Trajectory of fat-free mass and fat mass indices in small-for-date infants in India

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Background. Human growth during the first 2 years of life involves not only quantitative changes in body size, but also qualitative changes in body composition. Measuring fat-free mass (FFM) and fat mass (FM) in infants and children is of both scientific and public-health interest. The incidence of hypertension, type 2 diabetes and coronary heart disease is very high among south Asians compared with white people. In light of these findings, the measurement of body composition such as FFM and FM during the early development phase assumes importance.

Objectives. To establish the trajectories of the fat mass index (FMI), fat-free mass index (FFMI) and body mass index (BMI) of normal-birthweight (NBW) and low-birthweight (LBW) infants, and compare the age-related indices among NBW and LBW children.

Methods. This was a longitudinal study. A total of 240 NBW and LBW in six cohorts, aged 0, 45, 90, 180, 270 and 360 days at baseline, were enrolled from the neonatal care unit of a large charitable government hospital serving the urban poor population in the city of Kolkata, India. Weight and length (L) were measured, and total body water was determined by bio-electrical impedance analysis for estimation of FFM and FM. The indices FFM/L^2 and FM/L^2 were calculated, as were the indices FFM/L^p and FM/L^p, where p was selected in order to eliminate the correlation of these indices with length.

Results. The percentage of FFM gradually decreased in both NBW and LBW babies with an increase in age, and the percentage of FM gradually increased. The percentage of FFM in NBW babies was found to be lower than that in the LBW babies, and the percentage of FM in NBW babies was greater than in LBW babies.

Conclusion. The percentage of FM was consistently lower in LBW than the NBW infants. The fat percentage in all these infants was consistently lower, from birth to age 360 days, than in the reference data on healthy American infants in the West. BMI and FFMI gradually increased from 45 to 180 days of age, and then decreased up to 360 days. Similarly, FMI increased from 45 to 180 days of age, and from 180 to 270 days its growth remained constant. After that point, FMI gradually increased up to 360 days, but very slowly.

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Body size and growth in early childhood have been found to be associated with the risk of chronic adult diseases.[1] Recently, there has been increasing interest in factors that influence the trajectory of fat-free mass (FFM) and fat mass (FM) in young children. Methods based on anthropometry do not critically distinguish between FFM and FM. Bioelectrical impedance analysis (BIA) is an accepted method to estimate total body water (TBW). In a steady state condition TBW correlates with FFM, which can be calculated from TBW using age- and gender-specific hydration factors.[2] Body size and growth at birth in early childhood have been found to be associated with the risk of chronic adult diseases such as coronary heart disease (CHD), type 2 diabetes.[3] Modern BIA equipment is easily carried into the field for community-based studies.

Low birthweight (LBW) is one of the most serious challenges in maternal and child health in both developed and developing countries. Nearly 50% of neonatal deaths occur among LBW babies. The survivors among them are at a high risk of developing malnutrition, recurrent infections and neuro developmental handicaps. LBW rates, largely due to intrauterine growth retardation (IUGR), are high in South Asia, and an important cause of high morbidity and mortality in childhood.[4] Barker *et al*.[5] have shown that LBW and subsequent slow growth rate in early infancy are associated with adult diseases such as diabetes, hypertension and CHD. LBW (<2 500 g) infants suffer from very high rates of morbidity and mortality from infectious diseases, and are underweight, stunted or wasted from the neonatal period and through childhood. Infants weighing 2 000 - 2 499 g at birth are four times more likely to die than infants weighing 3 000 - 3 499 g. LBW is associated with impaired immune function, poor cognitive development and high risks of developing acute diarrhoea or pneumonia. Most studies on the association between birthweight and body size have used BMI and other anthropometric measures as proxy measures for body 'fatness'. Those of low birthweight had an increased death rate from CHD in later life.[5] People who were small at birth and during infancy and showed accelerated weight gain as a result of IUGR had an increased risk of heart disease.

