EMBJ.ORG FOR YOUNG DOCTORS

EUROMEDITERRANEAN BIOMEDICAL JOURNAL
2017,12 (30) 144–147
(*FORMERLY: CAPSULA EBURNEA*)

Original article

BLOOD LIPID LEVELS RELATED TO ALLERGIC RHINITIS: A SIGNIFICANT ASSOCIATION?

Ignazio La Mantia[1], Claudio Andaloro[1], Pasquale Gianluca Albanese[2], Attilio Varricchio[3]

1. Department of Medical Sciences, Surgical and Advanced Technologies, GF Ingrassia, University of Catania - ENT Unit, Santa Marta e Santa Venera Hospital, Acireale, Catania, Italy.

2. Department of Medical Sciences, Surgical and Advanced Technologies, GF Ingrassia, University of Catania, - ENT Unit, Policlinico "G. Rodolico" University Hospital, Catania, Italy.

3. ENT Unit, San Gennaro Hospital, ASL Na1, Naples, Italy.

ARTICLE INFO

Article history:
Received 15 May 2017
Revised 28 August 2017
Accepted 30 September 2017

Keywords:
Allergic rhinitis, dyslipidemia, cholesterol

ABSTRACT

Allergic rhinitis is a common problem increasing greatly over the past three decades. Several studies have found a possible link between dyslipidemia and allergic disease but the relating causal mechanisms remain elusive. The aim of this study is to investigate the association between blood lipid levels and the presence of allergic rhinitis.

A multicentre prospective study was carried out on 160 allergic rhinitis patients and 160 volunteers as a control according to age, gender, body mass index (BMI) values and full blood lipid profile. A possible correlation between abnormal dyslipidemia parameters and the severity of allergic rhinitis was studied too. Demographic characteristics didn't differ between groups. While levels of LDL-C, total cholesterol, as well as TC/HDL ratio and LDL/HDL ratio, were significantly higher ($p<0.001$) in patients with allergic rhinitis, there was a positive correlation between abnormal dyslipidemia parameters and moderate/severe allergic rhinitis symptomatology ($p<0.001$).

We support the hypothesis that dyslipidemia might play a role in in the manifestation of allergic rhinitis.

1. Introduction

Allergic diseases, including allergic rhinitis, asthma, and rhinoconjunctivitis, have increased greatly over the past three decades, especially in industrialized countries [1]. However, the origin of this increase is unknown [2], although the underlying pathology is attributed to an inflammatory process afflicting the nasal mucosa[3], conjunctival mucosa [4], or conducting airways [5].

The increasing incidence of allergic diseases, as populations become urbanized, suggests that factors related to a 'western lifestyle' are driving this increase [6]. In this context, special attention was paid to dietary factors which have been considered to contribute to the increment of this incidence. In fact, recently, several studies have found a possible link between allergic diseases and dietary factors [7-8].

Specifically, some authors demonstrated that excessive fat consumption and subsequent obesity, notable characteristics of the modern westernized diet pattern, are related to asthma, allergic rhinitis, and rhinoconjunctivitis [9-10].

In addition, dyslipidemia is known to potently impact the development of atopy as promotes pro-atopic Th2 immunity and allergic inflammation. Moreover, cholesterol enhances latex-specific IgE and Th2 cytokine production by mononuclear cells of patients with atopy [11-12].

Although several studies have suggested that metabolism factors are related to allergic diseases, the causal mechanisms relating to fat intake and allergic diseases remain elusive.

Few studies have concurrently analyzed this association, other than asthma, with allergic rhinitis, defined as a symptomatic disorder of the nose induced by an IgE-mediated inflammation after allergen exposure of the membranes lining the nose [13-14], or atopic dermatitis.

We speculated that cholesterol should be correlated with manifestations of atopy.

For that purpose, we investigated the association of serum lipid levels and the presence of allergic rhinitis.

