23 months	173	33.79
	24-35 months	101	19.73
	36-47 months	75	14.65
	48-59 months	46	8.98
Residence	Urban	182	35.55
	Rural	330	64.45
Health facility	Hospital	357	69.73
	Health centers	155	30.27

Regarding admission characteristics of SAM children, the majority 93.36 %(n=478) of the children failed an appetite during admission, 89.84 %(n=460) of them had no history of bottle-feeding, and more-than half (61.52% n=315) had breast-feeding.

5.2. Clinical presentation and co-morbidity-related characteristics

Concerning co-morbidity more than three-fourth (76.95% n=394) of severe acute malnutrition children had at least one complication during admission (Figure 4).



Figure 4: Major medical complications among U-5 children with severely acute malnutrition admitted at rehabilitation centers in public health facilities, Metekele Zone, NW Ethiopia, from January 1st, 2017 to December 30, 2021.

A significant proportion of children had deranged vital signs during admission. Of the total, more than half (69.14% n=158) of admitted children with SAM had altered respiratory rate during admission, and 15.82 %(n=81) children presented with altered body temperature. More than one-thirds (39.45% n=202) of children with SAM had vomiting, 10.94 %(n=56) had hypoglycemia, and 1.95 %(n=10) were presented with shock (Table 3).

Table 3: E	Baseline o	clinical	presentation	of U-5	children	with	SAM	admitted	at	rehabilita	ition
centers in	public he	alth faci	ilities, Metek	ele Zon	e, NW E	thiopi	a, 202	2.			

Variables	Characteristics	Frequency	Percent
Vomiting	Yes	202	39.45
	No	310	60.55
Hypoglycemia	Yes	56	10.94
	No	456	89.06
Temperature	Altered	81	15.82
	Normal	431	84.18
Pulse rate	Altered	89	17.68
	Normal	423	82.62
Respiratory rate	Normal	354	69.14
	Altered	158	30.86
Level of conscious	Conscious	481	93.95
	Impaired	31	6.05
Palmar pallor	Present	57	11.13
	Absent	455	88.87

Conjunctiva	Pink	441	86.13
5	Pale	71	13.87
Dehydration	Yes	44	23.28
	No	144	76.72
Shock	Yes	10	1.95
	No	502	98.05
Skin lesion	Present	45	8.79
	Absent	467	91.21

Key (Altered: bradycardia or tachycardia for respiratory and pulse rate), (alter: hypothermia or hyperpyrexia for temperature)

During the follow-up, $9.77 \ \%(n=50)$ of children admitted with SAM developed inpatient complications. Pneumonia 27 (5.27%) and malaria 11 (2.15%) were the leading common complications after admission.

5.3. Anthropometric and types SAM-related characteristics

Concerning anthropometric measurement at admission, more than half (56.45% n=289) of SAM children were WFH less than -3 Z-scores. The mean and SD of MUAC at admission were 104.3(\pm 28.2) mm respectively. Regarding types of admitted SAM children, more than half (58.39% n=299) were marasmus, whereas 21.68 %(n=110) and 20.31 %(n=103) of children were diagnosed as marasmic-kwashiorkor and kwashiorkor, respectively (Table 4). Table 4: Baseline nutritional status and types of SAM among U-5 children admitted with SAM at rehabilitation centers in public health facilities, Metekele Zone, NW Ethiopia, 2022.

Variables	Characteristics	Frequency	Percent
Nutritional edema	Yes	213	41.61
	No	299	58.39
Grade of edema	Grade one edema	13	6.10
	Grade two edema	45	21.13
	Grade three edema	155	72.77
MUAC	<115mm	345	67.38
	≥115mm	137	26.76
WFH z-score	Z score <-3	289	56.45
	Z score \geq -3	223	43.55
Types of SAM	Kwashiorkor	103	20.31
	Marasmus	299	58.20
	Marasmic-Kwashiorkor	110	21.68
Types of admission	New	451	88.09
	Re-admission	61	11.91

5.4. Medication-related characteristics

Of the total children enrolled, the majority (94.14% n=482) of children admitted with SAM received formula milk F-75, and nearly, three-fourth (70.12% n=359) of them received F-100 formula milk. Of the study participants, 363 (70.90%) of them received the medication orally and the rest 29.10 %(n=149) took it through a nasogastric tube. Nearly three-fourth (71.09% n=364), and more than half (55.66% n=285) of under-five children admitted with SAM received amoxicillin and Vitamin-A, respectively (Table5).

Table 5: Nutritional therapy and medication distribution for U-5 children admitted with SAM at rehabilitation centers in public health facilities, Metekele Zone, NW Ethiopia, 2022.

