Association of glutathione *S*-transferase M1 and T1 genotypes with asthma
A meta-analysis

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Abstract

Background: We performed an updated meta-analysis to clarify the relationship between glutathione *S*-transferase Mu and theta (GSTM1 and GSTT1, respectively) null/positive genotypes and asthma.

Methods: We performed a literature search using PubMed and Web of Science databases in August 2019. Pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to assess the role of GSTM1 and GSTT1 genotypes in the risk of asthma.

Results: Overall, we found a significant association with asthma risk in the general population for both the GSTM1 genotype (OR = 1.21; 95% CI: 1.07–1.35; $P < .001$; $I^2 = 69.5\%$) and the GSTT1 genotype (OR = 1.61; 95% CI: 1.30–2.00; $P < .001$; $I^2 = 83.6\%$). Moreover, significant associations between both genotypes and asthma risk were also found by age stratification. Furthermore, for GSTM1 we found significant associations in populations living in Asia, Europe, and Russia, but not in Africa. Conversely, for GSTT1, we found a significantly increased risk in populations living in Asia, Europe, Africa, and Russia. In addition, a significant association was found for both genotypes with a sample size <500, but not a sample size >2000.

Conclusion: Our meta-analysis provides evidence that GSTM1 and GSTT1 genotypes could be used as asthma-associated biomarkers.

Abbreviations: CI = confidence interval, GSTM1 = glutathione *S*-transferase M1, GSTs = glutathione *S*-transferases, GSTT1 = glutathione *S*-transferase T1, OR = odds ratio, ROS = reactive oxygen species.

Keywords: asthma, glutathione *S*-transferase M1, glutathione *S*-transferase T1, meta-analysis

1. Introduction

Glutathione *S*-transferases (GSTs) are a family of enzymes with an essential role in cells, such as the conjugation and detoxification of toxic or carcinogenic compounds like reactive oxygen species (ROS).[1] Polymorphisms in GSTs can lead to a decreased enzymatic function and inadequate detoxification of ROS might modulate the susceptibility to asthma.[2] Biopsies of the colonic mucosa of asthma patients showed an increased ROS production compared with healthy controls.[3] A reduced enzymatic function of GSTs coupled with impaired scavenging of ROS can contribute to a state of oxidative stress, which can trigger the onset of asthma.[4]

Human GSTs can be divided into 4 main classes: GST Alpha (GSTA), GST Mu (GSTM1), GST Pi (GSTP1), and GST Theta (GSTT1). For GSTM1, 3 alleles have been described so far. In particular, GSTM1*0 is characterized by gene deletion, leading to a nonfunctional protein. In the past decade, an increasing number of studies have been conducted to explore the associations between GSTM1 and GSTT1 null genotypes and the susceptibility to asthma in different populations. However, the role of GSTM1 and GSTT1 null genotypes in the progression of asthma is controversial.

In this study, we performed an updated meta-analysis to clarify the relationship between GSTM1 and GSTT1 null/positive genotypes with asthma.

2. Methods

2.1. Literature search, selection, and data collection

This meta-analysis included papers investigating the association between asthma risk and GSTM1 and GSTT1 null/positive genotypes that were published on PubMed and Web of Science [Information sources] between January 2000 and August 2019 [Protocol and registration]. The following search terms were used: asthma, asthmatic, GSTM1, GSTT1, polymorphism, mutation, and variant [Search]. Studies that met the following criteria were included: should include investigation on the asthma risk with either GSTM1 or GSTT1 null/positive genotypes; is a case–control study with an appropriate control group; genotype

distributions of both cases and controls need to be available for estimating the odds ratio (OR) with a 95% confidence interval (CI) and the *P*-value [Eligibility criteria, Study selection]. Data abstraction and analysis were performed by 2 different researchers (XS and YR) and reported on standardized forms including the first 3 authors, year of publication, country of origin, ethnicity, age, sample size, asthma definition, genotyping method, and genotype number in cases and controls [Data collection process, Data items]. Genotype distributions for both cases and controls were assessed as outcome measures. Additional subgroup analyses were performed in an attempt to gain more insight into the parameters or conditions that might improve the outcome in future studies [Data collection process, Data items]. The subgroup analyses were conducted including ethnicity, age, and sample size [Data collection process, Data items, Additional analyses].

This study was approved by the Ethic Committee of the First Affiliated Hospital of China Medical University.

2.2. Data analysis

For the meta-analysis, pooled ORs and 95% CIs were calculated using either the fixed effects model or the random-effects model. The chosen model was based on the results of a heterogeneity test, an Chi-squared-based *Q* test, as previously reported.[5] If the *Q* test reported a *P* value >.1, a fixed-effects model was used according to the Mantel–Haenszel method; otherwise, a random-effects model was used according to the DerSimonian and Laird method [Summary measures, Synthesis of results].

Publication bias was tested using Begg funnel plot and Egger test.[6] Publication bias was confirmed if the funnel plot was asymmetric and Egger test reported a *P* value <.05 [Risk of bias in individual studies, Risk of bias across studies].