The measurement of body fat is too complex to be of practical clinical application. Therefore, a high BMI may indicate either increased FM or FFM, or body composition, affected by ethnicity, growth pattern or socioeconomic, cultural and behavioural patterns: the same BMI in people of different ethnicities and backgrounds may reflect different fat content and distribution. FM and FFM are components of total body mass. When stature is taken into account, these become the FMI and FFMI, and represent the fat and lean components of BMI, respectively. Several reports support the use of FMI and FFMI instead of BMI for classifying the weight status of children.[6-9]

The purpose of this article is to establish normal trajectories for the FMI, FFMI and BMI of normal birthweight (NBW) and LBW babies in Kolkata, India, and the age-related changes of these indices.

Methods

This was a longitudinal study. A total of 240 NBW and LBW infants in six cohorts, aged 0, 45, 90, 180, 270 and 360 days at baseline, were enrolled from a government hospital in the city of Kolkata, India. The eligibility criteria for inclusion in the study were birthweight ≥ 1 700 g, the infant's mother being free of diabetes or other chronic diseases and the parents being willing to participate in the study. The socioeconomic and demographic features of the families are given in Table 1.

This study was approved by the international review board and the hospital ethics committee (ref. no. FWA00001757). Parental consent was obtained at the time of enrollment.

Data collection

Anthropometric and BIA measurements were obtained by two trained technicians. Weight was measured to the nearest 0.1 kg with a balanced-beam scale, which was calibrated at regular intervals. Recumbent length was measured to the nearest 0.1 cm with a wooden measuring board, as described in a previous article.[10] The board was made sufficiently broad to cover the shoulder blades.

Three values were averaged. FM and FFM were derived from a combination of BIA (using a bioelectrical impedance analyser BIA101-A), performed by placing electrodes on the right arm and right foot, and anthropometry.[11] FMI was calculated as FM (kg)/length (m)^2, and FFMI as FFM (kg)/length (m)^2.

Table 1. Socioeconomic status of families (*N*=240)

Variables	*n* (%)*
House with cement floor, walls and roof	127 (58)
Live and cook in one room	147 (61)
Family income, USD per month (median, IQR)	54 (42 - 70)
Mother's education	
Illiterate	3 (1.3)
1 - 5 years of school	28 (11.7)
6 - 10 years of school	97 (40.4)
>10 years of school	12 (46.4)
Father's education	
Illiterate	3 (1.3)
1 - 5 years of school	21 (8.7)
6 - 10 years of school	90 (37.5)
>10 years of school	126 (52.5)

IQR = interquartile range.
*Unless otherwise indicated.

Data analysis

EPI Info software version 6.0 (CDC, USA) and Stata software version 11.2 (StataCorp, USA) were used. Descriptive statistics (means and standard deviations (SDs)) for BMI, FMI and FFMI were calculated for cohorts defined by gender, age and birthweight. For anthropometric data, a software package based on the National Center for Health Statistics (NCHS) (Centers for Disease Control and Prevention; CDC) database, as provided with the EPI Info software, was used. The difference between two groups was identified using independent *t*-tests. $P<0.05$ was considered statistically significant.

Bioelectrical impedance analysis

The BIA measurements presented here were performed at a single frequency (RJL system, Quantum II & Quantum X Bioelectrical Impedance Analyzer), with one pair of electrodes placed on the dorsal surface of the right hand, and a second pair on the right foot. Bioelectrical impedance was measured in a standard manner while the subject was lying in a supine position on a flat and non-conductive bed. The arms were abducted slightly so that they did not touch the sides of the trunk. The legs were separated so that they did not touch each other. The first pair of electrodes was attached in the standard manner, with the detecting electrode edge placed on an imaginary line bisecting the ulnar hand (bone on the little-finger side of wrist), and the other electrode placed on the first joint of the middle finger. The interior surface detecting electrode edge was placed on an imaginary line bisecting the medial malleolus (bone on the big-toe side of the ankle), with the other electrode placed on the base of the second toe. The skin was cleaned with 70% alcohol before the electrodes were attached. To minimise changes in impedance due to gravity-induced shifts in the subjects, impedance measurements were taken within 5 minutes of lying down. Before each testing session, the calibration of the unit was checked using a 495 - 505 Ω precision resistor and –3 - 3 precision reactor.

