MEDICAL SCIENCE MONITOR BASIC RESEARCH

META-ANALYSIS

eISSN 2325-4416
© Med Sci Monit Basic Res, 2016; 22: 80-86
DOI: 10.12659/MSMBR.900193

Received: 2016.06.21
Accepted: 2016.07.13
Published: 2016.08.09

Association of HLA-DRB1 Gene Polymorphism with Risk of Asthma: A Meta-Analysis

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AB Yingshui Yao
C Lijun Zhu
D Jie Li
FG Yuelong Jin
EF Lianping He

School of Public Health, Wannan Medical College, Wuhu, Anhui, P.R. China

Corresponding Author: Yingshui Yao, e-mail: yingshuiyao@163.com
Source of support: Departmental sources

Background: The relationship between HLA-DRB1 alleles and asthma is controversial. The purpose of this study was to evaluate the relationship between HLA-DRB1 alleles and risk of asthma.

Material/Methods: We searched PubMed, Chinese National Knowledge Infrastructure (CNKI), Wan Fang (Chinese) database, and Chinese Biomedical Medical databases (CBM) to find studies on the relationship between HLA-DRB1 alleles and risk of asthma. We calculated the pooled odds ratio (OR) and 95% confidence interval (CI) using STATA 12.0. Finally, a total of 24 studies were included in this meta-analysis.

Results: The results revealed that DRB1*03 was positively associated with risk of asthma (OR=1.51, 95%CI=1.27–1.80), and DRB1*15 was negatively associated with risk of asthma (OR=0.63, 95%CI=0.42–0.93), but no association was found in other HLA-DRB1 alleles. Subgroup analysis by age revealed that DRB1*03, DRB1*04, DRB1*09, and DRB1*15 were associated with asthma in children. Subgroup analysis by ethnicity showed that DRB1*03 and DRB1*15 were associated with asthma in whites, and DRB1*07 and DRB1*14 were associated with asthma in Asians.

Conclusions: This results of this meta-analysis suggest that HLA-DRB1 alleles are associated with asthma.

MeSH Keywords: Anti-Asthmatic Agents • HLA Antigens • Meta-Analysis • Polymorphism, Single Nucleotide

Full-text PDF: http://www.basic.medscimonit.com/abstract/index/idArt/900193

Indexed in: [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Background

Asthma is characterized by recurrent episodes of airway obstruction, which reverse either spontaneously or after use of medication, and is usually associated with bronchial hyper-responsiveness and evidence of chronic airway inflammation [1]. There are more than 300 million people suffering from asthma worldwide, and it occurs in all countries regardless of the level of development [2]. Asthma prevalence increased from 7.3% in 2001 to 8.4% in 2010, when 25.7 million persons had asthma in the United States [3]. Asthma can increase mortality and morbidity, and is an important public health challenge [4]. Therefore, prevention and control of asthma have great significance.

Asthma is a multifactor disease caused by interactions between genetic and environmental factors. Genetic studies have attracted much attention with the development of genome-wide association studies and genome-wide linkage studies. For example, IREB2 gene rs2568494 polymorphism has been shown to be associated with susceptibility to chronic obstructive pulmonary disease [5]. IL13 gene polymorphisms contribute to the development of pediatric asthma [6]. The human leukocyte antigen (HLA) super-locus is a genomic region in chromosome position 6p21 that encodes the 6 classical transplantation HLA genes and at least 132 protein-coding genes that have important roles in the regulation of the immune system, as well as some other fundamental molecular and cellular processes [7]. The HLA region associated with asthma is the DR *loci* [8]. Cho et al. [9] found that HLA-DRB1*07 AND HLA-DRB1*04 were associated with asthma in Korean adults. Lama et al. suggested a significantly higher frequency of HLA-DRB1*03 in asthmatics than in controls among the Indian pediatric population [10]. Kauppinen et al. [11] showed that HLA-DRB1*0101, HLA-DRB1*0301 and HLA-DRB1*0404 were associated with asthma in people with allergic asthma in Finland [11]. However, some other studies have found no statistically significant associations between HLA-DRB1 alleles and asthma [12,13].

