

Determination of Fetal malnutrition in preterm newborns

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Abstract: Background: Fetal malnutrition has been associated with an increased risk of neonatal morbidities and mortalities and its proper documentation in a newborn is essential for optimal management of the child. Objective: To determine the nutritional status of preterm newborns at birth using CANSORE and anthropometry and to compare the relative efficiency of CANSORE and the anthropometric indices in detecting FM. Methods: The study was carried out on consecutive, singleton, live born babies of ≥ 28 completed weeks through 36 weeks gestation born at Lagos University Teaching Hospital, Lagos, Nigeria without any major congenital abnormalities or severe perinatal illness. Each infant was examined by the investigator within 48 hours of birth. Birth weights and lengths were recorded for each infant at birth. Using the Oloweintrauterine growth chart, birth weights for gestational age below the 3rd percentile and above the 97th percentile on the chart were taken as small for gestational age and large for gestational age respectively. PI was computed from the formula: $PI = \text{weight (g)} / \text{length}^3 \text{ (cm)} \times 100$. A PI < 2.2 was considered as malnutrition. The MAC/HC ratio was calculated for each infant and value plotted on and compared with a standard curve. Clinical assessment of nutritional status score (CANSORE) consisted of inspection and estimation of loss of subcutaneous tissues and muscles in the designated areas. A maximum score of 4 was awarded to each parameter with no evidence of malnutrition, and the lowest score of 1 was awarded to parameter with the worst evidence of malnutrition. Fetal malnutrition was defined as CANSORE less than 25. Statistical analysis was done using the Epi info statistics software version 3.5.1. Results: One hundred and forty preterm newborns were assessed. One hundred and eight (77%) of them were of LBW. CANSORE identified 34.3% of the babies as FM while PI, MAC/HC and birth weight identified 30.7%, 12.1 and 3.6% of the babies, respectively, as FM. The mean CANSORE and anthropometry between males and females were not significantly different ($p > 0.05$). Both CANSORE and PI detected significantly large numbers of FM in the study sample compared with birth weight. All the anthropometric parameters showed low sensitivity in detection of FM (which is the visible wasting or loss of subcutaneous tissues and muscles) but they all had high specificity. Conclusion: FM is still prevalent in our environment even in preterm babies. CANSORE identified more malnourished subjects than anthropometry.

Keywords: Preterm, CANSORE, Anthropometry, Newborns

1. Introduction

Fetal malnutrition (FM) is a state of poor nutrition in-utero resulting from inadequate supply and or utilization of nutrients [1] leading to the fetus failing to acquire adequate amount of fat, subcutaneous tissues and muscle mass during intrauterine growth [2]. Many factors affect fetal growth, including the nutritional state [3] and social habits / status [3] (e.g. smoking, literacy level) of the mother, the state of placental function [4] and the genetic makeup of the fetus [5]. FM describes the under-weight / wasting

aspect of the clinical syndrome seen in malnourished newborns. This clinical state may be present at almost any birth weight [2] and it has been described in preterm babies [6]. According to the World Health Organization, malnutrition is by far the biggest contributor to child mortality [7]. In about 50% of all childhood mortalities there is an underlying malnutrition [7]. In a Turkish study, Korkmaz et al [6] documented an incidence of FM of 54.8% in preterm newborns and demonstrated its association with an increased risk of neonatal morbidity and mortality [5,8]. The common feature of most causes of FM is

decrease in the delivery and utilization of nutrients or oxygen or both to the developing fetus. Numerous animal experiments have shown that poor nutrition and other influences that impair growth during critical periods of early life may permanently affect the structure and physiology of a range of organs and tissues [9,10]. Since different tissues mature during different periods of fetal life and infancy, the long term consequences of altered nutrition depend on its timing and duration. Therefore, the assessment of nutritional status of the fetus at birth becomes a major concern because of the potentially serious sequelae of malnutrition on multiple organ systems. Studies have shown that perinatal problems and /or long-term central nervous system sequelae occur primarily in babies with fetal malnutrition whether AGA or SGA [5,11]. Fetal malnutrition on its own can be a cause of preterm delivery [6]. Recent studies have also demonstrated the evidence that fetal malnutrition may have a far-reaching effect into adult life. Fetal under-nutrition has been linked to increased rates of cardiovascular disease and non-insulin dependent diabetes mellitus as adults [12,13,14].

