The Daily COVID-19 Literature Surveillance Summary

October 23, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Epidemiology

- Health policy researchers analyzed the COVID-19 and excess all-cause mortality rates across three periods (since the start of the pandemic, since 10 May 2020, and since 7 June 2020) between the U.S. and 18 nations and found that while the U.S. mortality rate since the start of pandemic is similar to that of other "High mortality" nations, its mortality rates since May 10th and June 7th far exceed that of any other nation.

- Investigators from multiple university hospitals in Denmark performed a retrospective cohort study comparing 473,654 Danish individuals tested for SARS-CoV-2 to 2.2 million non-tested individuals and found that those who tested positive for SARS-CoV-2 were less likely to have type O blood than A, B, or AB ($P<0.001$), suggesting a significantly reduced risk of COVID-19 infection in those with type O blood.

R&D: Diagnosis & Treatments

- Investigators within the fields of of toxicology and medical biochemistry found that lab testers working with SARS-CoV-2 need to be aware of potential contagiousness of samples, use disinfectants, and ample precautions; sampling of the airway and subsequent RT-PCR remains the best way to detect SARS-CoV-2 infection; and there is a growing body of literature suggesting cytokine, chemokine, blood, and serum parameters may help monitor severity of COVID-19 cases.

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COVID-19 AND EXCESS ALL-CAUSE MORTALITY IN THE US AND 18 COMPARISON COUNTRIES

Bilinski A, Emanuel EJ.. JAMA. 2020 Oct 12. doi: 10.1001/jama.2020.20717. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

Health policy researchers from Harvard University and University of Pennsylvania analyzed the COVID-19 and excess all-cause mortality rates across three periods (since the start of the pandemic, since 10 May 2020, and since 7 June 2020) between the U.S. and 18 nations (Table 1). While the U.S. mortality rate since the start of pandemic is similar to that of other “High mortality” nations, its mortality rates since May 10th and June 7th far exceed that of any other nation (Table 2). The authors speculate that this high U.S. mortality may be due to multiple factors, including a "weak public health infrastructure and a decentralized, inconsistent U.S. response to the pandemic."

FIGURES

Country	Date COVID-19 cases surpassed 1 per million	COVID-19 deaths per 100 000			Excess US COVID-19 deaths (% of reported deaths)		
		Since the start of the pandemic	Since May 10, 2020	Since June 7, 2020	Since the start of the pandemic	Since May 10, 2020	Since June 7, 2020
Low mortality (COVID-19 deaths, <5/100 000)							
South Korea	2/20/20	0.7	0.2	0.2	196 161 (99)	120 625 (61)	88 771 (45)
Japan	2/23/20	1.2	0.7	0.5	194 711 (98)	119 090 (60)	87 939 (44)
Australia	3/1/20	3.3	2.9	2.9	187 661 (94)	111 747 (56)	79 849 (40)
Moderate mortality (COVID-19 deaths, 5-25/100 000)							
Norway	2/29/20	5.0	1.0	0.5	182 099 (92)	118 074 (59)	87 655 (44)
Finland	3/2/20	6.1	1.4	0.3	178 373 (90)	116 698 (59)	88 432 (45)
Austria	3/1/20	8.6	1.7	1.0	170 247 (86)	115 874 (58)	86 066 (43)
Denmark	3/4/20	10.9	2.1	0.8	162 600 (82)	114 438 (58)	86 669 (44)
Germany	3/1/20	11.3	2.4	0.9	161 393 (81)	113 422 (57)	86 521 (44)
Israel	3/2/20	14.0	11.2	10.6	152 393 (77)	84 676 (43)	54 529 (27)
Switzerland	2/29/20	20.6	2.8	1.2	130 654 (66)	112 205 (57)	85 402 (43)
Canada	3/6/20	24.6	12.4	4.0	117 622 (59)	80 631 (41)	76 235 (38)
High mortality (COVID-19 deaths, >25/100 000)							
The Netherlands	3/3/20	36.2	5.2	1.5	79 318 (40)	104 177 (52)	84 514 (43)
France	3/1/20	46.6	7.5	3.2	45 142 (23)	96 763 (49)	78 947 (40)
Sweden	2/29/20	57.4	23.5	10.3	9581 (5)	44 210 (22)	55 607 (28)
Italy	2/23/20	59.1	9.1	3.1	4136 (2)	91 604 (46)	79 120 (40)
United Kingdom	3/3/20	62.6	16.3	5.0	−7459 (−4)	67 927 (34)	73 103 (37)
Spain	2/29/20	65.0	8.6	4.6	−15 204 (−8)	93 247 (47)	74 163 (37)
Belgium	3/2/20	86.8	12.4	4.2	−87 057 (−44)	80 475 (41)	75 572 (38)
United States	3/7/20	60.3	36.9	27.2			

