Best Evidence Topic report: does blood group type O decrease the risk of severe COVID-19 infection?

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ABSTRACT

A short-cut systematic review was conducted using a described protocol. The three-part question addressed was: In patients with COVID-19 infection, does blood group type O versus non-O blood groups lead to a lower risk of severe COVID-19 infection? MEDLINE, Embase, and Cochrane databases were searched for relevant evidence. Altogether, 238 papers were found using the search strategy developed. Seventeen provided the best evidence to answer the three-part question. The data on first author name, publication year, country of origin, study type, study sample size, participant's gender, reported effect sizes, main findings and limitations were extracted from the relevant studies and listed in a table. Finally, 4 out of 17 studies revealed that having blood group type O may be associated with a lower risk of severe COVID-19 among patients with COVID-19 infection and the 13 remaining studies reported no significant relationship between having O blood group and risk of COVID-19 severity among the infected individuals. Of three systematic reviews and meta-analyses identified, none detected a protective effect of blood group type O. The clinical bottom line is that the best available evidence does not support the notion that blood group type O is protective against serious outcomes in COVID-19.

THREE-PART QUESTION

In (patients with COVID-19 infection presenting to the ED), does (blood group type O compared with other blood groups) predict (less severe infection and lower mortality)?

CLINICAL SCENARIO

A young female with blood group type O was presented to the ED with mild COVID-19 and was discharged from the ED; however, her younger sibling, whose blood group was A, was admitted to the hospital due to severe COVID-19 infection at the same date. You are wondering whether blood group type O reduces the risk of severe COVID-19 infection among affected patients.

SEARCH STRATEGY

MEDLINE using the Ovid interface, inception—May 2023: [(exp covid 19/ OR exp covid 19 vaccines/ OR exp covid 19 serotherapy/ OR exp covid 19 nucleic acid testing/ OR exp covid 19 serological testing/ OR exp covid 19 testing/ OR exp sars cov 2/OR exp coronavirus/ OR "covid 19" .mp. OR "covid 19 vaccines" .mp. OR "covid 19 serotherapy" .mp. OR "covid 19 nucleic acid testing" .mp. OR "covid 19 serological testing" .mp. OR "covid 19 testing" .mp. OR "sars cov 2" .mp. OR "severe acute respiratory syndrome coronavirus 2" .mp. OR "ncov" .mp. OR "2019 ncov" .mp. OR "coronavirus" .mp. OR "cov" .mp. OR "coronavirus disease 2019" .mp.) AND (exp severity of illness index/ OR "index severity" .mp. OR "illness index severity" .mp. OR "severity of illness index" .mp.) AND (exp abo blood group system/ OR "abo blood group system" .mp. OR "blood group" .mp. OR "ABO factor" .mp. OR "factor ABO" .mp. OR "A blood group" .mp. OR "B blood group" .mp. OR "O blood group" .mp. OR "AB blood group" .mp.)] for general search and [("COVID-19" .mp. OR "SARS-CoV-2" .mp. OR "coronavirus disease 2019" .mp.) AND ("index severity" .mp. OR "illness index severity" .mp. OR "severity of illness index" .mp.) AND ("ABO blood group system" .mp. OR "ABO factor" .mp. OR "factor ABO" .mp. OR "A blood group" .mp. OR "B blood group" .mp. OR "O blood group" .mp. OR "AB blood group" .mp.) AND ("emergency*" .mp.)] for clinical query search.

Cochrane using the Ovid interface, inception—May 2023: [exp COVID-19/ OR exp Coronavirus/ OR exp Severe acute respiratory syndrome-related coronavirus/ OR exp COVID-19 Serological Testing/ OR exp COVID-19 Vaccines/ OR exp COVID-19 Testing/ OR exp COVID-19 Nucleic Acid Testing/ OR exp SARS-CoV-2/OR "COVID-19" .mp. OR "SARS-CoV-2" .mp. OR "coronavirus disease 2019" .mp.) AND (exp Severity of Illness Index/ OR "index severity" .mp. OR "severity of illness index" .mp. OR "illness index severity".mp.) AND (exp ABO Blood-Group System/ OR exp Blood Group Antigens/ OR "ABO factor" .mp. OR "factor ABO" .mp. OR "ABO blood group" .mp. OR "ABO blood group system" .mp.] for general search and PICO (population/intervention/comparison/outcomes) search.

