Int J Clin Exp Med 2024;17(12):221-233
www.ijcem.com /ISSN:1940-5901/IJCEM0158345

Review Article

Association of ABO blood type with diabetes mellitus: a systematic review and meta-analysis

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Received June 7, 2024; Accepted November 21, 2024; Epub December 15, 2024; Published December 30, 2024

Abstract: There is a growing interest in exploring the influence of ABO blood type on development of diabetes mellitus (DM). However, the association between the ABO blood type and DM is still controversial. This meta-analysis aimed to elucidate the potential role of ABO blood type as a risk factor for DM. PubMed, Embase, and the Cochrane Library were searched for studies evaluating the association of ABO blood with DM. Data were pooled using random-effects models to obtain the odds ratios (ORs) and 95% confidence intervals (CIs). A total of 19 studies were included in this meta-analysis. The combined results showed a similar prevalence of blood type A in DM cases compared to controls, with a pooled OR of 1.08 (95% CI: 1.00-1.16; P = 0.053). Moreover, there was no statistically significant difference in the risk of DM in subjects with blood type B, or AB compared with non-B, non-AB, respectively. However, there was a significantly lower prevalence of blood type O in subjects with DM than in controls, with a pooled OR of 0.89 (95% CI: 0.80-0.97; P = 0.013). Blood type O may be a protective factor against DM, which means that those with non-O blood may be more likely to have DM. This is of clinical importance for individuals with non-O blood types, who should pay more attention to the risk of diabetes and early prevention.

Keywords: ABO blood type, blood type, diabetes mellitus

Introduction

The ABO blood typing system contains four major phenotypes such as blood type A, B, O, and AB, according to the presence of A and B antigens on surface of red blood cells, which are produced by glycosyltransferases encoded by the ABO gene. As a well-known genetic risk factor, it is easily tested, and numerous studies have been designed to focus on the role of ABO blood type in health and disease. In addition to transfusion and organ transplantation compatibility, ABO blood typing is implicated in a wide variety of human diseases, including cardiovascular disease, venous thromboembolic events, longevity, cancer, and even virus susceptibility [1-4]. Based on the available data, individuals with blood type A are at increased risk for developing hyperlipidemia, atherosclerosis, and coronary artery disease compared with those with blood type O [3, 5]. Obviously, the variation in health outcomes across different blood types may be very important for us to make individualized approaches for the maintenance of health and the prevention and treatment of various diseases.

Diabetes mellitus (DM) has become a public health concern worldwide due to its increasing prevalence and involvement in the development of several diseases, including stroke, kidney failure, heart disease, and peripheral vascular disease [6]. Since the effect of ABO blood type on health and disease has been reported, there is a growing interest in exploring the influence of the ABO blood typing system on the development of DM. However, available studies on this topic have displayed inconclusive and inconsistent findings. There is evidence that compared with individuals with blood type O, those with either A or B types were at increased risk for type 2 diabetes [7, 8]. However, another study found that individuals with blood type O were more likely to have higher total cholesterol levels, glucose levels and blood pressure, with a decreasing trend from those with blood type A

https://doi.org/10.62347/VIBT7198

Table 1. Search strategies

Search strategy	
PubMed	1. "ABO blood type" [Text Word]
	2. "ABO blood group" [Text Word]
	3. "blood type" [Text Word]
	4. "blood group" [Text Word]
	5. 1 or 2 or 3 or 4
	6. diabetes mellitus [Text Word]
	7. DM [Text Word]
	8. diabet* [Text Word]
	9. 6 or 7 or 8
	10. 5 and 9
EMBASE	1. 'ABO blood type' OR 'ABO blood group'/exp OR 'ABO blood group' OR 'blood type' OR 'blood group'/exp OR 'blood group'
	2. 'diabetes mellitus'/exp OR 'diabetes mellitus' OR DM OR diabet*
	3. 1 AND 2
Cochrane Library	1. "ABO blood type" [All Text]
	2. "ABO blood group" [All Text]
	3. "blood type" [All Text]
	4. "blood group" [All Text]
	5. 1 or 2 or 3 or 4
	6. diabetes mellitus [All Text]
	7. DM [All Text]
	8. diabet* [All Text]
	9. 6 or 7 or 8
	10. 5 and 9

*, the asterisk is utilized as a wildcard character to expand the search scope.

to B, and then to AB [9]. In addition, other studies pointed out that there was no association between ABO blood type and DM [10, 11]. These inconsistent findings observed in the current studies may be attributed largely to methodological differences, including sample size, age range of subjects, gender distribution, as well as the ethnic makeup of the study groups. Therefore, we conducted this meta-analysis by incorporating the latest evidence with a focus on the association of ABO blood type with DM, which may be instructive for clinical practice.

Materials and methods

This study was conducted in accordance with the MOOSE group guidelines of observational meta-analyses [12].

Data sources and searches

PubMed, Embase and the Cochrane Library were searched for relevant studies from their inceptions to June 16, 2020. In order to maximize the search for articles on the same topic, the reference lists of included studies, relevant review articles and meta-analyses were screened for other suitable studies. The terms "ABO blood group", "ABO blood type", "blood group", "blood type", "diabetes mellitus", and "diabetes" were searched alone or in combination. The details of the search strategy are available in the **Table 1**.