Variables	Characteristics	Frequency	Percent
F-75 formula milk	Yes	482	94.14
	No	30	5.86
F-100 formula milk	Yes	359	70.12
	No	164	29.88
Means of feed	Orally	363	70.90
	NGT	149	29.10
Plumpy nut	Yes	360	70.31
	No	152	29.69
Vitamin A	Yes	285	55.66
	No	277	44.34
Deworming	Yes	202	39.39
	No	310	60.61
Folic acid	Yes	331	64.65
	No	181	35.35
Zink sup	Yes	182	35.55
	No	330	64.45
Antimalarial	Yes	79	15.43
	No	433	84.57
Amoxicillin	Yes	364	71.09
	No	148	29.91
IV antibiotic	Yes	495	96.68
	No	17	3.32
Resomal	Yes	175	33.18
	No	337	65.82
Blood transfusion	Yes	34	6.64
	No	478	93.36

5.5. Time to recovery of children with severe acute malnutrition

This study found that a total of 512 SAM children were followed for different periods for a minimum of one week and a maximum of 6.2 weeks between January 1^{st} 2017 to December 30^{th} 2021. In this study, 350 children recovered from SAM, making it an overall recovery rate of 68.36 % (95% CI: 64.32-72.40) while, 162(31.64%) SAM children were censored during the observations (Table 6).

In addition, the total times at risk for 512 under-five SAM children was 5479 days of observation. They had an overall incidence density rate of nutritional recovery was 6.4(95%:5.75-7.94) per 100 child-days of observation. Thus, the cumulative probability of recovery from SAM at 1st, 2nd, 3rd, and 4th weeks were 96%, 43%, 10%, and 0.3%, respectively (Table 7).

Moreover, the overall median time taken for recovery determined by Kaplan-Meier estimation in the entire cohort was 13days (IQR=10-16) (Figure 4), and the median length of stay in the rehabilitation centers was 10 days (IQR: 6-14).

Table 6: Performance indicators for children with SAM admitted at rehabilitation centers in public health facilities, Metekele Zone, NW Ethiopia, 2022.

Performance	Metekele Zone public health facilities	Sphere project reference		
indicators		Acceptance	Alarming	
Recovery rate	68.36%	>75%	<50%	
Defaulted rate	17.97%	<15%	>25%	
Death rate	10.94%	<10%	>15%	
Average LOS	11days	<28days	>42 days	

Life Table analysis shows that the cumulative probability of nutritional recovery rate was 96%, 43%, 10%, and 0.3% at weeks 1, 2, 3, and 4, respectively. This indicates the probability of recovery decreases as the length of stay increases and vice versa (Table 7).

Interval	Entering	Number	Number	Number	Proportion	Proportion	Cumulative
start	interval	censored	exposed	recovered	not	recovered	proportion
time			to risk		recovered		recovered
0-6	512	115	454.5	19	0.04	0.96	0.96
7-13	378	38	359	197	0.55	0.45	0.43
14-20	143	7	139.5	108	0.77	0.23	0.10
21-27	28	0	28	18	0.64	0.36	0.03
28-34	10	1	9.5	6	0.63	0.37	0.01
35-41	3	1	2.5	0	0.00	1.00	0.01
>=42	2	0	2	2	1.00	0.00	0.00

Table 7: Life table analysis for children with SAM managed at rehabilitation centers in public health facilities, Metekele Zone, NW Ethiopia, 2022.

As shown in the figure below, the Kaplan Meier survival curve decreases stepwise during the stay at rehabilitation centers (Figure 4).



Figure 5: Overall Kaplan-Meier survival estimation of time to recover among U-5 children with SAM admitted at public health facilities, Metekele Zone, NW Ethiopia, 2022.

5.6. Comparison of survival time for predictor variables

As shown in the table below, there was a significant difference in the median time of nutritional recovery among predictor variables. The highest median time of recovery difference was observed between children who developed inpatient complications and those who did not have a complication that was 25 days and 12 days respectively (Table 8).

Table 8: Median nutritional recovery time and log-rank tests across significantly predictor variables among U-5 children with SAM admitted at rehabilitation centers in public health facilities, Metekele Zone, NW Ethiopia, 2022.

