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Impact of early life undernutrition on adult health and nutrition outcomes: revisiting cohort studies undertaken by National Institute of Nutrition, Hyderabad

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Introduction

The ongoing epidemiological and nutrition transition in India has resulted in a rapid increase in non-communicable diseases (NCDs) including type 2 diabetes mellitus, hypertension, dyslipidemia and cardiovascular disease (CVD), all known to be associated with obesity[1-3]. However, the prevalence of obesity as assessed using body mass index (BMI) , although showing a rise in recent years, is still relatively low. In contrast, under-nutrition, especially childhood under-nutrition, continues to be widely prevalent and is still a priority area[4]. The double burden of under-nutrition and obesity-related chronic diseases has been highlighted as a key concern in societies in transition.

A large number of studies (mainly animal studies and observational studies in humans) during the past two to three decades have indicated that compromised nutrition and growth during early life may be associated with subsequent adiposity and metabolic syndrome[5-8]. Prospective cohort studies from India have made a major contribution to the advancement of our understanding in the area of 'developmental origins of health and disease (DOHaD)'. For example, studies based on birth cohorts in Pune and Mysore have shown that low birth weight is associated with an enhanced risk for type 2 diabetes and CVD in childhood[6,9]. In a recent study in the Pune children's cohort, an elevated cardio-metabolic risk in childhood was shown to predict higher glucose, insulin, insulin resistance, blood pressure, lipids and intima media thickness at 21 years[10]. Apart from birth weight, growth rate during infancy and childhood also influences the risk of metabolic syndrome and impaired glucose tolerance or type 2 diabetes as demonstrated by a study in the New Delhi Birth cohort, based on careful serial measurements of childhood BMI[11,12]. These studies that support the 'DOHaD' hypothesis have helped bring about a paradigm shift from the dominant view till the 1990s that diabetes and other chronic diseases are adult-onset diseases, to the current understanding that these diseases may originate much earlier in life. However, early nutritional influences cannot completely account for the enhanced risk of cardio-metabolic diseases in Indians. The role of nutritional influences operating throughout the life course cannot be ignored.

The body composition of South Asians (including Indians) , differs from that of other ethnic groups; Indians have 'high fat low muscle mass' as compared to other ethnic groups; this is considered an important determinant of a higher risk of metabolic syndrome. This is because muscle mass, which influences glucose clearance, is the most important indicator of the 'metabolic capacity' of the body. Evidence suggests that low muscle mass may, by itself, predispose to fat accretion by influencing the energy balance, given that the synthesis and breakdown of muscle protein are principally responsible for the energy expenditure of resting muscle[13].

In the absence of body composition measurements (that are generally unavailable widely in resource-constrained settings), adult height can be used as a valuable proxy for muscle mass and lean body mass and, hence, for metabolic capacity. Several studies from the developed as well as developing countries support the link between short stature and elevated risk of diabetes[14]. Interestingly, the relationship between diabetes risk and short stature was found to be stronger among populations of Asian and Australian origin than among Africans and Europeans[15]. It is therefore important to understand the influences that determine adult height.

It is now widely believed that stunting of adult height is largely determined during the first 2 to 3 years of life, with little catch-up growth in height possible thereafter[16]. This has led to concentration of efforts and nutritional interventions focused on the 'first 1000 days' of life. These efforts are no doubt important; but carry a risk of relative neglect of opportunities for improving growth at other time periods in life. A careful review of the available evidence to examine the patterns of growth and influence of childhood nutrition on adult height, muscle mass and metabolic health is therefore required.

Review of relevant studies carried out at NIN

Differing viewpoints on the effects of childhood under-nutrition and subsequent growth on adult health outcomes have elicited substantial controversy and heated debates. The National Institute of Nutrition (NIN) has contributed substantially to research on the impact of early life nutrition on nutritional status and health during

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later life. This article aims to review some of the major studies conducted at NIN in this area and synthesize the evidence to shed light on some of these important issues. These studies are organized as per the key research questions that could be addressed by them irrespective of the chronological order of the publication.

How does childhood under-nutrition influence adult nutritional status?

Some of the earliest studies conducted by NIN on the long-term effects of under-5 under-nutrition were based on the follow-up studies of children aged 1 to 6 years who were a part of the 'field prophylactic trial with a single annual oral massive dose of vitamin A'[17]. This study included anthropometric measurements recorded at six-monthly intervals during a four-year period from 1965-1969. After a gap of seven years subsequent studies were undertaken on the same children and anthropometric measurements were recorded annually from 1976 to 1984. Thus, over the 18-year study period, anthropometric data were collected regularly except for a gap of seven years during 1970-76. In the final year of the study (1984), the cohort members were aged between 19 and 24 years[18]. Height measurements of each subject were fitted with a Preece and Baines (PB) function which allowed estimation and comparison of growth parameters at uniform chronological and biological age points and periods across different cohorts[19]. Thus the values of adolescent growth parameters in this study were computed from PB coefficients and not observed.

