PERSPECTIVE

Micronutrients – An Essential Aid to Daily Growth in Children

KV RAMESHWAR SARMA

From National Institute of Nutrition (ICMR), Hyderabad, India.
Correspondence to: Dr KV Rameshwar Sarma, Senior Deputy Director (Retd), National Institute of Nutrition (ICMR), Hyderabad, India.
E-mail: rkramadhati@gmail.com

A human being is composed of about 10^{12} cells, which results from approximately 2^{38} mitoses since the moment of fertilization. During mitosis, cells differentiate into dozens of types of tissues and organs. This is the actual process of growth and development(1).

Human growth has been scientifically investigated and studied since the beginning of science; yet, the exact manner in which a child grows still remains unanswered. Although remarkable increases in body size and length occur during organismal growth, very little is known about the mechanism of the growth process(2). Longitudinal growth occurs through a process of cell proliferation, the addition of new cells to the growth plate of the bone and hypertrophy, resulting in the expansion of the growth plate.

GROWTH PATTERN IN CHILDREN

Growth of a child was considered to be a relatively smooth process traditionally–rapid growth during infancy followed by steady growth in midchildhood and finally the pubertal spurt during adolescence(3). But studies carried out globally have shown that human growth is a nonlinear process with marked variation in growth rate during the short-term. It is not known how long-term height gain or stature is influenced by short-term changes in height and weight.

Daily empirical observations modeled by several methods describe infant growth as an aperiodic saltatory or pulsatile process, separated by variable durations of stasis.

Daily empirical observations modeled by several methods describe infant growth as an aperiodic saltatory or pulsatile process, separated by variable durations of stasis(4). Butler, *et al*.(5), after studying the growth velocity data from normal prepubertal children, described growth spurts over 2-year intervals. Lampl, in 1993, identified a pattern of growth in the subjects that included intervals of no significant growth increments, or, stasis, for as long as 1-2 months(6). It was seen that growth itself occurred during short measurement intervals that punctuated these stases. These results led to the proposition that the actual mechanism of growth is a two-phase process–a short time duration growth of event accompanied by a longer refractory interval, or stasis. This is what is called as the saltatory model, which defines growth as a series of rapid growth intervals (saltations) separated by intervals of stasis (***Fig.* 1**)(5,6). ***Figure* 2** represents the schematic explanation of the characteristics of the height and weight.

Thalange, *et al*.(7), after studying 46 healthy prepubertal children showed that the growth in childhood over 1 year is represented by a biphasic process comprising 3–6 unpredictable growth spurts, each of mean length 56 days (range 13–155 days), separated by periods of stasis (≤0.05 cm height increment over more than 7 days), each lasting a mean of 18 days (range 8–52 days) and accounting for at least 20% of the period of observation.

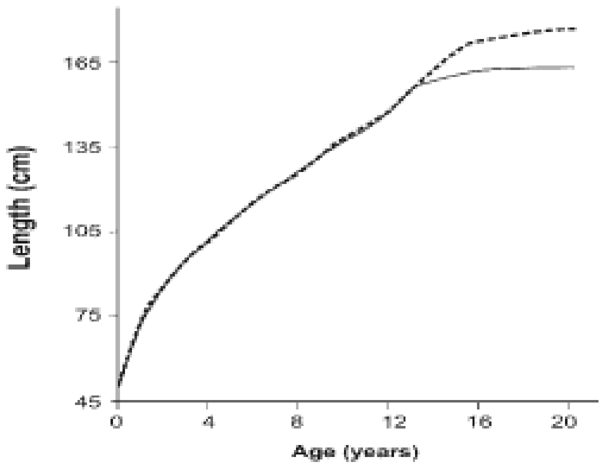

FIG. 1 *Standard growth curves from birth to 18 years. Data are mathematically smoothed and averaged over children. Dashed line represents boys. Solid line represents girls. Adapted from growth charts developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000).*

