The Association between Mannan Binding Lectin and Asthma in Children: a marker of severity?

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Background to the project

Mannan Binding Lectin (MBL) is a normal serum protein involved in opsonisation and complement activation via the lectin pathway. Polymorphisms affecting the MBL gene are found in 30-40% of the population.

Previous research into relationship of MBL with asthma has given conflicting results:

- Two reports of high levels of MBL in association with asthma – in both children and adults[1, 2]
- Other studies looking at risk of developing asthma after infection have reported an association with low levels of MBL[3]

Differences may be reflective of different phenotypes of asthma

Methods

The Leicestershire Child Cohort

The Cohort used is part of a population-based, random sample of children born in Leicestershire between 1993-1997

- south Asian and Whites included
- 154 serum samples measured in total

Surveys were conducted by repeated postal questionnaire and included questions on:

- demographic and environmental variables
- clinical features of wheeze
- treatment currently been taken for wheeze

Measuring MBL levels

- by commercial ELISA kit – using mannan coated plates, thus recognising functional oligomers of MBL only (HK 327 Hycult Biotechnology, Uden, Netherlands)
- method was validated by comparing results with assay measuring lectin pathway activation (C4 cleavage assay)

References:

(1) KAUR S. *et al*. 2005 Journal of Allergy and Clinical Immunology. 116: 1381-1383

(2) UGUZ A.*et al*. 2005 Paediatric Allergy and Immunology. 16: 231-235

(3) NAGY A .*et al*. 2003 Journal of Allergy and Clinical Immunology. 112: 729-34

(4) British Thoracic Society. 2003 Thorax. 58(Suppl1): i1-94.

The aims of the project

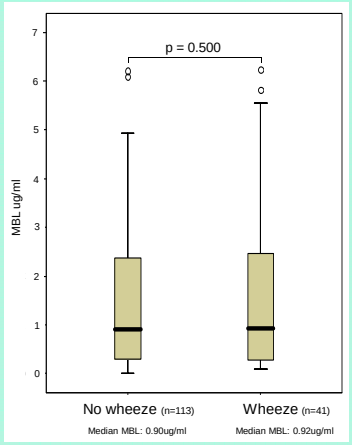
To use data collected from the Leicestershire Cohort to answer the following questions:

1. Are levels of MBL different between children with wheeze and children who do not wheeze
2. Are levels of MBL related to severity of wheeze

Results

(1) **Levels of MBL in children with and without wheeze**

No significant difference between levels of MBL in children with or without wheeze

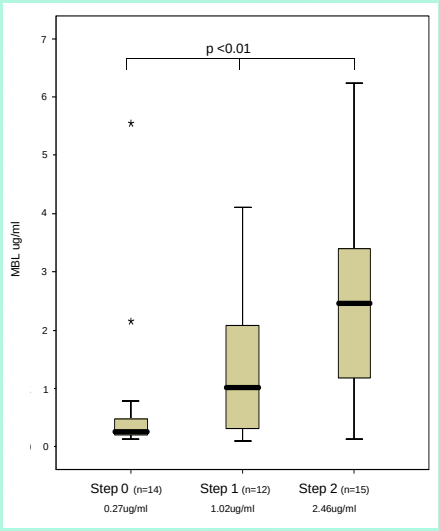


0.90ug/ml (0.30-2.37) compared to 0.92ug/ml (0.27-2.46) (median levels and IQR) p=0.500 (Mann-Whitney test)

Results

(2) **Levels of MBL in wheezers classified by treatment, BTS guidelines[4]**

- Step 0: no treatment
- Step 1: bronchodilator only
- Step 2: Inhaled corticosteroid



Significant difference between children who have been prescribed an inhaled corticosteroid compared to those whose wheezing is less severe.

- Step 0: 0.27ug/ml (0.20-0.48)
- Step 1: 1.02 (0.32-2.08)
- Step 2: 2.46 (1.10-3.62)

p=<0.01 (Kruskal-Wallis test)

Results: (3) Multivariable analysis

We performed a multivariable regression analysis on log transformed data to assess whether the relationship between inhaled corticosteroid and high MBL could be due to confounders.

	Unadjusted			Adjusted**		
Severity	**Coefficient**	**95% CI**	**P**	**Coefficient**	**95% CI**	**P**
Step 0	0			0		
Step 1	0.662	-0.221 - 1.544	0.137	0.664	-0.316 - 1.643	0.177
Step 2	1.549	0.716 - 2.383	0.001	1.361	0.308 - 2.415	0.013

Even after adjustment there is a significantly increased likelihood of having higher MBL when using an inhaled corticosteroid, compared to wheezers who were not prescribed this treatment (coefficient 1.361, p=0.013)

(**Adjusted for age, gender, cold frequency and exposure to smoking in household) (CI: confidence interval)

What does this mean?

- Levels of MBL appear to play a modulating role in childhood wheeze: high levels predispose to more severe wheeze
- Our study supports previous reports of high levels of MBL in hospital treated asthma patients. MBL could be a useful marker predicting susceptibility to more severe asthma.
- MBL is a pro-inflammatory molecule and it has also been associated with eosinophilia[1, 2]. It may therefore be involved in promoting airway inflammation and/or remodelling.
- Future research should include co-ordinated multi-centre units. Treatment (and compliance) should be recorded.