RESEARCH PAPER

Growth Patterns in Small for Gestational Age Babies and Correlation with Insulin-like Growth Factor-1 Levels

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Objective: Correlation of catch-up growth and Insulin-like Growth Factor -1 levels (IGF-I) in SGA babies. ***Methods***: 50 Full-term Small for Gestational Age children aged 12-18 months were analyzed for Catch-up growth (gain in weight and/or length, Standard Deviation Score/ SDS >0.67). IGF-1 was measured after post-glucose load using ELISA method and correlated with catch-up growth. ***Results*:** Mean (SD) birthweight and length were 2.1 (0.3) Kg and 44.4 (3.1) cm, respectively. At enrollment, mean (SD) age, weight and length were 15.0 (2.1) months, 7.7 (1.3) Kg, and 72.9 (5.6) cm, respectively. Catch-up growth was noted in 60% children. IGF-1 levels were significantly higher in children showing catch-up growth (56.6 (63.2) ng/mL) compared to those not having catch up growth (8.7 (8.3) ng/mL). IGF-1 was positively correlated with both weight and length catch-up. ***Conclusion***: Majority of Small for Gestational Age showed catch-up growth by 18 months, which had good correlation with IGF-1 levels.

Keywords: *Inslin sensitivity, Low birthweight, Outcome, Postnatal Growth.*

Majority of small for gestation (SGA) infants show rapid weight/length gain in early postnatal life [1-3], known as catch-up growth. In almost 90%, it is achieved by the age of 2 years; however, 10-15% continue to experience poor growth [1-4]. The patterns of these weight and length catch-up growth are regulated by genetically determined, pre-programmed, intrinsic ability of the growth plate that is coordinated by important biological regulators including GH-IGF 1 system, Insulin, Thyroxine, Cortisol, Leptin, Sex steroids, and nutrition - as explained by the Neuroendocrine hypothesis [4]. So, changes in IGF system coincide with the postnatal catch up growth, as IGF-I levels increase rapidly from birth in SGA [5,6]. Epidemiological studies have pointed out a link between being born SGA/IUGR and later risk of development of non-communicable diseases [7], the linkage between these associations could be due to alterations in the programming of insulin, IGF-1 and IGF-2.

No studies have been conducted on the role of IGF-1 in SGA and catch-up growth in our population. Therefore, this study was carried out to study the growth patterns and its correlation with IGF-1 levels in term SGA children.

METHODS

This was a cross-sectional study conducted in the Department of Pediatrics of a tertiary-care center. All children aged between 12-18 months attending the follow-up clinic in pediatric OPD from October 2009 to January 2012 were screened to identify term babies who at birth were SGA (<10^{th} percentile). Those with major congenital anomalies, chromosomal abnormalities, any gross neurological deficits, chronic illnesses, prolonged hospitalization, or children whose mothers had diabetes or gestational diabetes mellitus during the index pregnancy, were excluded from the study. The subjects were enrolled after obtaining informed consent from the parents. The study was approved by the institutional ethics committee.

All enrolled children were predominantly breastfed during first six months of life. A detailed history and clinical examination was done in all subjects. The birthweight and length was recorded from the hospital discharge record. Nude body weight was recorded using an electronic weighing scale to the nearest 5 grams. Length was recorded using an infantometer to the nearest 0.1 cm. Cohort was segregated into symmetrical and asymmetrical SGA according to Ponderal Index at birth. All the measurements were converted to standard deviation scores (SDS) using WHO growth charts as reference standards. Catch up growth was defined as gain in weight and/or length SD score of >0.67 between birth and enrollment [8].

A venous blood sample (1.5 mL) was taken 30 minutes after completion of a oral glucose load (1.75 g/

kg) [5,9]. The samples were transported within two hours of collection to the laboratory and centrifuged to separate the serum, which was stored at –70 ºC till testing. IGF-1 levels were measured after thawing the samples at room temperature. ACTIVE Non- Extraction IGF-1 ELISA Kit (DSL-10-2800) was used for quantitative measurement of IGF-1 in serum, using enzymatically amplified 'two-step' sandwich-type immunoassay [9].

The difference in IGF-1 levels with respect to catch-up growth was analyzed using Mann-Whitney U/ Wilcoxon Rank sum test. The difference in weight and length between the groups was assessed using Kruskal-Wallis Test for variables displaying non-normal distribution and ANOVA for normally distributed variables. A correlation coefficient between IGF-1 levels and catch-up growth was calculated. A probability of 5% (P<0.05) was taken as significant.

TABLE I GROWTH VARIABLES IN CHILDREN WITH CATCH-UP GROWTH AND NO CATCH-UP GROWTH

Variables	*CUG (n=30)*	*NCUG (n=20)*	*P value*
At Birth			
Weight (kg)	2.0 (0.31)	2.17 (0.29)	0.06
Weight SDS, no (%)			
< -3 SD	16 (53.3)	7 (35)	0.007
≥-3 to <-2SD	9 (30)	6 (30)	
≥-2 to <-1 SD	5 (16.6)	7 (35)	
Length (cm) (SD)	44.3 (3.1)	44.39 (3.3)	1.0
Length SDS			
< -3 SD	14 (46.6)	8 (40)	0.003
≥-3 to <-2SD	5 (16.6)	4 (20)	
≥-2 to <-1 SD	8 (26.6)	8 (40)	
≥-1 SD	3 (10)	0	
PI (SD)	2.2 (0.3)	2.5 (0.6)	0.1
At 12-18 months			
Weight (kg) mean (SD)	8.1 (1.2)	7.1 (1.1)	0.005
Weight SDS, no (%)			
< -3 SD	7 (23.3)	10 (50)	<0.001
≥-3 to <-2 SD	5 (16.6)	6 (30)	
≥-2 to <0 SD	13 (43.3)	4 (20)	
≥0 to <2SD	5 (16.6)	0	
≥2 SD	0	0	
Length (cm), mean (SD)	75.4 (5.3)	69.3 (4.0)	0.0
Length SDS, (%)			
< -3 SD	7 (23.3)	13 (65)	<0.001
≥-3to <-2 SD	3 (10)	5 (25)	
≥-2 to <0SD	12 (40)	2 (10)	
≥0 to <2SD	6 (20)	0	
≥2 SD	2 (6.6)	0	
BMI (SD)	14.4 (1.7)	14.8 (1.7)	0.3