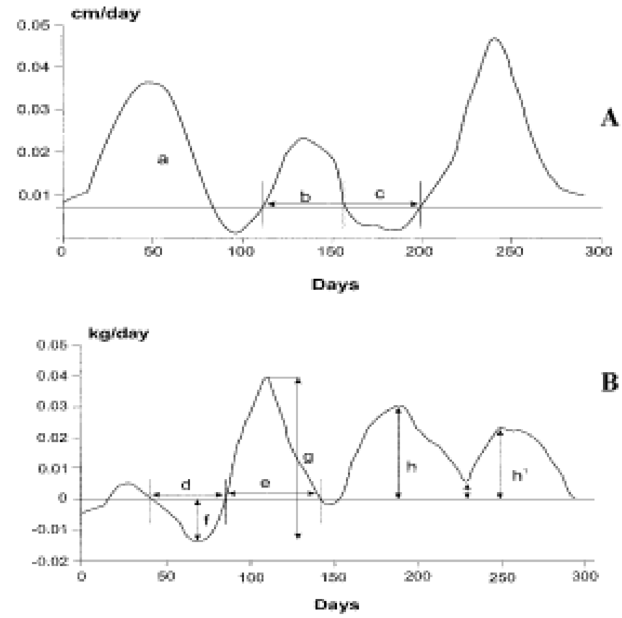

FIG. 2 *Schematic explanation of the characteristics of the height (A) and weight (B) velocity curves. Arrowed lines indicate the amplitude of a height velocity peak (a), length of a height velocity peak (b), and length of a stasis (c) in A. Length of weight loss (d), length of weight gain (e), amplitude of weight loss (f), total amplitude of weight velocity (g), and amplitude of weight gain (h) are shown by arrowed lines in B. If the minimum between two peaks (i) was less than half of the amplitude of the smaller peak (h'), then two separate periods of weight gain were identified.*

It has also been shown that seasonal variations play an important role in growth increments. There is a declining growth rate over the autumn months, which reached a nadir in midwinter. This is followed by a growth spurt in the spring(7). This points out to the fact that human growth over short periods is a continuous, irregular and unpredictable process.

The seasonal variation in growth velocity is probably the most well characterized cyclical pattern of human growth, with peak velocity in midsummer(8-10). Using knemometry, an accurate and noninvasive technique of lower leg length measurement, Hermanussen, *et al.*(11) showed that lower leg length increased in mini-growth spurts over 30–55 days intervals. In contrast, Lampl, *et al.*(12) proposed that all gain in length of normal infants occurred in irregular, brief, 1-day growth spurts saltations, separated by long periods of growth stasis. It has also been suggested that the growth process may be governed by the principles of chaos. Tillman, *et al*.(13) proposed that height gain during 1 year is a biphasic process, comprising intense growth spurts lasting an average 8 weeks, separated by periods of very slow growth or stasis over 2–3 weeks.

Despite the abundance of adolescent growth studies, comparatively little is known about sequential development of limb components and variation in this process. It has been observed that due to earlier maturation of girls, the length of each of their long bones exceeds that of boys to some degree during some period of adolescence. Peak velocities for leg bones occur earlier than those for arm bones, with the latter more closely coinciding with peak height velocity (peak velocities (years) females, males: humerus, 11.2, 13.8; radius, 10.7, 13.9; femur, 10.3, 12.7; tibia, indeterminate (linear), 12.4; height, 11.2, 14.0)(14).

The growth of children can be considered continuous when observed across years, with periods of spurts and stasis. Daily differences in growth may not be visible as growth is measurable only at certain frequencies.

The growth of children can be considered continuous when observed across years, with periods of spurts and stasis. Daily differences in growth may not be visible as growth is measurable only at certain frequencies. But there are growth changes happening in the child's body during the period of stasis which becomes evident during the period of growth spurt.

VARIATIONS IN THE NORMAL GROWTH PATTERN

Although most children follow the normal patterns of growth, a small number of children have growth patterns that differ from the typical model. These less common but normal patterns of growth include:

Growth rate changes in infancy: It is not unusual for normal children under 2 years of age to cross percentile lines in either direction. This happens because the factors that affect growth before birth are different from those that govern growth after birth(15).

Upward or downward shifts**:** Babies who are small at birth often shift to a higher growth channel during the first few months of life, as they 'catch up' to their own growth potential. On the other hand, large or average-size babies who have short parents may have slower-than-expected growth during the first months of life as they settle into their own growth channel. A downward shift in growth during the first 1.5–2 years of life may not be a cause for concern if the baby is healthy and thriving, if he or she has a good diet, and if height and weight are shifting together(16).

