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Cord IGF-I concentrations in Indian newborns: associations with neonatal body composition and maternal determinants

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Summary

Background: Indian newborns have been described as 'thin-fat' compared with European babies, but little is known about how this phenotype relates to the foetal growth factor IGF-I (insulin-like growth factor I) or its binding protein IGFBP-3.

Objective: To assess cord IGF-I and IGFBP-3 concentrations in a sample of Indian newborns and evaluate their associations with neonatal adiposity and maternal factors.

Methods: A prospective cohort study of 146 pregnant mothers with dietary, anthropometric and biochemical measurements at 28 and 34 weeks gestation. Neonatal weight, length, skin-folds, circumferences, and cord blood IGF-I and IGFBP-3 concentrations were measured at birth.

Results: Average cord IGF-I and IGFBP-3 concentrations were 46.6 (2.2) and 1269.4 (41) ng mL^{-1}, respectively. Girls had higher mean IGF-I than boys (51.4 ng mL^{-1} vs. 42.9 ng mL^{-1}; $P < 0.03$), but IGFBP-3 did not differ. Cord IGF-I was positively correlated with all birth size measures except length, and most strongly with neonatal sum-of-skin-folds ($r = 0.50$, $P < 0.001$). IGFBP-3 was positively correlated with ponderal index, sum-of-skin-folds and placenta weight ($r = 0.21$, 0.19, 0.16, respectively; $P < 0.05$). Of maternal demographic and anthropometric characteristics, only parity was correlated with cord IGF-I ($r = 0.27$, $P < 0.001$). Among dietary behaviours, maternal daily milk intake at 34 weeks gestation predicted higher cord IGF-I compared to no-milk intake (51.8 ng mL^{-1} vs. 36.5 ng mL^{-1}, $P < 0.01$) after controlling for maternal characteristics, placental weight, and newborn gestational age, sex, weight and sum-of-skin-folds. Sum-of-skin-folds were positively associated with cord IGF-I in this multivariate model (57.3 ng mL^{-1} vs. 35.1 ng mL^{-1} for highest and lowest sum-of skin-fold quartile, $P < 0.001$). IGFBP-3 did not show significant relationships with these covariates.

Conclusion: In this Indian study, cord IGF-I concentration was associated with greater adiposity among newborns. Maternal milk intake may play a role in this relationship.

Keywords: Cord IGF-I, maternal milk intake, neonatal anthropometry, 'thin fat' Indian baby.

Introduction

Newborns in India have been described as 'thin-fat', with relatively low weight and lean mass but high adiposity compared with European babies (1,2). This newborn phenotype has been associated with maternal nutrition, especially low vitamin B_{12} and high folate status (3). It persists in childhood and may predispose individuals to metabolic and cardiovascular disease later in life (2). It is unclear how foetal growth factors such as insulin-like growth factor I (IGF-I) or its major binding protein IGFBP-3 are related to this neonatal body composition. Nor is it known how maternal diet and nutritional status during pregnancy influence foetal IGF-I concentration, and especially how maternal milk consumption, which is an important source of vitamin B_{12} in India, influences foetal IGF-I and body composition. We aim to ascertain associations between foetal IGF-I, IGFBP-3, neonatal anthropometry and maternal diet.

IGF-I is a small peptide structurally similar to insulin. It is synthesized in the liver and most tissues; exhibits endocrine, paracrine and autocrine actions; and circulating levels are regulated by binding proteins (4,5). During pregnancy, both maternal and foetal IGF-I regulate foetal growth through positive effects on nutrient transport across the placenta and cellular proliferation and differentiation.

In humans, umbilical cord blood IGF-I has been positively associated with birth weight (6–8), ponderal index (8,9) and placental weight (10), with similar relationships reported for IGFBP-3 (11). Relationships to birth length are less consistent (6,9). Despite their smaller size, females have higher average IGF-I concentrations than males at birth (7,8), suggesting that foetal IGF-I may contribute to the differences in body composition.

