

Comparison between the presence of cow milk protein allergy in asthmatic and non-allergic children

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Abstract

Background: Hypersensitivity to cow milk proteins is one of the main food allergies and affects mostly but not exclusively infants, while it may also persist through adulthood and can be very severe. Different clinical symptoms of milk allergy have been established. The diagnosis of milk allergy differs widely due to the multiplicity and degrees of symptoms, and can be achieved by skin or blood tests. The aim of this study to assess the role of cow milk (CM) to induce asthma and compare between the presence of cow milk protein allergy in asthmatic and non-allergic children and to prevent occurrence of asthma among children, Subjects and methods: This is a case control study, was conducted on 154 patients divided into two groups (77 in each). This study was conducted in Pulmonology Unit of Pediatric Department in Zagazig University Hospital. Result: There was high statistically significant difference between the two studied groups as regards skin prick test. There was high significant increase in the severity recorded in respiratory function test in allergic group compared to control group. Conclusion: our study showed that CMA can exacerbate the symptoms in children with asthma. Therefore, it is worth considering a possible role of food allergy in asthma in young children, particularly when asthma is not adequately controlled in spite of proper routine management. Although SPT seemed to be more reliable than sIgE testing, both had suboptimal reliability. A definite decision should depend on performing a titrated oral challenge test.

Keywords; cow's milk protein allergy, Asthma, Food allergy, Immunoglobulin E.

INTRODUCTION

The most frequent chronic illnesses in children are food allergies and asthma. Since the second half of the twentieth century, the prevalence of asthma and allergy disorders such as allergic rhinitis in children has increased in several industrialised countries(1). Cow milk protein allergy is defined as a hypersensitivity reaction initiated by specific immunologic mechanism (3).

CMA refers to immune-mediated reactions to cow's milk that are categorized as immunoglobulin E (IgE)-mediated, non-IgE mediated, and mixed (IgE combined with non-IgE). This review focuses on IgE-mediated cow's milk allergy (CMA), a type I hypersensitivity reaction in which symptoms usually occur within minutes to 1 to 2 hours of ingestion. IgE antibodies to proteins in cow's milk bind to mast cells, and subsequent exposure to the protein leads to mast cell degranulation and release of mediators, including histamine. (4).

The omega-3 PUFAs linolenic acid, eicosapentaenic acid (EPA) and docosahexaenoic acid (DHA), and the omega-6 PUFAs linoleic acid and arachidonic acid, are key fatty acids; omega-3 fatty acids are generally considered to be anti-inflammatory and omega-6 fatty acids pro-inflammatory. It is thought that these molecules might influence susceptibility to allergic diseases. Indeed, in children who are allergic to cow's milk, higher levels of linoleic acid and total omega-6 PUFA levels in the blood are associated with an increased risk of atopic asthma (5)

The aim of this study is to determine the function of cow milk (CM) in causing asthma and to compare the presence of cow milk protein allergy in asthmatic and non-allergic children, as well as to prevent asthma in children.

PATIENTS AND METHODS:

This study was a case control study and was conducted in the Pulmonology Unit of the Pediatric Department at Zagazig University Hospital, with all 154 participants divided into two groups and investigated at the Medical Community and Immunology Department. Group A (77 patients) has bronchial asthma, while Group B has bronchial asthma (77 healthy control group).

Before prospective collection of patient data and after informed consent was received from patients, the work was carried out in line with the World Medical Association (Declaration of Helsinki) for studies involving humans.

Males and females of any age between the ages of 6 and 12 were eligible to participate. Asthma was identified by symptoms and a physical examination of the respiratory system. The existence of disorders other than cow milk protein allergy that could enhance the risk of asthma exacerbation, as well as the use of a systemic steroid within two weeks of the research, were both exclusion factors.

All child patients had a complete history taken, which included (chief complaint, previous medical history, pregnancy and birth history, developmental history, feeding history, and family history), a general examination of the child, which included (vital signs, weight in kilogrammes, and height in centimetres), and investigations including (complete blood picture, renal function test, liver test profile, skin prick test , total igE (serum specific igE for cow milk proteins) and respiratory function test)

Statistical analysis

IBM SPSS 23.0 for Windows (SPSS Inc., Chicago, IL, USA) and NCSS 11 for Windows were used to analyse the data (NCSS LCC., Kaysville, UT, USA). The mean and standard deviation were used to express quantitative data (SD). Frequency

and percentage were used to express qualitative data. The tests that were carried out were as follows: When comparing two means, an independent sample t-test of significance was utilised. When comparing two means of non-normally distributed data, the Mann-whitny test was used. To compare proportions between two qualitative factors, the Chi-square (X²) test of significance was applied. Fisher Exact test is a test of significance that is used in the place of chi square test in 2 by 2 tables, especially in cases of small samples. Probability (P-value): P-value <0.05 was considered significant, P-value <0.001 was considered as highly significant and P-value >0.05 was considered insignificant.

