Criteria for undernutrition screening in hospitalised infants under 6 months: A diagnostic accuracy study in a resource poor setting

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Conflict of interest statement

The authors declare that they have no conflict of interest

Contributor statement

CMW conceived the study design. IOE created the questionnaire, collected the data, undertook the initial analyses, and produced the first draft of the paper. CMW and ALG helped plan the study and supervised the analyses. CMW undertook further analyses and ALG drafted the paper. All authors contributed to successive drafts, and have approved the final draft.

Abstract

Purpose

We aimed to describe the prevalence of undernutrition in hospitalised infants aged under 6 months and test the utility of simple index measures to detect undernutrition.

Design

Diagnostic accuracy study: weight, length, mid upper arm circumference (MUAC), triceps and subscapular skinfolds were measured in infants aged 2 weeks to 6 months admitted to a Teaching Hospital in Enugu, Nigeria. ***Index criteria***: low (<-2SD) weight for age (WAZ), weight for length (WLZ); MUAC <11cm.   ***Reference definition*****:** weight faltering (conditional weight gain below 5th percentile for healthy Nigerian infants) or sum of skinfolds (SSF) <10 mm.

Results

Of 125 hospitalised infants, only 5% (6) were admitted specifically for undernutrition, but low SSF were found in 33% (41) and , 24% (25) with known birthweight had weight faltering, giving an undernutrition prevalence of 36%. Low WAZ was the most discriminating predictor of undernutrition (Sensitivity 69%, positive predictive value 86%, likelihood ratio 5.5; area under receiver operator curves 0.90) followed by MUAC (73%, 73%, 4.9; 0.86), while WLZ performed least well (49%, 67%, 2.9; 0.84). Where both MUAC and WAZ were low, there was Sensitivity 90%, positive predictive value 82% and likelihood ratio 8.7.

Conclusions

Infants aged under 6 months admitted to hospital in Nigeria had a high prevalence of undernutrition. In young, high risk population a low WAZ alone was a valuable screening criterion, while combining weight with MUAC gave even higher discrimination. Measurement of length to calculate WLZ was a less useful predictor in this population.

Keywords: malnutrition, nutrition indicators, prevalence, hospitalised infants, developing countries

Introduction

The prevalence of undernutrition at population level in the first six months of life has previously been assumed to be low[1] because of the relatively short time after birth and the assumption that infants will be protected by exclusive breastfeeding. However, recent studies in early infancy in countries with higher prevalence of undernutrition have challenged these assumptions and highlighted the scale of the problem, with reported rates for moderate wasting in healthy infants under 6 months of between 15-34%,[1 2 3] The main factors associated with high undernutrition prevalence in this age group are lack of exclusive breast feeding and underlying medical or neurodevelopmental problems[4].

Childhood undernutrition at hospital admission has been reported as a problem even in affluent countries[5 6] and when there is a higher background prevalence of malnutrition, admission may exacerbate and perpetuate the cycle of undernutrition, while malnutrition in hospitalised children increases the risk for complications and may prolong hospital stay[7]. Despite this, studies from hospitalized children living in resource poor settings are scarce. A prospective survey of infants aged 2-59 months in Gambia reported a high prevalence of wasting (41%), stunting (16.9%) and underweight (35.7%) in infants admitted to a paediatric ward of a rural health centre with a diagnosis of severe pneumonia[8], but this study included few children aged under 6 months. Undernutrition prevalence is usually reported using the common indicators for wasting (weight for length z scores, WLZ), stunting (height for age z scores, HAZ) and underweight (weight for age z scores, WAZ) based on WHO references. The pros/cons of different indicators to define undernutrition is a complex issue, because each of them measures different aspects, which will result in different prevalence rates. For example, it has been argued that using WAZ to define undernutrition in hospitalised infants rather than WLZ is likely to result in overestimation of undernutrition, because of the acute nature of disease-associated malnutrition[12]. On the other hand undernutrition can be the result of chronic deficit of energy and nutrient intake and prolonged periods of inflammation. Other common screening methods for undernutrition, such as mid-upper-arm circumference (MUAC) or skinfolds are less often in hospital settings. In more affluent countries, change in weight over time, rather than a single measurement are used, to avoid identifying naturally short, rather than undernourished children. The limitation of this approach is the need for at least two measurements and some allowance for baseline size, as healthy large infants will tend to drop towards average, while initially small infants will tend to rise[13].