All the statistical analyses were performed using Stata, version 12.0 (Stata Corporation, College Station, TX) and Comprehensive Meta-Analysis, version 2.0 (Englewood, NJ).

3. Results

3.1. Characteristics of the studies included in the meta-analysis

We performed a final search on August 31, 2019, which resulted in 292 articles. The majority of the articles were excluded for the following reasons: wrong type of study, animal studies, article duplication, review, or commentary articles. Of the remaining 45 articles, a total of 41 case–control studies[7–37] met the inclusion criteria and were included in the meta-analysis (Fig. 1).
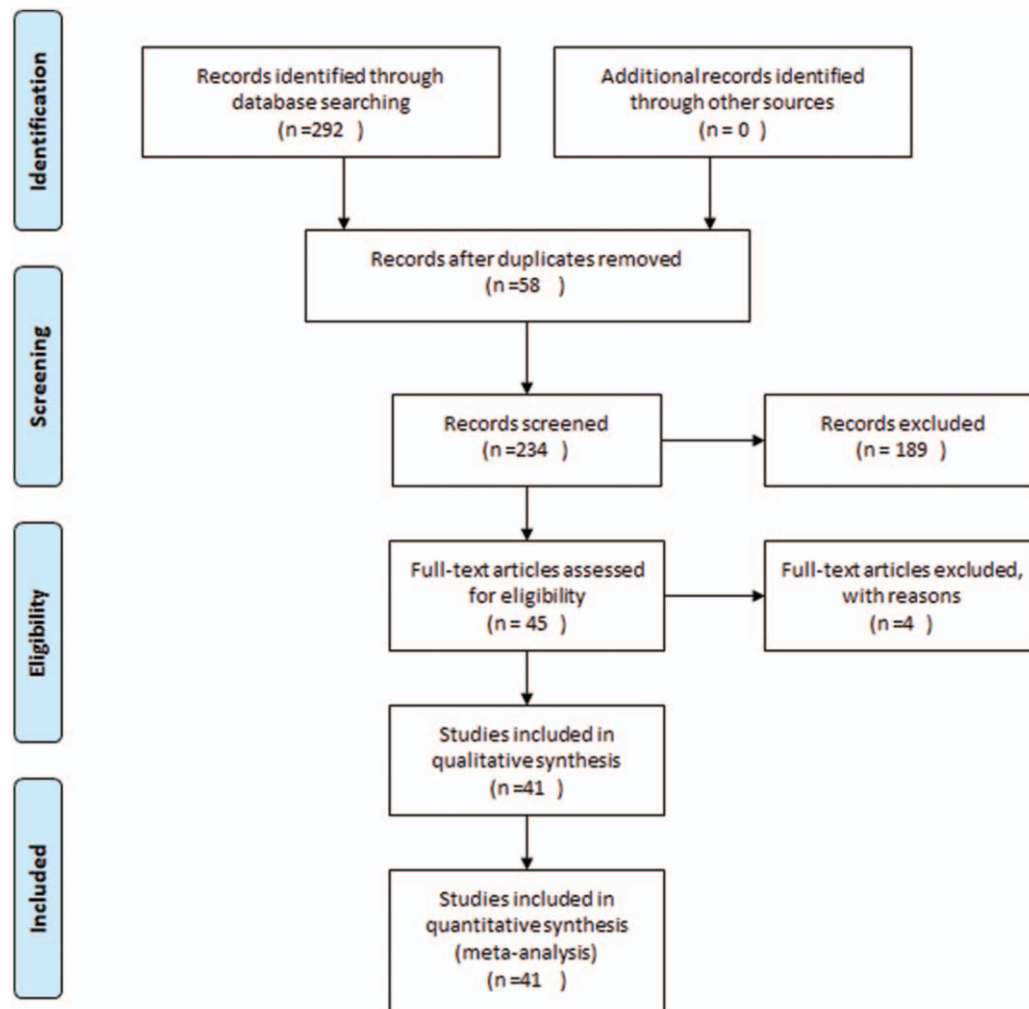

Figure 1. Flow diagram of study inclusion.

Table 1

Characteristics of included studies.