* *Corresponding author*: Ignazio La Mantia, igolama@gmail.com
DOI: 10.3269/1970-5492.2017.12.30
 ISSN: 2279-7165 - Available on-line at www.embj.org

2. Material and Methods

One hundred and sixty adult patients with allergic rhinitis and the same number of volunteers as a control group, were enrolled prospectively into the study performed from July 2016 to February 2017 at the ENT Unit, Santa Marta e Santa Venera Hospital, Acireale, Catania, Italy and the ENT Unit - San Gennaro Hospital, ASL Na1, Naples, Italy, after obtaining informed written consent and the approval of the study protocol by the local ethical committee.

Allergic rhinitis was diagnosed using a screening method for the determination of allergen-specific IgE levels (ImmunoCAP, Pharmacia Diagnostics AB, Uppsala, Sweden), against the most common inhalant allergens in Italy: mixed grass pollens (gm4: *Lolium perenne* (g5), *Phleum pratense* (g6), *Secale cereale* (g12), *Holcus lanatus* (g13)), *Parietaria Judaica* (w19), *Artemisia vulgaris* (w6), *Olea europaea* (t9), *Alternaria tenuis* (m6), *Dermatophagoides pteronyssinus* (d1) and *cat epithelium* (e1). Specific IgE values of 0.35 kU/L or greater were considered indicative of aeroallergen sensitization.

Patients belonging to the allergic rhinitis group were classified according to the 4 classes of ARIA (mild intermittent, mild persistent, moderate/severe intermittent, moderate/severe persistent) and defined as having a score of 2 or more on a 0 to 3 point scale (0, no symptoms and 3, severe symptoms) with regard to sneezing, itchy nose, running nose, stuffy nose and eye symptoms [16] .

Patients with respiratory tract infection or asthma exacerbation or a serious medical illness other than rhinitis or in treatment with corticosteroids for over 3 months were excluded from the study.

Demographic characteristics were recorded and body mass index (BMI) values were calculated (weight [kg]/height^2 (m^2)] for all patients. Venous, non-fasting serum samples were obtained from all patients to determine total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C). Blood samples were collected in serum separator tubes containing silica and a gel clot (Becton, Dickinson and Company, Franklin Lakes, NJ) and thereafter centrifuged at 4 °C and stored at –70 °C until an analysis was performed on a Cobas Integra 400 (Roche, Basel, Switzerland) at the local laboratory. Triglyceride, the total, as well as HDL and LDL serum cholesterol levels, were expressed in mg/dL.

Dyslipidemia parameters were based on the criteria of the National Cholesterol Education Program Adult Treatment Panel III [15]: high TC, TC level ≥240 mg/dL, or the use of lipid-lowering drugs; high TG, TG levels ≥200 mg/dL; and low HDL-C, HDL-C level <40 mg/dL. Additionally, we defined high non-HDL-C (non-HDL-C≥160 mg/dL), high TC to HDL-C ratio (TC/HDL-C≥4), high TG to HDL-C ratio (TG/HDL-C≥3.8), and high LDL-C to HDL-C ratio (LDL-C/HDL-C≥2.5) as abnormal dyslipidemia parameters [17-18] .

Statistical analysis

A descriptive analysis of demographic and relevant clinical parameters was done. Categorical variables are presented as frequencies and proportions, while metric variables are reported as the mean and standard deviation (SD).

Differences in proportions for categorical variables across the two groups of patients are analyzed using the Pearson's χ^2 test, for metric values the independent samples t-test or the non-parametric Mann-Whitney U test were used as appropriate. Thereafter, we investigated associations between blood lipid levels and study groups using both unadjusted and adjusted logistic regression models. In the analyses of the correlation between abnormal dyslipidemia parameters and allergic rhinitis, the Pearson correlation test was used for severity. All statistical tests were performed using the STATA SE 9.2 (STATA Corp., TX) and results with P-values less than 0.05 were considered statistically significant.

3. Results

The characteristics of the patients who participated in the study are shown in Table 1. There were no differences between the two groups (patients and controls) with respect to age, gender, height, and weight. There was only a minor difference in the BMI values, which was higher in the allergic rhinitis group, but not statistically significant (p > 0.05).