In order to assess the effect of early life under-nutrition, children were placed in one of three groups (groups I, II and III), based on height deficit at age 5 + years. Harvard reference standards were used, and those above -2 SD (group I) were considered as having normal nutritional status, a status between -2 and -4 SD (group II) was considered as mild to moderate under-nutrition and below -4 SD (group III) was considered as severe under-nutrition. The study included detailed assessment of various characteristics of pubertal growth spurt and the following parameters were calculated: a) height and linear growth rates at ages 3 years ($H_{3.0}$& $V_{3.0}$), and 5 years ($H_{5.0}$&$V_{5.0}$), b) age, height and velocity at take-off (ATO, HTO& VTO) of adolescent growth spurt (AGS), c) absolute height (HPHV) at the time (APHV) of peak height velocity (PHV), and d) adult height (h1), age at completion of linear growth (ACG) after PHV (estimated by reading age at height velocity less than 1.0 cm per year from height velocity curve predicted using PB coefficients), height gain during puberty and duration of adolescent growth spurt period (AGSP) from ATO to ACG.

It was noted (Table 1) that there was a delay of > 6 months for pubertal growth to begin in the severely undernourished (Group III) boys, though it was not significantly different from that observed among the boys of Group I. However, the delay of 1.1 year for APHV seen in Group III boys was significantly different from Group I boys. Growth velocities of Group III boys at the take-off of adolescent growth spurt (VTO) and at PHV were not different from those of Group I boys. On the other hand, the significant height deficit of Group III boys as compared to Group I boys at the start of the pubertal growth spurt continued to be significant at the peak of height velocity (HPHV) and adult height (h1). Boys in Group III had started with a deficit ranging from 11-14 cm in the third year itself, as compared to boys of Group I. However linear growth continued for a longer period and ACG was found to be 19.2 years in Group III boys with a delay of 1.4 years as compared to Group I boys. As a result, boys of Group III had attained heights similar to those of Group I during puberty.

The authors compared these growth patterns with those of British boys and found that the average adult height of British boys, 174.6 cm, consisted of 139 cm of pre pubertal height and about 36 cm of pubertal height gain. The gain in height during puberty continued for 6.6 years starting from the age of 10.7 years. The boys from Group I in the rural Hyderabad cohort had an average adult height of 167.9 cm and a pubertal height gain component of 37 cm. Group III boys had 158.2 cm of adult height and 38.6 cm was the pubertal component. Group I boys had 7.2 years AGSP from 10.6 years, while Group III boys had 7.9 years AGSP from 11.3 years. The pre-pubertal deficit of 19 cm observed in Group III boys for HTO at the initiation of AGS was carried into adult height as a 16cm deficit as compared to British boys. Boys of Group I had a deficit of 8 cm at HTO, as compared to British boys, which was carried on into adult height as a 7 cm deficit. Thus, whereas the Group I boys had similar timing, intensity, and duration of Adolescent Growth Spurt Period (AGSP) and gained a similar amount of height during puberty as did British boys, Group III boys, who entered late into puberty and with significantly depressed intensity, also gained a similar amount of height, as a result of a longer AGSP, which continued till19.2 years.

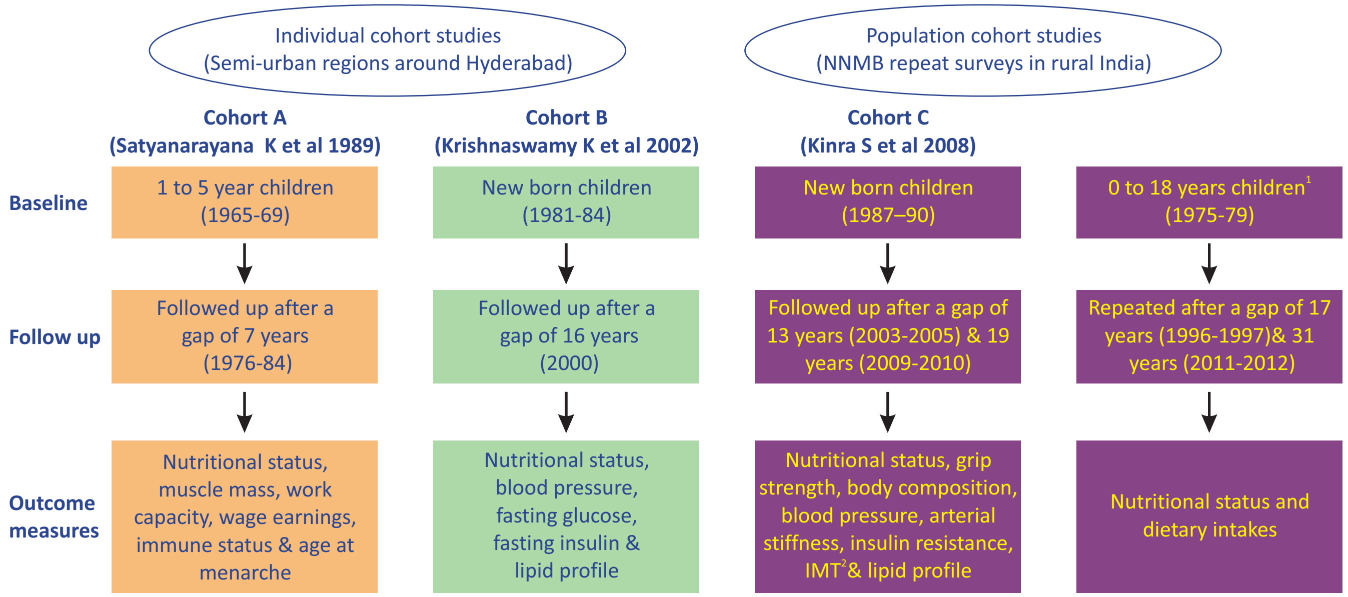
The authors concluded that rural Hyderabad children with differing childhood nutritional backgrounds had not experienced deficits in overall height growth once they entered pubertal age. Further, the deficits in height were lower by 3 cm in group III children than in Group I children (as compared to British boys), indicating partial catch up of linear growth during puberty. Another study in the same cohort studied weight patterns in these groups during pubertal growth. In contrast to the observations on height, the Group III boys had additional weight deficits during adolescence[20]. Compared to Group I boys, Group III boys gained significantly less weight (32.5 kg vs 36.3 kg) between their 5th and 20th years. The authors noted that the reasons for adequate height growth but simultaneous inadequate weight growth were not clear. This long term cohort study with rigorous data collection spanning almost two decades and complex analyses (with the help of Dr. R. Hauspie, Belgium) is a