[a] Data on coronavirus disease 2019 (COVID-19) deaths are from February 13, 2020, through September 19, 2020 (n = 198 589 US deaths). In columns 4-6, due to large sample sizes, all mortality rates are statistically significantly different from the corresponding US mortality rates ($P < .001$). Scenarios in the last 3 columns assume that compared with the country in a given row, (A) the US had a comparable cumulative mortality rate; (B) the US mortality rate was unchanged until May 10 (n = 77 180 deaths), when it became comparable to the other country's death rate; and (C) the US mortality rate was unchanged until June 7 (n = 109 143 deaths), when it became comparable to the other country's death rate.

Table 1. COVID-19 Mortality in the US Compared With That of Other Countries

Country	Excess all-cause mortality per 100 000			Excess US deaths from all causes (% of reported deaths)		
	Since the start of the pandemic	Since May 10, 2020	Since June 7, 2020	Since the start of the pandemic	Since May 10, 2020	Since June 7, 2020
Moderate mortality (COVID-19 deaths, 5-25/100 000)						
Norway	−2.6	−4.3	−2.1	235 610 (100)	102 598 (44)	63 952 (27)
Denmark	5.1	1.9	1.8	218 664 (93)	96 375 (41)	57 910 (25)
Israel	8	7.5	5.4	209 376 (89)	77 932 (33)	46 091 (20)
Germany	10.0	1.4	−0.2	202 547 (86)	97 905 (42)	63 952 (27)
Canada	13.3	−3.7	−7.6	192 009 (81)	102 598 (44)	63 952 (27)
Switzerland	17.0	−3.6	−2.7	179 545 (76)	102 598 (44)	63 952 (27)
Austria	17.1	3.2	1.4	179 208 (76)	92 042 (39)	59 375 (25)
Finland	19.1	8.7	5.4	172 706 (73)	74 116 (31)	46 264 (20)
High mortality (COVID-19 deaths, >25/100 000)						
Sweden	50.8	14.9	3.7	68 540 (29)	53 429 (23)	51 864 (22)
France	51.5	5.9	2.6	66 167 (28)	83 301 (35)	55 512 (24)
The Netherlands	55.1	0.1	−0.7	54 282 (23)	102 157 (43)	63 952 (27)
Belgium	67.8	−4.6	−6.4	12 638 (5)	102 598 (44)	63 952 (27)
United Kingdom	94.5	13.7	−1.2	−75 196 (−32)	57 659 (24)	63 952 (27)
Spain	102.2	2.1	1.8	−100 768 (−43)	95 784 (41)	57 948 (25)
United States	71.6	31.2	19.4			

[a] Data on deaths are through July 25, 2020 (week 30, n = 235 610 excess US deaths compared with 145 546 reported COVID-19 deaths). Countries lacking publicly available all-cause mortality data through this time are omitted. Excess deaths were estimated by week, compared with 2015-2019, beginning when a country surpassed 1 COVID-19 case per million population. In columns 3-5, due to large sample sizes, all mortality rates are statistically significantly different from the corresponding US mortality rates ($P < .001$). Scenarios in the last 3 columns assume that compared with the country in a given row: (A) the US had a comparable cumulative mortality rate; (B) the US excess all-cause mortality rate was unchanged until May 10 (week 20, n = 133 012 deaths), when it became comparable to the other country's death rate; and (C) the US excess all-cause mortality rate was unchanged until June 7 (week 24, n = 171 659 deaths), when it became comparable to the other country's death rate. Totals are truncated to avoid exceeding US estimated deaths. Due to reporting lags, these data include less follow-up time than Table 1, which in some cases produces lower cumulative death rates.

