Nutritional Assessment in Preterm Infants

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A practical approach for nutritional assessment in preterm infants under intensive care, based on anthropometric measurements and commonly used biochemical markers, is suggested.

Keywords: anthropometry ; biochemical markers ; body composition ; growth charts ; nutritional assessment ; preterm infant

1. Introduction

Growth faltering has been extensively documented in infants born very prematurely, being attributed to inadequate nutrient intake and lack of standardization in feeding practices [1][2]. Poor postnatal growth is associated with adverse neurocognitive outcomes [3]. Although fast postnatal growth is associated to better neurodevelopment in preterm infants, early fast weight gain may be associated with later obesity, high blood pressure, and adverse cardiovascular and metabolic outcomes [3][4][5]. Both undernutrition and overnutrition may predispose to obesity and cardiovascular disease [6][7].

Monitoring nutritional status is required to detect nutritional deficits early and to guide nutrition support in preterm infants under intensive care. Thus, nutritional assessment should be an essential skill of neonatal staff caring for preterm infants [8].

Tracking body composition rather than just body weight is more accurate for monitoring nutritional status and improving nutritional outcomes [9][10]. Dual-energy X-ray absorptiometry (DXA) and air displacement plethysmography (ADP) are validated and convenient methods for body composition assessment in small infants, since they are noninvasive, rapid to perform, and not affected by movements [10][11][12]. However, these methods are expensive and not accessible for the majority of clinical settings [10][13][14]. As an alternative, anthropometry may be a proxy for body composition [14]. This is a noninvasive and inexpensive method, suitable for bedside evaluation, despite limitations in the validity of several measurements in small infants [15][16]. In addition, most anthropometric prediction equations were developed based on cross-sectional studies at and near birth [12].

A comprehensive approach for the evaluation of nutritional status includes anthropometry, biochemical markers, clinical parameters, and dietary assessment [8]. While clinical signs of early malnutrition are largely imperceptible, certain clinical biochemical markers can provide a useful insight into nutritional status, particularly when used as a complement to anthropometric measurements [8][17].

2. Anthropometry

In preterm infants, anthropometry is useful for several purposes, including the diagnosis of fetal malnutrition and risk assessment of early metabolic complications, monitoring growth during hospital stay, and early recognition of undernutrition or overnutrition [16].

Revisited direct anthropometric measurements include body weight and length, head circumference (HC), mid-upper arm circumference (MUAC), and skinfolds [12][16]. Indices calculated from direct measurements have been proposed, assuming that some may provide a better insight into body composition than the original direct measurements [15][16]. Derived measurements herein revised include equations based on body weight and length, MUAC to HC ratio (MUAC:HC), and mid-arm cross-sectional areas.

Accurate anthropometry should rely on appropriate technique and instrumentation, and the obtained results interpreted by plotting on appropriate growth charts or comparing with appropriate reference values [11][16].

2.1. Body Weight

Body weight measurement is simple and reproducible, and it is the most used single parameter to monitor neonatal growth and nutritional status in clinical practice [18]. However, body weight does not give any information on the size of body compartments and, consequently, on the quality of growth [16][19]. In some preterm infants, weight gain may result from a positive balance of water and sodium rather than the accretion of fat or protein, as happens in sick infants affected by edema [18][20]. Nevertheless, in preterm infants measured shortly after birth, body weight unadjusted for length was found to be strongly associated (r^2 = 0.97) with ADP-determined fat-free mass [13]. It is not surprising that body weight is a good proxy of lean mass particularly in very- and extremely preterm infants since they are born with scarce fat mass [13][21]. In the fetus, body fat changes from a minimum deposit during the first trimesters of gestation to an exponential increase after 30 weeks, period in which 94% of all fat deposition occurs [22].

2.2. Crown-Heel Length

Body length reflects skeletal growth and fat-free mass [23][24]. In preterm infants, it was found to be a good predictor (r^2 = 0.85) of ADP-determined fat-free mass shortly after birth [13].

Length assessment is useful only if measurement has been accurately undertaken [23]. Length is frequently measured inaccurately or ignored in clinical practice because of the perceived difficulty in measurement of neonates [24][25]. The reluctance of the observer to extend the lower limbs forcefully is a factor affecting its accuracy in full-term neonates, who are more comfortable in flexion [25][26][27][28]. In spite of the lack of similar studies in preterm infants, the reluctance to fully extend the lower limbs as recommended seems to be widespread in these infants. Moreover, the accuracy of measured length is of utmost importance when it is squared or cubed in indices, since a small error in its measurement amplifies the distortion of final results [16][29].

