Age- and gender-dependent association of SLC11A1 polymorphisms with tuberculosis susceptibility

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Abstract

Background: Tuberculosis (TB) is an important health issue in our world. It is reported that various factors may effect on its pathogenesis. In this current study, we aimed to investigate the association between *SLC11A1* polymorphism and the risk of TB among 510 TB patients and 508 healthy controls.

Methods: Agena MassARRAY platform was conducted for genotyping. Odds ratios (ORs) and 95% confidence intervals (CIs) were analyzed through unconditional logistic regression adjustment confound factors, such as age and gender.

Results: The results suggested that the allele and genotype frequencies of polymorphisms in *SLC11A1* were not observed associated with TB risk. Subsequently, stratified analysis by age and gender confirmed that rs7608307 “A/A” and “C/T-T/T” genotypes were related with increased TB risk in age ≤ 41 group (p = 0.021) and males (p = 0.013), respectively. Besides, rs13062 “A/A” genotype was reduced TB risk in age > 41 group (p = 0.043). In addition, we observed that the “C/C” genotype of rs4674301 was noteworthy correlated with increased TB risk in females (p = 0.043).

Conclusion: Our results demonstrated the relationship between *SLC11A1* polymorphism and TB risk and confirmed for the first time that the correlation was restricted to age and gender in northwest Chinese population.

Introduction

Tuberculosis (TB) is a common public health issue with a high morbidity and infection rate in global (1, 2). According to the WHO reported in 2017, approximately 10.4 million persons were newly identified infection with TB and 1.3 million deaths occurred. Epidemiological investigation confirmed that the disease was main caused by Mycobacteria tuberculosis (MTB). However, approximately 10% of persons infected MTB develop clinical diseases during their lifetimes (3). Previous studies have provided evidences confirmed that several environment factors including age, gender, poverty and diabetes may affect TB development (4, 5). Recently researches demonstrated that host genetic factors also play a crucial role in the occurrence and development in TB. So far, multiples TB sensibility genes were confirmed through genome-wide association studies (GWAS) (6, 7). Nevertheless, the detailed molecular mechanisms of the genetic predisposition to TB still remain unknown.

The human solute carrier family 11 member 1 (*SLC11A1*) was also known as natural resistance-associated macrophage macrophage protein (*NRAMP1*) (8). Studies reported that the gene is located on 2q35, and encode a transport protein with multiple functions including the regulation of erythrophagocytosis and infections (9). Numerous studies have shown that the polymorphisms of *SLC11A1* are interacted with various inflammatory diseases, such as tuberculosis (10). The first case-control study was conducted among the Gambia, and demonstrated that *SLC11A1* polymorphisms were associated with TB susceptibility (11). Subsequently, plenty researches found the association between *SLC11A1* polymorphisms and TB susceptibility in Americans, Japanese and Turkish and so on (12, 13).

Although, there were some literatures reported the interaction between *SLC11A1* polymorphisms and the risk of TB in Chinese populations including Chinese Kazakh Population and Taiwanese (14, 15), no study investigated the correlation between *SLC11A1* polymorphisms and TB sensibility in northwest Chinese population.

Here, we performed this study to investigate the relationship between *SLC11A1* (rs11695562, rs7608307, rs4674301, rs2695343, rs13062 and rs1555529) polymorphism and TB risk in northwest Chinese population. These results provide important insights into *SLC11A1* function in the occurrence development of TB.

Materials And Methods

Subjects

All of 1018 subjects including 510 TB patients and 508 unrelated controls were enrolled from the Xi'an Chest Hospital, Shaanxi Province in the current study. All of the subjects were unrelated ethnic Chinese. TB patients were diagnosed through clinical characteristics, positive sputum smear and chest x–ray examination. Patients with familial hereditary diseases, chronic inflammatory and other autoimmune diseases were excluded. Healthy controls, without any clinical characteristics of TB and autoimmune history, were recruited from the same hospital. The guideline of this research was authorized by the clinical investigative ethical committee of the same hospital, and then all participants signed the written informed documents. Subsequently, blood samples were extracted from each subject for molecular analysis.