A further problem is a lack of suitable standards for very young infants. The WHO growth chart project published standards for subscapular and triceps skinfolds in 2007, which were only from age 3 months to 5 years[14 15]. MUAC has been recommended as the best case-detection method for severe malnutrition in field surveys, because of its high performance in terms of age-dependence, precision, accuracy, sensitivity, and specificity[16 17]. Its use in clinical settings in affluent countries with low malnutrition prevalence has been debatable, because of the sensitivity and cut-offs, but it is advocated for settings with high undernutrition prevalence[18]. MUAC measurement is simple, cheap, and acceptable; therefore, it is recommended that programmes screening and treating severe malnutrition move towards a MUAC-based case-detection, referral, and admission criteria[16]. However, as there are currently no threshold MUAC values for infants younger than 6 months, the recommended values for children 6 – 60 months of age are often applied and the performance of MUAC in hospitalised very young infants has not been explored. MUAC has been much promoted in recent years as a simple and useful measurement in clinical settings (Berkley et al., 2005) but the threshold to use in young infants is not clear. A study in rural Gambian infants aged 6 – 14 weeks[19] recommended using MUAC <11 cm, after finding this to be more effective than WFL Z-score of <-2 in predicting malnutrition-related mortality.

There is thus a need to establish which measures easily used in a hospital setting will identify undernutrition in very young infants in populations with high prevalence. Therefore, we aimed to:

1) Determine the prevalence of confirmed undernutrition in hospitalised infants aged under 6 months in a resource poor setting, using weight faltering (WF) defined by conditional weight gain (CWG) or low fat stores, as a reference definition.

2) Evaluate the performance and utility of WLZ, WAZ and MUAC as index screening methods to identify confirmed undernutrition in very young infants.

Methods

Study design and setting

This was a diagnostic accuracy study, conducted at the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria using cross-sectional data collected as part of a PhD study programme[20]. This is a large referral hospital with over 500 beds that serves Enugu city with a population of over 700,000[21] and community services that extend to various states in the country, particularly those in the southeast geopolitical zone. Social and economic activities in the zone are farming and small and medium scale trading. There is a high prevalence of childhood morbidity due to infectious diseases and inequality in maternal and child health care access are major public health issues.[20 22]

Subjects

Infants admitted to the paediatric wards aged up to 6 months were recruited using purposive sampling between February and July 2012. Power calculation conducted in advance suggested that 200 hospitalised children in total would give 95% power to estimate the prevalence of undernutrition estimated at 14% with a precision of +/- 5%. Infants under age 2 weeks were later excluded to avoid including children with newborn issues who in other centres would be managed in neonatal units.

Weight data were also collected on healthy infants attending the Infant Welfare Clinic at the same hospital to provide healthy norms for conditional the weight gain.

Ethics

Ethical approval was obtained from the College of Medicine Ethics Committee at the University of Glasgow (Reference No 2011018) and the Medical Research Ethics Committee of the University of Nigeria Teaching Hospital (UNTH), Enugu, southeast Nigeria (Reference No NHRE/05/01/2008B – FWA00002458 – IRB00002323).

Data collection

After obtaining informed consent from mothers of the participating infants, anthropometric measurements were taken using WHO-standard operating techniques[23] by one trained nutritionist-researcher. Weights were measured using a SECA 385 electronic baby scale, regularly calibrated with a known weight. Recumbent length was measured using a SECA 416 infantometer. MUAC was measured using a narrow, re-usable non-stretch tape. Skinfolds (triceps and subscapular) were measured using Holtain skinfold calipers. Each measure was collected at least three times until three were within acceptable range of each and the average of these three readings were usedfor each measurement. Gestational age, date of birth, weight at birth and information on diagnosis was obtained from each individual infant's hospital case note.

Data for the healthy comparison group were collected by approaching mothers attending the well-baby clinic and, with their consent, recording that days weight as well as transcribing all previous weights from the child's clinic card at birth, 6 weeks, 3 and 6 months. Children who were known to be malnourished or unwell were excluded. The infants were weighed in the nude using paediatric weighing scales with pan, which were routinely maintained and calibrated.

