Clinical and atopic parameters and airway inflammatory markers in childhood asthma: A factor analysis

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ABSTRACT

**Background:** Recent studies have repeatedly shown weak correlations among lung function parameters, atopy, exhaled nitric oxide level (FeNO), and airway inflammatory markers, suggesting that they are non-overlapping characteristics of asthma in adults. The objective of this study is to demonstrate, using factor analysis, whether the above features represent separate dimensions of childhood asthma.

**Methods:** Clinically stable asthmatic patients aged between 7 and 18 years old underwent spirometry, methacholine bronchial challenge, blood sampling for atopy markers and chemokine levels (macrophage-derived chemokine [MDC], thymus and activation-regulated chemokine [TARC] and eotaxin), FeNO, and chemokines (MDC and eotaxin) and leukotriene B4 measurements in exhaled breath condensate (EBC).

**Results:** The mean (standard deviation) FEV$_1$ and FeNO of 92 patients were 92.1 (15.9) % predicted and 87.3 (65.7) ppb, respectively. Fifty-nine percent of patients received inhaled corticosteroids. Factor analysis selected four different factors, explaining 55.5% of total variance. The Kaiser-Meyer-Olkin measure of sampling adequacy was 0.587. Plasma total and specific IgE levels, peripheral blood eosinophil percentage and FeNO loaded on factor 1; plasma TARC and MDC concentrations on factor 2; MDC, eotaxin and leukotriene B4 concentrations in EBC on factor 3; and plasma eotaxin concentration together with clinical indices including body mass index and Disease Severity Score loaded on factor 4. **Post hoc** factor analyses revealed similar results when outliers were excluded.

**Conclusions:** Our results suggest that atopy-related indices and airway inflammation are separate dimensions in the assessment of childhood asthma, and inflammatory markers in peripheral blood and EBC are non-overlapping factors of asthma.
Asthma is characterised by reversible airway obstruction, bronchial hyperresponsiveness (BHR) and atopy. A number of clinical and spirometric parameters are being used to evaluate the severity of disease and to assess response to therapy in chronic stable asthma. Traditionally, clinical symptomatology and disease scores as well as physiologic measures of airway function (e.g. spirometry, peak expiratory flow rate, bronchial provocation) have been the primary means of assessing asthmatic patients. There has been increasing interest in monitoring airway inflammation in asthma. The cellular inflammatory response of the bronchial mucosa in asthma is characterised by eosinophil infiltration. Sputum eosinophilia is also shown to reflect disease severity of asthma.

Our group published recently that type 2 T-helper lymphocyte (Th2)-specific chemokines were associated with eosinophilia in peripheral blood as well as increased in acute and chronic stable asthma. These patients also had increased nitric oxide (NO) and inflammatory mediators in exhaled breath. In many studies, however, there were poor interrelations among these outcome measures. For instance, the concentrations of Th2-specific chemokines (thymus and activation-regulated chemokine [TARC], macrophage-derived chemokine [MDC] and eotaxin) in exhaled breath condensate (EBC) did not show good correlations with those measured in PB in asthmatic children. The clinical, atopic and inflammatory variables might therefore provide complementary data for monitoring of the disease.

Factor analysis is commonly used to reduce a large number of disease parameters to a relatively small number of independent “factors”. As each factor groups associated parameters, the results help to provide insight into the pathogenesis of complex diseases. Being essentially free of a predetermined hypothesis on any interrelated parameters, this statistical technique can be viewed of as a hypothesis-generating tool. Factor analysis has been applied previously in studies of asthma in adults, and the results showed that clinical characteristics, spirometry, BHR, and sputum inflammatory markers are non-overlapping dimensions in asthma. Thus, assessment of disease control and severity in adults with asthma should include measurements of all these parameters. Relevant data on factor analysis in childhood asthma is also limited. Furthermore, most of the previous studies did not include atopic factors (e.g. plasma total and specific IgE levels) and emerging biomarkers of airway inflammation (e.g. NO and other mediators in exhaled air). The aim of this study was to objectively specify the heterogeneity of childhood asthma by categorising a number of functional, atopic and inflammatory features of chronic stable asthma into separate, complementary domains without a priori assumption. Such statistical evidence would further support the utility of routine measurement of all these dimensions.