EMBASE using the Ovid interface, inception—May 2023: [(exp coronavirus disease 2019/OR exp Severe acute respiratory syndrome coronavirus 2/OR exp SARS-CoV-2 vaccine/ OR exp COVID-19 testing/ OR exp COVID-19 pneumonia/ OR "COVID-19" .mp. OR "SARS-CoV-2" .mp. OR "coronavirus disease 2019") AND (exp severity of illness index/ OR "index severity" .mp. OR "illness index severity" .mp. OR "severity of illness index" .mp.) AND (exp blood group ABO system/ OR exp abo factors/ OR "ABO blood group" .mp. OR "ABO blood group system" .mp. OR "ABO factor" .mp. OR "factor ABO" .mp.)] for general search and PICO search.

Search results were limited to studies written in the English language, which evaluated humans.

SEARCH OUTCOMES

A total of 238 papers were found, of which 82 papers were identified after removing duplicates. Out of these, 43 papers were excluded based on title and abstract screening. Thirty-nine full-text articles were screened and assessed for eligibility. From these, 20 papers were eligible to be enrolled based on full-text screening. Among these 20 studies, 3 studies were excluded since they were reviewed in enrolled systematic review and meta-analysis studies. Finally, 17 studies were enrolled and provided the best evidence to answer the three-part question (figure 1).

RELEVANT STUDIES

See table 1.

COMMENTS

Out of relevant 17 studies,[1–17] four had supported the concept that having O blood group was a protective factor