			Median rec	covery time	Log-rank(X ²)	
Variables	Characteristic	Number	Estimate	IQR	test	P-value
ТВ	Yes	23	18	14-25	10.89	0.001
	No	489	12	10-16		
HIV	Yes	19	18	15-28	12.74	< 0.001
	No	493	12	10-16		
Inpatient	Present	50	25	16-31	17.87	< 0.001
complication	Absent	462	12	10-16		
Intake of F-100 milk	Yes	359	12	10-16	11.0	< 0.001
	No	153	15	10-22		
Intake of plumpy nut	Yes	360	12	10-16	15.94	< 0.001
	No	152	18	13-31		
Amoxicillin	Yes	364	12	10-15	20.78	< 0.001
	No	148	19	13-25		

(IQR: inter quartile range, X²: Chi square test)

5.7. Predictors of time to recovery from severe acute malnutrition

Bi-variable Cox proportional hazard regression was performed for each independent variable along with the dependent variable. During bi-variable analysis, 16 variables with a p-value of less than 0.25 were entered into multivariable cox regression analysis. Accordingly, residence, nutritional edema, history of bottle feeding, TB, HIV/AIDS, inpatient complication, intake of F-100 formula milk, intake of plumpy nut, means of feeding, intake of (vitamin-A, deworming, Zink, amoxicillin, intravenous fluid, Resomal) and blood infusion were significantly associated with time to recovery from SAM and entered into multivariable cox regression analysis.

After adjusting all variables for possible effects of confounding on the dependent variable, factors such as: absence of (TB, HIV/ AIDS, and inpatient complications), intake of (F-100 milk, plumpy nut, and amoxicillin) were found to be statistically significant predictors for time to recovery from SAM.

Hence, after controlling for confounding factors, those who had no HIV infection at baseline had an increased chance of recovery from SAM by 2.98 times compared to those who had HIV infections(AHR:2.98, 95% CI: (1.62-5.48), p-value<0.001). SAM children with no TB at

admission had 1.78 times higher chance of recovery when compared with those who had TB (AHR: 1.78, 95%CI :(1.08-2.92), p-value=0.023). Under-five children admitted with SAM who had no inpatient complication had 3.65 times increased time to recovery from SAM (AHR: 3.71, 95%CI :(1.32-10.44), P-value =0.013) as compared to counterparts. Besides, children taking F-100 milk after admission had 63% times higher probability of time to recover as compared to their counterparts (AHR=0.37: 95% CI :(0.16-0.89), P-value =0.027). Under-five children admitted with SAM who received plumpy nut had 4.23 times faster time of recovery as compared with children who did not receive (AHR: 4.22, 95%CI :(1.58-11.27), P-value=0.004). Similarly, children with SAM who received oral amoxicillin had a 1.86 times higher chance of time to recovery from SAM compared to their counterparts (AHR: 1.86, 95%CI :(1.17-2.94), p-value=0.009(Table 9).

Table 9: Bi-variable and Multivariable cox-regression analysis for time to recovery and its predictors among U-5 children with SAM admitted at rehabilitation centers in public health facilities, Metekele Zone NW Ethiopia from January 1st 2017 to December 30th 2021.

Variables		Survival status		P-	CHR	AHR(95%CI)	P-value	
		Recovery	Censored	value		· · · · ·		
Residence	Urban	120	62	0.02	0.78(0.62-0.97)	0.81(0.64-1.01)	0.07	
	Rural	230	100		1	1		
Tuberculosis	Yes	19	4		1	1		
	No	331	158	0.003	2.04(1.28-3.25)	1.78(1.08-2.92)	0.023*	
Bottle feeding	Yes	37	15		1	1		
	No	313	147	0.23	1.23(0.88-1.74)	1.20(0.85-1.71)	0.31	
HIV/ AIDS	Yes	12	7		1	1		
	No	338	155	0.001	2.76(1.50-5.08)	2.98(1.62-5.48)	< 0.001*	
Edema	Yes	137	76		1	1		
	No	213	86	0.23	1.14(0.92-1.429)	1.26(0.99-1.58)	0.051	
inpatient	Present	4	46		1	1		
complication	Absent	346	116	0.001	5.76(2.14-15.49)	3.71(1.32-10.44)	0.013*	
Intake of F-100	Yes	329	30	0.003	1.94(1.24-3.04)	0.37(0.16-0.89)	0.027*	
milk	No	21	132		1	1		
Means of feed	Orally	296	67	0.08	0.77(0.58-1.03)	0.97(0.69-1.35)	0.84	
	NGT	54	95		1	1		
Vitamin A	Yes	246	39	0.09	1.22(0.96-1.53)	0.88(0.67-1.19)	0.44	
	No	104	123		1	1		
Plumpy nut	Yes	334	26	< 0.001	2.53(1.53-4.20)	4.22(1.58-11.27)	0.004*	
1.2	No	16	136		1	1		
Deworming	Yes	175	27	0.08	1.23(0.98-1.54)	1.08(0.81-1.42)	0.61	
U	No	123	187		1	1		
Zink sup	Yes	141	41	0.23	1.14(0.92-1.42)	1.22(0.91-1.63)	0.19	
1	No	209	121		1	1		
Amoxicillin	Yes	328	36	< 0.001	2.49(1.61-3.84)	1.86(1.17-2.94)	0.009*	
	No	22	126		1	1		
IV-fluid	Yes	3	15	0.07	0.35(0.11-1.08)	0.32(0.09-1.05)	0.06	
	No	347	147		1	1		
ReSomal	Yes	118	57	0.16	1.17(0.94-1.46)	1.06(0.79-1.42)	0.71	
	No	232	105		1	1		
Blood transfusion	Yes	16	18	0.22	0.73(0.44-1.20)	0.88(0.53-1.48)	0.64	
	No	334	144		1	1		

