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Short- and medium-term outcomes of accelerated infant growth in a Hong Kong Chinese birth cohort

Key Messages

1. In a large, population-representative, Chinese birth cohort, higher birth weight and rapid growth, particularly at 0-3 months, were associated with higher body mass index (BMI) at 7 years.
2. Boys born heavy who had grown fast had the highest BMI, but rapid growth had the largest impact in lighter-born boys.
3. Rapid growth at 0-3 months or 3-12 months was not associated with a compensatory lower risk of serious infectious morbidity.
4. The ability to grow fast may be an embodiment of good health status rather than fast growth being causally protective.

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Introduction

Cardiovascular and metabolic diseases are leading causes of death and are becoming more prevalent in Asia. These diseases are increasingly seen within a framework where causation extends over the entire life and where humans work with a limited resource base and are forced to trade-off certain life-history parameters against each other, such as a strategy which promotes survival up to reproductive age against long-term health.[1] Until very recently one of the key components of early survival was resistance to infection.

Despite two decades of intensive research, the role of foetal and infant growth in metabolic and cardiovascular diseases remains controversial. Although much attention has been focused on low birth weight as the causative factor, evidence from experiments designed to test this hypothesis have highlighted the role of nutrition-driven post-natal growth as a possible missing link in the observed relation between birth weight and adult metabolic disease. To date, observational evidence in humans suggests that higher birth weight and faster infant growth are associated with childhood obesity,[2] and hence long-term risk. Although premature cardiovascular disease is more common in men, there has been little examination into whether birth weight or infant growth (singly or jointly) has different effects depending on sex. Less attention has also been paid to other potential positive outcomes of rapid infant growth, despite a cultural preference for 'fat' babies, particularly in locations such as China. One previous study has considered the potentially complimentary survival advantage of rapid infant growth. Faster infant growth was associated with a lower risk of serious infectious morbidity and possibly mortality.[3] The impact of infant growth on health is also less well understood in developed, non-western settings, such as Hong Kong, where birth weights are typically lower and there has been a history of rapid economic development. However, such populations may act as a sentinel for other rapidly developing locations.

Identifying optimal growth trajectories potentially has major public health implications. Using data from a large population-based, prospective Chinese birth cohort, we investigated the relation between infant growth rate and two complimentary outcomes: childhood adiposity and serious infectious morbidity.

Methods

This study was conducted from October 2005 to January 2007. The 'Children of 1997' birth cohort was initiated by the Department of Community Medicine, the University of Hong Kong and the Department of Health, of the Hong Kong SAR Government.[4] The sampling frame consisted of all infants born in April and May 1997 and brought to one of any of the 47 Maternal and Child Health Centres (MCHC) for their first postnatal visit. For the index year, 92% of infants born in Hong Kong visited the MCHC, which provides free-of-charge preventive care and immunisations, at least once. The study recruited 8327 mother-infant pairs, corresponding to 88% of all births in the recruitment period.

Mothers were approached at the MCHCs a few days after delivery for recruitment and baseline data collection, and were further followed up at 3, 9 and 18 months after birth. Mothers provided information on socio-demographics (age, parental education level, employment status and type of housing), mode of delivery, parity, breastfeeding and household smoking habits via a standardised self-administered questionnaire in Chinese. In addition to this prospectively collected data, in 2005-6 record linkage was used to obtain:

- Infant growth from the MCHC hardcopy records linked by MCHC number.
- Childhood weight and height from the Student Health Services (SHS) linked by birth certificate number. The SHS provides an annual examination at no cost to all students in any Hong Kong primary or secondary school.
- Lifetime public hospital use from the Hospital Authority (HA), which provides 94% of hospital care in Hong Kong, linked by birth certificate number.

All birth cohort members have a MCHC number and 97% have a birth certificate number. When the birth certificate number was missing, matching was by name, sex and date of birth, because there are only about 55 sex-specific births per day in Hong Kong. All potential matches were checked by the research team.

Exposure: growth rates

Infant growth rate was defined as change in weight z-score at 0-3 months and 3-12 months. Weight z-score was calculated relative to the 2006 World Health Organization growth standards for the exact age on the day of measurement. The closest measurements to 3 months (within 2 to 4 month) and 12 months (within 9 to 15 months) were used.

Outcomes

Childhood adiposity

Adiposity at about age 7 years was proxied by body mass index (BMI) z-score relative to the 2000 US Centers for Disease Control and Prevention growth references for the exact age on the day of measurement. The closest measurement between 5.5 and 8.5 years was used.

