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ORIGINAL ARTICLE

Association between complement gene polymorphisms and systemic lupus erythematosus: a systematic review and meta-analysis

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Abstract

Complement dysfunction results in impaired ability in clearing apoptotic cell debris that may stimulate autoantibody production in systemic lupus erythematosus (SLE). Herein, we provided a comprehensive search to find and meta-analyze any complement gene polymorphisms associated with SLE. The *ITGAM*, *C1q*, and *MBL* gene polymorphisms were included in this meta-analysis to reveal the exact association with SLE risk. Electronic databases, including Scopus, PubMed, and Google Scholar, were searched to find studies investigating the *ITGAM*, *C1q,* and *MBL* gene polymorphisms and SLE risk in different populations. The pooled odds ratio (OR) and its corresponding 95% confidence interval (CI) were used to analyze the association between *ITGAM*, *C1q,* and *MBL* gene polymorphisms and susceptibility to SLE. According to inclusion criteria, a total of 24 studies, comprising 4 studies for *C1QA* rs292001, 5 studies for *C1QA* rs172378, 9 studies for *ITGAM* rs1143679, 8 studies for *MBL* rs1800450, 3 studies for *MBL2* rs1800451, and 3 studies for *MBL2* rs5030737, were included in the final meta-analysis. A significant positive association was found between rs1143679 and SLE risk, while rs1800451 significantly associated with decreased SLE susceptibility. In summary, *ITGAM* gene rs1143679 SNP and *MBL* gene rs1800451 SNP were positively and negatively associated with SLE risk, respectively.

Keywords C1q · Complement · ITGAM · Meta-analysis · SNP · Systemic lupus erythematosus

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by autoantibodies production. These autoantibodies are against ubiquitous nuclear antigens and form immune complex deposits. Genetic is one of the crucial components in SLE etiology, as shown by the disease high-risk ratio between monozygotic twins over dizygotic twins [1–3]. Genetic deficiency in the complement system results in an increased risk of SLE development by reducing the ability in clearing apoptotic cells that may result in autoantibody production [4–6].

C1q is the first component of the classical pathway in complement activation. One of the important functions of C1q is the mediation of the clearance of apoptotic cells with binding to C1q/collectin receptors on phagocytes [7]. C1q is encoded by 3 genes, including *C1QA*, *C1QB,* and *C1QC,* that are harbored by chromosome 1p34.1–36.3 [8]. Mutations or single-nucleotide polymorphisms (SNPs) in C1q genes may result in C1q deficiency [9]. C1q deficiency results in impaired clearance of apoptotic cells and promotes autoreactivity and autoantibody production. Around 93% of individuals with C1q deficiency developed SLE or SLE-like symptoms [10–12]. The *Integrin-α-M* (*ITGAM*, also known as *CD11B*), which is located in chromosome 16p11.2, encodes CD11b. The CR3/Mac1/CD11b-CD18 modulates migration, leukocyte adhesion, and also has

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roles in phagocytosis of apoptotic cells that are coated by complement particles [13]. Variations, such as rs1143679 G/A polymorphism in the *ITGAM* gene, severely impair the phagocytosis of complement-coated particles [14]. M*annose-binding lectin 2* (*MBL2*) is located on chromosome 10q11.2–21, and it contains four exons [15]. MBL2 and C1q have similar structures and functions, and their deficiencies cause a higher risk of SLE [16]. There are three SNPs in the exon 1 of *MBL2* gene that include codon 52 (allele D: rs5030737), codon 54 (allele B: rs1800450), codon 57 (allele C: rs1800451) [17]. Any of these variants change the functional structure of MBL and results in the absence of functional MBL protein and impairing complement-coated particle clearance [15, 18].

In this systematic review, we performed the first meta-analysis for *C1QA* SNPs (rs292001, rs172378), *MBL2* SNPs (rs1800450, rs1800451, rs5030737) and also updated the last meta-analysis for *ITGAM* SNP (rs1143679) published in 2015 [19] to disclose an exact conclusion of the association between complement gene polymorphisms and SLE risk.

Methods

Searches and data sources

Herein, we searched the electronic databases, including PubMed, Scopus, and Google Scholar to include all eligible case–control studies between all complement gene polymorphisms and SLE risk up to June 2021. The following keywords were used to search the databases for finding many complement SNPs in SLE patients; (complement) AND (systemic lupus erythematosus OR SLE) AND (polymorphism OR variation OR single-nucleotide OR SNP OR mutation). Among all complement components, six SNPs had enough studies to include in the meta-analysis. The C1qA rs292001 (G > A) and rs172378 (A > G); ITGAM rs1143679 (G > A); MBL rs1800450 (G > A), rs1800451 (G > A) and rs5030737 (C > T) were selected to include in this study. The following keywords used to search each of these SNPs; (C1q OR Complement component 1q); (ITGAM OR Integrin Subunit Alpha M OR CD11b OR Component Receptor 3 OR CR3); (MBL OR Mannose Binding Lectin), AND (systemic lupus erythematosus OR SLE OR, in PubMed, "Lupus erythematosus, Systemic" [Mesh]) AND (polymorphism OR variation OR “single nucleotide” OR SNP OR mutation OR, in PubMed, "Polymorphism, Single Nucleotide" [Mesh]). In Google Scholar, the rs numbers were also used to limit the search results. Only English-language and human populations were included in this study. The protocol of the systematic review has been registered on the PROSPERO (ID: CRD42020170839).

