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# **Original Research Article**

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# Mortality outcome of hospitalized children aged six to fifty-nine months in relation to different anthropometric indices: an observational cohort study

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#### **ABSTRACT**

**Background:** Malnutrition among children is a major public health problem and an underlying cause of millions of child deaths across the globe. The WHO has provided criteria for identifying malnourished children aged 6-59 months however, these criteria have not been fully evaluated against the risk of in-patient mortality. The observational study was conducted to assess the predictability of in-patient mortality of children aged 6-59 months for different anthropometric criteria to understand which diagnostic criteria most accurately predict in-patient mortality.

**Methods:** Data from a cohort of children aged 6-59 months, admitted to Kalawati Saran Children's Hospital, New Delhi between January to October 2019 was analysed. The effect of anthropometric indexes, individually and in combinations, to predict in-patient mortality was assessed using cox regression survival analysis and receivers operating characteristics curves.

**Results:** A total of 3101 children aged 6-59 months were admitted, of which 123 (4.0%) died in the hospital. Among them, 30.1% were severely underweight, 19.3% were severely wasted and 23.0% were severely stunted. WHZ<-3 and/or MUAC<115 mm was the most sensitive predictor of mortality (sensitivity: 75.0%; specificity: 42.3%; PPV: 6.5%; NPV: 96.9%; AUC: 0.59, 95% CI: 0.53-0.64) with the largest adjusted hazard ratio (aHR=1.53; p value <0.05). **Conclusions:** WHZ<-3 and/or MUAC<115 mm was the most sensitive predictor out of all individual and combined anthropometric indexes in identifying children aged 6-59 months at risk of mortality. Children in this category should be properly managed during their inpatient stay.

**Keywords:** Children aged 6-59 months, In-patient mortality, Malnutrition, Mid-upper-arm-circumference, Weightfor-height z-score

# INTRODUCTION

Across the world, approximately twelve million children less than 5 years of age die every year and most of these deaths occur in developing countries. Though diarrhoea, acute respiratory illness, malaria, or measles are attributed to these deaths however, in many cases, the underlying cause of death is malnutrition, which is rarely cited among the leading causes of deaths.<sup>1</sup> Attempts have been

made to use different approaches to estimate contribution of malnutrition to all-cause mortality in children.<sup>2</sup> Studies have shown that malnutrition cause in about half of all deaths occurring among children in developing countries.<sup>3</sup> A study conducted in 13 Latin American countries suggested that 35% of all deaths to children less than 5 years of age involved malnutrition as an underlying cause.<sup>4</sup> Other long period studies conducted in India and Bangladesh also found strong nutrition-

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mortality linkage among children.<sup>5-7</sup> Such findings have drawn international attention on the potential impact that preventing and treating malnourished children will improve their survival. However, apart from these early studies, very limited efforts have been made to quantify the contribution of malnutrition to child mortality, especially in the low- and middle-income countries.

As undernutrition is an underlying cause of childhood deaths identification of children at higher risk remains a public health challenge. A study in a tertiary care hospital in New Delhi, India among children aged 6-59 months found MUAC<115 mm to be a significantly better predictor of in-patient mortality than WHZ<-3, however, both identified different sets of children and while MUAC<115 mm identified children at higher risk of dying, about a third of the children at risk were missed out using this criterion alone.8 Vella et al, in their study in Uganda also found MUAC as the most sensitive predictor of mortality followed by weight-for-age, height-for-age and weight-for-height.9 Many other studies have reported associations of stunting (low height-for-age), wasting (low weight-for-height), and underweight (low weightfor-age) with mortality where underweight was found to be the most sensitive predictor of mortality followed by wasting and stunting.<sup>3,10,11</sup> However, apart from these limited studies, we did not find other large studies in the context of developing nations to understand which anthropometric index or their combinations predicts better childhood mortality. We quantified the association between multiple anthropometric deficits and all-cause mortality among children aged 6-59 months using an observational study conducted in a hospital setting in order to understand which anthropometric criteria or combination of criteria predict in-patient mortality most accurately.