Analysis

Data were analysed using SPSS (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY, IBM Corp, USA). Anthropometric Z-scores were calculated using the WHO anthropometric software, adjusted for gestational age at birth[24]. Because of a lack of skinfold norms for infants under 3 months, a threshold of 10mm for sum of skinfolds was used to define low skinfolds, based on the empirical lower limit observed across the first year in a UK survey [7,20]. Conditional weight gain (CWG) is a measure of weight Z score change which adjusts for regression to the mean, the tendency for small infants to catch up towards the median and for larger infants to drift down towards the median[25]. In this study this was calculated as the change in weight Z-scores (SD scores) from birth to the later age when data was collected, as follows:

$$CWG = WAZ - \text{birth weight } Z * B$$

Where B is the regression coefficient of birth weight Z regressed onto later WAZ in a healthy population. Because of a lack of norms for CWG under age 4 weeks and uncertainty about local growth rates, regression constants and norms for weight gain were established using the retrospective weights of the healthy infants attending the hospital Infant Welfare clinic. Based on this data (see supplementary table) the threshold for WF in the hospitalised infants was defined as a CWG of -2SD[20]. The reference definition of undernutrition, was then defined as SSF 10mm or CWG <-2SD. Where there was no CWG due to lack of birthweight an infant was defined as test negative unless they had low SSF.

For each of the three index measures (WLZ, WAZ and MUAC) we calculated their sensitivity and positive predictive value (PPV) to detect undernutrition, as well as the likelihood ratio (LR): the ratio of the percentage test positive for each measure, to the prevalence in those who were test negative. The three indicators above were also compared using receiver operator curves (ROC).Thresholds for low WLZ and WAZ were set at -2 SD, the WHO thresholds for moderate malnutrition[23]. For MUAC a threshold of 11cm was used as described above.

Results

Date from the hospital Infant Welfare Clinic were obtained for 411 healthy infants, yielding 1480 measurements in total (Supplementary table). The regression constants of the later weight compared to birthweight decreased with age, but the lower limit for CWG remained around -2SD. A total of 125 hospitalised infants aged 2 weeks to 6 months were recruited. Overall 22% were born preterm, but prematurity was given as the reason for admission in only 9%. The commonest reason for admission was sepsis, followed by respiratory problems and surgical conditions. Only 6 cases were admitted specifically because of severe undernutrition, but the mean weight and CWG scores were low on average (Table 1).

The proportion with low WLZ WAZ or MUAC varied from 25% for WLZ to 36% for MUAC, while 24% had low CWG and 33% had low sum of skinfolds. (Table 2). This meant that overall 45 infants (36%) met our a-priori reference definition of undernutrition (low SSF or CWG). The great majority of these had low skinfolds, with only 4 (8%) having low CWG in isolation (Figure 1). A much higher proportion of infants aged under 3 months were below the thresholds for most measures, with the exception of WLZ.

MUAC had the highest sensitivity under 3 month, but the lowest at 3-6 months, while WLZ had the lowest sensitivity under age 3 months and overall detected only half of all cases. WAZ had the highest PPV at all ages and the highest sensitivity overall, detecting more than two thirds of the cases. The likelihood ratio (LR), was highest overall for low WAZ in infants aged 3-6 months, but in infants under 3 months MUAC had the higher LR (Table 3). When comparing the three values using ROC, WAZ consistently had the highest area under the curve (Table 3, Figure 2). Overall 42% of children had either low WAZ or MUAC or both and this criterion detected 90% of cases with a PPV of 82% and a likelihood ratio of 8.7 (Table 3).

Discussion

All anthropometric measures are only a screen for undernutrition rather than a gold standard measure of it and all have advantages as well as disadvantages. While the widely used WHO public health 'definitions' of acute malnutrition are important to allow consistency between countries and centres, it is important to remember that these are only screening definitions, which by their nature would be expected to misclassify some healthy children as undernourished, while missing other true cases. Some children with WAZ may be naturally short rather than undernourished, while other children with normal weight could be tall but emaciated. Weight for length and MUAC are intended to identify wasting, but low values for these might also screen in healthy children with a narrow build and in infancy it might not detect children who are growing slowly and becoming stunted. Thus is it important to validate these criteria against measures that are more specific to undernutrition. Here we have used skinfolds, which are a more direct assessment of the size of fat stores that are essential to sustain health, rather than lean mass. Conditional weight gain detects children whose weight has dropped below its expected trajectory, which should avoid the misclassification of genetically small or lean children as undernourished.

The performance of any screening measure, in terms of its positive or negative predictive values depends crucially on the underlying prevalence of the condition being targeted. In this study, though few of the hospitalised infants were admitted specifically for treatment of undernutrition, over a third had low fat stores, with or without slow weight gain, which likely reflects the high rates of pathology found in this hospitalised population. In practice most children with low WAZ were also thin or growing slowly so that, despite it theoretical limitations, it was actually a low WAZ that most reliable detected children with undernutrition, followed by MUAC, while weight for length performed least well. This presumably reflects a greater tendency for very young infants to respond to nutritional compromise by growing slowly, rather than wasting.

