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Review Article

Growth Trajectories among Toddlers in Rural Cambodia; Increased Risk for Severe Stunting in Poorer Communities

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Abstract

Objectives: Previous studies of a Cambodian birth cohort showed significant differences in birth weight, ponderal index and head circumference between newborns from two rural communities. The differences were associated with maternal anthropometrics and socioeconomic background, and the smallest babies were born to the mothers from the poorest communities. To see if the differences persisted postnatally, we followed the birth cohort for 18 months to investigate the children's physical growth and cognitive development.

Setting: A follow-up of a birth cohort from two rural Cambodian communities; Chroy Sdao commune (inland area) and Eak Phnom district (floating villages). The participants from the floating villages had significantly lower socioeconomic status than women from the inland area.

Participants: 152 children were included and examined at the age of approximately 18 months.

Main outcome measures: We measured the children' weight, height, and head circumference. Language, social and motoric skills were assessed using Ages and Stages Questionnaire adapted to a Cambodian setting.

Results: The significant differences in weight found at birth between the two areas had increased during the first 18 months of life. Birth length was similar, however, at the time of follow-up, the growth trajectory for children from Eak Phnom district was less favorable, leaving 53.3 % of them categorized as stunted compared to 20.7 % in children from Chroy Sdao ($p < 0.001$). The proportion for underweight children were 30 % versus 10 % ($p < 0.001$). The children from Eak Phnom district scored significantly lower in the cognitive development test.

Conclusion: Our findings show that growth trajectories in children from Eak Phnom continue to divert negatively compared to children with better living conditions. The same children also score lower in cognitive development tests. The differences are large, and there is an urgent need for interventions by local health authorities and policymakers.

INTRODUCTION

An adult's stature is the result of genetic background combined with influences on linear growth from conception through childhood and puberty [1]. Genes account for 10 % of variations in adult height. Linear growth is controlled by complex genetic, nutritional and hormonal signaling systems, and inflammations seem to play an important role inhibiting epiphysial development [1]. Studies on environmental enteric dysfunction (EED) and gut microbiome show that intestinal lining is altered [2], and resorption of nutrition reduced in various diseases and infections [3-5].

In addition, stress, unstable food supply and lack of clean water and safe sewage systems, manifest a cycle of poverty where short stature is passed on through the generations [6].

Children's growth and physical and mental development depend on an abundance of factors, many still neither fully investigated nor understood.

Bodyweight is commonly used for monitoring child growth, however, underweight (low weight for age) does not distinguish between stunting (low height for age) and wasting (low weight for height). In settings with high prevalence of stunting, but little or no wasting, the prevalence of underweight children most likely underestimates the total burden of malnutrition [1,7].

According to the joint report by United Nations Children's Fund (UNICEF), World Health organization (WHO) and the World Bank, 22% of children under 5 years worldwide were stunted in 2020; meaning their height is < -2 SD than normal for the chronological age (height/age). A large proportion of children in the global South are also underweight (weight/ age) or suffer from wasting (low weight/ height) [8]. In South-East Asia the prevalence of stunting is estimated to be 27.4%, underweight and wasting 8.2%. In Cambodia 29.9 % of children under 5 years of age were classified as stunted in 2020 [8].The aim of this study was to follow the physical and developmental growth in a birth cohort from two low-income settings in rural Cambodia. Our hypothesis was that growth faltering might continue during the first 18 months of life.

MATERIALS AND METHODS

Study population

The study has been described in detail previously [9]. Figure 1 shows the study's inclusion flowchart.

The study took place in two rural Cambodian communities, Chroy Sdao commune (inland areas) and Eak Phnom district (floating villages) from October 2015 through November 2017. The communities are located between Battambang and Siem Reap, two of the largest cities in Cambodia.