Characteristics	Allergic rhinitis group N=160	Control group N=160	*P value*
Age, in years			
Mean ± SD	40.52 ± 5.12	39.89 ± 4.82	0.651
Median	35	36	-
Range	20-47	20-45	-
Gender, n(%)			
Male	84 (52.5)	79 (49.4)	0.412
Female	76 (47.5)	81 (50.6)	
Height, cm			
Mean ± SD	171.95 ± 9.26	172.43 ± 9,98	0.353
Weight, kg			
Mean ± SD	79.55 ± 12.38	72.55 ± 9.41	0.101
BMI (weight/height^2)			
Mean ± SD	27,87	22,18	0.078
ARIA, n(%)			
Mild intermittent	39 (24.4)	/	/
Moderate/Severe intermittent	59 (36.9)	/	/
Mild persistent	21 (13.1)	/	/
Moderate/Severe persistent	41 (25.6)	/	/

Table 1 - General characteristics of allergic rhinitis and control patients included in the study (N=320)

Our data suggested that the increasing levels of LDL-C (OR: 1.85; 95% CI: 1.05-3.18; p=0.013) as well as total cholesterol (OR: 4.66; 95% CI: 3.28-6.62; p<0.001), TC/HDL ratio (OR: 1.14; 95% CI: 1.09-1.15; p<0.001) and LDL/HDL ratio (OR: 3.52; 95% CI: 2.15-4.24; p<0.001) were associated with increased risk of allergic rhinitis, which persisted after confounder adjustment, whereas neither HDL-C nor triglycerides levels were associated with allergic rhinitis (Table 2).

	Allergic rhinitis group N=160	Control group N=160	Crude		Adjusted*	
			Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Total Cholesterol	247 ±19.8	169 ±11.7	4.66 (3.28-6.62)	**<0.001**	4.78 (3.29-6.68)	**<0.001**
Triglycerides	205±11.3	202 ±10.1	1.06 (0.74-1.47)	0.712	1.07 (0.77-1.51)	0.719
HDL-C	41.7±4.9	49.3 ±5.1	0.74 (0.54-1.18)	0.259	0.77 (0.56-1.19)	0.263
LDL-C	132 ±31.2	78.7±9.3	1.85 (1.05-3.18)	**0.013**	1.86 (1.07-3.19)	**0.014**
TC/HDL ratio	5.86±2.65	3.82±0.7	1.14 (1.09-1.15)	**<0.001**	1.17 (1.11-1.16)	**<0.001**
LDL/HDL ratio	3.04±1.02	1.9±0.6	3.52 (2.15-4.24)	**<0.001**	3.54 (2.16-4.25)	**<0.001**

*Adjusted for age, gender and BMI.

Table 2 - Relationship between blood lipid levels and study groups

A correlation is found between abnormal dyslipidemia parameters and the severity of allergic rhinitis. Blood lipid levels were found to be higher in patients with moderate/severe symptoms, particularly with an intermittent symptomatology (p<0.001), as compared with patients presenting mild severity (Table 3).

	Allergic rhinitis severity	P value
Abnormal dyslipidemia	Mild intermittent	0.058
	Moderate/Severe intermittent	**<0.001**
	Mild persistent	0.119
	Moderate/Severe persistent	0.021

Table 3 - Correlation between abnormal dyslipidemia parameters and severity of allergic rhinitis

4. Discussion

Our results indicate that the levels of LDL-C, total cholesterol, as well as TC/HDL ratio and LDL/HDL ratio, were significantly higher in patients with allergic rhinitis than in controls.

This concurs with the findings of Kusunoki et al [19], in which the associations of total cholesterol, LDL-C, and atopy were investigated.

Similar findings were reported by Fessler et al [20], where the increases in total cholesterol and non-HDL-C increased the risk of atopy, but this association was race specific. This finding indicates that maybe human race or diet has an effect on the association of asthma and serum lipid profiles.

Although no significant correlation was found between HDL-C or triglycerides levels and allergic rhinitis, this is in contrast with the findings of Vinding et al [21], who found that both HDL-C and triglyceride levels were associated with aeroallergen sensitization and observed trends of association with FENO values, which are higher among children with allergic airway diseases.