Maternal parity (7,9) and height (7) have been positively associated with cord IGF-I, while mixed relationships between cord IGF-I and gestational age have been reported (8,9). Animal studies demonstrate that maternal undernutrition from protein restriction, feed reduction or starvation results in reduced foetal IGF-I and IGFBP-3 concentrations (4,12), but little is known about how maternal diet impacts foetal IGF-I or IGFBP-3 concentrations in humans (9). Several human studies have shown that maternal milk intake during pregnancy is positively related to neonatal size (13), and it has been suggested that this is due to milk's positive effects on either maternal or foetal IGF-I (14), as post-natal milk intake is positively associated with serum IGF-I concentrations and body size (15,16).

We report foetal cord IGF-I and IGFBP-3 concentrations and their associations with neonatal anthropometric measures and maternal characteristics, including macronutrient and milk intake and serum folate and vitamin B_{12} at 28 and 34 weeks gestation in a sample of Indian mothers and newborns.

Methods

Subjects and study design

This observational cohort study was undertaken in Pune, India, by the Diabetes Unit, King Edward Memorial Hospital (KEM) Research Centre to assess vitamin B_{12} status of mothers during pregnancy and its relationship to post-natal characteristics. Details of study recruitment have been described elsewhere (17). Participants were recruited among women attending an urban antenatal clinic in Pune and an associated rural health centre from May 2004 to February 2006. Records of over 900 pregnant women who attended either clinic were screened. Women who were beyond 28 weeks gestation, with multiple pregnancy, congenital anomaly of the fetus, previous Caesarean section, foetal or neonatal death, pre-eclampsia or underlying chronic disease were excluded. A total of 234 women agreed to participate, and 209 had births at the study centres. Of these, 146 singleton pregnancies with measures at 28 and 34 weeks and at birth were available for analysis.

The cohort study was approved by the KEM Hospital Research Centre Ethics Committee, Pune, India, and informed written consent was obtained from participants. Analysis of the cord blood samples was approved by the Institutional Review Board at Indiana University, Bloomington, IN, USA.

Materials and methods

Anthropometric measurements of mothers and newborns were performed by trained personnel using standardized protocols. The coefficient of variation between measures by different personnel was <2.0%. Maternal measurements included weight (to the nearest 0.005 kg, Conveigh, Mumbai, India) and height (to the nearest millimetre, Harpenden Stadiometer, CMS Instruments, London, UK). Neonatal measurements were taken within 72 h of delivery. Birth weight was measured to the nearest 1 g (ATCO, Mumbai, India) and crown-heel length to the nearest 0.1 cm (Pedobaby Babymeter, ETS J.M.B., Brussels, Belgium). The neonate was placed with the head touching the headboard and legs straightened and held in place until the reading was recorded. Circumferences were measured to the nearest 0.1 cm using a non-stretchable fibre glass measuring tape (Chasmors, London, UK). Mid-upper arm circumference (MUAC) was measured at a point midway between the tip of the acromion process and the tip of the olecranon process. Abdominal circumference was measured just above the umbilicus at the point of expiration. Triceps and subscapular skin-folds were assessed on the left side of the body to the nearest 0.2 mm using Harpenden skin-fold calipers (CMS Instruments). Triceps skin-fold was taken at the MUAC and the posterior most bulging portion of the arm, while subscapular skin-fold was measured at the inferior angle of the scapula. All neonatal measurements were carried out in the supine position.

Gestation was verified by ultrasonography at 12 weeks from antenatal records. The placenta had the membrane removed and was washed to remove clots before weighing.

Maternal diet during pregnancy (28 and 34 weeks) was assessed using a semi-quantitative food frequency questionnaire based on local practices to ascertain routine consumption of all foods. Milk was from either cow, buffalo or goats. Milk products included yogurt, buttermilk, cheese and milk-based puddings, which are common dairy items in the diet. Butter and ghee (clarified butter) were excluded. Milk and milk product intake were each classified into never, occasionally (less than once daily) and at least once daily. Macronutrient content of commonly consumed foods was calculated from a database created from local foods (18) to provide an estimate of daily macronutrient intake.