Table 2. Excess All-Cause Mortality in the US Compared With That in Other Countries

ADULTS

REDUCED PREVALENCE OF SARS-COV-2 INFECTION IN ABO BLOOD GROUP O

Barnkob MB, Pottegård A, Støvring H, Haunstrup TM, Homburg K, Larsen R, Hansen MB, Titlestad K, Aagaard B, Møller BK, Barington T.. Blood Adv. 2020 Oct 27;4(20):4990-4993. doi: 10.1182/bloodadvances.2020002657.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

Investigators from multiple university hospitals in Denmark performed a retrospective cohort study comparing 473,654 Danish individuals tested for SARS-CoV-2 between February 27 and July 30, 2020 to 2.2 million non-tested individuals (Figure 1). Those who tested positive for SARS-CoV-2 were less likely to have type O blood than A, B, or AB (P less than 0.001; Table 1), suggesting a significantly reduced risk of COVID-19 infection in those with type O blood.

ABSTRACT

Identification of risk factors for contracting and developing serious illness following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is of paramount interest. Here, we performed a retrospective cohort analysis of all Danish individuals tested for SARS-CoV-2 between 27 February 2020 and 30 July 2020, with a known ABO and RhD blood group, to determine the influence of common blood groups on virus susceptibility. Distribution of blood groups was compared with data from nontested individuals. Participants (29% of whom were male) included 473 654 individuals tested for SARS-CoV-2 using real-time polymerase chain reaction (7422 positive and 466 232 negative) and 2 204 742 nontested individuals, accounting for ~38% of the total Danish population. Hospitalization and death from COVID-19, age, cardiovascular comorbidities, and job status were also collected for confirmed infected cases. ABO blood groups varied significantly between patients and the reference group, with only 38.41% (95% confidence interval [CI], 37.30-39.50) of the patients belonging to blood group O compared with 41.70% (95% CI, 41.60-41.80) in the controls, corresponding to a relative risk of 0.87 (95% CI, 0.83-0.91) for acquiring COVID-19. This study identifies ABO blood group as a risk factor for SARS-CoV-2 infection but not for hospitalization or death from COVID-19.

FIGURES

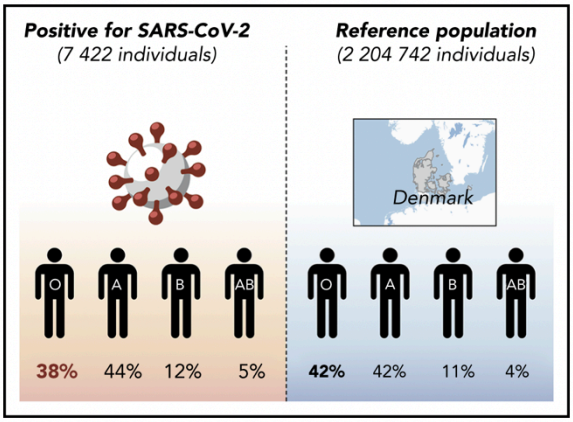

Figure 1. Reduced prevalence of SARS-CoV-2 infection in ABO blood group O

Blood group	SARS-CoV-2 tested, n (%)		Reference population, n (%)	*P*, SARS-CoV-2+ vs reference population	RR (95% CI), positive individuals vs reference population
	Positive	Negative			
O	2851 (38.41)	193 401 (41.48)	919 303 (41.69)	<.001	0.87 (0.82-0.91)
A	3296 (44.41)	199 211 (42.73)	934 421 (42.39)	<.001	1.09 (1.02-1.13)
B	897 (12.09)	52 838 (11.33)	252 559 (11.46)	.091	1.06 (1.03-1.19)
AB	378 (5.09)	20 782 (4.46)	98 459 (4.47)	.011	1.15 (1.05-1.31)
Total, n	7422	466 232	2 204 742		