METHODS

Study population

This study recruited patients aged 7 to 18 years with clinically stable asthma, diagnosed according to American Thoracic Society guideline, from the paediatric outpatient clinics of a university teaching hospital in Hong Kong. None of them were cigarette smokers. These patients were free from symptoms of infection for two weeks before study. Their anti-asthma treatments were also stabilised for at least three months. Asthma severity in these subjects was assessed by Disease Severity Score (DSS), a composite score that included daytime, nighttime and exercise-induced symptoms, frequency of asthmatic exacerbation, and the use of anti-asthma medications, as well as by the Global Initiative for Asthma (GINA) criteria. Body weight and height were measured with the subject lightly clothed and bare-footed using an electronic weighing scale (Model 708, Seca, Germany) and Harpenden stadiometer.
Subjects’ parents gave written informed consent, and the Clinical Research Ethics Committee of our University approved this study.

**Pulmonary function testing**

All patients underwent spirometric assessment (Compact II, Vitalograph, Buckingham, England) to measure their forced expiratory volume in one-second (FEV₁) and forced vital capacity (FVC), which were compared with the local reference values.[21] They were also tested for BHR by inhalation of methacholine according to the protocol reported by Yan et al.[22] PD₂₀, being the provocative dose of methacholine that resulted in 20% fall in FEV₁, was noted from the log dose-response curve.

**Exhaled NO measurement**

Fractional exhaled NO concentration (FeNO) was measured at an expiratory flow rate of 50 mL/sec using a chemiluminescence analyser (NOA280i, Sievers Instruments, Boulder, CO, USA) according to ERS/ATS standard.[23] Repeated exhalations were performed without nose clip until three NO plateau values agreed at the 10% level. The mean FeNO value was then recorded.

**Measurement of atopy and plasma inflammatory markers**

Eosinophils in EDTA-anticoagulated venous blood were enumerated using Coulter STKS counter (Beckman-Coulter, Miami, FL, USA). Plasma total IgE concentration was measured by micro-particle immunoassay (IMx analyser, Abbott Laboratories, Abbott Park, IL, USA) and specific IgE to *Dermatophagoides pteronyssinus*, being the most prevalent local Aeroallergen,[8] was measured by fluorescent enzyme immunoassay (AutoCAP analyser, Pharmacia Diagnostics AB, Uppsala, Sweden). Patients with *D. pteronyssinus*-specific IgE (levels ≥ 0.35 kIU/L) were considered atopic. Plasma concentrations of TARC, MDC and eotaxin were measured in duplicates by sandwich enzyme immunoassays (MDC and TARC by R & D Systems, Minneapolis, MN, USA; and eotaxin by Biosource International, Camarillo, CA, USA). The detection limits of these chemokines were 7, 62.5 and 2.2 pg/mL, respectively.

**Measurement of chemokines and LTB₄ in breath condensate**

Following mouth rinse, the subjects breathed tidally into the disposable RTube (Respiratory Research, Charlottesville, VA, USA) for 10 minutes.[10,11] EBC thus obtained was immediately stored at -70°C until being assayed for MDC and eotaxin in one batch using the commercial kits described above. The concentration of leukotriene B₄ (LTB₄) was also measured by acetylcholinesterase competitive enzyme immunoassay (Cayman Chemical, Ann Arbor, MI, USA). The detection limit of this assay for LTB₄ was 4 pg/mL.