RESULTS:

In groups 1 and 2, the age varied from 6 to 11 years, with a mean \pm SD of 7.9 \pm 1.7 years in group 1 and 8.0 \pm 1.9 years in group 2, with no statistically significant difference between the two groups. In terms of gender, there was no statistically significant difference between the two groups. There was no statistically significant difference in weight or length between the two groups.

In terms of the skin pick test, there was a substantial statistical difference between the two groups (**Fig. 1**). When compared to the control group, the allergic group (group 2) had statistically significant increases in both total and specific Ig E levels (group 1) (**Fig. 2,3**).

In the allergic group (group 2), the severity of the respiratory function test was significantly higher than in the control group (group 1) (**Fig. 4**).

In terms of GIT manifestation, there was no statistically significant difference between the two groups. In terms of cutaneous and respiratory signs, there was a substantial statistical difference between the two groups (**Fig. 5**).

When it came to family history of bronchial asthma, there was a substantial statistical difference between the two groups. When it came to family history of cow milk allergy, there was a statistically significant difference between the two groups (**Fig. 6**).

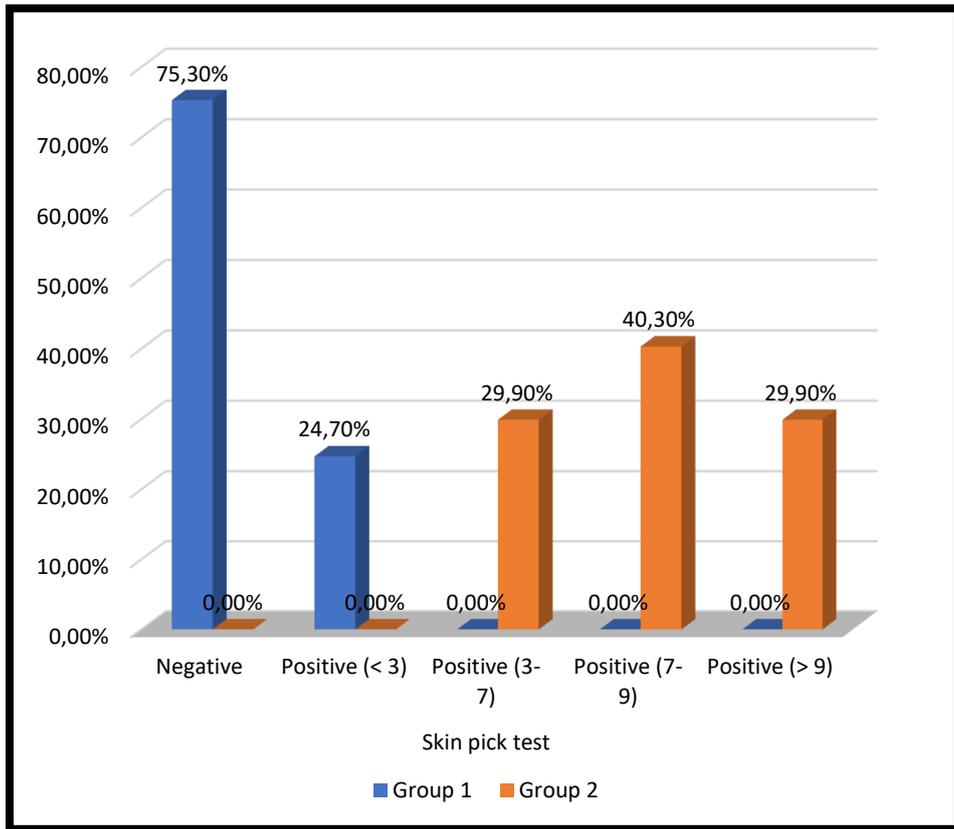


Figure (1): Bar chart showing comparison between studied groups regarding skin pick test.