Inclusion and exclusion criteria

The inclusion criteria for this meta-analysis were: (1) case–control studies that evaluate complement gene polymorphisms in SLE; (2) studies with available frequencies and numbers of each allele and different genotypes to calculate odds ratio (OR) and 95% confidence interval (CI); and (3) English-language research papers. The exclusion criteria were: (1) duplication or overlapping subjects and (2) article types of review, letter, and comment.

Data extraction and quality assessment

The following information was extracted: year of publication, first author’s last name, detection method, ethnicity of participants, number of cases and controls with minor A allele of rs292001, minor G allele of rs172378, minor A allele of rs1143679, minor A allele of rs1800450, minor A allele of rs1800451, minor T allele of rs5030737 and also the number of different genotypes for each SNPs in case and control subjects. The Newcastle–Ottawa Scale (NOS) was used for evaluation of methodological quality of included studies [20]. The quality of studies was scored by 0–3, 4–6, or 7–9 as low, moderate, or high quality, respectively.

Statistical methods

For evaluation of the mentioned complement gene polymorphisms and risk of SLE, we used pooled Odds Ratio (OR) as an effect size and its corresponding 95% CI for minor alleles in this meta-analysis. Hardy–Weinberg equilibrium was checked by Chi-squared test in the control group for each SNP. For assessing the heterogeneity and the variation in the pooled estimations, Cochran's Q test and I-squared index were used, respectively [21]. Meta-analysis was assessed with a random-effects model when heterogeneity existed between the individuals with a significant Cochran's Q test ($P < 0.1$), and the fixed-effects model was used if the heterogeneity was not detected. The Egger’s test and Begg’s test were used to checking the publication bias ($P < 0.05$) [22]. In addition, the influence of individual studies on the pooled OR (to assess the stability of the results) was calculated with re-estimating and plotting by omitting one of the studies each time (leave-one-out sensitivity analysis). Statistical software (STATA) (version 15.0; Stata

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

rs number	Author	Published year	Country/race	Detection technique	RA patients	Healthy controls	NOS score
rs292001, rs172378	Radanova et al. [23]	2015	Bulgarian	Real-time PCR	38	185	7
rs292001	Mosaad et al. [24]	2015	Egyptian	PCR–RFLP	130	208	7
rs292001	Zervou et al. [25]	2011	Turkish	PCR–RFLP	158	155	6
rs292001	Yunxia et al. [26]	2018	Chinese	DNA sequencing	245	245	8
rs172378	Cao et al. [27]	2012	Chinese	Sequenom MassArray system	748	750	9
rs172378	Racila et al. [28]	2003	Caucasian	SSP-PCR	19	62	6
rs172378	Chew et al. [29]	2008	Malaysian	PCR–RFLP	130	130	7
rs172378	Irshaid et al. [30]	2018	African, Americans, and Caucasians	PCR–RFLP	210	129	7
rs1143679	Toller-Kawahisa et al. [31]	2013	Brazilian	SSP-PCR	157	147	7
rs1143679, rs1800450	Sanchez et al. [36]	2010	Mestizo	Illumina Custom Bead system	795	650	8
			European, Amerindian		793	648	
rs1143679	Nath et al. [37]	2008	African-American, European American	Illumina Custom Bead system	2639	2736	7
rs1143679	Warchoł et al. [35]	2010	Polish Caucasian	PCR–RFLP	154	276	7
rs1143679	Han et al. [33]	2009	European American, Hispanic-American, Korean, Japanese, UK, Mexican, Colombian	TaqMan	3143	3074	9
rs1143679	Chunmei et al. [38]	2018	Han Chinese	PCR–RFLP	584	628	8
rs1143679	Gupta et al. [34]	2018	North Indian	TaqMan	394	583	8
rs1143679	Skonieczna et al. [32]	2017	Polish	Real-time PCR	35	50	6
rs1800450	Huang et al. [45]	2003	Chinese	DNA sequencing	82	222	6
rs1800450	Panda et al. [41]	2012	Odisha Indian	ASPCR	108	105	7
rs1800450	Tsai et al. [39]	2009	Chinese	DNA sequencing	150	100	7
rs1800450	Takahashi et al. [40]	2006	Japanese	PCR–RFLP	147	160	7
rs1800450, rs1800451, rs5030737	Lee et al. [44]	2005	European American, German	PCR–RFLP	381	296	7
rs1800450, rs1800451, rs5030737	Negi et al. [42]	2017	Indian Tamil	TaqMan	300	460	8
rs1800450, rs1800451, rs5030737	Hristova et al. [43]	2014	Bulgarian	PCR–RFLP	45	78	8
rs1143679	Julian Ramı´rez-Bello	2019	Mexican	TaqMan	359	609	8