Table 1: Mean age and height at the onset of puberty and predicted pubertal growth characteristics in the rural Hyderabad boys in comparison with published values in British boys (adapted from K Satyanarayana et al. 1989)

Groups	N	Height at 5 years	ATO (Years)	HTO (cm)	VTO (cm/year)	APHV (years)	PHV (cm/year)	ACG (years)	AGSP (years)	Height gain in puberty (cm)	Adult height (cm)
Group I	93	102.9	10.6	130.8	4.0	14.5	7.6	17.8	7.2	37.0	167.9
Group II	183	96.5	10.6	124.4	4.1	14.7	7.7	18.4	7.8	39.9	164.3
Group III	47	88.1	11.3	119.6	3.9	15.6	7.4	19.2	7.9	38.6	158.2
All Groups	323	96.9	10.7	125.5	4.0	14.8	7.7	18.3	7.6	38.9	164.4
British boys	35	105.8	10.7	138.9	4.5	14.2	8.2	17.3	6.6	35.7	174.6

ATO: Age at take-off; HTO: Height at take-off; VTO: Velocity at take-off; APHV: Age at peak height velocity; PHV: Peak height velocity; ACG: Age at completion of linear growth; AGSP: duration of adolescent growth spurt period

Figure 1.Long term cohort studies (discussed in this paper) that have assessed the impact of early life under-nutrition on later health and nutrition outcomes



[1]Included all age groups, [2]Carotid Intima Media thickness Note: Cohort A and B are non-intervention cohorts, while cohort C is an intervention cohort

seminal work contributing to the knowledge on catch-up (linear and ponderal) growth during puberty.

A subsequent study in girls showed findings similar to those observed in boys. In addition, a study in the girls from the cohort (12 to 18 years; n = 739) demonstrated delayed menarche in growth-retarded girls, which offered an opportunity for catch up in height[21]. The group of girls who were very short at five years of age (height < -4 SD as compared to Boston growth standards) attained menarche at a significantly later age (Mean (SD) 15.2 (0.13) years, 13.7 (0.19) years) than did tall girls or girls of average height (> 2 SD). In this study, differences of as much as four years in age at menarche were not accompanied by any significant differences in mean weights or heights and their ratio. It was concluded that the delay in menarche in most undernourished girls may be due to a delay in attaining adequate weight, build and other parameters.

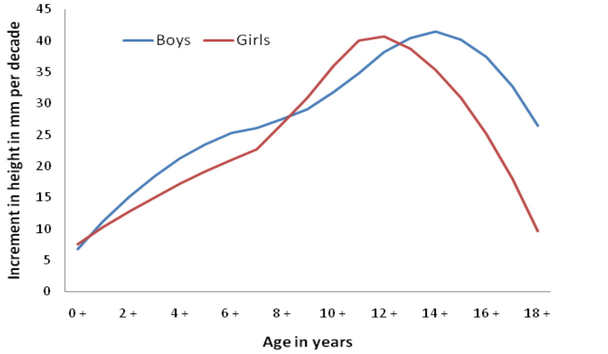
Is childhood undernutrition associated with decreased work capacity and reduced wages in later life?

