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COVID-19 Update September 23

Clinical Characteristics and Outcomes of Coronavirus Disease 2019 Among Patients With Preexisting Liver Disease in the United States: A Multicenter Research Network Study

- **Methods**
  - A real-time search to the electronic medical records of more than 49 million non-identified patients from 37 health care organizations in the US
  - Identified patients with COVID-19 were then stratified into 2 groups
    - Liver Disease (LD) defined as a diagnosis of chronic liver disease or cirrhosis
    - No liver disease (NLD)
- **Outcomes**
  - Mortality, hospitalization, and laboratory findings in the time window up to 30 days from the diagnosis of COVID-19

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Table 1. Outcomes and Baseline Characteristics Among Patients With COVID-19 Stratified Into Those With Preexisting Liver Disease and Without Liver Disease

	Before propensity matching			After propensity matching		
	COVID-19 with liver disease (n = 250)	COVID-19 without liver disease (n = 2530)	RR, RD, or *P* value	COVID-19 with liver disease (n = 250)	COVID-19 without liver disease (n = 250)	RR, RD, or *P* value
Outcomes						
Mortality, %, (n/total)	12.0 (30/250)	4.3 (110/2530)	RR: 2.8 (1.9, 4.0) RD: 7.7% (3.5%, 11.75%) *P* < .001	12.0 (30/250)	4.0 (10/250)	RR: 3.0 (1.5, 6.0) RD: 8.0% (3.3%, 12.7%) *P* = .001
Hospitalization rate	52.0 (130/250)	30.0 (760/2530)	RR: 1.7 (1.2, 2.0) RD: 22.0% (15.5%, 28.4%) *P* < .001	48.0 (120/250)	36.0 (90/250)	RR: 1.3 (1.1, 1.6) RD: 12.0% (3.4%, 20.6%) *P* = .006
Characteristics						
Age, ***y***, mean ± SD	55.2 ± 14.6	51.6 ± 17.8	<.01	55.4 ± 14.4	56.7 ± 15.3	.36
Female, n **(%)**	140 (56)	1570 (62)	.06	140 (56)	140 (56)	1.00
Race: white, n (%)	130 (52)	1220 (48.2)	.25	130 (52)	130 (52)	1.00
Nicotine dependence, n (%)	60 (24)	190 (7.5)	<.01	50 (20)	50 (20)	1.00
Body mass index >30.0 to 30.9 kg/m^2, **n (%)**	60 (24)	310 (12.5)	<.01	50 (20)	50 (20)	1.00
Race: black or African American, n (%)	100 (40)	1000 (39.5)	.88	100 (40)	110 (44)	.36
Hypertension, n (%)	170 (68)	1020 (40.3)	<.01	170 (68)	170 (68)	1.00
Diabetes mellitus, n (%)	120 (48)	520 (14.8)	<.01	110 (44)	110 (44)	1.00
Chronic lower respiratory diseases, n (%)	100 (40)	280 (11.0)	<.01	100 (40)	70 (28)	.01
Chronic kidney disease, n (%)	80 (32)	305 (7.2)	<.01	80 (32)	50 (20)	.01
Heart failure, n (%)	60 (24)	220 (8.7)	<.01	60 (24)	50 (20)	.28

NOTE. Outcomes and baseline characteristics are compared before and after propensity score matching of groups.

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Clinical Characteristics and Outcomes of Coronavirus Disease 2019 Among Patients With Preexisting Liver Disease in the United States: A Multicenter Research Network Study

- **A total of 2780 patients with COVID-19 were identified**
  - **LD**: 250 (9%) patients, **NLD:** 2530 (89%)
- ALT and AST were elevated after COVID-19 in both groups
- **Patients in the LD group had:**
  - Significantly higher risk of mortality
    - **RR, 2.8**; (95% CI,1.9–4.0; P < .001)
  - Higher risk of hospitalization
    - **RR, 1.7** (95% CI,1.2–2.0; P < .001)
  - Patients with cirrhosis had an even higher mortality
    - **RR, 4.6**; (95% CI, 2.6–8.3; P < .001).