SNP selection and genotyping

GoldMag DNA purification kit (GoldMag, China) was used to isolate the genomic DNA from samples, according to manufacturer's instructions. Soon afterwards, DNA purity and concentration were detected using NanoDrop 2000 (Thermo Fisher, USA). In accordance with minor allele frequency (MAF) > 0.05, five candidate single nucleotide polymorphisms (SNPs) involving in *SCL11A1* gene were selected from the 1000 Genomes Project data (http://www.internationalgenome.org/). The amplification and extension primer of each SNP was design through the Agena Bioscience Assay Design Suite V2.0 software. Moreover, the SNPs genotype and data management were performed by the MassARRAY iPLEX platform and Agena Bioscience TYPER 4.0 software, respectively.

Statistical analysis

The demographic characteristics of subjects involving age and sex were performed through the SPSS 20.0 software. Hardy-Weinberg equilibrium (HWE) *p* values of all controls were obtained from the χ^2 test. The values of odds ratios (ORs) and 95% confidence intervals (CIs) were used to estimate the correlation between individual alleles and genotype and TB risk. In addition, the PLINK software (version 1.07) was conducted to evaluate the relationship between *SCL11A1* polymorphism and TB sensibility under four

genetic models. Furthermore, the stratified analyses by age and gender were also performed. In this study, $p < 0.05$ in all statistical tests was thought to be statistically significant.

Results

Demographics

As summarized in table 1, the demographics characteristics of 510 TB cases and 508 unrelated controls were described. The mean age of TB cases was 41.90 ± 14.83 years old including 318 (62.35%) males and 192 (37.65%) females. For healthy controls, the mean age was 41.14 ± 18.42 year old containing 316 (62.20%) males and 192 (37.80%) females. Statistical analysis suggested that the age and gender among all participants were matched. No difference was observed regarding age and gender groups. The *p* values were 0.469 and 0.961, respectively.

Association between SLC11A1 polymorphism and TB risk

The detailed characteristics of five candidate SNPs in *SLC11A1* gene were displayed in table 2. In our study subjects, the MAF of SNPs was more than 0.05. At the same time, all SNPs were accordance with HWE ($p > 0.05$) among healthy controls. The allele and genotype frequencies distribution of all SNPs between participants were analyzed by χ^2 test, and the results were shown in table 3. However, all candidate SNPs of *SLC11A1* polymorphism did not present any difference in allele and genotype frequencies among TB patients and healthy controls (all $p > 0.05$).

Stratified analysis to assess the association between SLC11A1 polymorphism and TB risk

Subsequently, we performed the stratification analysis by age and gender. After analyzing the stratification by age, our results suggested that *SLC11A1* rs7608307 “C/T” genotype gene was significantly interacted with improved TB risk in the younger group (age ≤ 41) under the co-dominant genetic models (OR = 1.66, 95% CI = 1.04 – 2.65, $p = 0.035$). In contrast, rs13062 “A/A” genotype was associated with reduced risk of TB in the old group under the co-dominant genetic model (OR = 0.44, 95% CI = 0.20 – 0.98, $p = 0.043$) and the recessives genetic model (OR = 0.40, 95% CI = 0.18 – 0.87, $p = 0.021$) (Table 4). However, there was no significant difference between these remaining SNPs polymorphism and TB susceptibility ($p > 0.05$), all data was not shown.

The results of stratified analysis on gender demonstrated that a significant correlation between “C/T” and “C/T –T/T” genotypes of rs7608307 and TB risk was observed in males (co-dominant: OR = 1.69, 95% CI = 1.12 – 2.56, $p = 0.013$; dominant: OR = 1.61, 95% CI = 1.08 – 2.41, $p = 0.020$, respectively). We also found that the polymorphism of rs7608307 in *SLC11A1* gene was interacted with increased TB susceptibility in male under the log-additive genetic model (OR = 1.47, 95% CI = 1.01 – 2.13, $p = 0.043$). Furthermore, the “C/A” genotype of rs13062 was related to improved TB risk in males (OR = 1.52, 95% CI = 1.10 – 2.12, $p = 0.012$). For females, the results presented that the “C/C” genotype of rs4674301 was noteworthy increase the risk of TB under the co-dominant genetic model (OR = 3.82, 95% CI = 1.04 – 4.03,

p = 0.043) and the recessive genetic model (OR = 3.85, 95% CI = 1.06 – 4.02, *p* = 0.041). Table 5 displayed all results.