CUG: Children with Catch-up growth; NCUG: Children with no CUG; PI: Ponderal index.

RESULTS

A convenience sample of 50 children (54% boys) with mean (SD) age of 15 (2.1) mo was enrolled. The mean Ponderal Index (PI) of the study population at birth was 2.4 (0.5), suggestive of all being symmetrical SGA. Catch-up growth was noted in 30 (60%) of the children. CUG in both weight and length was seen in 13 (26%), length alone in 12 (24%) and only weight in 5 (10%) (***Table* I**).

The IGF-1 in the study group followed a non-normal distribution with a mean of 37.4 (54.4) ng/mL; ranging from 1.66 ng/mL in the non-catch up group to 203.71 ng/mL in the catch-up group. The mean (SD) level was significantly higher in the catch-up group [56.6 (63.2) *vs* 8.7 (8.3) ng/mL; P<0.001]. The mean IGF-1 levels in those showing only weight catch-up (66.1 (73.4) ng/mL) was higher as compared to those with only length catch-up (37.8 (52.8) ng/mL).

IGF-1 levels in the study cohort were found to have a significant correlation (P<0.001) with the weight (r=0.533) (***Fig.* 1**), and length SDS (r=0.478, P<0.001) change from birth.

DISCUSSION

Our data suggest that circulating levels of IGF-I in childhood have correlation with weight-gain and height-velocity particularly in the first two years of life. The

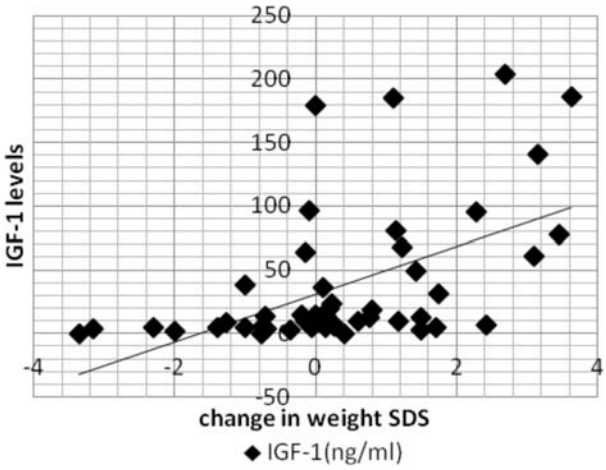

FIG. 1 *Correlation between IGF-1 and change in weight SDS.*

WHAT THIS STUDY ADDS?

- Around 60% of Indian infants born SGA show catch-up growth by 18 months, which correlates with higher IGF-1 levels.

IGF-1 levels were significantly higher in the catch-up group than in the non-catch up group, suggesting its role in catch-up growth. There was wide inter-individual variation in serum IGF-I levels with skewed distribution, which could be partially attributed to a genetic influence. Poorer nutrition and growth may explain the greater positive skewness of the distribution of IGF-1 concentrations in the Indian children. This marked variation in serum concentration in first 18 months of life might limit its usefulness in assessment of growth disorders in early life.

The strength of this study is the early age of evaluation to detect those who do not catch-up by 18 months of age, so that they can be closely monitored for further evaluation. The limitation is the small size of our cohort and the results could not be compared with AGA babies due to ethical issues.

IGF-I level of our cohort (4.85 nmol/L or 37.4 ng/L) was less than the mean of reference population of Low, *et al*. [10] at 12 months 9.7 (5.1) nmol/L and at 18 months 13.6 (8.5) nmol/L of age. There are no Indian studies on SGA in this age group. On comparison with the previous Indian data [11] of healthy term babies (mean IGF-1 level at 1 year 23.1 (16.7) ng/mL), our results were found to be similar. When compared with the Western data (67-108 ng/mL) [5,10,12,13], IGF-I levels were found to be lowest in our cohort at the same age measured using the same assay, likely to indicate delayed catch-up [6,11,14]. As IGF-I levels are largely nutritionally regulated [5,7,12,14], these findings are consistent with the smaller size and chronic malnourished state of Indian children. This may explain the lowest gain in weight and length SDS in our study group when compared with children in other studies.

Our study concludes that majority of Indian infants born SGA show catch-up growth as early as 12-18 months. IGF-I levels in these are positively associated with postnatal weight and height gain, and may potentially be used to assess growth, and correlate with catch-up growth as early as 12-18 months of age. However, due to small sample size, definitive conclusions are not possible.

Contributors: DR: collected the data, analyzed and interpreted the data, wrote the paper; SY: conceptualized and designed the study, gave critical inputs to the paper, reviewed and approved the final manuscript; SR: data analysis, revised and reviewed the manuscript for critical content, approved the final draft; TKM: inputs in designing of methodology for biochemical analysis, reviewed the final manuscript.

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