**Statistical analysis**

Results were expressed as proportions, mean and standard deviation (SD) or median and interquartile range (IQR). Variables with non-Gaussian distribution were logarithmically transformed before analysis. Exploratory factor analysis included the following 12 variables: clinical (body mass index [BMI], DSS); atopic (total and *D. pteronyssinus*-specific IgE, peripheral blood eosinophils), and inflammatory markers in peripheral blood (TARC, MDC and eotaxin) and EBC (FeNO, MDC, eotaxin and LTB₄). Because only 68 patients could successfully perform lung function measurements (FEV₁, FVC, FEV₁/FVC and PD₂₀; Table 1), these spirometric parameters were not included in our factor analysis so as to maintain an acceptable ratio between sample size and number of variables included.[24] Bartlett’s test of sphericity was used to test for the possibility to perform factor analysis. The Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy was also evaluated. A high KMO
(maximum 1.0; minimum acceptable 0.5) indicates that data is likely to factor well since correlations between pairs of variables can be explained by the other variables (low partial correlation coefficients). Correlation coefficients were analysed by principal component analysis and subsequent rotation according to the standard varimax criterion.[24][25] In this type of analysis, the correlation between parameters is attributed to their common dependence on independent entities called “factors”. The coefficients that link parameters to factors are called “factor loadings”, the number of factors is chosen to be as small as possible but large enough to account for most of the variation within the data. It was decided a priori that the number of factors in the varimax rotation would be based on the number of eigenvalues ≥ 1.0 in the principal component analysis.[26] To assess the robustness of our findings, we repeated the factor analysis after excluding outliers from the data set, defined as data outside the range of mean ± 3 SD, to determine the stability of the factor structures. Because no procedure is known for estimating standard errors of factor loadings, this study did not evaluate any statistical significance. Instead, we adopted one common and conventional rule of thumb to consider “factor loadings” of 0.45 or larger to be “high”. [24] All analyses were performed with the Statistical Package of Social Sciences for Windows version 10.1 (SPSS Inc., Chicago, IL, USA).

RESULTS

Subjects
Ninety-two consecutive asthmatic children were approached and all consented to participate. Table 1 summarises their clinical and laboratory characteristics. Forty-five (49%) of these patients received ICS treatment and nine received a combination of ICS and inhaled long-acting β-agonist. Eighty-eight patients (96%) were atopic. BHR was present in 26 (68%) steroid-naive and 21 (70%) of ICS-treated patients, respectively (p=0.889).

Asthma severity and study parameters
According to the GINA criteria, 31 patients (34%) suffered from intermittent asthma, 34 (37%) from mild persistent asthma, 12 (13%) from moderate persistent asthma and 15 (16%) from severe persistent asthma. Plasma TARC and MDC concentrations were significantly higher in patients with persistent asthma than those with intermittent disease (p = 0.006 and p = 0.009 respectively as analysed by ANOVA; Fig. 1). Other measured clinical, atopic, spirometric or inflammatory parameters did not differ among the various GINA groups (results not shown).