A limitation of this study was that it was undertaken in only one centre and there is a need to replicate this study in other units with different case mixes, where results might be different. However so far there have been very few studies in this young age group. A similar recent study in infants aged 1- 12 months found low rates of malnutrition in hospitalised infants in the UK, but much higher rates in a tertiary referral unit in Iran.[7] Similar rates of undernutrition have been reported previously in another Nigerian hospital-based study[26] but it was not clear there how much this simply reflected the high background prevalence of undernutrition in Nigeria[27]. However in our study it was clear that undernutrition was much commoner in hospitalised infants than in the well-baby clinic, since rates of weight faltering were four to five time the lower 5th percentile found in healthy Nigerian children. This suggests that in a Nigerian setting, levels of undernutrition are high for very young sick infants during hospitalisation, which could have implications for recovery and prolonged hospital stay.

The limitation of any study of malnutrition is the absence of any gold standard measure and the results of different studies will vary depending on the measure used. In more affluent, low prevalence settings measures of weight gain, rather than a single weight are favoured as they are assumed to be more specific. Their limitation is the need for at least two measures collected over time s and any velocity measure of this kind is thus more prone to error, as it relies on weights at two time points. In this sample we cannot assume that the birthweight was collected accurately, but it is reassuring that most infants with low CWG also had low skinfolds, suggesting that most were accurate. Around one in six children did not have a recorded birth weight and this is more likely in settings without universal maternity provision, making velocity measures impractical for general use. A very similar CWG measure, also using a 5th percentile threshold has been successfully used in another study to identify infants at risk for growth faltering in Nigerian infants at the 6 – 8 week postpartum check [28]. The 5% threshold for CWG, although apparently less stringent than the -2 z scores threshold (equivalent to the 2nd centile), was in fact comparably stringent to the other measures used. The lower limits were established for this study using healthy Nigerian infants, but the average weight gain seen there was slower than rates seen in UK infants[9]. It must also be recognised that for some infants the exact date of birth may not be known accurately, which would also introduce some imprecision into the weight for age Z scores. Skinfolds have not yet been much used in a developing world context to assess undernutrition, although norms for skinfolds were included in the WHO growth chart project[14] and it is the level of fat reserves that is most likely to determine the level of severity of undernutrition. The problem for our study was that the WHO norms only started at three months, which would exclude over half of the children screened. However we had already observed that skinfolds levels showed little variation across the first year, making a single lower threshold probably valid[20]. Skinfolds will not allow any assessment of abdominal fat, but it seems reasonable to assume that these will be quite closely correlated.

Whatever measure is used, what matters is the extent to which that measure reflects underlying functional impairment or long term risk, so future studies of this kind should consider functional outcomes such later morbidity or mortality and longer term growth impairment.

Conclusions

This highlights the importance of screening for malnutrition at hospital level in these very young infants and that a low WAZ alone is the most valuable screening criterion, while

MUAC is also helpful. Combining weight with MUAC gives even higher discrimination, but the addition of a length measurement does not.

“**What is already known on this topic**”

- Undernutrition is more common in hospitalised infants due to disrupted feeding and underlying disease effects.
- In low and middle income countries undernutrition is usually identified using measurements of weight, height and mid-upper arm circumference.
- Screening criteria for children aged under 6 months are lacking.

“What this study adds”

- Undernutrition in hospitalised infants under 6 months of age in Nigeria is common.
- MUAC and WAZ are the best performing measures to screen for undernutrition in very young infants.
- Using WLZ in a hospital setting missed many cases of low body fat and faltering growth.

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Table 1: Variation in characteristics of subjects by age

