Postnatal catch-up fat after late preterm birth

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BACKGROUND: Late preterm birth accounts for 70% of preterm births. The aim of the study was to investigate the postnatal weight gain and weight gain composition changes in a cohort of late preterm infants.

METHODS: A total of 49 late preterm infants (mean birth weight $2,496 \pm 330$ g and gestational age 35.2 ± 0.7 wks) underwent growth and body composition assessment by an air displacement plethysmography system on the fifth day of life, at term, and at 1 and 3 mo of corrected age. The reference group was composed of 40 healthy, full-term, breast-fed infants.

RESULTS: The late preterm infants showed a Δ fat mass gain between birth and term-corrected age equal to 182%. As compared with full-term infants, at term and 1 mo of corrected age mean weight ($3,396 \pm 390$ vs. $3,074 \pm 409$ g and $4,521 \pm 398$ vs. $4,235 \pm 673$ g, respectively) and percentage of fat mass (16.1 ± 4.6 vs. 8.9 ± 2.9 and 22.6 ± 4.2 vs. 17.4 ± 4.0 , respectively) were significantly higher in late preterm infants, whereas no difference among groups was found at 3 mo.

CONCLUSION: Rapid postnatal catch-up fat was found in these infants. Further studies are needed to investigate whether this short-term increase in fat mass may modulate the risk of chronic diseases or represent an adaptive mechanism to extrauterine life.

Late preterm birth is defined as a birth that occurs between 34 0/7 and 36 6/7 wk of gestation. The proportion of late preterm births has markedly increased during the past two decades, accounting for 70% of preterm births (1). Late preterm infants have been recognized as a high-risk group of infants as they present unique physiology and greater risks in terms of mortality and morbidity as compared with full-term infants (2,3).

There is evidence that monitoring not only the quantity but also the quality of growth, in terms of body composition changes, may play an important role in gaining further insight into the relationship between birth weight and time *in utero* on early growth pattern and future health (4–6). Indeed, extremely preterm infants, assessed at term-corrected age, have been found to be at increased risk for developing increased and/or aberrant adiposity, which is a known risk marker for cardiovascular disease (7,8). However, it has been reported that preterm infants born appropriate for gestational age succeed in recovering growth and fat mass within the third month of corrected

age (9). To our knowledge, data regarding the early dynamic features of growth and body composition changes of late preterm infants are scarce. Santos *et al.* recently reported that late preterm infants are at increased risk of failure to thrive during the first 2 years of life (10).

The aim of our study was to investigate the body composition of late preterm infants at birth and to evaluate the postnatal weight gain and changes in body composition in a cohort of late preterm infants during the first 3 mo of corrected age in comparison with full-term infants.

RESULTS

Growth and body composition were assessed in 49 late preterm infants. Basic subject characteristics of the late preterm and full-term infants at birth are shown in Table 1. As expected, gestational age, birth weight, length, and head circumference in the late preterm infants were significantly smaller than in the full-term infants, whereas no significant difference in the percentage of males between the two groups was found. Sixty-seven percent ($n = 33$) of the late preterm infants were born by vaginal delivery. All late preterm infants were breastfed for at least 50% of total milk intake. No difference in maternal characteristics between the late preterm and the full-term infants was found (Table 2). Anthropometric parameters of the late preterm and full-term infants at each study point are shown in Table 3. The late preterm infants showed higher mean weight values than the full-term infants at term and 1 mo of corrected age, whereas at 3 mo no significant difference between the two groups was found. No difference in terms of length and head circumference values were found between the late preterm and full-term infants through the study.

Mean percentage (SD) of fat mass in the late preterm infants on the fifth day of life was significantly lower than that of the full-term infants at birth (5.7 (3.9) vs. 8.9 (2.9), respectively, $P < 0.0001$). Mean percentage of fat mass was significantly higher in the late preterm infants as compared with the full-term infants at term and 1 mo of corrected age (Table 4). The late preterm infants showed a mean (SD) Δ fat mass gain between the fifth day of life and term corrected age equal to 182% (43). Mean Δ fat mass gain from term up to the third month of corrected age was significantly lower than that of the full-term infants (Figure 1). However, at 3 mo of corrected age,

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Table 1. Characteristics of the late preterm and full-term infants at birth

	Males, <i>n</i> (%)	GA (wk)	Weight (g)	Length (cm)	Head circumference (cm)
Late preterm infants	21 (43)	35.2 (0.7)*	2,496 (330)*	44.8 (1.7)*	31.6 (1.2)*
Full-term infants	17 (42)	39.2 (1.29)	3,074 (409)	49.3 (2.0)	34.2 (1.1)

Data are expressed as mean (SD) or *n* (%).

GA, gestational age.

*P < 0.0001.