ASPCR allele-specific polymerase chain reaction, *PCR–RFLP* restriction fragment length polymorphism polymerase chain reaction, *SSP-PCR* single specific primer-polymerase chain reaction, *RA patients* the number of reported patients with RA disease

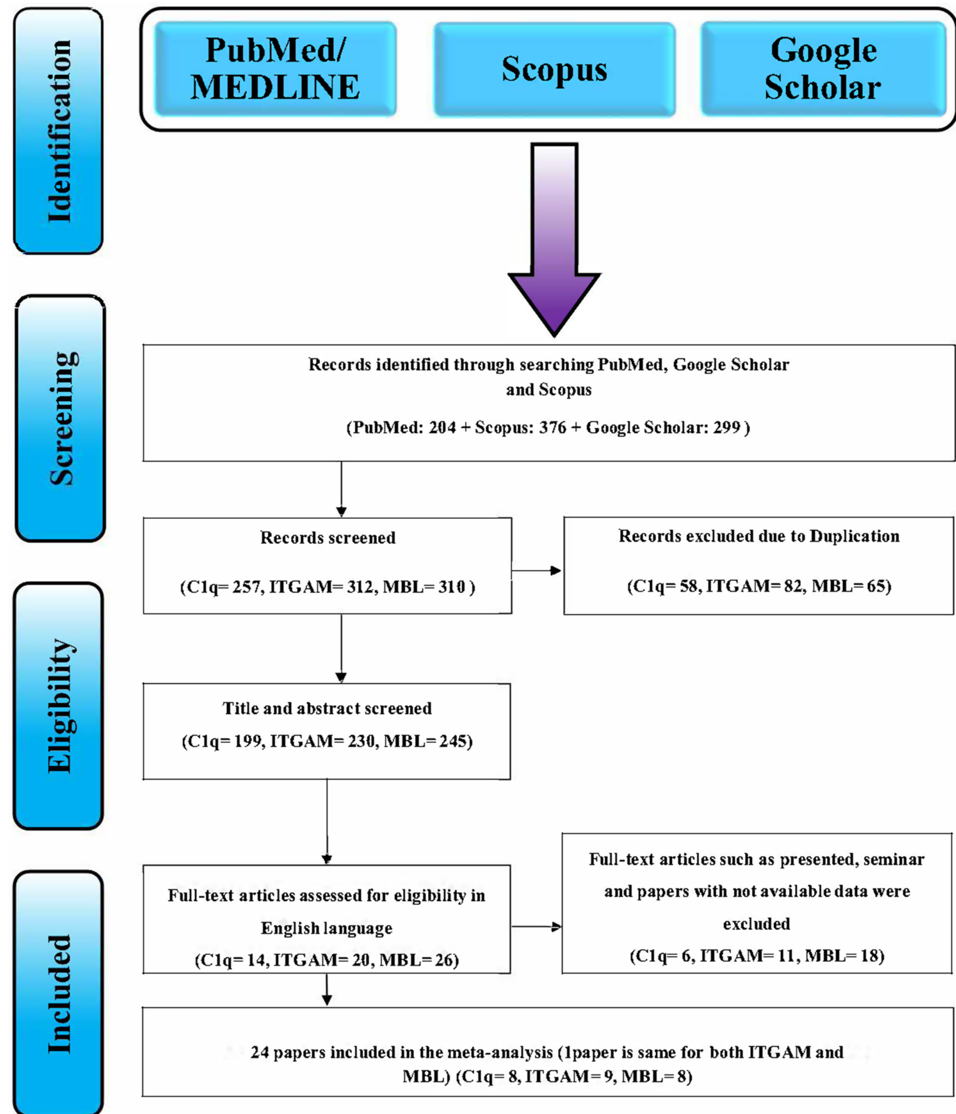


Fig. 1 Flowchart of literature search for selection of 24 studies in the meta-analysis

Corporation, College Station, Texas 77845 USA) was used for data analysis.

Results

Characteristics of eligible studies

In the initial search, 257, 312, and 310 studies for C1q, ITGAM, and MBL complement SNPs were found, respectively. After removal of irrelevant papers, presentations, seminars, letters, case reports, reviews, non-English papers, duplications, and also with using mentioned criteria, 4 case–control studies comprising 571 cases and 793 healthy subjects for rs292001 [23–26], 5 case–control studies comprising 1145 cases and 1256 healthy subjects for rs172378 [23, 27–30], 9 case–control studies comprising 8260 cases and 8753 healthy subjects for rs1143679 [31–38], 8 case–control studies comprising 2006 cases and 2069 healthy subjects for rs1800450 [36, 39–45], 3 case–control studies comprising 726 cases and 834 healthy subjects for rs1800451 [42–44], and 3 case–control studies comprising 726 cases and 834 healthy subjects for rs5030737 [42–44] were included for meta-analysis. The papers were investigated in different nations of Asian, European, African, and American countries. The ranges of publication were between 2003 and 2019. The mean NOS score was 7.30 (range: 6–9) (Table 1, Fig. 1).

