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DETERMINANTS OF TIME TO CURE FROM SEVERE ACUTE MALNUTRITION OF UNDER FIVE CHILDREN ADMITTED TO THERAPEUTIC FEEDING UNIT: IN WOLDIA GENERAL HOSPITAL, NORTH ETHIOPIA

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Abstract:

Severe acute malnutrition (SAM) is still among the major health problems especially in low and middle-income countries.According to the report of the new standards for the management of acute malnutrition in Ethiopia, every month over 25,000 children with severe acute malnutrition are admitted to hospitals, if not identified early and treated properly, these children could die (WHO, 2019). Therefore, the aim of this study is to assess time to cure and its determinants among under-five children with SAM admitted to inpatient therapeutic feeding unit.The hospital record based retrospective cohort study the data for this study is from September 2017 to August 2019. The statistical method survival analysis is appropriate to assess the stated objectives of this study. Non parametric, semi parametric and AFT models are used. The estimated median survival time of the patient was 14 days (2 weeks) with inter- quartile range 1.2 to 3.3 weeks, which is the acceptable time of recovery in the therapeutic feeding centers according to the SAM management protocol. CoxPH model and common AFT models (Weibull, lognormal and log logistic) are compared with AIC. Weibull AFT model was best fitted model. The finding of the study showed that among the accounted cures was 66.7%, which was below the recommended sphere standard which should be >75%. The median length of stay for recovered children in the ITFU of 2 weeks (14 days) is acceptable recovery time.Residence, age of the children, appetite status, breast feeding status, weight, MUAC, admission types, edema status, cough, vomiting, anemia, antibiotic treatment and vitamin A are the covariates that have significant effect on time to cure from SAM of under-five children at 5% level of significance.Addressing these risk factors for cure of children is vital to decreasing the child mortality due to malnutrition.

Key Words: Severe Acute Malnutrition, Non-Parametric, Semi-Parametric, AFT Models, Woldia General Hospital

1. Introduction:

Background:

Today's children are tomorrow's world or tomorrow's fatherthis slogan is riding a massive wave of concern throughout the world. But children, all over the world are deprived of many facilities. The growth, dynamic and continuous process expressed by the increase in body size is considered one of the most important indicators of child health. This is because stature delay is the most effective anthropometric characteristic for the determination of nutritional deviations in this people(Desai, 2018).Nutrition is a key determinant of good health and is critical for survival, good quality of life and well-being. Adequate nutrition is essential in early childhood to ensure healthy growth, proper organ formation and function, a strong immune system, and neurological and cognitive development.

Malnutrition is a pathological state resulting from a relative or absolute deficiency or excess of one or more essential nutrients.Malnutrition refers to deficiencies in a person's intake of energy and/or nutrients(Musa et al., 2014).Acute Malnutrition is classified into severe acute malnutrition1 (SAM) and moderate acute malnutrition (MAM) according to the degree of wasting and the presence of oedema. It is severe acute malnutrition if the wasting is severe (W/H < 70% or a low MUAC) or there isoedema.

According to the global nutrition report of 2018 the burden of malnutrition across the world remains unacceptably high, and progress unacceptably slow. Malnutrition is responsible for more ill health than any other cause. Children under five years of age face multiple burdens: 150.8 million are stunted, 50.5 million are wasted and 38.3 million are overweight. Meanwhile 20 million babies are born of low birth weight each year (GNR, 2018).

Therefore this study aimed to assess the survival time to cure and its determinants among under-five children with severe acute malnutrition admitted to inpatient therapeutic feeding unit (ITFU) in Woldia General

Hospital, North Ethiopia. Thus, these findings could be essential to provide evidences for decision makers, health facilities, and care providers to take measures to target those children at highest risk of slow recovery.

Statement of the Problem:

Severe acute malnutrition (SAM) is still among the major health problems especially in low and middle income countries. Globally, 52 million children of age less than five years were affected by acute malnutrition from which 17 million were severely wasted. Data shows that more than half of all wasted children in the world live in Southern Asia and Sub-Sahara African countries. In Africa, 14.0 million children under 5 are wasted, of which 4.1 million are severely wasted (UNICEF, WHO and WB, 2012). Children with severe acute malnutrition are nine times more likely to die than well-nourished children as a direct result of malnutrition itself. There are also indirect deaths as a result of childhood illnesses like diarrhea and pneumonia among malnourished children (UNICEF, 2015).

Ethiopia remains in a precarious situation where under nutrition is an underlying cause to half of its child deaths and wasting contributing to 23% of these deaths (UNICEF, 2015). According to the report of the new standards for the management of acute malnutrition in Ethiopia, Everymonth over 25,000 children with severe acute malnutrition are admitted to hospitals,if not identified early and treated properly, these children could die (WHO, 2019).

Objectives of the Study:

General Objective:

The main objective of this study is to assessthe time to cure andits determinants of under-five children with severe acute malnutrition admitted to therapeutic feeding unit in Woldia General Hospital, North Ethiopia.

Specific Objective:

- To estimate the survivorship function(time to cure)of under five children from severe acute malnutrition admitted to therapeutic feeding unit.
- To test the hypotheses of equality of the estimated survivalfunctions across groups.
- To fit the appropriate model for SAM dataset.
- To identify the possible predicators of time to cure of under five children with severe acute malnutrition admitted to therapeutic feeding unit.

2. Methodology:

Source of Data:

The study used secondary data sourcethat consider the recorded data of two years (September 2017 to August 2019)under five children admitted to the therapeutic feeding unit of Woldia General Hospital that fulfills theinclusion criteria. From the recorded 2 year data of 200 underfive children with SAM 150 patientsfulfils the inclusion criteria are included in this study.

Study Variables:

DependentVariable:

The response variable is time-to-cure from SAM is obtained by calculating the difference (inweeks) from the start of admission to the child was cured (recovered)or censored. The length of stay (Time) in admission to hospital until the cure (recovery) or censored can be coded as (1= cure,0= censored).

Independent Variables:

The independent variables (covariates)in this study include Socio-demographic variables, anthropometric measurements and history of the patient, routine medications assummarized in the following table.

