Int J Clin Exp Med 2016;9(2):5264-5268
www.ijcem.com /ISSN:1940-5901/IJCEM0008931

Original Article

GSTM1 polymorphism and cataract risk: a systematic review and a meta-analysis

Yi Zhu[1], Sicong Wang[1], Jing Yuan[1], Dai Li[2,3], Xiaojun Cai[1]

[1]Department of Ophthalmology, Zhongnan Hospital, Wuhan University, Wuhan 430071, China; [2]Department of Ophthalmology, Hubei University of Science and Technology, Xianning 437100, China; [3]China State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou 510275, China

Received January 13, 2015; Accepted December 21, 2015; Epub February 15, 2016; Published February 29, 2016

Abstract: Background: Many studies were conducted to assess the relationship between GSTM1 polymorphism and cataract risk. However, results of these studies remained inconclusive. Thus, we performed this systematic review and meta-analysis to clarify the association between GSTM1 polymorphism and cataract risk. Method: PubMed, EMBASE, and Cochrane databases were searched to find relevant studies by two authors. The data were extracted by these two authors independently. The strength of association between the GSTM1 polymorphism and cataract risk was assessed by calculating OR with 95% CI. Results: A total of 16 studies with 3177 cases and 2217controlson the association between GSTM1 polymorphism and cataract risk were included for this meta-analysis. GSTM1 null genotype was associated with a significantly increased risk of cataract (OR=1.44; 95% CI, 1.15-1.80; I^2=72%). In the race subgroup analysis, both Asians (OR=1.65; 95% CI, 1.16-2.36; I^2=68%) and Caucasians (OR=1.44; 95% CI, 1.09-1.90; I^2=69%) with GSTM1 null genotype had increased cataract risk. In the subgroup analysis according to gender, both women and men were not associated with risk of cataract (OR=1.06; 95% CI, 0.88-1.27; I^2=0% and OR=0.74; 95% CI, 0.49-1.14; I^2=68%, respectively). In the subgroup analysis by cataract type, subjects with GSTM1 null genotype did not show increased cortical cataract risk (OR=0.97; 95% CI, 0.74-1.27; I^2=64%), nuclear cataract risk (OR=1.19; 95% CI, 0.93-1.52; I^2=22%), and posterior subcapsular cataract risk (OR=1.18; 95% CI, 0.83-1.69; I^2=54%). Conclusion: This meta-analysis suggested that GSTM1 null genotype may be associated with the risk of cataract.

Keywords: Cataract, GSTM1, meta-analysis, association

Introduction

Cataract is a major cause of visual impairment among senior citizens worldwide [1]. According to the World Health Organization (WHO), cataract is responsible for nearly 50% of blindness across the world [2]. The importance of risk factors identification for cataract is therefore evident.

Genetic variations in the antioxidant genes coding for the glutathione S-transferase (GST) enzymes may lead to decreased or impaired regulation of their enzymatic activity and alter ROS detoxification. Therefore, genetic variations among enzymes that protect the cell against ROS may modulate disease risk [3]. A number of studies investigated the association betweenGSTM1 polymorphism and cataract risk. However, the results remained inconclusive [4-19]. Thus, we performed a meta-analysis to clarify the association of GSTM1 polymorphism and cataract risk.

Methods

Publication search

Online electronic databases (PubMed, EMBASE, and Cochrane database) was searched using the search terms: Cataract and glutathione S-transferase M or GSTM1. Additional studies were identified by a hand search from reference of original studies or review articles on this topic. There was no language restriction.

Inclusion and exclusion criteria

The following inclusion criteria were used: (1) the study should have evaluated the associa-