While cross sectional studies have shown a relationship between under-nutrition and decreased work capacity[22], there was less clarity on the long-term effect of under-nutrition in early life on physical work capacity of adults in the developing world. In order to examine this aspect, a sub-sample of 14-17 year old adolescent boys (N=96) from the previously described main cohort was assessed for physical work capacity and physical activity[23]. Physical activity was assessed using a questionnaire and was cross-checked with parents and peers. Investigators who set up a field laboratory also observed their activity for 2 typical days in their environment. Physical work capacity was assessed using a magnetically braked Collin's bicycle ergometer and was based on the work performed in a seated position. Heart rate was recorded on an electrocardiogram at 2, 4 and 6 minutes after each work load. The participants were encouraged to continue to pedal up to complete exhaustion; otherwise, the experiment was terminated at heart rate above 170 per minute. The physical work performed (kpm/minute, 1 watt =61.12 kpm) at a heart rate of 170 (physical work capacity (PWC), 170 kpm/minute) was obtained by interpolation using approximate linear relationship between heart rate and work load. The Nutritional status of the participants was determined using western standards. The participants were divided into four groups, with the last group consisting of those with severe under-nutrition as assessed by height and weight. Among the 94 boys, only seven had normal nutritional status at both points of the study (i.e. status at 5 years and 14-17 years). As expected, the PWC was significantly greater in the older children as compared to younger children. Physical work capacity was significantly correlated with current weight, height and habitual physical activity. Current weight alone explained 63.6% (P <0.001) of the total variation; this was followed by habitual physical activity (10%, P <0.001) in the multiple regression analysis. When PWC was compared with early-life nutritional status, severely undernourished children at age 5+ had significantly lower PWC and higher heart rates when they performed the same task as compared to the other children. The work capacity per unit weight was lower in children who had been undernourished, but this difference disappeared when their physical activity levels were taken into consideration.

The main observation of the study was that the capacity to perform submaximal work was clearly related to body size, and nutritional status during early childhood influenced later life work capacity in proportion to the body weights at the time of the study. The authors concluded that early under-nutrition had no qualitative effect on work performance based on the work capacity per unit body weight. However, they advised caution while interpreting the findings of the study as there were only two normally nourished children at a later point who had been previously severely under nourished. Within an occupational group, low body weight appeared to be associated with lower PWC .But this difference narrowed in those who had higher habitual physical activity.

The cohort study also offered an opportunity to test whether the reduced physical work capacity impacted wage earning capacity during later life[24]. Children (N=723, 13 to 18 years) from the main cohort were classified into four groups based on nutritional status [normal (group 1), mild (group 2), moderate (group 3) and severe growth retardation (group 4) using Boston growth standards. About two-thirds of these boys had attended school for at least one year and half of them had completed primary education. At the time of

Figure 2 Tempo of growth in boys and girls from Kerala as assessed by Loess curves of increments in height (mm per decade)



the study, 40% were still at high school or college; and the remaining 60% were working in different fields of the rural economy. Among them, 301 boys worked in agriculture, 150 on their own family farms and 151 as agricultural labourers employed by other farmers. For the purpose of the study, 140 boys who were agricultural labourers were included for assessment of wage earning capacity. The nature of work included light activities such as grazing cattle (lowest wages) and intense activities such as ploughing (highest wages). Wages earned per day by the subjects were directly related to their body weight ($r = 0.60$, $P < 0.001$), age ($r = 0.41$, $P < 0.001$), and height ($r = 0.53$, $P < 0.001$). Wage earning capacity was divided into three groups from< 1 rupee, 1-2 rupees and > 2 rupees per day. Among those who earned <1 rupee per day, the largest proportion (71%) were those who had been under-nourished at 5 years. Among those who earned > 2 rupees per day, the corresponding proportion was the lowest (32%). Those who earned the lowest wages also had the lowest body weights at the time of the study, indicating that poor nutritional status in early life leads to low adolescent body weight, low physical work capacity as well as lower wage earnings.

Is childhood under-nutrition associated with decreased muscle mass in later life?

As the physical work capacity of under-nourished children was significantly lower than that of their peers in the other groups in the study, the researchers were interested in examining whether lower muscle mass could be the reason for this finding. In a sub-sample of 50 boys aged between 13 to 15 years from the main cohort who had been examined annually for heights and weights since 1976, an estimate was obtained of creatinine in 24-hour urinary excretion (an indirect measure of muscle mass that has an almost perfect correlation with it)[25]. The 24-hour urine samples were collected on two consecutive days in all participants, who were also requested to avoid meat for 3 days before and during the period of collection. In 19 of them, the samples were collected for 6 consecutive days to determine the extent of intra-individual variation. The 48-hour urinary creatinine value gave 98% predictability for 6 days of urinary excretion, and was utilized to obtain the daily average for all the participants. Heights and weights as percentages of American standards were used for classifying them into the four groups on the basis of nutritional status.. When the data were compared to those of American boys, all the groups had significantly lower values of creatinine excretion per kg body weight or per cm height. Further, Group 4 boys had the lowest excretion (total as well as per unit weight or height). However, the authors were of the opinion that it was unclear whether this reduction in creatinine index represents a reduction in muscle mass or an altered creatinine turnover on account of nutritional status per se and recommended that there was a need to assess body composition in under-nourished persons using direct methods.

Is childhood labour related to adult nutritional status?