	First author	Year	Country	Ethnicity	Case age, yrs	Asthma definition	Genotyping method	GSTM1 (null/present) Cases null	Cases present	Controls null	Controls present	GSTT1 (null/present) Cases null	Cases present	Controls null	Controls present
[1]	Arbag H[13]	2006	Turkey	Asia	Adults (36.37 ± 14.17)	Diagnosed by a physician	PCR	12	19	47	55	11	20	24	78
[2]	Babusikova E[14]	2009	Slovakia	Europe	Children (12 ± 0.3)	GINA criteria	PCR	NA	NA	NA	NA	45	156	2	22
[3]	Birbian N[15]	2012	India	Asia	Adults (38.11 ± 16.20)	Diagnosed by a physician	PCR	191	219	163	251	164	246	55	359
[4]	Castro-Giner F[2]	2009	Sweden, UK, Spain, Germany, France and Belgium	Europe	Adults (20–44)	Based on a questionnaire	PCR	152	175	996	1254	69	258	385	1865
[5]	Chung HW[16]	2002	Korea	Asia	Not available	According to symptom	PCR	16	17	31	35	24	45	15	42
[6]	Ebrahimi M[38]	2004	Ukraine	Europe	Adults (44.68 ± 1.22)	Diagnosed by a physician.	Multiplex PCR	39	56	128	125	25	70	36	217
[7]	El-Aal AAA[38]	2012	Egypt	Africa	Children (5–14)	GINA criteria	Multiplex PCR	12	32	11	19	26	18	4	26
[8]	El Rifai N[8]	2014	Egypt	Africa	Children (7.65 ± 1.916)	GINA guidelines criteria	PCR	33	34	14	13	59	8	23	4
[9]	Ercan H[17]	2006	Turkey	Asia	Children (8.1–13.2)	Diagnosed by a physician	PCR	124	179	100	151	64	246	48	202
[10]	Fedorova I[18]	2009	Russia	Asia	Children (1–18)	Based on clinical and laboratory data	PCR	35	47	53	49	13	69	22	80
[11]	Freidin MB[19]	2002	Russia	Asia	Not available	Diagnosed by a physician	PCR	52	17	42	15	NA	NA	NA	NA
[12]	Fryer AA[20]	2000	UK	Europe	Adults (36.1 ± 11.4)	Diagnosed by a physician	PCR	72	53	24	20	24	103	7	37
[13]	Gravina P[21]	2009	Italy	Europe	Children	GINA criteria	PCR	31	15	30	27	31	15	30	27
[14]	Hanene C[22]	2007	Tunisia	Africa	Children (5–16)	Diagnosed by questionnaire categories	PCR	84	37	111	115	41	80	67	159
[15]	Hersoug LG[38]	2012	Denmark	Europe	Adults (18–69)	Asthma diagnosis was based on a self-administered questionnaire	PCR	186	173	892	832	54	301	246	1468
[16]	Holla LI[23]	2006	Czech	Europe	Both (27.9 ± 13.5)	GINA criteria	PCR	166	140	166	165	59	247	73	258
[17]	Imboden M	2008	Switzerland	Europe	Adults (18–60)	Asthma diagnosis was based on a self-report of physician-diagnosed asthma	TaqMan PCR	124	132	1995	1802	41	215	707	3090
[18]	Ivaschenko TE[24]	2002	Russia	Europe	Both	According to symptom	PCR-RFLP	83	26	43	23	73	36	21	45
[19]	Kabesch M[38]	2004	Germany	Europe	Children (9–11)	ISAAC questionnaire	PCR	148	120	382	355	42	226	120	617
[20]	Kamada F[38]	2007	Japan	Asia	Children (4–18)	American Thoracic Society criteria	PCR	57	57	95	80	NA	NA	NA	NA
[21]	Kamada F[25]	2007	Japan	Asia	Both (4–75)	American Thoracic Society criteria	PCR	178	189	326	287	52	74	59	108
[22]	Karam RA[9]	2012	Egypt	Africa	Children (9.8 ± 2.8)	American Thoracic Society Statement	PCR	80	46	78	90	NA	NA	60	NA
[23]	Lee YL[26]	2005	china	Asia	Children (11.9 ± 1.5)	Diagnosed by a physician	PCR	49	33	97	87	NA	NA	NA	NA
[24]	Li YF[38]	2009	Taiwan	Asia	Children (6–12)	modified from the Chinese translated version of ISAAC core questionnaire	Taqman-PCR	101	114	448	429	NA	NA	NA	NA
[25]	Lima CS[27]	2010	Brazil	Latin America	Children (7–17)	GINA criteria	PCR	52	34	104	154	14	72	45	213
[26]	Mak JC[28]	2007	China	Asia	Adults (42.6 ± 15.4)	According to symptom	PCR-RFLP	161	150	185	130	144	167	168	147
[27]	Ozcan C	2010	Turkey, South region	Asia	Adults (44.14 ± 8.73)	NA	Real time PCR	7	15	75	92	8	14	25	142
[28]	Piacentini S[29]	2010	Italy	Europe	Adults (47.53 ± 2.05)	Global Initiative on Asthma criteria	PCR-RFLP	46	18	35	32	34	30	16	51
[29]	Piacentini S[30]	2012	Italy	Europe	Adults 52.4 (1.2)	GINA criteria	PCR	109	90	101	99	72	127	59	141
[30]	Piacentini S[31]	2012	Italy	Europe	Children	GINA criteria	PCR	81	46	62	64	29	98	26	100
[31]	Polonikov AV[38]	2009	Russia, Central Russia	Europe	Adults (43.3 ± 11.4)	Diagnosed by a physician on the basis of characteristic symptoms (i.e., reversibility of airway obstruction, airway hyperresponsiveness to methacholine)	PCR-RFLP	114	101	106	108	30	185	30	184
[32]	Saadat M[32]	2004	Iran	Asia	Adults (38.7 ± 14.7)	Diagnosed by a physician	PCR	42	43	20	65	55	30	35	50
[33]	Salam MT[38]	2007	USA	American	Children (10–16)	Asthma diagnosis was based on parental report of physician-diagnosed asthma	Real time PCR	589	558	1266	1300	232	915	537	1989
[34]	Sideleva O[33]	2002	Russia	Europe	Both (1–65)	Diagnosed by a physician	PCR	83	26	43	47	73	36	21	69
[35]	Tamer L[34]	2004	Turkey	Asia	Adults (45.53 ± 1.85)	Diagnosed by a physician	PCR	64	37	42	61	27	74	25	78
[36]	Tatarskyy P[35]	2011	Ukraine	Europe	Children	ND	PCR-RFLP	54	60	47	39	54	60	47	39
[37]	Undarmaa S[38]	2010	Japan	Asia	Adults (45 [16–83])	American Thoracic Society criteria Group or the ISAAC questionnaire	PCR	194	165	331	293	NA	NA	NA	NA
[38]	Undarmaa S[38]	2010	Japan	Asia	Children (9.9 [4–15])	American Thoracic Society criteria Group or the ISAAC questionnaire	PCR	152	168	164	172				
[39]	Vavilin VA[36]	2002	Russia	Europe	Children	Diagnosed by a physician	PCR	52	48	44	60	26	74	12	92
[40]	Wang JJ[10]	2017	China	Asia	Children	ISAAC questionnaire and GINA Guidelines 2015	Taqman SNP PCR	58	68	124	203	NA	NA	NA	NA
[41]	Wu CC[11]	2014	China	Asia	Children (6)	Diagnosed by a physician	Multiplex PCR	77	61	347	244	NA	NA	NA	NA
[42]	Yucesoy B[38]	2012	Canada	Caucasian French-Canadians	Adults (42.4 ± 1.2)	Specific inhalation challenge	PCR	47	48	55	61	23	72	17	99
[43]	Zhang YQ[37]	2004	China	Asia	Adults (15–78)	Bronchial asthma diagnostic criteria	PCR	49	11	18	42	43	17	7	53