Factor analysis
Bartlett’s test of sphericity indicated a correlation between the presently used variables because the correlation matrix was statistically different from an identity matrix ($\chi^2 = 135.8$, degree of freedom = 66, p<0.0001). The KMO measure of sampling adequacy was 0.587. Factor analysis yielded four separate factors that could explain 55.5% of the total variance in the data set when the ‘eigenvalue=1’ criterion was used. The addition of one more factor only resulted in an increase of the total explained variance to 63.8%. Thus, factor analysis with four components was presented (Table 2). When factor analysis was repeated after excluding outliers > 3 SD, the KMO measure of sampling adequacy was 0.580. A total of 5 factors were identified (Table 3). The robustness of the original factor structure was confirmed by the finding that all parameters except those in the original factor 4 (DSS, BMI and plasma eotaxin concentration) were clustered into the same factors when outliers were excluded. Plasma eotaxin interestingly ‘returned’ to the same factor as plasma TARC and MDC concentrations, and DSS and BMI were separated into two independent factors.
DISCUSSION
This study focused on the factor analysis of asthma-related parameters solely in 92 children and adolescents with chronic stable asthma. Most of these patients had normal or mildly obstructed airways (mean FEV₁ 92%) but with significant airway inflammation (mean FeNO 87.3 ppb). Factor analysis reduced 12 parameters into mostly 4 different factors with satisfactory sampling adequacy. Plasma total and D. pteronyssinus-specific IgE levels, peripheral blood eosinophil percentage and FeNO loaded on factor 1, plasma Th2-specific chemokines (TARC and MDC) loaded on factor 2, MDC, eotaxin and LTB₄ levels in EBC loaded on factor 3, and DSS, BMI and plasma eotaxin level loaded on factor 4. Post hoc factor analyses revealed similar clustering of the parameters when outliers were excluded. In particular, this is the first study to show using factor analyses that the inflammatory markers (MDC and eotaxin) being measured in both peripheral blood and EBC are assigned into separate factors. Although the results from this limited study should not be generalisable to other biomarkers, our findings support that inflammatory mediators may be differentially regulated in these compartments in childhood asthma.

The present factor analysis has clearly demonstrated weak correlations between clinical, atopic and inflammatory parameters in childhood asthma. These differences can probably be explained by the fact that asthma health status has a number of distinct components. If the poor correlations are due mainly to measurement error of a single concept, the asthma parameters will not be separated into such clinically sensible dimensions. BMI, plasma IgE levels and airway inflammatory markers were consistently segregated into different components. Besides, although it was specified a priori that the number of factors in the varimax rotation would be based on the number of eigenvalues ≥1.0 in the principal component analysis, exploratory rotations with both three and five factors were also conducted. The distributions on these alternative numbers of factors did not significantly alter the total variance explained. Lastly, all “factor loadings” were larger than 0.45 (Table 2) and our final model explained more than 50% of the total variance.[24] These results suggest a good assignment of the variables into the four factors.

Factor analysis reduces a large number of related or even seemingly unrelated parameters into relatively small number of “factors”. As this method does not require a predetermined hypothesis on any interrelated parameters, this statistical technique offers tremendous help to guide us on possible ways to categorise the many dimensions of complex diseases such as asthma. Nonetheless, this approach does not offer any mechanistic link between variables that cluster in the same factor. In addition, the clustering of variables obtained may apparently be unexplained from the clinical point of view. We should thus be very careful in deciding on the optimal number of factors (with the help of Scree plot, eigenvalues, etc) while making the best biological sense out of the results.[24][25][26] Factor analysis has not been widely applied in studying asthma-related parameters in children. Among Chinese children, Qian and colleagues conducted factor analysis to examine the associations between respiratory health outcomes and household risk factors.[18] They found that the five factors of heating coal smoke, socioeconomic status, ventilation, environmental tobacco smoke and parental asthma were independently associated with asthma. In another study on asthmatic children, principal components and factor analysis suggested two independent factors: atopy-related indices and loci on chromosome 5q31-33 that encoded the cytokine gene cluster.[19] The present study provides data to this expanding field by suggesting different non-overlapping clinical, atopic and inflammatory factors in childhood asthma.

Clinical measures of asthma were shown to have poor correlations with subjective
quality-of-life indicators [17], and the occurrence of asthma symptoms was also independent of subjects' BMI and measures of airway function. [27] These observations opened up a new dimension of clinical trials - any new asthma treatment should aim at reducing asthma-specific mortality and morbidity and improving patient well-being, daily activities and emotional stability. [28] In asthma, the conventional clinical outcomes address the first concern and quality of life assessment addresses the latter. Thus, subjective patient status has to be measured and interpreted independently. To complicate the issue, the present study suggests that airway inflammatory markers in peripheral blood and EBC are different dimensions in the assessment of childhood asthma. It will also be interesting and important to know the ways different asthma interventions bring about improvements in clinical, immunological and quality-of-life outcomes in the patients.