### **METHODS**

The study was conducted in a tertiary care hospital of Delhi. Children aged 6-59 months who were admitted in the paediatric wards for a range of medical complaints like sepsis, pneumonia, meningitis and other illnesses between January to October 2019 were enrolled into the study within twelve hours of their hospitalization. These children were managed using the standard hospital protocol in three pediatric wards equipped with a dedicated high dependency unit for critical cases. Nutritional rehabilitation for malnourished children was done as per the Facility Based Management of Severe Acute Malnutrition (FSAM) Guidelines of Government of India. The primary outcome was discharge from the hospital as cured or died. For the current study, successfully discharged was defined as children whose medical conditions improved, course of antibiotic was complete, weight gain on three consecutive days, ageappropriate immunization was completed, and caregivers were educated on appropriate child caring and feeding, as per the FSAM guidelines of Government of India and the WHO.<sup>12,13</sup> Children with congenital anomalies, known chronic medical illnesses, surgical conditions and known human immunodeficiency virus (HIV) exposed children were excluded from the study. The study was approved by Institutional Ethical Committee of Lady Hardinge Medical College, New Delhi (Approval Letter Ref. No.: LHMC/IEC/2020/50 dated 19.08.2020).

All severely malnourished children at discharge were attached to a follow-up clinic. At the time of admission, after taking informed consent from the parent or guardian, information on the child and their medical history was taken including age, sex, reason for admission into the hospital, birth and hospitalization history. Height, weight and MUAC were measured using WHO recommended taking standard methods for anthropometric measurements. For weight measurement, SECA 334 digital weighing scales were used and for height measurement, wooden infanto-cum-stadiometers were used. For MUAC measurement, non-stretchable MUAC tapes were used. Weighing equipment was calibrated using standard calibration weights on daily basis and infantometer-cum-stadiometer was calibrated calibration rods. Height was measured to the nearest 0.1 cm, weight to the nearest 0.01 kg and MUAC to the nearest 1 mm. All children were also examined for bilateral pitting edema. All anthropometric measurements were taken by trained workers who had experiences in conducting anthropometric assessments and they were also re-trained on conducting anthropometric assessments every quarter.

Data was analyzed using SPSS 20 (IBM). WAZ, HAZ and WHZ were calculated using Emergency Nutrition Assessment (ENA) software (WHO 2006 reference). Descriptive statistics were used to summarize the study variables. Chi-square test was performed to assess crude association of categorical forms of individual and combinations of each anthropometric index for their association with mortality. Cox regression survival analysis method was used to investigate the effect of continuous and categorical forms of individual and combinations of each anthropometric index for their association with time to mortality after adjusting for sex and age (in months). Receiver operating characteristic (ROC) curves were used to assess the discriminatory ability of anthropometric indexes to predict inpatient mortality.14

We created individual and combined indicators of WAZ<-2, HAZ<-2, WHZ<-2, WAZ<-3, HAZ<-3, WHZ<-3, MUAC<115 mm and MUAC<125 mm. Sensitivity of these anthropometric indices and their combinations was defined as the proportion of children who died among those who were below the cut-off. Specificity was defined as the proportion of surviving children among those who were above the cut-off. The positive predictive value (PPV) was defined as the proportion of children who died among children classified as malnourished using these anthropometric cut-offs and their combinations. The negative predictive value (NPV)

was defined as the proportion of children who did not die among those not classified as malnourished using these indices and their combinations. For a given marker, area under the curve (AUC) is an index of the marker's ability to discriminate between true positives and true negatives. AUC was calculated to evaluate the overall prognostic ability of these anthropometric indices and their combinations to detect mortality.