Variable	2 weeks – 3 months	3 – 6 months	Total	Chi^2 P-value
Female	23 (39.7)	36 (53.7)	59 (47.2)	0.116
Born before <37 weeks	15 (25.9)	13 (19.4)	28 (22.4)	0.388
Birthweight <2500g	8 (16.0)	5 (9.1)	13 (12.4)	0.283
Diagnosis				
Sepsis	17 (29.3)	21 (31.3)	38 (30.4)	
Respiratory Tract Disorder	9 (22.4)	14 (20.9)	23 (18.4)	
Surgical condition	11 (19.0)	10 (14.9)	21 (16.8)	
Malaria	5 (8.6)	7 (10.4)	12 (9.6)	
Prematurity	6 (10.3)	5 (7.5)	11 (8.8)	
Neonatal jaundice	5 (8.6)	0 (0.0)	5 (4.0)	
Diarrhoea & Vomiting	3 (5.2)	6 (9.0)	9 (7.2)	
Severe undernutrition	2 (5.2)	4 (6.0)	6 (4.8)	0.329
Mean (SD)				
Birthweight (kg)	3.1 (0.66)	3.3 (0.62)	3.2 (0.64)	
Birthweight Z scores	-0.44 (1.5)	-0.05 (1.4)	-0.23 (1.4)	0.17
At assessment				
Weight (kg)	3.9 (1,2)	6.4 (1.2)	4.3 (1.8)	
Weight for Age scores (WAZ)	-1.40 (1.8)	-1.10 (1.7)	-1.24 (1.7)	0.34
Length (cm)	53 (5.0)	64 (3.8)	55 (8.0)	
Length for Age scores (LAZ)	-1.11 (1.9)	-0.34 (1.5)	-0.69 (1.7)	0.01
Weight for length scores (WLZ)	-1.00 (1.6)	-1.13 (1.7)	-1.07 (1.7)	0.67
Conditional weight gain	-1.26 (1.2)	-0.99 (1.6)	-1.11 (1.4)	0.34
MUAC (cm)	10.6 (1.9)	12.8 (1.6)	11.8 (2.1)	<0.001
Sum of skinfolds	10.2 (3.8)	12.9 (3.6)	11.7 (3.9)	<0.001

Table 2: Prevalence of undernutrition using different criteria, broken down by age.

Values are Percentage (Number) below threshold

	2 weeks – 3 months	**3 – 6 months**	**Total**	**Chi^2 P-value**
Number	58	67	125	
Weight-for-age Z<-2SD	34.5 (20)	23.9 (16)	28.8 (36)	0.13
MUAC <11 cm	60.3 (35)	14.9 (10)	36.0 (45)	<0.001
WLZ <-2SD (n = 120)	20.8 (11)	28.4 (19)	25.0 (40)	0.23
Conditional weight gain <5th centile[1]	30.0 (15)	18.2 (10)	23.8 (25)	0.12
Sum of skinfolds <10 mm	48.3 (28)	19.4 (13)	32.8 (41)	0.001
Undernutrition (LSSF or CWG or both)	50.0 (29)	23.9 (16)	36.0 (45)	0.002

[1]Available for 105

Table 3: Extent to which field measures (MUAC, WLZ, and WAZ) predict undernutrition (low CWG and /or low skinfolds)

Risk factor	Sensitivity	Positive predictive value	% (N) with actual undernutrition Below risk factor threshold	 Above risk factor threshold	Likelihood ratio
2 weeks to <3m					
MUAC <11 cm	90%	74%	74.3 (26)	13.0 (3)	5.72
WLZ <-2SD	36%	82%	81.8 (9)	38.1 (16)	2.15
WAZ <-2SD	66%	95%	95.0 (19)	26.3 (10)	3.61
3-6m					
MUAC <11 cm	44%	70%	70.0 (7)	15.8 (9)	4.43
WLZ <-2SD	69%	58%	57.9 (11)	10.4 (5)	5.57
WAZ <-2SD	75%	75%	75.0 (12)	7.8 (4)	9.62
Total					
MUAC <11 cm	73%	73%	73.3 (33)	15.0 (12)	4.89
WLZ <-2SD	49%	67%	66.7 (20)	23.3. (21)	2.86
WAZ <-2SD	69%	86%	86.1 (31)	15.7 (14)	5.48
MUAC <11cm or WAZ <-2SD	90%	82%	74% (39)	8.3% (6)	8.67