Various methods have been used to identify babies that suffered suboptimal fetal growth such as birth weight for gestational age [15,16], ponderal index (PI) [15-17], mid arm circumference /head circumference ratio [16,18,19] and CANSORE. Clinical assessment of nutritional status score (CANSORE) - contains nine clinical signs viz hair, cheeks, neck, arms, chest, abdomen, back, buttocks and legs –which was developed by Metcoff [11] to differentiate malnourished from appropriately nourished babies [11]. Routinely used anthropometric indices may not have been able to answer all the questions about FM. There is need for new and better methods of determining FM especially in preterm babies. CANSORE has been used widely by researchers to determine FM in term babies. It is therefore, hypothesized, that if CANSORE has been effective in detecting fetal malnutrition in term neonates, its applicability in preterm newborns is deserving of evaluation. There is a dearth of research in the use of CANSORE as a means of assessing FM in preterm newborns in the West African sub region.

The aims of the present study are to assess the nutritional status of preterm neonates at birth using CANSORE and anthropometry and to compare the relative efficiency of CANSORE and the anthropometric indices in detecting FM. The findings from this study could contribute to baseline data for subsequent research and planning in this area.

2. Methodology

The study was carried out on consecutive, singleton, live born babies of ≥ 28 completed weeks through 36 weeks gestation born at Lagos University Teaching Hospital, Lagos, Nigeria between 1st May and 30th November 2010.

Exclusion criteria were any obvious major congenital abnormalities or severe perinatal illness. Ethical clearance

was obtained from the Research and Ethics Committee of the Lagos University Teaching Hospital. Informed parental consent was obtained for each newborn recruited.

Sample size of 140 was calculated using the formula for descriptive study: $n = Z^2Pq / d^2$.

Each infant was examined by the investigator within 48 hours of birth. All the anthropometric measurements, except birth weight, were carried out by the investigator with trained assistance where needed, within 48 hours of baby's birth. All the neonates were weighed completely nude at birth by the delivery room staff using the infant weighing scale (Weighmaster model[®], USA), which records the weight to the nearest 10g. Using the Oloweintrauterine growth chart [20], birth weights for gestational age below the 3rd percentile and above the 97th percentile on the chart were taken as small for gestational age and large for gestational age respectively. The infant's length was measured using the infants measuring board, Infantometer. It was measured to the nearest 2mm. The infant was laid in supine position on the board with the head held at the fixed end by an assistant. The knees were brought together, straightened out and steadied. The movable foot piece was then applied to the sole of the feet after stabilizing and straightening the baby's knees and trunk against the board. The length was read off the board at the level of the soles of the feet with the slide gently touching the heels. The head circumference was measured using non-metallic non-stretchable tape measure at the level of the occiput, parietal prominences and above the supra-orbital ridge [21]. The measurement was to the nearest 0.1cm. The mid arm circumference was measured using a flexible non-stretchable tape at the midpoint between the acromion and the olecranon process with the forearm flexed at 90° at the elbow [21]. In the abducted arm with the elbow flexed (in almost all the term babies), a skin crease appears which corresponds approximately with the midpoint of the arm [17,21,22]. The readings obtained were recorded to the nearest 0.1cm.

PI was computed from the formula: $PI = \text{weight (g)} / \text{length}^3 \text{ (cm)} \times 100$. A PI < 2.2 was considered as malnutrition. The MAC/HC ratio was calculated for each infant and value plotted on a standard curve designed for Nigerian newborn [22,23]. This MAC/HC standard consists of the regression line of MAC/HC and gestational age and the corresponding 95% confidence belt. Infants above the belt are overnourished and those below the belt are malnourished [22,23].