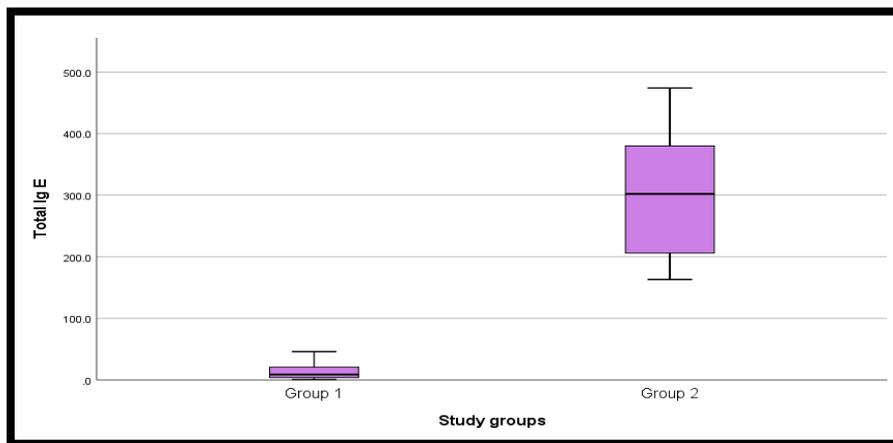


Figure (2): Boxplot showing comparison between Group 1 and Group 2 regarding total Ig E level.

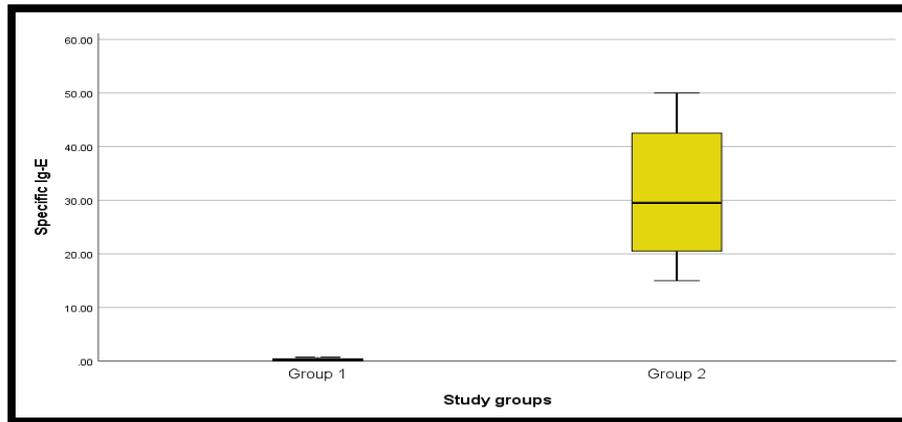


Figure (3): Boxplot showing comparison between Group 1 and Group 2 regarding specific Ig E level.

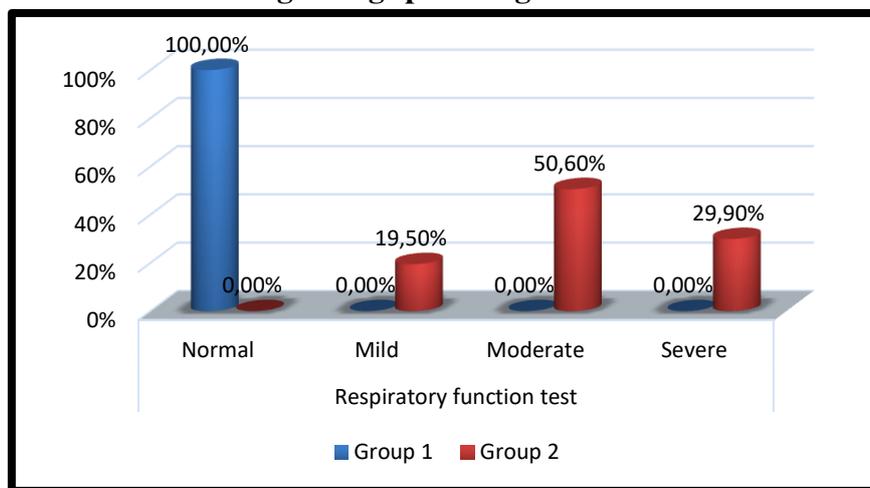


Figure (4): Bar chart showing comparison between studied groups regarding respiratory function test.