In view of several contradictory conclusions based on small sample size studies, we performed the current meta-analysis to determine if there is an association between HLA-DRB1 alleles and asthma.

Material and Methods

Literature search

PubMed, Chinese National Knowledge Infrastructure (CNKI), Wan Fang (Chinese) databases, and Chinese Biomedical Medical databases (CBM) were searched using the search terms: 'asthma' or 'asthmatic', 'human leukocyte antigen' or 'HLA', and 'polymorphism' or 'mutation' or 'variant' or 'allele'. The date of the last search was December 10, 2015.

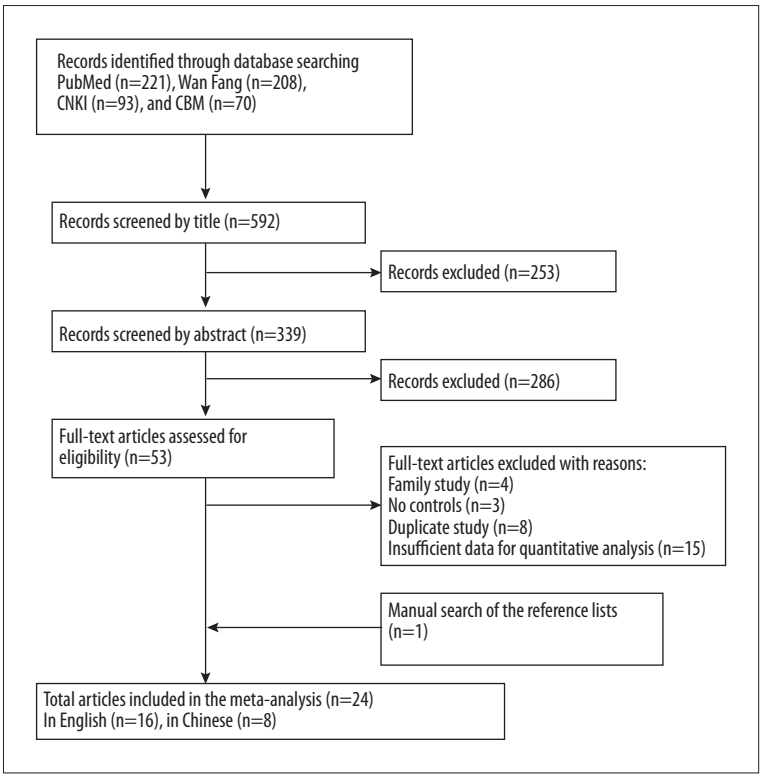

Figure 1. Flow chart of this meta-analysis.

Indexed in: [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 1. Characteristics of studies included in the meta-analysis.

First author	Year	Country (ethnicity)	Children or not	No. of DRB1 alleles studied	Detection methods	No. of cases	No. of controls
Bignon JS	1994	Italy (whites)	Not	2	PCR-SSP	56	32
Soriano JB	1997	Spain (whites)	Not	11	PCR-SSP	145	168
Cho SH	2000	Korea (Asians)	Not	11	PCR-SSP	91	98
Horne C	2000	Canada (whites)	Not	6	PCR-SSP	56	63
Mapp CE	2000	Italy (whites)	Not	2	PCR-SSP	67	128
Wang CG	2000	China (Asians)	Not	3	PCR-SSP	64	104
Li L	2003	China (Asians)	Children	9	PCR-SSOP	40	92
Choi JH	2004	Korea (Asians)	Not	3	PCR-SSP	149	91
Li CP	2005	China (Asians)	Not	3	PCR-SSP	60	30
Lu JR	2006	China (Asians)	Children	11	PCR-SSP	78	82
Juhn YJ	2007	USA (whites)	Children	2	PCR-SSP	81	231
Munthe-Kaas MC	2007	Norway (whites)	Children	7	PCR-SSOP	330	1260
Wang JW	2007	China (Asians)	Children	12	PCR-SSP	45	45
Movahedi M	2008	Iran (whites)	Children	12	PCR-SSP	112	80
Choi JH	2009	Korea (Asians)	Not	3	PCR-SSP	84	174
Ivković-Jureković I	2011	Croatia (whites)	Children	8	PCR-SSOP	143	163
Zhu SF	2011	China (Asians)	Not	2	PCR-SSP	45	46
Chen LP	2012	China (Asians)	Not	1	PCR-SSP	100	100
Kauppinen A	2012	Finland (whites)	Not	6	PCR-SSP	40	151
Dzurilla M	2013	Slovakia (whites)	Not	13	PCR-SSP	109	130
Xie QL	2013	China (Asians)	No	1	PCR-SSP	84	168
Mishra MN	2014	India (whites)	Children	13	PCR-SSP	103	152
Bottero P	2014	Italy (whites)	Not	8	PCR-SSP	159	1808
Lama M	2014	India (whites)	Children	4	PCR-SSP	105	110