Serious morbidity

Serious morbidity was proxied by number of in-patient admissions to any public hospital in Hong Kong from the age of 3 months (or 12 months for growth at 3-12 months) to 8.0 years. Admissions were classified as respiratory infections, all infections, accidents and all other causes using the International Classification of Diseases 9, Clinical Modification (ICD9-CM), of the primary discharge code. Cohort members without any record of hospital admission were assumed to have no hospital admission.

Statistical analyses

Initial analysis of the association between infant weight growth rate and childhood adiposity revealed that the associations with 0-3 month growth rate were not consistent by birth weight (P-value for interaction 0.001) or sex and birth weight (P-value for interaction 0.007). We used multivariable linear regression to assess the association of growth rate tertile, initial weight tertile (ie at start of the period) and sex with childhood BMI z-score, adjusted for gestational age (complete weeks based on date of the last menstrual period) and growth rate in the other period (as a continuous variable). Other potential confounders such as birth order, infant feeding, parental education and maternal smoking changed the estimates by less than 5% and were not included in the model.

There was no evidence that the association between either growth rate and hospital admission differed by sex or initial weight. We used multivariable negative binomial regression to calculate the relative risk of admission by growth rate tertile in each period. We adjusted for initial weight, growth rate in the other period, gestational age, sex and parental education. We additionally adjusted for disease status, ie congenital or other life-long conditions that might affect infant growth or risk of infection. Children born in private hospitals had higher socio-economic status and were more likely to use private hospitals. We also adjusted for hospital type at birth (private or public) to correct for the probable greater use of public hospitals by children from less-advantaged families. Birth order, breastfeeding and housing changed the estimates by less than 5% and were not included in the model.

The University of Hong Kong–Hong Kong Hospital Authority West Cluster Joint Institutional Review Board and the Ethics Committee of the Department of Health, Government of Hong Kong SAR approved the study.

Results

We linked 7999 of the birth cohort (96%) with the MCHC records, 7809 (94%) with the SHS records and 3746 (45%) with the HA records; not all children were expected to have a hospital admission by the age of 8 years.

Of the surviving 7832 full-term births, 7153 had weight growth rates for 0-3 months and 6874 for 3-12 months. Faster growth was more common in infants with lower birth weight, lower gestational age and more socio-economically advantaged families (Table).

Higher initial weights and higher growth rates were associated with higher childhood BMI (Fig 1). The heaviest born children with the fastest growth rate from 0-3 months had the highest BMI at 7 years, but rapid growth at 0-3 months had a greater impact on BMI in lighter-born boys.

Growth rates were not associated with admissions for respiratory infections, all infections or accidents (Fig 2). Slower growth at 0-3 months was associated with admission for other causes.

Discussion

Consistent with findings elsewhere,[2] in this understudied

Table. Baseline characteristics by growth rate tertile at 0-3 and 3-12 months for term subjects in the Hong Kong 'Children of 1997' birth cohort