BIA-based published equation

The prediction equation for TBW using weight, length and resistance that we evaluated in this study is given below.

We used Fjeld's BIA-based equation for children aged 3 - 30 months (where H = height, R = resistance and W = weight):[12]

$$TBW\ (kg) = 0.76 + 0.18 \times H^2/R + 0.39 \times W$$

The FFM was calculated as TBW divided by an age- and sex-specific hydration factor for FFM, and for this age group that ranged from 80.7 to 77.0 for boys and 80.7 to 78.0 for girls.[2]

Results

The parents of the infants in the study came from a relatively poor metropolitan city in India. The average family income was USD80 per month, and 61% of the families lived in one room. Eighty-five percent of the mothers had school education of ≤6 years. A total of 240 newborn babies (120 NBW and 120 LBW (<2500 g) infants, 112 (47%) boys and 128 (53%) girls)

were included in our study. On developmental follow-up at the hospital clinic we saw 187 (91 NBW and 96 LBW) infants at 45 days, 163 (82 NBW and 81 LBW) at 90 days, 145 (73 NBW and 72 LBW) at 180 days, 126 (65 NBW and 61 LBW) at 270 days and 116 (58 boys and 58 girls) at 360 days old.

The characteristics of the study infants and mothers are shown in Table 2. The TBW of the infants gradually decreased from the age of 45 to 360 days. Using the BIA method, we calculated TBW using the Fjeld equation.[12] The table shows that the percentage FFM differences between NBW and LBW babies are highly significant at 45 days and at 90 days of age, but at 180 days, 270 days and 360 days are not significant. The mean, SD and standard error (SE) values of the differences in percentage FFM in NBW and LBW infants, and the 95% confidence interval (CI) of these differences, are shown in Table 3. For NBW infants, BMI gradually increased with age from 45 days to 180 days, and then decreased up to 360 days. For LBW infants, BMI increased up to 270 days, and then decreased up to 360 days. The indices of FFM and FM are shown in Table 4.

As expected, the mean indices of BMI, FFM and FM in NBW infants tended to be higher than those in the LBW babies. The mean, SD, SE and 95% CI values of these differences are shown in Table 5.

Table 2. Characteristics of the study infants and mothers (*N*=240)

Variable	Normal birthweight	Low birthweight	*p*-value
Mother's age (years), mean (SD)	23.29 (3.77)	24.56 (4.25)	0.02
Mother's postnatal weight (kg), mean (SD)	55.03 (7.97)	52.45 (8.60)	0.02
Mother's postnatal height (cm), mean (SD)	151.19 (5.28)	149.79 (5.59)	0.05
Past pregnancy outcome of the mother, %			
Infant death	10	10.8	
Abortion	19.17	14.17	
Preterm	17.8	32.8	
Type of delivery, %			
NVD	39.1	41.67	
Breech	0	0.83	
Forceps	1.67	4.17	
LUCS	59.17	53.33	
Gestational age, weeks, ^			
≤37	3	8	
38	11	28	
39	32	50	
≥40	74	34	
House with cement floor, walls and roof	59%	54%	
Baby's birthweight, g (mean (SD))	2 865 (249.84)	2 212 (183.57)	<0.001
Sex ratio, boys:girls	63:57	49:71	
Birth length, cm (mean (SD))	48.66 (1.84)	45.79 (1.47)	<0.001

SD = standard deviation; NVD = normal vaginal delivery; LUCS = lower uterine segment caesarean section.

Table 3. Mean, SD, SE and 95% CI of the differences in percentage of FFM between NBW and LBW infants (NBW – LBW)

Age (days)	Mean	SD	SE	95% CI	*p*-value
45 (*n*= 187)	–3.66	4.46	0.64	–4.92 - –2.39	<0.0001
90 (*n*= 163)	–2.43	3.29	0.51	–3.43 - –1.43	<0.0001
180 (*n*=145)	–0.96	3.08	0.51	–1.96 - 0.05	0.0618
270 (*n*=126)	–0.04	2.82	0.51	–1.04 - 0.96	0.9337
360 (*n*= 116)	–0.45	2.52	0.47	–1.38 - 0.48	0.3377

SD = standard deviation; SE = standard error; CI = confidence interval; FFM = fat-free mass; NBW = normal birthweight; LBW = low birthweight.