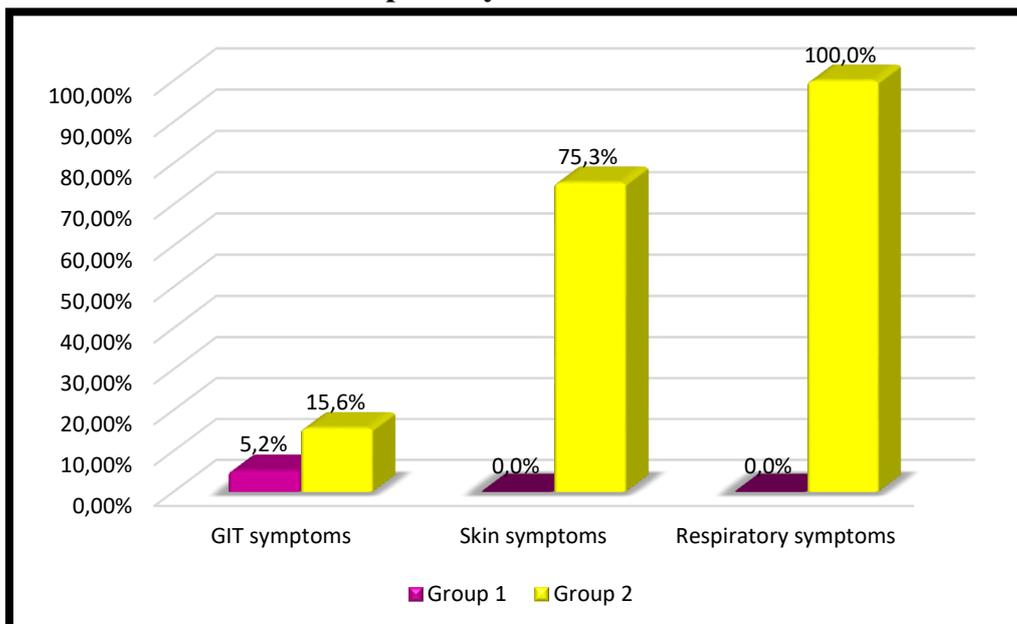


Figure (5): Bar chart showing comparison between studied groups regarding manifestations.

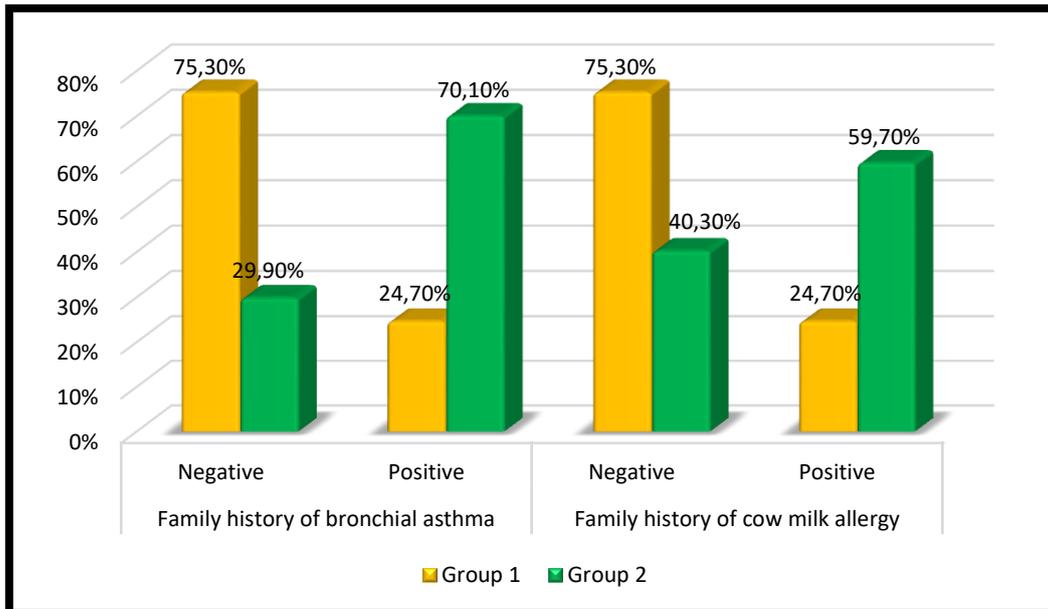


Figure (6): Bar chart showing comparison between studied groups regarding family history.

DISCUSSION:

CMA is the most common allergy in children with prevalence between 1.8% and 7.5% during the first year of life. The variability between studies may be attributable to different methods used for diagnosis, the different ages of the populations studied or to geographical factors (5).

This is particularly relevant in CMA as it may appear with a variety of clinical symptoms, many of which can be difficult to attribute to an allergic reaction, particularly in infants. In general, the frequency of self-reported adverse reactions to cow's milk proteins (CMP) is much higher than the number of medically confirmed diagnoses, not only in children but also in adults (6).