Table 1: covariates of time to cure from SAM and their discriptionof underfive children

A. Socio Demographic Variables

Variable	Description	Category
Sex	Sex of the child	0= female, 1=male
Residence	Residence of the child	0= urban, 1=rural
Age	Age of children at admission	0= 12-23 months, 1= <6 months, 1= 6-11 months,3=24-35months, 4= 36-47 months,5=48-59 months
Appetite	Appetite status at admission	0=good, 1= poor
Breast	Breast feeding at admission	0=good,1=poor

B. Anthropometric measurements and history of the patient

Variable	Description	Category
MUAC	MUAC of the child at admission	0= > 12.5 cm, 1= 11.5-12.5 cm 2= <11.5 cm
Weight	Weight of the child at admission	0=3-6.9kg, 1=<3kg, 2=7-9.9kg, 3=>=10kg
Height	Weight of the child at admission	1= <60 cm, 0=60-79cm 2= >=80cm
Criteria	Admission criteria	0= only oedema 1= only wasting 2= both oedema and wasting

		3= MUAC
Types	Admission types	0= re admission ,1= new
Refer	The child where refered from	0=self 1=health center
Cough	Cough at admission	0=no,1=yes
Oedema	Oedema grade	0= no oedema 1= grade 1, 2= grade 2, 3= grade 3.
Fever	High fever	0=no1=yes,
Anemia	Severe anemia	0=no1=yes,
Pneumonia	Pneumonia	0=no1=yes,
Vomiting	Vomiting at admission	0=no1=yes,
Diarrhea	Diarrhea	0=no1=yes,
HIV	Human Immune Deficiency Virus	0=no1=yes,
TB	Tuberculosis	0=no1=yes

C. Routine medications

Variable	Description	category
Fluid	I.V Fluid	0=no,1=yes
Antibiotic	I.V antibiotic	0=no,1=yes
Amoxicillin	Amoxicillin	0=no,1=yes
Pencilline	Pencilline	0=no,1=yes
Folic acid	Folic acid	0=no,1=yes
Vitamin A	Vitamin A	0=no,1=yes
Parastamol	Parastamol	0=no,1=yes

DataAnalysis Method:

Survivaldata Analysis:

The response variable is time-to-cure from SAM was obtained by calculating the difference (inweeks) from the admission of the child in hospital until the child was cured (recovered) or censored and discharged.Cured children according to the SAM treatmentprotocol are defined as children who have weightfor height >85% and no bilateral oedema. Children wereconsidered to be cured and discharged, which is ourevent of interest, if they fulfilled the discharging criteriafor SAM.The statistical method called survival analysis is appropriate to assess the stated objectives of this study.

Non Parametric Methods:

Non parametric methods are known as distribution free methods. The aim of non-parametric estimation of the survival function is to come up with graphical summaries of the survival times for a given group of individuals considered in the study. These graphical summaries are for the hazard and the survival function. After estimating the survival function, the median and other percentiles can be obtained which help to give a more detailed analysis.Among the various non-parametric tests one can find in the statistical literature, the Mantel- Haenzeltest, currently called the "log-rank" test is used. Here is thebrief description of these Kaplan-meier and the log-ranktest that are useful for our analysis.

Semi-Parametric Methods:

A Cox model is a statistical technique for exploring the relationship between the survival time and several explanatory variables. The most commonly used regression model is the Cox-proportional hazard model. With this model the distribution for the baseline hazard function is not specified implies vary with time and that is why it is called a semi-parametric model. The Cox-proportional hazard model is a more general model in modeling the hazard and survival function because it does not place distributional assumptions on the baseline hazard (Prentice, 1992). The Cox model was introduced by Cox (1972) is written as:

$$h_i(t \mid x) = h_o(t)\exp(X_i^t \beta)$$

Where,$h_o(t)$ is the baselinehazard function; X_i is a vector of covariates and β is a vector of parameters for fixed effects.

AcceleratedFailure Time Model:

The Accelerated Failure Time model presents a way to easily describe and interpret survival regression data. It approaches the data differently than the widely used and well described Cox proportional hazard model, by assuming proportional effect of the covariates on the log-failure time rather than on the hazard function. It is an alternative if the proportional hazards assumption does not hold. Denote the survival functions of two groups by S_1 (t) and S_2(t), respectively, then the AFT model is given by:

$$S_1(t) = S_2(\phi t)$$

Where, t≥ 0 and ϕ is acceleration factor. This model implies that rate of group 1 is ϕ times as much as that of group 2. The hazard function of the i^{th} individual at time t of the AFT regression model can be written in the form:

$$h_i(t) = e^{-\eta_i} h_o(t/e^{\eta_i})$$

Where, $\eta_i = \alpha_1 x_{1i} + \alpha_2 x_{2i} +, \ldots, \alpha_p x_{pi}$ is the linear component of the model, in which x_{ji} *is* the value of the jth explanatory variable. X_j, j = 1, 2… p, for the ith individual, i = 1,2,…,n. The baseline hazard function$h_o(t)$ is the hazard of death at time t for an individual for whom the value of the p explanatory variables are all equal to zero.

3. Statistical Data Analysis:

This chapter focuses on the analysis of results about the effect of covariates on time to cure from SAM of under-five childrenadmitted to therapeutic feeding unit in Woldia General Hospital from September 2017 to August 2019. This chapter is divided into four sections. The first section presents the results ofdescriptive statistics and non parametric survival analysis; the second section,analysis of the results obtained from semiparametric survival analysis; the third section, analysis of the results obtained from parametric AFT (Weibull) regression model and the fourth section discussion of all survival analysis results .

Descriptive Statistics:

Descriptive analysis is the beginning of any statistical analysis before proceeding to more complicated models. It is mainly concerned with describing the data interms of graphs tables and percentages to understand the nature of the data. This research has taken 150 under five children with SAM who were followed up during the time from September 2017 to August 2019 at Woldia General Hospital therapeutic feeding center.

Table 2: Survival status and median survival time for under five children with SAM from September 2017 to August 2019

Cures	Censored	Total	Median Survival Time	[95% Conf. Interval]	
				LCL	UCL
100(66.7%)	50(33.3%)	150	2 weeks	1.2 weeks	3.3 weeks

The accounted cures (recovery) and censored of patients in the study period was 100 (66.7%) and 50 (33.3%), respectively. Since patients might cures beyond the study period, lost to follow up (defaulters) and might died, the observations follow right censoring mechanism, random type in particular. The estimated median survival time of the patient was 14 days (2 weeks) with inter- quartile range 1.2 to 3.3 weeks, which is the acceptable time of recovery in the therapeutic feeding centers according to the SAM management protocol.The variable included in this study is categorized into three parts for better description.These are socio-demographic characteristics, anthropometric measurements, patient history of co-morbidity and routine medication given in the therapeutic feeding center. The summary for each category is as follows.

Table 3 : Socio-demographic characteristics of the under-five children with SAM in Woldia General Hospital from September 2017 to August 2019.

Covariate	Category	Status				Median Time (Week)
		Event		Censored		
		Freq	%	Freq	%	
Sex	Female	52	69.3	23	30.7	2
	Male	48	64	27	36	2
Residence	Urban	17	68	8	32	2.5
	Rural	83	66.4	42	33.6	2
Age in Months	<6 months	29	63.2	14	36.8	2
	6-11 months	24	63	17	37	3
	12-23	25	73.5	9	26.5	2
	24-35	16	72.7	6	27.3	2
	36-47	3	42.9	4	57.1	2
	48-59months	3	100	0	0	2
Appetite	Good	27	73	10	27	2
	Poor	73	64.6	40	35.4	2
Breast	Good	51	68.9	23	31.1	2.5
	Poor	49	64.5	27	35.5	2

From the above table, 75 (50%) were female and 75 (50%) were male. Under five children with SAM that are female patients were followed up for a median survival time 2 weeks (inter quartile range 1.2 – 3 weeks) also male patients followed up for a median survival time 2 weeks (inter quartile range 1.2 – 4 weeks). From this we can observe that in order to cure from SAM sex of the patients does not make difference on the median survival time of recovery. Out of the 150 patients included, 125 (83.3%) were from rural and 25(16.7%) were from urban. This suggests that most of SAM patients of under-five children at Woldia General Hospital therapeutic feeding center come from rural areas of the zone.