Discussion

In the current case-control researches, there was a population-based inheritance correlation study conducted among unrelated Chinese Han population in northwest in China. We investigated the *SLC11A1* polymorphism and TB susceptibility. Our results revealed that *SLC11A1* polymorphism does not present any difference in allele and genotype frequencies among TB patients and healthy controls ($p > 0.05$). Subsequently, stratified analysis by age and gender confirmed that *SLC11A1* rs7608307, rs13062 and rs4674301 polymorphism was correlated with TB susceptibility ($p < 0.05$).

SLC11A1 was identified as a proton cation antiporter which localizes to lysosomes or late endosome. Several studies suggested that it might change the microenvironment of the phagosome to influence microbial killing(11). Epidemiology investigation have provided evidence that *SLC11A1* was a candidate gene for genetic susceptibility to disease caused by intracellular pathogens (16, 17). Recently, numerous studies demonstrated that *SLC11A1* polymorphism was associated with TB risk(13, 18). A study investigated 855 individuals (435 families) and reported that *SLC11A1* polymorphism rs3731865 was associated with TB in African-Americans(19). In addition, four SNPs distributed across the *SLC11A1* gene, such as rs17235416 in the 3' untranslated region, a GTn repeat in the 5' promoter region and two SNPs in intron 4 (rs3731865) and exon 15 (rs17235409) were significantly considered to be related with TB risk in West Africans(20, 21). The results of Two meta-analysis researches, which respectively identified 82 case-control studies in 35 articles and 131 case-control studies, showed that *SLC11A1* polymorphism was associated with TB risk(18, 22). Nevertheless, this is the first time to assess the relationship between *SLC11A1* polymorphism and TB risk in northwest China. The results confirmed that *SLC11A1* rs11695562, rs7608307, rs4674301, rs2695343, rs13062 and rs1555529 polymorphisms were not associated with TB risk in northwest China.

Several studies reported that demographic factors including age and gender as confounding factors affected the candidate gene with TB susceptibility(12, 23). A case- control study in which individuals were unrelated ethnic Chinese in Hong Kong, suggesting that *SLC11A1* polymorphism was correlated with TB risk in age ≤ 65 years group and the females. However, no differences were noted in either the older age group or the males (24). In this study, we observed that the “C/T” and “C/T –T/T” genotypes of rs7608307 and rs13062 “C/A” genotype were associated with increased risk of TB in the younger group (age ≤ 41) and males, respectively. However, the “A/A” genotype of rs13062 was correlated with reduced TB risk in the old group (age > 41).

Conclusion

Although, there are several problems need to be considered in our study, such as the molecular mechanism which considered to be perform in future research, this is the first time to confirm the

relationship between *SLC11A1* polymorphism and TB risk in northwest China. The study provides an important direction to understand the occurrence and development mechanism of TB in Chinese population.

Declarations

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Conflicts of Interest

The authors have declared that they have no conflict of interest.

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Author contributions

Tianbo Jin conceived and designed the study; Xue He and Zhongtao Wang wrote the paper and analyzed the data; Yuhe Wang, Li Wang and Mei Bai performed research; Dongya Yuan and Yongjun He collected and checked information. All authors have read and agreed with the final manuscript.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (name of institute/committee) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent for Publication

Not applicable

Availability of supporting data

Not applicable

References

1. Wang B, Wang Y, Wang L, He X, He Y, Bai M, et al. The role of FOXO3 polymorphisms in susceptibility to tuberculosis in a Chinese population. Molecular genetics & genomic medicine. 2019:e770.