Clinical assessment of nutritional status was done within 48 hours of life on the basis of the superficial readily detectable signs of malnutrition in the newborn as described by Metcoff [11]. The researcher alone did the assessments. This consisted of inspection and estimation of loss of subcutaneous tissues and muscles in the designated areas. Hair, cheeks, neck and chin, arms, back, buttocks, legs, chest and abdomen were examined and then scored. The range of scores for each varied between 1 and 4. A maximum score of 4 was awarded to each parameter with

no evidence of malnutrition, and the lowest score of 1 was awarded to parameter with the worst evidence of malnutrition. The total rating of the 9 CANS signs was the CANSORE for the subject. Fetal malnutrition was defined as CANSORE less than 25 [11,24,25].

STATISTICAL analysis was done using the Epi info statistics software version 3.5.1. The variables were presented by frequency tables and cross-tabulations. Student's t-test was used to compare the mean anthropometry between males and females. Non parametric data were analyzed using Mann Whitney U test. Chi-squared analysis was used to assess association between categorical variables. Fisher's exact test was used for variables less than five. P-value < 0.05 was considered significant at 95% confidence level.

3. Results

Over a period of seven months, a total of 140 preterm babies who met the study criteria were recruited. Of these, 108 were of LBW. There were 67 males and 73 females giving a male: female ratio of 1:1.08.

Table 1. Distribution of gestational age by sex

Gestational age (week)	Frequency (%)		Total n (%)
	Male n (%)	Female n (%)	
28 – 30	3 (4.5)	17 (23.3)	20 (14.3)
31 – 33	19 (28.4)	15 (20.5)	34 (24.3)
34 – 36	45 (67.2)	41 (56.2)	86 (61.4)

Using the Olowe intrauterine growth chart, out of the 140 preterm newborns, 124 (88.6%) were AGA, 11 (7.9%) were LGA and 5 (3.6%) were SGA. Table 2 shows the mean \pm SD of anthropometric measurements viz. birth weight, length, head circumference (HC) and mid arm circumference (MAC). The anthropometric indices increased with gestational age.

There was no demonstrable significant difference between the anthropometric parameters of nutritional assessments in both males and females as shown in table 3.

The mean of the ages of the mothers were 30.9 \pm 4.6 years. Sixty percent of the babies were born to multiparous mothers. Educational levels of the mothers had no significant influence on whether they had preterm delivery. About 65% of the mothers suffered various illnesses during pregnancy (high blood pressure (62%), malaria (6.5%), retroviral disease (17.5%), and others (14%).

3.1. Clinical Assessment of the Nutritional Status of the Newborns

Table 4 shows the prevalence of FM, in preterm newborns, using CANSORE, PI, birth weight and MAC/HC ratio. The prevalence of FM using CANSORE was 34.3% (48 babies) while it was 30.7% (43 babies) and 3.6% (5 babies) using PI and birth weight respectively. There was no significant difference between

the clinical parameters of nutritional assessments in both males and females except for MAC/HC which detected more males with low MAH/HC ratio as shown in table 4.

Table 5 shows the comparison of the anthropometric indices and the CANSORE among preterm babies. PI identified FM in 29.2% of the preterm babies that CANSORE identified as FM. All the SGA babies were classified as fetal malnourished by CANSORE. CANSORE also identified 43 (31.8%) of the 135 preterm AGA babies as FM. Also, 41% of the preterm babies with low MAC/HC showed features of FM.

Table 2. Distribution of mean \pm SD of the anthropometric indices according to gestational age

Gestational age (weeks)	No of babies (%)	Birth weight (g)	Mean \pm SD		
			Length (cm)	HC (cm)	MAC (cm)
28 – 30	20 (14.3)	1300 \pm 300	37.0 \pm 2.8	28.4 \pm 1.9	7.1 \pm 0.5
31 – 33	34 (24.3)	1600 \pm 300	40.4 \pm 3.8	29.7 \pm 1.8	7.9 \pm 0.8
34 – 36	86 (61.4)	2400 \pm 500	45.7 \pm 3.8	32.8 \pm 2.2	9.3 \pm 1.4