At enrolment, data were collected on the woman's reproductive history and household demographic characteristics. Socioeconomic status was assessed using the Standard of Living Index (SLI) devised by the National Family Health Survey (19).

Biochemistry

Maternal folate and vitamin B_{12} status were assessed through blood draws at 28 and 34 weeks, as described in a previous publication (17). At birth, umbilical cord blood was collected after the baby was separated from the placental end of the cord. Free flowing blood was collected and centrifuged (4°C, 2500 *g* for 15 min) within an hour of collection, and the plasma was stored at –70°C. IGF-I and IGFBP-3 measurements were carried out on stored samples using the ELISA (enzyme-linked immunosorbent assay) method (Mediagnost, Reutlingen, Germany), with a sensitivity of 0.09 ng mL^{-1}. All steps were performed according to manufacturer's instructions. Calibration was carried out against the World Health Organization (WHO) International standard preparation IGF-I, WHO NIBSC 02/254. Inter- and intra-batch coefficients of variation were 8.5% and 2.8%, respectively.

Statistics

STATA SE13 was used for all statistical analyses (20). Means and frequencies are reported with standard errors. Pearson's correlations were calculated to test for associations between cord IGF-I and IGFBP-3 concentrations and maternal and neonatal characteristics. Neonatal anthropometric measures were standardized for age and sex. Sex differences in birth size and cord IGF-I were evaluated with a two-tailed *t*-test. Multivariate regression was used to assess predictors of cord IGF-I and IGFBP-3 and adjust for potential confounders.

Results

Of the 209 deliveries, 205 mothers had complete dietary, demographic and anthropometric data at 28 and 34 weeks. Among those, 175 newborns had anthropometry, 156 had placenta weight and 146 had IGF-I data. The characteristics of the included mothers were similar to the 59 excluded mothers except that study mothers had higher SLI scores (38 vs. 35), higher intake of energy (8127 kJ vs. 6969 kJ), protein (51 g vs. 45 g) and fat (44 g vs. 38 g) at 34 weeks, and were more likely to be multiparous (36% vs. 19%) and urban (53% vs. 37%). There were no differences in gestational age or birth size between neonates in the study and those excluded.

Maternal characteristics are presented in Table 1. There were 77 urban and 69 rural women. Women were young and most (64%) were primiparous. Average height was slightly above national Indian norms (152.0 cm) (21). Twenty-three per cent was qualified as stunted (*z*-score below –2; 150.1 cm) by the WHO standards (22). Body mass index (BMI) at 28 weeks was 22.1 kg m^{-2} (range: 17.1–31.0), but weight gain from 28 to 34 weeks gestation averaged only 2.1 kg, which was well below the Institute of Medicine's recommendations for non-overweight women (23). Maternal energy intake increased from 28 to 34 weeks; protein intake was below the European recommendations at 28 weeks (49 g vs. recommended 53 g), and well below at 34 weeks (51 g vs. 73 g) (24). Serum folate and vitamin B_{12} concentrations were in the normal range for the second and third trimesters (25). Average milk intake was low and did not increase from 28 to 34 weeks. Nineteen per cent of women reported drinking no milk in either trimester, and 20% reported not consuming any milk product.

Urban women in the sample were older, taller, had greater BMIs and weight gain in pregnancy, higher serum folate and vitamin B_{12} at 28 and 34 weeks, and were from households with higher SLI than rural women. Calorie, milk and milk product intake was similar, but protein intake at 34 weeks was greater among urban women (54.9 g vs. 47.6 g; $P < 0.01$).

