

## TYPE 1 DIABETES MELLITUS AND ATOPIC DERMATITIS - SYSTEMATIC REVIEW AND META-ANALYSIS

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received: December 12, 2011      accepted: March 07, 2012

available online: May 31, 2012

### Abstract

Both diabetes mellitus and allergic diseases presented an ascendant trend in the last years. The association between the two diseases represents an extremely discussed subject from the pathophysiological and clinical point of view, since the two diseases should exclude each other, but a unitary conclusion has not been reached yet.

**Objectives.** The aim of this study is to perform a systematic review and a meta-analysis of the existent studies regarding the association between these two pathologies. **Material and Method.** We carried out an extensive search in the international databases, where we identified 557 articles treating these subjects, but only 12 articles have analyzed the relation between type 1 diabetes and atopic dermatitis. **Results.** The meta-analysis comprised 81519 subjects and suggests that the occurrence of type 1 diabetes is protective for atopic dermatitis ( $OR=0,68$ ,  $CI=0,61-0,77$ ,  $p<0,0001$ ). **Conclusion.** Patients with type 1 diabetes have a decreased risk of atopic dermatitis occurrence.

**key words:** diabetes mellitus, atopic dermatitis, infantile eczema, atopy.

### Introduction

Both type 1 diabetes mellitus (DM 1) and atopic dermatitis (AD) represent diseases where immune system plays an important role. In DM 1 is an increased activity of Th1 lymphocytes unlike AD where is an increased activity of Th2 lymphocytes. Beginning with the specified pathogenic differences, the two diseases should mutually exclude each other. The articles which analyse the association between the two diseases are numerous, carried out in different populations, but a

unitary conclusion has not been reached yet. Our purpose is to carry out a meta-analysis and a systematic review of the studies existent in the literature.

### Material and methods

During the period November 2011 - February 2012, we carried out a search in the following databases: Medline (1967 - to present), Scopus (1966 - to present), Web of knowledge (1998 - to present). We included the studies which have been in English

language and which have analyzed the risk of occurrence of AD in patients with type 1 DM.

The searches were carried out by two independent reviewers (PM and IDA) who analyzed the titles and the abstracts of the initial studies identified in order to determine if they satisfy the selection criteria. The integral text of selected titles was extracted and the reference list of selected articles was consulted in order to find out other relevant publications.

### Data extraction

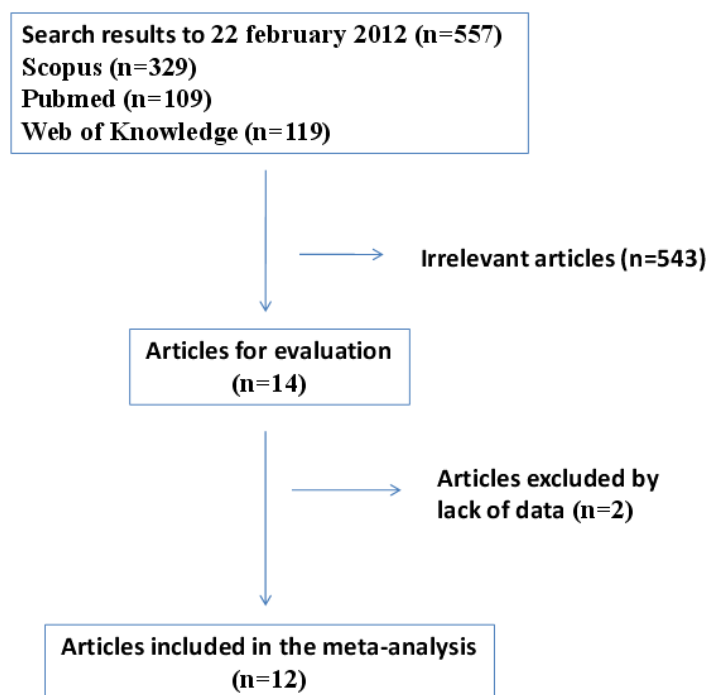
Before implementing the search strategy we decided upon the data we were interested in. The collected data included the studies features (date when the study was published, the country, study design, the number of patients with type 1 DN and AD) ([Table 1](#)).

