

The relationship between anthropometric measurements at birth: asthma and atopy in childhood

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Summary

Background Recent studies have reported that a large head circumference at birth is associated with an increased risk of raised serum IgE in adult life, and asthma during childhood.

Objective To examine the relationship between head circumference and other anthropometric measurements at birth and asthma and indices of atopy in childhood.

Methods The presence of asthma and measures of atopic status (total serum IgE level and skin prick tests to common allergens) were assessed prospectively in offspring of families participating in a community-based genetic study in Southampton, UK. Measures of perinatal variables including birth weight, head circumference at birth, and gestational age were obtained from hospital records of 239 offspring aged 6–23 years.

Results Children with a head circumference of 37 cm or more at birth had a relative risk of an elevated serum total IgE (> 150 IU) of 3.2 (95% CI 1.0–10.4). There were no consistent relationships between head circumference at birth and either skin prick positivity or the development of clinical asthma. There was no significant association between other perinatal markers and measures of atopic status or clinical asthma.

Conclusion The study has identified that a large head circumference at birth is associated with an increased risk of an elevated total serum IgE in childhood. The reasons for this association, and the lack of an association with asthma are unclear and will require further research.

Keywords: anthropometric measurements, asthma, Atopy, childhood, head circumference at birth

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Introduction

It is now recognized that perinatal events affecting fetal development may contribute to the risk of developing diseases in later life [1]. Barker has termed this process 'programming', in which an early stimulus or exposure during critical periods of fetal development leads to permanent or long-term effects on the structure or function of different organ systems. One situation in which programming is thought to occur is that of enhanced fetal growth

of the brain in which a large head circumference at birth has been associated with an increased risk of a raised serum total IgE level in adult life [2] and asthma during childhood [3]. Both of these studies found that the increased risk was particularly strong for a head circumference at birth above the 85th percentile. To investigate these relationships further we have analysed data obtained in the Southampton Asthma Genetics Study [4] in which anthropometric measurements at birth, clinical data during childhood and measures of atopic status including serum total IgE and skin prick tests were available in over 200 subjects. The primary objective of the study was to investigate whether a large head circumference at birth was associated with an

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increased risk of a raised serum IgE or asthma symptoms in childhood.

Methods

The Southampton study

In the Southampton Asthma Genetic Study parents of 1800 children aged 11–14 years randomly selected from the practice lists of all children registered with 104 general practitioners in the Southampton area, UK were sent a questionnaire enquiring about their general health and the number of children in the family [4]. The questionnaire was open ended and did not specifically mention atopy or atopic diseases. All families that replied and had three or more children were contacted to determine their willingness to participate in further studies. For those who agreed, a full verbal and written explanation of the study was given to each family member. The study was approved by the Southampton University Hospitals Joint Ethics Committee. The children gave informed verbal consent and the parents gave informed written consent.

Clinical data

Members of each family involved in the study completed a structured written asthma questionnaire derived from the International Union Against Tuberculosis and Lung Disease Questionnaire. Asthma was primarily assessed by the questions 'Have you had wheezing or whistling in the chest in the last 12 months?', and 'Are you currently taking any medication for asthma?'

Measurements of atopic status

The serum total IgE was measured by an enzyme-linked immunosorbent assay (ELISA). Skin prick testing by stylet was performed for 14 common allergens (*Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cat, dog, horse, feathers, egg white, egg yolk, cows' milk, mixed grass, mixed trees, *Alternaria*, *Aspergillus fumigatus* and *Cladosporium*; Bayer Corporation, Spokane, WA, USA) and the mean of perpendicular diameters of each weal recorded.

Perinatal measures

From the Hospital medical records perinatal information regarding birth weight, head circumference and gestational age were obtained.

Data analysis

The data was analysed using PC SAS (SAS Institute, Cary

NC, USA). The measurements of head circumference at birth and birth weight were categorized into low, medium and high values, and the odds ratios were calculated using the middle category as the reference. The prevalence odds ratios for each parameter were then adjusted for each other, and the gestational age using logistic regression [5]. *P*-values for trend were calculated using logistic regression on the continuous values of these three variables.

Results

One hundred and thirty-one families agreed to participate, comprising 262 parents and 423 offspring. For the offspring, hospital records were traced in 270, which represents 64% of the total. Twenty multiple births were excluded from the analysis, and information (anthropometric measurements) was available for 239 of the remaining 250 participants. The mean (range) age of the offspring was 13 years (6–23 years).

Asthma symptoms and medication use

Gestational age, birth weight and head circumference showed no consistent relationship with wheeze in the last 12 months, or asthma treatment (Tables 1 and 2).

Total serum IgE/skin prick tests

The prevalence of an elevated IgE (≥ 150 IU/L) was significantly raised in children who were born with large head circumferences (Tables 1 and 2). The relationship appeared to be nonlinear to the extent that variations in head circumference under 37 cm were not related to systematic variation in the risk of an elevated IgE. As a result, there was not a statistically significant overall association between elevated IgE and head circumference at birth ($P = 0.17$). For the different categories of head circumference less than 37 cm, the proportion of children who had a raised IgE was between 28% and 38%, whereas 63% of children born with a head circumference of 37 cm or greater had a raised IgE. The geometric mean total serum IgE level for children born with a head circumference 37 cm or more was 164.0 IU compared with 69.2 IU for those less than 37 cm. The odds ratio of risk of an elevated IgE with head circumference in excess of 37 cm in comparison with children with a head circumference of between 34 and 36.9 cm was 3.2 (95% CI 1.0–10.4). There was no significant relationship between birth weight, or gestational age and raised serum IgE levels. There was no significant relationship between any of the anthropometric measures and the number of positive skin prick tests (weal ≥ 3 mm diameter) (Tables 1 and 2), or positive skin prick response to house dust mite or cat allergen alone (data not shown).

