Airway and systemic inflammation in obese children with asthma

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ABSTRACT Obese asthma presents *via* altered airway and systemic inflammation in adults. This has not been comprehensively described in children. The aim of the present study was to compare airway and systemic inflammation in obese and nonobese asthmatic children and controls.

In a cross-sectional study, children aged 8–17 years were assigned to one of four groups: obese asthma (OA, n=74); nonobese asthma (NOA, n=249); obese control (OC, n=9); nonobese control (NOC, n=29). Lung function, and both sputum and systemic inflammatory biomarkers were measured.

Non-eosinophilic asthma was more prevalent among OA females (60.0%) *versus* OA males (30.8%). However, there were no differences in the percentage of eosinophils or neutrophils between OA and NOA. Leptin was higher in OC, but not OA, *versus* NOA and NOC, while adiponectin was reduced in OA *versus* NOC only. Expiratory reserve volume was reduced in OA, *versus* NOC. Residual volume (RV) and RV/total lung capacity were reduced in OC *versus* OA, and OC *versus* OA and NOA, respectively.

Obesity was associated with significant lung restriction in children with and without asthma. Obesity was not associated with significantly altered airway or systemic inflammation in asthmatic children. However, the higher prevalence of non-eosinophilic asthma in female obese asthmatics, compared to males, warrants further investigation.

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Introduction

Overweight and obesity is highly prevalent among children with asthma, and exceeds the general population rate in Australia, Denmark and the USA [1–4], with a recent report that up to 45% of asthmatic children are carrying excess weight [4]. Obesity appears to complicate the management of childhood asthma, with previous studies indicating that obesity is associated with an increased risk of exacerbations, poorer asthma control and increased medication use, including steroids [5, 6]. Recently, significant reductions in lung volume indices have also been associated with overweight and obesity in asthmatic children [7, 8].

While the alarmingly high rates of obesity among asthmatic children warrant the development of specific interventions for this population, the first step is to better understand the presentation of obese asthma in order to inform clinical management. The mechanisms linking obesity and asthma remain poorly understood and multiple hypotheses have been proposed. Obesity may be associated with respiratory symptoms *via* cardio-respiratory de-conditioning, physiological restriction of the chest wall by excess mass, or comorbidities, including gastrooesophageal reflux and sleep-disordered breathing [9]. Alternatively, chronic systemic inflammation, characteristic of obesity, has been hypothesised as an underlying factor in obese asthma that may contribute to altered airway inflammation and poorer clinical outcomes [10].

As a chronic inflammatory disease of the airways, asthma is traditionally characterised by eosinophilic airway inflammation. However, in adults, obese asthma has been described as a distinct clinical phenotype, involving non-eosinophilic airway inflammation and being unresponsive to current pharmacological treatment [11–13]. Levels of airway interleukin (IL)-8 have been shown to be raised in neutrophilic asthma [14]. Raised systemic inflammation is also characteristic of obese asthma in adults, including IL-6, and has been linked to airway inflammation and poorer clinical outcomes [13]. However, airway inflammation in obese asthmatic children has not been adequately described. Therefore, the aim of this study is to characterise obese asthma in children by describing airway inflammation, systemic inflammation and clinical asthma outcomes in obese and nonobese children, with and without asthma.

Methods

Subjects

Obese and nonobese children, with and without asthma, aged 8–17 years, were recruited from the general community and John Hunter Hospital outpatient clinics, Newcastle NSW, Australia, from July 2004–2011. Asthma was defined by physician diagnosis and current respiratory symptoms. Obesity was defined as a body mass index (BMI) z-score $\geqslant$1.64 standard deviation score. Participants were assigned to one of four groups: obese asthma (OA, n=74); nonobese asthma (NOA, n=249); obese control (OC, n=9); or nonobese control (NOC, n=29). Exclusion criteria included unexplained weight change during the past 3 months, inflammatory/endocrine disease, or respiratory disorder other than asthma. The Hunter New England and University of Newcastle Human Research Ethics Committees, Newcastle, NSW, Australia, approved this study (09/05/20/5.08). Participant assent and guardian consent were obtained.