#### **RESULTS**

# Characteristics of study population

A total of 3101 children, with a mean age of 21.7 months (SD 13.8 months), were admitted of which 64.1% were boys. 63.2% of children were aged six to twenty-three months at the time of admission. Characteristics of the

study participants are presented in Table 1. Weight and MUAC were measured in all 3101 children. Height was measured in 3094 children. Of all admissions, 30.1% had a WAZ<-3, 54.2% had a WAZ<-2, 23.0% had a HAZ<-3, 44.2% had a HAZ<-2, 19.3% a WHZ<-3 and 41.7% a WHZ<-2. 19.4% children had a MUAC<115 mm while 41.3% children had a MUAC<125 mm. The authors found 9 (0.3%) children with bilateral pitting edema. Further information on anthropometry at admission is presented in Table 1. Mean duration of hospital stay for all children was 6.8 days (SD:  $\pm 6.5$  days). A total of 123 (4.0%) children died during treatment. 36% of children who died were diagnosed (primary diagnosis) with sepsis, 32.5% were diagnosed with pneumonia, 15.4% with GI tract infection, 11.4% with meningitis and 4.9% were diagnosed with other causes.

Table 1: Characteristics of sample population.

Variable		Admissions; N (%)	Inpatient mortality; N (%)
Total number of adm	nissions	3101 (100.0)	123 (4.0)
Sex	Boys	1987 (64.1)	69 (3.5)
Sex	Girls	1114 (35.9)	54 (4.8)
	6 to <12 month	949 (30.6)	46 (4.8)
	12 to <24 months	1010 (32.6)	43 (4.3)
Age (months)	24 to <36 months	537 (17.3)	17 (3.2)
	36 to <48 months	401 (12.9)	12 (3.0)
	48 to <59 months	204 (6.6)	5 (2.5)
	Anthropometry	Total number measured; N (%)	N (% of total measured)
	WHZ<-3	3094 (99.8)	598 (19.3)
	WHZ<-2	3094 (99.8)	1292 (41.7)
Anthropometry at admission	WAZ<-3	3101 (100.0)	934 (30.1)
	WAZ<-2	3101 (100.0)	1680 (54.2)
	HAZ<-3	3094 (99.8)	712 (23.0)
	HAZ<-2	3094 (99.8)	1369 (44.2)
	MUAC<115 mm	3101 (100.0)	602 (19.4)
	MUAC<125 mm	3101 (100.0)	1282 (41.3)
		Mean (SD score)	
Mean	WHZ (n=3094)	-2.23 z-score (1.62)	
anthropometry at	WAZ (n=3101)	-1.70 z-score (1.60)	
admission	HAZ (n=3094)	-1.86 z-score (1.80)	
	MUAC (n=3101)	126.5 mm (15.7)	
Mortality status	Mortality status	n (% of total)	
	Alive	2978 (96.0)	
	Death	123 (4.0)	

# Mortality association with anthropometry

Five hundred and ninety-eight (19.3%) children had a WHZ<-3 of whom a significantly greater proportion died (6.2%) compared to children with WHZ≥-3 (3.4%). 934 (30.1%) children had a WAZ<-3, 51 (5.5%) of whom died compared to children with WAZ≥-3 (3.3%). 712 (23.0%) children had a HAZ<-3, 38 (5.3%) of whom died compared to children with HAZ≥-3 (3.6%). Among

different cutoffs for MUAC, 602 (19.4%) children had a MUAC less than 115 mm, of whom a significantly higher percentage of children died (7.0%) compared to those with a MUAC greater than 115 mm (3.2%). Among different combinations of anthropometric indices, 796 (25.7%) children had WHZ<-3 and/or MUAC<115 mm, of whom a significantly higher percentage of children died (6.5%) compared to those who were above with this cut-off (3.2%). Further analysis of associations between death and anthropometry are presented in Table 2.

Table 2: Association of different anthropometric indexes and their combinations with in-patient mortality.