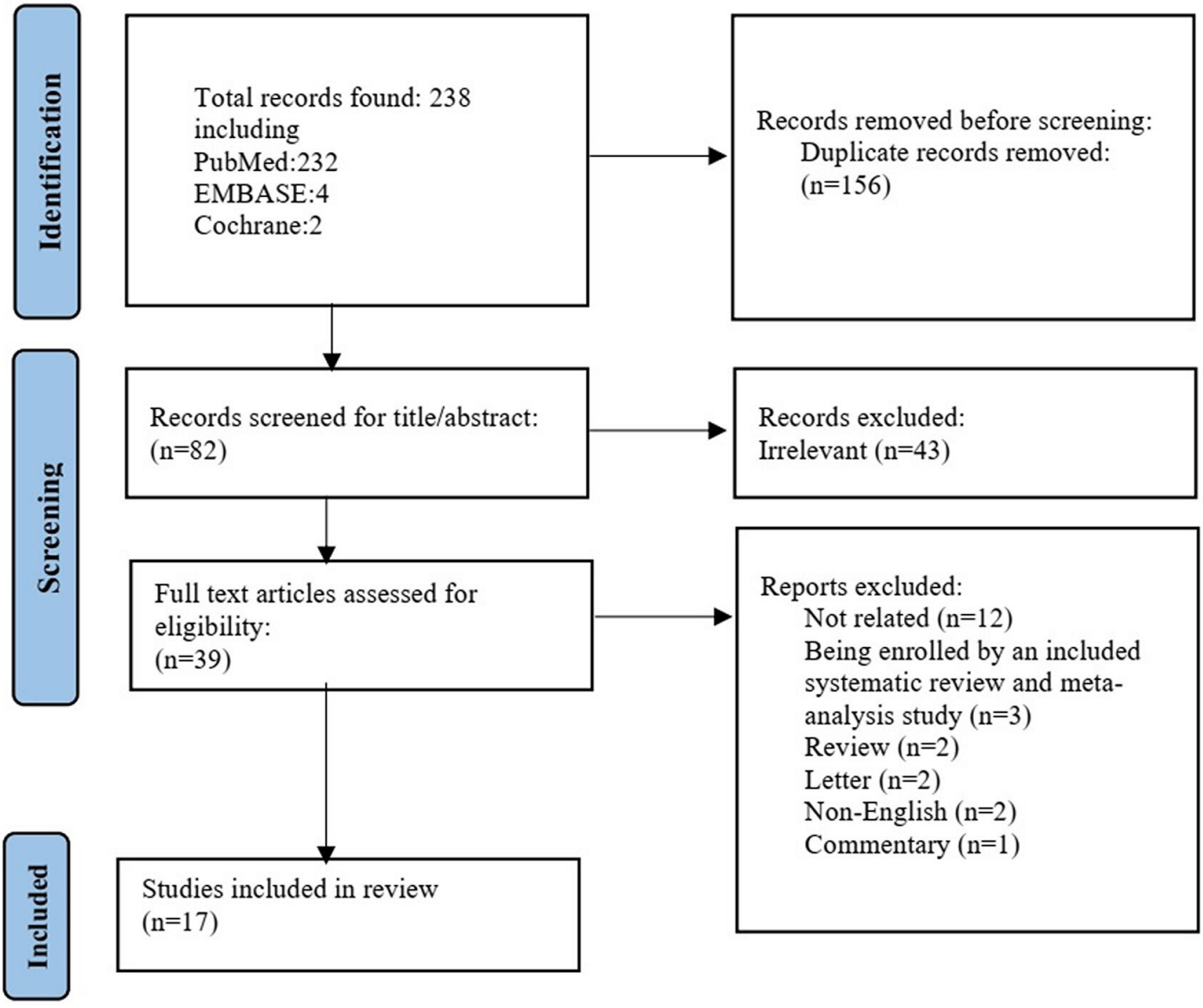

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

against severe COVID-19 infection[6 8 9 17] and 13 demonstrated that O blood group had no significant effect on COVID-19 severity among patients with COVID-19.[1–5 7 10–16] Although numerous studies have been conducted which evaluated the association between ABO blood groups and severity of COVID-19 among affected patients, their results are conflicting. Regarding limitations, most of the studies were conducted on a limited population with limited diversity, which might further affect the generalisability of findings.[5 8 10 12 14–17] Furthermore, some studies reported that considerable differences regarding the frequency of various types of blood groups might affect the results since usually type O blood group were the most predominant type and blood types such as B and AB were less common.[4 9 15] In addition, a considerable number of the cohort studies had a small sample size of patients with COVID-19.[4 7 8 10 12 14] Moreover, among cohort studies, 13 were retrospective in design.[4–16] The majority of studies were subject to potential confounding effects because of the lack of a control group or adjustments for potential confounding variables.[5–7 11 14 15] Finally, the systematic reviews and meta-analyses reported some degrees of publication bias and notable heterogeneity between the studies.[1–3]

To the emergency physicians who manage patients with COVID-19 in the ED, there is always a serious concern: Does this patient need to be hospitalised due to COVID-19-related adverse outcome(s)? Many risk stratification scores were introduced in this issue according

Clinical bottom line

⇒ The currently available best evidence suggests that blood group O is not protective against serious outcomes in COVID-19.