2. Bharti D, Kumar A, Mahla RS, Kumar S, Ingle H, Shankar H, et al. The role of TLR9 polymorphism in susceptibility to pulmonary tuberculosis. Immunogenetics. 2014;66(12):675-81.
3. Chen C, Liu Q, Zhu L, Yang H, Lu W. Vitamin D receptor gene polymorphisms on the risk of tuberculosis, a meta-analysis of 29 case-control studies. PloS one. 2013;8(12):e83843.
4. Liu Q, Wang J, Sandford AJ, Wu J, Wang Y, Wu S, et al. Association of CYBB polymorphisms with tuberculosis susceptibility in the Chinese Han population. Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases. 2015;33:169-75.
5. Du B, Hua D, Droma C, Zhang H, Qu J, Yang L, et al. Association between TAP2 and SEC14L2 polymorphisms and pulmonary tuberculosis risk in the Tibetan Chinese population. 2017;10(11):11188-94.
6. Mahasirimongkol S, Yanai H, Mushiroda T, Promphittayarat W, Wattanapokayakit S, Phromjai J, et al. Genome-wide association studies of tuberculosis in Asians identify distinct at-risk locus for young tuberculosis. Journal of human genetics. 2012;57(6):363-7.
7. van Tong H, Velavan TP, Thye T, Meyer CG. Human genetic factors in tuberculosis: an update. Tropical medicine & international health : TM & IH. 2017;22(9):1063-71.
8. Soe-Lin S, Apte SS, Andriopoulos B, Andrews MC, Schranzhofer M, Kahawita T, et al. Nramp1 promotes efficient macrophage recycling of iron following erythrophagocytosis in vivo. 2009;106(14):5960-5.
9. Soe-Lin S, Apte SS, Mikhael MR, Kayembe LK, Nie G, Ponka PJEh. Both Nramp1 and DMT1 are necessary for efficient macrophage iron recycling. 2010;38(8):609-17.
10. van Crevel R, Parwati I, Sahiratmadja E, Marzuki S, Ottenhoff TH, Netea MG, et al. Infection with Mycobacterium tuberculosis Beijing genotype strains is associated with polymorphisms in SLC11A1/NRAMP1 in Indonesian patients with tuberculosis. 2009;200(11):1671-4.
11. Awomoyi AA, Marchant A, Howson JM, McAdam KP, Blackwell JM, Newport MJJTJoid. Interleukin-10, polymorphism in SLC11A1 (formerly NRAMP1), and susceptibility to tuberculosis. 2002;186(12):1808-14.
12. Solğun HA, Taştemir D, Aksaray N, Inan I, Demirhan OJTvt. Polymorphisms in NRAMP1 and MBL2 genes and their relations with tuberculosis in Turkish children. 2011;59(1):48-53.
13. Harishankar M, Selvaraj P, Bethunaickan RJFim. Influence of genetic polymorphism towards pulmonary tuberculosis susceptibility. 2018;5.
14. Liaw Y-S, Tsai-Wu J, Wu C, Hung C, Lee C, Yang P, et al. Variations in the NRAMP1 gene and susceptibility of tuberculosis in Taiwanese. 2002;6(5):454-60.
15. Wu F, Zhang W, Zhang L, Wu J, Li C, Meng X, et al. NRAMP1, VDR, HLA-DRB1, and HLA-DQB1 gene polymorphisms in susceptibility to tuberculosis among the Chinese Kazakh population: a case-control study. 2013;2013.
16. McDermid JM, Prentice AMJCS. Iron and infection: effects of host iron status and the iron-regulatory genes haptoglobin and NRAMP1 (SLC11A1) on host–pathogen interactions in tuberculosis and HIV. 2006;110(5):503-24.

17. Liu Y, Zhao E, Zhu L, Zhang D, Wang Z. 3'UTR polymorphisms in NRAMP1 are associated with the susceptibility to pulmonary tuberculosis: A MOOSE-compliant meta-analysis. Medicine. 2019;98(23):e15955.
18. Archer NS, Nassif NT, O'Brien BAJG, immunity. Genetic variants of SLC11A1 are associated with both autoimmune and infectious diseases: systematic review and meta-analysis. 2015;16(4):275.
19. Velez D, Hulme W, Myers J, Stryjewski M, Abbate E, Estevan R, et al. Association of SLC11A1 with tuberculosis and interactions with NOS2A and TLR2 in African-Americans and Caucasians. 2009;13(9):1068-76.
20. Li X, Yang Y, Zhou F, Zhang Y, Lu H, Jin Q, et al. SLC11A1 (NRAMP1) polymorphisms and tuberculosis susceptibility: updated systematic review and meta-analysis. 2011;6(1):e15831.
21. Bellamy R, Ruwende C, Corrah T, McAdam KP, Whittle HC, Hill AVJNEJoM. Variations in the NRAMP1 gene and susceptibility to tuberculosis in West Africans. 1998;338(10):640-4.
22. Meilang Q, Zhang Y, Zhang J, Zhao Y, Tian C, Huang J, et al. Polymorphisms in the SLC11A1 gene and tuberculosis risk: a meta-analysis update. 2012;16(4):437-46.
23. Li H, Zhang T, Zhou Y, Huang Q, Huang JJTIJoT, Disease L. SLC11A1 (formerly NRAMP1) gene polymorphisms and tuberculosis susceptibility: a meta-analysis. 2006;10(1):3-12.
24. Leung KH, Yip SP, Wong WS, San Yiu L, Chan KK, Lai WM, et al. Sex-and age-dependent association of SLC11A1 polymorphisms with tuberculosis in Chinese: a case control study. 2007;7(1):19.