Study selection

Studies were considered eligible if they fulfilled the following criteria: (1) participants were diagnosed with DM; (2) separate data for participants with or without DM were provided; (3) information regarding proportions of ABO blood type were provided; (4) published in English. Studies were excluded if they were conference abstracts, editorials, case reports, reviews, nonhuman studies, had a lack of proper controls, or did not report clear data on the distribution of ABO blood type. Moreover, the studies

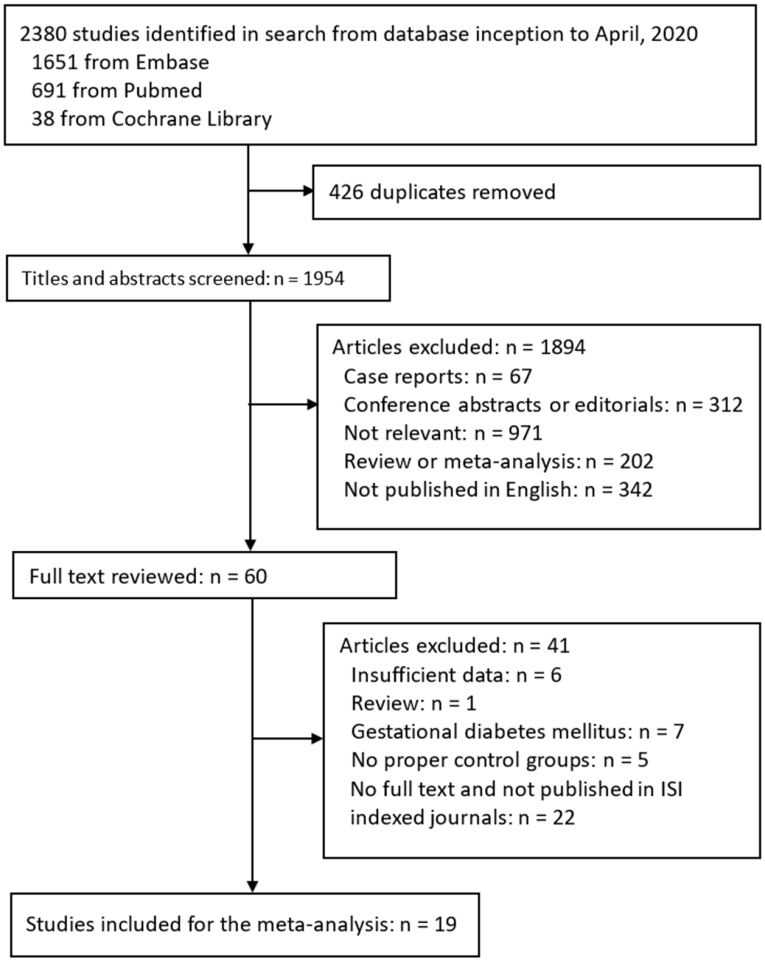

Figure 1. Literature search and study selection.

published in non-ISI indexed journals without available data were also excluded.

Two authors (JC and YTD) independently reviewed the titles and abstracts to identify potentially relevant articles. After being identified as relevant articles, full texts were individually analyzed by both authors, independently, to determine whether the article was qualified for eligibility criteria. If suitable data were not available or unclear in the published papers, the corresponding authors were contacted to request this information.

Data extraction and quality assessment

The following information from eligible studies were extracted by two independent authors (JC and YTD): author name, publication year, region, sample size, baseline characteristics of participants, distribution of ABO blood type in subjects with or without DM. The quality of studies was assessed using the Newcastle-Ottawa Scale [13]. We rated cohort studies with a maximum of 4 stars for selection, 2 stars for comparability, and 3 stars for outcome assessment. For case-control studies, the maximum score for selection, comparability, and exposure assessment was 4, 2, 3, respectively. More stars meant better quality, and the highest score was 9. Disagreements were resolved by discussion between the two authors.

Data synthesis and statistical analysis

Statistical analyses were undertaken using STATA (version 15.0, College Station, Texas). Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to evaluate the correlation of ABO blood type with the risk of DM. The heterogeneity was evaluated using the Q test and I^2 statistic. $I^2 > 50\%$ or $P < 0.1$ was considered to have a significant heterogeneity. Potential moderating factors were evaluated by subgroup analyses, including study regions (Asia, Europe, Africa, North America), study design, and sample size of case group. Publication bias was assessed using Begg's and Egger's tests, with the $P < 0.1$ indicative of significance. Sensitivity analyses were performed to evaluate the robustness of our findings. A 2-sided $P < 0.05$ was set for statistical significance.

Results

Study selection and characteristics

The study selection process and search results are shown in **Figure 1**. In total, 2,380 articles were identified, with 1,651 articles identified in Embase, 691 articles identified in Pubmed, 38 articles identified in the Cochrane Library. After excluding 426 duplicates, 1,954 potentially eli-

gible articles were selected. Of these articles, 60 were searched for full-text assessment after screening of titles and/or abstracts, with 19 considered eligible for inclusion.

Of the 19 included studies, 18 articles were case-control studies, 1 article was a prospective cohort study. The selected studies were published from 1956 to 2016 [7-11, 14-27]. The number of participants with DM ranged from 70 to 3,553 and the number of controls ranged from 55 to 78,551 for a total of 15,350 individuals with DM and 236,001 controls. The detailed characteristics of the 19 studies included in the meta-analysis are presented in **Table 2**.

Study quality

Table 3 shows the assessment of quality using the Newcastle-Ottawa Scale for 19 studies included in this meta-analysis. The total scores ranged from 5 to 8. Higher scores indicate better quality.