A study was conducted in a sub-sample of the main cohort (N=410) in 1983-8420 to assess whether child labour could influence the adult height and body mass. Children were classified into 3 groups: normal, mild to moderate under-nutrition, and severe undernutrition (at age 5 years) based on Harvard reference values. Occupations during childhood were divided into four categories: (1) students (2) agricultural workers on family farms (3) agricultural workers working for wages and (4) non-agricultural workers. The last three groups were studied together as a 'child labour' group. The child labour participation was 52% and some children had started working from 6 -8years of age Prevalence of severe under-nutrition at 5 years of age was lower among students (13%) as compared to child labourers (25%). Since the social status of students was expected to be different from that of other groups, comparisons of heights and weights were carried out within the three groups of under-nutrition Group 3 boys were significantly taller than those of Group 1. Increase in weight between the ages of 5 and 20 years was the lowest in Group 1, but the increase in height between the ages of 5 and 20 years was the highest in Group 3. In fact, children in Group 3 showed a larger gain in stature (68.6 cm as compared to 67.9 cm) than had been recorded in western studies up to that time. Within each group, there were no significant differences in height or weight between students and child labourers. The results indicated that even severe malnutrition at the age of 5 years does not impair the capacity for linear growth after 5 years; however, the rate of gain was not enough to make up the deficit. While the marked reduction in adult stature due to labour in childhood was apparent, the difference also reflected the lower socio-economic levels of the child labourers as compared to the students. This study also suggests that later childhood life environment plays a significant role in the final adult heights attained.

Is childhood under-nutrition associated with altered immunocompetence in later life?

It was believed that under-nutrition during early childhood has a lasting effect on the immune status, but there was very little documented evidence for this belief. A subsample of boys aged less than 15 years during the period 1977-78 from the NIN main cohort were requested to participate in the study to assess immune status 26. The boys were classified into 4 groups based on Boston growth standards with grades of Normal (greater than - 2SD, N=22), Mild (-2 to -3SD, N=25), Moderate (-3 to -4 SD, N=29) and Severe (less than -4 SD, N=18) under-nutrition at age 5+ years. In this cohort there were a few children with a history of Marasmus and Kwashiorkor. Bactericidal activity (BCA) of leukocytes (N = 36 children), Humoral immune response, Cell mediated Immunity (CMI), and Total serum complement (CH 50, N =31) were measured in all the children. BCA activity measurement was also carried out over a two-year period to assess the impact of changes in body weight on BCA.

BCA of leukocytes and Humoral immunity (B cells and Immunoglobulin) decreased from Group 1 to Group 4, but this decrease was not statistically significant. Current body weight was significantly correlated ($r = 0.33$, $P < 0.05$) with BCA. There was a reduction in CMI with increasing grades of under-nutrition, with children in (Group 4) having significantly lower ($P < 0.01$) CMI as assessed by T lymphocyte count as compared to children in other groups. The mean haemolytic complement levels (CH50) were not related to the degree of under-nutrition. It was observed that children with Kwashiorkar had lower counts of T cells and B cells as compared to children who had Marasmus. It was concluded that, while CMI was significantly impaired in severely growth-retarded children, humoral response was unaltered even in that group and was intact in about 80% of the children in a poor community. Interestingly, the changes in the current nutritional status were significantly associated with similar changes in BCA over a 2-year period.

Is low birth weight associated with increased cardiovascular risk in later life?

A new cohort study was established in 2000 to assess the relationship between birth weight and cardio-metabolic risk indicators. This arose from the opportunity provided by a previous study conducted to determine the effects of birth weight and childhood protein energy malnutrition on physical growth and psychological development[27]. The cohort children (n=125) at the time of recruitment were aged 16 -19 years and 40% of them had birth weight < 2.5 kg. Most of the children continued to remain in the semi urban and rural areas. The low birth weight (LBW) children were further grouped as per their current weights into two groups: under-nourished or better nourished, using the current median weights of normal birth weight children (NBW). The outcome parameters included systolic and diastolic blood pressure, fasting glucose, fasting insulin and a complete lipid profile. There were no clear differences in any of the outcome parameters in relation to the birth weight group. Only the current BMI had a significant influence on systolic and diastolic blood pressure (both P <0.05). Participants who were born LBW and continued to be thin were relatively at lower risk of CHD. The sample size was adequate to prove that this was not due to the confounding effect of continued under-nutrition in adult life in those born with LBW.

Is nutrition intervention in early life associated with decreased cardiovascular disease risk in later life?

The evidence in support of intrauterine programming of adult body composition and chronic diseases is largely circumstantial, based on experiments in animals and observational studies in humans. Most of these studies have used birth weight as a proxy measure of foetal nutrition. A major criticism of these studies is that birth weight is a poor measure of intrauterine nutrition because it is multi-factorial in origin and a more direct assessment of exposure is desirable[28,29]. However, the direct evidence of a relationship between maternal nutrition during pregnancy and later health outcomes is very scarce due to the difficulties in conducting longitudinal studies with many years of follow-up. Data from nutrition supplementation trials in pregnant women provide an opportunity for the direct assessment of the long-term impact of the nutrition intervention on the health of the offspring[30,31].

Nutrition supplementation during pregnancy is one of the public health measures implemented in many developing countries to help undernourished women meet the extra energy requirements during pregnancy. However, whether such nutrition interventions result in a positive long-term impact on adult health has not been researched adequately.