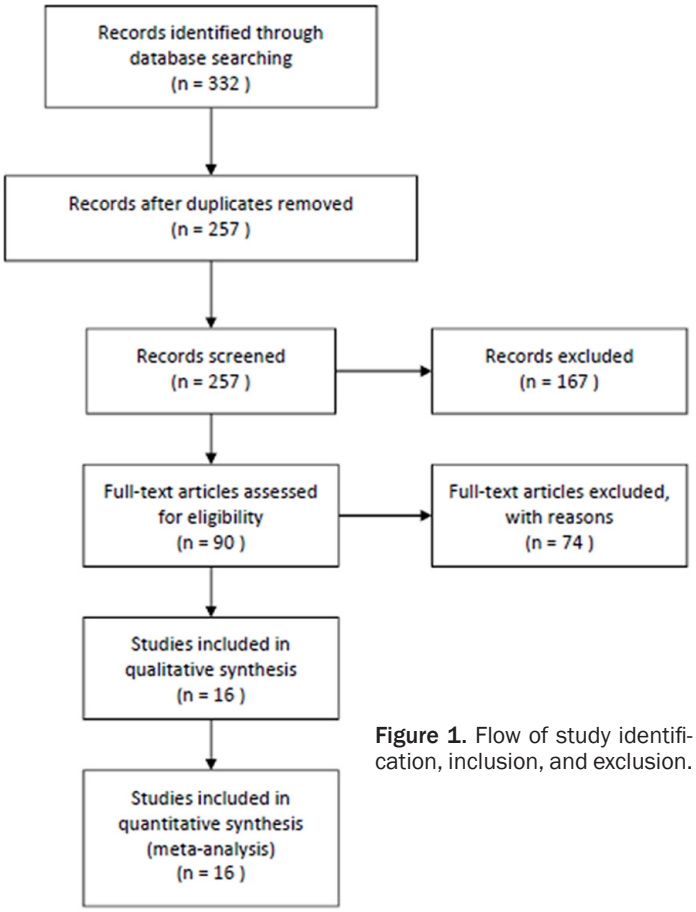

Figure 1. Flow of study identification, inclusion, and exclusion.

Table 1. Characteristics of included studies

First author	Year	Ethnicity	Age	Gender	Case (n)	Control (n)	Quality score
Sekine	1995	Asian	Adult	Mixed	138	62	6
Alberti	1996	Caucasian	Adult	Mixed	202	98	7
Pi	1996	Asian	Adult	Mixed	59	112	6
Hao	1999	Asian	Adult	Mixed	77	76	7
Juronen	2000	Caucasian	Adult	Mixed	503	202	8
Saadat	2004	Caucasian	Adult	Mixed	150	150	9
Saadat	2006	Caucasian	Adult	Mixed	95	95	6
Guven	2007	Caucasian	Adult	Mixed	195	136	7
Xu	2007	Asian	Adult	Mixed	120	118	8
Azeem	2009	African	Adult	Mixed	53	73	7
Zhou	2010	Asian	Adult	Mixed	279	145	6
Othman	2012	Caucasian	Adult	Mixed	112	112	7
Sireesha	2012	Caucasian	Adult	Mixed	455	205	8
Jiang	2012	Asian	Adult	Mixed	422	312	8
Saadat	2012	Caucasian	Adult	Mixed	186	195	7
Chandr	2014	Caucasian	Adult	Mixed	131	126	8

tion between the GSTM1 polymorphism and cataract risk; (2) the study should have a case-control or cohort design; (3) sufficient data should have been provided in order to calculate odds ratios (OR) and 95% confidence interval (CI). Studies were excluded if any of the following conditions applied: (1) only abstracts or reviews were available, without sufficient data; (2) animal studies; (3) studies were repeated or publications overlapped.

Data extraction

The following data were recorded from each article: first author, years of publication, ethnicity, gender, age, numbers of subjects. The data were extracted by two of the authors independently. Discrepancies between these two authors were resolved by discussion.

Quality assessment

The included studies were assessed independently by the two reviewers using the Newcastle-Ottawa Scale (NOS). The NOS employs a star rating system to assess quality from 3 broad perspectives of the study: (1) selection of the study groups, (2) comparability of the groups, and (3) identification of the exposure (for case-control studies) or outcome of interest (for cohort studies). Scores ranged from 0 to 9 stars.

Statistical analysis

The strength of association between the GSTM1 polymorphism and cataract risk was assessed by calculating OR with 95% CI. A statistical test for heterogeneity was performed based on the Q statistic. The $P>0.10$ of the Q-test indicated a lack of heterogeneity among studies. The summary OR estimate of each study was calculated by the random-effects model or fixed-effects model. Stratified analysis was performed by race, gender, and cataract type. Potential publication bias was examined by funnel plot and Egger's test. All statistical tests

Table 2. Results of meta-analysis and subgroup analyses

	No. of studies	OR (95% CI)	*P* Value	Model	I^2 (%)
Overall	16	1.44 (1.15-1.80)	0.002	R	72
Race					
Asian	6	1.65 (1.16-2.36)	0.006	R	68
Caucasian	9	1.44 (1.09-1.90)	0.01	R	69
Gender					
Male	4	1.06 (0.88-1.27)	0.54	F	0
Female	4	0.74 (0.49-1.14)	0.17	R	68
Cataract type					
Cortical	4	0.97 (0.74-1.27)	0.83	R	64
Nuclear	4	1.19 (0.93-1.52)	0.17	F	22
Posterior subcapsular	3	1.18 (0.83-1.69)	0.36	R	54

R, random-effects model; F, fixed-effects model.