Parameters	Number	Number (%) of deaths	Yes (%)	No (%)	P value
WHZ<-3	3094	123 (4.0)	37 (6.2)	86 (3.4)	0.002
WHZ<-2	3094	123 (4.0)	65 (5.0)	58 (3.2)	0.010
WAZ<-3	3101	123 (4.0)	51 (5.5)	72 (3.3)	0.005
WAZ<-2	3101	123 (4.0)	85 (5.1)	38 (2.7)	0.001
HAZ<-3	3094	123 (4.0)	38 (5.3)	85 (3.6)	0.034
HAZ<-2	3094	123 (4.0)	70 (5.1)	53 (3.1)	0.004
MUAC<115 mm	3101	123 (4.0)	42 (7.0)	81 (3.2)	< 0.001
MUAC<125 mm	3101	123 (4.0)	70 (5.5)	53 (2.9)	< 0.001
WAZ<-3 and/or WHZ<-3	3101	123 (4.0)	55 (5.5)	68 (3.3)	0.003
WAZ<-3 and/or HAZ<-3	3101	123 (4.0)	57 (5.2)	66 (3.3)	0.012
WHZ<-3 and/or HAZ<-3	3094	123 (4.0)	58 (5.4)	65 (3.2)	0.003
WAZ<-3 and/or WHZ<-3 and/or HAZ<-3	3101	123 (4.0)	61 (5.2)	62 (3.2)	0.007
WHZ<-3 and/or MUAC<115 mm	3101	123 (4.0)	52 (6.5)	71 (3.1)	< 0.001
WAZ<-3 and/or MUAC<115 mm	3101	123 (4.0)	56 (5.4)	67 (3.2)	0.003
HAZ<-3 and/or MUAC<115 mm	3101	123 (4.0)	56 (5.5)	67 (3.2)	0.002

Table 3: Association between different anthropometric indexes and inpatient mortality adjusted for sex and age.

Variable	Coeff.	Coeff.	Coeff.	Coeff.	Coeff.	Coeff.	Coeff.	Coeff.	Coeff.
Age of the children in months	0.98**	0.98***	0.98***	0.98*	0.98***	0.98**	0.98**	0.98**	0.98*
Sex (Male=1, Female=0)	0.71*	0.71*	0.70**	0.76	0.72*	0.71*	0.71*	0.74*	0.73*
WAZ	0.84***								
WHZ		0.88**							
HAZ			0.88***						
MUAC				0.98***					
WAZ<-3					1.31				
WHZ<-3						1.39*			
HAZ<-3							1.35		
MUAC<115 mm								1.47*	
MUAC<125 mm									1.35

<sup>\*\*\*</sup>p value<0.01, \*\*p value<0.05, \*p value<0.10

Table 4: Association between combinations of different anthropometric indexes and inpatient mortality adjusted for sex and age.

Variables	Coeff.	Coeff.	Coeff.	Coeff.	Coeff.	Coeff.	Coeff.
Age of the children in months	0.98***	0.98**	0.98***	0.98***	0.98***	0.98***	0.98***
Sex (Male=1, Female=0)	0.71*	0.73*	0.69**	0.72*	0.71*	0.71*	0.71*
WAZ<-3 and/or WHZ<-3	1.35						
WHZ<-3 and/or MUAC<115 mm		1.53**					
WAZ<-3 and/or MUAC<115 mm			1.31				
WAZ<-3 and/or WHZ<-3 and/or MUAC<115 mm				1.40*			
WAZ<-3 and/or HAZ<-3					1.27		
WHZ<-3 and/or HAZ<-3						1.38*	
WAZ<-3 and/or WHZ<-3 and/or HAZ<-3							1.31

