

*Review Article***Size at Birth: Effect on Nutrition and Adult Onset Disease**

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There is an increase in the burden of adult cardiovascular diseases and Type 2 diabetes in low and middle income countries, including India. Non-communicable diseases contribute to almost 60% of all deaths in India. This is the result of nutrition transition and the emergence of overnutrition as major public health problem. Globally and in India, increasingly sedentary life style and in some segments of population habitual intake of high fat, high sugar energy dense food stuffs have been responsible for the rising overnutrition rates. In India, there is an additional factor: the high burden of low birth weight infants who undergo fetal programming. LBW not only contributes to high burden of under nutrition in under 5 children, but when accompanied by accelerated weight gains in childhood and early adulthood, it increases the risk for adult chronic disorders.

Keywords: Low Birth-Weight; Non-Communicable Diseases; Fetal Programming; Nutrition Transition

There has been a global increase in the burden of non-communicable diseases (NCD), but the increase in past decade or more has been greater in low and middle income countries (LMICs) including India. The Global Burden of Disease (GBD) Study estimated that for 2016, NCDs accounted for 72% of all deaths (Naghavi *et al.*, 2017). The contribution of NCDs to total DALYs for India increased from 30.5% in 1990 to 55.4% in 2016 (ICMR 2017). Similarly, the proportion of all deaths due to NCDs increased from 37.9% in 1990 to 61.8% in 2016. While India as a whole has demonstrated this epidemiologic transition, the rate of change across different states has not been uniform. The highest level of epidemiologic transition (ETL) in 2016 was observed in states of Kerala, Goa, Tamil Nadu, Punjab and Himachal Pradesh, with the lowest levels being seen in states such as Bihar, Uttar Pradesh, Rajasthan, Madhya Pradesh, and Jharkhand. Interestingly, Kerala had a high ETL even in the 1990s (Dandona *et al.*, 2017).

While life style changes have been identified as important contributors to obesity, hypertension, altered glucose metabolism and dyslipidemia (risk factors for NCDs such as ischemic heart disease, type 2 diabetes and stroke), there has also been growing evidence

over the last two decades of the role of size at birth on adult NCDs (Fall 2013).

Size at Birth and Nutritional Status

National Family Health Survey-4 (NFHS 4 -2015) reported that 18% of newborn were documented to have a birth weight of <2.5kg (estimated from the 78% of surveyed sample having birth records). This burden increased from 15% amongst births to mothers in households in the highest income quintiles to 20% amongst mothers in the lowest quintile households. When the survey used the mother's estimate of infant size at birth (a proxy to birth weight), 12% women reported their infants to be smaller than average or very small at birth. The NFHS-4 also noted that the proportion of children whose weight for age was <-2SD or <-3SD rose as the age increased from <6 months (26.5% and 9.5% respectively) to 48-59 months (39.1% and 10.7% respectively). The proportion of under-5 children with weight for age <-2SD or <-3SD were highest in women who were underweight (BMI <18.5kg/m²). The states which had higher levels of ETL (as noted in the GBD 2016 study) had lower proportion of under-5 children who were underweight compared to the low ETL states.

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Transitioning societies such as India and other LMICs are faced with the dual burden of under-nutrition in childhood and obesity amongst its adult population. Studies now support the relationship between childhood nutrition and adult lean body mass (LBM). Observations from the Birth-To-Twenty cohort from urban South Africa (Kagura *et al.*, 2012) noted that underweight at one year had significant association with lower lean body mass at 10 years. They also noted that body fat at 10 years of age was positively associated with infant WAZ score change during the second year.

The Cebu Longitudinal Health and Nutrition Survey in Philippines (Borja, 2013) documented that babies who were small at birth were more likely to be stunted at adolescence, and had a higher risk for adult cardiovascular disease. The data from this cohort reported that breast feeding protected against both morbidity and stunting. They also noted that delayed complementary feeding reduced the likelihood of obesity in adulthood. The study also recorded a transgenerational effect of a positive association of maternal birth weight and the weight of her offspring at birth.

The association of birth weight and changes in WAZ score with fat mass and fat free mass was also documented in studies from the SKOT Danish cohort (Ejlerskov *et al.*, 2015). Ejlerskov *et al.* reported on the relationship of birth weight z-scores (BWZ) and change in WAZ scores from 0 to 5, 5 to 9, 9 to 18 and 18 to 36 months with body composition (measured by anthropometry and bioelectrical impedance analysis) at 3 years of age. They observed a significant positive association between BWZ and WAZ scores change at 0-5 months, and BMI, fat free mass index and fat mass index at 3 years. As in the Cebu longitudinal study, they noted that exclusive breast feeding for 6 months eliminated the positive association of BWZ and early growth at 0-5 months on fat mass index.