Figure Legends

Figure 1: Degree of overlap between slow weight gain and low skinfolds

Values are percentage of all children with each characteristic

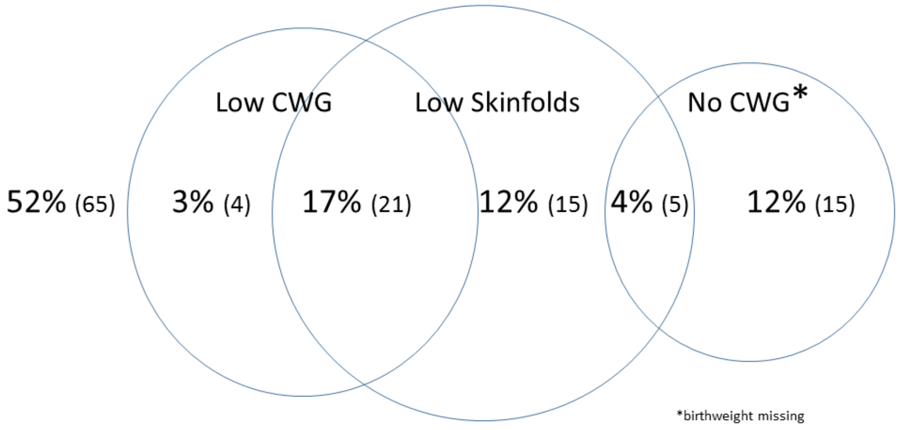
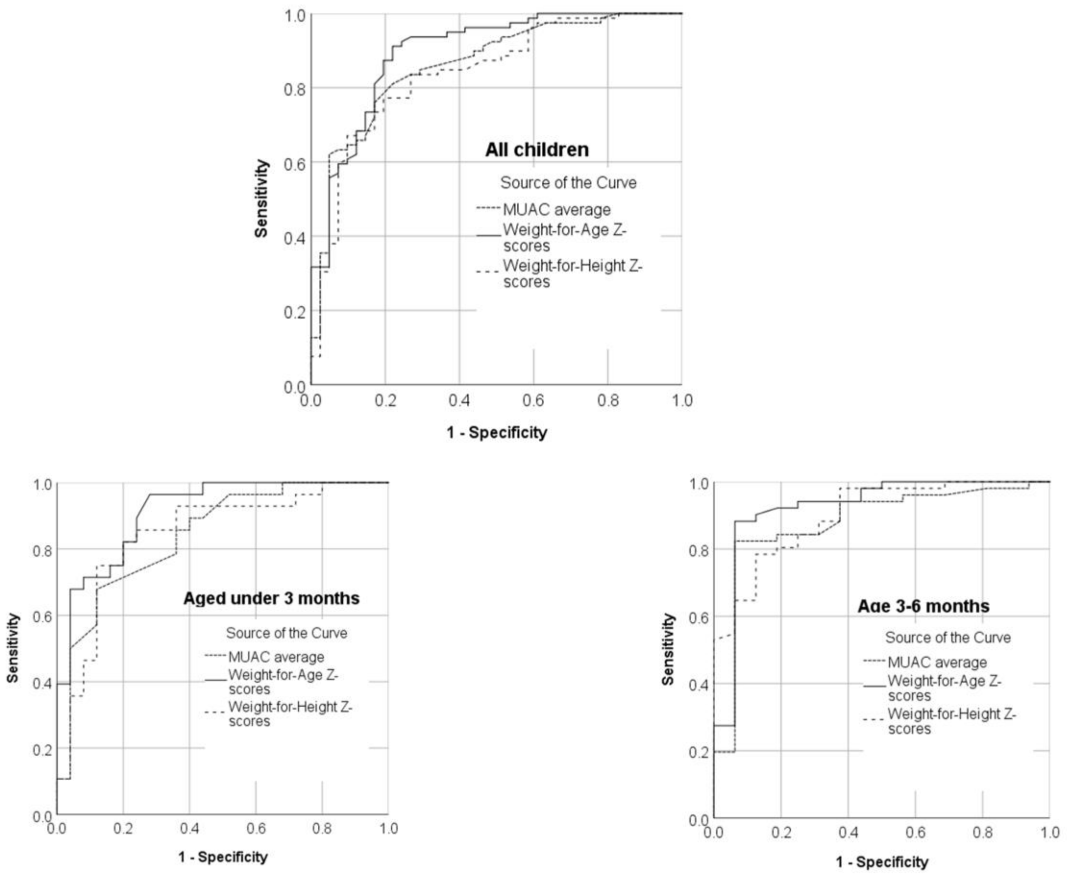


Figure 2: WLZ, WAZ and MUAC compared using receiver operator curves (ROC) with the outcome of undernutrition.



Supplementary table: Weight data for healthy infants collected in child welfare clinic (n=411)

Age	N	Weight (kg) Median	Weight-for-age Z-scores Mean (SD)	Regression constant	5th percentile for CWG
Birth	382	3.3	-0.0 (1.2)		
6 weeks	400	4.7	-0.3 (1.1)	0.60	-1.9
3 months	391	6.0	-0.3 (1.2)	0.53	-2.1
6 months	307	6.8	-0.4 (1.2)	0.30	-2.2