Clinical assessment

Participants attended the John Hunter Hospital for clinical testing after an overnight fast and withholding antihistamines and asthma medications. Clinical asthma pattern, current asthma status, and quality of life was assessed using the Global Initiative for Asthma guidelines [15], Juniper Asthma Control Questionnaire (ACQ) [16] and Paediatric Asthma Quality of Life Questionnaire (standardised) [17], respectively. Asthma stability was confirmed, defined as no exacerbation, respiratory tract infection or oral corticosteroid use in the past 4 weeks. The sequence of tests is shown in fig. 1. Exhaled nitric oxide (eNO) was measured (NiOX chemiluminescent detector unit; Aerocrine, Solna, Sweden). Atopy was determined by positive skin prick test to common allergen(s) (*Aspergillus fumigatus*, *Alternaria tenius*, dust mite (*Dermatophagoides pteronyssinus*), cockroach mix and Grass mix). Tobacco exposure was measured by urinary cotinine (NicAlert; Nymox Pharmaceutical Corp., Hasbrouck Heights, NJ, USA). Weight and height were measured using 150 kg maximum scales (EB8271 NuWeigh; Newcastle Weighing Services, Newcastle, NSW, Australia) and 2 m wall-suspended measuring tape with wall stop (Surgical and Medical Supplies Pty Ltd, Rose Park, SA, Australia). BMI was calculated (weight (kg)/height $(m)^2$) and converted to BMI z-scores [18]. All participants performed spirometry (Windows KoKo PFT System Version 4.9 2005; PDS Inc., Louisville, KY, USA). Forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) are expressed as a percentage of the predicted value (% pred) [19]. A subset of participants (OA, n=31; NOA, n=12; OC, n=9; and NOC, n=15) performed lung plethysmography (MedGraphics Elite Series Plethysmograph, USA; Breeze Suite 6.4.1.14 Version 510 2008; MedGraphics Corp., St. Paul. MN, USA). Total lung capacity (TLC), functional residual capacity (FRC), expiratory reserve volume (ERV) and residual volume (RV) are presented as % pred [20]. FEV_1/TLC% is also presented as an additional measure of obstruction [21, 22].

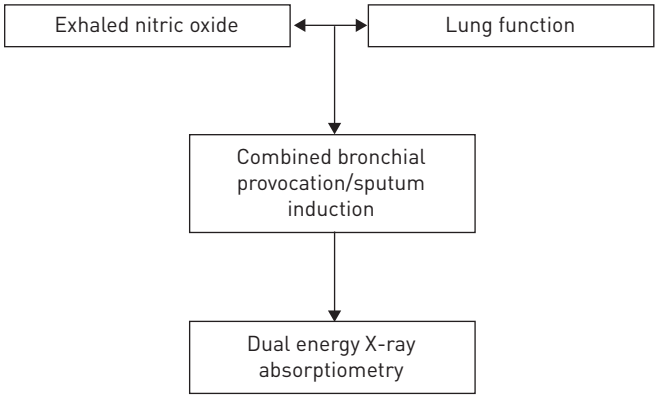

FIGURE 1 Sequence of testing for participants during clinic visit. All patients fasted ⩾12 h and attended clinic to begin first test between 07:30–09:30 h. Lung function and/or exhaled nitric oxide conducted prior to combined bronchial provocation and sputum induction. Blood was collected at any time-point between 07:30–10:00 h. Questionnaires and skin prick testing were completed at any time-point during clinic visit.

Sputum inflammatory cells

Participants underwent combined bronchial provocation testing and sputum induction with hypertonic saline (4.5%) (ULTRA-NEB ultrasonic nebuliser, Model 2000; DeVilbiss, Tipton, UK), as previously described [23]. Airway hyperresponsiveness (AHR) was defined as a fall in FEV1 ⩾15% from baseline. The dose–response slope and log-transformed provocation dose (log-PD_{15}) were calculated. Sputum was selected, dispersed with dithiothreitol, and total cell counts and viability determined. Cytospins were prepared, stained (May–Grünwald Geimsa) and a differential cell count obtained. Eosinophilic asthma was defined as sputum eosinophilia ⩾2.0% [24].