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Conclusions

- Liver injury can be seen in most patients with COVID-19
- Patients with preexisting liver disease, notably cirrhosis, are at higher risk for hospitalizations and mortality
- Early isolation, intensive surveillance, and timely diagnosis are essential in these patients
- Further research identifying interventions to reduce poor outcomes in high-risk patients with COVID-19 is needed

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Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women

METHODS

- Women in the US having a confirmed SARS-CoV-2 infection and concurrently breastfeeding were invited to participate in the study
- Breast milk samples were self-collected and mailed to the study center
- A SARS-CoV-2 RT-PCR in breast milk as well as tissue culture was validated
- Conditions of pasteurization commonly used in human milk banks were mimicked

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Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women:

RESULTS

- **Eighteen women with confirmed SARS-CoV-2 infection enrolled**
  - 77.7% White non-Hispanic, mean age 34.4 years [SD, 5.2 years]
  - Their offspring ranged in age from newborn to 19 months
  - A total of 64 samples collected before and after the positive SARS-CoV-2 RT-PCR test.

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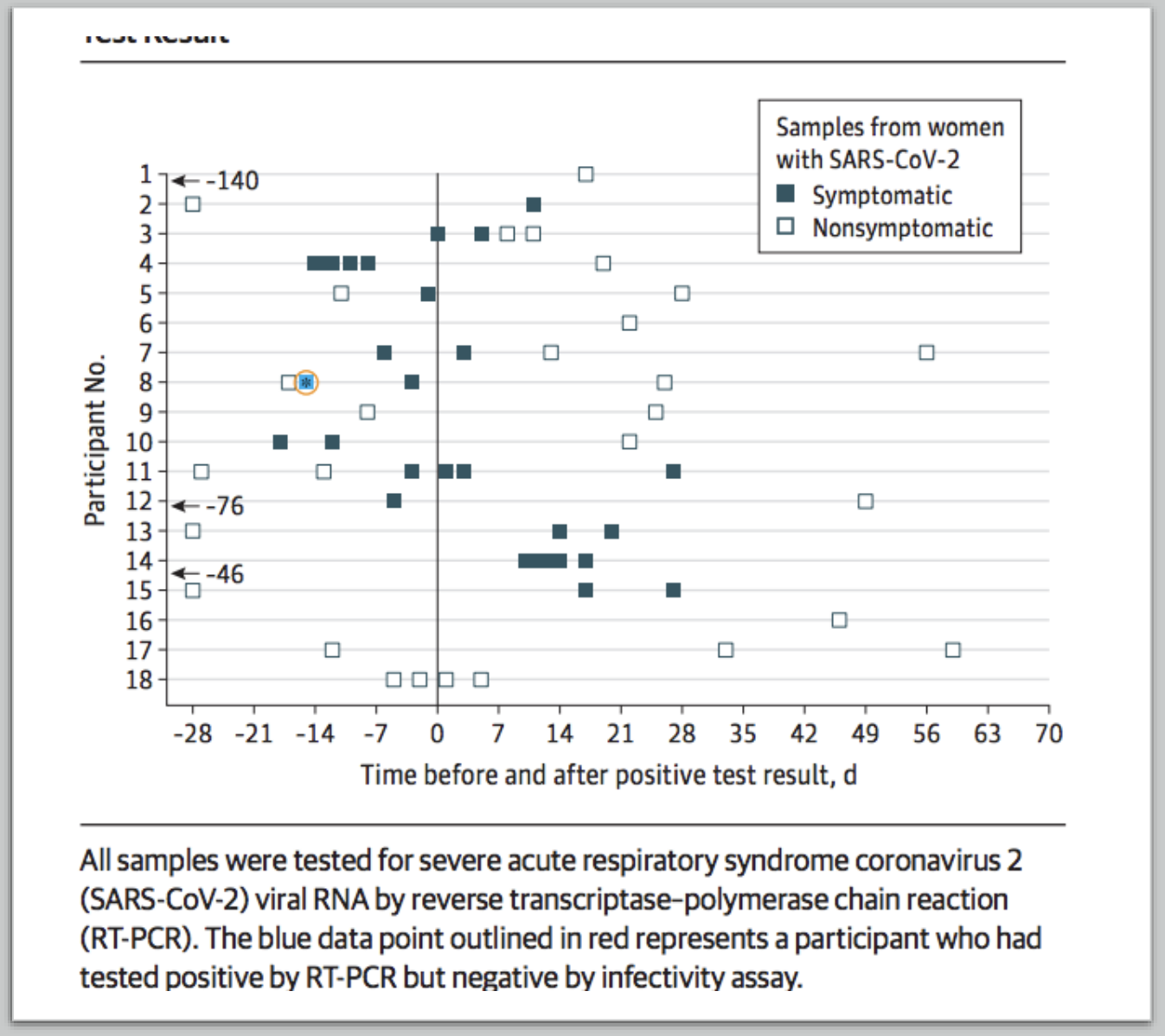
Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women