Previous studies have demonstrated that increases in BMI have been associated with increased prevalence of atopic disorders. Ciprandi et al [22] found BMI values to be significantly higher in patients with allergic rhinitis (P = 0.0002) or allergic asthma (P < 0.0001), compared with control subjects.

Other reports, as Sybilski et al [23], stated that there was no correlation between BMI and sensitization to aeroallergens, so a higher BMI was negatively associated with the prevalence of allergic rhinitis.

Following this last report, in our study we found higher values of BMI in the allergic rhinitis group compared to the control group but it did not reach statistical significance.

We found a statistically significant correlation between allergic rhinitis severity and abnormal dyslipidemia levels as the intensity of moderate/severe symptoms were observed more often among the rhinitis patients group compared to the mild symptomatology.

This can be explained by the mechanism of how lipoproteins take part in the pathogenesis of allergy mechanisms. In other words, dyslipidemia induces a shift toward an immunologic TH2-oriented response and then enhances allergic inflammation, which has been found in mice [24-25].

Serum cholesterol may also potentiate eosinophilic inflammation in those with genetic susceptibility for atopy, with a significant correlation between serum cholesterol and elevated inflammatory markers, such as eosinophil counts, interleukin-5, prostaglandin E 2 and monocyte chemoattractant protein-1. Authors also found that the administration of pravastatin decreased pulmonary allergic inflammation. A similar anti-inflammatory effect of statins at varying doses has been demonstrated in other animal studies indicating its therapeutic potential in asthma [26].

This study has some limitations. First, we relied only on the determination of Allergen-specific IgE levels (ImmunoCAP) for the diagnosis of AR without differentiating between AR subtypes or non –allergic rhinitis (NAR). Second, the study design does not permit us to prove if allergic manifestations preceded the rising of lipid levels as determining the relationship of causality would require a comparison over time between the two groups. We assume, however, that parameters of the fat metabolism have an impact on the occurrence of allergies and not vice versa.

5. Conclusions

In conclusion, through this study, we support the hypothesis that lipid metabolism plays a role in the manifestation of allergic rhinitis. Our findings suggest a potential role of lipoproteins in the pathogenesis of allergic status and may help to partially explain the positive association between dyslipidemia and asthma. The underlying metabolic mechanisms, however, remain to be elucidated and further, larger studies are necessary to explain these mechanistic pathways.