Table 4. BMI, FFMI and FMI of LBW and NBW babies

Variable (by age)	NBW Mean (SD)	LBW Mean (SD)
45 days		
BMI	14.24 (1.19)	13.51 (1.14)
FFMI	12.70 (0.69)	12.57 (0.75)
FMI	1.54 (0.60)	1.03 (0.54)
90 days		
BMI	15.62 (1.30)	14.79 (1.44)
FFMI	13.11 (0.84)	12.76 (0.90)
FMI	2.45 (0.58)	1.98 (0.66)
180 days		
BMI	16.63 (1.70)	16.08 (1.68)
FFMI	13.38 (1.00)	13.09 (1.02)
FMI	3.25 (0.81)	2.99 (0.77)
270 days		
BMI	16.47 (1.46)	16.14 (1.73)
FFMI	13.23 (0.94)	12.95 (1.00)
FMI	3.24 (0.68)	3.19 (0.79)
360 days		
BMI	16.23 (1.53)	15.66 (1.84)
FFMI	12.93 (0.98)	12.53 (1.16)
FMI	3.31 (0.69)	3.13 (0.76)

BMI = body mass index; FFMI = fat-free mass index; FMI = fat mass index; NBW = normal birth weight; LBW = low birthweight; SD = standard deviation.

Table 5. Comparative indices of NBW and LBW babies (*N*=240)

Variable (by age)	Mean (SD) difference	SE	95% CI	*p*-value
45 days (*n*=187)				
BMI	0.73 (1.22)	0.17	0.39 - 1.08	<0.001
FFMI	0.14 (0.72)	0.12	–0.09 - 0.37	0.2377
FMI	0.51 (0.63)	0.09	0.32 - 0.69	<0.001
90 days (*n*=163)				
BMI	0.83 (1.43)	0.22	0.41 - 1.26	0.0002
FFMI	0.35 (0.88)	0.14	0.07 - 0.63	0.0162
FMI	0.47 (0.66)	0.10	0.26 - 0.67	<0.001
180 days (*n*=145)				
BMI	0.54 (1.71)	0.28	–0.01 - 1.10	0.0543
FFMI	0.29 (1.02)	0.17	–0.04 - 0.62	0.0875
FMI	0.26 (0.80)	0.13	–0.004 - 0.52	0.0537
270 days (*n*=126)				
BMI	0.33 (1.60)	0.28	–0.23 - 0.89	0.2419
FFMI	0.28 (0.98)	0.17	–0.06 - 0.62	0.1071
FMI	0.05 (0.73)	0.13	–0.21 - 0.31	0.6862
360 days (*n*=116)				
BMI	0.57 (1.71)	0.31	–0.05 - 1.19	0.0707
FFMI	0.40 (1.09)	0.20	0.006 - 0.790	0.0467
FMI	0.18 (0.72)	0.13	–0.09 - 0.45	0.1841

NBW = normal birthweight, LBW = low birthweight; SD = standard deviation; CI = confidence interval; BMI = body mass index; FFMI = fat-free mass index; FMI = fat mass index.

Discussion

Recent findings on the association of fetal growth, early postnatal growth and rate of growth in childhood[14-17] with diseases in adults such as hypertension, type 2 diabetes and CHD has generated considerable new interest in studying postnatal growth and development. In South Asian countries, the rate of LBW is very high,[18] largely due to IUGR, while the incidence of hypertension, type 2 diabetes and CHD is high.[19] Population-based studies on growth and its components such as FFM in infancy may be useful in understanding these phenomena.