Analysis of our findings revealed that the age ranged from 6 to 11 years in group 1 and 2 with mean \pm SD= 7.9 \pm 1.7 years while the in group 2 the mean \pm SD was 8.0 \pm 1.9 years with no statistical significant difference ($p=0.924$) between the two groups. There was no statistical significant difference between the two groups as regards gender ($p=1.00$). There was no statistical significant difference between the two groups regarding weight and hight ($p=0.212$ & 0.793 respectively). **Sardecka et al.(7)** reported that the age in group 1(control group) was with mean \pm SD= 7.4 \pm 7.2 years while the in group 2(patient group) the mean \pm SD was 8.2 \pm 6.2 years with no statistical significant difference ($p=0.052$) between the two groups. There was no statistical significant difference between the two groups as regards gender ($p=0.74$).

In the current study, as regard skin pick test among the two studied groups. Skin pick test was significantly positive in patient group than control group ($p < 0.001$). In comparison with the study of **Murray et al. (8)** in which 32 children (5 months to 11 years; median 24 months; mean 34 months) with asthma and a suspected history of cow's milk allergy were studied. They underwent skin prick testing (SPT) and

specific IgE (sIgE) testing to whole cow's milk (WCM), casein, -lactalbumin, and -lactoglobulin, followed by single-blind oral milk challenge. Results: Reactions to milk challenge occurred in 12 (37.5%) including wheezing in 5 (41.7%, or 15.6% of the whole group). Children who developed wheezing at the time of challenge were younger than those who had negative challenge (23.0 months versus 34.8 months). Challenge was positive in 33.3% of subjects who had a positive SPT, and SPT was positive in 50% of challenge positive subjects.

In the study on our hands, we measured the mean and median levels of total Ig E and specific Ig E among the two studied groups. There was statistically significant increase in the levels of both total and specific Ig E ($p < 0.001$) in allergic group (group 2) compared to control group (non-allergic group). **Sandeep et al. (9)** who found that levels of IgE increased as the severity of asthma increased. In contrast, **Davila et al. (10)** showed increase of total serum IgE in both mild and moderate asthma, whereas no significant differences was found between them.

In the current study, respiratory function test was recorded among the two studied groups, There was high significant increase in the severity recorded ($p < 0.001$) in respiratory function test in allergic group (group 2) compared to control group (group 1). In comparison with the study of **Kim et al. (11)** they reported that in the asthma group, the ratio of forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) increased according to breastfeeding duration: 86.6 ± 8.7 for not breastfed group, 87.2 ± 8.6 for < 6 months group, and 88.8 ± 7.7 for ≥ 6 months group. Within asthma group, only the non-atopic subjects showed a significant increase of FEV₁/FVC, maximal mid-expiratory flow, and increase of maximal response to BD according to breastfeeding duration. Increase in FEV₁/FVC was seen in the exclusive breastfeeding for ≥ 6 months group compared with those partially breastfed .

The categorization of milk feeding behavior has not been consistent between studies and the most commonly measured lung function outcome parameter in association with duration of breast milk has been FEV₁. A more consistent association between breastfeeding and increased FVC has been observed, while MEF has been rarely assessed in previous research **(12)**.

In most children with CMPA, IgE-mediated CMPA predominates as manifested by generalized systemic reactions (anaphylaxis) or cutaneous, gastrointestinal and/or respiratory reactions along with positive skin tests and/or serum milk sIgE antibodies. Disorders involving non-IgE-mediated CMPA only occur in a subset of children and are mainly localized to the gastrointestinal tract, while skin (atopic dermatitis) and rarely respiratory tract reactions may also occur along with negativity of tests for IgE antibodies. **(13)**

In the present study, the manifestations recorded among the two studied groups revealed that there was no statistically significant difference between the two groups regarding GIT manifestation ($p = 0.292$). There was a high statistically significant difference between the two groups regarding skin and respiratory manifestations ($p < 0.001$). In **Murray et al. (8)** study on children with asthma, wheezing was the most

common symptom (in 41.7%) to milk challenge, although it was always associated with other symptoms.

CONCLUSION:

Our study showed that CMA can exacerbate the symptoms in children with asthma. Therefore, it is worth considering a possible role of food allergy in asthma in young children, particularly when asthma is not adequately controlled in spite of proper routine management. Although SPT seemed to be more reliable than sIgE testing, both had suboptimal reliability. A definite decision should depend on performing a titrated oral challenge test. However, it should also be kept in mind that currently there is no evidence-based protocol for the strategy of tolerance in most children with CMPA, and further studies are needed. Given the recently described different clinical phenotypes of food allergy, it seems necessary to adopt an individualized nutrition and treatment algorithm that is tailored to each individual's needs and medical conditions in the management of CMPA.

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