Catch-up growth**:** The brain regulates the body's growth by controlling the feelings of hunger and fullness and makes the system function to keep each child's size and shape relatively stable over the time. During sickness like fever and diarrhea, the quantity of food and in turn, nutrients consumed by children is less; this results in the body being depleted of essential nutrients, which makes the immune system weaker. This results in a lack of growth, both in terms of height and weight. But once the illness is past, the weight gets back to normal. This pattern of catch-up growth is a good sign of a healthy body and a healthy growth-control mechanism(17).

FACTORS DETERMINING EVERYDAY GROWTH

What makes one child long and thin, another short and stout? Growth varies with age. Many factors influence how much and how rapidly a child grows, and how tall he or she will be as an adult (***Fig. 3***). Some of these factors can be controlled and others cannot. Human growth rate is determined by a complex interaction of physical, endocrine and nutritional factors, of which growth hormone (GH) and nutrition are the key determinants of child growth(1).

Heredity or the genetic potential is one of the most important factors influencing a child's growth. Growth varies among different ethnic groups, among different families within the same ethnic group and even among members of the same family. Growth hormone releasing hormone stimulates GH pro-duction in the pituitary gland and releases it into the bloodstream, which in turn helps in the stimulation of IGF-1 resulting in growth. A well-balanced, age-appropriate diet that includes the essential nutrients especially micronutrients has a positive effect on how well a child grows(18).

ROLE OF NUTRIENTS IN INFLUENCING GROWTH

Adequate nutrition from fetal stage, in childhood, during adolescence, pregnancy and lactation is of fundamental importance for human develop-ment(19). Nutrition is also important for the skeletal development, which is a part of the growth process. Deficiency of nutrients can adversely affect the

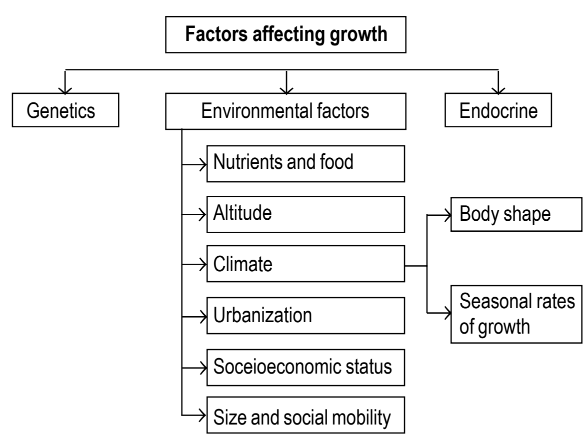

FIG. 3 *Factors affecting growth.*

linear growth, cognition and muscle development. While the role of energy and proteins on physical growth is well-established, recent studies have stressed on the importance of micronutrients in enhancing the full growth potential(20). These nutrients are essential for the assimilation, absorption and utilization of even the macro nutrients from the daily foods i.e., carbohydrates, proteins and fats.

Inadequate nutrient intake during childhood leads to undernutrition, which results in growth retardation, reduced work capacity and poor mental and social development(21-26). A study carried out by Satyanarayana, *et al*.(27) among Indian preadolescent boys of 5+ years of age for 18 years showed that boys who were nutritionally deficient were less tall than their counterparts and entered late into puberty with significantly depressed intensity.

As growth of children can be considered continuous when observed across years, a daily intake of essential nutrients is necessary for maintaining this growth. Deficiencies, particularly energy and micronutrient deficiencies, begins from early fetal life and continues through childhood, adolescence and reproductive stages of life, resulting in a vicious cycle of transgenerational events. Strong evidences for iron and iodine deficiencies compromising cognition and growth are well-documented. Inadequate nutrient intake will also increase the body's susceptibility to infections, which is another causative factor in delayed or slow growth(28-31).

Only recently is the role of micronutrients in the etiology of growth is being appreciated. Micronutrient deficiencies represent a hidden form of hunger with severe consequences on physical growth, immune functions and cognition. As many of the micronutrients are water soluble and get excreted, not all of them can be stored in the body. All of them are not available in required amounts in all the food one eats everyday.