Impedance to the flow of current in body tissues is a function of resistance (R) and reactance. Cell membranes act as small capacitors, and thus offer a reactive resistance (i.e. reactance) to the flow of current. Based on electrical theory, current at relatively higher frequencies passes through both extracellular and intracellular fluid, and can provide an index of TBW. Thus the BIA method can distinguish between FFM and FM.[20]

This analysis provides trajectories for FMI, FFMI and BMI for NBW and LBW babies. In Fig. 1, we see that the percentage of TBW was comparatively higher in LBW than NBW babies. This percentage decreased gradually in both groups, and at 270 days old the percentage TBW is almost the same in both the LBW and NBW babies. After 270 days, it decreased gradually in both groups, until the age of 360 days. The growth pattern and rate of length increase were similar in NBW and LBW boys, and both were below those in the reference data for boys in the USA, according to the CDC (Fig. 2A).[21] Among girls, the LBW babies had shorter length than the CDC norm. However, in NBW girls aged 0 - 60 days, their length gradually increased, similarly to the CDC girls, from 60 to 90 days, with both having similar length, but after 90 days, the girls in this study's length did not. At 360 days, LBW and NBW babies' length was the same (Fig. 2B). Fig. 3 shows that FFMI was lower in the LBW than the NBW babies. Fig. 4 shows the relationship between the body composition indices (FMI, FFMI, BMI) according to age (from 45 to 360 days old). Here we see that the growth pattern of BMI and FMI were similar. Both BMI and FMI increased symmetrically, and increased with age up to 180 days. After 180 days, their growth rate decreased.

The median spline BMI and FMI growth curve represents a J-shaped curve in both NBW and LBW babies. In contrast, the FFMI

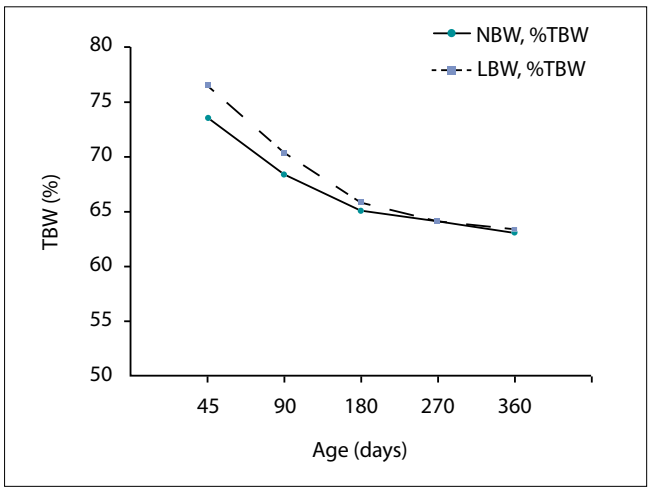
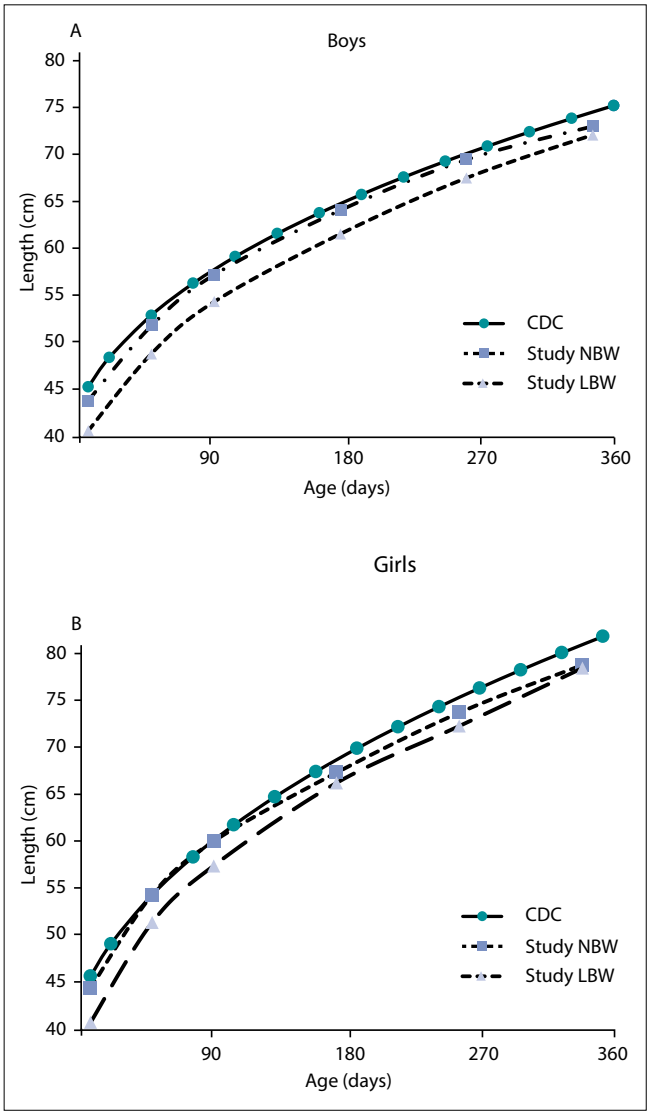