Association between ABO blood type and DM

Blood type A was present in 6,187 of the 15,350 individuals with DM (40.3%) and in 96,897 of the 236,001 (41.1%) individuals without DM, leading to a similar prevalence of blood type A in DM cases than in controls with a pooled OR of 1.08 (95% CI: 1.00-1.16; P = 0.053) (**Figure 2**). Since the evidence collected in our meta-analysis showed heterogeneity, a random-effects model was performed. In addition, there was no statistically significant difference in the risk of DM in subjects with blood type B, or AB compared with non-B, or non-AB, respectively (**Figures 3** and **4**). However, a significantly lower prevalence of blood type O in subjects with DM than in controls was observed, with a pooled OR of 0.89 (95% CI: 0.80-0.97; P = 0.013) (**Figure 5**).

Subgroup analysis

Further subgroup analyses according to regions (Asia, Europe, Africa, North America), study design, and sample size of case groups were undertaken to evaluate the presence of heterogeneity in this meta-analysis. Detailed results of subgroup analyses are shown in **Table 4**. Although the overall effect was determined to be not statistically different when comparing blood type A with non-A for the risk of DM, significant increased risk of DM in subjects with blood type A was observed in studies with the number of cases greater than 1000 (OR = 1.06, 95% CI = 1.01-1.11, P = 0.016). Additionally, a positive association between blood type B and DM risk was found in the subgroup of more than 1000 cases, but not in studies with a relatively small number of cases. Furthermore, significant reduction in the risk of DM was observed in the Asian population with blood type O (OR = 0.83, 95% CI = 1.79-0.88, P < 0.001). However, analyses of populations from other regions, such as Europe, Africa, and North America, showed no evidence of benefit of blood type O on the risk of DM. Besides, the negative association between blood type O and DM was observed in studies with the number of cases greater than 1000 (OR = 0.94, 95% CI: 0.91-0.96, P < 0.001), but not in studies with a relatively small number of cases.

Sensitivity analysis

Sensitivity analyses were conducted to evaluate the robustness of our conclusions. The associations of blood types A, B, AB and O with DM did not change considerably after exclusion of any one study from the analyses, suggesting that the pooled results were reliable.

Publication bias

No statistical evidence of publication bias was observed among the included studies overall for the association between blood type A and DM (Begg's test, Pr > |z| = 0.944, Egger's test, P = 0.579). In addition, significant publication biases were also not observed for the associations of blood types B, AB, and O with the risk of DM, as suggested by Begg's test and Egger's test (**Table 5**).

Discussion

Although there is accumulating evidence that ABO blood type is closely correlated with health and diseases, the link of ABO blood type with DM is still unclear due to inconsistent and inconclusive findings. Our meta-analysis did not provide adequate evidence that individuals with blood type A were more likely to have DM than those with non-A. Meanwhile, we investigated the correlations of blood type B, and AB compared with non-B, and non-AB, respective-

Table 2. Characteristics of studies included in this meta-analysis

Study and year	Country	Design	Age, year	Male, %	Blood group A	Blood group B	Blood group AB	Blood group O
Lamba DL et al. 1974	India	Case-control study	Case: 50.05 ± 14.08	Case: 249 (59.9%)	Case: n = 71	Case: n = 178	Case: n = 29	Case: n = 138
			Control: NA	Control: NA	Control: n = 1383	Control: n = 2481	Control: n = 610	Control: n = 1864
Sidhu LS et al. 1988	India	Case-control study	Case: aged 25-58 years	Case: 306 (58.8%)	Case: n = 138	Case: n = 172	Case: n = 106	Case: n = 104
			Control: age ≥ 20 years	Control: NA	Control: n = 1373	Control: n = 2382	Control: n = 537	Control: n = 1912
Fagherazzi G et al. 2015	France	Prospective cohort study	Blood group A: 49.02 ± 6.6; Blood group B: 49.03 ± 6.5; Blood group AB: 49.07 ± 6.4; Blood group O: 49.05 ± 6.5	0	Case: n = 1622	Case: n = 344	Case: n = 147	Case: n = 1440
					Control: n = 34906	Control: n = 6591	Control: n = 2949	Control: n = 34105
Jassim WE et al. 2012	Iraq	Case-control study	Case: (blood group A: 36.8 ± 17; blood group B: 37.2 ± 14; blood group AB: 37.9± 12; blood group O: 38.2 ± 13) Control: (blood group A: 38.0 ± 13; blood group B: 38.0 ± 12; blood group AB: 37.4 ± 11; blood group O: 37.0 ± 12)	Case: 488 (53.0%)	Case: n = 331	Case: n = 150	Case: n = 38	Case: n = 401
				Control: 117 (58.5%)	Control: n = 70	Control: n = 30	Control: n = 10	Control: n = 90
Kamil M et al. 2010	Malaysia	Case-control study	Age ≥ 18 years	Case: 33 (47.1%)	Case: n = 11	Case: n = 25	Case: n = 10	Case: n = 24
				Control: 66 (47.1%)	Control: n = 35	Control: n = 31	Control: n = 19	Control: n = 55
Abu-Bakare A et al. 1983	Nigeria	Case-control study	NA	Case: 110 (54.46%)	Case: n = 59	Case: n = 38	Case: n = 6	Case: n = 99
				Control: NA	Control: n = 2740	Control: n = 1791	Control: n = 268	Control: n = 6008
Macafee AL et al. 1964	Northern Ireland	Case-control study	NA	Case: 343 (39.65%)	Case: n = 307	Case: n = 91	Case: n = 21	Case: n = 446
				Control: NA	Control: n = 4192	Control: n = 1229	Control: n = 384	Control: n = 5522
Andersen J et al. 1960	Denmark	Case-control study	NA	Case: 509 (51.31%)	Case: n = 401	Case: n = 94	Case: n = 34	Case: n = 463
				Control: NA	Control: n = 21276	Control: n = 5209	Control: n = 2309	Control: n = 20342
Pontiroli AE et al. 1984	Italy	Case-control study	Case: aged 18-80 years	Case: 72 (46.15%)	Case: n = 67	Case: n = 21	Case: n = 6	Case: n = 62
			Control: aged 18-77 years	Control: 22 (40%)	Control: n = 24	Control: n = 8	Control: n = 2	Control: n = 21
Bener A et al. 2014	Qatar	Case-control study	Age ≥ 18 years	Case: 842 (51.56%)	Case: n = 474	Case: n = 419	Case: n = 111	Case: n = 629
				Control: 850 (51.52%)	Control: n = 456	Control: n = 337	Control: n = 107	Control: n = 750
Navabi J et al. 2020	Iran	Case-control study	Case: 50.5 ± 15.1	Case: 122 (32.53%)	Case: n = 154	Case: n = 67	Case: n = 32	Case: n = 122
			Control: 51.1 ± 14.2	Control: 99 (26.4%)	Control: n = 126	Control: n = 64	Control: n= 36	Control: n = 149
Iyengar S et al. 1989	USA	Case-control study	NA	NA	Case: n = 113	Case: n = 18	Case: n = 6	Case: n = 150
					Control: n = 193	Control: n = 44	Control: n = 7	Control: n = 256
Williams DR et al. 1979	UK	Case-control study	NA	Case: 314 (43.55%)	Case: n = 309	Case: n = 73	Case: n = 18	Case: n = 321
				Control: 268 (52.04%)	Control: n = 197	Control: n = 47	Control: n = 16	Control: n = 255
Oner C et al. 2016	Turkey	Case-control study	42.6 ± 13.4	Case: 254 (52.48%)	Case: n = 279	Case: n = 69	Case: n = 27	Case: n = 109
				Control: 161 (37.27%)	Control: n = 180	Control: n = 69	Control: n = 18	Control: n = 165
Scholz W et al. 1975	Germany	Case-control study	NA	Case: 441 (42.73%)	Case: n = 473	Case: n = 118	Case: n = 35	Case: n = 406
				Control: 1351 (57.51%)	Control: n = 1027	Control: n = 254	Control: n = 117	Control: n = 951
Buckwalter JA et al. 1964	USA	Case-control study	NA	Case: 612 (41.1%)	Case: n = 634	Case: n = 164	Case: n = 35	Case: n = 656
				Control: NA	Control: n = 21144	Control: n = 4695	Control: n = 1748	Control: n = 22392