This study included BMI in our factor analysis in view of a number of recent publications on an epidemiological association between asthma and obesity. [27][29][30][31] This relation seemed to be present irrespective of atopy and eosinophil counts. [27][31] In the Childhood Asthma Management Program, BMI was independently associated with FEV₁, FVC and FEV₁/FVC but not with asthma symptoms or atopy. [27] Our recent study also could not find any association between BMI and spirometric variables, peripheral blood eosinophil percentage, FeNO or LTB₄ levels in EBC. [11] Whereas the mechanical properties of the respiratory system associated with obesity may account for this linkage, obese patients were found to have increased levels of leptin and pro-inflammatory cytokines. [32] These pathways may be independent of Th2-specific chemokines, and thus our factor analyses failed to reveal any correlation between BMI and inflammatory markers in peripheral blood or EBC.

Although 12 asthma-related parameters are grouped into four factors in this study, the finding do not mean that childhood asthma is determined only by four factors. There may be other factors that are not captured by these 12 items. For example, quality-of-life factor was found to be an important component of asthma [17] but this has not been measured in our patients. Although it is too invasive to use bronchial biopsy samples to monitor asthma, the presence of inflammatory markers (e.g. eosinophils and chemical mediators) in induced sputum has not been evaluated. The inflammatory markers included in this study may also be associated with other, as yet unidentified, factors. Additional studies should be done to explore the mechanisms that link up the four components of childhood asthma that are identified in this study.

In conclusion, this study suggests that the asthma-related parameters including atopic factors and airway inflammatory markers are non-overlapping dimensions in the assessment of chronic stable asthma in children. Specifically, inflammatory markers in peripheral blood and EBC should be considered separate dimensions. The results support the usefulness of routine measurement of these dimensions in monitoring childhood asthma.

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COMPETING INTEREST STATEMENT
None of the authors of this article has any competing interest.
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Figure Legend

Figure 1 The distribution of plasma concentrations of (A) TARC and (B) MDC among asthmatic patients with intermittent (INT), mild persistent (MP) and moderate-to-severe persistent (MSP) disease. Horizontal bars indicated the mean values for the respective groups.
REFERENCES


shows 2 major components, one of which is linked to markers on chromosome 5q. *J Allergy Clin Immunol* 2001;108:772-80.