Fig. 1. Percentage total body water (%TBW) of normal birthweight (NBW) and low birthweight (LBW) infants.



Figs 2A and B. Increase in length, in comparison with reference data.[20] A = boys; B = girls.

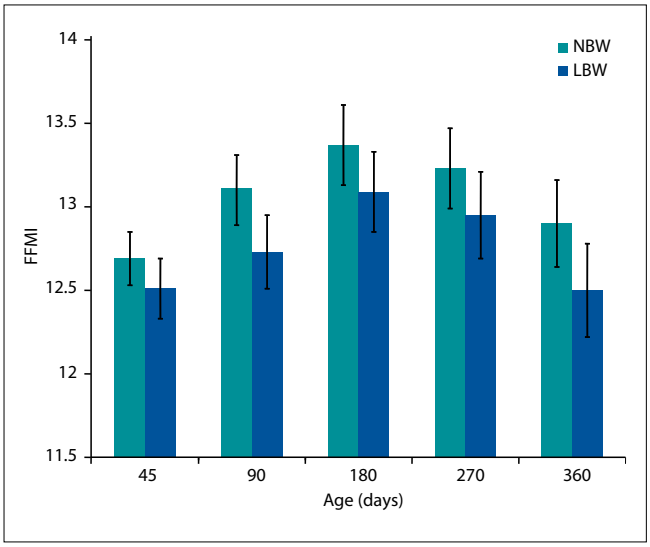


Fig. 3. Fat-free mass index (FFMI) of normal birthweight (NBW) and low birthweight (LBW) babies.