(Key 1: Reference group, CHR: Crude hazard ratio, AHR: Adjusted hazard ratio, and CI: Confidence interval, * significant at p-vale <0.05)

6. DISCUSSION

According to the finding of this study, about 68.36 % of children recovered from severe acute malnutrition during the follow-up. The finding of this study is in line with studies reported from Hawassa (68%), Nekemet (66.8%), Assossa(64.5%), and Gondar (69.2%) (26,27,43,50). However, the finding of the current study is higher than studies conducted in Felege-Hiwot (51.9%), Aksum(56%), Afar (62.89%), and Bahir-Dar (58.4%)(28,30,33,39). This discrepancy between studies might be explained by variations in socio-demography, patient load, and adherence of health providers to SAM treatment guidelines.

The finding of this study is lower than the minimum humanitarian charter standards sets and the national management protocol for severe acute malnutrition at a therapeutic feeding center (>75%)(19). Moreover, it is also lower than the finding of a study conducted at East Amhara (74.5%), WagHimra Zone(80.4%), Jimma medical Center(73.1%), and Debre-Markos and Finote-Selam (77.9%)(24,31,38,45). This discrepancy might result from variations in settings, health care setup, patient load, late presentation, and the presence of comorbidities during admission. Moreover, the possible explanation might be, that high numbers of SAM children defaulted and died in the TFUs and this could be responsible for the observed low recovery rate compared to other studies. In addition, it might be the resident in the study area are pastoralist dwellers in the countryside; this makes little access to a treatment center. Similarly, the power of maternal decision-making ability for sick children at the house level has a great impact and has an indispensable variation role(2).

In the present study the median nutritional recovery time is 13 days (IQR 10-16days). This is within the recommended range of international standards set by the sphere project less than 28 days(19). This finding is consistence with a study reported from Hawassa 12 days(26). In the present study, the median nutritional recovery time is faster than studies conducted in Malawi 49 days(21), Bahir Dar 16 days (28), Jima hospital 26 days (25), Felege-Hiowt referral hospital 18 days(39), and Afar 21 days(30). This discrepancy might be due to variation in the study setting as the latter studies were conducted in referral and specialized hospitals where SAM children with the most severe SAM cases are referred and adhere to the standard treatment protocol.

However, the nutritional recovery time is longer than studies reported from different parts of Ethiopia: East Amhara, Debere-markos, Gondar, and Waghimra Zone which were 11

days(24,27,45,46). The possible discrepancy might be due to the differences in underlying comorbidities, inpatient complications, the caring practice of healthcare providers, health facility setup, and variation in the socioeconomic status of the population.

The study showed that there were significant differences in median nutritional recovery time between children with SAM who had TB, HIV/ADIS at admission, inpatient complication, and children who had not, (TB), (HIV), and inpatient complications. Likewise, there was a significant difference in the median recovery time among predictor variables like intake of F-100 formula milk, provision of plumpy nut, and provision of amoxicillin compared to counterparts. The highest median recovery time difference was observed between children who received amoxicillin and those who did not and children who had inpatient complications and who didn't have inpatient complications.

In this study, children with severe acute malnutrition who had no tuberculosis at admission were 1.78 times more likely to recover than SAM children who had tuberculosis keeping the other variables constant. This finding is in line with the study done at a multicenter level in Amhara region, St. Paul's Hospital Millennium Medical College, Gondar referral hospital, and Ayder hospital(27,29,49,59). This might be explained by the fact that the presence of malnutrition facilitates the progress of TB infection to an active disease due to its immunosuppressive effects. Moreover, tuberculosis creates a potentially lethal cycle of worsening illness and deteriorating nutritional status, ultimately resulting in a longer recovery time(63). The prognosis of SAM largely depends on the presence of complications during admission. This might be because those children's depressed humeral and cell-mediated immunity are attributable reasons for the prevalence of infection(52). This suggested that children with SAM and having additional disease needs more recovery time compared to their counterpart.