The age distribution of patients of SAM is 34(22.7%) were under six months, 46 (30.7%) were between 6 and 11months, 38 (25.3%) were between 12 and 23 months and 22(14.7%) were 24 and 35 months, 7(4.7%) were between 36 and 48 months 3(2%) were between age of 49 to 58 months. From this SAM is more experienced in under age one.

Table 4: Anthropometric measurements of the under-five children with SAM in Woldia General Hospitalfrom September 2017 to August 2019

Covariate	Category	Status				Median time(wee)
		Event		Censored		
		Freq	%	Freq	%	
Weight	< 3 kg	68	66	35	34	2
	3-6.9 kg	8	80	2	20	1
	7-9.9 kg	21	63.6	11	34.4	3
	>=10 kg	3	60	2	40	2
Height	<60 cm	62	65.3	33	34.7	2
	60-79 cm	34	81	8	19	2
	>=80 cm	4	30.8	9	69.2	-
MUAC	>12.5 cm	3	50	46	50	2
	11.512.5cm	6	85.7	1	14.3	1
	<11.5 cm	91	66.4	3	33.6	3
Admission Type	Readmission	6	83.7	1	14.3	1.3
	New	94	63.7	49	34.3	1
Admission Criteria	Only Oedema	28	65.1	15	34.9	3
	Only Wasting	27	67.5	13	32.5	2
	Oedema& Wasting	10	71.4	4	28.6	3
	MUAC	35	76	18	34	2
Oedema	No oedema	84	67.2	41	32.8	2
	Grade 1	2	50	2	50	3
	Grade 2	8	72.7	3	27.3	2
	Grade 3	6	60	4	40	2
Referred From	Self	6	46.2	7	53.8	2
	Health centers	94	68.6	43	31.4	2

Majority of the patients, 137 (91.3%) were with MUAC less than 11.5 cm 7 (4.7%) were 11.5 to 12.5 cm and 6(4%) patients were with MUAC above 12.5 cm. This implies that the majority of the patients have the MUAC less than the cutoff point of the WHO SAM case identification.When we see the admission criteria 43(28.7%) wasonly oedema (kuashorkor) 40(26.7%) were only wasting (marasmus) 14(9.3%)were both oedema and wasting 53(35.3%) were by MUAC. Out of 150 patients 68.7% have weight of the less than 3kg.and also about 143(95.33%) were newly admitted children in to the center.

Table 5 : Co-morbidities of underfive children with SAM in woldia general hospital ,September 2017 to August 2019

Covariate	**Category**	**Status**				**Median Time (Week)**
		Event (cures)		**Censored**		
		Freq	**%**	**Freq**	**%**	
Fever	No	39	66.1	20	33.9	2
	Yes	61	67	30	33.0	2
Cough	No	37	61.7	23	38.3	2
	Yes	63	70	27	30.0	2
Pneumonia	No	88	66.2	45	33.8	2
	Yes	12	70.6	5	29.4	2
Vomiting	No	28	73.7	10	26.3	2.5
	Yes	72	64.3	40	35.7	2
Diarrhea	No	35	8.3	25	41.7	3
	Yes	65	72.7	25	27.8	2
HIV	No	92	68.1	43	31.9	2
	Yes	8	53.3	7	46.7	2
TB	No	94	67.6	45	32.4	2
	Yes	6	54.5	5	45.5	1.1
Anemia	No	89	65.9	46	34.1	2
	Yes	11	3.3	4	26.7	3

Among the common co-morbidities of underfive children with SAM in the area , out of 150 patients of SAM 90 (60%) were with diarhea, 91(60.7%) were with fever, 90 (60%) cough 111(74%) were with vomiting, when they are admitted to the therapeutic feeding center.

Table 6: Routine medications given for underfive children with SAM in woldia general hospital, September 2017 to August 2019

Covariates	Category	Status				Median Time (Week)
		Event		Censored		
		Freq	%	Freq	%	
IVfluide	No	13	61.9	8	38.1	2
	Yes	87	67.4	42	32.6	2
IV antibiotic	No	13	68.4	6	31.6	1.5
	Yes	87	66.4	44	33.6	2
Amoxacilline	No	16	57.1	12	42.9	2
	Yes	84	68.9	38	31.1	2
Vitamin A	No	10	66.7	5	33.3	3
	Yes	90	66.7	45	33.3	2
Folic acid	No	11	68.8	5	31.2	3
	Yes	89	66.4	45	33.6	2
Pencilline	No	31	72.1	12	27.9	2
	Yes	69	64.5	38	35.5	2
Parastamol	No	62	70.5	26	29.5	2
	Yes	38	61.3	24	38.7	2

As shown in the above table ,Out of different rutine medicatins given in the feeding center of 150 admitted underfive children in the hospital 135(90%) were taken the vitamin A nutrient as medication and 131(87.33%) take IVantibiotics, 134(89.33) takes folic acid ans so on.

Non Parametric Survival Analysis:

It is also imperative to do some basic descriptive analysis that could used as initiation to our subsequent finding. The log-rank test and Kaplan-Meier survival estimates that have been used to glance the significance of the difference among the different groups of covariates.

The Kaplan- Meier Estimate For Under-Five Children:

Survival time distributions of time-to-cure from SAM under-five children were estimated for each group using the KM method in order to compare the survival curves of two or more groups.The Kaplan-Meier curves by admission type figure 1 below the survival curve have been observed that new admittedand the re admitted in the therapeutic feeding center have difference on the experience of cure. The cumulative survival proportion of thenew admitted underfive children ishigherthanthere-admitted one.