### Statistical analysis

We evaluated the risk of occurrence of AD in patients with type 1 DM. Data collected from the found studies have been analyzed with the help of Mix 2.0.1.4. Pro (BiostatXL) software [[1](#)].

### Results

We identified 557 articles, when we used, for our search, the following keywords: „diabetes mellitus”, „atopic dermatitis”, „infantile eczema”, „atopy”. Following their selection by eliminating the abstracts, duplicates and articles not related to the subject, 14 articles left, which comprised data related to diabetes and AD.



**Figure 1.** Selection diagram of the studies.

Out of the 14 articles, one article [[2](#)] comprised data regarding gestational diabetes and risk of occurrence of AD, and one comprised data regarding type 2 diabetes

mellitus [[3](#)], reason for which these were excluded, eventually remaining 12 articles [[4-14](#)] which analyzed the risk of occurrence of AD in patients with type 1 DM ([Figure 1](#)). The

studies' features included in the meta-analysis are conveyed in [Table 1](#).

**Table 1.** Features of studies included in the meta-analysis

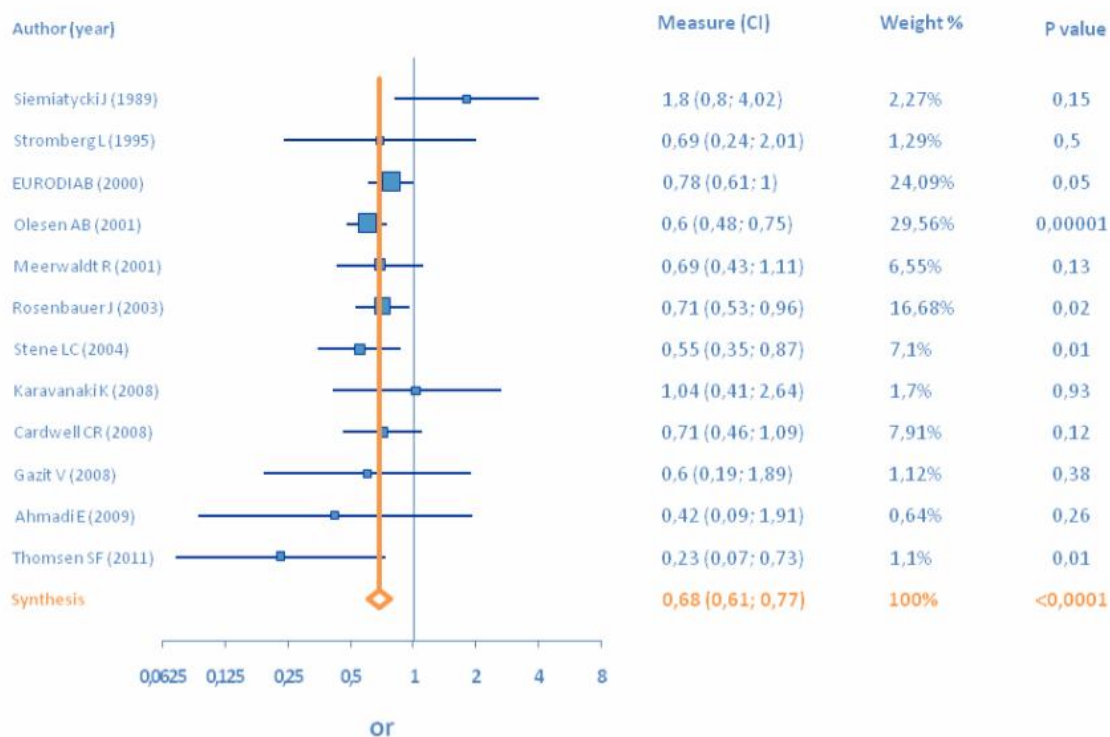
Id	Author	Journal	Year	No. of patients with type I DM	No. of patients without DM	Total number of patients in the study	Country	Design
1	Siemiatycki J	Diabetes Care	1989	161	321	482	Canada	case-control
2	Stromberg L	J Allergy Clin Immunol	1995	102	118	220	Sweden	case-control
3	EURODIAB	J Pediatr	2000	1028	2744	3772	Austria, Lithuania, Latvia, Luxembourg, England, Romania, Bulgaria	case-control
4	Olesen AB	Lancet	2001	817	7683	10652	Denmark	case-control
5	Meerwaldt R	Clin Allergy Exp	2001	188	781	969	Netherlands	case-control
6	Rosenbauer J	Diabetologia	2003	760	1871	2631	Germany	case-control
7	Stene LC	Clin Allergy Exp	2004	545	1668	2213	Norway	case-control
8	Karavanaki K	Pediatric Diabetes	2008	127	150	277	Greece	case-control
9	Cardwell CR	Pediatric Diabetes	2008	175	4859	5034	Ireland	case-control
10	Gazit V	Allergy and Clinical Immunology	2008	65	74	139	Israel	case-control
11	Ahmadi E	American Journal of Immunology	2009	150	450	600	Iran	case-control
12	Thomsen SF	Allergy	2010	143	54387	54530	Denmark	cross-sectional