Main results, subgroup, and sensitivity analysis

Significant associations were found between two SNPs, including *ITGAM* gene rs1143679 polymorphism and

Table 2 Meta-analysis of the pooled associations between *C1qA*, rs292001 (G > A), rs172378 (A > G); *ITGAM*, rs1143679 (G > A); *MBL2*, rs1800450 (G > A), rs1800451 (G > A), rs5030737 (C > T) polymorphisms, and risk of SLE disease

SNPs	Variation	Frequency		Association test			Heterogeneity test (Q, I^2, *P*-value)	Publication bias (Begg's test, *P*-value; Egger's test, *P* value)
		Case	Control	*P* value	Pooled (OR)	95% (C.I)		
C1QA rs292001 (G > A), 4 studies, HWE for controls = 0.07	G	530	870					
	A	612	716					
	GG	120	226					
	GA	290	418					
	AA	161	149					
	A versus G			0.104	1.252	(0.955–1.640)	(11.55, 65.39%, 0.02)	(0.99, 0.90)
	AA versus GG			0.280	1.676	(0.657–4.275)	(15.9, 81.13%, 0.001)	(0.73, 0.87)
	GA versus GG			0.678	1.102	(0.832–1.459)	(6.57, 54.3%, 0.09)	(0.73, 0.43)
	AA + GA versus GG			0.539	1.162	(0.719–1.877)	(8.86, 66.2%, 0.03)	(0.65, 0.56)
	AA versus GA + GG			0.152	1.649	(0.831–3.269)	(12.68, 76.3%, 0.005)	(0.81, 0.78)
C1QA rs172378 (A > G), 5 studies, HWE for controls = 0.22	G	1256	1293					
	A	1022	1171					
	GG	347	350					
	AG	562	593					
	AA	230	289					
	G versus A			0.546	0.948	(0.799–1.126)	(11.18, 55.3%, 0.04)	(0.99, 0.73)
	GG versus AA			0.627	0.941	(0.735–1.204)	(8.59, 53.5%, 0.07)	(0.46, 0.59)
	AG versus AA			0.538	0.932	(0.745–1.166)	(7.94, 49.6%, 0.09)	(0.81, 0.51)
	GG + AG versus AA			0.522	0.873	(0.577–1.322	(10.72, 62.7%, 0.03)	(0.63, 0.49)
	GG versus AG + AA			0.642	0.958	(0.799–1.148)	(6.03, 33.7%, 0.19)	(0.72, 0.62)
ITGAM rs1143679 (G > A), 9 studies, HWE for controls = 0.01	G	14,129	16,063					
	A	2391	1461					
	GG	6105	7382					
	AG	1919	1299					
	AA	236	80					
	A versus G			**< 0.001**	**1.966**	(1.757–2.20)	(8.58, 6.8%, 0.379)	(0.17, 0.19)
	AA versus GG			**< 0.001**	**3.608**	(2.762–4.713)	(3.01, 0.0%, 0.93)	(0.76, 0.25)
	AG versus GG			**< 0.001**	**1.923**	(1.706–2.168)	(22.79, 60.50%, 0.007)	(0.27, 0.33)
	AA + AG versus GG			**< 0.001**	**2.037**	(1.811–2.293)	(18.89, 52.4%, 0.026)	(0.17, 0.22)
	AA versus AG + GG			**< 0.001**	**3.202**	(2.452–4.180)	(3.81, 0.0%, 0.874)	(0.19, 0.39)

Table 2 (continued)