Characteristics	Growth rate tertile, 0-3 months (%)				Growth rate tertile, 3-12 months (%)			
	No.	Slow (n=2483)	Medium (n=2453)	Fast (n=2217)	No.	Slow (n=2343)	Medium (n=2327)	Fast (n=2204)
Sex								
Male	3766	34.9	34.4	30.6	3633	37.7	31.9	30.4
Female	3387	34.5	34.2	31.4	3241	30.0	36.1	33.9
Birth weight								
1st tertile	2169	14.6	32.4	53.0	2101	27.2	33.6	39.2
2nd tertile	2568	32.8	37.5	29.6	2460	33.8	33.7	32.5
3rd tertile	2416	54.8	32.5	12.7	2313	40.6	34.3	24.1
Size for gestational age								
Small	702	12.0	27.6	60.4	681	26.0	31.9	42.1
Appropriate	6451	37.2	35.0	27.8	6193	35.0	34.1	31.0
Gestational age (weeks)								
37-39	4376	30.2	33.9	36.0	4203	32.5	33.1	34.4
40	1787	40.0	35.5	24.6	1722	36.1	34.3	29.6
≥41	990	45.4	34.0	20.6	949	37.3	36.4	26.3
Birth order								
1	3268	33.5	35.6	30.9	3175	29.4	34.6	36.0
2	2858	34.7	33.2	32.1	2726	38.4	33.1	28.5
3+	768	40.4	33.5	26.2	730	39.0	33.7	27.3
Mother's age (years)								
<24	882	32.0	36.3	31.8	826	35.5	31.6	32.9
25-29	2212	35.0	34.9	30.2	2119	33.6	33.8	32.6
30-34	2722	34.5	34.2	31.3	2633	34.3	34.0	31.7
35-39	1162	36.5	31.8	31.8	1123	33.8	34.9	31.3
40-44	131	36.6	37.4	26.0	130	33.1	33.9	33.1
≥45	8	25.0	12.5	62.5	8	50.0	50.0	0
Breastfeeding for 4 weeks								
No	4255	35.8	34.6	29.6	4093	33.8	33.7	32.5
Yes	2591	32.9	34.2	32.8	2508	34.6	34.3	31.1
Highest parental education attainment								
9th grade or below	2077	38.1	34.0	27.9	1914	37.8	34.0	28.3
10-11th grade	2999	35.3	34.6	30.1	2912	32.7	33.9	33.5
12th grade or above	1867	30.2	34.4	35.4	1805	32.6	33.8	33.6
Housing								
Public	3039	36.5	34.2	29.4	2895	36.0	33.3	30.7
Private	3840	33.5	34.4	32.1	3721	32.7	34.4	32.9
Birth hospital								
Public	5057	36.8	34.3	28.9	4839	34.4	34.2	31.4
Private	2049	29.5	34.3	36.2	1988	33.6	33.1	33.4
With congenital conditions								
Yes	106	49.1	33.0	17.9	101	26.7	38.6	34.7
No	7047	34.5	34.3	31.2	6773	34.2	33.8	32.0

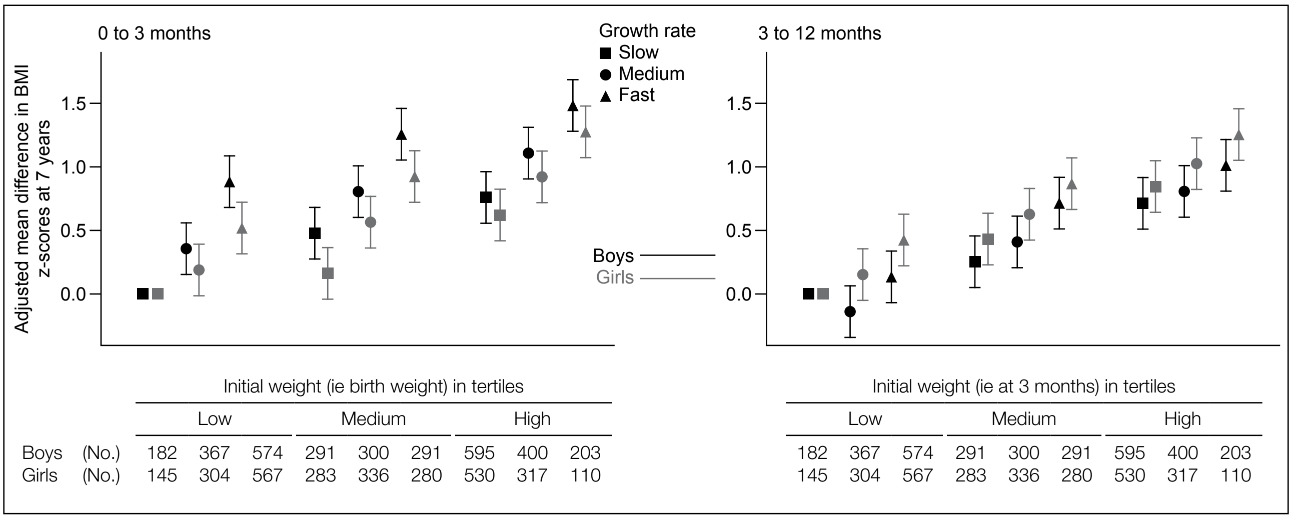

Fig 1. Adjusted* mean difference with 95% confidence intervals in body mass index (BMI) z-score at 7 years jointly by tertiles of initial weight and growth rate at 0-3 months and 3-12 months in boys and girls