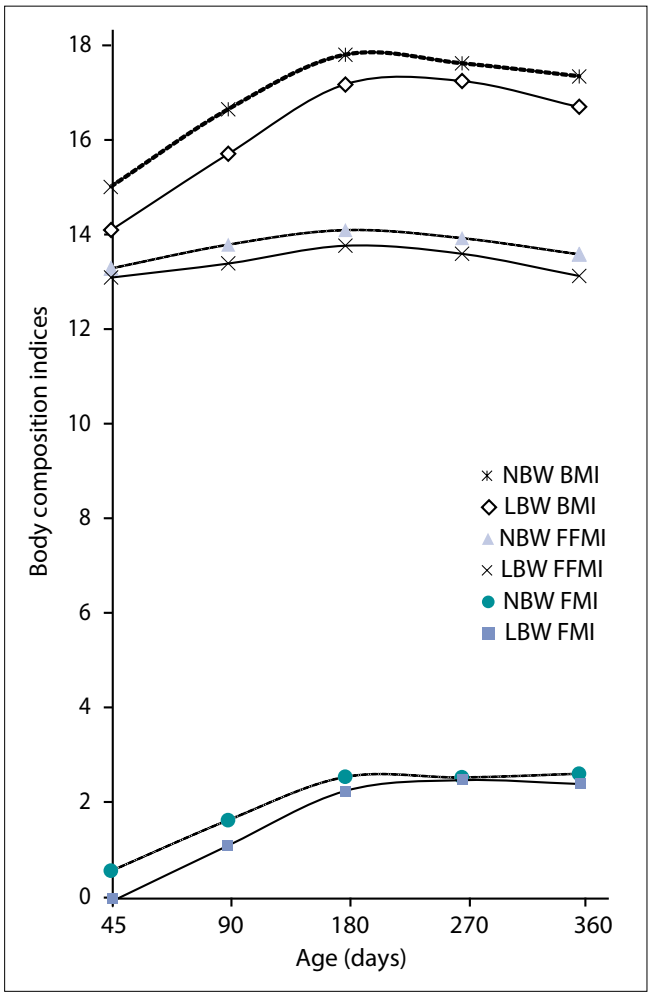


Fig. 4. Mean body mass index (BMI), fat-free mass index (FFMI) and fat mass index (FMI) of normal birthweight (NBW) and low birthweight (LBW) babies, by age.

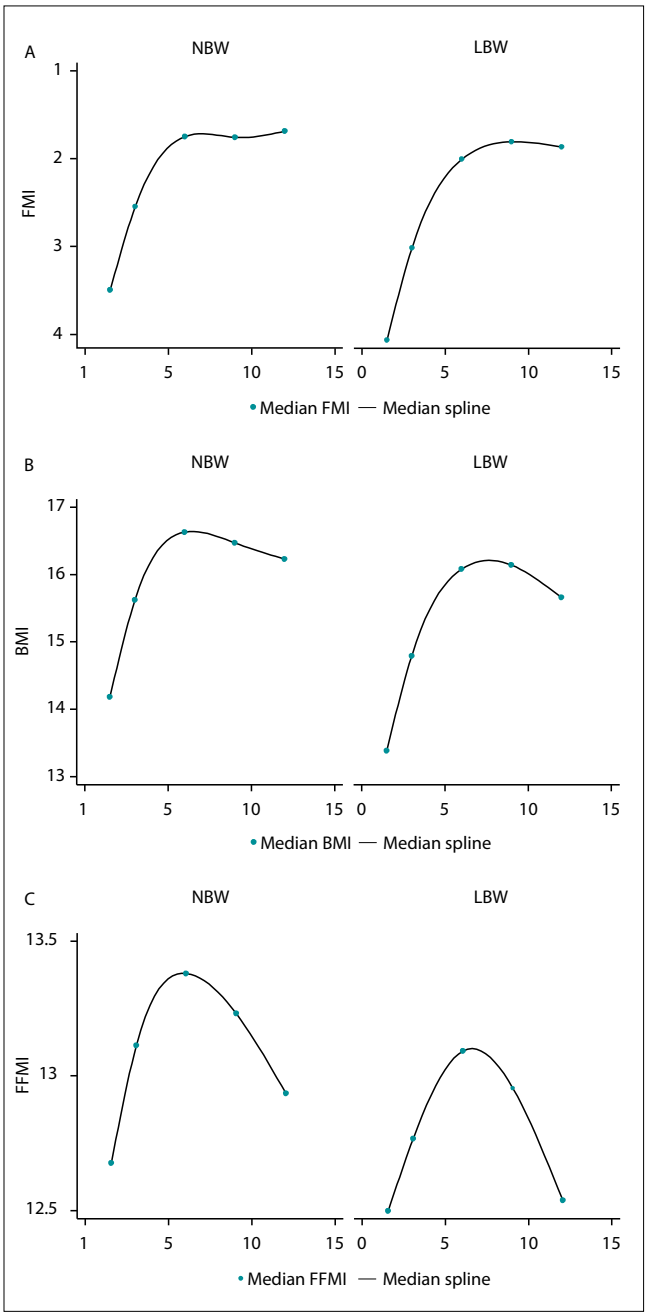


Fig. 5A - C. Stata-generated median spline curves for fat mass index (FMI; A), body mass index (BMI; B) and fat-free mass index (FFMI; C).

curve shaped is an inverted U shape (Figs 5A - C). A number of retrospective studies have clearly established that birthweight and rapid changes in the pattern of growth in early infancy are associated with increased risks for obesity, hypertension, cardiovascular disease, diabetes and some cancers later in life.[20,22-24] Ellis[25] has shown that birthweight has been associated with increased disease risks in adults, although not necessarily all of the same magnitude, or for the same diseases, resulting in both J-shaped and U-shaped response curves. Also, rapid weight gain during early infancy, whether as 'catch-up' growth to compensate for undernutrition or as a result of overnutrition in NBW infant, has been identified as a potential predictor of later adverse health.