RESULTS



All samples were tested for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral RNA by reverse transcriptase–polymerase chain reaction (RT-PCR). The blue data point outlined in red represents a participant who had tested positive by RT-PCR but negative by infectivity assay.

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Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women:

RESULTS

- **One breast milk sample had detectable SARS-CoV-2 RNA**
  - Positive sample collected on the day of symptom onset;
  - 1 sample taken 2 days prior to symptom onset and 2 samples collected 12 and 41 days later tested negative
- **No replication-competent virus** was detectable in any sample
- **Pasteurized aliquots**
  - Viral RNA not detected in the spiked milk samples
  - No culturable virus detected in the spiked milk samples
- **Non pasteurized aliquots**
  - Virus was detected by culture in one of the same 2 milk-virus mixtures.

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Evaluation for SARS-CoV-2 in Breast Milk From 18 Infected Women

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- SARS-CoV-2 RNA was detected in 1 sample, but the culture was negative
- Breast milk may not be a source of infection for the infant
- When control samples spiked with RCV were pasteurized, no RCV or viral RNA was found
- Limitations
  - Small sample size
  - Nonrandom sample
  - Self-report of RT-PCR positivity
  - Self-collection of milk samples

RCV: replication competent virus

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Probative Value of the d-Dimer Assay for Diagnosis of Deep Venous Thrombosis in the Coronavirus Disease 2019 Syndrome

METHODS

- Only patients with confirmed SARS-CoV-2 infection by RT PCR included
- Serial d-dimer, troponin-I, LDH, C-reactive protein (CRP), interleukin (IL)-6, and fibrinogen
- Assessment for LeDVT with two clinical prediction tools used (Wells score and the Dutch Primary Care Rule)
- LeDVT US done in those patients with a positive screening prediction tool

LeDVT: Lower extremity Deep Vein Thrombosis

Probative Value of the d-Dimer Assay for Diagnosis of Deep Venous Thrombosis in the Coronavirus Disease 2019 Syndrome

RESULTS

- Seventy-two patients with severe COVID-19 had 102 Lower extremity US performed
- Twelve patients (17%) developed LeDVT.
- Screening tools were not useful
- Except for d-dimer, not other marker discriminated between patients with and without a LeDVT
- Using a d-dimer cutoff value of 3,000 ng/mL
  - Sensitivity was 100%, specificity was 51.1%
  - PPV was 21.8%, NPV was 100%

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TABLE 1. Demographics, Inflammatory Biomarkers, and Renal Function Variables

Variable (Normal Reference)	Overall	Lower Extremity Deep Venous Thrombosis ($n = 12$)	No Evidence of Deep Venous Thrombosis ($n = 60$)
Age	64	66.2	63.7
% Male	79	75	80
% Mortality	24	8	27
C-reactive protein (≤ 0.9 mg/dL)			
Median	17.3	21.8	14.1
IQR	7.9–26.7	15–32.2	6.5–24.8
% Positive		100	96
D-dimer (0–229 ng/mL)[a]			
Median	2,512	12,858	2,087
IQR	727–4,491	3,176–30,770	638–3,735
% Positive		100	99
Fibrinogen (180–400 mg/dL)			
Median	578	570	585
IQR	483–793	503–813	460–761
% Positive		91	85
Interleukin-6 (≤ 5 pg/mL)			
Median	27.5	20	36.5
IQR	15–117.5	13.8–49.3	15–121.8
% Positive		100	91
Creatinine (0.64–1.27 mg/dL)			
Median	1.04	1.37	1.04
IQR	0.69–1.92	0.61–1.88	0.71–1.97
% Positive		50	57
Glomerular filtration rate (≥ 60 mL/min)			
Median	64	60	64
IQR	34–101	32–113	34–100
% Positive		50	52

% Positive = proportion of tested patients with values exceeding the upper limit of the reference range, IQR = interquartile range.
[a]$p < 0.0001$ by Mann-Whitney *U* test.
Median values are shown for laboratory data. Values other than D-dimer showed no statistical significance.