Data collection

A total of n = 194 women (n = 120 from the inland and n = 74 from the floating area) were recruited during their third trimester of pregnancy. The inclusion period was between October 2015 and May 2016. The data collection took place at their local health centers. Blood and urine samples were given, and socioeconomic, anthropometric and medical data were recorded by medical personnel at enrollment. The newborns were included consequently at birth. Due to missing data 22 babies were excluded. Thus, 172 neonates were eligible for the study. We initiated a follow-up to look at physical and cognitive development of the cohort at 18 months of age. Out of the original 172 babies, 20 children could not be located at the time of follow up. 152 children were included. Height, weight, and head circumference were measured by medical personnel at local health centers. The child's social and motor skills were assessed using the Ages and Stages Questionnaire. The questionnaire was adapted to a Cambodian context and filled in by parental report and then recorded in the survey form by a member of the Cambodian research team.

Patient and public involvement

The public was not involved in the design of the study. The results are, however, important to disseminate among local stakeholders and also to the communities who participated in the study. Local involvement will be crucial.

Statistical analysis

The Mann-Whitney U test and Chi-square test were applied to compare the maternal sociodemographic characteristics and child growth and development characteristics between the two study sites. Fisher exact test was used when the data failed the assumption for Chi-square test. Breastfeeding status, weight, height, head circumference, communication, gross and fine motor, problem solving, and personal social skills were assessed at the 18 months follow-up. Underweight, stunting and wasting were calculated as proportion less than – 2 SD using the World Health Organization Child Growth Standards median. The WHO standards display normal growth of children under optimal environmental conditions and are thus applicable for any ethnic groups. Complete case analysis was used for handling missing data. A significance level of $p < 0.05$ (two-tailed) was used for all analyses. Data analyses were performed using IBM SPSS Statistics for Windows (version 26; SPSS Inc., Chicago, IL, USA).

RESULTS AND DISCUSSION

A total of 194 women were recruited while in their third trimester of pregnancy. There was no statistically significant difference in age or parity between the two study areas (Table 1). Mean body mass index (BMI) at the time of inclusion was less than 25 kg/m^2 in both groups, however, the women from the inland were heavier ($p = 0.001$) and taller than ($p < 0.001$) the women from the floating area. The average educational level was significantly lower in floating area (4.6 *vs.* 7.1 years, $p < 0.001$), and the gestational length was 10 days shorter compared to the inland villages (38.4 vs. 40.0 weeks, $p < 0.001$). In inland area, 49.2% women were primipara versus 31.1 % in the floating area. Due to missing data, 22 babies were excluded, leaving 172 newborns eligible for study. The percentages of male and female babies were different between inland and floating area ($p = 0.002$), male to female newborns ratio was 1.32 and 0.49, respectively. Table 2 presents the anthropometric measurements of the children at birth and 18 months. There were 152 children included at the 18 months of follow up, 92 from the inland area and 60 from the floating area. The mean birthweight in the floating area was 200 grams lower compared to infants from the inland area ($p < 0.001$). The discrepancy increased during the first 18 months of life; resulting in 1200 grams lower weight among the children from floating area ($p < 0.001$). Despite similar birth length between the two study sites, children from inland area were 3.3 cm taller than those living in the floating area at 18 months ($p < 0.001$). At birth head circumference and ponderal index (PI) were higher for children from the inland ($p < 0.001$ for

Table 1: Maternal characteristics at the time of inclusion; original study.

Variables	N (Missing data)	Inland area	Floating area	*P* value	Total
All participants	194	120	74		194
Maternal age (years), mean (SD)	194 (0)	26.7 (6.5)	26.6 (5.7)	0.79[a]	26.7 (6.2)
Maternal weight (kg), mean (SD)	194(0)	60.3 (7.9)	56.4 (8.0)	0.001[a]	58.8 (8.1)
Maternal height (cm), mean (SD)	194(0)	156.9 (4.8)	152.6 (4.7)	< 0.001[a]	155.3 (5.2)
Maternal body mass index (BMI)	194 (0)	24.5(2.9)	24.2(3.2)	0.53[a]	24.4(3.0)
Maternal education (years), mean (SD)	156 (38)	7.1 (3.0)	4.6(2.0)	< 0.001[a]	6.3(3.0)
Parity	194 (0)				
Nulliparous, n (%)		59 (49.2)	23 (31.1)	0.01[b]	82 (42.3)
Multiparous, n (%)		61 (50.8)	51 (68.9)		112 (57.7)
Infant gender	172 (22)				
Boy, n (%)		58 (56.9)	23 (32.9)	0.002[b]	81 (47.1)
Girl, n (%)		44 (43.1)	47 (67.1)		91 (52.9)
Gestational age(weeks), mean (SD)	144 (50)	40.0(0.8)	38.4(0.7)	< 0.001[a]	39.1(1.0)