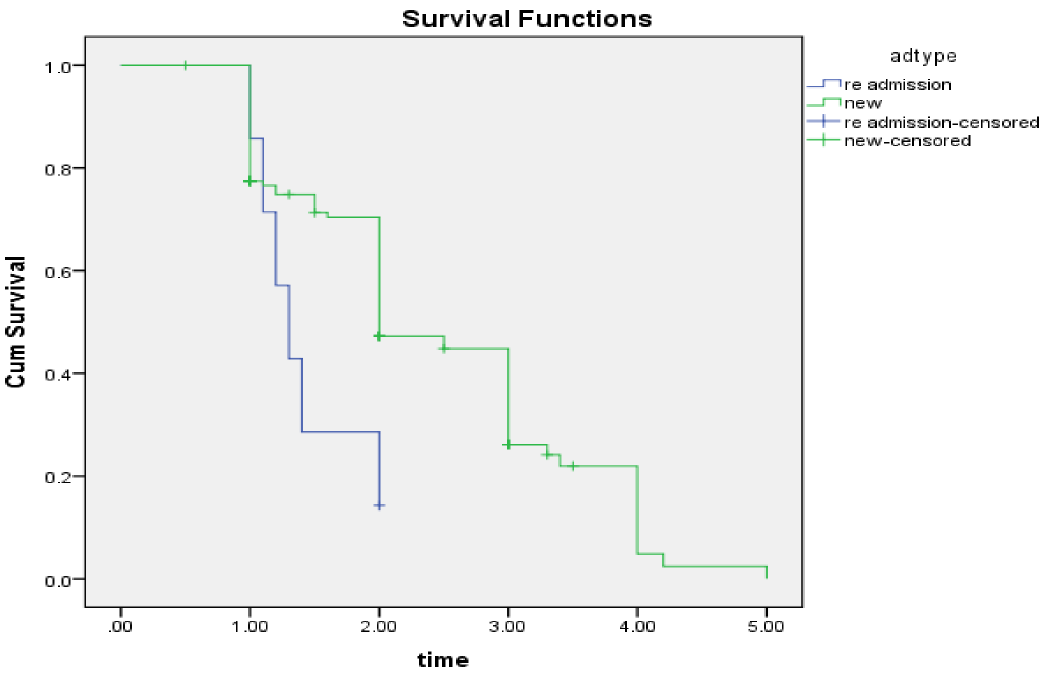

Figure 1: The K-M curve of time to cure from SAM of under-five children by Admission type

The Kaplan-Meier curves by weight figure 2 below, as it can be observed from the curves the cumulative survival proportion ofunder-five children with the weight category 2 (7 - 9.9 kg) had highest followed by weight < 3kgthan other groups.

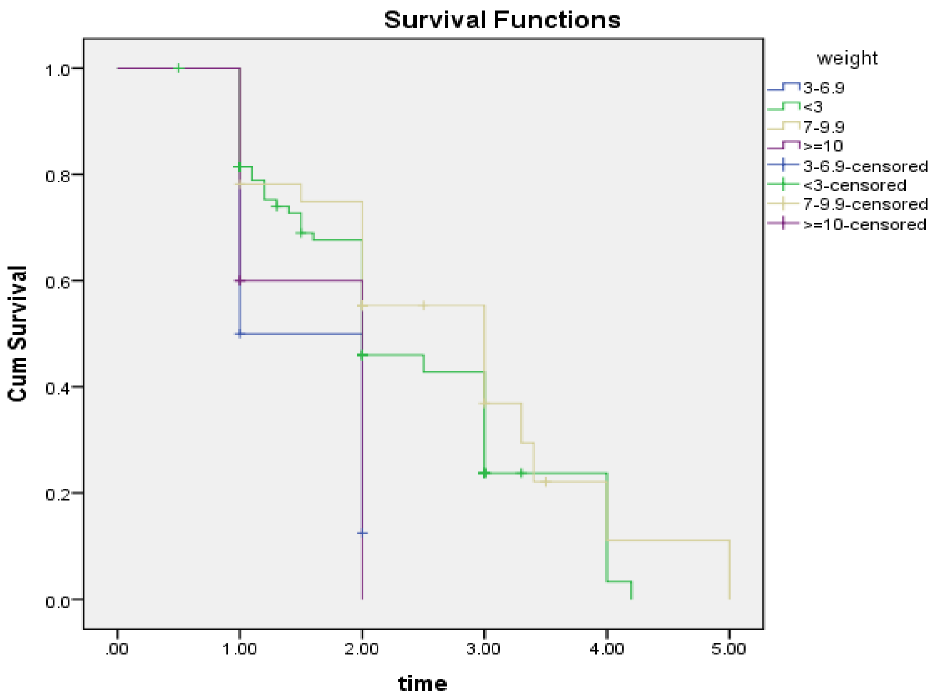

Figure 2 : The K-M curve of time to cure from SAM of under-five children by weight

The Kaplan-Meier curves by diarrhea status of under five children figue 3 below, the survival curves are varied through the study time, implies thatthe cumulative survival proportionof underfive children with diarrhea is higher than with out diarhea.

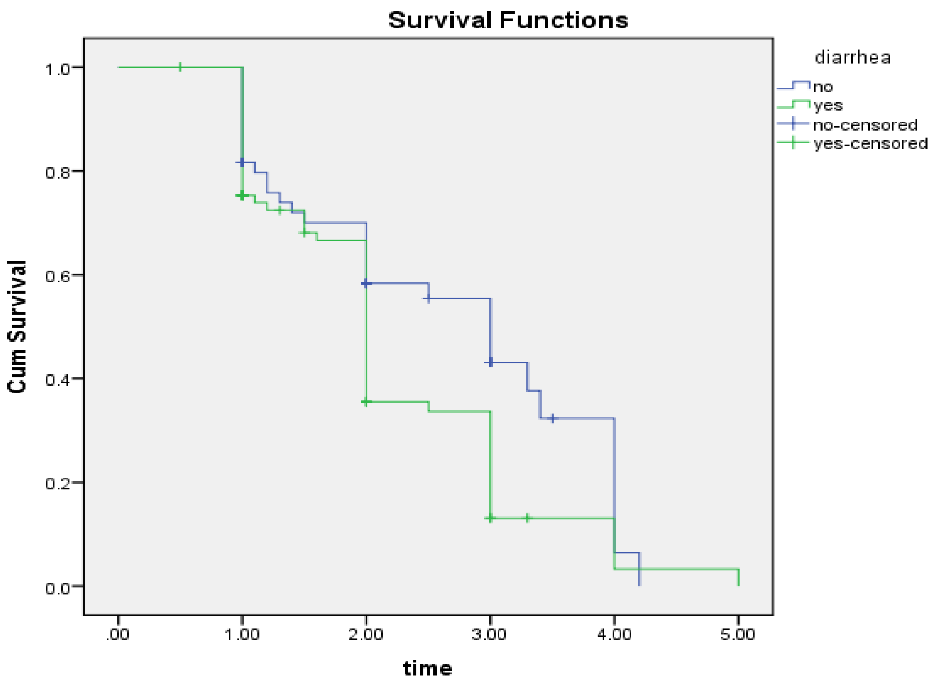

Figure 3: The K-M curve of time to cure from SAM of under-five children by Diarrhea

The Kaplan-Meier curves by routine medication IVantibiotics figure 4 below, the cumulative survival proportion that takes the medication IVantibiotics is higher than the patients do not take the IV antibioptic treatment.