Mcconnell RB et al. 1956	UK	Case-control study	Men: mean age 44.65; Women: mean age 52.53	Case: 484 (36.3%) Control: NA	Case: n = 596 Control: n = 6008	Case: n = 103 Control: n = 1238	Case: n = 55 Control: n = 423	Case: n = 579 Control: n = 6580
Berg K et al. 1966	Norway	Case-control study	Aged 14-86 years	NA	Case: n = 91 Control: n = 1521	Case: n = 13 Control: n = 259	Case: n = 3 Control: n = 110	Case: n = 69 Control: n = 1199
Pontiroli AE et al. 1986	Italy	Case-control study	Case: (men: mean age 33.02; women: mean age 33.31) Control: NA	NA	Case: n = 57 Control: n = 46	Case: n = 10 Control: n = 6	Case: n = 7 Control: n = 5	Case: n = 52 Control: n = 48

NA, not available.

Table 3. Assessment of the quality of all studies included in the Meta-analysis

	Selection	Comparability	Measurement	Total
Case-control studies				
Lamba DL et al. 1974	4	0	2	6
Sidhu LS et al. 1988	3	0	2	5
Jassim WE et al. 2012	4	1	2	7
Kamil M et al. 2010	4	1	2	7
Abu-Bakare A et al. 1983	4	0	2	6
Macafee AL et al. 1964	4	0	2	6
Andersen J et al. 1963	4	0	2	6
Pontiroli AE et al. 1984	4	1	2	7
Bener A et al. 2014	4	1	3	8
Navabi J et al. 2020	4	1	2	7
Iyengar S et al. 1989	4	0	2	6
Williams DR et al. 1979	4	1	2	7
Oner C et al. 2016	3	0	2	5
Scholz W et al. 1975	4	0	2	6
Buckwalter JA et al. 1964	4	0	2	6
Mcconnell RB et al. 1956	4	0	2	6
Berg K et al. 1966	4	0	2	6
Pontiroli AE et al. 1986	3	0	2	5
Cohort study				
Fagherazzi G et al. 2015	4	2	2	8