LBW serves as a proxy not just for fetal but also for adult health.[4] Barker[4] also showed that LBW is associated with a host of chronic diseases including coronary artery disease (CAD), type 2 diabetes mellitus, cancer and osteoporosis. Birth weight and CAD were shown to have an inverse J- or U-shaped relationship.[4,26,27]

A conventional measure of neonatal 'thinness' is the ponderal index (PI). Our findings suggest that LBW babies have a lower PI (are thinner) than NBW babies. The present analysis provides trajectories of FFMI, FMI and BMI in NBW and LBW infants. LBW is used as an indicator of fetal undernutrition. A better characterisation of the body composition at birth of Indian babies may improve our understanding of the 'thrifty phenotype', and the fetal origin of adult disease.

The utility of BMI is that it is highly correlated with weight and body fatness, but it has a relatively low correlation with height in adults. Andersen *et al*.[28] have shown that neonates with LBW have reduced lean mass as well as lower fat mass. This study has

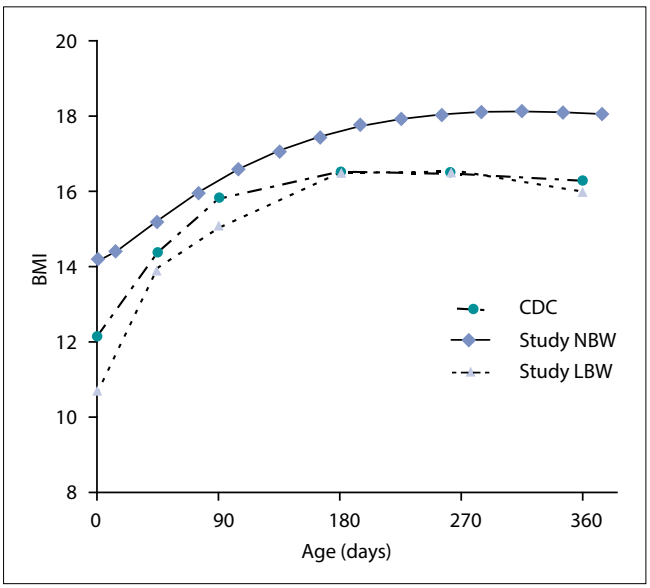


Fig. 6. Body mass index (BMI) comparison between normal birthweight (NBW) and low birthweight (LBW) children in the study and Centers for Disease Control (CDC)[20] US norms.

provided a growth chart for the FFM and FM percentile between NBW and LBW babies. Shelgikar *et al.*[29] have shown that in general, Indians are thin by conventional criteria (low BMI), but are centrally obese.[29]

Fig. 6 shows that the BMI of the children in the present study was lower than that of the Western children in the CDC reference data.[21]

Conclusion

Growth in infants has relevance for adult diseases. The trajectory of weight and height gain does not truly reflect FFM and FM in infants.

Indian babies generally have a high rate of LBW and retarded growth during the first year of life. Both have long-term implications for chronic adult diseases.

Weight-for-length (or height) or indicators such as body mass do not differentiate between FFM and FM. Precise numerical indicators such as FFMI and FMI may provide a better understanding of the intriguing relationship between early growth and adult disease.

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Author contributions. BS carried out the study procedures, took part in the analysis and in writing the manuscript. DM conceived the study design and experiment and statistical analysis, supervised her work, and took part in data analysis and interpretation and in writing the manuscript. AS assisted BS in the standardisation of procedures for anthropometry and BIA methods. He also took part in study design, analysis and interpretation of the findings.
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