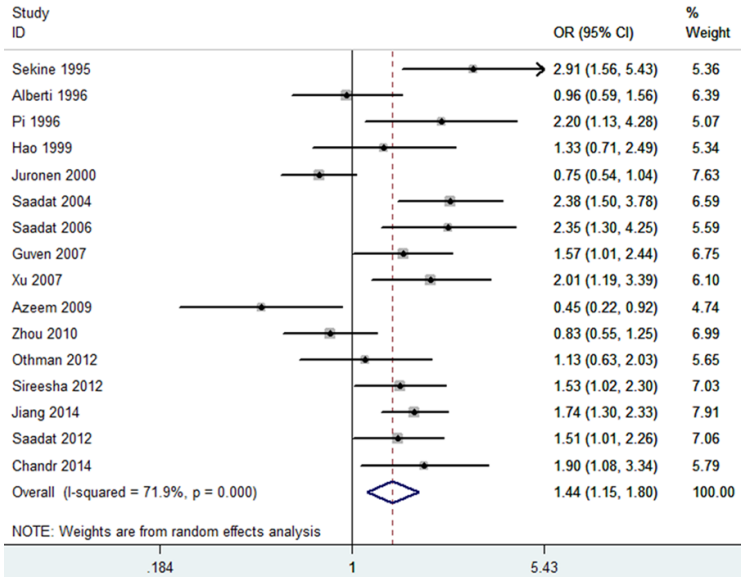

Figure 2. Meta-analysis for the association between GSTM1 polymorphism and cataract risk.

were performed with the software STATA version 11.0 (Stata Corporation, College station, TX, USA). A *P* value <0.05 was considered statistically significant.

Results

Study characteristics

According to the searching strategy, 332 papers were found. We reviewed the titles, abstracts and the full texts of all retrieved articles through defined criteria. **Figure 1** showed the flow diagram. A total of 16 studies with 3177 cases and 2217controlson the association between GSTM1 polymorphism and cataract risk were included for this meta-analysis. There were 6 studies of Asian population, 9 studies of Caucasian population, and 1 study of African population. The characteristics of each study are presented in **Table 1**.

Results of meta-analysis

The results of the association between GSTM1 polymorphism and cataract riskier summarized in **Table 2**. GSTM1 null genotype was associated with a significantly increased risk of cataract (OR=1.44; 95% CI, 1.15-1.80; I^2=72%; **Figure 2**). In the race subgroup analysis, both Asians (OR=1.65; 95% CI, 1.16-2.36; I^2=68%) and Caucasians (OR=1.44; 95% CI, 1.09-1.90; I^2=69%) with GSTM1 null genotype had increased cataract risk. In the subgroup analysis according to gender, both women and men were not associated with risk of cataract (OR=1.06; 95% CI, 0.88-1.27; I^2=0% and OR=0.74; 95% CI, 0.49-1.14; I^2=68%, respectively). In the subgroup analysis by cataract type, subjects with GSTM1 null genotype did not show increased cortical cataract risk (OR=0.97; 95% CI, 0.74-1.27; I^2=64%), nuclear cataract risk (OR=1.19; 95% CI, 0.93-1.52; I^2=22%), and posterior sub capsular cataract risk (OR=1.18; 95% CI, 0.83-1.69; I^2=54%).

The Galbraith plot was used to find the source of the heterogeneity. As shown in **Figure 3**, five studies were the outliers. After excluding these studies, the heterogeneity decreased significantly (I^2=0%). Funnel plot was performed to assess the publication bias of literatures. The shape of the funnel plot showed symmetry (**Figure 4**). Egger's test found no evidence of publication bias (*P*=0.55).

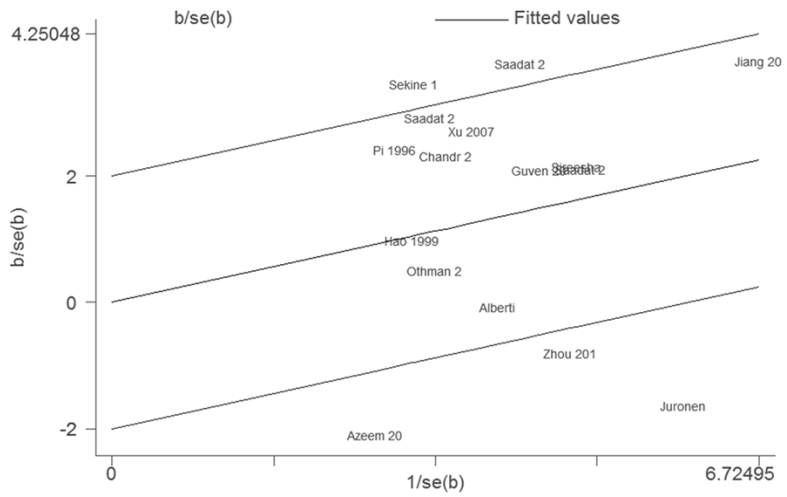

Figure 3. Galbraith plot of GSTM1 polymorphism and cataract risk.