Table 2. Maternal characteristics

	Late preterm	Term
Age (y)	34.2 (5.2)	33.1 (4.7)
BMI (kg/m ²)	22.7 (4.2)	22.6 (4.5)
Weight gain during pregnancy (kg)	11.3 (3.7)	12.1 (4.6)
Gestational hypertension/preeclampsia, <i>n</i> (%)	4 (8)	None
Smokers, <i>n</i> (%)	6 (12)	None

Data are expressed as mean (SD) or *n* (%).

mean percentage of fat mass in the late preterm infants reached values comparable with those of full-term infants.

DISCUSSION

This explorative study presents data related to the body composition changes in a cohort of late preterm infants during the first 3 mo of corrected age. As expected, late preterm infants at birth showed a significantly lower birth weight and percentage of fat mass as compared with full-term infants. Indeed, it is well known that the last trimester of pregnancy is characterized by a major accretion in body weight and fat mass (11). However, at term and 1 mo of corrected age, the late preterm infants were heavier than the full-term infants and achieved a mean body weight value comparable with their counterparts by the third month of corrected age. In addition, between birth and term-corrected age, the late preterm infants showed a great increase in fat mass so that they were fatter than their counterparts at birth. From term up to the third month of corrected age, the late preterm infants showed lower fat mass gains than the full-term infants and, as a result, the percentage of fat mass was comparable between the two groups at 3 mo of age.

To our knowledge, there is a paucity of data concerning the postnatal growth and body composition changes in late preterm infants. Santos *et al.* (10) aimed to evaluate the consequences of being born late preterm on later growth. These authors reported that 3.4% and 3% of a cohort of 371 late preterm infants were at increased risk of being underweight at 1 and 2 years of age, respectively. These findings could be partly explained by the negative effect on growth associated with the higher hospitalization rates reported for late preterm infants in the first years of life (12,13). In addition, as the prevalence of late preterm birth in the population studied was higher in the low-income families, the late preterm infants enrolled in that study could present environmental and economic constraints on growth.

With regard to body composition, this study reports longitudinal data on the dynamic changes in body composition

of late preterm infants during the first months of corrected age in comparison with full-term infants. On the basis of our results, the rapid weight growth shown by the late preterm infants is accompanied by a major increase in the percentage of fat mass that takes place mostly during the first weeks of life. These findings are consistent with previous results reported by other authors with regard to extremely preterm infants. It has been found that extremely preterm infants, including those born small for gestational age, show a major deposition of fat mass in early postnatal life so that they show an increased adiposity at term-corrected age (7,14). However, within the first 3–4 mo of corrected age, extremely preterm infants succeed in achieving fat mass values similar to those of full-term infants (9,15).

The rapid fat deposition experienced by the late preterm infants could represent an adaptive mechanism to postnatal life. It is well acknowledged the fetus and preterm infant are different with regard to the environment and the nutritional supply. Indeed, late preterm infants, as they switch from intrauterine to extrauterine life, have to maintain thermoregulation, fluid balance, and breathing even in the absence of major clinical problems. Moreover, amino acid delivery immediately after birth does not match the high fetal protein intake (16). In addition, it has been suggested that catch-up growth may lead to a state of skeletal muscle insulin resistance, which seems to be strictly associated with an accelerated rate of deposition of fat mass rather than fat-free mass (FFM) (17). The adipose tissue appears to exert a specific control of thermogenesis, i.e., thermogenesis is suppressed by the depleted adipose fat stores during starvation, to spare energy. When refeeding takes place, deposition of fat mass is greater than that of FFM due to the fact that thermogenesis remains suppressed to promote catch-up fat. Instead of being used in the skeletal muscle glucose is redistributed for lipogenesis and storage in the adipose tissue. This preferential “catch-up fat” can eventually lead to an increased adiposity that, in association with adipose tissue hyper-responsiveness and hyperinsulinemia, may represent an additional risk factor for the development of the metabolic syndrome in young adulthood (17). On the basis of these experimental studies, the rapid catch-up fat shown by the late preterm infants could be partially explained by the fact that the infants enrolled in this study were relatively “underfed” in the first days of life.

This explorative, longitudinal study provides preliminary evidence regarding growth and weight gain composition of late preterm infants vs. full-term infants during the first

Table 3. Anthropometric parameters of the late preterm and full-term infants at each study point

	Weight (g)		Length (cm)		Head circumference (cm)	
	Late preterm	Full term	Late preterm	Full term	Late preterm	Full term
Term/birth	3,396 (390)**	3,074 (409)	49.5 (1.9)	49.3 (2.0)	34.8 (1.0)	34.2 (1.1)
1 mo	4,521 (398)*	4,235 (673)	53.6 (2.3)	53.8 (2.5)	37.1 (1.1)	36.7 (1.2)
3 mo	6,050 (485)	5,978 (580)	59.6 (2.1)	60.6 (2.5)	40.4 (1.2)	39.9 (1.3)

Data are expressed as mean (SD).