Andhra Pradesh Children and Parents Study (APCAPS) birth cohort represents a long term follow up of Hyderabad Nutrition Trial conducted in 29 villages near Hyderabad (1987–90), using an opportunity afforded by the stepwise expansion of the Integrated Child Development Services (ICDS) programme. In two adjacent administrative areas (one with an ongoing programme, the other awaiting implementation), all villages within a 20 km radius of a central village were selected to serve as intervention (n =15) and control (n=14) areas, with unselected intervening villages to avoid contamination. In the intervention villages, a nutritional supplement based on corn–soya blend was given daily to all pregnant and lactating women and to children <6 years of age; the supplement provided a daily average of 500 Kcal and 20–25 g protein to pregnant/lactating women and 300 Kcal and 8–10 g protein to children. The supplement had to be collected daily by the women (or their children) from the ICDS centre, but they were not obliged to eat it there. The supplementation was associated with a small but statistically robust (61 g, 95% C.I. 18 to 104; p = 0.007) increase in birth weight of the offspring (n=2601).

Children born within this trial were traced in 2003-5 to examine the prevalence of risk factors for cardiovascular disease (including body composition assessment by anthropometry) in relation to the food supplementation. The first follow-up study which included 1165 of the children (then aged between 13 and 18 years) showed that adolescents from the intervention villages were 14 mm (95% confidence interval 4 to 23; P=0.007) taller than controls but had similar body composition. The data suggested a lower risk of cardiovascular disease (as evidenced by arterial stiffness and insulin resistance) in adolescents from the intervention villages, as compared to controls,32 a finding which was consistent with the DOHaD hypothesis,

The index participants of the cohort study were further followed up in 2009-2010 (second follow-up of the APCAPS birth cohort) when they were young adults aged 18-21 years to assess their body composition (using dual energy X-ray absorptiometry (DXA) and their propensity to develop Type II diabetes and coronary heart disease. This study included a total of 1,446 (56%) of the 2,581 surviving children. Data collection included detailed assessment of socio-economic status, dietary intake (over the past year) and physical activity (over the past week) using validated questionnaires in addition to anthropometric and grip strength measurements. Fasting blood glucose, cholesterols (HDL, total), triglycerides, and insulin were measured in all the children. Assessment of cardiovascular risk indicators such as blood pressure, arterial stiffness (augmentation index and pulse wave velocity), and carotid intima media thickness was also carried out. Data from this study showed that nutritional supplementation did not have any significant long term impact on body composition, muscle strength and bone density in young adulthood; these parameters were influenced mainly by contemporary lifestyle factors[33,34].

It appears that the favourable impact of nutrition intervention in early life on lean body mass and cardio-metabolic disease risk does not persist beyond adolescence due to “dilution” of the programming effect of early nutrition by diet and other lifestyle changes over the years. The findings could also be explained by a confounding influence exerted by imperfectly measured or unmeasured confounders on the observed relationship. Studies based on long-term follow up of birth cohorts in transitioning communities are faced with challenges of dealing with complex confounding influences related to rapid socio-economic and lifestyle changes. Anecdotal evidence from the study area suggests that the intervention villages have undergone more rapid urbanization than the control villages in the past few years. The lower muscle mass and strength observed in the intervention participants could be attributed to their relatively urbanized sedentary lifestyles. The third follow-up of the cohort in 2010-12 largely corroborated the findings of the second follow-up study.

The major strength of this study is the comprehensive assessment of early and later life influences on the adult lean body mass and other health indicators In contrast, a majority of previous studies had examined either only “programming” of the adult disease risk by early nutrition or only the role of contemporary lifestyle determinants, each in isolation. The findings of this study highlight the need to ensure that an assessment of the relationship of early life factors with adult health outcomes should include precise measures of current life factors so as to make adequate adjustment for their potential confounding influences. The study suggests that there are opportunities for interventions such as improvement in diet and physical activity throughout the life course, and that these should be emphasised.

Does early life under-nutrition affect the pattern and rate of linear growth?

Studies assessing the secular trends in heights in India (using cross sectional data measured periodically) have indicated wide variations across the states, showing both positive (Kerala) and negative (Meghalaya) secular trends in heights[35]. It was therefore interesting to examine the extent of actual improvement in heights over a period of time. The landmark paper by Prof. Cole suggested that changes in adult height were similar to those of the height at age 2 years in Japanese children. He also suggested that secular trends in height have occurred even without changes in birth weights[36].The question then was whether the pattern and rate of growth are affected by low birth weight and under-nutrition in childhood as seen in rural India.

An analysis of the reported NNMB data from the first survey (baseline) in 1975-79 (N=6018) and the third repeat survey (end line) in 2012-13 (N=11910) was taken up to assess the increments in heights and weights of boys and girls during this period. The data used for this analysis included height and weight measurements in boys and girls for the first 2 decades of life (0+ to 18+) in all the states covered by NNMB except three states that were not a part of the baseline survey.

Secular trends in height

Increments in height were highest in 12-year-old girls (19 mm per decade) and 15-year-old boys (21 mm per decade). The increments at 18 years were 9 mm per decade in boys and 3 mm per decade in girls. The pattern of change in height in rural India was strikingly similar to that in Japanese children. While it was found that the increments in adult height were similar to that at 18 years in boys, this was not so in girls, thereby suggesting poor nutritional status of adolescent girls in rural India.