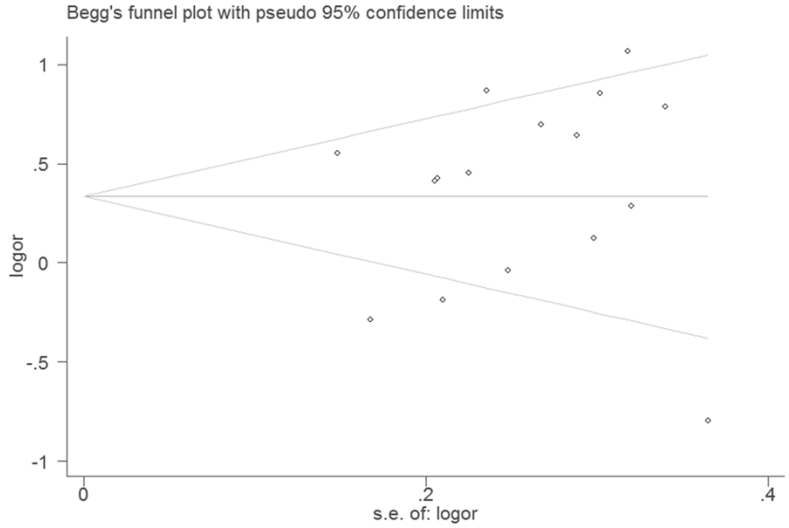

Figure 4. Funnel plot for the association between GSTM1 polymorphism and cataract risk.

Discussion

In this meta-analysis, we investigated the association between the GSTM1 polymorphism and cataract risk including 3177 cases and 2217 controls. We found that individuals with GSTM1 null genotype showed an increased risk of cataract in the overall population. In the stratified analysis by ethnicity, the significant association was observed in Asians and Caucasians. Only one study conducted in African population was included in this meta-analysis. Thus, more studies with African are still needed. In the subgroup analysis by gender and cataract type, we did not found any positive results. The possible reason might be the low sample size. Thus, more studies with large sample size should be conducted in the future.

The pathophysiologies of age-related ocular diseases are complex and remain poorly understood. Oxidative stress, associated with cellular damage caused by reactive oxygen intermediates (ROIs), has been implicated in the development of cataract [20]. A previous meta-analysis also suggested that GSTM1 null genotype was significantly associated with cataract risk [21]. That study found that GSTM1 null genotype was significantly associated with cataract risk in Caucasians. More studies with Caucasians were reported recently. Thus, our result might be different from that study.

In this meta-analysis, significant heterogeneity was observes. Galbraith plots were applied to explore the sources of heterogeneity. Five studies were spotted as outliers. I^2 value was decreased significantly after excluding the outliers. However, some limitations should be addressed. First, due to the limited availability of published results, the number of studies included in each meta-analysis was small. Second, the studies investigating genetic associations should be based on a large sample size, similar study designs and standardized case and control definitions. Third, we did not have enough data to conduct any gene-gene interaction analyses. Finally, our results were based on single-factor evaluations without adjustment for other risk factors, including BMI, tobacco, alcohol, environmental factors, or lifestyle.

In conclusion, this meta-analysis suggested that GSTM1 null genotype may be associated with the risk of cataract.

Disclosure of conflict of interest

None.

Address correspondence to: Xiaojun Cai, Department of Ophthalmology, Zhongnan Hospital, Wuhan University, Donghu Road No. 169, Wuhan 430071, China. Tel: 86-027-67812622; E-mail: caixiaojunwh@163.com

References

[1] Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. Br J Ophthalmol 2012; 96: 614-8.

[2] Resnikoff S, Pascolini D, Etya'ale D, Kocur I, Pararajasegaram R, Pokharel GP, Mariotti SP. Global data on visual impairment in the year 2002. Bull World Health Organ 2004; 82: 844-51.

[3] Forsberg L, de Faire U, Morgenstern R. Oxidative stress, human genetic variation, and disease. Arch Biochem Biophys 2001; 389: 84-93.