Table 1. Prevalence of asthma, elevated IgE levels and skin test positivity.

	<i>n</i>	Wheeze in last 12 months	Asthma treatment	IgE ≥ 150 IU	IgE geometric mean level	Any skin test test ≥ 3 mm
<i>Head circumference (cm)</i>						
<34	30	17.86	21.43	33.33	70.40	40.74
34–34.9	54	11.32	15.09	27.66	57.76	39.62
35–35.9	56	36.36	23.64	38.30	85.32	47.17
36–36.9	36	22.86	11.43	34.38	65.46	52.78
37+	20	26.32	26.32	62.50	163.99	57.89
<i>Birth weight (kg)</i>						
<2.5	7	28.57	28.57	80.00	248.63	28.57
2.5–2.9	24	21.74	21.74	28.57	46.48	39.13
3.0–3.4	107	20.75	16.98	34.41	74.26	47.57
3.5–3.9	87	21.95	19.51	30.00	64.17	43.90
≥4.0	24	36.36	27.27	59.09	146.73	60.87
<i>Gestational age (weeks)</i>						
<37	7	16.67	16.67	50.00	145.76	33.33
37–38	30	16.67	16.67	32.14	61.45	46.67
39–40	140	22.56	18.80	38.05	87.37	46.15
≥41	73	26.39	22.22	33.33	59.34	47.95

Discussion

In this study data gathered in the Southampton Asthma Genetics Study was used to examine the relationships between head circumference and other anthropometric measurements at birth and the risk of developing asthma or a raised serum total IgE in childhood. The major finding

was that a large head circumference at birth was associated with an increased risk of an elevated serum IgE measured 6–23 years later. This is consistent with the previous report of Godfrey, Barker and Osmond who reported an association between large head circumference at birth and elevated serum IgE concentration at the age of 50 [3]. This suggests that the relationship may persist throughout life.

Table 2. Adjusted prevalence odds ratios for asthma, elevated IgE levels and skin test positivity.

	<i>n</i>	Wheeze in last 12 months OR (95% CI)	Asthma treatment OR (95% CI)	IgE ≥ 150 IU OR (95% CI)	Any skin test test ≥ 3 mm OR (95% CI)
<i>Head circumference (cm)</i>					
- Adjusted for age & birth weight					
<34	30	0.6 (0.2–2.2)	1.1 (0.3–3.5)	1.0 (0.4–2.9)	1.0 (0.4–2.5)
34–36.9	146	1.0 (–)	1.0 (–)	1.0 (–)	1.0 (–)
≥37	20	0.8 (0.2–2.9)	1.5 (0.4–5.0)	3.2 (1.0–10.4)	1.4 (0.5–3.9)
(<i>p</i> -value for trend)		(0.17)	(0.74)	(0.17)	(0.57)
<i>Birth weight (kg)</i>					
- Adjusted for age & head circumference					
<3.0	31	1.5 (0.5–4.7)	1.5 (0.5–4.7)	1.3 (0.5–3.8)	0.7 (0.3–1.9)
3.0–3.9	194	1.0 (–)	1.0 (–)	1.0 (–)	1.0 (–)
≥4.0	24	1.6 (0.5–5.0)	1.3 (0.4–4.4)	1.7 (0.6–5.1)	1.6 (0.6–4.5)
(<i>P</i> -value for trend)		(0.81)	(0.83)	(0.95)	(0.64)

Head circumference at birth is determined by the growth of the brain which is influenced by numerous factors which are both complex and vary depending on gestational age. These include maternal factors such as nutrition and smoking, placental function including production of growth factors, and fetal factors such as genetic growth potential [6–10]. The potential role of these different risk factors has not been addressed in this study.

In contrast with our recent New Zealand study [2], we did not observe an association between head circumference at birth and the occurrence of asthma, when recorded as either 'wheeze in the last 12 months', or 'requirement for asthma treatment'. This may relate to the smaller number of subjects in the Southampton study, although the interpretation of this current study may also be limited by the wide age range of the offspring included. It was to some extent unexpected, in view of the recognized association between elevated serum total IgE and clinical asthma in childhood [11,12]. An alternative explanation is that variations in examiner technique in measuring head circumference may have reduced the ability to identify statistically significant differences, should they exist.

The findings in relation to birth weight were intriguing, with high birth weights generally being associated with an increased risk of asthma, elevated IgE levels and skin test positivity, although none of these differences reached statistical significance. The possibility exists that these findings are real but that the current study has insufficient power.

In conclusion, this study has extended previous observations that enhanced fetal growth of the brain, leading to large head circumference at birth, may lead to an increased risk of elevated serum IgE levels in childhood. The reasons for this association are unclear and will require further research.

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