The effects of deficiencies are multiple and severe in children and may affect the linear growth, cognition and muscle development which are often irreversible. While the role of energy and proteins on physical growth is well-established, a deficiency in the micronutrient intake may add to the insult. The genetic potential of children for physical growth and mental development will be compromised and the susceptibility to infections is increased even in subclinical deficiencies of multiple vitamins and minerals (***Table* I**). Children who suffer from malnutrition are more likely to have slowed growth, delayed development, difficulty in school and high rates of illness, and they may remain malnourished into adulthood(33).

Studies have shown that the nutrient intake, especially the micronutrient intake of Indian school going children do not meet the Recommended Dietary Allowances suggested by Indian Council of Medical Research. Countrywide surveys conducted by the National Nutrition Monitoring Bureau (NNMB, 1998) showed that Indian diets were qualitatively adequate in proteins but deficient in some micronutrients. Thus, if caloric needs are met, protein requirements too are fulfilled, but the requirement of several micronutrients (***Fig.* 4**) remains unmet. Since Indian diets have not changed substantially over the years, these observations apply even today. While dietary deficiencies of vitamin A and riboflavin are seen in all age, sex and physiological groups, those of other micronutrients, such as iron, calcium, thiamine, niacin and vitamin C are seen high in children(34).

TABLE I ROLE OF MICRONUTRIENTS IN GROWTH

Vitamin D and calcium	Deficiency affects bone development, which manifest as rickets
Potassium, zinc magnesium and copper	Deficiency disturbs the GH/IGF-I system and affects growth
Manganese	Deficiency leads to skeletal abnormalities including retarded growth, which may be mediated through detects in proteoglycan physiology in the growth plate
Iron and iodine	Helps in cognitive development and growth
Vitamin A	Indirectly helps in growth
Zinc	Overall growth
Vitamin E	Muscle development

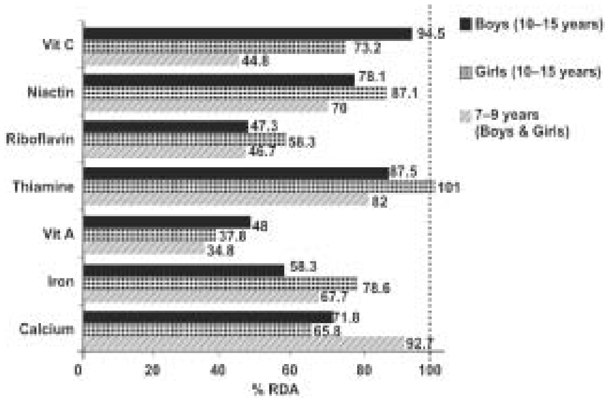

FIG. 4 *Graph depicting the micronutrient intake of Indian children (Boys and girls) in the age group of 7-15 years as compared to 100% RDA as per NNMB 1996 Data. (RDA marked as dotted line).*

GAPS IN INDIAN DIET

A study carried out recently by the National Institute of Nutrition showed that subclinical micronutrient deficiencies among those who have adequate protein and calorie intake may be an important contributing factor for not achieving the growth potential. The study was carried out in semi-urban middle-income residential schoolchildren aged 6–16 years(35). It was observed that the extent of inadequacy at baseline was almost 100% for folic acid, 65% for vitamins B_2 and B_6 and 55% for vitamin C and 44% for vitamin A. The prevalence of anemia among subjects was 54%, with inadequacy of vitamin B_{12} being 40% and that of vitamin D being 30%(36).

ENSURING OPTIMAL NUTRIENT INTAKE

Prevention against growth failure and ensuring full growth potential is therefore, of primary importance and is possible at several stages of life through focused approaches. Assuring adequate nutrient intake is one approach to prevent and overcome growth failure problems. We have moved away from protein gap to energy gap and currently our focus of attention is on micronutrient deficiencies as impediments for linear growth(37).

However, it is seen that the children are not taking the required vitamins and minerals on a daily basis. Fast foods are gaining an upper hand over conventional foods resulting in multimicronutrient deficiencies. The high activity level of children coupled with the frequent childhood infections, their life style to withstand the competition, in the prevailing environment of urbanization and globalization further increase the nutrients required, which call for the need for more nutrients in addition to that from their diet.

Several approaches may be taken to improve the intake of growth-promoting nutrients, including daily administration of micronutrient supplements, forti-fication of food with micronutrients or improved dietary intake on a daily basis.