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Conclusions

- Patients with severe COVID-19 are at increased risk for VTE
- D-dimer concentration less than 3,000ng/mL is sensitive to preclude further investigation for LeDVT
- Considering the high risk for VTE posed by COVID- 19, we recommend aggressive anticoagulation in severe cases.

VTE: Venous Thromboembolism

Cytokine Levels in Critically Ill Patients With COVID-19 and Other Conditions

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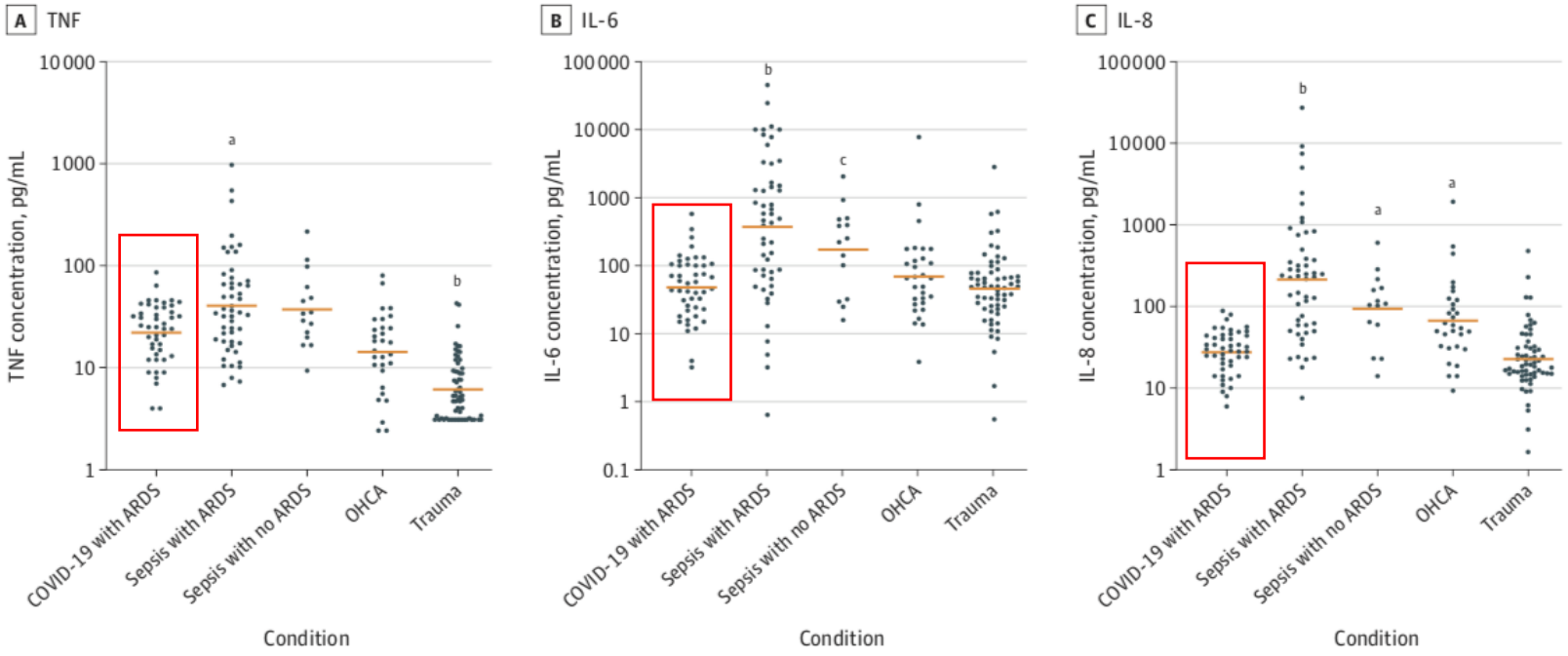
Figure. Cytokine Levels in Critically Ill Patients With Coronavirus Disease 2019 (COVID-19) and Other Conditions