GINA = Global Initiative on Asthma, ISAAC = International Study of Asthma and Allergies in Childhood, NA = not available, ND = no data, PCR = polymerase chain reaction, RFLP = restriction fragment length polymorphism.

Characteristics and genotype distribution of each included study are shown in Table 1.

3.2. Meta-analysis results

The meta-analysis of the association between GSTM1 and GSTT1 null/positive genotypes with asthma risk is summarized in Figures 2–4. When we pooled all groups, we chose the random effects model since we found statistically significant heterogeneity.

3.3. Analysis of the overall population

For the GSTM1 null/positive genotypes, 40 studies with a total of 7733 cases and 18,986 controls were included in the meta-analysis. For the GSTT1 null/positive genotype, 34 studies with a total of 6185 cases and 15,166 controls were included. The pooled results showed a significant association for both the GSTM1 genotypes (OR = 1.21; 95% CI: 1.07–1.35; $P < .001$; $I^2 = 69.5\%$) and GSTT1 genotypes (OR = 1.61; 95% CI: 1.30–2.00; $P < .001$; $I^2 = 83.6\%$) and asthma risk in the overall population.

3.4. Subgroup analysis by age

In the subgroup analysis by age, we found a significantly increased risk of asthma for GSTM1 in children (OR = 1.18; 95% CI: 1.02–1.37; $P = .000$; $I^2 = 59.6\%$), adults (OR = 1.22; 95% CI: 0.99–1.49; $P = .000$; $I^2 = 76.5\%$), and in the studies with both types of patients (OR = 1.46; 95% CI: 0.86–2.50; $P = .000$; $I^2 = 85.3\%$), but not in the studies with nonavailable related information (OR = 1.08; 95% CI: 0.60–1.93; $P = .963$; $I^2 = 0.0\%$) (Fig. 2A). Regarding GSTT1, we found a significant association in children (OR = 1.19; 95% CI: 0.95–1.48; $P = .008$; $I^2 = 54.3\%$), adults (OR = 1.79; 95% CI: 1.27–2.51; $P < .001$; $I^2 = 86.8\%$), and in the studies with both types of patients (OR = 2.85; 95% CI: 0.71–11.42; $P < .001$; $I^2 = 94.8\%$) (Fig. 2B).

3.5. Subgroup analysis by ethnicity

Since Russia stretches across Europe and Asia, it was considered an independent ethnic group for the present meta-analysis. Based on the subgroup analysis by ethnicity, we found a significant association between GSTM1 and asthma risk in populations living in Asia (OR = 1.17; 95% CI: 0.95–1.43; $P < .001$; $I^2 = 76.1\%$), Europe (OR = 1.09; 95% CI: 0.94–1.27; $P = .045$; $I^2 = 45.0\%$), and Russia (OR = 1.40; 95% CI: 0.92–2.13; $P = .007$; $I^2 = 68.9\%$). We found no significant association in Africa (OR = 1.50; 95% CI: 0.88–2.53; $P = .05$; $I^2 = 61.6\%$) and North America (OR = 1.08; 95% CI: 0.95–1.24; $P = .995$; $I^2 = 0.0\%$) (Fig. 3A). Regarding GSTT1, we found a significantly increased risk of asthma in Asia (OR = 2.19; 95% CI: 1.20–4.02; $P < .001$; $I^2 = 90.9\%$), Europe (OR = 1.21; 95% CI: 0.98–1.48; $P = .007$; $I^2 = 55.9\%$), Africa (OR = 1.77; 95% CI: 0.91–3.46; $P = .019$; $I^2 = 70.0\%$), and Russia (OR = 2.22; 95% CI: 0.95–5.22; $P < .001$; $I^2 = 88.1\%$), but not North America (OR = 1.21; 95% CI: 0.63–2.32; $P = .062$; $I^2 = 71.3\%$) (Fig. 3B).