ROLE OF NUTRITIONAL SUPPLEMENTS IN CHILDREN

Bioavailability of the nutrients, especially that of the micronutrients, are reduced due to factors like the nature of Indian diet, cooking methods followed and high prevalence of fast food consumption among children. Hence, one cannot be really sure about the particular nutrients children derive from their food, owing to the loss of nutrients as a result of cooking and due to the presence of preservatives, colors and pesticides. As growth may be affected by more than one growth-limiting nutrient, intervention studies focus on the importance of multiple micronutrients. Hence, in ensuring adequate nutrient intake, multimicronutrient supplementation is essential in addition to food on a daily basis.

- Nutritional intake plays a major role in the performance at school and in the general understanding and retention capacity of the students.
- Well-nourished children not only are better physically but also mentally(38).

Meta-analyses of studies conducted to assess the effects of vitamin A, iron and multimicronutrient interventions on the growth of children <18 years showed that interventions limited to only vitamin A or iron did not improve child growth. Multi-micronutrient interventions on a daily basis, on the other hand, improved linear and possibly ponderal growth in children(39).

Bhandari, *et al*.(40) examined the impact of daily multimicronutrient supplementation on linear growth either singly or in combination for various

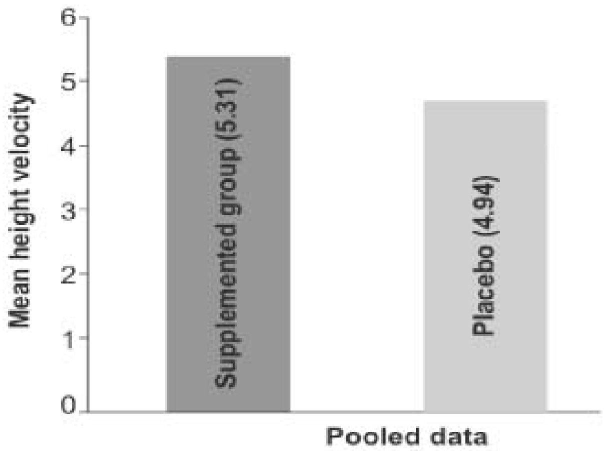

FIG. 5 *Height velocity.*

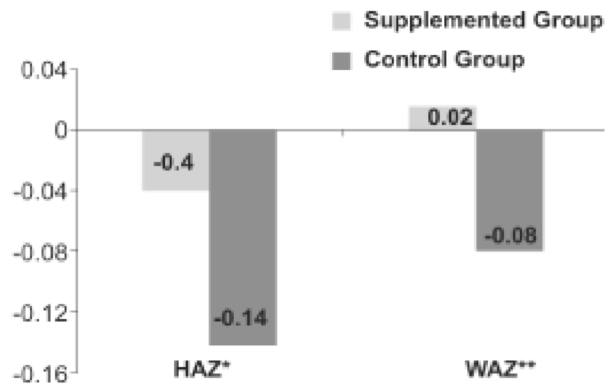

FIG. 6 *Mean Z-scores of increments in height and weight in the study groups. HAZ, height-for-age Z score; WAZ, weight-for-age Z- score. *P=0.016. **P=0.002.*

age groups such as infants, preschoolers and school going children. Single nutrients did not impact linear growth. Zinc supplements had a small effect on length (0.22 SD units) in children of 0–13 years of age. Sarma, *et al*.(41) in a double-blind placebo-controlled, matched paired, cluster randomized study in children aged 6–16 years after 14 months of multimicronutrient rich beverage administration on a daily basis observed a significant increase in mean increments of height and weight *Z* scores of 0.04 and 0.02, respectively. Velocity of weight (3.56 vs. 3.0) was also significantly higher in supplemented group. In this study, the usual diets provided 80% of their energy requirements (***Figs.*** **5** and **6**)(41).

CONCLUSION

Growth in children can be considered continuous when observed across years with periods of spurts and stasis. Daily differences in growth may not be visible as growth is measurable only at certain frequencies. However, there are growth changes happening in the child's body even during the period of stasis which become evident during the growth spurt. Hence, adequate nutrition is required everyday for normal growth to happen.