Inclusion and exclusion criteria

Inclusion criteria were: cohort study or case-control; enough data available; and English or Chinese language.

Data extraction

Two reviewers (Yingshui Yao and Jie Li) selected all potential studies separately. If there was disagreement, the reviewers would solve it by discussion or judgement by a third reviewer (Lijun Zhu). The following data were extracted: first author, year of publication, country, ethnicity, age (children or not), number of HLA-DRB1 alleles studied, detection methods, and numbers of cases and controls.

Statistical analysis

The pooled OR with 95% CI was analyzed using the Z test to assess the strength of the associations between HLA-DRB1 alleles and asthma. Heterogeneity assumption was evaluated by the χ^2-based Q-test and I^2 test [14]. If $P>0.10$ (Q-test) or I^2 <50%, the fixed-effects model (the Mantel-Haenszel method) was used [15]. Otherwise, the random-effects model (the DerSimonian and Laird method) was used [16]. The Begg's rank correlation method and the Egger's linear regression method were used to assess potential publication bias [17,18]. The meta-analysis was carried out using STATA version 12.0 (Stata Corp, College Station, TX) software. $P<0.05$ meant there was statistically significant. All P values are 2-tailed.

Indexed in: [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 2. Meta-analysis of associations between HLA-DRB1 alleles and asthma.

Alleles	No. of study	Case	Control	Heterogeneity			Model	Test of association			P value for Egger's (Begg's) test
				χ^2	P value	I2(%)		OR (95%CI)	Z	P	
01	10	180/1216	306/2336	15.31	0.083	41.2	F	1.04 (0.84–1.28)	0.36	0.721	0.366 (0.210)
03	11	276/1389	607/4247	12.32	0.264	18.9	F	1.51 (1.27–1.80)	4.61	0.000	0.728 (1.000)
04	14	359/1601	839/4449	40.61	0.000	68.0	R	1.09 (0.82–1.46)	0.61	0.540	0.904 (0.913)
07	12	300/1415	774/4108	27.32	0.004	59.7	R	1.23 (0.91–1.67)	1.35	0.177	0.040 (0.115)
08	8	86/723	98/847	7.68	0.361	8.9	F	1.02 (0.74–1.41)	0.13	0.896	0.103 (1.000)
09	7	57/725	86/2530	3.38	0.760	0.0	F	1.39 (0.93–2.09)	1.59	0.111	0.575 (1.000)
10	7	44/611	47/767	6.47	0.373	7.2	F	1.23 (0.79–1.91)	0.92	0.358	0.569 (0.764)
11	11	314/1355	1238/4078	18.85	0.042	47.0	R	1.18 (0.89–1.56)	1.16	0.245	0.732 (0.876)
12	10	92/987	138/2765	9.12	0.426	1.3	F	1.18 (0.86–1.61)	1.04	0.298	0.599 (0.858)
13	10	242/1277	766/3996	12.63	0.180	28.8	F	0.93 (0.77–1.11)	0.84	0.403	0.979 (0.474)
14	9	97/819	318/2651	21.48	0.006	62.8	R	0.93 (0.57–1.54)	0.28	0.783	0.410 (0.754)
15	6	136/808	389/1832	11.91	0.036	58.0	R	0.63 (0.42–0.93)	2.31	0.021	0.762 (0.707)
16	4	42/433	63/527	0.67	0.881	0.0	F	0.74 (0.49–1.13)	1.41	0.160	0.866 (1.000)
0101	5	60/441	100/559	16.57	0.002	75.9	R	0.85 (0.39–1.83)	0.42	0.673	0.039 (0.027)
0301	6	55/477	85/521	8.31	0.140	39.8	F	0.75 (0.51–1.12)	1.42	0.156	0.404 (0.452)
0701	4	51/280	92/488	2.51	0.473	0.0	F	0.75 (0.50–1.12)	1.43	0.153	0.076 (0.308)
0901	7	112/483	129/674	35.76	0.000	83.2	R	1.23 (0.50–3.05)	0.45	0.649	0.786 (0.764)
1001	6	20/401	36/612	5.71	0.336	12.4	F	0.81 (0.46–1.43)	0.73	0.466	0.895 (1.000)
1401	4	20/264	18/326	1.97	0.578	0.0	F	1.20 (0.60–2.41)	0.51	0.608	0.868 (0.734)