SNPs	Variation	Frequency		Association test			Heterogeneity test (Q, I^2, *P*-value)	Publication bias (Begg's test, *P*-value; Egger's test, *P* value)
		Case	Control	*P* value	Pooled (OR)	95% (C.I)		
MBL2 rs1800450 (G > A), 8 studies, HWE for controls = 0.003	G	3225	3317					
	A	705	599					
	GG	1346	1422					
	AG	533	473					
	AA	86	63					
	A versus G			0.089	1.218	(0.971–1.528)	(18.45, 62%, 0.01)	(0.27, 0.28)
	AA versus GG			0.215	1.599	(0.773–3.148)	(18.16, 61%, 0.01)	(0.39, 0.42)
	AG versus GG			0.202	1.101	(0.950–1.277)	(4.42, 0.0%, 0.79)	(0.54, 0.90)
	AA + AG versus GG			0.073	1.137	(0.988–1.309)	(7.07, 1%, 0.42)	(0.54, 0.27)
	AA versus AG + GG			0.235	1.542	(0.754–3.153)	(19.02, 63.2%, 0.008)	(0.42, 0.77)
MBL2 rs1800451 (G > A), 3 studies, HWE for controls = 0.003	G	1414	1598					
	A	38	70					
	GG	690	769					
	AG	34	60					
	AA	2	5					
	A versus G			0.114	0.70	(0.45–1.089)	(0.54, 0.0%, 0.76)	(0.30, 0.16)
	AA versus GG			0.670	0.763	(0.22–2.646)	(0.41, 0.0%, 0.81)	(0.99, 0.99)
	AG versus GG			0.051	0.645	(0.416–1.002)	(0.001, 0.0%, 0.97)	(0.99, 0.12)
	AA + AG versus GG			**0.044**	0.641	(0.416–0.988)	(0.0, 0.0%, 0.98)	(0.30, 0.11)
	AA versus AG + GG			0.699	0.782	(0.226–2.712)	(0.39, 0.0%, 0.82)	(0.95, 0.43)
MBL2 rs5030737 (C > T), 3 studies, HWE for controls = 0.001	C	1381	1600					
	T	71	68					
	CC	663	775					
	CT	55	50					
	TT	8	9					
	T versus C			0.469	1.128	(0.798–1.595)	(0.36, 0.0%, 0.83)	(0.99, 0.68)
	TT versus CC			0.567	1.315	(0.514–3.363)	(1.11, 0.0%, 0.57)	(0.30, 0.07)
	CT versus CC			0.716	1.079	(0.716–1.627)	(1.28, 0.0%, 0.53)	(0.99, 0.91)
	TT + CT versus CC			0.581	1.113	(0.761–1.628)	(0.24, 0.0%, 0.88)	(0.30, 0.28)
	TT versus CT + CC			0.582	1.301	(0.510–3.319)	(1.23, 0.0%, 0.54)	(0.30, 0.19)

SNPs single-nucleotide polymorphisms, *HWE* Hardy–Weinberg equilibrium, *MBL2* mannose-binding lectin 2, *ITGAM* the Integrin-α-M

Bold pooled (OR) indicates statistically significant values at the 0.05 level

MBL2 gene rs1800451 polymorphism with SLE risk. The minor A allele of the *ITGAM* gene rs1143679 was significantly associated with an increased SLE risk (OR = 1.966, 95% CI = 1.757–2.20, $P < 0.001$). Moreover, the AA (OR = 3.608, 95% CI = 2.76–4.71, $P < 0.001$) and AG (OR = 1.923, 95% CI = 1.70–2.16, $P < 0.001$) genotypes significantly increased the disease risk. As such, the dominant (OR = 2.037, 95% C = 1.81–2.29, $P < 0.001$) and recessive (OR = 3.202, 95% CI = 2.45–4.18, $P < 0.001$) models of inheritance were significantly associated with increased susceptibility to SLE (Table 2, Fig. 2a). On the other side, the dominant genetic model of *MBL2* gene rs1800451 SNP significantly decreased SLE proneness (OR = 0.641, 95% CI = 0.416–0.988, $P = 0.044$), but the allelic model of this SNP has a non-significant effect on SLE risk (Table 2, Fig. 2b).