Tables

Table 1.Characteristics of samples

Variables	Case (n=510)	Controls (n=508)	*p*
Age, year (mean ±SD)	41.90 ± 14.83	41.14 ± 18.42	0.469
Gender			0.961
Male	318 (62.35%)	316 (62.20%)	
Female	192 (37.65%)	192 (37.80%)	

p values were calculated from χ2 test.

**p*<0.05 indicates statistical significance.

Table 2. Basic characteristics and allele frequencies among *SLC11A1* SNPs

SNP	Genes	Chr	Alleles	MAF		HWE *p*-Value	OR (95% CI)	p^a
				Case	Control			
rs11695562	*SLC11A1*	2	C/T	0.28	0.28	0.101	0.98 (0.81-1.19)	0.839
rs7608307	*SLC11A1*	2	T/C	0.11	0.10	0.804	1.12 (0.84-1.49)	0.439
rs4674301	*SLC11A1*	2	C/T	0.19	0.19	0.886	1.00 (0.80-1.25)	0.989
rs2695343	*SLC11A1*	2	A/G	0.35	0.35	0.096	1.02 (0.85-1.23)	0.795
rs13062	*SLC11A1*	2	A/C	0.29	0.29	0.101	1.01 (0.84-1.23)	0.890

Chr, chromosome; CI, confidence interval; HWE, Hardy-Weinberg equilibrium; MAF, minor allele frequency, OR, odds ratio; SNP, single nucleotide polymorphism;

p values calculated with two-sided χ2;

**p* < 0.05 indicates statistical significance.

Table 3. The association between SNPs within the *SLC11A1* gene and the risk of tuberculosis

SNP	Model	Genotype	TB	Controls	OR (95%CI)	P^a
rs11695562	Co-dominant	T/T	267	268	1	
		T/C	200	191	1.05 (0.81-1.37)	0.715
		C/C	43	49	0.87 (0.56-1.36)	0.549
	Dominant	T/T	267	268	1	
		T/C–C/C	243	240	1.01 (0.79-1.30)	0.916
	Recessive	T/T– T/C	467	459	1	
		C/C	43	49	0.86 (0.56-1.32)	0.478
	Log-additive	-			0.98 (0.81-1.18)	0.818
rs7608307	Co-dominant	C/C	403	414	1	
		C/T	104	89	1.21 (0.88-1.66)	0.237
		T/T	3	5	0.60 (0.14-2.54)	0.489
	Dominant	C/C	403	414	1	
		C/T –T/T	107	94	1.18 (0.86-1.60)	0.304
	Recessive	C/C – C/T	507	503	1	
		T/T	3	5	0.58 (0.14-2.45)	0.460
	Log-additive	-			1.13 (0.84-1.51)	0.417
rs4674301	Co-dominant	T/T	339	333	1	
		T/C	147	156	0.92 (0.70-1.20)	0.535
		C/C	24	19	1.24 (0.67-2.30)	0.501
	Dominant	T/T	339	333	1	
		T/C–C/C	171	175	0.95 (0.73-1.24)	0.712
	Recessive	T/T– T/C	486	489	1	
		C/C	24	19	1.27 (0.69-2.35)	0.445
	Log-additive				1.00 (0.80-1.24)	0.971
rs2695343	Co-dominant	G/G	216	225	1	
		G/A	228	213	1.12 (0.86-1.46)	0.412
		A/A	66	70	0.96 (0.66-1.42)	0.854
	Dominant	G/G	216	225	1	

		G/A - A/A	294	283	1.08 (0.84-1.38)	0.548
	Recessive	G/G - G/A	444	438	1	
		A/A	66	70	0.91 (0.63-1.31)	0.621
	Log-additive	-			1.02 (0.85-1.22)	0.850
rs13062	Co-dominant	C/C	246	265	1	
		C/A	230	192	1.28 (0.99-1.66)	0.061
		A/A	34	51	0.71 (0.45-1.14)	0.155
	Dominant	C/C	246	265	1	
		C/A - A/A	264	243	1.16 (0.91-1.49)	0.232
	Recessive	C/C - C/A	476	457	1	
		A/A	34	51	0.64 (0.40-1.00)	0.050
	Log-additive	-	-	-	1.01 (0.83-1.22)	0.935

CI, confidence interval; OR, odds ratio; SNP: single nucleotide polymorphism.