Regional trends in changes in height

Secular trends in height were highest in Kerala, with an increment of 46 mm per decade in 15-year-old boys and 49 mm per decade in 13-year-old girls from baseline to final survey (Figure 2). The rate of reduction in stunting was high - 1.5% per year in both boys and girls over a period of more than 30 years. This has happened despite 16.2% (unadjusted) and 18.2% (adjusted for heaping of digits) of all new born children with LBW from the NFHS-3 analysis. Thus, as suggested by Prof Cole, birth weight may not influence long-term changes in linear growth despite its short term effects on early-life stunting.

Catch up growth in height

While the definition of catch-up growth is clear, the outcome parameter that should be chosen to express catch-up growth (whether it should be change in Height for age Z (HAZ) score or absolute change in height) is debatable; using different parameters has resulted in opposite conclusions and controversy from analysis and reanalysis of the COHORTS studies[37]. The arithmetical explanation for this apparent paradox has been linked to the calculation of HAZ with larger SDs from birth to adulthood, resulting in a decrease in HAZ over period of time and therefore an apparent catch-up. It was suggested that absolute differences in heights from the reference may also be presented to assess catch-up growth. However, there is an essential flaw in this "horses for courses approach" in that if HAZ attenuates over a period, this should have happened even during the first 2 years of life during which stage growth faltering in linear growth is known to be at its maximum. The analysis would be more helpful if the rate of change in linear growth after mid-childhood (48 months) is compared with the reference gain, as was done in earlier studies at NIN. Nevertheless, studies on secular trends in height in developed countries in the 19th century have shown that the highest increments in height were seen in school children, followed by adolescents and adults[36]. If catch-up growth in height after the first two years of life is considered to be absent, then the rate of absolute increments in height after the first two years should have been similar. In our study, in rural India, height gain seen in the adolescent age group in most states was much higher than that in children below 2 years. Further, in both surveys, the HAZ scores of adolescents were also much higher than those of children younger than 5 years. This has been interpreted as suggestive but not conclusive evidence of catch-up growth. There was a gross deficit in adolescent weight gain to the extent of about 23.1 and 17.7 kg in 15-year-old boys and 12-year-old girls, respectively, as compared to the WHO median. This is a cause of concern.

The analyses showed that the age at the maximum increment in height was 12 years in girls and 15 years in boys (similar to the findings in previous studies), and thereafter increments in height reduced by 2- to 3-fold till the age of 18 years, suggesting earlier maturation in growth. Demographic health surveys (DHS) in developing countries conduct periodic measurements of heights of children < 5 years and heights of women aged >15 years but do not include the age group 6-14 years, where peak increments in height are noticed. The findings of this study emphasize the need for measurement of heights in the adolescent age group.

Key questions and Future research

The studies conducted at NIN and elsewhere in the first thousand days of life using different interventions (single micronutrient supplements (zinc)[38], multiple micronutrient supplements[39], food supplements and nutrition education[40], and community mobilization[41]) have shown either minimal or no impact on birth weight and linear growth. It is important to examine why the effect sizes of these interventions are so small and whether these marginal benefits have any meaningful impact on the nutritional status in later life, especially in the rapidly changing environments of transitioning societies. Other key questions include: If the delivery of nutrition intervention is the major constraint, what programmatic delivery approach of nutrition intervention would be most useful during the first 1000 days of a child's life? Are growth standards appropriate for children of developing countries where adults have not attained their peak heights? Is the change in final adult height as reflected at 2 years of age a cause or an effect? Do nutrition interventions beyond or within the1000-days window work? These are some important questions that need to be addressed. In this context, NIN is organizing an international conference as a part of the centenary celebrations on the theme "Nutrition before, beyond and during the first 1000 days of life-evidence and action" (November 26-28, 2017) at Hyderabad.

Summary and the way forward

The body of evidence from the review of NIN studies suggests that, although early-life under-nutrition has a significant influence on nutritional status, muscle mass, physical work capacity, and immune competence in later life, its impact on cardiovascular disease risk indicators was minimal. There was a strong influence of contemporary factors including body weight, habitual physical activity and diet on cardio-metabolic risk outcomes in later life.

Although the nutrition in the first 1000 days of life is crucial for linear growth, opportunities to improve growth during adolescence should be not be neglected. DHS surveys did not collect data on heights and weights of children in the age group of 6 to 14years. The lack of nationally representative data on adolescent growth, when peak increments in heights are seen and could be sensitive to nutritional interventions, represents a missed opportunity to understand the factors affecting the attainment of adult height in different regions. Given that most of the developing countries have not reached their full growth potential, it would be useful if the DHS extends the weight and height measurements to all age groups. Nutritional status is a reflector of living conditions of the society and is the simplest and most inexpensive, sustainable and direct marker for assessing the development of the population of a nation.

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FOUNDATION NEWS

NAMS-NFI symposia:

1. NAMS-NFI technical orientation programme on Assessment of Nutritional status in the Dual Nutrition Burden Era

India is undergoing economic, social, demographic, health and nutrition transitions. This has resulted in a dual nutrition burden of under- and over-nutrition as public health problems. The dual nutrition burden is accompanied by the dual disease burden with persistence of high morbidity due to communicable diseases on the one hand, and rising prevalence of non-communicable diseases on the other.