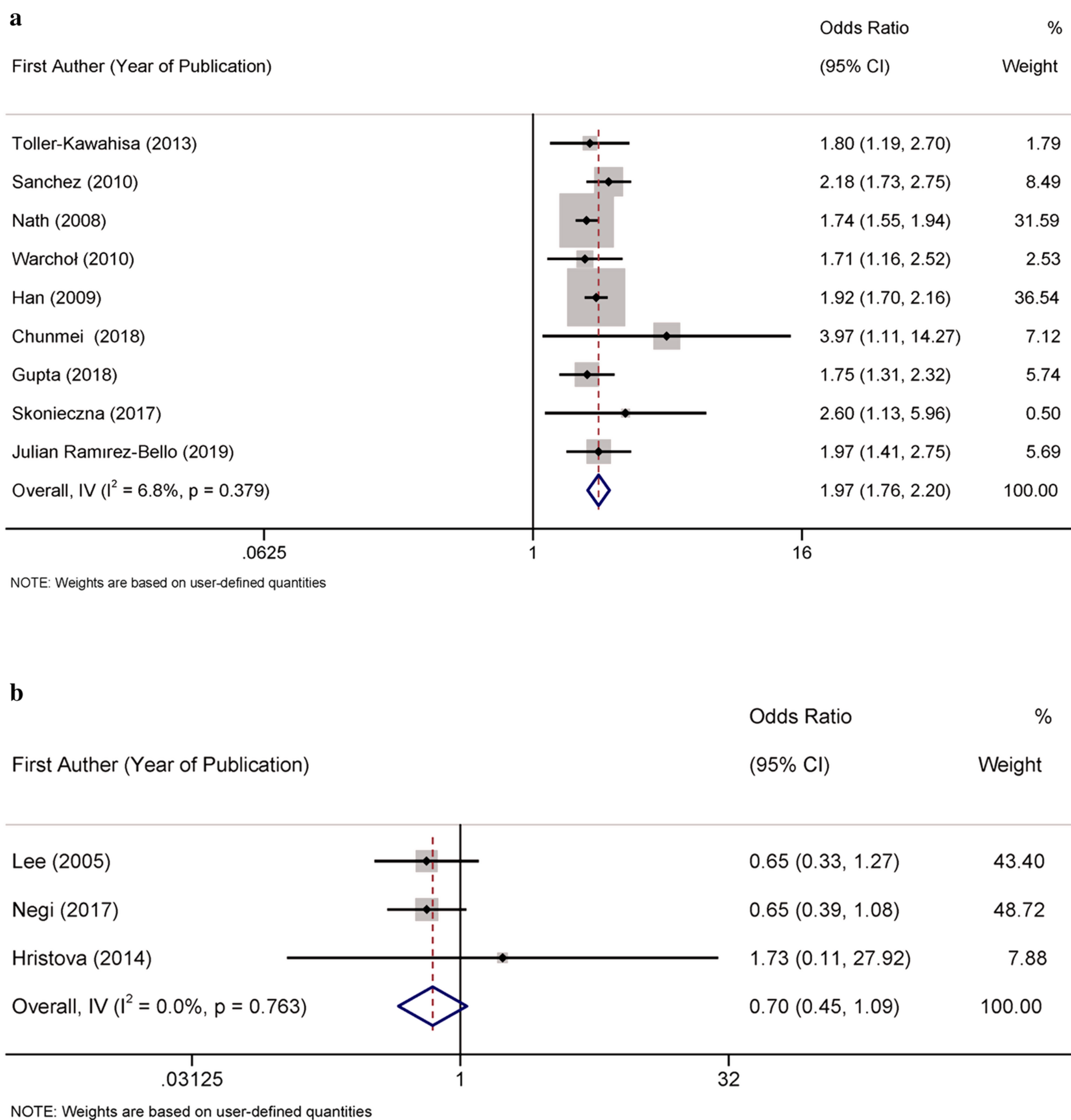


Fig. 2 Forest plots of the pooled ORs for the allelic model of **a** *ITGAM* gene rs1143679 SNP and **b** *MBL2* gene rs1800451 SNP, pooled associations between the SNPs and SLE risk (A versus G)

Heterogeneity and publication bias

Cochran's Q test and I^2 test were conducted for analyzing the heterogeneity of the studies. The ($I^2\% > 50\%$, $P_{\text{Heterogeneity}} < 0.10$) considered as significant heterogeneity between the studies.

Heterogeneity was observed in *C1QA* gene rs292001 SNP for the comparisons A versus G ($I^2\% = 65.39\%$, $P_{\text{Heterogeneity}} = 0.02$) and AA versus GG ($I^2\% = 81.13\%$, $P_{\text{Heterogeneity}} = 0.001$), GA versus GG ($I^2\% = 54.3\%$, $P_{\text{Heterogeneity}} = 0.09$), AA + GA versus GG ($I^2\% = 66.2\%$, $P_{\text{Heterogeneity}} = 0.03$), and AA versus GA + GG ($I^2\% = 76.3\%$, $P_{\text{Heterogeneity}} = 0.005$). Moreover, for *C1QA* gene rs172378 SNP, heterogeneity was detected for G versus A ($I^2\% = 55.3\%$, $P_{\text{Heterogeneity}} = 0.04$) and GG versus AA ($I^2\% = 53.5\%$, $P_{\text{Heterogeneity}} = 0.07$), GG + AG versus AA ($I^2\% = 62.7\%$, $P_{\text{Heterogeneity}} = 0.03$). The only comparison that had heterogeneity for *ITGAM* gene rs1143679 SNP was AG versus GG ($I^2\% = 60.5\%$, $P_{\text{Heterogeneity}} = 0.007$). On the

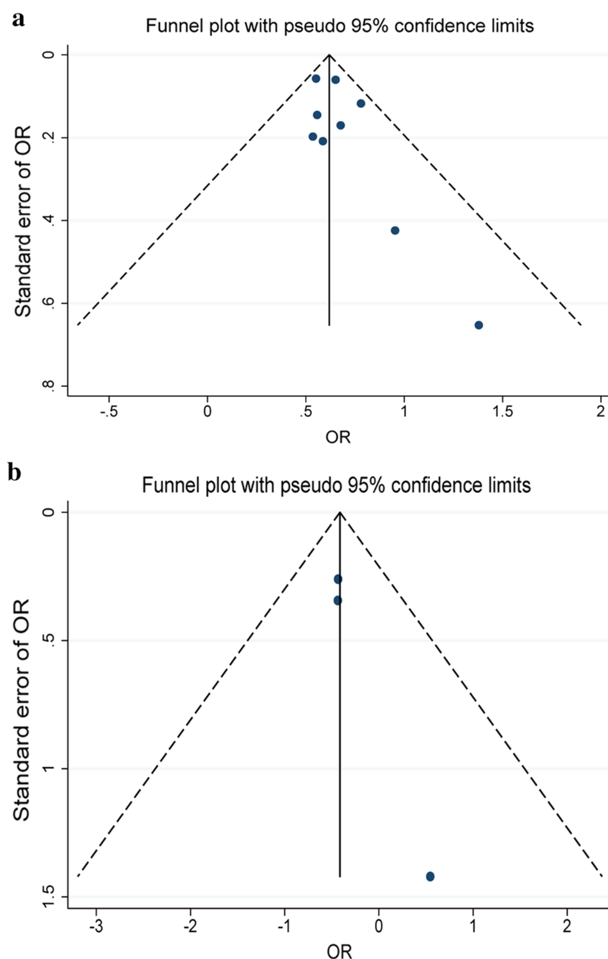


Fig. 3 Funnel plots to detect the publication bias for the allelic model of **a** *ITGAM* gene rs1143679 SNP and **b** *MBL2* gene rs1800451 SNP