Newborn characteristics are summarized in Table 1. Females had higher average cord IGF-I than males (51.4 ng mL^{-1} vs. 42.9 ng mL^{-1}, $P < 0.03$) but there was no difference in IGFBP-3. Most (92%) neonates were full term, and gestational age ranged from 34 to 43 weeks. Newborns were light on average (2819 g, range: 1706–3900 g) relative to the WHO standards (22). Males and females had similar weights, but females were shorter and had higher sum-of-skin-folds (subscapular + triceps) and ponderal index ($P < 0.01$ for each). Compared with rural newborns, urban newborns were heavier and longer, and placental weight was greater, but gestational age, sex ratio, sum-of-skin-folds, and cord IGF-I and IGFBP-3 concentrations did not differ.

Cord IGF-I concentration was positively correlated with placenta weight ($r = 0.20$, $P < 0.02$), birth weight ($r = 0.39$, $P < 0.001$), ponderal index ($r = 0.40$, $P < 0.001$), abdominal circumference and MUAC ($r = 0.39$, 0.34, respectively, $P < 0.001$), and showed the strongest association with sum-of-skin-folds ($r = 0.50$, $P < 0.001$). It was not correlated with neonatal length or gestational age. IGFBP-3 was positively correlated with ponderal index, sum-of-skin-folds and placenta weight ($r = 0.21$, 0.19, 0.16, respectively; $P < 0.05$). Principal component analysis confirmed the associations between cord IGF-I concentration and neonatal size, particularly adiposity (Supporting Information Table S1).

There were no correlations between cord IGF-I or IGFBP-3 concentration and maternal weight, height, BMI at 28 or 34 weeks, weight gain from 28 to 34 weeks, serum folate or vitamin B_{12}, age, energy, protein and fat at 28 or 34 weeks, SLI, and milk or milk product intake at 28 weeks. Cord IGF-I, but not IGFBP-3, concentration was positively correlated with parity ($r = 0.27$, $P < 0.001$). There were no differences in cord IGF-I or IGFBP-3 concentration by tertile of total protein or fat intake. Cord IGF-I was marginally higher among births to women with daily milk intake at 34 weeks compared with those who consumed no milk (49.3 ng mL^{-1} vs. 39.3 ng mL^{-1}, $P < 0.06$; Supporting Information Table S2). Neither IGF-I nor IGFBP-3 varied by type of milk or frequency of milk product intake. Daily milk product intake at 34 weeks was associated with lower ponderal index and greater placenta weight compared to no intake. No other neonatal characteristics differed by category of maternal milk or milk product intake.

Table 1 Sample maternal and newborn characteristics, reported as means (SEM); $n = 146$

Mothers	Mean	28 weeks	34 weeks
Age	23.1 (0.3)		
Height (cm)		154.2 (0.5)	
Weight (kg)		52.6 (0.6)	54.7 (0.6)
Sum of triceps and subscapular skin-folds (mm)		29.8 (1.0)	30.3 (1.0)
BMI (kg m^{-2})		22.1 (0.2)	22.9 (0.3)
Weight gain 28–34 weeks (kg)	2.1 (0.1)		
Serum folate (pmol L^{-1})		30.8 (1.5)	35.9 (1.8)
Serum B-12 (pmol L^{-1})		143.3 (4.8)	133.3 (4.7)
Energy intake (kJ d^{-1})		7635 (213)	8127(205)
Protein intake (g d^{-1})		49 (1)	51 (1)
Fat intake (g d^{-1})		38 (2)	44 (2)
Milk intake (g d^{-1})		159 (13)	172 (15)
Milk intake (kJ d^{-1})		643 (55)	679 (64)
% never drinking milk		19	19
% drinking milk at least once daily		38	45
% drinking cow milk		34	38
% drinking buffalo milk		45	41
Milk product intake (kJ d^{-1}; excluding ghee and butter)		238 (36)	342 (59)
% never consuming milk products		19	20
% consuming milk products at least daily		8	12
Newborns	**All ($n = 146$)**	**Males ($n = 82$)**	**Females ($n = 64$)**
Cord IGF-I (ng mL^{-1})	46.6 (2.0)	42.9 (2.9)	51.4 (2.4)*
Cord IGFBP-3 (ng mL^{-1})	1269.4 (41)	1221.7 (57)	1330.5 (58)
Gestational age (weeks)	39.0 (0.1)	39.0 (0.2)	39.0 (0.2)
Birth weight (g)	2819 (31)	2823(41)	2813 (46)
Birth length (cm)	48.8 (0.2)	49.2 (0.2)	48.3 (0.2)**
Ponderal index (kg m^{-3})	24.2 (2.0)	23.7 (3.0)	25.0 (3.0)**
Abdominal circumference (cm)	29.3 (0.2)	29.2 (0.2)	29.4 (0.2)
Mid-upper arm circumference (cm)	9.5 (0.1)	9.5 (0.1)	9.6 (0.1)
Sum of triceps and subscapular skin-folds (mm)	8.5 (0.2)	8.1 (0.2)	9.0 (0.3)**
Placental weight (g)	434 (8)	436 (11)	432 (11)