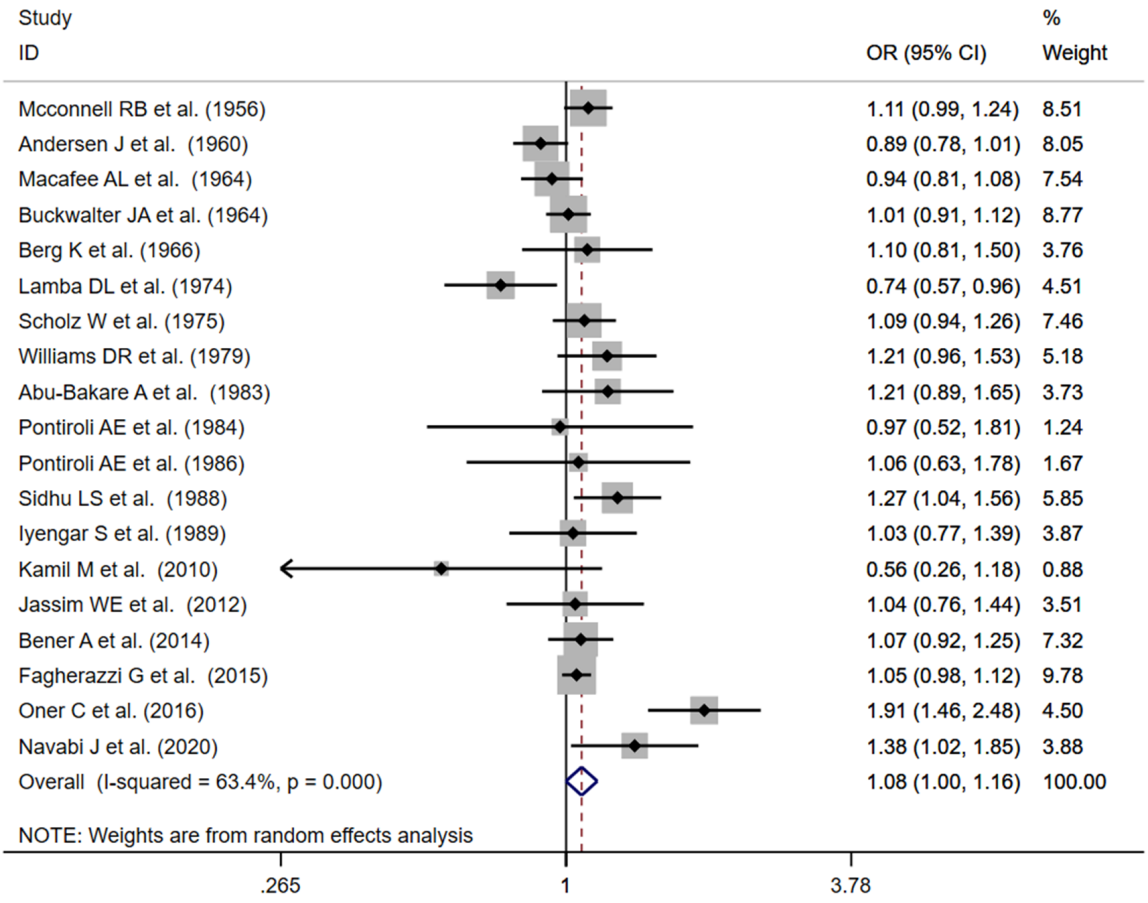

Figure 2. Forest plot of studies evaluating the association between blood type A and the risk of diabetes.

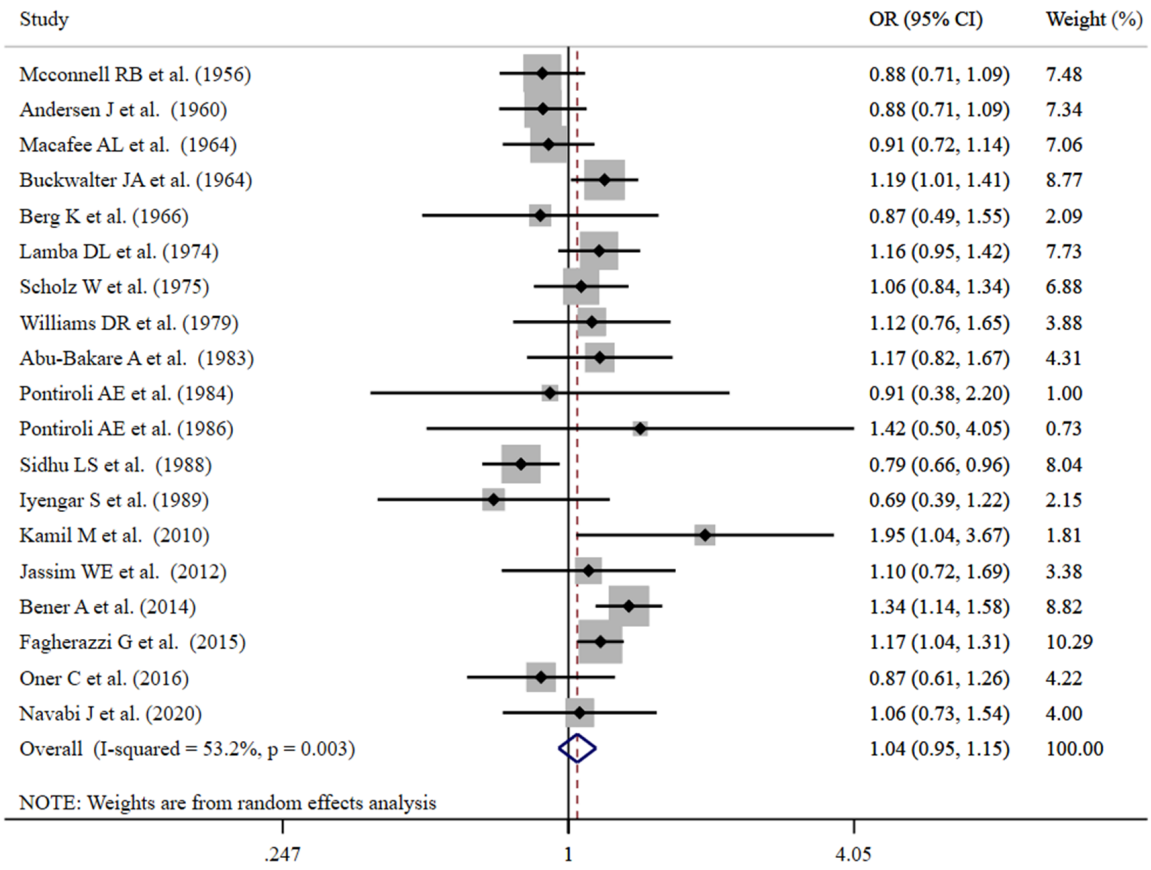

Figure 3. Forest plot of studies evaluating the association between blood type B and the risk of diabetes.