Systemic inflammatory mediators

Blood samples collected from a participant subset were centrifuged at 17 230 × *g* (3000 rpm) at 4°C for 10 min. High sensitivity C-reactive protein (CRP) was measured from serum mixed with monoclonal antibody-coated polystyrene particles, specific for human CRP (CRP Flex reagent cartridge, Dimension Vista System; Siemens Healthcare Diagnostics Inc. 2008, Newark, NJ, USA). Commercial ELISAs were used to measure plasma IL-6 (R&D Systems, Minneapolis, MN, USA), and serum leptin and adiponectin (Bio-Rad, Hercules, CA, USA). Assay sensitivity was 0.039 pg·mL^{-1}, 3.1 pg·mL^{-1} and 32.7 pg·mL^{-1}, respectively. All samples were tested in duplicate.

Statistical analysis

Data is presented as mean±SD, median (interquartile range) or proportion (n (%)). Data variables were assessed for normality prior to analysis using one-way-ANOVA with *post hoc* two-sample unpaired t-testing or Kruskal–Wallis with *post hoc* Wilcoxon rank sum testing for continuous data, and Pearson's Chi-squared test for categorical data. Alpha was set at ⩽0.05 for all tests, and ⩽0.017 for *post hoc* testing. Statistical analysis was performed using Intercooled Stata Version 11.0 for Windows (StataCorp, College Station, TX, USA).

Results

Subject characteristics

Subject characteristics are presented in table 1. The prevalence of atopy was higher in the OA *versus* the OC group and higher in the NOA *versus* the OC and NOC groups. All participants were Caucasian, with the exception of one Asian participant in the NOC group. FEV1 % pred, FVC % pred and TLC % pred did not differ by statistical significance across the four groups. However, FEV1/TLC% was significantly lower in both asthma groups compared with the NOC group. ERV % pred was lower in the OA *versus* the NOC group, and RV % pred was higher in the OA *versus* the OC group. Likewise, RV/TLC % was significantly higher in the OA and NOA groups *versus* the OC group.

Mean±SD asthma duration was similar between the OA and NOA groups (8.7±3.0 *versus* 8.5±4.1 years; p=0.815). The prevalence of AHR was similar in the OA and NOA groups (42.5 *versus* 35.3%; p=0.346), as was the median (interquartile range) dose–response slope (1.02 (0.53–2.9) *versus* 1.25 (0.38–3.22) percentage fall per millilitre; p=0.798) and log-PD_{15} (1.26±1.47 *versus* 1.24±1.06 mL; p=0.928). The OA group had a significantly lower Paediatric Asthma Quality of Life Questionnaire (standardised) score (5.9 (4.7–6.4) *versus* 6.4 (6.0–6.6); p=0.035) and a smaller proportion used inhaled corticosteroids (ICS)

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TABLE 1 Subject characteristics and lung function summarised by obesity and asthma status

Subject characteristics	OA	NOA	OC	NOC	p-value
Subjects n	74	249	9	29	
Age years	11.1±2.8	11.1±3.0	12.4±2.2	11.8±2.9	0.344
Females	47.3	38.6[¶]	44.4	69.0	**0.014**
Height cm	150.5±15.3[+]	143.8±16.1	154.0±12.0	151.5±15.9	**0.001**
Weight kg	65.4±24.7[¶,+]	39.1±13.4	70.9±18.8[¶,+]	44.1±15.2	**<0.001**
BMI z-score SDS	2.1±0.3[¶,+]	0.2±0.9	2.1±0.4[¶,+]	0.1±0.8	**<0.001**
Atopic[#] yes/no (% yes)	27/12 (69.2)[§]	42/8 (84.0)[¶,§]	2/7 (22.2)	14/14 (50.0)	**<0.001**
FEV1 % pred	96.1±14.1	96.3±14.0	94.3±12.7	97.8±13.1	0.908
FVC % pred	100.5±11.2	97.4±11.9	97.4±12.5	97.0±11.8	0.581
FEV1/FVC % pred	79.2±6.6[¶]	80.7±8.2[¶]	84.1±4.4	88.0±7.8	**<0.001**
TLC % pred	106.8±13.3	100.3±10.7	97.3±9.5	99.1±9.3	0.568
FEV1/TLC[#] %	88.5±12.9[¶]	86.5±9.4[+]	96.7±5.3	99.1±8.0	**0.003**
FRC[#] % pred	102.2±23.6	116.7±18.7	93.5±22.0	112.0±16.2	**0.046**
ERV[#] % pred	86.1±37.1[¶]	112.3±23.7	117.8±24.5	121.3±27.2	**0.004**
RV[#] % pred	121.4±50.1[§]	120.9±29.6[§]	64.9±36.0	101.1±30.7	**0.003**
RV/TLC[#] %	24.0±8.0[§]	26.0±7.0[§]	14.0±7.0	22.0±0.6	**0.005**