2.3. Head Circumference

An increase in occipitofrontal circumference reflects brain growth, although it is not a sensitive or specific measure [19]. Some factors should be taken into account when interpreting HC measurements in neonates. During the first postnatal week, HC may decrease by about 0.5 cm due to extracellular fluid space contraction [19]. If HC values are above or below the reference limits it may represent a variant of normal, and therefore, the parents' HC should be measured and plotted [16].

In infants born prematurely, a non-expected deviation of head growth in the presence of good weight and linear growth should be investigated for causes other than inadequate nutrient intake. These may be related with prematurity-related morbidity, including post-hemorrhagic hydrocephalus or brain atrophy [19][30]. In addition, magnetic resonance imaging measurements recently revealed that in "encephalopathy of prematurity", increased size of the extra-axial spaces may artificially increase HC [31].

In preterm infants, postdischarge head growth seems to be a better predictor of cognitive outcomes than intra-hospital head growth [32].

2.4. Mid-Upper Arm Circumference

The MUAC reflects the combined arm muscle and fat; a decrease in its value indicates a reduction in body muscle and/or fat mass [23][33]. As the upper arm is less affected by fluid status changes than other areas of the body, in the presence of edema, the MUAC may be a more accurate estimate than other measurements [23].

In preterm infants, measurements of MUAC are reproducible and detect changes over time [33]. In moderately preterm infants, adiposity defined by ADP-determined percent of fat mass (%FM), accounts for 60.4% of the variation of MUAC [34].

2.5. Skinfolds

Skinfolds measurement is an inexpensive and suitable method for bedside nutritional assessment in neonates [10][16]. The triceps and biceps skinfolds are used mainly to assess peripheral subcutaneous fat, whereas subscapular and suprailiac skinfolds are used to assess central subcutaneous fat [35].

The use of skinfolds to estimate body fat assumes that the thickness of subcutaneous fat reflects a constant proportion of total body fat and the sites used for the measurements reflect the average thickness of the subcutaneous fat layer. Although these assumptions have been questioned [36], a good correlation was reported between skinfolds and DXA- [37][38] and ADP-determined body fat [34]. Contrarily, skinfolds seem to overestimate total body fat comparing with body water dilution measurements [39]; however, this method assumes a constant of lean tissue hydration that in fact is not constant

and varies with age [10]. Some reasons have been reported for the discrepant results between studies. Skinfolds do not reflect intra-abdominal fat; the hydration status affects skinfold compressibility; and reproducible measurements require skill and practice of the observer [15][16][36][40]. Particularly in preterm infants, the rapidly changing distribution of fat accretion makes it difficult to generate an accurate equation for predicting total body fat [36].

2.6. Weight-to-Length Based Equations

Indices based on weight and length commonly used to assess body proportionality and body composition in neonates include the weight-for-length ratio, the body mass index (BMI) (weight/length^2), and the ponderal index (weight/length^3) [12][13][16].

The reliability of these indices is highly dependent on the accuracy of length measurement [16]. It has been described that accurate crown-heel length measurement is difficult to obtain at least in term neonates [28]. Inaccurate length squared in the BMI magnifies the error while leading to the index decreasing its ability to differentiate over- from underestimation. When cubed to obtain ponderal index, the inaccuracy of the length measurement is further magnified, despite the fact that it still differentiates overestimation from underestimation [29].

Ponderal index has been the traditional measure used to assess proportionality at birth and to distinguish between asymmetrical and symmetrical types of intrauterine growth restriction [41]. More recently, BMI has been reported to be more appropriate to assess body proportionality than either weight-for length ratio or ponderal index [42].

When used to assess body composition, BMI accounts for more than 81% of the variance of DXA-determined lean mass in AGA term infants measured shortly after birth [38]. Compared with ADP-determined %FM (adiposity), all weight-to-length based equations were found to be poor predictors of adiposity in preterm infants [10][13], even though the BMI z-score predicts adiposity better than the ponderal index (r^2 = 0.43 vs. 0.29) [43].