* $P = 0.002$; ** $P < 0.0001$.

Table 4. Mean fat mass values (%) in the late preterm and full-term infants

	Late preterm	Full term
Term	16.1 (4.6)**	8.9 (2.9)
1 mo	22.6 (4.2)*	17.4 (4.0)
3 mo	26.7 (4.3)	27.1 (3.9)

Data are expressed as mean (SD).

* $P = 0.002$; ** $P < 0.0001$.

Figure 1. Mean Δ fat mass gains in the late preterm and full-term infants. Black bars, full-term infants; white bars, late preterm infants. * $P = 0.007$ full-term vs. preterm infants; ** $P = 0.004$ full-term vs. late preterm infants.

months of corrected age. Larger studies are needed to confirm these data and further elucidate the clinical implications of the early postnatal catch-up fat shown by the late preterm infants.

METHODS

Informed consent was obtained from the infants' parents and the study design was approved by the Departmental Ethics Committee, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano, Italy.

Patients

A total of 49 late preterm infants were included in the study. Forty full-term, healthy, breast-fed infants constituted the reference group (18).

Inclusion criteria were the following: gestational age from 34 0/7 to 36 6/7 wk; singleton pregnancy; being born appropriate for gestational age according to Fenton's growth chart (19); and Caucasian parentage. Exclusion criteria were the presence of congenital diseases;

chromosomal abnormalities; severe cardiac, brain, renal, endocrinologic, or gastrointestinal diseases; sepsis documented by positive blood culture; need of intravenous fluids or parenteral nutrition; prepregnancy maternal BMI > 30 ; and prepregnancy diseases.

Study Design

We conducted an explorative, observational, longitudinal study. Infants were enrolled at birth. At enrollment, basic subject characteristics (birth weight, length, head circumference, gestational age, and gender) were recorded prospectively. Gestational age was based on the last menstrual period and first trimester ultrasonogram. Corrected age was calculated using the chronologic age and adjusting for gestational age, that is, for the number of additional weeks from term (40 wk). The following maternal variables were also recorded: age; prepregnancy BMI; smoking; weight gain during pregnancy; gestational hypertension and/or preeclampsia, defined, respectively, as *de novo* hypertension (systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg) arising after mid-pregnancy and gestational hypertension associated with new-onset proteinuria (≥ 300 mg/24 h); and mode of delivery.

Nutritional Practices

With regard to late preterm infants, breastfeeding practice was encouraged in all mother-infant pairs. In case of insufficient breastfeeding, a term formula was used. Full-term infants were exclusively breastfed.

Growth and Body Composition Assessment

With regard to the late preterm infants, anthropometric measurements and body composition were assessed on the fifth day of life, at term, and at 1 and 3 mo of corrected age. The full-term infants were measured at birth (third day of life), and at 1 and 3 mo of age. Body weight, length, and head circumference were measured according to standard procedures (20). The weight of each baby was measured on an electronic scale accurate to ± 0.1 g (PEA POD Infant Body Composition System; Cosmed, Concord, CA). Body length was measured to the nearest 1 mm on a Harpenden neonatometer (Holtain, Crymmych, UK). Head circumference was measured to the nearest 1 mm using nonstretch measuring tape. All measurements were performed by trained nurses.

Body composition was assessed using an air displacement plethysmography system (PEA POD Infant Body Composition System). A detailed description of the PEA POD's physical design, operating principles, validation, and measurement procedures is provided elsewhere (21,22). Briefly, the PEA POD assesses fat mass and "FFM" by direct measurements of body mass and volume and the application of a classic densitometric model in which percentage of body fat is calculated using body density and predetermined fat and FFM density values. Body fat was defined as body weight minus FFM. A constant fat mass density value of 0.9007 g/ml was used. FFM density values are calculated as the sum of the contributions of the various components in the FFM compartment. Age and sex-specific FFM density values extrapolated from data reported in previous multicompartiment model studies were used.

The changes in fat mass [$100 \times (\text{fat mass at second examination} - \text{fat mass at first examination}) / \text{fat mass at first examination}$] were also calculated. With regard to the late preterm infants, the changes in fat mass were calculated between birth and term-corrected age, term-1 mo, and 1-3 mo of corrected age, whereas in the full-term infants, the changes were calculated between birth and 1 mo, and 1-3 mo.

Statistical Analysis

A χ^2 test was used for comparisons between discrete variables. Differences between and among infants in repeated measurements of growth parameters and fat mass were assessed by ANOVA. Statistical significance was set at a level of 0.05. All statistical analyses were performed using SPSS (SPSS, version 12; SPSS, Chicago, IL).

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