ly, but failed to confirm statistical differences. However, our meta-analysis revealed that the risk of DM in subjects with blood type O was significantly decreased compared with those with non-O blood. Furthermore, according to the results of subgroup analyses, potential factors, such as regions, study design, and sample size of case groups should be considered when exploring the association between ABO blood type and the risk of DM. The present study suggests that blood type O may be a protective factor for DM.

The study by Bener A et al. reported that the percentage of blood type A was slightly higher in subjects with DM than those without DM, yet this difference did not reach significance (29% vs 27.6%, P = 0.214) [7]. However, Navabi J et al. argued that participants with blood type A were the most vulnerable for type 2 diabetes [21]. Our data showed that the risk of DM had no statistically significant difference in participants with blood type A compared with those with non-A blood types (OR = 1.08, 95% CI: 1.00-1.16; P = 0.053). Nevertheless, it is noteworthy that the risk of DM was significantly higher in individuals with blood type A than those with non-A type blood in studies with a relatively large number of cases (**Table 4**). Therefore, these inconsistent findings may partly be explained by variations in the number of cases.

Previous study revealed that blood type B was significantly more common in individuals with DM as compared with the healthy population (25.7% vs. 20.4%; P < 0.001) [7]. However, our study showed that there was no significant difference in the risk of DM between subjects with blood type B and those with non-B blood (**Figure 3**). According to subgroup analyses, the number of cases may have a potential impact on the results. Future studies with larger sample sizes are warranted to confirm our findings. In

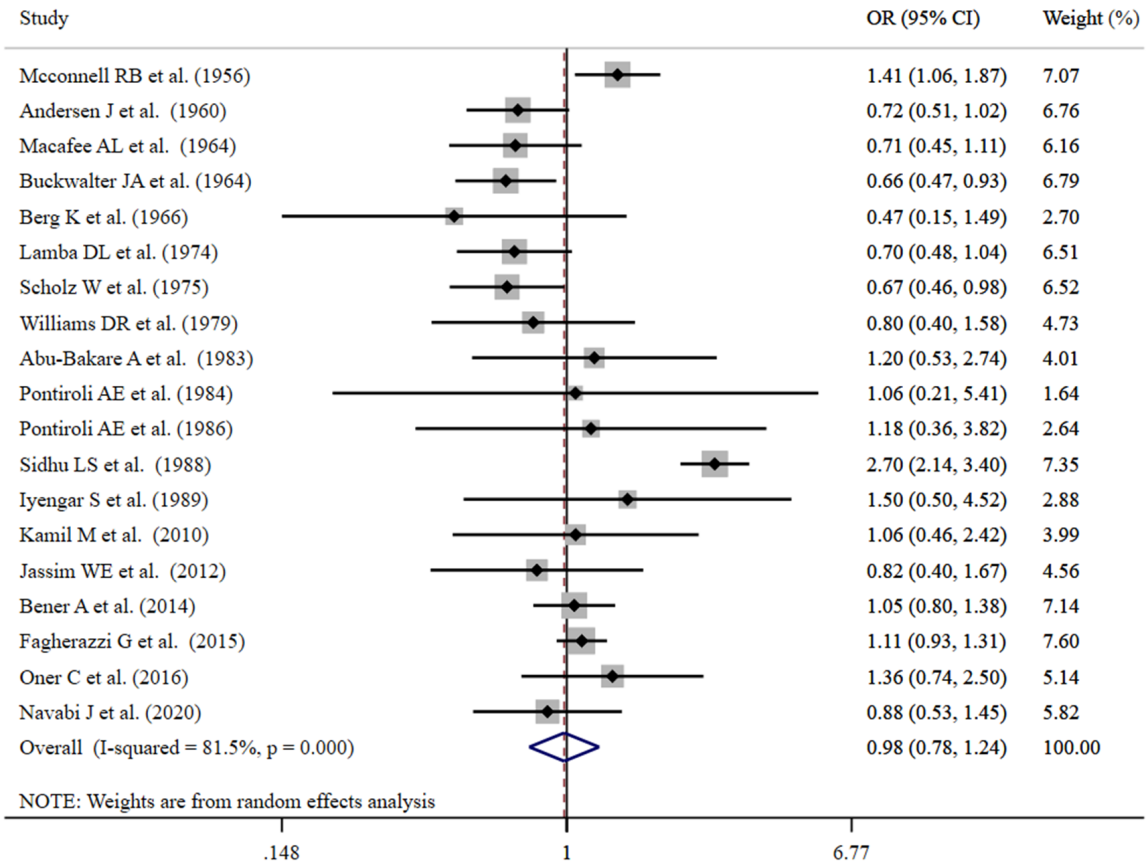

Figure 4. Forest plot of studies evaluating the association between blood type AB and the risk of diabetes.

addition, the result regarding study design should be interpreted with caution as only one prospective cohort study was available for inclusion.