Table 1 The main characteristics and key findings of the 17 included studies

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Liu *et al*, 2021, China[1]	10 studies including 8 case–control and 2 cohort studies 54 218 subjects including 9383 patients with COVID-19 and 44 835 uninfected individuals	Systematic review and meta-analysis	COVID-19 mortality	OR (95% CI): A compared with non-A=1.24 (1.02 to 1.21) B compared with non-B=0.97 (0.77 to 1.24) AB compared with non-AB=1.57 (0.90 to 2.72) O compared with non-O=1.07 (0.87 to 1.31)	Significant heterogeneity was found. Potential confounding factors could not be ruled out.
Wu *et al*, 2020, China[2]	Four studies including four retrospective cohort studies 34 794 COVID-19-infected and non-infected individuals	Systematic review and meta-analysis	COVID-19 severity COVID-19 mortality	OR (95% CI): A=1.055 (0.783 to 1.422) B=1.271 (0.894 to 1.806) AB=2.424 (0.934 to 6.294) O=0.748 (0.556 to 1.077) A=1.124 (0.879 to 1.124) B=0.891 (0.669 to 1.422) AB=1.348 (0.507 to 1.348) O=0.972 (0.746 to 1.265)	The source of samples was not diverse. Prospective cohorts were not collected to determine when healthy patients were infected with COVID-19.
Franchini *et al*, 2021, Italy[3]	21 studies including 11 case–control and 10 cohort studies 922 145 participants with COVID-19 and uninfected individuals	Systematic review and meta-analysis	ICU admission/severe disease Hospitalisation Death Intubation Proning Acute kidney injury Shock Thrombosis	RR (95% CI): Non-O=ref. O=1.00 (0.92 to 1.09) Non-O=ref. O=0.94 (0.87 to 1.02) Non-O=ref. O=0.95 (0.89 to 1.02) Non-O=ref. O=0.98 (0.93 to 1.04) Non-O=ref. O=1.22 (0.71 to 2.10) Non-O=ref. O=0.87 (0.51 to 1.49) Non-O=ref. O=0.79 (0.62 to 1.01) Non-O=ref. O=0.88 (0.42 to 1.85)	Risk of bias and considerable heterogeneity were found in some enrolled studies.
Muñoz-Culla *et al*, 2021, Spain[4]	412 patients with COVID-19 (130 males/282 females) and 17 796 blood donors	Retrospective cohort	Comparable COVID-19 severity between blood groups	P>0.05	The prevalence of blood groups was not uniform in various ethnicities and the findings were not validated with appropriate controls in each ethnicity and region. The sample size of patients with COVID-19 was relatively small. The study was retrospective in design.
Latz *et al*, 2020, USA[5]	1289 patients with COVID-19 (417 males/872 females)	Retrospective cohort	COVID-19 severity	Adjusted OR (95% CI): A=ref. B=0.72 (0.42 to 1.26) AB=0.78 (0.33 to 1.87) O=0.77 (0.51 to 1.16)	The study was retrospective in design. There was lead-time bias. The unmeasured confounding affected the results.
Ray *et al*, 2020, Canada[6]	225 556 individuals with SARS-CoV-2 laboratory test (65 566 males/159 990 females)	Retrospective cohort	COVID-19 severity/ mortality	Adjusted relative risk (RR) (95% CI): A=ref. B=1.04 (0.92 to 1.19) AB=1.09 (0.88 to 1.33) O=1.00 (0.90 to 1.10) O (compared with non-O)=0.98 (0.90 to 1.07)	The study was retrospective in design. There was some degrees of selection bias.
Badedi *et al*, 2021, Saudi Arabia[7]	404 patients with COVID-19 (251 males/153 females)	Retrospective cohort	COVID-19 severity	OR (95% CI): A=1.2 (0.14 to 1.74) B=1.9 (0.74 to 7.57) AB=1.1 (0.96 to 1.4) O=1.1 (0.44 to 2.93)	The sample size was small. The study was retrospective in design. The causal associations were not established. The X^2 test was not adjusted for confounders.
Zalba Marcos *et al*, 2020, Spain[8]	225 patients with COVID-19 (81 males/144 females) and 182 384 healthy blood donors	Retrospective cohort	Respiratory complications Thrombotic complications Other infections	OR (95% CI): O=ref. A=1.22 (0.31, 4.84) AB+B=1.01 (0.10, 9.82) A=ref. AB+B=6.16 (1.75, 21.8) O=2.09 (0.67, 6.54) A=ref. AB+B=3.05 (1.11, 8.39) O=2.36 (1.11, 5.01)	Study population was recruited from a limited geographical area and was not diverse. The sample size of patients with COVID-19 was small. The study was retrospective in design.
Jericó *et al*, 2022, Spain[9]	1399 hospitalised patients with COVID-19 (807 males/592 females) (365 admitted to the ICU) and 182 384 healthy blood donors	Retrospective cohort	COVID-19 severity	Adjusted OR (95% CI): A=ref. B=1.27 (0.55 to 2.90) AB=0.60 (0.17 to 2.08) O=0.52 (0.33 to 0.81)	The prevalence of blood groups was not uniform, with the O blood group having the highest prevalence which might lead to over-representation. The study was retrospective in design. Variation of ICU admission criteria was not controlled.
Al-Youha *et al*, 2021, Kuwait[10]	3305 hospitalised SARS-CoV-2-positive patients (2288 males/1017 females)	Retrospective cohort	Pneumonia development	Adjusted OR (95% CI): A=1.32 (1.01 to 1.71) B=0.85 (0.64 to 1.11) AB=0.93 (0.58 to 1.43) O=0.91 (0.71 to 1.17)	The sample size of patients with severe COVID-19 was small. The study was retrospective in design.
Amoroso *et al*, 2021, Italy[11]	56 304 transplanted and waitlisted patients (37 565 males/18 728 females)	Retrospective cohort	COVID-19 mortality	OR (95% CI): A=0.95 (0.55 to 1.65)	The study population were at a greater risk of COVID-19 infection and mortality. Availability of COVID-19 testing was not homogeneous at the national level. The study was retrospective in design.