<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Value*</th>
<th>Reference range**</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>92</td>
<td>12.7 (3.4)</td>
<td>NA</td>
</tr>
<tr>
<td>Male gender, n (%)</td>
<td>92</td>
<td>64 (70)</td>
<td>NA</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>92</td>
<td>19.0 (3.5)</td>
<td>NA</td>
</tr>
<tr>
<td>Disease Severity Score, range 6 - 30</td>
<td>92</td>
<td>11 (9 - 14)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Atopic features</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma total IgE concentration, kIU/L</td>
<td>92</td>
<td>611 (271 - 1256)</td>
<td>≤ 160 for 7 years; ≤ 180 for ≥ 8 years</td>
</tr>
<tr>
<td>Specific IgE to <em>D. pteronyssinus</em>, kIU/L</td>
<td>92</td>
<td>105 (39 - 145)</td>
<td>&lt; 0.35</td>
</tr>
<tr>
<td>Peripheral blood eosinophil percentage, %</td>
<td>92</td>
<td>8 (5 - 10)</td>
<td>≤ 3</td>
</tr>
<tr>
<td>Absolute eosinophil count, 10⁹/L</td>
<td>92</td>
<td>0.52 (0.35 - 0.77)</td>
<td>≤ 0.25</td>
</tr>
<tr>
<td><strong>Lung function †</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV₁ predicted, %</td>
<td>80</td>
<td>92.1 (15.9)</td>
<td>≥ 80</td>
</tr>
<tr>
<td>FVC predicted, %</td>
<td>80</td>
<td>104.8 (17.3)</td>
<td>≥ 80</td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>80</td>
<td>80.0 (9.6)</td>
<td>≥ 80</td>
</tr>
<tr>
<td>PD₂₀, µmol</td>
<td>68</td>
<td>1.95 (0.58 - 6.00)</td>
<td>&gt; 7.8</td>
</tr>
<tr>
<td><strong>Inflammatory markers ‡</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FeNO, ppb</td>
<td>92</td>
<td>72.4 (39.5 - 117.8)</td>
<td>≤ 30</td>
</tr>
<tr>
<td>Plasma TARC concentration, pg/mL</td>
<td>92</td>
<td>45.0 (26.8 - 85.3)</td>
<td>≤ 70</td>
</tr>
<tr>
<td>Plasma MDC concentration, pg/mL</td>
<td>92</td>
<td>540 (411 - 702)</td>
<td>≤ 480</td>
</tr>
<tr>
<td>Plasma eotaxin concentration, pg/mL</td>
<td>92</td>
<td>39.0 (33.5 - 47.5)</td>
<td>≤ 45</td>
</tr>
<tr>
<td>EBC MDC concentration, pg/mL</td>
<td>92</td>
<td>113 (93 - 126)</td>
<td>≤ 105</td>
</tr>
<tr>
<td>EBC eotaxin concentration, pg/mL</td>
<td>92</td>
<td>37.0 (33.0 - 43.3)</td>
<td>≤ 35</td>
</tr>
<tr>
<td>EBC LTB₄ concentration, pg/mL</td>
<td>92</td>
<td>39.9 (31.4 - 47.7)</td>
<td>≤ 35</td>
</tr>
</tbody>
</table>

EBC=exhaled breath condensate; FeNO=fractional exhaled nitric oxide concentration; FEV₁=forced expiratory volume in 1-second; FVC=forced vital capacity; LTB₄=leukotriene B₄; NA=not applicable or available; PD₂₀=provocative dose of methacholine that caused a 20% drop in FEV₁; SD=standard deviation.

* Results were expressed in mean (SD) or median (IQR) unless stated otherwise.

** The reference ranges for “inflammatory markers” were established in-house from non-atopic and non-allergic.
† Only 80 and 68 patients could successfully perform spirometry and methacholine bronchial challenge, respectively.
‡ Mean (SD) volume of EBC collected was 1.26 (0.44) mL.

### Table 2 Varimax rotated factor-loading matrix for all 92 asthmatic patients*

<table>
<thead>
<tr>
<th>Factor</th>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Factor 3</th>
<th>Factor 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma total IgE conc.</td>
<td><strong>0.710</strong></td>
<td>0.034</td>
<td>-0.009</td>
<td>-0.270</td>
</tr>
<tr>
<td>Specific IgE to <em>D. pteronyssinus</em></td>
<td><strong>0.684</strong></td>
<td>0.031</td>
<td>-0.016</td>
<td>-0.020</td>
</tr>
<tr>
<td>Peripheral blood eosinophil percentage</td>
<td><strong>0.609</strong></td>
<td>0.158</td>
<td>-0.037</td>
<td>0.147</td>
</tr>
<tr>
<td>FeNO</td>
<td><strong>0.576</strong></td>
<td>-0.392</td>
<td>-0.215</td>
<td>0.408</td>
</tr>
<tr>
<td>Plasma TARC conc.</td>
<td>0.088</td>
<td><strong>0.839</strong></td>
<td>-0.020</td>
<td>0.222</td>
</tr>
<tr>
<td>Plasma MDC conc.</td>
<td>0.089</td>
<td><strong>0.795</strong></td>
<td>-0.183</td>
<td>-0.187</td>
</tr>
<tr>
<td>EBC LTB4 conc.</td>
<td>-0.141</td>
<td>-0.100</td>
<td><strong>0.726</strong></td>
<td>0.199</td>
</tr>
<tr>
<td>EBC MDC conc.</td>
<td>-0.295</td>
<td>0.007</td>
<td><strong>0.628</strong></td>
<td>0.037</td>
</tr>
<tr>
<td>EBC eotaxin conc.</td>
<td>-0.301</td>
<td>-0.130</td>
<td><strong>0.590</strong></td>
<td>0.018</td>
</tr>
<tr>
<td>Disease Severity Score</td>
<td>0.014</td>
<td>0.097</td>
<td>0.217</td>
<td><strong>0.681</strong></td>
</tr>
<tr>
<td>Body mass index</td>
<td>-0.025</td>
<td>-0.073</td>
<td>0.037</td>
<td><strong>0.579</strong></td>
</tr>
<tr>
<td>Plasma eotaxin conc.</td>
<td>-0.009</td>
<td>0.461</td>
<td>-0.341</td>
<td><strong>0.550</strong></td>
</tr>
<tr>
<td>Eigenvalue</td>
<td>1.89</td>
<td>1.77</td>
<td>1.52</td>
<td>1.49</td>
</tr>
<tr>
<td>Total variance explained, %</td>
<td>15.7</td>
<td>14.8</td>
<td>12.6</td>
<td>12.4</td>
</tr>
</tbody>
</table>