<sup>\*\*\*</sup>p value<0.01, \*\*p value<0.05, \*p value<0.10

WAZ, HAZ and WHZ were significantly associated with in-patient death, even after adjusting for sex and age of the child at hospitalization using a Cox regression (survival analysis) model. The lower the z score value,

the higher the chance of in-patient mortality. Along with WHZ, HAZ and WAZ, age and sex of the child were significantly associated with in-patient mortality. Younger children were associated with higher risk of

death. Similarly, female children were associated with higher risk of mortality. MUAC status was also significantly associated with in-patient mortality. The lower the MUAC value, the higher the chance of inpatient mortality. It was also found that, MUAC<115 mm was a better predictor of in-patient mortality with the largest adjusted hazard ratio (aHR=1.47 p value <0.1) after adjusting for age and sex, compared to other individual markers (WAZ<-3, HAZ<-3 and WHZ<-3) of severe malnutrition (Table 3).

To understand the most sensitive anthropometry (and cutoff value) in predicting the risk of in-patient mortality, comparisons of multiple combinations of anthropometric indexes with severe categories were made. It was found that, WHZ<-3 and/or MUAC<115 mm was a better predictor of in-patient mortality with the largest adjusted hazard ratio (aHR=1.53; p value <0.05) after adjusting for age and sex, compared to all other combinations (Table 4).

Table 5: PPV, NPV, sensitivity, specificity and AUC of different anthropometric indexes and their combinations for inpatient mortality.

Criteria	PPV	NPV	Sensitivity	Specificity	ROC area (95% CI)
MUAC<115 mm	7.0%	96.8%	34.1%	81.2%	0.58 (0.52, 0.63)
MUAC<125 mm	5.5%	97.1%	56.9%	59.3%	0.58 (0.53, 0.63)
WAZ<-3	5.5%	96.7%	41.5%	70.3%	0.56 (0.51, 0.61)
WHZ<-3	6.2%	96.6%	30.1%	81.1%	0.56 (0.50, 0.61)
HAZ<-3	5.3%	96.4%	30.9%	77.3%	0.54 (0.49, 0.60)
WAZ<-2	5.1%	97.3%	69.1%	46.4%	0.58 (0.53, 0.63)
WHZ<-2	5.0%	96.8%	52.8%	58.8%	0.56 (0.51, 0.61)
HAZ<-2	5.1%	96.9%	56.9%	56.3%	0.57 (0.51, 0.62)
WAZ<-3 and/or WHZ<-3	5.5%	96.7%	44.7%	68.0%	0.56 (0.51, 0.62)
WAZ<-3 and/or HAZ<-3	5.2%	96.7%	46.3%	64.8%	0.56 (0.50, 0.61)
WHZ<-3 and/or HAZ<-3	5.4%	96.8%	47.2%	65.9%	0.57 (0.51, 0.62)
WHZ<-3 and/or MUAC<115 mm	6.5%	96.9%	42.3%	75.0%	0.59 (0.53, 0.64)
WAZ<-3 and/or MUAC<115 mm	5.4%	96.8%	67.3%	43.3%	0.56 (0.51, 0.62)
HAZ<-3 and/or MUAC<115 mm	5.5%	96.8%	45.5%	67.9%	0.57 (0.51, 0.62)

To further understand the most sensitive anthropometry (and cut-off value) in predicting the risk of in-patient mortality, area under the curve (AUC), sensitivity, specificity, PPV and NPV of all anthropometric indexes and combinations (only of severe indexes) were compared. The AUC was highest for WHZ<-3 and/or MUAC<115 mm (sensitivity: 75.0%; specificity: 42.3%; PPV: 6.5%; NPV: 96.9%; AUC: 0.59, 95% CI: 0.53-0.64) (Table 5). In the Cox regression (survival analysis) model, adjusting for confounding factors (age and sex), it was again found that WHZ<-3 and/or MUAC<115 mm was a better predictor of in-patient mortality with the largest adjusted hazard ratio (aHR=1.53; p value <0.05), compared to other individual anthropometric indexes and their combinations (Table 4).