Moreover, in the current study, an overall effect was not statistically different when comparing blood type AB with non-AB blood for the risk of DM. Of interest, another study pointed out that blood type AB was a protective factor against gestational diabetes mellitus [28]. Due to the differences in glucose values for diagnosis [29], the present meta-analysis included research on type 1 and type 2 diabetes, but articles on gestational diabetes mellitus were excluded. Moreover, there is a lack of sufficient data to recommend the cut-off values for oral glucose tolerance testing in early pregnancy [30]. Nevertheless, it is worth investigating the association of ABO blood types with different types of diabetes.

Partly in agreement with our finding, the prior review paper by Meo SA et al. had also observed that individuals with blood type O were at low risk of developing type 2 diabetes [31]. However, our study, which included more research, extended the findings through introducing subgroup analyses and exploring the potential moderators. Besides, after excluding the studies that had no detailed data on the distribution of ABO blood type in subjects with or without DM, a comprehensive analysis of the data was conducted, which was not performed in the study by Meo SA et al. According to the data of our meta-analysis, subjects with blood type O were less likely to have DM, which also could be evidenced by the findings from other studies [8, 17]. However, a recent study indicated that blood type O independently increased the risk of gestational diabetes mellitus [29], which may be attributed to the limited sample size and the different types of diabetes. In addition, based on subgroup analyses, the negative association between blood type O and DM was observed in the Asian population, but not in other populations. Moreover, the analysis of studies with a relatively large number of cases showed a negative correlation between

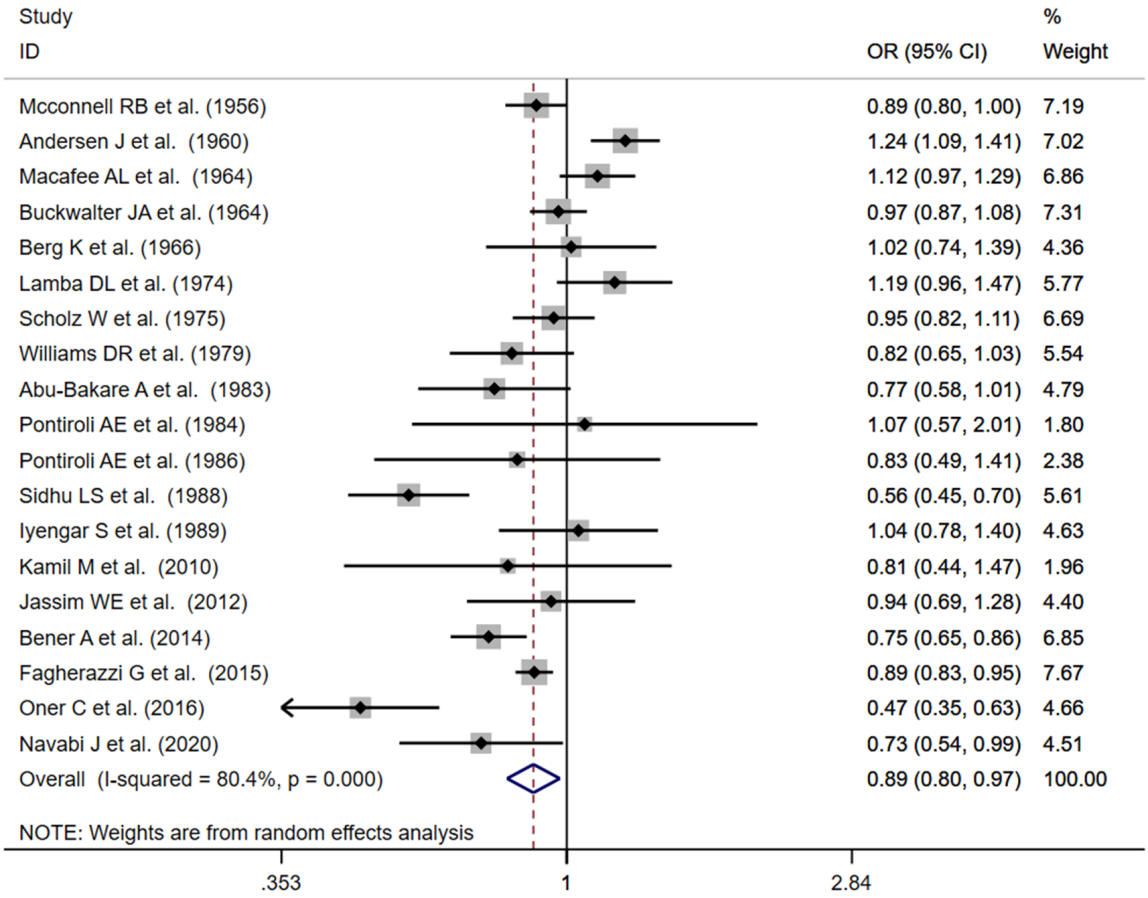

Figure 5. Forest plot of studies evaluating the association between blood type O and the risk of diabetes.

blood type O and DM, whereas such association was not observed in studies with a relatively small number of cases. To date, many risk factors for DM are well known and have been studied for decades, such as excessive energy intake, lack of physical activity, and genetic factors. The observed association between ABO blood type and DM risk may be the combined effect of multiple risk factors. However, we did not take these confounding factors into consideration due to the lack of detailed data. Future studies focused on this topic should eliminate the influence of these confounders.