Data shows that the typical Indian diet does not provide adequate quantity of all essential micronutrients. Further, studies have conclusively shown that daily micronutrient supplementation improved height even in apparently healthy children. Hence, it can be concluded that the process of growth happens on a daily basis; therefore it becomes critical to provide all key micronutrients in adequate quantities to children on a daily basis.

Funding: None.

Competing interests: None stated. Conclusions in this Perspective are those of author and do not necessarily represent the views of the funding agency.

REFERENCES

1. Bogin B. Patterns of Human Growth. London: Cambridge University Press; 1999.
2. Johnson ML, Veldhuis JD, Lampl M. Is growth salutatory. The usefulness and limitations of frequency distributions in analyzing pulsatile data. Endocrinology 1996; 137: 5197-5204.
3. Malina RM. Motor development during infancy and early childhood: Overview and suggested directions for research. Int J Sport Health Sci 2004; 2: 50-66.
4. Michelle L, Johnson ML. Identifying saltatory growth patterns in infancy: A comparison of results based on measurement protocol. Am J Hum Biol 1997; 9: 343-355.
5. Butler GE, McKie M, Ratcliffe SG. The cyclical nature of prepubertal growth. Ann Hum Biol 1990; 17: 177-198.
6. Lampl M. Evidence of saltatory growth in infancy. Am J Hum Biol 1993; 5: 641-652.
7. Thalange NKS, Foster PJ, Gill MS, Price DA, Clayton PE. A model of normal prepubertal growth. Arch Dis Child 1996; 75: 427-431.

8. Fitt AB. Seasonal Influence on Growth Function and Inheritance. Wellington: New Zealand Council for Educational Research; 1941.
9. Bransby ER. The seasonal growth of children. Med Officer 1945; 73: 149-165.
10. Marshall WA. Evaluation of growth rate in height over periods of less than one year. Arch Dis Child 1971; 46: 414-420.
11. Hermanussen M, Geiger-Benoit K, Burmeister J, Sippell WG. Periodical changes of short-term growth velocity ('mini growth spurts') in human growth. Ann Hum Biol 1988; 15: 103-109.
12. Lampl M, Veldhuis JD, Johnson ML. Saltation and stasis: A model of human growth. Science 1992; 258: 801-803.
13. Tillman V, Thalange NKS, Foster PJ, Gill MS, Price DA, Clayton PE. The relationship between stature, growth and short-term changes in height and weight in normal prepubertal children. Pediatr Res 1998; 44: 882-886.
14. Smith SL, Buschang PH. Longitudinal models of long bone growth during adolescence. Am J Hum Biol 2005; 17: 731-745.
15. Manly T, Cornish K, Grant C, Dobler V, Hollis C. Examining the relationship between rightward visuo-spatial bias and poor attention within the normal child population using a brief screening task. J Child Psy Psychiatry 2005; 46: 1337-1344.
16. Vogiatzi MG, Copeland KC. The short child. Pediatr Rev 1998; 19: 92-99.
17. Adair LS. Filipino children exhibit catch-up growth from age 2 to 12 years. J Nutr 1999; 129: 1140-1148.
18. Eveleth PB, Tanner JM. Worldwide Variation in Human Growth. Cambridge: Cambridge University Press; 1990.
19. The World Health Report 2002. Reducing risks, promoting healthy life: Overview, Geneva, World Health Organisation, 2002 (WHO/WHR/02.1).
20. Graham GG. Environmental factors affecting the growth of children. Am J Clin Nutr 1972; 25: 1184-1188.
21. Sandstead HH, Penland JG, Alcock NW, Dayal HH, Chen XC, Li JS, *et al*. Effects of repletion with zinc and other micronutrients on neuro-psychologic performance and growth of Chinese children. Am J Clin Nutr 1998; 68: S470-S475.
22. Harahap H, Jahari AB, Husaini MA, Saco-Pollitt C, Pollitt E. Effects of an energy and micronutrient supplement on iron deficiency anemia, physical activity and motor and mental development in undernourished children in Indonesia. Eur J Clin Nutr 2000; 54: S114-S119.
23. Bates CJ, Evans PH, Allison G, Sonko BJ, Hoare S, Goodrich S, *et al*. Biochemical indices and neuromuscular function tests in rural Gambian school children given a riboflavin, or multivitamin plus iron supplement. Br J Nutr 1994; 72: 601-610.
24. Bamji MS, Sarma KVR, Radhaiah G. Relationship between biochemical and clinical indices of B-vitamin deficiency in rural school boys. Br J Nutr 1979; 41: 431-440.
25. Sarma KVR, Radhaiah G, Bamji MS. Impact of long term low dose supplementation of B-complex vitamins on clinical and anthropometric status of rural school children. Nutr Rept Int 1981; 24: 2.
26. Bamji MS, Arya S, Sarma KVR, Radhaiah G. Impact of long term low dose supplementation of B-complex vitamins on biochemical and psychomotor status of rural school children. Nutr Res 1982; 2: 147-153.
27. Satyanarayana K, Radhaiah G, Mohan KR, Thimmayamma BV, Rao NP, Rao BS, *et al*. The adolescent growth spurt of height among rural Indian boys in relation to childhood nutritional background: An 18 year longitudinal study. Ann Hum Biol 1989; 16: 289-300.
28. Gibson RS, Hotz C. Nutritional causes of linear growth faltering in infants during the complementary feeding period. In: Martorell R, Haschke F, editors. Nutrition and Growth. Nestle Nutrition Workshop Series No. 2006; 47: 159-192.
29. Bhan MK, Bahl R, Bhandari N. Infection: How important are its effect on child nutrition and growth. *In*: Martorell R, Haschke F, editors. Nestle Nutrition Workshop Series 2006; 47: 197-222.
30. Brown KH, Peerson JM, Rivera J, Allen LH. Effect of supplemental zinc on the growth and serum zinc concentrations of prepubertal children: A meta-analysis of randomized controlled trials. Am J Clin Nutr 2002; 75: 1062-1071.
31. Rivera JA, Hotz C, Gonzalez-Cossio T, Neufeld L, Garcia-Guerra A. The effect of micronutrient deficiencies on child growth: A review of results from community-based supplementation trials. J Nutr 2003; 133: 4010S-4020S.