[a] Mann-Whitney U test.
[b] Chi-Square test.

both). We found no differences between the two study groups in the same parameters at the follow-up at 18 months.

More than half of children in floating area could be classified as stunted at 18 months of age; the proportion being 2.5 times higher than among children from the inland area ($p < 0.001$) (Table 2). One third of children from floating area were underweight compared to less than 10 % from the inland sites. About 5% of children were wasted in both inland and floating area at 18 months ($p = 0.91$). The cognitive development screening revealed that children from the inland area scored higher in communication ($p = 0.01$) and gross motor skills ($p < 0.001$) compared to toddlers from floating villages (Table 2).

The women from the floating area breastfed longer ($p = 0.003$), however, their children had the slowest growth trajectory. In both study groups the mean length of breastfeeding was more than one year. We did not record the duration of exclusive breastfeeding (EBF).

In this follow-up study from two low-income communities in rural Cambodia, we found high proportions of stunting, underweight and wasting. The children from the floating villages had the least favorable physical development, and more than half of them could be categorized as stunted. The anthropometric differences found at birth between the two study groups increased during the first 18 months of life. The toddlers from the floating villages weighed 1200 grams less and were 3.3 cm shorter compared to the inland children. In addition, they had a lower score when tested for social and motoric skills. The proportion of stunting in the inland area was lower than the estimated prevalence in Cambodia (29.9%), but like the global prevalence (22%). A stunting rate of >50 % among children from the floating villages indicates that growth faltering is severe in this specific area compared to Cambodian and global estimates [8, 10].

Stunting, in contrast to wasting, which is the result of more acute malnutrition, is an indication of a longstanding suboptimal food supply combined with unfavourable living conditions. The Lancet series on Optimizing Child and Adolescent Health highlights early-life poverty's negative effect on children's physical and cognitive development, thus, supporting our findings [11].

Longitudinal growth in humans happens mainly during four phases in life, prenatal period, infancy, childhood and puberty. Growth spurts are episodical and occur after shorter or longer spans of stasis [12]. The longitudinal growth rate in children is similar after the first two years of life; thus, enhanced growth later will most likely not compensate for stunting manifested in early childhood. In addition, it is estimated that 10-20 % of stunting originates from antenatal growth retardation; small for gestational age (SGA) [1,13]. The infants from the floating villages were not shorter at birth but weighed less and had a lower ponderal index. They also had smaller head circumferences. This is an indication of less favorable intrauterine conditions [9].

Leroy also argues that growth faltering continues after the first 24 months of life. Recalculating findings from 51 LMIC the authors state that approximately 30 % of stunting happen after two years of age [13]. This is supported by Millward [1] who found that continued growth faltering after 24 months was most common in poorer communities. Both articles confirm our results; the difference in height between the children in our study at 18 months, is almost the same as the height difference we found in their mothers. The toddlers and their mothers from the floating areas were 3.3 cm and 4.3 cm shorter compared to the inland population [9]. The growth trajectory for head circumference was satisfactory for both study groups, however, despite this finding, the smallest children scored lower when tested for social and motoric skills. Our results are in accordance with multiple studies investigating the association between stunting and cognitive development both regionally and globally [10,11,14,15].