Data are presented as mean±SD or %, unless otherwise stated. OA: obese asthma; NOA: nonobese asthma; OC: obese control; NOC: nonobese control; BMI: body mass index; SDS: standard deviation score; FEV1: forced expiratory volume in 1 s; % pred: % predicted; FVC: forced vital capacity; TLC: total lung capacity; FRC: functional residual capacity; ERV: expiratory reserve volume; RV: residual volume. [#]: data available on a subset of participants only (OA n=31; NOA n=12; OC n=9; and NOC n=15); [¶]: *versus* NOC; [+]: *versus* NOA; [§]: *versus* OC; p<0.017 for *post hoc* analyses. Bold indicates statistical significance.

(52.0 *versus* 75.8%; p=0.004) compared with NOA group. However, there was no significant difference in the median ACQ score (0.6 (0.3–1.3) *versus* 0.7 (0.4–1.0); p=0.933) or steroid dose (400 (400–800) *versus* 400 (200–675) beclomethasone equivalents; p=0.721) between OA and NOA. A statistically significant difference (p=0.034) in the proportion of OA *versus* NOA classified as intermittent (35.7 *versus* 24.1%), mild (19.1 *versus* 44.8%), moderate (33.3 *versus* 27.6%) and severe (11.9 *versus* 3.5%) asthma was detected. Urinary cotinine levels were negligible in all participants and are, therefore, not presented.

Airway inflammation

Compared with all groups, eNO was significantly lower in the OC group (table 2). However, there was no difference between the OA and NOA groups. Sputum induction was collected in a subset of participants (OA, n=52; NOA, n=185; OC, n=9; and NOC, n=16). The number and proportion of airway eosinophils did not differ by statistical significance between the four groups. Conversely, the airway percentage of neutrophils were significantly different across the four groups, with a trend towards a higher proportion in the asthmatic groups *versus* the control groups. However, *post hoc* analysis did not detect a statistically significant difference between the groups. Significantly lower airway percentage of macrophages were detected in the NOA compared with both control groups, while absolute airway macrophage numbers were significantly lower compared with all groups. Among OA participants, females had significantly lower airway percentage of eosinophils *versus* males (table 3), and a significantly higher proportion of females compared with males had non-eosinophilic asthma, based on percentage of sputum inflammatory cells (fig. 2). This was not true for NOA participants. However, no statistically significant sex differences were evident in airway neutrophils (table 3). Given the difference in airway percentage of eosinophils in the OA group, we compared medication usage between females and males. There was no difference in ICS or short-acting β-agonist usage, with a similar median steroid dose between female and male OA participants (400 (400–800) *versus* 400 (200–400) beclomethasone equivalents; p=0.199). Atopic status (53.3% *versus* 79.2%) and age (10.8±2.9 *versus* 11.5±2.8 years) were similar between female and male OA participants, while the BMI z-score was not (2.0±0.3 *versus* 2.2±0.3 standard deviation score; p=0.045).

