INVITED COMMENTARY

Growth Faltering in Small and Sick Newborn Infants: Does it Matter?

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In an important prospective study, Joseph, et al.[1] describe the depreciation of growth (mainly weight for age *z*-scores using the Intergrowth 21 standards for preterm infants) among small and sick new-born infants [2]. These infants represented 31% of all admissions to public sector newborn care facilities in two districts of Himachal Pradesh. The authors describe growth faltering among 30% of term infants and 52.6% of preterm infants between 1-4 months of discharge from hospitals, underscoring inadequate recognition and intervention by ASHA workers in primary care settings.

These are important data on high-risk newborn outcomes and quality of care from rural settings in South Asia. However, there are also important limitations in the information that was captured. We have limited information on gestational weight gain and maternal nutrition in the cohort and sub-categories at excess risk for potential targeting [3]. Preterm infants who are also small for gestational age (SGA) represent subsets with 17-39 folds excess risk for newborn mortality [4]. These infants also have 4-5 folds higher odds for stunting, a fifth or more of which is established by 6 months of age [5]. Given the known association of early growth in infancy with maternal nutrition status prior to and during pregnancy [6], there could well be differing patterns of growth among their infants, an aspect not fully covered in the current study.

Regardless, the data provide strong evidence of growth faltering in these high-risk infants, and the need for focused attention towards their care and community follow up. The authors use the term "catch down growth" and growth faltering interchangeably, which may not be strictly correct in this setting. The term "catch down" growth has been used in the literature to account for adjustment of growth patterns in young infants to their genetically programmed growth patterns and has often been used in the context of large for dates infants and others. In the context of the average birth cohort in India, this downwards growth trajectory is neither normal nor ordained. As was underscored by the late Prof Ramalingaswami and colleagues decades ago [7], these small babies may represent the contribution of systemic disadvantage that many women face and indeed the consequence of intergenerational effects of undernutrition [8].

The subject of postnatal growth and drivers is of special interest (especially under 6 months of age), and requires attention to social determinants of growth failure in these circumstances. It is also evident that much of the long-term risks of non-communicable diseases and obesity could be determined and programmed in utero. In a recent multi-country prospective observational study of 3598 pregnant women, Villar, et al. [9] observed distinct patterns of intrauterine growth (by measurements of abdominal circumference) between 20-25 weeks gestation, metabolic signals and postnatal growth and development patterns up to 24 months of age. The group with faltering intrauterine growth pattern remained significantly small with minimal catch-up growth in the first year of life. The early catch-down growth pattern was only seen among those with the early fetal growth acceleration pattern. Importantly, in comparing maternal and cord blood samples, most metabolites associated with the faltering growth phenotype had ORs close to 1·5, indicative of an upregulation of metabolic pathways associated with impaired fetal growth. In contrast these metabolites had a reciprocal relationship with the early accelerating growth phenotype, which suggests that the same path-ways are down-regulated when fetal growth is accelerated.

The Women First Trial [6] also followed the growth trajectory of 2337 infants over the first two years of life and documented that length at birth was the best predictor of linear growth at 24 months. For infants with ultrasound-determined gestational age (n=1329), the strongest predictors of stunting were birth LAZ <–2 and <–1 to ≥– 2

with adjusted relative risk of 1.62 (95% CI: 1.39, 1.88; *P*<0.001) and 1.46 (95% CI: 1.31, 1.62; *P*<0.001), respectively.These data underscore the importance of maternal health and nutrition for child growth and the need for gestational age adjusted weight and length mea-sures at birth and thereafter; measures which are unfor-tunately lacking in large scale surveys. In a cross-sectio-nal analysis of predictors of growth among Pakistani children, maternal BMI and height were found to be independent predictors of linear growth among children suggesting that there is likely an intergenerational conse- quence of poor growth and maternal undernutrition [10].