In the current study, SAM children who had no HIV/AIDS at baseline were increased time of recovery by three-fold compared to those who had HIV/AIDS infections. This finding is supported by the study conducted at Debre-Markos and Finote-Selam hospital, Amhara region, Bahir-Dar, and Assosa (28,29,43,45). Both malnutrition and HIV have a complex and multidirectional relationship that causes progressive immune system damage, with a synergistic effect. HIV/ADIS being an immune-suppressed disease it leaves SAM patients at higher risk of developing a critical illness. It increases the nutrition requirement and poor

intake of nutrients which causes poor survival. HIV/IDS also accelerates the progression of immune impairment and repeated hospitalization through increasing loss of aptitude and micronutrient deficiency following poor gastrointestinal absorption as a result of diarrhea and gastrointestinal erosion and even microorganisms could compete with patients' cells by consuming nutrients(64). Malnutrition can also increase viral replication and accelerates the progression of HIV disease by decreasing CD4 T cells, suppressing delayed hypersensitivity, and altering β -cell responses(65).

This study revealed that SAM children who had no inpatient complication had 3.71 times more likely to recover from SAM as compared to their counterparts. It is supported by a study conducted at Hawassa(26). The possible explanation is that in fact, children with severe acute malnutrition are highly susceptible to life-threatening infection, because of a secondary immunodeficiency(66). This could be explained by the fact that those children who developed inpatient complications returned to phase I treatment, which might lead to a reduction in their nutritional recovery rate(26). Co-morbidities further increase nutrient loss and nutrient requirement by the body on one hand and decrease nutrient absorption and utilization on the other hand.

In this study, severe acute malnutrition children who received plumpy nut during their treatment were 4.23 times more likely to recover compared with those who did not received plumpy nut. This is in line with studies conducted at Felege-Hiwot, Tigray, and Aksum(33,39,51). This might be explained by the fact that plumpy nut is an energy-dense mineral/vitamin-enriched food, which is equivalent to F-100 milk. It is a combination of food and medicine that is administered to children with SAM throughout the transition phase and phase II to help them gain weight (4). The possible explanation could be due to children who received plumy nut at admission might achieve rapid weight gain and fulfilling the discharge criteria early compared to those SAM children who didn't get the chance to consume plumpy nut(26). Children treated with RTUF have a higher proportion of recovery and weight gain than children who received a local diet supplemented with additional vitamins and minerals(67).

In the current study, SAM children who take F-100 milk had 63% times higher chance of time to recovery as compared to their counterparts. This is supported by a study done at St. Paul's Hospital Millennium Medical College, Ayder hospital, and Southern Ethiopia(42,49,59). This

might be explained by the fact that F-100 has higher calories 100 kcal/100 ml, which increases the daily weight gain and improves the treatment outcome of children with SAM(42). Supplementation of F-100 formula milk in the form of either undiluted or diluted has a great role in restoring the normal physiology of children with SAM after reductive adaptation and it could help to achieve catch-up growth and to gain target weight(68). This indicated that appropriate nutritional therapy in conjunction with the national SAM management protocol promotes early recovery from SAM.

In the present study, children with SAM who received oral amoxicillin had 1.86 times more likely to recover from SAM compared to their counterparts. It is in line with a study conducted at JUMC(31). It also come up with a consistence finding of a randomized, doubleblind, placebo-controlled trial study done in Southern Malawi that reported the proportion of children who received placebo had significantly lower recovery as compared to children who received antibiotics(69). It is also agreed with the recent updates of WHO and the national guideline for SAM management that recommend the provision of a broad spectrum of antibiotics like amoxicillin for all severely malnourished children regardless of signs of infection and complications. In fact, provisions of antibiotic like amoxicillin for routine treatment is active against small bowel bacterial overgrowth and leads to an increase in the progression of recovery in SAM children (4).

On the other hand, variables such as age, sex, residence, nutritional edema, MUAC pneumonia diarrhea, and anemia, and were not significantly associated with time to recovery from severe acute malnutrition even though they were significant in other previously conducted studies. A possible explanation for the difference might be the number of differences among participants with the characteristics of difference in the previous study and our study. For instance, age of less than six months was included in the current study make difference from the previous one. Additionally, the number of complications like pneumonia, diarrhea, and anemia is less than the provisions studies.