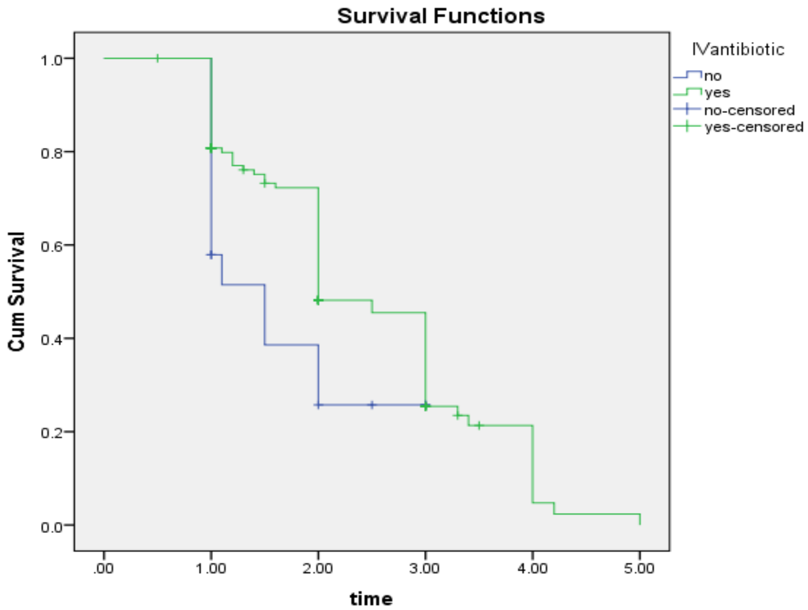

Figure 4: The K-M curve of time to cure from SAM of under-five children by IV Antibiotic

Log Rank Test for Survival Curves of Underfive Children:

The log-rank test was used at 5% level of significance to validate the differences in the survival time of each factor. There is no difference between the probabilities of an event occurring at any time point was the null hypothesis that has been tested. The next portion of this paper shows that the KM estimates and the corresponding logrank test of equality of the survival curves of covariates is summerized below.

Table 7:Results of the Log-rank test for catagorical covariates of underfive children with SAM in Woldia General Hospital, September 2017 to August 2019

Covariates	Chi Square	DF	P Value
Sex	0.33	1	0.565
Residence	0.109	1	0.741
Age	4.65	5	0.459
Appetite	1.325	1	0.250
Breast	2.289	1	0.093
Weight	8.10	3	0.044
Height	3.633	2	0.163
MUAC	1.143	2	0.565
Admission type	5.316	1	0.021
Admission criteria	1.028	3	0.795
Oedema	1.33	3	0.722
Refer	0.12	1	0.729
Fever	0.033	1	0.856
Cough	0.473	1	0.491
Pneumonia	0.25	1	0.874
Vomiting	0.003	1	0.955
Diarrhea	5.34	1	0.021
HIV	0.005	1	0.941
TB	0.430	1	0.512
Anemia	0.740	1	0.390
IV flude	0.554	1	0.457
IVantibiotic	3.941	1	0.047
Amoxcilline	0.109	1	0.741
Vitamine A	1.515	1	0.218
Folic acid	0.138	1	0.711
Pencilline	0.027	1	0.869
Parastamol	0.319	1	0.572

From table of the logrank test result weight,admission type, diarrhea and IV antibiotic treatments have p value less than alpha value 0.05. This implies that there is difference between the probabilities of cureoccurring at any time point of the study time. But most of the covariates are insignificant this may indicates that the proportionality assumption of the cox PH model may not be reasonable for the given data analysis.

Semi Parametric Survival Analysis:

Cox PH Model:

A Cox PH model is a statistical technique for exploring the relationship between the survival time and several explanatory variables. The most commonly used regression model in survial analysis is the Cox-proportional hazard model. With this model the distribution for the baseline hazard function is not specified, implies it varys with time and that is why it is called a semi-parametric model.Before developing the final model of the given study, selecting candidate covariates that may be included for the final model is a crucial step of any model development. There are different techniques of variable selection in statistical modeling.

Univariate Analysis:

Is the prelimnary step of model development. From the"APPENDIX 1a," we have covariates which have alpha less than 0.25 are breast feeding status, weight of children, admission types,diarrhea and IVantibiotic. The point is that including these variables on final multivariable model to assess their effect on time to cure from SAM. But we lost important covariates that have an effect on the time to cure from SAM as we have seen in different litratures in related area of research done before.Similarly Automatic stepwise backward variable selection (LR) is applied at 0.25 level of significance as shown "APPENDIX 1b," From the output of the stepwise backward LR we have got age of the childen, breast feeding status at admission, wheght of the children,admission type, IVantibiotic treatment and vitamin A treatment are candidate covariates with alpha value less than 0.25 level of significance. In both techniques we lost important predictors (e.g. existence of co morbidity, residence, appetite status)on the survival status of underfive children with SAM.

Multivariable Analysis:

Variables, that were not important on their own, may become important in the presence of others. Sowe useall predictors to fit the model at 5% alpha level of significance and we try to asses the predictors of time to cure from SAM of underfive childrenadmitted in the therapeutic feeding center of Woldia General Hospital. As shown in "APPENDIX2a"that the estimated multivariableCOX PH model of those all covarietes in the study at 0.05 level of significance to assess their effect on the survival time to cure from SAM of under five children. From the estimated cox PH model we have Liklihood ratio is 46.46 with 39 degree of freedom and the over all goodness of fit test p-value 0.1920which is larger than alpha 0.05. meaning that the Cox PH model do not fits the data well.

The Proportionality Assumption:

Making inference without the fulfilment of the proportionality assumption is not reasonable in cox PH estimated model. It is better to assess the basic assumption of cox PH model assumes that the hazards of the groups is proportional over time. To do so, we apply theformal test and graphical method *i.e.* plot of $ln(-ln(S(t))$ vs $ln(time)$ if the PH assumption is satisfied this plot looks like parallel through study time. Let we see the plot of some covariets that have significant effect on the survival time of the multivariable cox PH model and try to assess the PH assumption as follows.From the $ln(-ln(S(t))\ vsln(time)$ plots below (Figure 5) of different covariates that are significant in the final model we observed that the plots of the diferent categories of these covariates is not parallel. This implies that the proportionality assumption is violated.

A.For Admission Type B. For Vitamin A

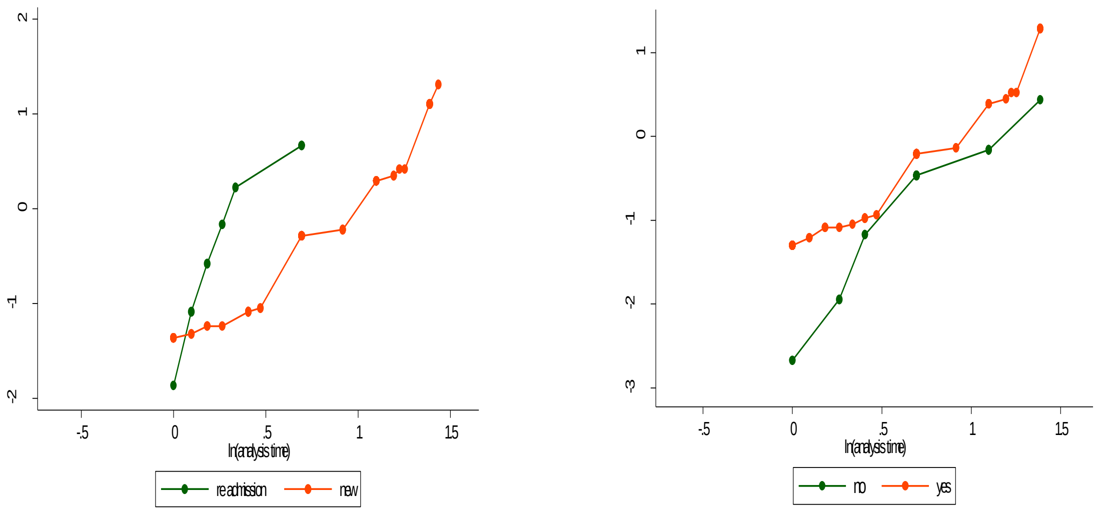

Figure 5 : Plots ln(-ln(S(t)) vs ln(time) of admission type and vitamin A treatment