3.6. Subgroup analysis by sample size

Based on the subgroup analysis by ethnicity, we found a significant association between GSTM1 and asthma risk for a study sample size <500 (OR = 1.42; 95% CI: 1.16–1.75; $P < .001$; $I^2 = 70.2\%$), while we found no significant association for a sample size between 500 and 2000 (OR = 0.99; 95% CI: 0.89–1.11; $P = .153$; $I^2 = 22.0\%$) and >2000 (OR = 1.03; 95% CI: 0.93–1.14; $P = .381$; $I^2 = 2.3\%$) (Fig. 4A). Regarding GSTT1, we found a significantly increased risk of asthma for a sample size <500 (OR = 1.93; 95% CI: 1.46–2.55; $P < .001$; $I^2 = 75.4\%$) and a sample size between 500 and 2000 (OR = 1.24; 95% CI: 0.64–2.41; $P < .001$; $I^2 = 94.0\%$), but not a sample size >2000 (OR = 1.02; 95% CI: 0.85–1.21; $P = .181$; $I^2 = 38.5\%$) (Fig. 4B).

3.7. Publication bias

Publication bias was assessed using Begg funnel plot and Egger test. We detected a significant publication bias for the GSTM1
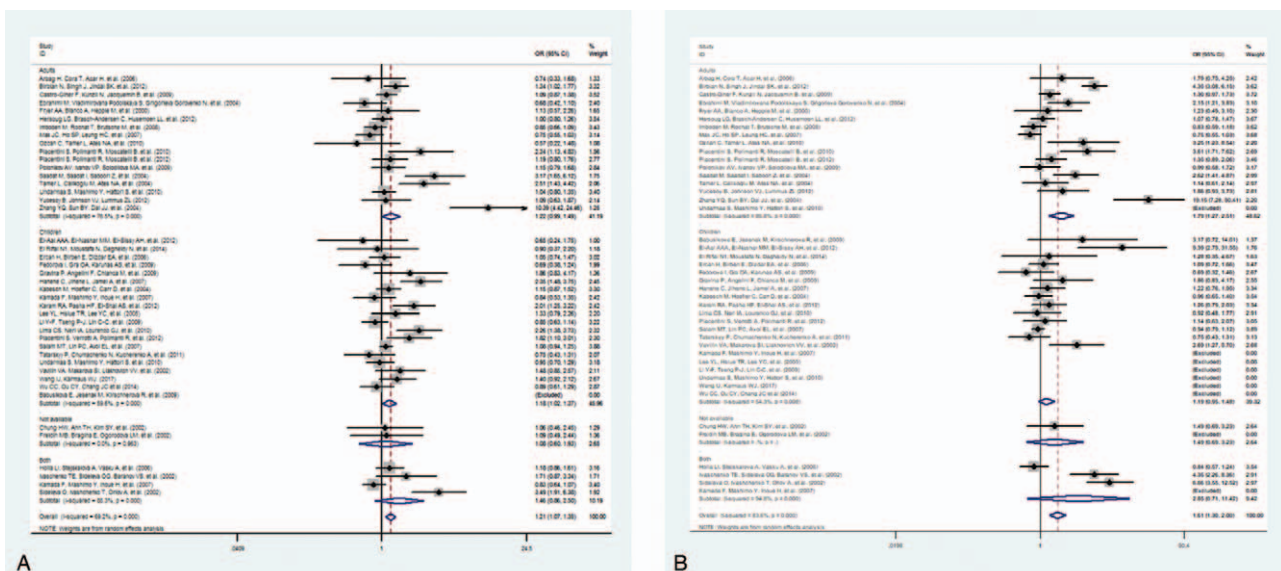