In this period,accurate assessment of nutritional status is essential:

- At individual level for
  - early detection of under- and over-nutrition
  - initiation of appropriate management on the basis of the findings during assessment and
  - monitoring the improvement in nutritional status over time
- At community level surveys for assessment of
  - magnitude and determinants of dual nutrition burden
  - impact of ongoing public health interventions to combat the dual nutrition burden

NFI in collaboration with NAMS is organising a technical orientation programme on "Assessment of Nutritional status in the Dual Nutrition Burden Era" on 6.10.2017 at Kamla Raheja Auditorium, JS Bajaj Centre for Multi-professional Education, NAMS House, Ansari Nagar New Delhi.

The objectives of the technical orientation programme are to familiarise the participants about:

- Dual nutrition burden: perspective, determinants, dimensions and health consequences
- Assessment of nutritional status in the dual nutrition burden era using:
  - o Dietary intake
  - o Physical activity
  - o Anthropometric assessment of nutritional status
  - o Body fat and its distribution
- Quality assurance procedures for ensuring accuracy and reliability of measurement
- Through a video demonstration, to explain methods of ensuring the accuracy of measurements and measuring instruments during
  - o Measurement of height
  - o Measurement of weight
  - o Circumferential measurements
  - o Measurement of fat fold thickness
  - o Body fat measurement using BIA

2. NAMS-NFI symposium on "Food fortification for improving micronutrient intakes"

Micronutrient deficiencies - referred to as hidden hunger - are the most common type of nutritional deficiencies in India, as indeed globally. It is estimated that over 2 billion persons in the world, including a majority of the 1.3 billion Indians, are deficient in one or more micronutrients. Deficiencies in iodine, iron, folate, vitamin B12, and vitamins A and D are recognised as major public health problems in India. With fortification of appropriate food stuffs, it is possible to achieve sustained improvement in intakes of micronutrients and a reduction in micronutrient deficiencies at population level, even without any dietary modification. Five decades ago, India initiated fortification of salt with iodine to combat iodine deficiency disorders. The mandatory fortification of salt with iodine in the last decade gave an impetus to the programme, and the country is now nearing the goal of universal household access to iodized salt.

The success of the Iodine Deficiency Disorder (IDD) control programme led to an exploration of ways to use a similar strategy to combat other even more widespread micronutrient deficiency diseases such as iron deficiency anaemia. Rapid improvements in the technology of fortification, and improved packaging, transport and marketing have made food fortification a viable, sustainable, effective and inexpensive strategy to combat widespread micronutrient deficiencies.

Globally and in India, iron deficiency is the most common micronutrient deficiency and is the major cause of anaemia. Iron-fortified iodised salt (DFS) represents the most feasible, economical and sustainable method of increasing iron intake by an average of 10 mg/day (without any major dietary change) and reduce the prevalence of iron deficiency. The FSSAI has set the standards and has approved two technologies for DFS manufacture. Currently there are ongoing studies to explore the feasibility and efficacy of fortifying atta and rice with iron, folic acid and vitamin B12 to combat anaemia.

Voluntary fortification of vegetable oils with vitamins A and D by manufacturers is underway. Vitamins A and D are lost when milk fat is removed during processing for production of toned, double-toned and skimmed milk. Voluntary replenishment fortification of toned, double-toned and skimmed milk with vitamins D and A is being taken up by some major milk producers.

One of the potential problems in the widespread use of fortification of multiple food stuffs with multiple micronutrients is the possibility that some segments of the population whose intake of nutrients is adequate, may consume many of these fortified products and the total amount consumed may exceed the required amount of nutrients. Occasionally such sustained high intake of some nutrients may have potential adverse health consequences either due to excessive intake and/or imbalance of intake of inter-related micronutrients.

The NAMS-NFI symposium on "Food fortification for improving micronutrient intakes" aims to update the participants about:

- the current global, South-East Asian scenario regarding food fortification
- Indian efforts to improve micronutrient nutritional status through food fortification
- regulatory frame work for food fortification in India
- ongoing efforts to ensure that intake of nutrients are well within the tolerable upper limits of intake

The symposium will be held on 29.11.2017 at Kamla Raheja Auditorium, JS Bajaj Centre for Multi professional Education, NAMS House, Ansari Nagar New Delhi.

NUTRITION NEWS

- The 49th Annual National Conference of the Nutrition Society of India will be held from 2-4 November, 2017 at Assam Agricultural University, Jorhat Assam. The theme of the conference is "Biodiversity, Traditional Food Systems and Wellness: Connecting Global Priorities".
- Two pre-conference workshops will be held on 2nd November, 2017. The topics for the pre-conference workshops are:
  - Designing, planning and execution of nutrition research
  - Management of food analysis laboratories
- The 50th Annual National Conference of Indian Dietetic Association will be held from 18-20 December, 2017 at Science City, Kolkata. The theme of the conference is "Let's nourish to flourish – Nutrition for Health & Economic Development".

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