The data from the Dutch cohort (De Beer *et al.*, 2015) also have noted similar results on the association of birth weight, weight gain in early childhood, breast and complementary feed on fat mass measured at 5-6 years of age. Data was analyzed from 2227 children in the cohort and body composition was assessed using bioelectrical impedance analysis. Birth weight and relative weight gain at all ages in infancy was positively associated with fat mass and

fat free mass. Exclusive breast feeding beyond 6 months and complementary feeding initiated after 6 months were associated with a significantly lower fat mass.

Goncalves *et al.* in a longitudinal study of 167 term babies from Brazil (Goncalves *et al.*, 2014) observed that LBW term babies (irrespective of whether they were stunted at birth or not) were associated with lower BMI and waist circumference at 8 years of age. However increased BMI and waist circumference at 8 years was significantly associated with rapid weight gain in the first 6 months of life, shorter breastfeeding duration, higher socioeconomic status and maternal BMI.

The evidence from all the studies demonstrate the positive association between birth weight and weight gain changes in early childhood with fat mass all through life (late childhood, adolescence and early adulthood). However, it appears that exclusively breast feeding upto 6 months or more and delaying complimentary feeding beyond 6 month has a mitigating effect on fat mass and obesity.

Size at Birth, Childhood Nutrition and Adult Chronic Disease

The important risk factors for NCDs include obesity, elevated glucose and hypertension. As per NFHS-4 (NFHS-4 2015), in the age group 15-49 years, the proportion of women who were obese in India during 2015-16 was 5.1% and it was 3% amongst men. There has been an increase in proportion of women and men who are either overweight or obese in the decade between NFHS-3 (2005-2006) and NFHS-4 (2015-16). Amongst women, it has increased from 13 to 21% and amongst men from 9.3 to 19%. The highest proportion of overweight or obese women (>30%) are in states of Kerala, Goa, Andhra Pradesh and Tamil Nadu- the states with the highest levels of epidemiologic transition.

As per NFHS-4, in the age group 15-49 years, 11% of women and 15% of men were detected to be hypertensive, and 30% of women and 43% of men were pre-hypertensive. As expected, prevalence of hypertension was greater amongst obese women and men compared to those with normal BMI. Similarly 6% women and 8% men had random blood sugar values > 140 mg/dL. Larger proportion of population

in high ETL states had elevated blood sugar values compared to low ETL states.

The effect of birth weight and weight gain in early childhood has been documented to be associated with increased risk of diabetes and cardiovascular disease in adult life. The Cebu longitudinal study in the Philippines (Borja, 2013) observed increased risk of adult cardiovascular disease amongst those born small at birth. Amongst the males in cohort, it was noted that those born thin but with high adult BMI had higher risk of elevated systolic blood pressure. Studies amongst subjects of the New Delhi Birth Cohort (Bhargava *et al.*, 2004) demonstrated that those who were diabetics or had impaired glucose tolerance at ages 26-32 years, had low BMI till 2 years of life, followed by rebound adiposity in early childhood, consequently followed by accelerated increase in BMI till adulthood. Observations from a Danish Cohort (Rytter *et al.*, 2014) reported an inverse association between birth weight and insulin levels, triglycerides and insulin resistance in adults aged 20 years.

There is increasing evidence to indicate that the effect of “programming” for adult chronic disorders amongst those with small size at birth can be detected early in childhood. de Jong *et al.* (de Jong *et al.*, 2014)

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studied the components of metabolic syndrome amongst very low birth weight infants at 2 years of life. Amongst 38 VLBW term and preterm infants followed at 2 years, 63% had elevated blood pressure, and 30% had high triglycerides. Bavdekar *et al.*, (Bavdekar *et al.*, 1999) in a study in 8 year old children in Pune noted that children born with low birth weight but currently relatively heavy had higher blood pressure, serum lipids and insulin resistance. Other birth cohort studies from Mysore (Krishnaveni *et al.*, 2010) and New Delhi (Bhargava *et al.*, 2004) in India have reported similar findings. The results from these studies indicate that the metabolic changes consequent to fetal programming could be seen early in childhood.

Conclusion

An alarming increase in the burden of adult cardiovascular diseases and Type 2 diabetes in low and middle income countries including India, is not only a result of economic transition these nations are experiencing, but also related to the high burden of low birth weight infants who undergo fetal programming, which when superimposed by accelerated weight gains in childhood and early adulthood, increase the risk for the adult chronic disorders.

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