Figure 2. Meta-analysis of glutathione *S*-transferase M1 null/positive (A) and glutathione *S*-transferase T1 null/positive (B) genotypes correlation with asthma after stratified analysis by age. CI = confidence interval, OR = odds ratio.
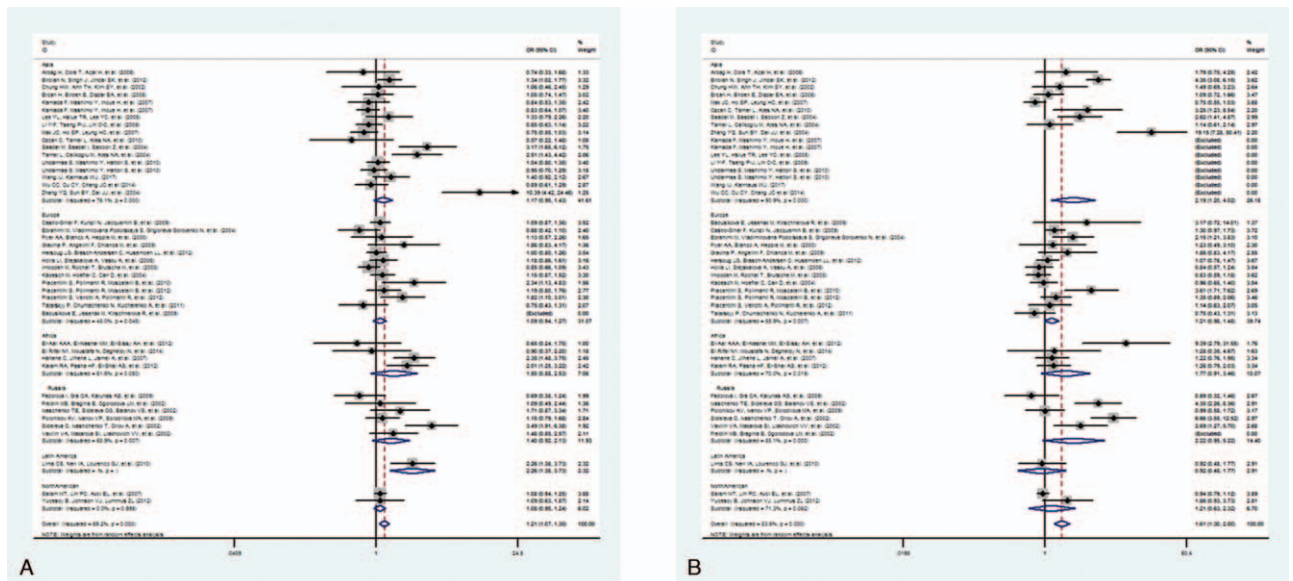
Figure 3. Meta-analysis of glutathione *S*-transferase M1 null/positive (A) and glutathione *S*-transferase T1 null/positive (B) genotypes correlation with asthma after stratified analysis by ethnicity. CI = confidence interval, OR = odds ratio.

null/positive genotypes ($t=2.32$, $P=.03$, Fig. 5A) and GSTT1 null/positive genotypes ($t=3.16$, $P=.003$, Fig. 5B).

4. Discussion

In a previous meta-analysis about the association between GSTM1, GSTT1, and asthma, Liang et al[39] included a total of 26 case–control studies. They found a significant association in the overall population, both for the GSTM1 (OR = 1.452; 95% CI: 1.192–1.770) and GSTT1 polymorphism (OR = 1.792; 95% CI: 1.293–2.483). In the subgroup analysis by age, they found that GSTM1 significantly increased the risk of asthma in both

children (OR = 1.368; 95% CI: 1.051–1.781) and adults (OR = 1.859; 95% CI: 1.183–2.921). Regarding GSTT1, they found a significant association only in the adult population (OR = 2.312; 95% CI: 1.204–4.439). When they performed the analysis by ethnicity, they found a significant association between GSTM1 genotypes and asthma risk in Europe (OR = 1.303; 95% CI: 1.018–1.667), Africa (OR = 2.175; 95% CI: 1.560–3.031), and Latin America (OR = 2.265; 95% CI: 1.375–3.729). Regarding GSTT1, they found a significantly increased risk of asthma only in Asia (OR = 2.105; 95% CI: 1.101–4.025) and Russia (OR = 2.747; 95% CI: 1.071–7.046). Based on these results, they concluded that GSTM1 and GSTT1 polymorphisms could be risk
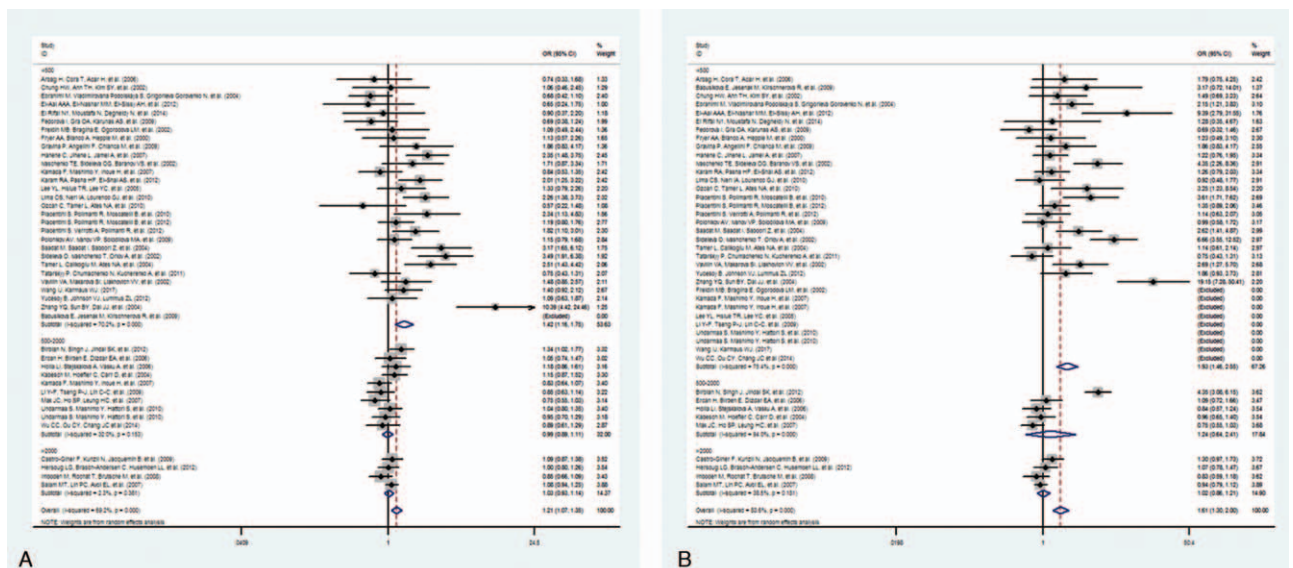