References

1. Schafer T, Ring J: Epidemiology of allergic diseases. Allergy 1997; 52(Suppl. 38):14-22.
2. Ring J, Kramer U, Schafer T, Behrendt H: Why are allergies increasing? Curr Opin Immunol 2001; 13:701-8.
3. La Mantia I, Andaloro C: Demographics and clinical features predictive of allergic versus non-allergic rhinitis in children aged 6–18 years: A single-center experience of 1535 patients. Int J Pediatr Otorhinolaryngol 2017; 98:103-109
4. Mishra GP, Tamboli V, Jawla J, Mitra AK: Recent patents and emerging therapeutics in the treatment of allergic conjunctivitis. Recent Pat Inflamm Allergy Drug Discov 2011; 5:26-36
5. Murdoch JR, Lloyd CM. Chronic inflammation in asthma. Mutat Res 2010; 690:24-39
6. Ring J: Allergy and modern society: does ‘‘Western Life Style’’ promote the development of allergies? Int Arch Allergy Immunol 1997; 113:7-10.
7. Tamay Z, Akcay A, Ergin A, Guler N: Dietary habits and prevalence of allergic rhinitis in 6 to 7-year-old schoolchildren in Turkey. Allergol Int 2014; 63:553-562.
8. Nwaru BI, Takkinen HM, Kaila M, Erkkola M, Ahonen S, Pekkanen J, Simell O, Veijola R, Ilonen J, Hyöty H, Knip M, Virtanen SM: Food diversity in infancy and the risk of childhood asthma and allergies. J Allergy Clin Immunol 2014; 133:1084-1091.
9. Raj D, Kabra SK, Lodha R: Childhood obesity and risk of allergy or asthma. Immunol Allergy Clin North Am 2014; 34:753-765.
10. Erdol S, Mazzucco W, Boccia S. Cost effectiveness analysis on childhood obesity primary prevention programmes: a systematic review. Epidemiology, Biostatistics and Public Health 2014; 11.3.
11. Kimata H: Cholesterol selectively enhances in vitro latex-specific IgE production in atopic dermatitis patients with latex allergy. Life Sci 2005; 76:1527-1532.
12. Gelardi M, Ciprandi G, Buttafava S, Quaranta N, Squeo V, Incorvaia C, Frati F: Nasal inflammation in Parietaria-allergic patients is associated with pollen exposure. J Investig Allergol Clin Immunol 2014; 24:352-353.
13. Marchese D, Gullo F, Gallina S, Speciale R. Profile of intranasal corticosteroids in italy: Safety, cost/effectiveness, local and systemic adverse effects. EuroMediterranean Biomedical Journal 2014;9:102-111.
14. La Mantia I, Andaloro C: Effectiveness of intranasal sodium hyaluronate in mitigating adverse effects of nasal continuous positive airway pressure therapy. Am J Rhinol Allergy. 2017 Sep 19. [Epub ahead of print]
15. Bousquet J, Neukirch F, Bousquet PJ: Severity and impairment of allergic rhinitis in patients consulting in primary care. J Allergy Clin Immunol 2006;117:158-62.
16. Expert Panel on Detection E, Treatment of High Blood Cholesterol in A. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001; 285:2486-2497.
17. Natarajan S, Glick H, Criqui M, Horowitz D, Lipsitz SR, Kinosian B: Cholesterol measures to identify and treat individuals at risk for coronary heart disease. Am J Prev Med 2003; 25:50-57.
18. Hanak V, Munoz J, Teague J, Stanley A, Bittner V: Accuracy of the triglyceride to high-density lipoprotein cholesterol ratio for prediction of the low-density lipoprotein phenotype B. Am J Cardiol 2004; 94:219-222.
19. Kusunoki T, Morimoto T, Sakuma M, Mukaida K, Yasumi T, Nishikomori R, Fujii T, Heike T: Total and low-density lipoprotein cholesterol levels are associated with atopy in schoolchildren. J Pediatr 2011; 158:334-336.
20. Fessler MB, Jaramillo R, Crockett PW, Zeldin DC: Relationship of serum cholesterol levels to atopy in the US population. Allergy. 2010; 65:859-864.
21. Vinding RK, Stokholm J, Chawes BL, Bisgaard H: Blood lipid levels associate with childhood asthma, airway obstruction, bronchial hyperresponsiveness, and aeroallergen sensitization. J Allergy Clin Immunol 2015.
22. Ciprandi G, Pistorio A, Tosca M, Ferraro MR, Cirillo I: Body mass index, respiratory function and bronchial hyperreactivity in allergic rhinitis and asthma. Respir Med 2009; 103:289-95.
23. Sybilski AJ, Raciborski F, Lipiec A, Tomaszewska A, Lusawa A, Furmańczyk K, Krzych-Fałta E, Komorowski J, Samoliński B: Obesity - a risk factor for asthma, but not for atopic dermatitis, allergic rhinitis and sensitization. Public Health Nutr 2014; 18(3):530-536.
24. Robertson AK, Zhou X, Strandvik B, Hansson GK: Severe hypercholesterolaemia leads to strong Th2 responses to an exogenous antigen. Scand J Immunol 2004; 59:285-293.
25. La Mantia I, Varricchio A, Ciprandi G: Bacteriotherapy with Streptococcus salivarius 24SMB and Streptococcus oralis 89a nasal spray for preventing recurrent acute otitis media in children: a real-life clinical experience. Int J Gen Med 2017;10:171-175
26. Ramaraju K, Krishnamurthy S, Maamidi S, Kaza AM, Balasubramaniam N: Is serum cholesterol a risk factor for asthma? Lung India 2013; 30(4):295-301