There are different alternatives that uses as a remadial measures and making further survival analysis. Among thes we used the parametric approaches. AFT model is used with the specification of the distribution of the baseline hazard. The common parametric AFT models are wuibull, log logistic and log normal models is estimated and their godness of fit is compared with AIC and BIC.

Estimated AFT Models:

The Accelerated Failure Time model presents a way to easily describe and interpret survival regression data. It approaches the data differently than the widely used and well described Cox proportional hazard model, by assuming proportional effect of the covariates on the log-failure time rather than on the hazard function. The common parametric AFT models are wuibull, log logistic and log normal models were estimated at 5% level of significant to assess the significant factrs on the time to cure from SAM of under five children and their godness of fit is compared with AIC and BIC as shown table .

Table 8 : Model comparisons of common AFT models for SAM data set

Models	LR	AIC	BIC	P value
Weibull	85.7	214.37	337.81	0.0000
Log logistic	83.78	216.61	340.05	0.0000
Log normal	75.08	215.45	338.89	0.0005

After fitting the common baseline AFT models, comparison of models by using Akaike's Information Criterion (AIC) and BIC is done. i.e.the minimum AIC or BIC indicates the model fits the data well. As shown in table 8 above, compared to the others the baseline Weibull have minimum AIC and BIC, 214.37 and 337.81 respectively. Hence the Weibull AFT model is used for the analsis of this study.

Table 9 : Time to cure from SAM of under five children using parametric AFT model (Weibull regression) at alpha 0.05

No	Covariate	Category	T R	S.e	Z	P>|Z|
1.	Residence	Urban (ref)				
		Rural	1.250377	.1268222	2.20	0.028
2.	Ageof Children	<6 months	.7297676	.0828642	-2.77	0.006
		6-11months	1.410785	.1632408	2.97	0.003
		12-23 (ref)				
		24-35months	.8289596	.123242	-1.26	0.207
		36-47months	1.347564	.3591459	1.12	0.263
		48-59months	.8187295	.1857087	-0.88	0.378
3.	Appetite	Good (ref)				
		Poor	1.217594	.1188933	2.02	0.044
4.	Breast Feeding	Good (ref)				
		Poor	.7724381	.0703798	-2.83	0.005
5.	Weight	< 3kg	1.847078	.2656825	4.27	0.000
		3-6.9kg (ref)				
		7-10 kg	1.523416	.2774983	2.31	0.021
		> 10kg	1.097439	.3066177	0.33	0.739
6.	MUAC	>12.5cm(ref)				
		11.5-12.5 cm	.6112461	.1196365	-2.52	0.012
		<11.5 cm	1.147982	.2443548	0.65	0.517
7.	Admission types	Readmit (ref)				
		New	1.885657	.3167658	3.78	0.00
8.	Oedema Status	Nooedema (ref)				
		Grade 1	2.36116	.8510726	2.38	0.017
		Grade 2	.830751	.1206766	-1.28	0.202
		Grade 3	.6267494	.1328857	-2.20	0.028
9.	Cough	No (ref)				
		Yes	.8434482	.0715076	-2.01	0.045
10.	Vomit	No (ref)				
		Yes	.7554637	.0758744	-2.79	0.005
11.	Anemia	No (ref)				
		Yes	1.308174	.1698978	2.07	0.039
12.	IVantibiotic	No (ref)				
		Yes	1.965331	.2471276	5.37	0.000
13.	Vitamin A	No (ref)				

		Yes	.628807	.0895531	-3.26	0.001
		Cons	.895227	.3108329	0.32	0.750
		/ln_p	1.238876	.0808106	15.	0.000
		P	3.45173	.2789364		
		1/p	.2897098	.0234116		

S.e= standard error, TR = time ratio = exp(B), 95% CI=Confidence Interval for Time ratio, LCL=lower class limit, UCL= upper class limit, TR=exp(B), Ref=Reference, z= z-statistics, P>|Z|=p- value

Model Diagnostics of Weibull AFT Model:

After the model has been fitted, it is desirable to determine whether a fitted parametric model adequately describes the data or not. Therefore, the appropriateness of model with Weibull baseline can be graphically evaluated by plotting log(-log(S(t)) versus log(time) of covariates. If the plot is approximately linear, the given baseline distribution is appropriate for the given dataset. Accordingly, the respective plots of some covariates are given in figure 6 below and the plot for the weibul baseline distribution make linear. This evidence also strengthens the decision made by AIC value that the weibull baseline distribution is appropriate for the given dataset.

a.Residence b.Appetite

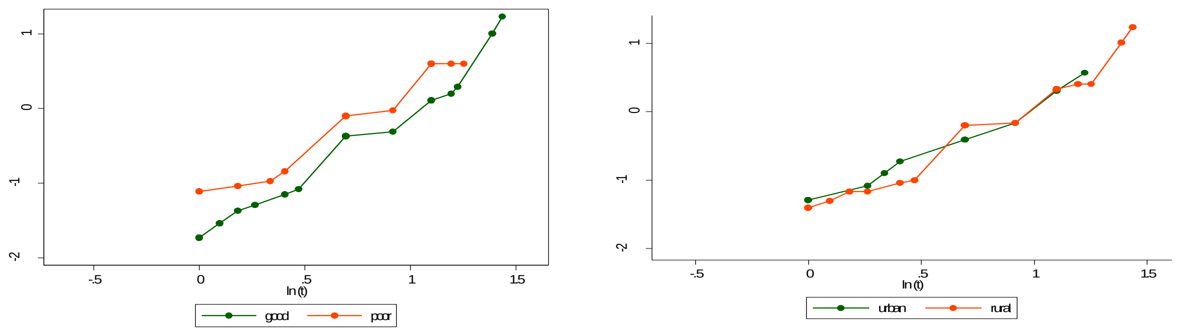

Figure 5: Model diagnosis plot of some covariates in the webull AFT model

Assessing the Goodness of Fit of the Model:

After fitting the model we should check the goodness of fit of themodel whether it fits the data well or not. We use both the formal (global test of BETA=0) likelihood ratio testand the most common graphical method, (Cox-Snell) of checking the goodness of fit of the final selected model, Weibull AFT model.From the likelihood ratio test we have likelihood ratioat 39 degree of freedom is 85.7 and the p- value is 0.0000, implies that the model fits the data well.