Systemic inflammation

Serum leptin (p=0.032), serum adiponectin (p=0.010) and plasma IL-6 (p=0.025) levels differed significantly across the four groups, while serum CRP levels did not (p=0.197). In *post hoc* analysis, serum

TABLE 2 Exhaled nitric oxide and sputum inflammatory cell counts in obese and nonobese children, with and without asthma

Airway inflammatory markers	OA	NOA	OC	NOC	p-value
Subjects	52	185	9	16	
Exhaled nitric oxide ppb	27.9 (10.5–46.7)[#]	27.5 (16.8–55.7)[#]	6.1 (2.4–10.4)	15.0 (9.3–28.9)[#]	**0.002**
Interleukin-8 pg·mL^{-1}	1.7 (0.4–6.4)	1.2 (0.3–3.1)	n/a	n/a	0.242
Total cell count ×10^6 per mL	2.5 (1.3–4.6)	1.7 (0.7–3.7)[¶]	3.7 (2.9–6.5)	3.4 (2.3–6.0)	**0.007**
Eosinophils %	0.8 (0–5.9)	1.1 (0–7.0)	0.0 (0.0–0.3)	0.5 (0.0–1.5)	0.136
Eosinophils ×10^6 per mL	0.02 (0–0.1)	0.02 (0–0.1)	0.00 (0.0–0.02)	0.02 (0.0–0.04)	0.508
Neutrophils %	20.6 (9.5–39.5)	27.5 (13.0–53.5)	9.1 (2.0–17.5)	12.3 (5.0–21.1)	**0.012**
Neutrophils ×10^6 per mL	0.5 (0.2–1.5)	0.4 (0.2–1.2)	0.5 (0.1–1.2)	0.3 (0.1–1.0)	0.794
Macrophages %	61.8±22.6	51.9±25.9[#,¶]	79.6±20.6	75.7±22.8	**<0.001**
Macrophages ×10^6 per mL	1.8 (1.1–2.5)[+]	1.0 (0.5–1.6)[#, ¶]	2.7 (1.8–5.4)	2.6 (1.7–3.7)	**<0.001**
Lymphocytes %	0.9 (0–2.4)	0.5 (0–1.5)	1.1 (0.0–1.3)	1.3 (0.5–3.1)	0.139
Lymphocytes ×10^6 per mL	0.02 (0–0.1)	0.01 (0–0.04)[¶]	0.04 (0.0–0.1)	0.1 (0.02–0.1)	**0.047**
Epithelial %	2.3 (0.5–5.5)[¶]	3.0 (0.5–7.0)[¶]	0.3 (0.0–2.3)	0.4 (0.0–2.4)	**0.005**

Data are presented as n, median (interquartile range) or mean±SD, unless otherwise stated. OA: obese asthma; NOA: nonobese asthma; OC: obese controls; NOC: nonobese control. [#]: *versus* OC; [¶]: *versus* NOC; [+]: *versus* NOA; p<0.017 for *post hoc* analyses. Bold indicates statistical significance.

leptin levels were significantly higher in the OC group compared with the NOA and NOC groups, and serum adiponectin levels were lower in OA compared with NOC participants, while no statistically significant difference was detected for plasma IL-6 (fig. 3). Sex differences were not evident in systemic inflammatory biomarkers.

Discussion

Obese asthma was not associated with elevated airway inflammation or elevations in the systemic inflammatory markers, leptin, IL-6 and CRP, in this group of children. However, based on percentage of sputum inflammatory cells, a higher proportion of obese females had non-eosinophilic asthma compared with obese males, suggesting that sex differences in airway inflammation exist. Obesity was associated with lung restriction, which manifested itself as reduced ERV in asthma and reduced RV in controls. Furthermore, obesity was associated with a clinically significant reduction in quality of life in asthmatic children.