Environmental Enteric Dysfunction (EED) is a syndrome initiated by gastric infections where the intestinal villi become flattened, and the mucosa develops inflammatory infiltrations. The process initiates increased intestinal permeability, which is

Table 2: Anthropometric measurements of the child at birth and 18th month and breasting feeding status, child development screening, underweight, stunting and wasting at 18th month of age.

Time points of measurements	At time of birth				18th month		
	Inland area (n = 83)	Floating area (n = 64)	P value		Inland area (n = 92)	Floating area (n = 60)	P value
Mean weight in kg (SD)	3.2(0.4)	3.0(0.4)[a]	0.001[d]		10.1 (1.4)	8.9 (0.9)	< 0.001[d]
Mean length in cm (SD)	48.5(3.4)	49.5(2.2)	0.31[d]		78.0 (4.3)	74.7 (3.8)	< 0.001[d]
Mean head circumference in cm (SD)	32.8(2.6)[b]	30.2(2.6)[c]	< 0.001[d]		46.3 (1.4)	46.1 (1.6)	0.34 [d]
Mean ponderal index in kg/m^3 (SD)	28.6(8.9)	24.7(3.4)	< 0.001[d]		21.5 (3.8)	21.6 (3.4)	0.96 [d]
Median breastfeeding months (Min-Max)	-	-	-		13 (0-21)	16.5 (0-24)	0.003 [d]
Median communication (Min-Max)	-	-	-		60 (35-60)	50 (25-60)	0.01[d]
Median gross motor (Min-Max)	-	-	-		60 (40-60)	55 (20-60)	< 0.001[d]
Median fine motor (Min-Max)	-	-	-		53 (20-60)	50 (30-60)	0.69 [d]
Median problem solving (Min-Max)	-	-	-		53 (20-60)	60 (25-60)	0.15 [d]
Median personal social (Min-Max)	-	-	-		55 (25-60)	55 (30-60)	0.42 [d]
Stunting less than - 2 SD (%)	-	-	-		19 (20.7)	32 (53.3)	< 0.001[e]
Underweight less than - 2 SD (%)	-	-	-		8 (8.7)	19 (31.7)	< 0.001[e]
Wasting less than - 2 SD (%)	-	-	-		5 (5.4)	3 (5.0)	1.00 [f]

[a] Number of birth weight in floating area is n = 66.

[b] Number of head circumference in inland area at time of birth is n = 82.

[c] Number of head circumference in floating area at time of birth is n = 65.

[d] Mann-Whitney U test.

[e] Chi-Square test.

[f] Fisher's exact test.

negatively associated with growth in children [2]. The intestinal infection triggers chronic inflammation and thus suppresses insulin-like growth factor (IGF). Stunting is, therefore, not just a result of insufficient nutrition and lack of calories, but also an inflammatory disease originating partly from gut pathology. Environmental enteric dysfunction could be one explanation for why only one-tenth of growth-faltered children respond to supplemental feeding regimes [4,7]. The women and children from the floating areas have limited access to safe drinking water, and they spend most their lives on waterways with high likelihood of contaminants, bacteria, virus and parasites [9]. We did not test the water quality from the rivers, however, the chances for an infant from the floating areas to develop environmental enteric dysfunction with all its implications, are much higher than for babies living in areas with safe drinking water. Eriksen found in her study from Gambia that despite exclusive breastfeeding, growth faltering could be detected already at the age of 3.5 months [16]. Almost half of the children were partially breastfed when they were 2 years old, however, still 26 % were classified as stunted and 23 % were underweight. The findings underscore the impact of unfavourable living conditions with high prevalence of infectious diseases, unclean water and unstable food supply [16]. The Gambian study supports the theory that Environmental enteric dysfunction may develop in babies despite being exclusively breastfed if living conditions are not optimal. A study from Ghana found insufficient nutrition and unclean water supplies to be the main drivers for stunting among children 6 – 24 months. The negative effect was greater when the child was exposed to both factors [17].