Results

Characteristics of studies

We finally identified 24 studies, including 2346 cases and 5506 controls [9–12,19–38]. The retrieval process is presented in Figure 1. The characteristics of each study are shown in Table 1. Thirteen studies were conducted in whites and 12 studies were conducted in Asians. Nine studies were conducted in children. We also extracted the number of DRB1 alleles for each study.

Meta-analysis of HLA-DRB1 alleles and risk of asthma

We took 19 HLA-DRB1 alleles into consideration, including 13 HLA-DRB1 allele families and 6 HLA-DRB1-specific alleles. The detailed results of the association between HLA-DRB1 alleles and asthma are presented in Table 2.

Among the allele families, significant associations were found in HLA-DRB1*03 and HLA-DRB1*15 alleles (DRB1*03: OR=1.51, 95%CI=1.27–1.80; DRB1*15: OR=0.63, 95%CI=0.42–0.93). HLA-DRB1*03 was significantly increased the risk of asthma and HLA-DRB1*15 was associated with significantly decreased risk of asthma. No evidence of correlations was found in other allele families. Heterogeneity was observed in DRB1*04, DRB1*07, DRB1*11, DRB1*14, and DRB1*15 ($P>0.10$ or $I^2<50\%$). Thus, the random-effect model was used to analyze these alleles. Begg's and Egger's tests were carried out to estimate the publication bias, and the results showed that there was no publication bias among any of the allele families ($P>0.05$). There was no significant difference between asthma and the specific alleles (DRB1*0101, DRB1*0301, DRB1*0701, DRB1*0901, DRB1*1001, DRB1*1401). Among these specific alleles, heterogeneity was observed in DRB1*0101 and DRB1*0301 ($P>0.10$ or $I^2<50\%$). Publication bias was found in DRB1*0101 ($P<0.05$).

Subgroup analysis by ethnicity and age were carried out among allele families. For ethnicity (categorized as whites and Asians),

Indexed in: [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Table 3. Meta-analysis stratified by ethnicity and age.