Strength and Limitations of the study

Strengths

The data were collected by health professions who had trained and experienced on severe acute malnutrition which has an essential role in ensuring data quality. This study addressed the status of stabilizing centers at multicenter level (wider geography) and used a strong model (cox-proportional hazard model) to identify predictor variables.

Limitations

The incomplete nature of secondary review data can produce potential bias associated with excluding the records of some children and a lack of control over the quality of the measurements that were made might be a setback to this study. Secondly, the difference in health professionals' skills in the management of SAM could have influenced the appropriate treatment of cases and record keeping. Since the data were, secondary data collected from medical records some important variables like parental socioeconomic characteristics, and perception of caregivers on therapeutic feeding programs might have influenced outcomes.

7. Conclusion and Recommendations

7.1. Conclusion

The finding of the current study indicated that the overall nutritional recovery rate from severe acute malnutrition managed at public health facilities in Metekele Zone was less than the minimum sphere standard and national management protocol for SAM. While the median time of nutritional recovery was within the recommended ranges of national and international standards set to manage SAM as an in-patient. Absence of (tuberculosis, HIV, and inpatient complications), and intake of (F-100, plump nut, and amoxicillin) during admission were statistical predictors of time to recovery from severe acute malnutrition.

7.2. Recommendations

Based on the above finding the following recommendations are forwarded to the concerned bodies including:

For health care providers:

- > Treatments of complications like tuberculosis and HIV/ AIDS need more attention.
- Proper management of SAM children according to national guidelines needs more attention.
- Special emphasis should be given to preventing and treating comorbidities besides therapeutic feeding.
- Efforts should be strengthened to facilitate the early recovery of children by considering the identified predictors of time to recovery.

For district health offices

Screening and early identification of children with severe acute malnutrition are enhanced through outreach programs.

For Zonal health department

> Continuous follow-up and coordination experience sharing among stabilizing centers

For regional health bureau and NGOs

- Basic and refreshment training should be provided for health care providers on the management of SAM.
- > Program supervision and monitoring need attention.

For Researcher

For the future researcher, a prospective cohort study is recommended to identify important variables like parental socioeconomic status and perception of caregivers on therapeutic feeding programs.

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ANNEX Annex I:-Information sheet and consent form

My name is ______. I am working as a data collector for the research being conducted to assess time to recovery and its predictor/s among under-five children with SAM admitted to SCs at public health facilities in Metekele Zone by <u>Hika</u> <u>Mosissa</u> who is an MPH in Epidemiology student in the Faculty of Public Health, Jimma University. I kindly request you to lend me your attention to explain to you the study and study participants.

The study Topic: Time to recovery and its predictors among under-five children with SAM admitted at rehabilitation centers in, Metekele Zone, Northwest Ethiopia, 2017-2021 G.C.

Purpose of the study: This study aims to write a thesis as a partial requirement for the fulfillment of a master's degree in Epidemiology for the principal investigator. The result of the study will be used as evidence and input for Zone health department, district health office, HCs, hospital, and NGOs working in the area.

Procedure and duration: The data collectors will collect the necessary information from patient files using structured data extraction tools to have pertinent data that is helpful for the study. The duration of data collection will be 22 days.

Risk: By participating in this research project, no risk comes to the SCs in general and the client whose records are reviewed. Information is only from the Unique SAM logbook and patient's medical registration sheet no personal contact is needed.

Benefit: The research has no direct benefit to those who have participated in this project. However, the indirect benefit of the research for the participant and all other clients in the program is great. As identifying areas of improvement and taking appropriate decisions helps to improve the service, increase access and overall effectiveness of the program and reduce the length of stays in SCs among under-five children with SAM.

Confidentiality: The information acquired from the patient file will be confidential. There will be no information that will identify in particular. The findings of the study will be general for the study community and will not reflect anything, particularly of individual persons.

The data extraction tools will be coded to exclude showing names and other personal information. No reference will be made in oral or written reports that could link participants to the study.

Contact address: This research project will be reviewed and approved by the ERB of the Institute of Health, Jimma University. If in any case, you want to know more information about the research and its undertakings, you can contact the committee through the address of the principal investigator.

Principal investigator: Hika Mosissa (BSc in PH).

Annex II Assurance of principal investigator

The undersigned agrees to accept responsibility for the scientific, ethical, and technical conduct of the research project and for the provision of required progress reports as per terms and conditions of the Faculty of Public Health in effect at the time of grant forwarded as the result of this application.