* Adjusted for gestational age and growth rate in the other period

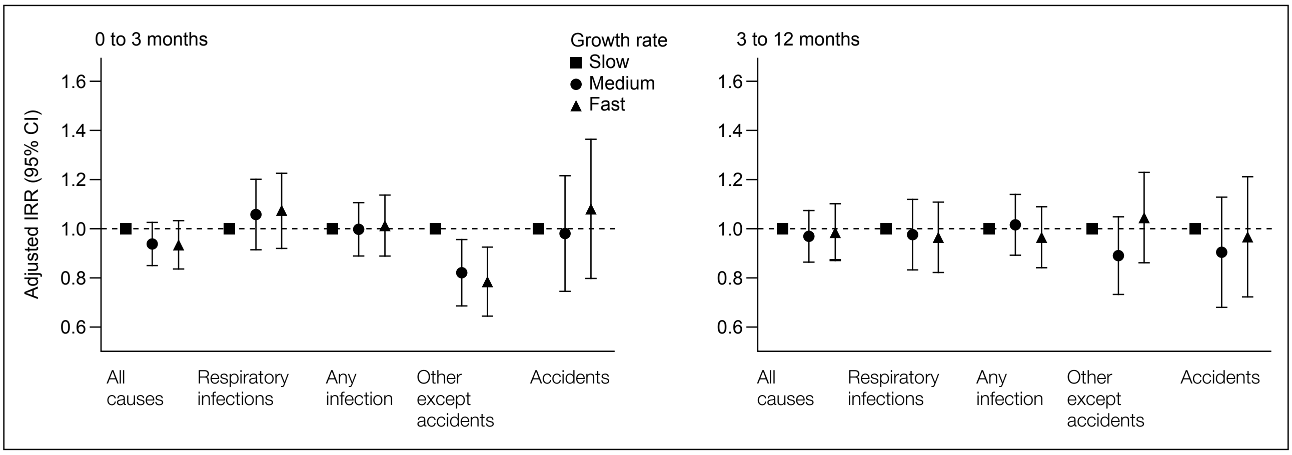

Fig 2. Adjusted* incidence rate ratio (IRR) with 95% confidence intervals (CIs) for number of hospital admissions by cause† and growth at 0-3 months and 3-12 months

* Adjusted for initial weight, growth rate in the other period, gestational age, sex, parental education, birth hospital and disease status

† Respiratory infections: ICD9-CM 033, 034.0, 381-382, 460-466, 477, 480-487 and 493; any infections: ICD9-CM 001-009, 033, 034.0, 381-382, 460-466, 477, 480-487, 493 787.91, 599.0, 780.6 and 780.3; accidents: ICD9-CM 800-999; and other except accidents: all other ICD9-CM except the above

population with scarce appropriate data, higher birth weight and faster infant weight growth were associated with higher BMIs at 7 years. Fast growth at 0-3 months was more strongly associated with higher BMI in boys born light, but not girls born light. Infants born light were also more likely to grow fast than heavier born infants. Nevertheless, the relatively small number of infants of either sex born heavy who grew fast had the highest BMI at 7 years. In contrast, rapid infant growth was not associated with a lower risk of admission for infections, but was associated with a lower risk of admission for causes other than infections or accidents. As such our study does not provide evidence that better immunity is a developmental trade-off for later metabolic risk resulting from fast infant growth. It does, however, suggest that maximal growth may not be optimal for metabolic risk.

Our study concerned a large, representative, population-based birth cohort, but had limitations. First, greater muscle mass and heavier build may explain some of the higher BMIs in high-birth-weight babies. However, muscle mass or build is unlikely to explain the differences in BMI by infant growth rate. Second, our cohort was largely fed formula milk; the impact of growth could be different in exclusively breastfed babies. Third, children with rapid infant growth may have been more likely to use private hospitals, so we cannot rule out the possibility that rapid infant growth increased the risk of hospital admission. However, we can be more confident that there was no protective effect of fast growth against serious infectious illnesses.

Most investigations into the effects of faster infant growth on metabolic risk has been from the perspective of infant growth as an outcome of, or in combination with detrimental restricted intrauterine growth. A detrimental effect of faster infant growth regardless of birth weight requires a different perspective. Disruption of hypothalamic circuit development and leptin regulation by early over-feeding could result in poorer appetite control in later life.[5] Leptin levels may also be suppressed by androgens, and hence be relevant to the differences between boys and girls.

Given the lack of benefit associated with fast growth, it is possible that traditionally valued fast infant growth (or fatness) is a marker of underlying health state, rather than a protective response to poor foetal growth. Faster growth at 0-3 months was associated with less risk of admissions for causes other than infections and accidents, of which over 50% were related to congenital anomalies, which would not always be immediately apparent.

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