Continued

Table 1 Continued

Author, date, country	Patient group	Study type	Outcomes	Key results	Study weaknesses
Bahardoust *et al*, 2021, Iran[12]	1002 patients with COVID-19 (665 males/337 females) including 81 patients with liver disease (56 males/25 females) and 921 patients without liver disease (609 males/312 females)	Retrospective cohort	COVID-19 severity	Adjusted OR (95% CI): In patients with liver disease: A=1.59 (1.15 to 2.11) In patients without liver disease: A=0.67 (0.39 to 0.96)	The number of patients with COVID-19 suffering from liver diseases was small. The study was retrospective in design.
Dal *et al*, 2021, Turkey[13]	39 850 patients with laboratory-confirmed COVID-19 (24 088 males/15 762 females)	Retrospective cohort	Hospitalisation ICU admission Mechanical ventilation Case fatality rate	OR (95% CI): B=ref. A=1.027 (0.961 to 1.097) AB=1.004 (0.921 to 1.095) O=1.018 (0.950 to 1.090) B=ref. A=1.216 (1.023 to 1.446) AB=1.019 (0.811 to 1.281) O=1.123 (0.938 to 1.344) B=ref. A=1.206 (0.983 to 1.480) AB=1.135 (0.871 to 1.478) O=1.098 (0.888 to 1.359) B=ref. A=1.120 (0.898 to 1.397) AB=1.011 (0.756 to 1.351) O=1.059 (0.842 to 1.331)	The study was retrospective in design.
Hafez *et al*, 2022, United Arab Emirates[14]	303 adult patients with COVID-19 (221 males/82 females)	Retrospective cohort	Pneumonia development Disease severity Mortality Viral clearance rate	Crude OR (95% CI), adjusted OR (95% CI): O=ref. A=1.35 (0.78 to 2.38), 1.57 (0.77 to 3.25) B=1.20 (0.67 to 2.13), 0.89 (0.44 to 1.77) AB=1.94 (0.75 to 5.41), 1.45 (0.47 to 4.82) O=ref. A=1.68 (0.76 to 3.73), 2.02 (0.80 to 5.16) B=1.04 (0.41 to 2.50), 1.05 (0.38 to 2.79) AB=3.09 (0.97 to 9.05), 3.35 (0.93 to 11.51) O=ref. A=0.87 (0.17 to 3.63), 1.36 (0.23 to 7.58) B=0.31 (0.02 to 1.98), 0.47 (0.02 to 3.96) AB=2.46 (0.34 to 12.37), 3.57 (0.38 to 28.53) O=ref. A=1.21 (0.89 to 1.66), 1.37 (0.45 to 4.15) B=0.96 (0.68 to 1.34), 0.272 (0.076 to 0.968) AB=1.07 (0.63 to 1.82), 1.16 (0.67 to 1.997)	The study had a small sample size and regarding the multiethnicity of the UAE population, due to variation of blood group distribution in different ethnicities, the precise risk comparison was not possible. The study was retrospective in design. In the comparison analysis, only hospitalised patients with COVID-19 were enrolled and no healthy individual was included. No control for a variety of confounding factors was performed.
Jawdat *et al*, 2022, Saudi Arabia[15]	373 patients with COVID-19-positive PCR (218 males/155 females)	Retrospective cohort	Mild COVID-19 Moderate COVID-19 Severe COVID-19	OR (95% CI): A=0.88 (0.57 to 1.36) B=1.57 (0.98 to 2.44) AB=1.31 (0.47 to 2.96) O=0.79 (0.53 to 1.16) A=0.78 (0.46 to 1.30) B=1.73 (1.02 to 2.83) AB=1.74 (0.615 to 0.98) O=0.75 (0.477 to 1.167) A=1.07 (0.75 to 1.50) B=1.36 (0.91 to 1.98) AB=1.17 (0.49 to 2.39) O=0.76 (0.55 to 1.04)	The study population was limited to Saudi population and not diverse. Prevalence of various blood groups was not uniform so that the sample size was small in AB blood group. The study population was small. The study was retrospective in design. No adjustment for possible confounding factors was performed.
Kofahi *et al*, 2022, Jordan[16]	2148 Jordanian patients recovered from COVID-19 (903 males/1245 females)	Retrospective cohort	Disease severity Hospitalisation	Adjusted OR (95% CI): A=ref. B=1.027 (0.671 to 1.57) AB=1.021 (0.619 to 1.685) O=1.054 (0.75 to 1.48) A=ref. B=0.969 (0.597 to 1.574) AB=1.147 (0.667 to 1.973) O=1.315 (0.906 to 1.908)	Fatal COVID-19 cases were not enrolled. Data regarding ABO blood groups of 42 patients were missing. The study was retrospective in design. Data were self-reported and data validation with other methods was not conducted. No stratification according to geographical area was performed. Response rate varied between different groups which can lead to over-representation and under-representation of some groups.
Tamayo-Velasco *et al*, 2021, Spain[17]	108 hospitalised patients with COVID-19 (47 males/61 females)	Prospective cohort	Mechanical ventilation or death	HR (95% CI): Non-O=ref. O=0.463 (0.213 to 1.004)	The study only enrolled hospitalised patients. The study took place at a single centre.

CI, confidence interval; HR, hazard ratio; ICU, intensive care unit; OR, odds ratio; PCR, polymerase chain reaction; Ref, reference; RR, relative risk; UAE, United Arab Emirates.

to the published studies. Among patients with COVID-19 infection without known risk factors for poor outcomes (including unstable vital signs upon arrival at ED, older age, uncontrolled diabetes mellitus, immunosuppression, chronic diseases of liver, kidney, heart or lung), emergency physicians may have heard that type O blood group was protective against serious outcomes. However, the evidence retrieved does not back that conclusion.

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