Alleles	Ethnicity				Age			
	Whites		Asians		Children		Not	
	I^2 (%)	OR (95%CI)	I^2 (%)	OR (95%CI)	I^2 (%)	OR (95%CI)	I^2 (%)	OR (95%CI)
01	42.7	1.10 (0.88–1.38)	40.5	0.73 (0.42–1.26)	52.5	1.11 (0.84–1.45)	31.3	0.95 (0.69–1.32)
03	24.2	1.54 (1.28–1.84)	20.9	1.13 (0.56–2.30)	27.2	1.71 (1.37–2.14)	0.0	1.25 (0.94–1.65)
04	50.6	1.22 (0.95–1.57)	80.2	0.82 (0.34–1.95)	53.5	1.38 (1.01–1.87)	77.3	0.70 (0.39–1.24)
07	12.9	1.01 (0.82–1.23)	63.6	2.82 (1.13–7.09)	0.0	1.18 (0.92–1.50)	82.2	1.54 (0.77–3.05)
08	0.0	1.42 (0.88–2.31)	40.5	0.77 (0.50–1.20)	30.9	0.82 (0.52–1.29)	0.0	1.29 (0.81–2.05)
09	0.0	0.98 (0.37–2.57)	17.6	1.50 (0.96–2.36)	0.0	1.88 (1.08–3.27)	0.0	0.97 (0.52–1.79)
10	0.0	0.93 (0.52–1.67)	0.0	1.82 (0.91–3.62)	17.8	1.30 (0.78–2.15)	25.8	1.04 (0.42–2.60)
11	63.8	1.21 (0.87–1.67)	0.0	1.01 (0.49–2.05)	38.6	1.16 (0.80–1.68)	66.8	1.20 (0.71–2.00)
12	22.4	1.30 (0.83–2.02)	0.0	1.08 (0.70–1.66)	37.0	1.34 (0.93–1.95)	0.0	0.87 (0.49–1.54)
13	23.0	0.91 (0.75–1.10)	54.1	1.09 (0.62–1.90)	0.0	0.97 (0.76–1.23)	60.6	0.88 (0.68–1.15)
14	0.0	1.35 (0.98–1.86)	52.5	0.38 (0.15–0.96)	48.5	0.70 (0.20–2.50)	71.6	0.98 (0.54–1.79)
15	34.6	0.68 (0.50–0.93)	83.8	0.41 (0.06–2.68)	56.4	0.57 (0.37–0.87)	–	1.01 (0.56–1.82)
16	0.0	0.70 (0.44–1.12)	–	0.94 (0.36–2.45)	0.0	0.71 (0.44–1.15)	–	0.84 (0.36–1.97)

DRB1*03 significantly increased the risk of asthma and DRB1*15 significantly decreased the risk of asthma in whites. DRB1*07 significantly increased the risk of asthma and DRB1*14 significantly decreased the risk of asthma in Asians. For age (categorized as children or not), DRB1*03, DRB1*04, and DRB1*09 suggested the risk-enhancing role and DRB1*15 suggested a protective role. The detailed information of the subgroup analysis is presented in Table 3.

Discussion

Asthma is a complex heterogeneous respiratory disease. The pathogenesis of asthma involves many different cells. IgE and an imbalance between T helper cell 1 (Th1) and T helper cell 2 (Th2) are thought to play a key role in the pathogenesis of asthma [39–41]. The human major histocompatibility complex (MHC) is localized to chromosome 6p21 and is thought to play a role in regulating inflammation on T helper cells [7,42,43]. For the past 2 decades, many studies have focused on the relationship between HLA-DRB1 alleles and asthma, which may help to disclose the pathogenesis of asthma [44–48]. Use of meta-analysis could resolve the inconsistent results, which have harmful effect on false-positive and false-negative associations [49]. Thus, we performed this meta-analysis to clarify the association between HLA-DRB1 alleles and asthma.

Two alleles (DRB1*03 and DRB1*15) were found have statistically significant associations with risk of asthma among 13 HLA-DRB1 allele families. The results showed that individuals who carry HLA DRB1*03 have a 51% higher risk of asthma compared with those who do not carry this allele. Similar conclusions were reported in other studies. A study by Juhn et al. [28] found that the 12-year cumulative incidence of asthma by age among children who carry HLA DRB1*03 was 33%, compared to 24.2% among those who did not carry this allele. Lama et al. [10] demonstrated a significantly higher frequency of HLA-DRB1*03 in asthmatics than in controls. HLA DRB1 may have an effect on asthma through regulating Th1 *vs.* Th2 immune response. Murray et al. [43] showed that the interaction between T cell receptor, peptide, and major histocompatibility complex (MHC) can determine Th1/Th2 dominance through a differential T cell receptor affinity and ligand density between different MHC genes. In this study, we also found that DRB1*15 was a protective factor for asthma. A similar protective role of DRB1*15 was reported in other studies [30,37]. Although the precise mechanism of this effect is still unknown, we hypothesis that HLA-DRB1 alleles have different effects on asthma. In addition, we also examined the association between HLA-DRB1 specific alleles and asthma, but no significant difference was found between them. Because of the limited number of studies, we only chose 6 HLA-DRB1-specific alleles in this meta-analysis. These results of specific alleles still require evaluation by further studies.