To our knowledge, this is the first study to report airway inflammatory cell counts in obese children. In adults, obese asthma follows a non-eosinophilic steroid-resistant pattern of airway inflammation, characterised by neutrophilia and predominant among females [11, 13]. An association between airway percentage neutrophils and BMI has been reported in female, but not male, adults with asthma [13]. Our data did not detect altered airway neutrophils in obese female children with asthma. However, among obese asthmatics, airway percentages of eosinophils were higher in males, and a significantly higher proportion of

TABLE 3 Exhaled nitric oxide and sputum inflammatory cell counts in asthmatic children, summarised by sex and obesity status

Airway inflammatory markers	OA		NOA		p-value
	Males	Females	Males	Females	
Subjects	26	26	120	65	
Exhaled nitric oxide	33.5 (12.8–49.8)	11.2 (8.6–28.2)	28.0 (20.3–73.7)	23.2 (13.3–55.7)	0.301
Interleukin-8 pg·mL^{-1}	2.27 (0.5–5.56)	1.67 (0.03–6.84)	1.19 (0.15–3.29)	1.25 (0.47–2.7)	0.692
Eosinophils %	3.8 (0.5–9.8)[#]	0.0 (0–1.0)	1.4 (0.0–7.5)	0.5 (0.0–6.3)	**0.021**
Eosinophils ×10^6 per mL	0.11 (0.01–0.12)	0.0 (0.0–0.04)	0.03 (0.0–0.14)	0.01 (0.0–0.10)	0.053
Neutrophils %	21.6 (8.5–29.8)	19.6 (9.5–42.0)	28.0 (13.0–56.5)	26.5 (12.7–48.5)	0.403
Neutrophils ×10^6 per mL	0.5 (0.2–2.4)	0.5 (0.1–1.3)	0.4 (0.2–1.2)	0.4 (0.1–1.1)	0.892
Macrophages %	60.0±22.4	63.7±23.1	51.9±25.6	53.2±26.3	0.088
Macrophages ×10^6 per mL	1.8 (1.1–3.0)[¶,+]	1.7 (1.1–2.5)[¶,+]	1.0 (0.5–1.8)	0.9 (0.4–1.6)	**0.003**

Data are presented as n, median (interquartile range) or mean±SD, unless otherwise stated. OA: obese asthma; NOA: nonobese asthma. [#]: *versus* OA females; [¶]: *versus* NOA males; [+]: *versus* NOA females; p<0.017 for *post hoc* analyses. Bold indicates statistical significance.

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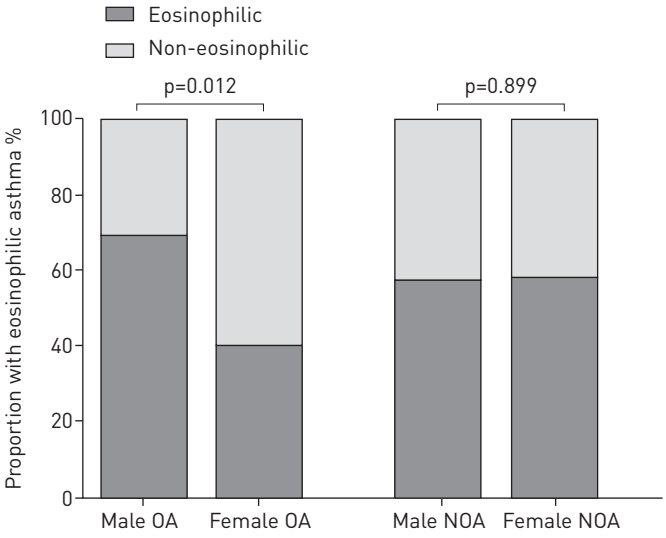

FIGURE 2 The proportion of eosinophilic asthma (⩾2% sputum eosinophils) and non-eosinophilic asthma among obese and nonobese male and female children. OA: obese asthma; NOA: nonobese asthma.

obese females had non-eosinophilic asthma, based on percentage of sputum inflammatory cells. The obese female children also had a lower eNO, consistent with a non-eosinophilic pattern of airway inflammation. This requires further examination in a larger cohort.