Table 1. Distribution of ABO blood groups among individuals tested and not tested for SARS-CoV-2 in Denmark

SARS-COV-2 - A NEW CHALLENGE FOR LABORATORY MEDICINE

Dodig S, Čepelak I, Čepelak Dodig D, Laškaj R.. Biochem Med (Zagreb). 2020 Oct 15;30(3):030503. doi: 10.11613/BM.2020.030503. Epub 2020 Aug 5.
Level of Evidence: Other - Review / Literature Review

BLUF

Investigators within the fields of of toxicology and medical biochemistry review lab testing techniques and diagnostic protocols for COVID-19 and examine the biomarkers that may aid in predicting COVID-19 progression. The authors reached the following conclusions:
1) lab testers working with SARS-CoV-2 need to be aware of potential contagiousness of samples and need to use disinfectants and ample precautions
2) sampling of the airway and subsequent RT-PCR remains the best way to detect SARS-CoV-2 infection
3) there is a growing body of literature suggesting cytokine, chemokine, blood, and serum parameters may help monitor severity of COVID-19 cases (Table 2).

These observations provide insight into the best current practices for working with SARS-CoV-2 in the lab, testing protocols, and monitoring of disease progression while ensuring patient and lab tester safety.

ABSTRACT

The new corona virus SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona Virus 2) causes a disease called COVID-19 (coronavirus disease 2019), that develops mostly in subjects with already impaired immune system function, primarily in the elderly and in individuals with some chronic disease or condition. The reasons for this should be sought in the processes of aging and chronic latent inflammation, i.e. immunosenescence and inflammaging. Laboratory medicine specialists are currently focused on proving the presence of the virus and defining biomarkers that would enable the prediction of disease progression. For now, it has been shown that useful biomarkers can include general biomarkers of inflammation (parameters of complete blood count, C-reactive protein, interleukin-6, procalcitonin), biomarkers of myocardial damage (high sensitivity troponin I/T, B-type natriuretic peptide, and N-terminal B type natriuretic peptide), and vascular biomarkers (D-dimer, prothrombin time, fibrinogen). Their actual diagnostic specificity, sensitivity and predictive value need to be tested on a larger number of subjects. In addition, it is important to find and evaluate specific biomarkers of immunosenescence.

FIGURES

Phase of disease	Serum cytokines and chemokines profiles	Blood and serum parameters related to inflammation
Initial phase	(↑) IL-1β, IL-1RA, IL-7, IL-8, IL-10, IFN-γ, MCP-1, MIP-1A, MIP-1B, G-CSF, TNF-α	(↑) leukocytes, neutrophils, monocytes (↓) eosinophils (↑) acute phase proteins
Worsening of the disease	(↑) IL-2, IL-6, IL-8, IL-10, TNF-α	(↑) lymphocytes, monocytes, platelets, N/L, M/L (↓) eosinophils (↑) CRP, D- dimer, fibrinogen, ferritin
Non-ICU patients	(↑↑) IL-2, IL-7, IL-17, IL-10, IP-10, MCP-1, MIP-1A, TNF-α	(↑) lymphocytes, monocytes, eosinophils, platelets, N/L, M/L, P/L (↑↑) D-dimer, fibrinogen ferritin, procalcitonin
ICU patients	(↑↑↑) IL-2, IL-6, IL-8, IL-10, TNF-α (higher than in non-ICU)	(↓) lymphocytes, monocytes, eosinophils, platelets (↑↑) N/L, D-dimer, fibrinogen, ferritin, procalcitonin

CRP – C-reactive protein. G-CSF – granulocyte-colony stimulating factor. ICU – intensive care unit. IFN – interferon. IL – interleukin. MCP – monocyte chemoattractant peptide. IP-10 – 10 kDa IFN γ-induced protein. MIP – macrophage inflammatory protein. M/L – monocyte/lymphocyte ratio. N/L – neutrophil/lymphocyte ratio. P/L – platelet/lymphocyte ratio. TNF-α – tumour necrosis factor-alpha. Adapted according to references 37-40.

Table 2. Trend of variations over time of laboratory parameters related to inflammation

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