other side, *MBL2* gene rs1800450 SNP demonstrated heterogeneity for comparisons below: A versus G ($I^2\% = 62\%$, $P_{\text{Heterogeneity}} = 0.01$) and AA versus GG ($I^2\% = 61\%$, $P_{\text{Heterogeneity}} = 0.01$), AA versus AG + GG ($I^2\% = 63.2\%$, $P_{\text{Heterogeneity}} = 0.008$) (Table 2).

Assessing of publication bias was done by using a funnel plot, Egger's and Begg's tests. The shapes of the funnel plots did not reveal any evidence of an obvious significantly asymmetry in all comparison models. Also, nonsignificant publication bias was found in all analyses by the tests (Table 2, Fig. 3).

Sensitivity analysis

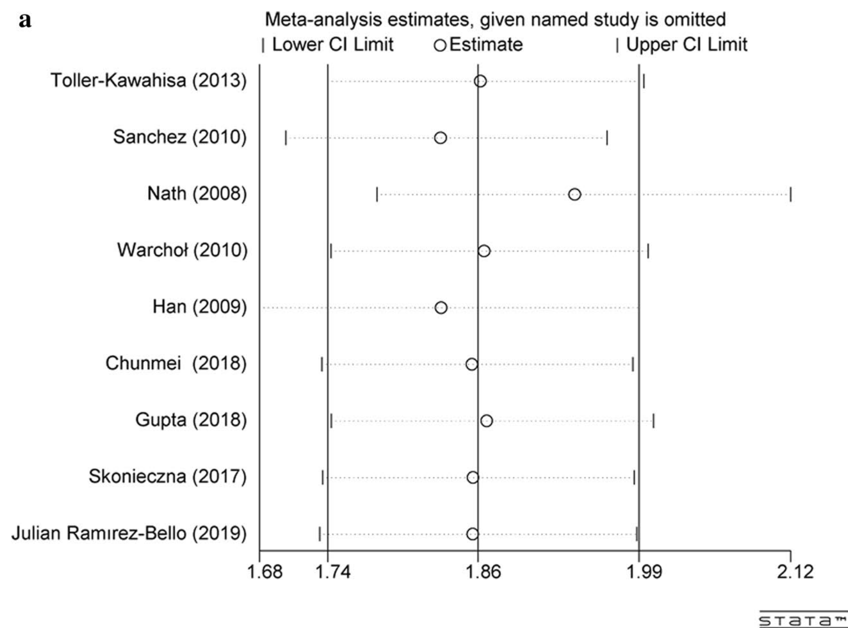
The stability of the meta-analysis was evaluated; as the results suggested, no individual study significantly affected the pooled ORs. The result of leave-one-out sensitivity analysis was shown for the allelic model of *ITGAM* gene rs1143679 SNP (Fig. 4a) and *MBL2* gene rs1800451 SNP (Fig. 4b).

Discussion

SLE is a chronic autoimmune disease in which both genetic and environmental factors are contributed [46, 47]. A bulk of evidence has revealed that complement deficiencies result in a reduced ability in the clearance of apoptotic cells that increase the risk of autoantibody production and, therefore, SLE development in susceptible subjects. The complement system has an intricate role in SLE, and either complement deficiency or aberrant complement activation contributes to SLE risk [4–6].

The deficiency or malfunction of several complement proteins has been important in SLE pathogenesis. The C1q component that plays a significant role in the removal of apoptotic cells is associated with SLE. The lupus autoantigens that are located in apoptotic debris may stimulate an inappropriate immune response. C1q can also inhibit the interferon alpha (IFN-α) production via the inhibitory receptor leukocyte-associated immunoglobulin-like receptor 1 (LAIR-1, also called CD305) and, hence, is involved in SLE development [5, 48, 49]. Several studies reported an association between low serum levels of MBL and autoimmune disease development. In SLE patients, MBL deficiency may result in insufficient removal of apoptotic debris same as C1q deficiency. Genetic polymorphisms that are associated with decreased serum levels of MBL as well as the presence of anti-MBL autoantibodies which bind to MBL and decrease its serum level may increase the risk of SLE development [50–55]. ITGAM, a component of CR3 or Mac1, is expressed on most myeloid cells, such as macrophages and dendritic cells (DCs). CR3 binds to the complement protein iC3b and mediates the phagocytosis of iC3b-coated particles and, hence, has an important role in the removal of apoptotic cells. Some studies reported other essential roles for CR3 that are also associated with autoimmune responses in SLE patients. Mac1 could inhibit some immunological processes such as DC maturation and function, DC-induced T cell activation, Toll-like receptor (TLR) signaling, and macrophage activation. CR3 deficiency may result in impaired phagocytosis of apoptotic cells, activation of T cells, increased TLR signaling, and Th17 differentiation, which are contributing to the increased systemic inflammation and SLE development [56–61].