SD = standard deviation

HC = Head circumference

MAC = Mid-arm Circumference

Table 3. Comparison of anthropometrics between male and female babies

Variable	Mean \pm SD			Student's t statistic	P
	Total	Male	Female		
Length	43.2 \pm 5.0	43.4 \pm 4.8	43.0 \pm 5.1	0.52	0.61
HC	31.4 \pm 2.7	31.7 \pm 2.6	31.1 \pm 2.9	1.27	0.21
MAC	8.6 \pm 1.5	8.6 \pm 1.4	8.6 \pm 1.5	0.05	0.96
BWT	2.1 \pm 0.6	2.1 \pm 0.4	1.9 \pm 0.5	0.21	0.81
PI	2.5 \pm 0.5	2.59 \pm 0.51	2.5 \pm 0.4	1.81	0.07

Table 4. Nutritional status of preterm newborns using CANSORE, PI, Birth weight and MAC/HC ratio

Assessment Tool	All (n=140) no (%)	M (n=67) no (%)	F (n=73) no (%)	X ²	P
CANSORE < 25	48 (34.3)	19 (28.4)	29 (39.7)	1.53	0.22
PI < 2.2	43 (30.7)	16 (23.9)	27 (37.0)	2.22	0.14
SGA	5 (3.6)	4 (6.0)	1 (1.4)		0.15**
MAC/HC low	17 (12.1)	13 (19.4)	4 (5.5)		0.04**

Figures in brackets are percentages of n

M = males

F = Females

PI = Ponderal Index

SGA = Small for gestational age

MAC = Mid-arm circumference

HC = Head circumference

** = Fisher exact test

The sensitivity and specificity of the anthropometric indices in comparison to CANSORE were 29.2%, 14.6%, and 10.4% for PI, MAC/HC and BWT respectively; while their positive and negative predictive values were 68.5%, 89.1% and 100% respectively. All the parameters had low

sensitivity for detecting FM compared to CANSCORE. However they all had very high specificity. BWT had a specificity of 100% for detecting FM. (Table 6)

Table 5. Comparison of CANSCORE and anthropometric indices in detection of FM in preterm newborns

Anthropometrics	CANSCORE (%)		Total N=140(%)	P
	Malnourished n = 48(%)	Not malnourished n = 92(%)		
PI				
Malnourished	14 (29.2)	29(31.5)	43 (30.7)	0.93
Not malnourished	34 (70.8)	63 (68.5)	97(69.3)	
MAC/HC ratio				
Malnourished	7 (14.6)	10 (10.9)	17(12.1)	0.001
Not malnourished	41 (85.4)	82 (89.1)	123(87.9)	
Birth weight				
Malnourished (SGA)	5 (10.4)	0 (0)	5 (3.6)	0.000 2
Not malnourished (AGA + LGA)	43 (89.6)	92 (100)	135(96.4)	

Table 6. Statistical details of the various anthropometric indices in comparison to CANSCORE

Statistical indices	PI	MAC/HC	BWT
Sensitivity	29.2	14.6	10.4
Specificity	68.5	89.1	100
Positive predictive value	32.6	41.2	100
Negative predictive value	64.9	66.7	68.1

4. Discussion

Fetal malnutrition is a common problem in the developing countries [5,26]. Several studies have documented that the nutritional status of the newborn is important for identifying perinatal risks [11,27,28]. An easy to use tool for bedside diagnosis of FM is much needed especially in preterm newborns.

Most of the work done on CANSCORE had been on term babies. Only Korkmaz et al [6] had exclusively assessed preterm babies with CANSCORE. When CANSCORE was applied to the preterm babies in the present study, the prevalence of FM was 34.3%. This is lower than the 54.8% prevalence recorded in preterm newborns in Turkey by Korkmaz et al [6] but higher than the prevalence documented by most literature on term babies [5,11,16,29]. This could be explained by the high incidence of prenatal risk factors such as maternal or obstetric diseases and placental disorders, leading to both prematurity and fetal malnutrition in preterm infants. For example in the present study, 62% of the preterm mothers were hypertensive. Adverse maternal obstetric histories were also found to be significantly higher in mothers of preterm babies with FM in the study by Korkmaz et al [6]. Prolonged maternal hypertension results in placental insufficiency and fetal malnutrition which may ultimately

lead to preterm labor or demise of the fetus if very severe.