Sex differences by two-tailed t-test. *$P < 0.05$; **$P < 0.01$. BMI, body mass index; IGF-I, insulin-like growth factor I.

Table 2 Maternal and neonatal predictors of cord IGF-I (insulin-like growth factor I) concentration[ab]

	Parity (1 – primiparous; 2 – multiparous)	Sex female (1 –males, 2 – females)	Gestational age (weeks)	Daily milk intake at 34 weeks[c]	Placenta weight (g)	Birth weight (g)	Highest quartile of neonatal sum-of skin-folds[d]
Model 1	13.5 (4.6)**	6.5 (3.8)^{NS}	–1.0 (1.4)^{NS}	14.4 (5.7)*			
Model 2	12.0 (4.6)**	7.1 (3.8)^{NS}	–1.7 (1.4)^{NS}	15.1 (5.6)**	0.05 (0.02)*		
Model 3	7.3 (4.5)^{NS}	8.1 (3.6)*	–1.44 (1.3)^{NS}	15.6 (5.3)**	0.02 (0.02)^{NS}	0.02 (0.01)†	
Model 4	7.8 (4.3)^{NS}	5.1 (3.6)^{NS}	–1.2 (1.3)^{NS}	14.7 (5.1)**	0.003 (0.02)^{NS}	0.01 (0.01)*	22.3 (5.8)†

[a]Values are B coefficients (SEM). [b]All models include adjustment for Standard of Living Index (SLI) and urban/rural residence, maternal age (years), height (cm) and weight gain 28–34 weeks (kg), energy (kJ) and protein intake (g) at 34 weeks. [c]Reference category is no milk intake. [d]Reference category is lowest quartile of neonatal sum-of-skin-folds. *$P < 0.05$; **$P < 0.01$; $^{\dagger}P < 0.001$; NS = $P > 0.05$.

To further investigate the relationships between cord IGF-I concentration and maternal and neonatal characteristics, we ran multivariate regressions including neonatal gestational age and sex and maternal parity, age, height, weight gain 28–34 weeks, energy and protein intake at 34 weeks, SLI, rural/urban residence and frequency of milk consumption at 34 weeks (Table 2). Milk intake's association with cord IGF-I concentration was strengthened in each multivariate model. In model 1, cord IGF-I was predicted to be 51.4 ng mL^{-1} for women with daily milk intake compared to 37.0 ng mL^{-1} for those reporting no intake.

We then added placenta weight (model 2), birth weight (model 3) and neonatal sum-of-skin-fold quartiles (model 4). Placental weight and birth weight were each associ-