In the present study, we meta-analyzed the previously published data to attain conclusive outstanding of the genetic associations between the *ITGAM* (rs1143679), *C1QA* (rs292001 and rs172378), and *MBL* (rs1800450, rs1800451, and rs5030737) gene polymorphisms and susceptibility to SLE. The previous meta-analysis in 2015 [19] reported 1.77 pooled OR (95% CI = 1.65–1.90, $P < 0.001$) for the minor A allele of the *ITGAM* gene rs1143679 SNP which was also confirmed with our meta-analysis with 1.966 pooled



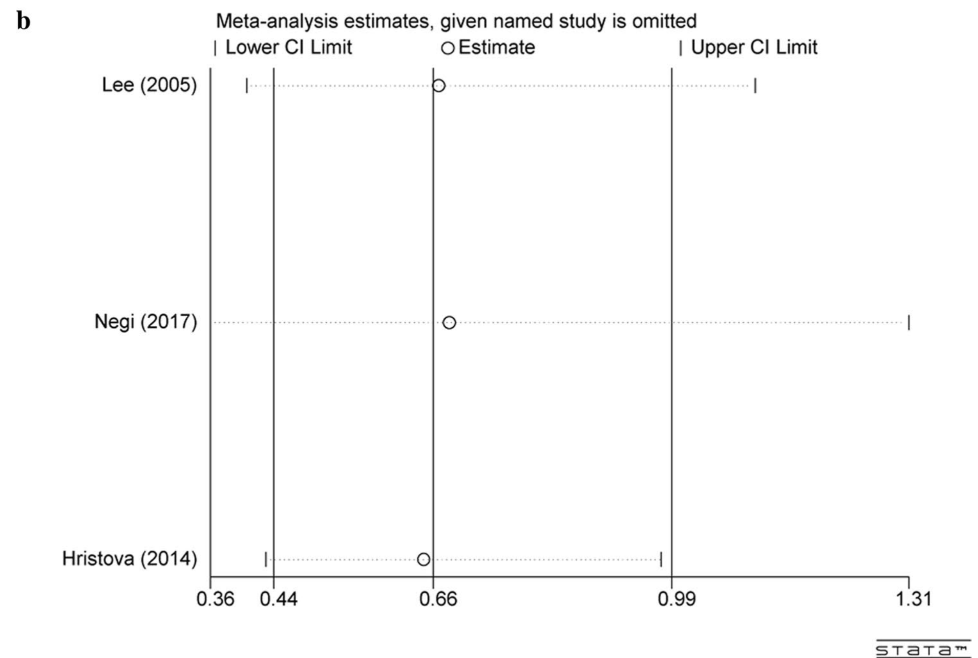


Fig. 4 Leave-one-out sensitivity plots to assess the robustness of the pooled OR against each included study for the allelic model of **a** *ITGAM* gene rs1143679 SNP and **b** *MBL2* gene rs1800451 SNP

OR (95% CI = 1.757–2.20, $P < 0.001$). The pooled OR of other genetic comparisons for *ITGAM* gene rs1143679 SNP reported in the previous meta-analysis was also included in the currently updated meta-analysis.

Some of the previous studies investigating the *C1QA* gene polymorphisms reported a significant association between these polymorphisms with SLE pathogenesis. Significant ORs that were reported include 1.80 for rs172378 [23] and 1.57 for rs292001 [24]. However, our meta-analysis resulted in no significant pooled ORs for the minor A allele of rs292001 and the minor G allele of rs172378. Some researchers reported significant associations between *MBL* gene polymorphisms (rs1800450, rs1800451, and rs5030737) with SLE risk [62]. However, others reported no significant association for these SNPs [44]. The current meta-analysis revealed non-significant associations between rs1800450 and rs5030737 SNPs with SLE risk, while a significant protective association was shown for rs1800451 (on the dominant genetic model). Other complement gene polymorphisms that were investigated had not enough data to be analyzed in this meta-analysis.

Conclusion

In summary, this meta-analysis study provides a comprehensive and up-to-date conclusion of the association between the complement SNPs and SLE risk until June 2021. The present meta-analysis revealed that the *ITGAM* gene rs1143679 SNP significantly increased the SLE risk. However, the dominant genetic model of *MBL2* gene rs1800451 SNP was significantly associated with decreased SLE risk. Further studies of different ethnicities are still needed to attain a more comprehensive and conclusive understanding of the association between complement gene SNPs and SLE development.

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Declarations

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