* Bold values represent the highest factor loadings.
Table 3  Distribution of parameters into different factors after exclusion of outliers

<table>
<thead>
<tr>
<th>Parameter</th>
<th>With outliers</th>
<th>No outliers*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma total IgE concentration</td>
<td>Factor 1</td>
<td>Factor 1</td>
</tr>
<tr>
<td>Specific IgE to <em>D. pteronyssinus</em></td>
<td>Factor 1</td>
<td>Factor 1</td>
</tr>
<tr>
<td>Peripheral blood eosinophil percentage</td>
<td>Factor 1</td>
<td>Factor 1</td>
</tr>
<tr>
<td>FeNO</td>
<td>Factor 1</td>
<td>Factor 1</td>
</tr>
<tr>
<td>Plasma TARC concentration</td>
<td>Factor 2</td>
<td>Factor 2</td>
</tr>
<tr>
<td>Plasma MDC concentration</td>
<td>Factor 2</td>
<td>Factor 2</td>
</tr>
<tr>
<td>EBC LTB4 concentration</td>
<td>Factor 3</td>
<td>Factor 3</td>
</tr>
<tr>
<td>EBC MDC concentration</td>
<td>Factor 3</td>
<td>Factor 3</td>
</tr>
<tr>
<td>EBC eotaxin concentration</td>
<td>Factor 3</td>
<td>Factor 3</td>
</tr>
<tr>
<td>Disease Severity Score</td>
<td>Factor 4</td>
<td>Factor 4</td>
</tr>
<tr>
<td>Body mass index</td>
<td>Factor 4</td>
<td>Factor 5</td>
</tr>
<tr>
<td>Plasma eotaxin concentration</td>
<td>Factor 4</td>
<td>Factor 2</td>
</tr>
<tr>
<td>Total variance explained</td>
<td>55.5%</td>
<td>64.6%</td>
</tr>
</tbody>
</table>

* Five factors were obtained after the exclusion of all outliers, with the respective Eigenvalues being 1.92, 1.75, 1.55, 1.30 and 1.23 and % of total variances explained being 16.0%, 14.6%, 12.9%, 10.9% and 10.2%.
Figure 1A

Plasma TARC Conc. (pg/mL)

INT 41
MP 79
MSP 92

Asthma Severity

p < 0.005
p < 0.01
Clinical and atopic parameters and airway inflammatory markers in childhood asthma: a factor analysis

Ting Fan Leung, Gary W. K. Wong, Fanny W. S. Ko, Christopher W. K. Lam and Tai Fai Fok

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