Finally, the meta-analysis comprised 81519 subjects, out of which 4261 patients with type 1 DM. The result of the meta-analysis is that patients with type 1 DM present a decreased risk of occurrence of AD (OR=0,68, CI =0,61 – 0,77, p<0,0001) ([Figure 2](#)).

### Discussions

Our result is in compliance with the physiopathological theory of mutual exclusion of the two diseases due to antagonism between dominant answers either of type Th1 or Th2.

In spite of this theory, there also exist studies which show the association between immune-mediated diseases driven by Th1 and Th2 [15]. However, most of the studies included in this meta-analysis support the idea of a decreased risk for occurrence of AD in patients with type 1 DM. Only two studies sustained the contrary idea of association between type 1 DM, (mediated by Th2 lymphocytes) and AD (mediated by Th1 lymphocytes), but without statistical significance.



**Figure 2.** Meta-analysis of studies on the association between type 1 diabetes mellitus and atopic dermatitis.

### Exploration of heterogeneity and publication bias

Following the statistical analysis of heterogeneity, it results that the studies included in our meta-analysis were relatively homogenous - Q statistic (13,56;  $p=0,25$ ), I-square (18,8%; 95% CI=0,00–57,9) and a tau-square (0,012; 95% CI=0.00–0,07). Following the funnel plot type analysis, most of the studies were framed by the distribution expected in the absence of heterogeneity, except from the study of Siemiatycki J et al, whose results did not reach the statistical significance.

### Strengths and limitations of the study

The meta-analysis which we have carried out comprises the articles existent in the literature, presenting data regarding the risk of occurrence of AD in patients with type 1 DM.

Unfortunately, we have analysed only the articles existent in English language, this representing a limitation of our study.

### Conclusion

Patients with type 1 diabetes present a decreased risk of occurrence of atopic dermatitis. Moreover it seems interesting to study further the association between the two pathologies in order to understand which are the regulatory mechanisms of the immune system which will allow us to prevent the occurrence of both diseases.

**Acknowledgements:** M.P. and N.M.P. have been supported by the Sectoral Operational Programme – Human Resources Development (SOP-HRD), financed from the European Social Fund and by the Romanian Government under the contract numbers POSDRU/89/1.5/S/64331 (M.P.), respective POSDRU/89/1.5/S/64109 (N.M.P.).

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