[4] Abdel Azeem AA, Mahmoud AA, Salaheldine MM, Amr K. Implication of glutathione S-transferase M1 and T1 polymorphisms in the development of senile cataract among Egyptians. Bratisl Lek Listy 2009; 110: 678-683.

[5] Alberti G, Oguni M, Podgor M, Sperduto RD, Tomarev S, Grassi C, Williams S, Kaiser-Kupfer M, Maraini G, Hejtmancik JF. Glutathione S-transferase M1 genotype and age-related cataracts: lack of association in an Italian population. Invest Ophthalmol Vis Sci 1996; 37: 1167-73.

[6] Guven M, Unal M, Sarici A, Ozaydin A, Batar B, Devranoglu K. Glutathione-S-transferase M1 and T1 genetic polymorphisms and the risk of cataract development: a study in the Turkish population. Curr Eye Res 2007; 32: 447-454.

[7] Hao Y, He S, Gu Z, Zhao Y, Li X, Wang C, Li Q, Liu T. [Relationship between GSTM1 genotype and susceptibility to senile cataract]. Chin J Ophthalmol 1999; 35: 104-6.

[8] Juronen E, Tasa G, Veromann S, Parts L, Tiidla A, Pulges R, Panov A, Soovere L, Koka K, Mikelsaar AV. Polymorphic glutathione S-transferases as genetic risk factors for senile cortical cataract in Estonians. Invest Ophthalmol Vis Sci 2000; 41: 2262-7.

[9] Pi J, Bai Y, Zheng Q. A study on relationship between glutathione S-transferase mu gene deletion and senile cataract susceptibility. Chin J Ophthalmol 1996; 32: 224-226.

[10] Saadat M, Farvardin-Jahromi M. Occupational sunlight exposure, polymorphism of glutathione S-transferase M1, and senile cataract risk. Occup Environ Med 2006; 63: 503-504.

[11] Saadat M, Farvardin-Jahromi M, Saadat H. Null genotype of glutathione S-transferase M1 is associated with senile cataract susceptibility in non-smoker females. Biochem Biophys Res Commun 2004; 319: 1287-1291.

[12] Sekine Y, Hommura S, Harada S. Frequency of glutathione-S-transferase 1 gene deletion and its possible correlation with cataract formation. Exp Eye Res 1995; 60: 159-163.

[13] Xu MF, Fu SH, Zhang LH. Relationship between GSTM1 gene deletion and susceptibility to senile cataract. Acta Acad Med Jiangxi 2007; 47: 33-38.

[14] Zhou J, Hu J, Guan H. The Association between copy number variations in glutathione s-transferase M1 and T1 and age-related cataract in a Han Chinese population. Invest Ophthalmol Vis Sci 2010; 51: 3924-3928.

[15] Othman H, Gholampour AR, Saadat I, Farvardin-Jahromoi M, Saadat M. Age-related macular degeneration and genetic polymorphisms of glutathione S-transferases M1 (GSTM1) and T1 (GSTT1). Mol Biol Rep 2012; 39: 3299-303.

[16] Sireesha R, Laxmi SG, Mamata M, Reddy PY, Goud PU, Rao PV, Reddy GB, Vishnupriya S, Padma T. Total activity of glutathione-S-transferase (GST) and polymorphisms of GSTM1 and GSTT1 genes conferring risk for the development of age related cataracts. Exp Eye Res 2012; 98: 67-74.

[17] Jiang Z, Liang K, Zhang Q, Tao L. Glutathione S-transferases polymorphisms confer susceptibility to senile cortical cataract in the Han Chinese population. Mol Vis 2012; 18: 1247-52.

[18] Saadat I, Ahmadi Z, Farvardin-Jahromi M, Saadat M. Association between cataract and genetic polymorphisms of GSTM1, GSTT1, and GSTO2 with respect of work place. Mol Vis 2012; 18: 1996-2000.

[19] Chandra A, Raza ST, Abbas S, Singh L, Rizvi S, Ahmed F, Eba A, Mahdi F. Polymorphism of GST and FTO Genes in Risk Prediction of Cataract among a North Indian Population. Ophthalmic Genet 2015; 1-6.

[20] Reiter RJ. Pineal melatREonin: cell biology of its synthesis and of its physiological interactions. Endocr Rev 1991; 12: 151-80.

[21] Sun L, Xi B, Yu L, Gao XC, Shi DJ, Yan YK, Xu DJ, Han Q, Wang C. Association of glutathione S-transferases polymorphisms (GSTM1 and GSTT1) with senile cataract: a meta-analysis. Invest Ophthalmol Vis Sci 2010; 51: 6381-6.