Name of the student: Hika Mosissa Biftu

 Date: 9/16/2022
 Signature: ______

 Approval of Advisor(s)

 1.
 Mrs. Zerihun Kura (MSc, Assistant professor)

 Date: _______
 Signature: _______

 2.
 Abraham Lomboro (BSc, MPHE)

 Date: ________
 Signature: ________

Annex III Data Extraction Tools

 Topic: Time to recovery and its predictors among under-five children admitted with severe acute malnutrition at stabilizing centers in Metekele Zone, Northwest Ethiopia, from January 1st, 2017, to December 30, 2021.

 Date of data collection: ____/____

 Mame of data collector: ______

 Date: __/____

 Sign:

 Name of field supervisor: ______

 Date: __/_____

 Stop: _______

 Stop: _______

Guide to data collectors: Read the variables and fill the data extraction form carefully by making an appropriate circle or writing the response on the space provided accordingly.

Section 1: Socio-demographic characteristics								
S/N <u>o</u>	Variables	Response category Skip						
101	Age	(month)						
102	Sex	1. Male2. Female						
103	Residence	1. Urban2. Rural						
104	Admission type	1. New 2. Re-admission						
105	Health facility type	1. Health center 2. Hospital						
	Section 2: Anth	ropometric characteristics at admission						
201	Weight	(Kg)						
202	Height/length	(cm)						
203	MUAC	(cm)						
204	WFH/L	(%)						
205	Nutritional edema	1. Yes 2. No If 2 go to Q#	207					
206	If yes for Q#205 grade of edema	1. Grade one edema						
		2. Grade two edema(moderate)						
		3. Grade three edema(generalized)						
207	Appetite test at admission	1. Passed appetite						
		2. Failed appetite						
208	Has a history of Bottle-feeding?	1. Yes, 2. No						
	Section 3: Severe acute n	nalnutrition diagnosed and co-morbidity						
301	Types of SAM	1. Kwashiorkor						
		2. Marasmus						
		3. Marasmic-kwashiorkor						
302	Co-morbidity at admission	1. Present2. AbsentIf 2 go to Q#	401					
303	Presences of HIV	1. Yes 2. No						
304	Presences of TB	1. Yes 2. No						
305	Presences of pneumonia	2. Yes 2. No						
306	Presences of malaria	3. Yes 2. No						
307	Presences of diarrhea	4. Yes 2. No						
308	Presences of anemia	5. Yes 2. No						
Section 4: Clinical characteristics during and after admission								

401	Vomiting		1.	Prese	nt	2. /	Absent	
402	Hypoglycemia		1.	Prese	nt	2. Ał	osent	
403	Temperature					_(in	C ⁰)	
404	Pulse rate					(cou	int per minute)	
405	Respiratory rate					(bre	eaths per minute)	
406	Level of consciousness		1.	Conse	ciou	ıs 2	2. Impaired	
407	Conjunctiva color		2.	Pink		2	2. Pale	
408	Palmar pallor 1		1.	Prese	nt	4	2. Absent	
409	Skin lesion 1		1.	Prese	nt	4	2. Absent	
410	Diarrhea		1.	Prese	nt	4	2. Absent	If 2 go to Q#414
411	If for Q,#410 is a present type of	of	1.	Wate	ry			
	diarrhea		2.	Dyser	nter	у		
412	Dehydration		1.	Prese	nt	4	2. Absent	
413	If for Q, #412 is a present degree of			Some	del	hydrati	ion	
	dehydration).		2.	2. Severe dehydration				
414	Present in shock		1.	Yes,2	2. No	0		
			Fo	llow uj	р			
415	Hemoglobin level					(g/dl		
416	HIV test	1.	React	ive2. N	Non	- react	ive 3. Unknown	
417	Malaria blood film	1.	Positi	ve	2.	Negati	ve 3. Unknown	
418	Inpatient complication	1.	Yes		2.	No		If 2 go to Q#501
419	If yes for Q#418 types of	1.	HIV					
	comorbidity developed after	2.	Tuber	rculosi	S			
	admission (possible to choose	3.	Pneur	nonia				
	more than one answer).	4.	Mala	ria				
		5.	Anen	nia				
		6.	Other	,(speci	ify)_			
	Section 5:1	Med	licatio	n relat	ted	chara	cteristics	
Therape	eutic diet							
501	Phase		1.	Phase	1			
			2.	Transit	tion	n phase		