32. Tandon N, Marwaha RK, Kalra S, Gupta N, Dudha A, Kochupillai N, *et al*. Bone mineral parameters in healthy young Indian adults with optimal vitamin D availability. Natl Med J India 2003: 16: 298-302.

33. Bhan MK, Sommerfelt H, Strand T. Micronutrient deficiency in children. Br J Nutr 2001; 85: S199-203.

34. Brahmam GNV. National Nutrition Monitoring Bureau in India: An overview. Indian J Comm Med 2007; 32: 5.

35. Sivakumar B, Vijayaraghavan K, Vazir S, Balakrishna N, Shatrugna V, Sarma KV, *et al*. Effect of micronutrient supplement on health and nutritional status of schoolchildren: Study design. Nutrition 2006; 22: S1-S7.

36. Sivakumar B, Nair KMN, Sreeramulu D, Suryanarayana P, Ravinder P, Shatrugna V, *et al*. Effect of micronutrient supplement on health and nutritional status of schoolchildren: Biochemical status. Nutrition 2006; 22: S15-S25.

37. Allen LH. Interventions for micronutrient deficiency control in developing countries: Past, present and future. J Nutr 2003; 133: 3875S-3878S.

38. Vazir S, Nagalla B, Thangiah V, Kamasamudram V, Bhattiproulu S. Effect of micronutrient supplement on health and nutritional status of schoolchildren: Mental function. Nutrition 2006; 22: S26-S32.

39. Ramakrishnan U, Aburto N, McCabe G, Martorell R. Multimicronutrient interventions but not vitamin A or iron interventions alone improve child growth: Results of 3 meta-analyses. J Nutr 2004; 134: 2592-2602.

40. Bhandari N, Taneja S, Mazumder S, Bahl R, Fontaine O, Bhan MK, *et al*. Zinc Study Group. Adding zinc to supplemental iron and folic acid does not affect mortality and severe morbidity in young children. J Nutr 2007; 137: 112-117.

41. Sarma KVR, Udaykumar P, Balakrishna N, Vijayaraghavan K, Sivakumar B. Effect of micronutrient supplementation on health and nutritional status of schoolchildren: growth and morbidity. Nutrition 2006; 22: S8-S14.