As a major blood group classification, ABO blood typing is widely used in clinical practice. Although not fully understood, it is speculated that the observed association of ABO blood type with DM might be underlined by the following mechanism. Studies have demonstrated significant associations of genetic variants in different ABO blood types with various inflammatory markers, such as soluble levels of E-selectin (E-selectin), vascular cell adhesion molecule 1 (VCAM1), intercellular adhesive molecule 1 (ICAM1), and P-selectin (P-selectin) [32, 33]. Noteworthy, chronic low-grade inflammation is one of the most important causes of insulin resistance [34, 35], a key element in the pathogenesis of type 2 diabetes. It has been reported that blood type B associates primarily with VCAM1 level, while the A1 subtype shows a robust effect on E-selectin and ICAM1 levels [33]. The levels of ICAM-1 and E-selectin have been found to be significantly higher at baseline in women who developed diabetes than in those who remained nondiabetic during follow-up [34]. Further investigations are needed to clarify whether ABO blood types affect the development of DM by the above-mentioned mechanism.

Despite a comprehensive exploration of ABO blood grouping and DM, this meta-analysis has some limitations. First, since there was certain heterogeneity in this study, a random-effects

Table 4. Subgroup analyses of the association between ABO blood type and DM

Subgroup analysis	No. of study	No. of subject		OR (95% CIs)	*P* value
		Case group	Control group		
Blood type A and DM					
Region					
Asia	7	4418	15339	1.13 (0.89-1.42)	0.313
Europe	9	8954	159376	1.03 (0.97-1.10)	0.303
Africa	1	202	10807	1.21 (0.89-1.65)	0.213
North America	2	1776	50479	1.01 (0.92-1.12)	0.788
Study design					
Case-control study	18	11797	157450	1.08 (0.99-1.18)	0.079
Prospective cohort study	1	3553	78551	1.05 (0.98-1.12)	0.154
Sample size of case group					
< 1000	14	6310	89223	1.09 (0.95-1.24)	0.233
≥ 1000	5	9040	146778	1.06 (1.01-1.11)	0.016
Blood type B and DM					
Region					
Asia	7	4418	15339	1.09 (0.89-1.34)	0.387
Europe	9	8954	159376	1.01 (0.91-1.12)	0.917
Africa	1	202	10807	1.17 (0.82-1.67)	0.397
North America	2	1776	50479	0.98 (0.58-1.63)	0.928
Study design					
Case-control study	18	11797	157450	1.03 (0.93-1.14)	0.554
Prospective cohort study	1	3553	78551	1.17 (1.04-1.31)	0.007
Sample size of case group					
< 1000	14	6310	89223	0.98 (0.88-1.09)	0.689
≥ 1000	5	9040	146778	1.14 (1.00-1.29)	0.042
Blood type AB and DM					
Region					
Asia	7	4418	15339	1.13 (0.70-1.82)	0.615
Europe	9	8954	159376	0.90 (0.71-1.13)	0.352
Africa	1	202	10807	1.20 (0.53-2.74)	0.658
North America	2	1776	50479	0.84 (0.41-1.73)	0.637
Study design					
Case-control study	18	11797	157450	0.97 (0.74-1.28)	0.836
Prospective cohort study	1	3553	78551	1.11 (0.93-1.31)	0.241
Sample size of case group					
< 1000	14	6310	89223	1.00 (0.68-1.45)	0.979
≥ 1000	5	9040	146778	0.96 (0.75-1.24)	0.768
Blood type O and DM					
Region					
Asia	7	4418	15339	0.83 (0.79-0.88)	< 0.001
Europe	9	8954	159376	0.98 (0.95-1.00)	0.060
Africa	1	202	10807	0.88 (0.77-1.02)	0.081
North America	2	1776	50479	0.99 (0.94-1.04)	0.661
Study design					
Case-control study	18	11797	157450	0.96 (0.93-0.98)	0.001
Prospective cohort study	1	3553	78551	0.93 (0.90-0.97)	0.001
Sample size of case group					
< 1000	14	6310	89223	0.97 (0.94-1.01)	0.154
≥ 1000	5	9040	146778	0.94 (0.91-0.96)	< 0.001

DM, diabetes mellitus.

Table 5. Publication bias calculated by Egger's and Begg's test

	Egger's test	Begg's test
Blood type A and DM	0.579	0.944
Blood type B and DM	0.455	0.944
Blood type AB and DM	0.233	0.484
Blood type O and DM	0.446	0.576

model was used, an approach that takes into account the variance among the studies and could provide more conservative results than fixed-effects model [36]. Second, the diagnostic criteria for diabetes have changed over years, which may have a potential impact on the result. Therefore, more convincing evidence is needed to confirm our findings. Additionally, other potential confounders, such as lifestyle and eating habits, may cause heterogeneity and should be considered in future studies. Third, any articles without full text could be retrieved and were not published in ISI indexed journals were excluded, which may cause a publication bias. Although no significant publication biases were observed in the present study, as suggested by Begg's test and Egger's test, additional research is necessary toward providing high-quality evidence on this topic. Despite the aforementioned limitations, the present study may still provide valuable information to help understand the association of ABO blood type with DM.

In conclusion, this meta-analysis suggests that blood type O may be a protective factor against DM, which means that those with non-O blood types may be more likely to have DM. This is of clinical importance for individuals with non-O blood, who should pay more attention to the risk of diabetes and early prevention. Notably, such an association appears to be affected by other factors, like regions and the number of cases. Future research should take these confounders into consideration and confirm the results of our study.

Acknowledgements

This study was supported by grants from Outstanding Young Doctoral Talents Cultivation Program (2024QB022).

Disclosure of conflict of interest

None.

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