Systemic inflammation occurs in adult obese asthma, with IL-6 almost 2–3 times higher and CRP ~7–8 times higher in obese *versus* nonobese adults [13, 25]. Previous studies have also reported adiponectin to be 50% lower in obese children and adults, compared with their nonobese counterparts [26, 27]. In our study, serum adiponectin was reduced in asthmatic and nonasthmatic obese children, compared with nonobese controls. However, this reduction was statistically significant in obese asthmatics only, and may reflect the small sample of obese controls. Leptin has been suggested as a mediator between asthma and obesity, with systemic leptin levels reportedly 2–5 times higher in obese adults with asthma [13, 25, 27]. Studies in asthmatic and nonasthmatic children have found systemic leptin levels to be 2–3 times higher in the obese *versus* nonobese children [10, 26]. In contrast, serum leptin levels in the current study were not elevated in obese asthmatics compared with nonobese asthmatics or controls, but were only significantly raised in obese children without asthma. This is a novel finding and requires further investigation. However, it should be noted that there was considerable variability in serum leptin levels in the OA, and a number of individuals had elevated serum leptin levels.

Plasma IL-6 and serum CRP were not significantly raised in the asthmatic or nonasthmatic obese children in our study population, which agrees with previous paediatric studies that did not detect elevated systemic CRP, IL-6 or tumour necrosis factor-α levels in obese children [26, 28]. We hypothesise that the point at which adipose tissue becomes pathological may be an important distinction between children and adults when considering the effects of obesity on inflammatory and clinical outcomes. In contrast to adults [13], it is difficult to conclude from the present data that adipose tissue inflammation contributes to obese asthma in children.

Obesity exerts its greatest detriment on lung volume measurements, with reductions observed in ERV and FRC in adults, with and without asthma [29]. Similarly, reductions in ERV were detected in obese asthmatic children, compared with nonobese children without asthma. However, in contrast to recent reports in children [7, 8], the obese controls had a significantly reduced RV % pred and RV/TLC% , which was not observed in the obese asthmatic children. RASTOGI *et al.* [7] recently reported RV % pred and RV/TLC% to be significantly lower in OA children, compared with nonobese children without asthma. Likewise, MAHUT *et al.* [8] reported RV/TLC to be lower in overweight and obese children, compared with normal-weight children with asthma, identifying a negative relationship between BMI z-score and FRC and RV, expressed both as % pred and relative to TLC. Preserved RV in the asthmatic children in the presented study may be attributable to the obstructive effect of asthma, causing ''air-trapping'' in the distal airways and an inflated RV [30]. Importantly, reductions in lung function associated with obesity were not detected through routine spirometry, and our data identifies lung volume assessment as an important clinical measure in this group of children.

Among asthmatic children, quality of life was both clinically and statistically significantly lower in the obese *versus* nonobese subjects. Although some studies have found obesity is associated with poorer quality of life