The prevalence of fetal malnutrition using CANSCORE in various weight-for-gestational age groups infants had been reported. Different researchers had demonstrated that not all SGA babies had FM and that some AGA babies may have features of FM. In the study by Metcalf [11], the prevalence of fetal malnutrition was reported to be 5.5% in AGA infants and 54.0% in SGA infants. Naveen et al [16] documented features of FM in 57.1% of SGA and 3.8% of AGA newborns. Adebami et al [5] detected FM in 11.5% of term AGA babies using CANSCORE. The present study also documented a high prevalence of fetal malnutrition in preterm AGA and SGA infants of 31.8% and 100% respectively. This is in conformity with the prevalence documented by Korkmaz et al [6] in preterm AGA (44%) and SGA (100%) infants in Turkey; and it corroborates the evidence that preterm SGA babies may also have visible features of FM.

Aside from the nutritional condition of the fetus, birth weight depends on the gestational age. The marked difference in birth weight at gestational age 34-36 weeks (Table 2) may not be unexpected and it is in accord with other studies which have demonstrated that subcutaneous fat accretion commences around 28 weeks gestational age and peaks around 36 weeks and, thereafter, the rate of accretion decreases [30,31]. By 39 weeks gestational age the placenta ceases to grow and the supply of nutrient stabilizes and then gradually declines in prolonged gestation [32-34]. The data from the present study shows that fat accumulation may be highest in the gestational age 34-36 weeks hence the marked increase in weight and MAC observed at these gestational ages. The prevalence of SGA in preterm babies in the present study is 3.6% which is also lower than the prevalence documented by Korkmaz et al [6] in preterm newborns in Turkey. The low prevalence of SGA in the present study may be due to the different intrauterine growth curves used. The Olowe intrauterine growth chart [20] used in this study classified babies less than minus two standard deviations from the mean or below the 3rd percentile as SGA whereas the Brenner intrauterine growth chart which uses the 10th percentile as the cut-off for SGA was used in the study by Metcalf [11] and Adebami et al [5]. Korkmaz et al [6] used the Denver growth chart which also used the 10th percentile as cut-off for SGA. It is possible that the Olowe growth chart used may not have identified all the SGA babies as Brenner or Denver growth charts would have done. A similar study in India by Naveen et al [16] had also reported a lower prevalence of SGA when local Indian intrauterine growth chart was used (9.1%) compared to when international growth charts which had higher cut-off weights at each gestational age was used (45.4%) resulting in higher sensitivity but low specificity.

Ponderal index has been used by various authors to classify intrauterine growth and FM infants. The present study recorded FM prevalence of 30.7% using PI. This was lower than the 49.5% reported by Orbark et al [35] in

preterm newborns. The observed difference may be explained by the fact that different definitions were used for low PI. While Orbak *et al* [35] used $\pm 1SD$ from the mean to classify the PI, the present study used a static cut-off of 2.2 to define low PI in the preterm babies. However, a normal PI may not always indicate adequate intrauterine nutrition. Some babies with normal PI were found to be malnourished using other indices in the present study. For example, CANSORE identified 34 babies with normal PI as malnourished. It may be that these babies with normal PI, who were found to be FM using other indices, were of symmetrical growth restriction with proportionate decrease in weight and length but have features of FM. PI being a ratio may not be markedly affected by gestational age. However, its sensitivity in chronic malnutrition may be decreased. When compared with CANSORE in the present study, PI had a very low sensitivity for FM.