Indexed in: [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

Considering ethnicity and age, we performed subgroup analysis in HLA-DRB1 allele families. DRB1*03 significantly increased the risk of asthma and DRB1*15 significantly decreased the risk of asthma in whites. DRB1*07 significantly increased the risk of asthma and DRB1*14 significantly decreased the risk of asthma in Asians. For age, DRB1*03, DRB1*04, and DRB1*09 were suggested to affect risk and DRB1*15 was suggested to have a protective role. Publication bias is another factor to consider in meta-analysis. In this meta-analysis, the Begg's rank correlation method and the Egger's linear regression method showed that there was no publication bias in any alleles except DRB1*0101.

There are some limitations to the present study that should be addressed. First, we only chose some of the HLA-DRB1-specific alleles in this study due to the scarcity of data in the literature. Second, the relationship between the HLA-DRB1 alleles and asthma did not consider confounding factors such as sex, lifestyle factors, and other risk factors. It is best to adjust these factors when conducting the studies. Third, asthma is the result of the interaction of genetic and environmental factors, but we could not extract sufficient data on these factors from the primary publications. Thus, this meta-analysis could not elucidate gene-gene and gene-environment interactions. More studies should be designed to analyze these associations in the future. Results of the present study must be interpreted cautiously in light of its limitations.

Conclusions

Despite these limitations, this meta-analysis suggests that DRB1*03 is positively associated with asthma risk and DRB1*15 is negatively associated with asthma risk. Additional studies on the association between DRB1-specific alleles and asthma are required.

Conflict of interest

The authors declare no conflict of interest.

References:

1. Martinez FD, Vercelli D: Asthma. Lancet, 2013; 382 1360–72
2. Olin JT, Wechsler ME: Asthma: Pathogenesis and novel drugs for treatment. BMJ, 2014. 349 g5517
3. Akinbami LJ, Moorman JE, Bailey C et al: Trends in asthma prevalence, health care use, and mortality in the United States, 2001–2010. NCHS Data Brief, 20121-8
4. Ali Z, Dirks CG, Ulrik CS: Long-term mortality among adults with asthma: A 25-year follow-up of 1,075 outpatients with asthma. Chest, 2013; 143: 1649–55
5. Du Y, Xue Y, Xiao W: Association of IREB2 gene rs2568494 polymorphism with risk of chronic obstructive pulmonary disease: A meta-analysis. Med Sci Monit, 2016; 22: 177–82
6. Liu Z, Li P, Wang J et al: A meta-analysis of IL-13 polymorphisms and pediatric asthma risk. Med Sci Monit, 2014; 20: 2617–23
7. Shiina T, Hosomichi K, Inoko H et al: The HLA genomic *loci* map: Expression, interaction, diversity and disease. J Hum Genet, 2009; 54: 15–39
8. Kontakioti E, Domvri K, Papakosta D et al: HLA and asthma phenotypes/endotypes: A review. Hum Immunol, 2014; 75: 930–39
9. Cho SH, Kim YK, Oh OH et al: Association of HLA-DRB1(*)07 and DRB1(*)04 to citrus red mite (*Panonychus citri*) and house dust mite sensitive asthma. Clin Exp Allergy, 2000; 30: 1568–75
10. Lama M, Chatterjee M, Chaudhuri TK: A study of the association of childhood asthma with HLA alleles in the population of Siliguri, West Bengal, India. Tissue Antigens, 2014; 84: 316–20
11. Kauppinen A, Perasaari J, Taivainen A et al: Association of HLA class II alleles with sensitization to cow dander Bos d 2, an important occupational allergen. Immunobiology, 2012; 217: 8–12
12. Dzurilla M, Vrlik M, Homolova M et al: No association between bronchial asthma and HLA-DRB1, -DQB1 alleles in the Slovak population. Bratisl Lek Listy, 2013; 114: 93–95
13. Rihs HP, Barbalho-Krolls T, Huber H et al: No evidence for the influence of HLA class II in alleles in isocyanate-induced asthma. Am J Ind Med, 1997; 32: 522–27
14. Higgins JP, Thompson SG: Quantifying heterogeneity in a meta-analysis. Stat Med, 2002; 21: 1539–58
15. Mantel N, Haenszel W: Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst, 1959; 22: 719–48
16. Rogers WJ: What is the optimal tool to define appropriate therapy: The randomized clinical trial, meta-analysis, or outcomes research? Commentary. Curr Opin Cardiol, 1994; 9: 401–3
17. Begg CB, Mazumdar M: Operating characteristics of a rank correlation test for publication bias. Biometrics, 1994; 50: 1088–101
18. Egger M, Davey Smith G, Schneider M et al: Bias in meta-analysis detected by a simple, graphical test. BMJ, 1997; 315: 629–34
19. Bignon JS, Aron Y, Ju LY et al: HLA class II alleles in isocyanate-induced asthma. Am J Respir Crit Care Med, 1994; 149: 71–75
20. Soriano JB, Ercilla G, Sunyer J et al: HLA class II genes in soybean epidemic asthma patients. Am J Respir Crit Care Med, 1997; 156: 1394–98
21. Horne C, Quintana PJ, Keown PA et al: Distribution of DRB1 and DQB1 HLA class II alleles in occupational asthma due to western red cedar. Eur Respir J, 2000; 15: 911–14
22. Mapp CE, Beghe B, Balboni A et al: Association between HLA genes and susceptibility to toluene diisocyanate-induced asthma. Clin Exp Allergy, 2000; 30: 651–56
23. Chunfang M, Runfang G: Study of HLA-DRB1 allele in bronchial asthma. Shanxi Clin Med, 2000; 9: 417–19
24. Lin L, Lanfang C, Ticheng G et al: Study on gene frquency of HLA-DRB1 expression in children with mycoplasma pneumonia and bronchial. Journal of Clinical Pediatrics, 2003; 21: 29–31
25. Choi JH, Lee KW, Oh HB et al: HLA association in aspirin-intolerant asthma: DPB1*0301 as a strong marker in a Korean population. J Allergy Clin Immunol, 2004; 113: 562–64
26. Chaopin L, Qinggui Y, Li T: Relationship between HLA-DRB1 gene and acarian asthma. Acta Universitatis Medicinalis Anhui, 2003; 40: 244–46
27. Jirong L, Lixin J, Chengxun W: A study of correlation between childhood asthma and HLA. Journal of Clinical Pediatrics, 2006; 24: 16–24
28. Juhn YJ, Kita H, Lee LA et al: Childhood asthma and human leukocyte antigen type. Tissue Antigens, 2007; 69: 38–46
29. Munthe-Kaas MC, Carlsen KL, Carlsen KH et al: HLA Dr-Dq haplotypes and the TNFA-308 polymorphism: Associations with asthma and allergy. Allergy, 2007; 62: 991–98
30. Jiawei W, Gesheng W, Licheng D et al: [Immunogenetic analysis of leukocyte antigen DRB1 and DQB1 in childhood asthma.] Zhejiang Practical Medicine, 2007; 12: 240–41 [in Chinese]

Indexed in: [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]