As shown in the figure7 below, We also usethe Cox-Snell residual plot,From the graph we can observe that the cumulative hazard function follows the 45 degree line except for large values of time, common for models with censored data to have some wiggling at large values of time. Therefore, we can conclude that the final Weibull AFT model fits the data well. Hence it is used for analysis of identifying significant factors time to cure from SAM of under-five children in the feeding unit.

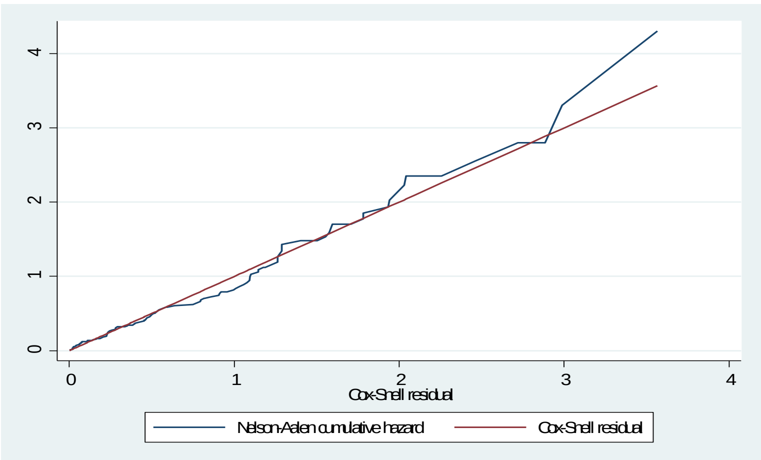

Figure 6 : Cox snell residual plot of Weibull AFT model of SAM data set

Interpretation for Weibull Regression Model Result:

Under the Weibull AFT model output residence,age of the chidren, appetite status, breast feeding status, weight, MUAC, admission types, oedema status, cough, vomiting, anemia, antibiotic treatment and vitamin A are the covarites that have significant effect on time to cure from SAM of underfive children at 5%

level of significance. Here is the detail interpretation of each covariates based on theestimated acceleration factor(time ratio) of SAM dataset.

The acceleration factor for the residene of the children is 1.25 with 95% CI [1.024, 1.525]and p- value 0.028, indicates that the children whose residence is rural have prolonged survival of time to cure from SAM than that of urban.The estimated time ratio for age of children with age less than 6 months is 0.729 p-value 0.006 and 95% CI [0.584, 0.911], implies that children whoseage is below 6 months have short time to cure from SAM than that of the (11-23 months). This may be the early detection of the SAM for the age group < 6 months have positive effect on time to cure from SAM. Time ratio for age group (6-11 months) is 1.41, p-value 0.003 and 95%CI [1.124, 1.769]indicates that children with (6-11 months) age group have prolonged survival time thanthat of11-23 months old. If not identified early, as the age increases the complication of SAM also increases & increases the time to cure. Others groups of age are not different at 5% level of significance.

The estimated acceleration factor for breast feeding status of the children poor is 0.772 with p-value 0.005and 95%CI [0.646,0.923], which indicates that children with poorbreast feeding status have short survival time to cure from SAM than that of with good status. This might be the emidiate allocation (when the case was identified early on time) of children to the center couse the cureof the children in short period of time after admission.The estimated acceleration factor for appetite status of the children poor is 1.217 with p-value 0.044 and 95% CI [1.0055, 1.27703], which indicates that children with poor appetite status have prolonged survival time to cure from SAM than that of with good appetite satus.

When we see the weight of children taking (3-6.9kg) as reference category, the acceleration factor for weight group <3kg is 1.84 with p-value 0.000 and 95% CI [1.393, 2.448], this implies that children who have weight <3kg have prolonged survival time than that of the reference group. This mighet be due to children are underweighted(wasted)& it increases the stay of time in the center.SimmilarlyTR of weight group 7-10 kg is1.52 with p-value 0.021 and 95% CI [1.066, 2.177], which indicates that children that have weight 7-10 kg have prolonged survival time than that of(3-6.9kg).This maightbe the weight of the children increases (over weighted) due to the the oedema existence at admission.

The estimated acceleration factor for MUAC status of the children having 11.5-12.5 cm is 0.611 with p-value 0.012and 95%CI [0.416, 0.897], which depicts that children with this MUAC group have shortersurvival time to cure from SAM than that of with MUAC >12cm. This is due to the MUAC interval 11.5-12.5 cm is moderately malnurished stage of the children (WHO, 2013). This decreases the time to cure from SAM.MUAC <11.5cm have high p-value meanig that have no difference from the reference category(MUAC >12cm.The estimated acceleration factor for the admission types of newly admitted childrenis 1.88with p-value 0.000and 95%CI [1.35, 2.62], it implies that the newly admitted children have prolonged survival time to cure from SAM than that of withthe re-admitted ones .This might be due to the fact that children with re-admission have strict follow up status as directed by the judgement on theirfollow up chart than the newly admitted.

When we see the oedema status of children taking (no oedema) as reference category, the acceleration factor for children with grade 1 oedema is 2.36 with p-value 0.017 and 95% CI [1.164, 4.785],which indicates that children that have grade 1 oedema have prolonged survival time than that of the reference group (no oedema). Among the common co morbidities the acceleration factor for the cough is 0.843 with 95% CI [0.714, 0.995] and p- value 0.045 indicates that children who have cough when admitted have shorter survival of time to cure from SAM than that of no cough.

Time ratio for vomiting status of children the acceleration factor for the cough is 0.755 with 95% CI [0.620, 0.919] and p- value 0.005 indicates that children who have vomit when admitted have shorter survival of time to cure from SAM than that of no vomit.This might be due to the simplicity in differentiating the signs of cough and vomitting in SAM patients. Proper diagnosis and treatment for these co morbidities decreases the stayng time of child with SAM in the therapeutic feedingcenter.

Time ratio for anemia status of children is 1.30 with 95% CI [1.014, 1.687] and p- value 0.005 indicates that children who have anemia when admitted have prolonged survival of time to cure from SAM than that of no anemia.

Routine medication of IVantibiotic have time ratio of 1.96 with 95% CI [1.536, 2.514] and p- value 0.000 indicates that children who takes IVantibiotic have prolongedsurvival of time to cure from SAM than that of patients who have not taken it.This isdue to antibiotics may be of benefit in uncomplicated malnutrition in preventing opportunistic infections. Since there is high risk of bacterial infections in hospitals children with SAM,the antibiotic treatments may enlongates the staying time in hospital than that of donot take it (WHO, 2012).Routine medication of vitamin A have time ratio of0.628 with 95% CI [0.475,0.831] and p- value 0.001 indicates that children who takesvitamin A have shortersurvival of time to cure from SAM than that of patientes have not taken it.

Discussion of Survival Analysis Results:

This study investigated the determinants of time to cure from severe acute malnutrition among under five children who were admitted at therapeutic feeding unitWoldia General Hospital from September 2017 to August 2019.