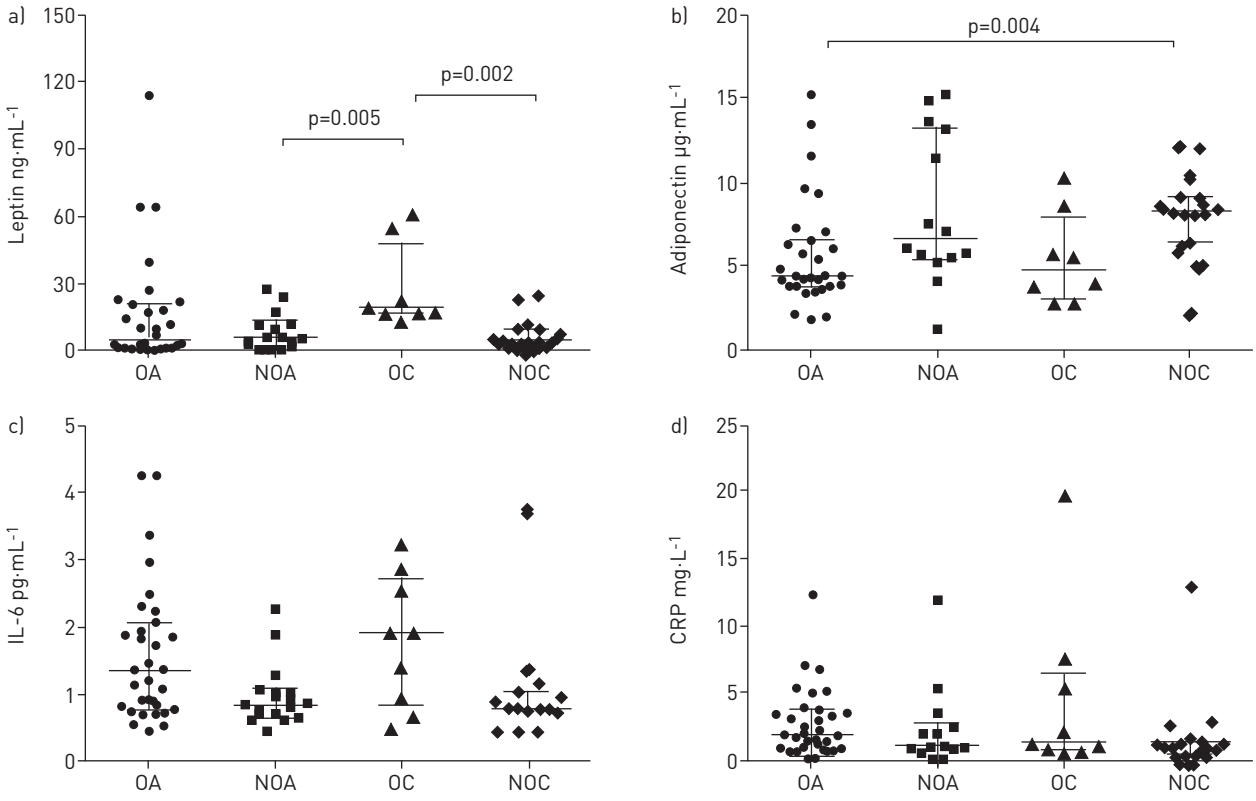

FIGURE 3 Systemic inflammatory biomarkers a) serum leptin, b) serum adiponectin, c) plasma interleukin (IL)-6 and d) serum C-reactive protein (CRP). OA: obese asthma (n=32); NOA: nonobese asthma (n=14); OC: obese control (n=9); NOC: nonobese control (n=16).

in asthmatic children, other studies have found no difference between obese and nonobese children, and it has been suggested that obesity may interfere with the perception of respiratory symptoms in children [5, 31]. Alternatively, obese asthmatic children may perceive worse symptoms related to a clinically significant reduction in ERV. Indeed, one could hypothesise that the poorer quality of life is due to poorer asthma control, in addition to obesity. However, despite fewer obese asthmatics being on controller medications, obesity was not associated with poorer asthma control, as measured by ACQ. Furthermore, airway reactivity to hypertonic saline did not differ between obese and nonobese asthmatics in our study. Previous studies examining obesity and AHR in children and adults provide conflicting results, with some reporting a higher prevalence or severity of AHR in obese compared with nonobese asthmatics, while others report no difference [5]. Previous studies also report increased medication use in obese asthmatic children and adults [5, 6]. Our data do not detect a difference in steroid dose between obese and nonobese children with asthma. In fact, a smaller proportion of obese children were reportedly taking ICS medication. However, our data is limited by patient/guardian report of medication use, which may not reflect actual practice by this group. This study is limited by the small number of control subjects, particularly the obese, which may have impacted on the power to detect differences between asthma and control subjects. The limited number of systemic inflammatory measures may also limit conclusions regarding the role of obesity associated inflammation in childhood asthma.

In a large cohort of asthmatic children, stratified to mild obesity or no obesity, obesity was associated with chest wall restriction and poorer quality of life, as seen in adult obese asthma. However, it was difficult to confirm that obesity-associated inflammation contributed to asthma in this group of children. Noting the absence of contribution from obesity-associated inflammation to asthma in this group of children, one may hypothesise that obesity is a comorbidity, as opposed to a causative or precipitating factor in childhood asthma. Obese asthma in adults is associated with distinct airway and systemic inflammatory alterations, which may become apparent in this group of children as they transition through adolescence into adulthood. Therefore, longitudinal studies, including repeated measures of sputum and systemic inflammatory markers, are needed to improve our understanding of obese asthma.

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