31. Movahedi M, Moin M, Gharagozlou M et al: Association of HLA class II alleles with childhood asthma and Total IgE levels. Iran J Allergy Asthma Immunol, 2008; 7: 215–20
32. Choi JH, Lee KW, Kim CW et al: The HLA DRB1*1501-DQB1*0602-DPB1*0501 haplotype is a risk factor for toluene diisocyanate-induced occupational asthma. Int Arch Allergy Immunol, 2009; 150: 156–63
33. Ivkovic-Jurekovic I, Zunec R, Balog V et al: The distribution of HLA alleles among children with atopic asthma in Croatia. Coll Antropol, 2011; 35: 1243–49
34. Shufen Z: [Association between Human Leukocyte antigen DRB1(HLA-DRB1) gene polymorphisms and Cough variant.] Journal of Clinical Pulmonary Medicine, 2011; 16: 371–73 [in Chinese]
35. Liping C, Hong X, Jingmei L et al: [Association between Human Leukocyte antigen-DRB1 allele and asthma.] Chinese Journal of Practical Internal Medicine, 2012; 32: 956–57 [in Chinese]
36. Qinglin X, Hong Z, Ling Q et al: Study on the association between Human Leukocyte antigen gene-DR and -G polymorphisms and children. Chinese Journal of New Clinical Medicine, 2013; 6: 109–11
37. Mishra MN, Dudeja P, Gupta RK: Association of HLA-Class II and IgE serum levels in pediatric asthma. Iran J Immunol, 2014; 11: 21–28
38. Bottero P, Motta F, Bonini M et al: Can HLA-DRB4 Help to Identify Asthmatic Patients at Risk of Churg-Strauss Syndrome? ISRN Rheumatol, 2014; 2014: 843804
39. Kim Y, Lee S, Kim YS et al: Regulation of Th1/Th2 cells in asthma development: a mathematical model. Math Biosci Eng, 2013; 10: 1095–133
40. Brand S, Kesper DA, Teich R et al: DNA methylation of TH1/TH2 cytokine genes affects sensitization and progress of experimental asthma. J Allergy Clin Immunol, 2012; 129: 1602–10e6
41. Arroyave WD, Rabito FA, Carlson JC: The relationship between a specific IgE level and asthma outcomes: results from the 2005–2006 National Health and Nutrition Examination Survey. J Allergy Clin Immunol Pract, 2013; 1: 501–8
42. Lin KL, Hsieh KH, Huang JH et al: Major histocompatibility complex (MHC) class II restriction, lymphokine production, and IgE regulation of house dust mite-specific T-cell clones. J Clin Immunol, 1992; 12: 271–80
43. Murray JS: How the MHC selects Th1/Th2 immunity. Immunol Today, 1998; 19: 157–63
44. Knutsen AP, Vijay HM, Kariuki B et al: Association of IL-4RA single nucleotide polymorphisms, HLA-DR and HLA-DQ in children with Alternaria-sensitive moderate-severe asthma. Clin Mol Allergy, 2010; 8: 5
45. Martyn MB, Molis W, Jacobson RM et al: Human leukocyte antigen type and progression from onset of symptoms to development of asthma. Allergy Asthma Proc, 2010; 31: 120–25
46. Hanchard NA, Jacobson RM, Poland GA et al: An assessment of the association between childhood asthma and HLA DRB1*03 using extended haplotype analysis. Tissue Antigens, 2010; 76: 491–94
47. Smit LA, Strachan DP, Vermeulen R et al: Human leukocyte antigen class II variants and adult-onset asthma: Does occupational allergen exposure play a role? Eur Respir J, 2014; 44: 1234–42
48. Muro M, Mondejar-Lopez P, Moya-Quiles MR et al: HLA-DRB1 and HLA-DQB1 genes on susceptibility to and protection from allergic bronchopulmonary aspergillosis in patients with cystic fibrosis. Microbiol Immunol, 2013; 57: 193–97
49. Wang J, Pan HF, Hu YT et al: Polymorphism of IL-8 in 251 allele and gastric cancer susceptibility: A meta-analysis. Dig Dis Sci, 2010; 55: 1818–23

Indexed in: [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS] [Index Copernicus]