What are the implications of these findings for public policy? This growth depreciation occurs at a period of life when there are no satisfactory alternatives to exclusive breastfeeding. Although full feeding patterns and intakes for the cohort were not described, only about half the infants were fully breastfed, which makes it quite challenging to propose nutrition solutions in this age group. Much greater emphasis must be placed on prevention of fetal growth retardation and preterm births, and optimizing maternal health and nutrition. Additionally, substantial investments are needed to support small and sick babies in the health system, not only during hospital stay but also postnatally during the follow up period. India has invested in a substantial workforce that can provide this support in primary care settings. They need to be trained for optimizing maternal health and nutrition and supporting mothers in community kangaroo care [11]. The strong evidence emerging on the role of mother newborn care units in optimizing newborn outcomes is an additional strategy worth emulating at scale [12]. India can lead the way for the region by prioritizing such investments in early child growth and human capital development [13].

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REFERENCES

1. Joseph J, Jalal R, Nagrath M, et al. Growth faltering among discharged babies from inpatient newborn care facilities: learnings from two districts of Himachal Pradesh. Indian Pediatr. 2022 Jul 12:S097475591600440.
2. Villar J, Giuliani F, Bhutta ZA, et al. International Fetal and Newborn Growth Consortium for the 21(st) Century (INTERGROWTH-21(st)). Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21(st) Project. Lancet Glob Health. 2015; 3:e681-91.
3. Ashorn P, Black RE, Lawn JE, et al. The Lancet Small Vulnerable Newborn Series: science for a healthy start. Lancet. 2020;396:743-45.
4. Katz J, Lee AC, Kozuki N, et al. Cherg Small-for-Gestational-Age-Preterm Birth Working Group. Mortality risk in preterm and small-for-gestational-age infants in low-income and middle-income countries: a pooled country analysis. Lancet. 2013;382:417-25.
5. Christian P, Lee SE, Donahue Angel M, et al. Risk of childhood undernutrition related to small-for-gestational age and preterm birth in low- and middle-income countries. Int J Epidemiol. 2013;42:1340-55.
6. Krebs NF, Hambidge KM, Westcott JL, et al. Women First Preconception Maternal Nutrition Study Group. Birth length is the strongest predictor of linear growth status and stunting in the first 2 years of life after a preconception maternal nutrition intervention: the children of the Women First trial. Am J Clin Nutr. 2022;116:86-96..
7. Ramallingaswmi V, Rohde J, Johnson U. Commentary; The Asian Enigma. The Progress of Nations. UNICEF. 1996. Accessed Sept 2, 2022. Available from:*https:// advocacy.thp. org/ 1996/12/commentary-the-asian-enigma/*
8. Selling KE, Carstensen J, Finnström O, Sydsjö G. Intergenerational effects of preterm birth and reduced intrauterine growth: a population-based study of Swedish mother-offspring pairs. BJOG. 2006;113:430-40.
9. Villar J, Ochieng R, Gunier RB, et al. Association between fetal abdominal growth trajectories, maternal metabolite signatures early in pregnancy, and childhood growth and adiposity: prospective observational multinational INTERBIO-21st fetal study. Lancet Diabetes Endocrinol. 2022 Aug 25:S2213-8587 (22)00215-7. Epub ahead of print.
10. Di Cesare M, Bhatti Z, Soofi SB, Fortunato L, Ezzati M, Bhutta ZA. Geographical and socioeconomic inequalities in women and children's nutritional status in Pakistan in 2011: an analysis of data from a nationally representative survey. Lancet Glob Health. 2015;3:e229-39.
11. Taneja S, Sinha B, Upadhyay RP, et al. ciKMC development study group. Community initiated kangaroo mother care and early child development in low birth weight infants in India-a randomized controlled trial. BMC Pediatr. 2020;20:150.
12. Chellani H, Arya S, Mittal P, Bahl R. Mother-Newborn Care Unit (MNCU) Experience in India: A Paradigm Shift in Care of Small and Sick Newborns. Indian J Pediatr. 2022;89:484-89.
13. Heidkamp RA, Piwoz E, Gillespie S, et al. Mobilising evidence, data, and resources to achieve global maternal and child undernutrition targets and the Sustainable Development Goals: an agenda for action. Lancet. 2021;397:1400-18.