# **DISCUSSION**

This study assessed multiple anthropometric criteria in children aged 6-59 months at admission to in-patient care in a tertiary care hospital of Delhi, with the aim of identifying the criteria which most accurately predicts mortality risk. An assessment of MUAC, WAZ, WHZ and combinations of multiple indices found WHZ<-3 and/or MUAC<115 mm to be the most accurate in predicting risk of in-patient mortality among children

aged 6-59 months. WHZ<-3 and/or MUAC<115 mm had the largest AUC and the highest hazard ratio after adjusting for sex and age of the child at hospitalization. This indicates that WHZ and MUAC should be assessed for all children aged 6-59 months on admission to hospital. Those categorized as WHZ<-3 and/or MUAC<115 mm should be treated as at-risk with close monitoring during their inpatient stay.

The World Health Organization and UNICEF define non-oedematous severe acute malnutrition (SAM) either by a MUAC<115 mm or by a WHZ<-3. The same criteria are also used for children aged 6-59 months for admission into a therapeutic feeding programme in the facility-based setting. The current finding signifies that, in the hospital setting, combining these two diagnostic criteria for identifying children with a high risk of death provides better results compared to all the individual and combined diagnostic criteria. ROC analysis of the study conducted in a district hospital in Kenya also found that MUAC<115 mm and WHZ<-3 were independently associated with inpatient mortality among children 12-59 months with high sensitivities and specificities compared to other anthropometric criteria. The same criteria and specificities compared to other anthropometric criteria.

Other studies had shown that MUAC criteria had high sensitivities and specificities compared to other anthropometric criteria such as HAZ, WHZ and WAZ.9, <sup>17-20</sup> A study in a tertiary care hospital in New Delhi, India among children aged 6-59 months also found MUAC<115 mm to be a significantly better predictor of in-patient mortality compared to WHZ<-3.8 The same was also true in our study where MUAC<115 mm alone was found to be a better predictor of in-patient mortality compared to all other individual criteria with high hazard ratio (aHR=1.47; p value <0.1) and AUC (AUC: 0.58, 95% CI: 0.52-0.63). However, these studies did not assess the predictability by combining different anthropometric indexes as it was done in the current study. Studies have shown that MUAC<115 mm as a sole criterion fails to identify one-third of the children at risk of dying.8 This is synchronous with other studies which have shown that MUAC<115 mm and WHZ<-3 SD identify different sets of children with partial overlap and if only one criterion is used, there is a high chance that we miss some of the high-risk children.<sup>21-23</sup>

Since, in the current study WHZ<-3 and/or MUAC <115 mm was identified as the most suitable anthropometric index in identifying children at risk of in-patient mortality, weight, height and MUAC measurements should be taken for all inpatient admissions. Children with WHZ<-3 and/or MUAC<115 mm should be properly managed. As this study was conducted in a large government-run hospital for children in the country, the findings represent a wide range of population and can therefore be generalized for in-patient care. However, a multicentric study with large sample size needs to be conducted in future to evaluate the predictability of inpatient mortality of different anthropometric criteria to confirm the study findings.

The limitation of the study is that it did not follow the children post discharge to assess mortality thereafter which may have revealed further nuances in the most accurate anthropometry. Also, this study has only assessed children aged 6-59 months, excluding the six months of life when the risk of mortality is high. Therefore, the findings should not be extrapolated to this age group without further analysis.

# **CONCLUSION**

A high prevalence of malnutrition was found in this study population of hospitalized children aged 6-59 months and was found to be associated with in-patient mortality. In this in-patient setting, WHZ<-3 and/or MUAC<115 mm was found to be the strongest predictor of mortality in comparison to other anthropometric indices and combinations of anthropometric indices. The findings of this study suggest that WHZ<-3 and/or MUAC<115 mm should be used to identify at-risk children aged 6-59 months. Also, they should be treated as at-risk preferably

in high dependency unit and closely monitored during their inpatient stay.

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