The human body hosts vast numbers of microbes (microbiota) and their genes (microbiomas), including gut microbiota. If the colonization of microbes in early life is disturbed, it can induce detrimental effects on development and physical growth. Immature and less enriched microbiomas may even have intergenerational effects. Robertson et al support our findings [5]. The growth faltering found in children from the floating villages is not just due to calorie shortage, but most likely the result of unfavourable living conditions in generations.

Contrary to linear growth and weight gain, the growth trajectories for head circumference in the children were satisfactory for both study groups (Table 2). Maximum human brain volume is achieved when a child is between 5 and 10 years old. The growth rate is highest in late gestational weeks and the first 12 months of life [18], and 75 % of the brain volume develops within the first 1000 days from conception. During this same period up to 50 % of the body's basal metabolism is diverted to the brain [5]. The brain's high energy demand may explain why the smallest children in our study had a satisfactory growth of the head circumference while still being very short for their age.

The prenatal period and early childhood are crucial windows of opportunities for the child's ability to achieve his or her cognitive and physical potential. A meta-analysis of 68 studies from 29 LMIC showed a strong positive association with longitudinal growth during the first 2 years of life and cognitive and motor development [19]. The smallest children in our studies scored lower in social and motor skills, affirming previous findings, including a study from Bangladesh [20] and also results from studies where children from India, Ethiopia, Peru and Vietnam were followed until they turned 12 years old [21]. Interestingly, the smallest children in our study were breastfed longer which should contribute positively to cognitive development [22]. However, negative environmental factors such as poor sanitation and unsafe water supplies may have a stronger impact and thus outweigh the breastmilk's benefits in our cohort [16]. Breastfeeding is also negatively associated with longitudinal growth in a recently published article from the same areas in Cambodia as we conducted our research. Lai's cross-sectional study showed significant reduction in stunting for babies under 6 months in clusters with improved access to clean water, sanitation and hygiene, however, the results were not conclusive for older children [10].

Most of the children in the floating villages come from families with low socioeconomic status and unstable incomes. They grow up in unfavourable conditions and most likely suffer from mental stress where they experience the adult's worries for the future. The living quarters are restricted, and the quality of sleep may be hampered due to stress, noise and crowded dwellings [1]. Sleep deprivation inhibits the release of growth hormones, and also raises cortisol levels. High levels of cortisol can be detrimental for healthy brain development [23]. Cortisol inhibits linear growth, and cortisol levels are increased in both situations of energy deficiencies and inflammatory diseases. In addition, inflammation and sleep deprivation inhibit production of growth hormone [1].

STRENGTHS AND LIMITATIONS

The main limitation of the study is the small sample size. Some studies show that boys are more exposed to stunting. We were not able to stratify results by gender due to the low number of participants; However, our other findings are in corroboration with established knowledge in the field. Thus, we assume the results are trustworthy. The main strength of the study is that we were able to follow the birth cohort despite challenging conditions for the field workers. The families in the floating villages live seminomadic lives, and the Cambodian authors invested time and resources to track down the children. The inland families also migrate during harvest seasons, making follow-up difficult. We are quite confident that the prevalence of growth faltering is not overestimated. The most disadvantaged families hardly ever come to the health centers, and we presume they are probably not represented in either of our study groups. Differences in anthropometrics are unlikely to be from ethnicity. To our knowledge this is the first article to present data from a follow up-study of birth cohorts in rural Cambodia.

CONCLUSION

Stunting is an indicator for multiple adverse environmental influences prenatally, in infancy and early childhood. Inflammatory responses, including gut pathology, probably play a vital role. Intergenerational epigenetic effects are strong. WASH (water, sanitation and hygiene) is important as well as sufficient nutrition and calories. In our study we found increasing growth faltering from birth to 18 months of age in the most disadvantaged groups. Cambodia has made impressive economic progress in recent years; however, the population still experiences unfair distribution of power, income, health services and commodities. The high prevalence of childhood stunting in our poorest study group is a strong indicator of this inequality. We have reason to assume that similar findings can be detected in vulnerable groups in most low- and middle-income countries.

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