The finding of the study showed that among children treated for severe acute malnutritionthe accounted cures (recovery) of patients in the study period was66.7%.The proportion of recovery in this study was below the recommended Sphere standard which should be >75%. However this finding is lower than previous study done in Haramaya dilchora hospital (69.9%) (Oumer, Mesfin and Demena, 2016), Debremakos (70.5%) (Wagnew et al., 2019), South wollo (75.4%) (Hassen et al., 2019) and larger than Felege Hiwot hospital (58.4%).This difference may be due to the differences in health seeking behavior, availability as well as accessibility of therapeutic foods and medications and also use of updated SAM treatment guideline.The finding from Haramaya, Debremakos and felegehiwot hospital were consistent with the finding of this study.

The median length of stay for recovered children in the ITFU of 2 weeks (14 days) was in the international standard (Sphere) set for the management of SAM which is less than 28 days(4 weeks).In the same way, It was also lower than reported in Bahir Dar Felege Hiwot Referral hospital(18.00 day). But it was similar with study report at wolliso St luke hospital 14 day (Banbeta et al., 2015). and longer than study at south wollo (11 day) and study zambia (9 days).The main difference between the total percentage of (cure is below standad) and median survival time to cure (in standard of sphere) is thatthere is positive association between longer duration of hospital stay with recovery. SAM children who stay more than 21 days were 7 times more likely to recover than those children with shorter duration of hospital stay (Moges T. and Hayder J., 2009).

The study finding showed majority 125(83.33%) of the children admitted to therapeutic feeding center were from rural area which is consistent with the study done in Debre markos and Finote Selam hospital (Mekuria, G.et al., 2017).The similarity of the study finding may be due to similar pattern of SAM distribution in Ethiopia. The acceleration factor of residenceis 1.25 meaning that rural children have 25%higer length of time to cure from SAM than that of urban.

In this study the age of the children at admission was with less than 6 months is 30.67% and from 6-11 months is 25.35% indcates that majority of the children are below 1 year.Similarwith the finding at Wolisso St. Luke catholic hospital, south west Ethiopia (Banbeta et al., 2015).The reason for the high proportion of cases of SAM to be among the age group less than 12 months could be due to sub optimal breast feeding and poor complementary feeding practices of the community. In this study the estimated time ratio of children with age less than 6 months is 0.729 with p-value 0.006 and 95% CI [0.584, 0.911] , implies that children who are below 6 months old have short time to cure from SAM than that of the (11-23 months).

The estimated acceleration factor of breast feeding status of the children poor is 0.772 with p-value 0.005 and 95%CI [0.646,0.923] which indicates that children with poor breast feeding status have shorter survival time to cure from SAM than that of with good status. This is mainly might be children reach the therapeutic feeding center on time after developing complications may cousescure with in short time.

The estimated acceleration factor the appetite status of the children poor is 1.217 with p-value 0.044 and 95% CI [1.0055, 1.27703] which indicates that children with poor appetite status have prolonged survival time to cure from SAM than that of with good status. This finding is in line with previous study conducted atSouth Wollo Zone(Hassen et al., 2019).

This study finding showed that more than two third of the study subject have at least one form of co morbidities at admission among thesevomiting, cough and anemia with their respective prevalence being (60%), (74.67%), and (10%) respectively. Other studies done in different area had also indicated these co morbidities are common in children with severe acute malnutrition (Oumer, Mesfin and Demena, 2016).

The acceleration factor of anemia is1.30 which means children with anemia have 30% more stayng time in hospital than that of without anemia.This finding is in line with previous study conducted at Debremarkoswhich reported anemia was a predictors of death in severe mal-nourished children (Wagnew et al., 2019).

Routine medication of vitamin A has time ratio of 0.628 with 95% CI [0.475,0.831] indicates that children who have taken vitamin A have shorter survival of time to cure from SAM by 37.2 % than that of children who have not taken it. This finding is in line with previous study conductedin Bahirdar Felege Hiwot Referral Hospital (Desyibelew, Fekadu and Woldie, 2017). Routine medication of IVantibiotic have time ratio of 1.96 with 95% CI [1.536, 2.514] indicates that children who have taken IVantibiotic have prolonged survival of time to cure from SAM than that of have not taken it. This is due to antibiotics may be of benefit in uncomplicated malnutrition in preventing opportunistic infections. Since there is high risk of bacterial infections in hospitals children with SAM, the antibiotic treatments may enlongates the staying time in hospital than that of have not taken it (WHO, 2012).

4. Conclusion and Recommendations:

Conclusion:

This study tried to assess thedeterminants of time to cure from SAM of under-five children with severe acute malnutrition admitted to therapeutic feeding unit in Woldia General Hospital, North Ethiopia.Proper management of severe acute malnutrition and high proportion of recovery has vital role to save the lives of many children. Accordingly proportion of cures from SAM is 66.7% which is beow the acceptable range of global Sphere standards which is to be >75%. The median length of stay for recovered children in the

ITFU was2 weeks (14 days). It is within the international standard (sphere) set for the management of SAM which is less than 28 days(4 weeks).

Residence,age of the chidren, appetite status, breast feeding status, weight, MUAC, admission types, oedema status, cough, vomiting, anemia, antibiotic treatment and vitamin A are the covarites that have significant effect on time to cure from SAM of underfive children at 5% level of significance.

Childen from rural area takes more time to cure from SAM than urban. Children with good appetite have less time to cure from SAM than that of the poor. Treatment vitamin A and having no anemia at admission were found to be associated with higher likelihood of cure by decelerating the stay time of underfive children in the therapeutic feeding center.Children whose age <6 months have shorter survival time to cure where as the age 6-11 months have prolonged time to cure than that of children ageg 12-23 months (ref).Children with weight<3kg and 7-10 kg have prolonged survival time to cure than who have 3-6.9 kg. co morbidities oedema grade3, cough and vomiting may shortens the survinal time to cure. Children who take IVantibiotics, the new admitted children,oedema grade 1 increases stay time of underfive children in the therapeutic feeding center than their corrosponding reference group.

Recommendations:

Based on the finding of this study the following recommendations were forwarded:

For the hospitals

Children admitted to therapeutic feeding center in this hospital are below the standard of Sphere. So it is better to have:

- Proper diagnosis and management of cases in accordance with the protocol.
- Treatment of complication like, anemia, cough and vomiting needs special attention.
- Proper monitoring and documentation of records needsimprovement by computerizing the data handling mechanisms.

For zonal health office

As the majority patients are from the rural parts of the zone,

- The zonal health office is better to work with all concerned bodies to create awareness mainly in the rural community for early detection of severity of malnutrition in the area.
- Providinggood health care and guidance for maternal and children in rural areas of the zone is important to control the death of the children with SAM.
- Increasing breast feeding and complementary feeding practices of the community.

For researchers

Researchers are better to conduct further prospective studies using both qualitative and quantitative techniques that better investigate time to cure from SAM and its determinants.

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