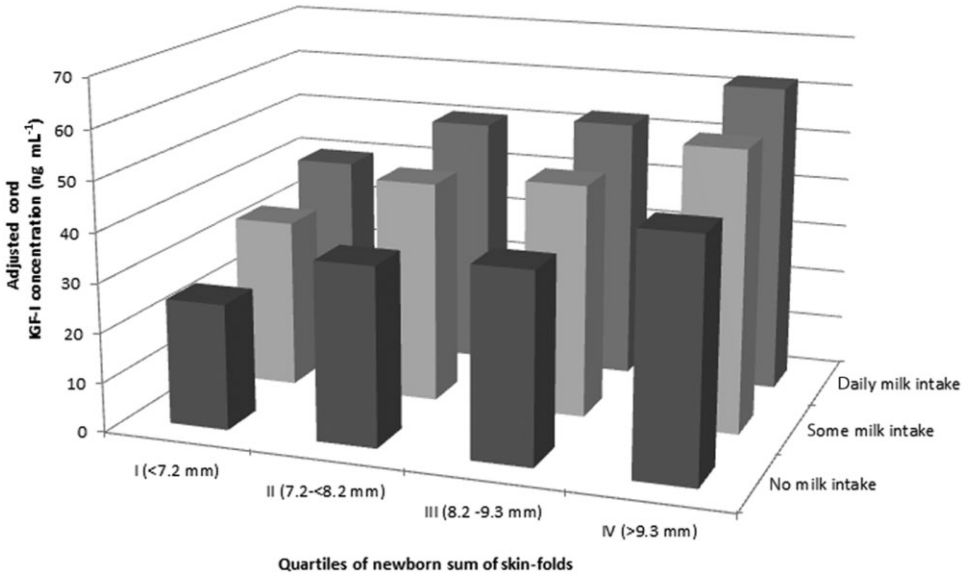

Figure 1 Cord IGF-I (insulin-like growth factor I) concentration (ng mL^{-1}) by quartile of neonatal sum-of-skin-folds and maternal milk intake at 34 weeks.
Legend: Data represent adjusted means across the quartiles of neonatal sum-of-skin-folds and categories of maternal milk intake at 34 weeks, adjusted for baby's gestational age, sex and birth weight, and maternal parity, age, height, weight gain from 28 to 34 weeks, energy (kJ) and protein intake at 34 weeks, and placental weight.

ated with greater cord IGF-I, but placental weight's influence disappeared after adjustment for birth weight. For a given birth weight, female newborns had higher IGF-I levels than males.

As model 4 indicates, newborns in the top quartile of sum-of-skin-folds had higher IGF-I compared to those in the lowest quartile (57.3 ng mL^{-1} vs. 35.1 ng mL^{-1}, $P < 0.001$; P for trend = 0.001), sex differences were no longer significant, and newborns of women with daily milk intake had higher average cord IGF-I than those who consumed none (51.8 ng mL^{-1} vs. 36.5 ng mL^{-1}, $P < 0.01$; $P < 0.004$ for trend). Overall, newborns in the highest quartile of sum-of-skin-folds born to mothers with the greatest reported milk intake at 34 weeks had substantially higher cord IGF-I than those in the lowest quartile of fatness whose mothers reported no milk consumption (62.6 ng mL^{-1} vs. 25.2 ng mL^{-1}, $P < 0.01$). Figure 1 shows the independent contributions of maternal milk intake and neonatal adiposity to variation in cord IGF-I.

The same models were run to predict IGFBP-3, but only placenta weight had a significant association with IGFBP-3 (B = 1.1, $P < 0.03$, same covariates as model 2).

Discussion

Cord IGF-I and IGFBP-3 concentrations in our studies were comparable to those reported by others (26), and the positive relationships with birth weight and parity were consistent with other studies (7–9). Cord IGF-I concentration was unrelated to length but was greater among newborns with higher skin-fold measures at any birth weight, and among those newborns whose mothers drank milk daily at 34 weeks of pregnancy after controlling for overall energy and protein intake and other confounders. The higher cord IGF-I found among female newborns could be attributed to their higher adiposity. Another study also reported that cord IGF-I was more closely related to fat mass than lean body mass (27).

In the context of this Indian study, where maternal size, caloric intake and weight gain during pregnancy were low, deposition of foetal fat may be privileged over linear growth or muscularity. This 'thin-fat' phenotype is characterized by low weight and skeletal measurements, but greater adiposity compared with European babies (1). Newborns in our sample conform to this description and the association of their cord IGF-I concentration with higher skin-fold measures, even after controlling for birth weight, suggests that foetal IGF-1 may be involved in the privileging of fat deposition during foetal growth. IGFBP-3 may also be involved through its positive associations with neonatal sum-of-skin-folds and ponderal index.