2.7. Mid-Upper Arm Circumference to Head Circumference Ratio

The MUAC:HC ratio may contribute to the estimation of body composition; its usefulness as a complementary index was assessed, comparing with DXA measurements [38]. This index was proposed to identify acute intrauterine malnutrition at birth, assuming that in acute protein-energy deprivation the brain is spared in relation to muscle and fat [44]. It may be particularly useful to identify symptomatic malnourished AGA neonates who are not diagnosed based exclusively on birth weight [45]. Longitudinal MUAC:HC measurements were reported to be useful for monitoring growth, seeming to not overestimate malnourishment in apparent protein-energy sufficiency [46].

2.8. Upper-Arm Cross-Sectional Areas

Upper-arm fat and muscle areas have been used in the assessment of nutritional status in infants [47]. For their calculation, it is assumed that the upper arm is cylindrical, the subcutaneous fat is a concentric ring evenly distributed around a circular core of muscle, the fat thickness is half the triceps skinfold, and the muscle includes the humeral diameter [48]. Two equations derived from MUAC and triceps skinfold have been proposed relying on different geometrical assumptions [48][49].

Upper-arm fat and muscle areas measurements should be interpreted with caution in neonates, since their ability to predict total body fat and muscle has been questioned [38]. In term infants assessed shortly after birth, the added value of cross-sectional arm areas contributed little to detect the variation of DXA-determined body lean and fat mass, compared with weight and length alone [38]. The ability of cross-sectional arm areas to predict mid-upper arm muscle and fat was also questioned. In full-term infants, a poor correlation of arm areas with ultrasound measurements was found, leading to overestimation of muscle and underestimation of fat [50]. In preterm infants, arm muscle and fat areas were inaccurate predictors (r^2 < 0.56) of magnetic resonance imaging measurements [51]. These poor correlations may be explained by the limited reliability of MUAC [34] and triceps skinfold [39] measurements and by the oversimplification of geometrical assumptions used for the calculation of cross-sectional arm areas [16].

3. Biochemical Markers

In preterm infants, some biochemical markers are useful in the assessment of nutritional status, helping to detect nutritional deficiencies before the appearance of clinical signs [17]. These markers should be interpreted with caution and used to complement other nutritional data, including anthropometric measurements [17].

Markers for metabolic and electrolyte, iron, protein, and bone status have been reviewed previously [8][17][52]. Markers to monitor protein status and bone status are summarized in **Table 1**.

Table 1. Biochemical markers of protein and bone status in preterm infants [8][17][18][53].

Measurement	Advantages	Limitations
Protein status		
Blood urea nitrogen (BUN)	Low BUN is a good marker of low protein intake in enterally fed, clinically stable infants.	High BUN is not easy to interpret, since it may represent appropriate amino acid intake, low energy intake relative to protein intake, or amino acid intolerance.
Serum prealbumin	Half-life of approximately 2 days. A low level reflects current protein deficit.	Inflammation or infection may decrease prealbumin levels.
Retinol-binding protein (RBP)	Half-life of approximately 12 h. A low level reflects current protein deficit.	RBP levels may be also be affected by suboptimal iron, zinc, and vitamin A status. Measuring RBP is more expensive than prealbumin, providing equivalent information.
Serum transferrin	A complementary marker of protein status.	In iron deficiency, transferrin concentration increases regardless of nutritional status. It is seldom used.
Bone status		
Serum calcium		It is a poor marker of MBD.
Serum phosphate	High specificity and positive predictive value as a marker of MBD.	Low sensitivity and negative predictive value as a marker of MBD. Insufficient evidence as a reliable marker of MBD.
Serum alkaline phosphatase	Levels >900 U/L yield a specificity of 71% and a sensitivity of 88% as a marker of MBD	Insufficient evidence as a reliable marker of MBD.
Serum alkaline phosphatase plus serum phosphate	Alkaline phosphatase >900 U/L plus phosphate <1.8 mmol/L (5.6 mg/dL) yield a specificity of 70% and a sensitivity of 100% as a marker of MBD	Insufficient evidence as a reliable marker of MBD.
Urinary calcium and phosphate markers	Urinary calcium-creatinine ratio, phosphate concentration and tubular reabsorption of phosphate may be complementarily used in the diagnosis of MBD	Levels are dependent on whether infants are formula-fed or breastfed.

BUN, blood urea nitrogen; MBD, metabolic bone disease; RBP, retinol binding protein.

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