*p^a < 0.05 indicates statistical significance.

Table 4. The association between three SNPs within the *SLC11A1* gene and the risk of tuberculosis stratified by gender

SNP	Model	Genotype	Male		Female	
			OR (95% CI)	*P*	OR (95% CI)	*P*
rs7608307	Co-dominant	C/C	1		1	
		C/T	**1.69 (1.12-2.56)**	**0.013***	0.75 (0.46-1.23)	0.255
		T/T	0.79 (0.17-3.56)	0.753	/	/
	Dominant	C/C	1		1	
		C/T –T/T	**1.61 (1.08-2.41)**	**0.020***	0.73 (0.45-1.20)	0.219
	Recessive	C/C – C/T	1		1	
		T/T	0.72 (0.16-3.24)	0.666	/	/
	Log-additive	-	**1.47 (1.01-2.13)**	**0.043***	0.72 (0.44-1.17)	0.185
rs4674301	Co-dominant	T/T	1		1	
		T/C	0.89 (0.63-1.26)	0.508	0.98 (0.63-1.51)	0.921
		C/C	0.77 (0.36-1.63)	0.490	**3.82 (1.04-4.03)**	**0.043***
	Dominant	T/T	1			
		T/C–C/C	0.87 (0.63-1.21)	0.414	1.11 (0.73-1.69)	0.626
	Recessive	T/T– T/C	1			
		C/C	0.79 (0.37-1.68)	0.546	**3.85 (1.06-4.02)**	**0.041***
	Log-additive		0.88 (0.67-1.16)	0.371	1.24 (0.86-1.78)	0.249
rs13062	Co-dominant	C/C	1		1	
		C/A	**1.52 (1.10-2.12)**	**0.012***	0.98 (0.64-1.49)	0.914
		A/A	0.76 (0.42-1.36)	0.352	0.64 (0.29-1.41)	0.269
	Dominant	C/C	1		1	
		C/A - A/A	0.79 (0.37-1.68)	0.546	0.91 (0.61-1.37)	0.663
	Recessive	C/C - C/A	1		1	
		A/A	0.63 (0.36-1.10)	0.104	0.65 (0.30-1.39)	0.267
	Log-additive	-	1.10 (0.86-1.40)	0.453	0.88 (0.64-1.20)	0.414

CI, confidence interval; OR, odds ratio; SNP: single nucleotide polymorphism.

*$p < 0.05$ indicates statistical significance.

Table 5. The association between two SNPs within the *SLC11A1* gene and the risk of tuberculosis stratified by age

SNP	Model	Genotype	≤ 41		> 41	
			OR (95% CI)	*P*	OR (95% CI)	*P*
rs7608307	Co-dominant	C/C	1		1	
		C/T	**1.66 (1.04-2.65)**	**0.035***	0.99 (0.63-1.57)	0.972
		T/T	0.34 (0.06-1.99)	0.232	/	/
	Dominant	C/C	1		1	
		C/T –T/T	1.50 (0.95-2.36)	0.080	1.01 (0.64-1.60)	0.970
	Recessive	C/C – C/T	1		1	
		T/T	0.32 (0.05-1.83)	0.198	/	/
	Log-additive	-	1.30 (0.86-1.97)	0.209	1.03 (0.66-1.62)	0.902
rs13062	Co-dominant	C/C	1		1	
		C/A	1.19 (0.82-1.72)	0.362	1.25 (0.85-1.86)	0.260
		A/A	0.96 (0.51-1.80)	0.892	**0.44 (0.20-0.98)**	**0.043***
	Dominant	C/C	1		1	
		C/A - A/A	1.14 (0.80-1.63)	0.458	1.08 (0.74-1.56)	0.703
	Recessive	C/C - C/A	1		1	
		A/A	0.88 (0.48-1.63)	0.692	**0.40 (0.18-0.87)**	**0.021***
	Log-additive	-	1.06 (0.81-1.38)	0.694	0.90 (0.67-1.22)	0.498

CI, confidence interval; OR, odds ratio; SNP: single nucleotide polymorphism.

*$p < 0.05$ indicates statistical significance.