		3.	Completed both phases
502	Intake of F-75	1.	Yes 2. No
503	Intake of F-100	1.	Yes 2. No
504	Means of feed	1.	Orally 2. Nasogastric tube
505	Plumpy nut	1.	Yes 2. No
506	Breastfeeding status	1.	Exclusive breastfeeding
		2.	Mixed
		3.	Not breastfeed
Routine	e medication		
507	Vitamin A	1.	Yes 2. No
508	De-worming	1.	Yes 2. No
509	Folic acid	1.	Yes 2. No
510	Measles supplementation	1.	Yes 2. No
511	Zinc supplementation	1.	Yes 2. No
512	Anti-malaria treatment	1.	Yes 2. No
513	Intake of amoxicillin	1.	Yes 2. No
514	Vaccination status	1.	Ever not started
		2.	Not completed
		3.	Fully vaccinated
Special	medication		
515	Intravenous antibiotics	1.	Yes 2. No
516	Intravenous fluid	1.	Yes 2. No
517	ReSomal	1.	Yes 2. No
518	Blood transfusion	1.	Yes 2. No
	Section 6:Overall summary	and	l outcome status of children with SAM
601	The outcome of the children with	1.	Recovered
	SAM at the end (discharge status)	2.	Defaulted during follow up
		3.	Died during follow up
		4.	Transferred out
		5.	Not responded for treatment
602	Discharged weight		KG

603	Discharged length/length	cm
604	Discharged MUAC	
605	Discharged date	//DD/MM/YY.
606	Discharged time	(Am/Pm)
607	Length of stay in the SC	(day)

Figures



Figure 6: Kaplan-Meier survival estimate across categories of tuberculosis at admission among U-5 children with SAM admitted at SCs at public health facilities, Metekele Zone NW Ethiopia, 2022.



Figure 7: Kaplan-Meier survival estimate across categories of HIV/AIDS at admission among U-5 children with SAM admitted at SCs at Public health facilities, Metekele Zone, NW Ethiopia, 2022.



Figure 8: Kaplan-Meier survival estimate across categories of inpatient complications among U-5 children with SAM admitted at SCs at Public health facilities in Metekele, NW Ethiopia, 2022.



Figure 9: Kaplan-Meier survival estimate across categories of receiving F-100 formula milk among U-5 children with SAM admitted at SCs at public health facilities, Metekele Zone NW Ethiopia, 2022.



Figure 10: Kaplan-Meier survival estimate across categories of receiving plumpy nut among U-5 children with SAM admitted at SCs at Public health facilities, Metekele Zone, NW Ethiopia, 2022.



Figure 11: Kaplan-Meier survival estimate across categories of receiving oral amoxicillin among under-five children admitted at SCs at Public health facilities, Metekele Zone NW Ethiopia, 2022.

Annex IV Cox-proportional hazard assumption

To apply the cox regression model, it has to be checked proportional hazed assumption effect of the covariate on the hazard ratio remains constant over time. It was tested by using a graphical presentation and Schoenfeld residual test.

 Schoenfeld residual test: it is a statistical test to assess the proportional hazard assumption which says the null hypothesis hazard rate over time is constant and if the statically Pvalue is less than 0.05 null hypothesis is not rejected and the proportional hazard assumption will be fulfilled.

. estat phtest

Test of proportional-hazards assumption

Time: Time

	chi2	df	Prob>chi2
global test	17.05	16	0.3822

2. log-log plot: for two data sets if the distance between two curves is parallel then the proportional hazard assumption is satisfied it is a graphical test of plotting -log(-log(survival)) versus time graph.



Figure 12: log-log plots for significantly predictor variables among U-5 children with SAM admitted at SCs at Public health facilities, Metekele Zone, NW Ethiopia, 2022.

Annex V Model adequacy test



Figure 13: Model adequacy for time to recovery and its predictors among U-5 children admitted with SAM at public health facilities, Metekele Zone NW Ethiopia, 2022.

Annex VI Declaration

I, the undersigned, Master of Pub	olic Health in Ep	idemiology student	declare that this thesis
my original work in partial fulfill	ment of the requ	irement for the deg	ree of Master of Public
Health in Epidemiology.			
Name: Hika Mosissa Biftu	Signature	Date	
Place of submission: Department	t of Epidemiolo	gy, Faculty of Pub	olic Health, Institute of
Health, Jimma University.			
Date of Submission:			
This thesis has been submitted wit	h the approval of	the advisor and int	ernal examiner(s).
Name of major advisor		Signature	Date
Zerihun Kura (MSc, Assistant Pro	ofessor)		
Name of Co-advisor:			
Abraham Lomboro (BSc, MPHE)			
Abraham Lomboro (BSc, MPHE) Name of internal examiner	_		