The MAC/HC ratio is another indicator of FM widely used by researchers. It considers the fat accumulation on the arm compared with the size of the head. The fat mass is affected by changes in nutritional status and it is readily mobilized as a source of calories during periods of stress [36]. The prevalence of FM in the present study using MAC/HC ratio was 12.1%. This is lower than the 49.76% recorded in term babies in India by Mehta *et al* [37]. An explanation for the low values of FM detected by MAC/HC ratio in the present study may be the different cut off values used in determining FM. Mehta *et al* [37] and Naveen *et al* [29] used a MAC/HC cut off value of 0.27 for defining FM in both term and preterm babies. The present study showed that MAC/HC increased as gestational age increased hence a static cut-off point may not be ideal. The present study used the intrauterine growth curve for MAC/HC developed by Eregie *et al* [22] in Nigeria. However, when compared with CANSORE as an index for detecting FM in the present study, it recorded a very low sensitivity.

It is of interest to note that not all babies classified as malnourished by anthropometry were found malnourished by CANSORE and vice versa. The present study like others in the literature had shown that CANSORE identified more babies with FM compared to anthropometry. Does it mean that CANSORE over-diagnosed FM or that other methods under-diagnosed it or a mixture of both? The question of possible over diagnosis of FM by CANSORE is an important one. FM can predispose to certain metabolic derangements like hypoglycaemia at birth and when it is not anticipated and monitored it may cause some adverse neurological damage before it is detected. The additional assessment and monitoring required with CANSORE may be considered cost effective if these adverse effects can be prevented.

The results from the present study have shown that the mean anthropometry increased as the gestational age increased. This is partly due to increased fat accumulation as the gestational age increases. Hence, babies born before this optimal fat accumulation age may be at a disadvantage if the same parameters and cut-off points were used for

identifying FM in them. The issue now is that considering that acquisition of fat and subcutaneous tissues actually commences around 26 weeks gestation and peaks around 36 to 40 weeks gestation [38], it is conceivable that the same cut-off of CANSORE (and anthropometry) in both term and preterm babies may contribute to the apparent increase in the number of malnourished preterm babies seen in this study. This may indeed be the reason why previous researchers have not used CANSORE in very preterm newborns. It is understandable that if adjustments were to be made in the parameters for different gestational age groups of preterm infants, multiple criteria may need to be developed and therefore complicate nutritional status assessment in these babies. It is also obvious from different studies that preterm babies suffer FM just like term babies but the use of CANSORE in preterm newborns may require further study. Using an arbitrary cut-off for CANSORE as 25 may not give a true picture of FM in these babies.

The newborn baby with FM is a high risk newborn and his postnatal survival greatly depends on careful observation and documentation of the evidence of his adverse intrauterine life and a proactive management of his anticipated complications. A simple and easy way of identifying FM at birth is ideal and will make for judicious use of scarce resources in developing countries. The different anthropometric indices measure different aspects of the wellbeing of a newborn while CANSORE measures the visible wasting observed in malnourished newborn. All the parameters, in one way or the other, reflect the adverse intrauterine nutrition these newborns suffered. Therefore, the use of multiple methods of determining FM will increase the likelihood of identification of most babies with FM. The addition of CANSORE to the routine assessment of preterm newborns at birth may further improve newborn care and buttress the need to look out for these high risk babies for anticipatory care and follow up.

5. Conclusions

1. The present study has shown that FM is still prevalent in our environment even in preterm babies.
2. CANSORE identified more malnourished subjects than Ponderal Index, MAC/HC ratio and birth weight.
3. Fetal malnutrition is prevalent in preterm babies irrespective of method of assessment.

Recommendations

- The use of CANSORE at birth is recommended in order to identify cases of FM for proactive intervention to minimize morbidity and mortality of these at risk group of babies.
- Though CANSORE may be useful in the

identification of FM in preterm infants, it may require some modifications in order to capture peculiarities relating to lower deposition of adipose tissue.

Limitations of the Study

CANSCORE increases with increasing gestational age so the use of same cut-off point of CANSCORE for both term and preterm babies may not give the true picture of FM in preterm babies.

Future Research Needs

- 1 A study involving a large cohort of preterm babies with enough babies in each gestational age band to demonstrate:
 - a) The relationship between gestational age and CANSCORE.
 - b) The best cut-off point for defining fetal malnutrition.
- 2 A study that will assess the value of CANSCORE as a proxy for body fat by comparing with more direct measures of subcutaneous fat like skin-fold thickness.

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