Figure 4. Meta-analysis of glutathione *S*-transferase M1 null/positive (A) and glutathione *S*-transferase T1 null/positive (B) genotypes correlation with asthma after stratified analysis by study sample size. CI = confidence interval, OR = odds ratio.
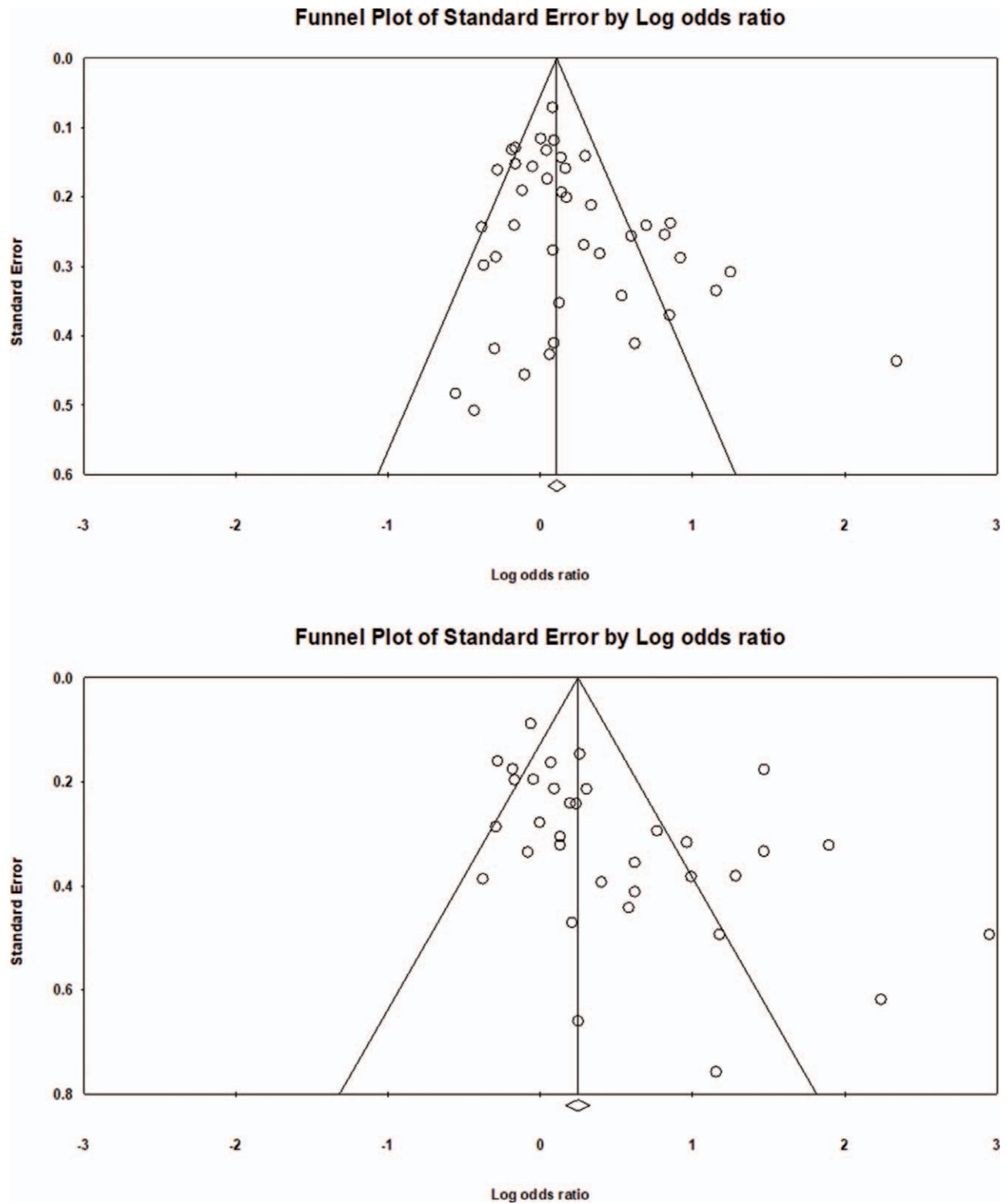
Figure 5. Funnel plot of glutathione *S*-transferase M1 null/positive (A) and glutathione *S*-transferase T1 null/positive (B) genotypes correlation with asthma.