The association of serum IGF-I with fat deposition but not length during foetal growth differs from IGF-I's positive relationship to post-natal height (16). Among Indian children, Fall *et al*. (15) reported that serum IGF-I concentrations were associated with both weight and height at 4 years, and were greatest among those who had the lowest birth weights but highest current weight. Higher IGF-I at 4 years predicted greater height and adiposity (triceps and subscapular skin-folds) at 8 years ($P < 0.05$) and greater height and weight at 21 years ($P < 0.05$) (unpublished data).

Although maternal milk consumption in late pregnancy was not associated directly with neonatal adiposity in this or other studies from the region (3), it may contribute to this outcome through its positive effects on foetal IGF-I. Furthermore, data from the Pune Maternal Nutrition Study (PMNS) showed that total dairy intake in mid-pregnancy was associated with increased adiposity at 6 and 12 years, and homeostatic model assessment insulin resistance (HOMA-IR) at 6 years (28). Thus, milk intake in pregnancy may have long-term programming effects on body composition.

To our knowledge, there is no other study of the relationship between maternal milk consumption in pregnancy and cord IGF-I. Olsen *et al*. (14) suggested that higher IGF-I levels might explain their finding that greater maternal milk intake contributed to higher birth weight. In addition, they found that milk protein contributed to higher birth weight, but milk fat and protein from other dairy products did not. Serum concentrations of IGF-I are higher among individuals consuming more milk (16), but there are less consistent results for other dairy products, which may explain the lack of associations between milk product intake and cord IGF-I concentration observed here. There is likely a combination of milk components that stimulate IGF-I and growth, and processing may alter their properties. Studies of milk and milk protein intake's effects on IGFBP-3 have yielded mixed results (29,30).

The mechanism by which maternal milk consumption could influence foetal IGF-I is not clear. Maternal and foetal IGF-I levels are independently regulated and maternal IGF-I does not cross the placenta, but both maternal and foetal IGF-I are correlated with placental size (10). In our study, milk consumption was correlated with cord IGF-I concentration after controlling for placental weight, so aspects of placental function, including placental lactogen and IGF-I signalling pathways, may be involved in the interactions between maternal milk intake, foetal IGF-I and foetal growth. These require further investigation.

Limitations of the study include a small sample size and the sample may have been biased towards urban women of higher socioeconomic status, parity and macronutrient intake at 34 weeks than other women in the study. Skinfold measurements were used as a surrogate for body fat due to unavailability of equations to calculate body fat in neonates. Furthermore, in this observational design, we could not distinguish causal relationships between maternal diet, birth size and foetal IGF-I. Follow-up data on the children in our study will allow us to investigate the associations of cord IGF-I with growth, adiposity and cardiovascular risk factors. Larger intervention studies would be required to evaluate the effects of milk consumption during pregnancy on later adiposity and IGF-I's involvement in any such relationships.

In summary, in this study of Indian mothers and newborns, we found that foetal IGF-I was associated with greater birth size, especially adiposity. Despite the overall low nutritional status of mothers and low newborn weights, foetal fat deposition is relatively spared. Intriguingly, maternal milk intake was the only dietary item related to cord IGF-I concentration even after adjustment for a variety of maternal factors. This needs to be studied in other populations.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author contributions

CSY and HGL designed the research; HGL, DSB, LVR, AAG, NVT and VUD conducted the research; ASW provided IGF-I analysis kits; ASW, HGL and SMJ analysed the data; ASW wrote the paper; ASW, HGL, DSB and CSY had primary responsibility for the final content. All authors read and approved the final manuscript.

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Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. Rotated component matrix of Principal Components and Pearson correlation coefficients with cord IGF-I (ng/ml).

Table S2. Neonatal characteristics by category of maternal milk or milk product intake at 34 weeks of pregnancy.