factors for asthma. Furthermore, Piacentini et al[38] performed a meta-analysis that included independent genetic association studies on GSTM1 and GSTT1, and they also evaluated the effects of potential confounding variables (i.e., ethnicity, population age, and urbanization) using a fixed-effects or, where

appropriate, a random-effects model. In this meta-analysis, the authors found no significant association between GSTM1 gene polymorphisms and asthma susceptibility, whereas a significant association was detected for the GSTT1 genotypes (pooled OR = 1.33; 95% CI: 1.10–1.60). However, they also observed high

inter-study heterogeneity in all their general analyses (P value of the heterogeneity test <.05). However, their subsequent stratification analysis could only explain the heterogeneity in few cases. Therefore, they concluded that the interaction between genetics and the environment characterizes the disease pathogenesis. For this reason, further studies on the interactions between GST genes and potential oxidative stress sources and other antioxidant genes are needed. Recently, Turner et al[40] investigated the frequency of *GSTM1* and *GSTT1* null genotypes in 3 cohorts (2362 children). They found that *GSTT1* null alleles (but not other genotypes) were associated with minor increased risk for an asthma attack. However, they found no significant association between *GST* genotypes and asthma severity. In the same study, the interactions between *GST* genotypes and second-hand smoking exposure or asthma severity were nonsignificant. They concluded that there is no convincing evidence correlating GST genotypes to asthma outcomes. In contrast, Zhao et al[41] showed that there is a significant association between GSTT1 null genotype and the increased risk of asthma in children (OR = 1.25; 95% CI: 1.02–1.54; P = .032). In the same study, population analyses showed that the GSTT1 null genotype is associated with an increased risk of asthma in Caucasians children (OR = 1.46; 95% CI: 1.04–2.03; P = .027), but not in Asians (OR = 1.03; 95% CI: 0.55–1.94; P = .928) and Africans (OR = 1.33; 95% CI: 0.92–1.91; P = .127). Moreover, Zhao et al found no evidence of publication bias in the Caucasians' analysis. They concluded that there is a significant association between the GSTT1 null genotype and the risk of asthma in Caucasian children, but more well-designed epidemiological studies are needed to further assess this association in Asian and African children.

In the present study, we found in the overall population a significant association for both the GSTM1 null/positive genotypes (OR = 1.21; 95% CI: 1.07–1.35; P < .001; I^2 = 69.5%) and GSTT1 null/positive genotypes (OR = 1.61; 95% CI: 1.30–2.00; P < .001; I^2 = 83.6%) with asthma risk. Moreover, we found a significant association between GSTM1 and asthma risk in children (OR = 1.18; 95% CI: 1.02–1.37; P = .000; I^2 = 59.6%), adults (OR = 1.22; 95% CI: 0.99–1.49; P = .000; I^2 = 76.5%), and in studies enrolling both types of patients (OR = 1.46; 95% CI: 0.86–2.50; P = .000; I^2 = 85.3%), but not in studies with not available related information (OR = 1.08; 95% CI: 0.60–1.93; P = .963; I^2 = 0.0%). Regarding GSTT1 genotypes, a significant association was found in children (OR = 1.19; 95% CI: 0.95–1.48; P = .008; I^2 = 54.3%), adults (OR = 1.79; 95% CI: 1.27–2.51; P < .001; I^2 = 86.8%) and in studies enrolling both types of patients (OR = 2.85; 95% CI: 0.71–11.42; P < .001; I^2 = 94.8%). Furthermore, we found a significant association between GSTM1 and asthma risk in populations living in Asia, Europe, and Russia, but not in Africa, while for GSTT1, we found a significantly increased risk of asthma in populations living in Asia, Europe, Africa, and Russia. In addition, we found a significant association between GSTM1 and GSTT1 genotypes and asthma risk when the sample size was <500, but not when it was >2000.

Our study has some limitations. The first is the insufficient sample size in some of our subgroup meta-analysis, especially when the number of studies was <3. Second, considering the publication bias, quality control of the included studies should be performed a priori to distinguish high- and low-quality studies, to perform subgroup analysis according to the studies' quality. Third, a more accurate subgroup classification should be performed according to the patient number. Therefore, further

subgroup analyses are required to achieve more robust conclusions.

In conclusion, as supported by our meta-analysis of 41 studies (40 studies with a total of 7733 cases and 18,986 controls investigating GSTM1 null/positive genotypes, whereas 34 studies with a total of 6185 cases and 15,166 control investigating GSTT1 null/positive genotypes), our study suggests that GSTM1 and GSTT1 null/positive genotypes are correlated with increased asthma risk. Although there are some limitations, our meta-analysis provides valuable information on the use of GSTM1 and GSTT1 genotypes as asthma-associated biomarkers.

Author contributions

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