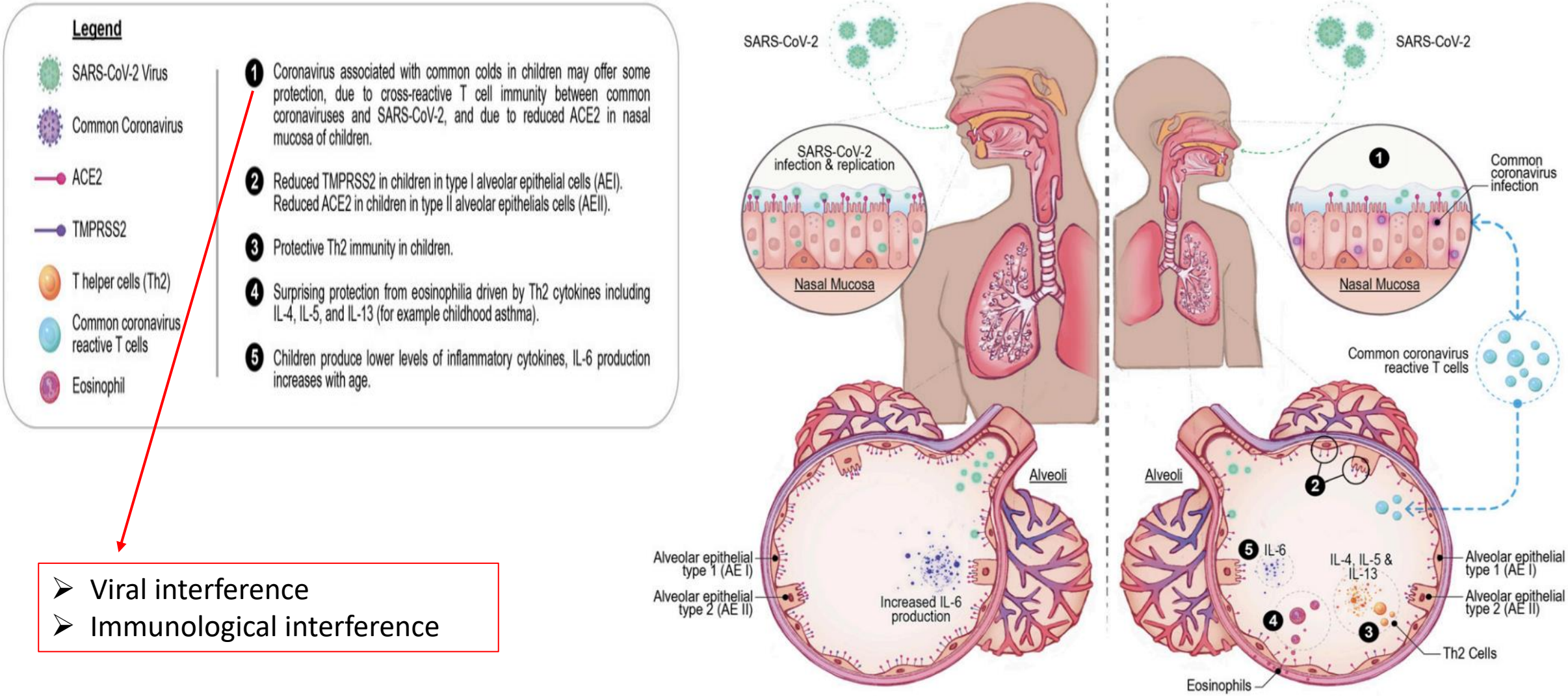


Plasma concentrations of tumor necrosis factor (TNF) (A), IL-6 (B), and IL-8 (C) in patients with COVID-19 and acute respiratory distress syndrome (ARDS) (n = 46), septic shock with ARDS (n = 51), septic shock without ARDS (n = 15), out-of-hospital cardiac arrest (OHCA; n = 30), and multiple traumas (n = 62). Data are presented as scatter plots with red horizontal bars indicating the geometric mean levels.

[a] $P < .01$ vs COVID-19 with ARDS.

[b] $P < .001$ vs COVID-19 with ARDS.

[c] $P < .05$ vs COVID-19 with ARDS.



- Viral interference
- Immunological interference

Reduced development of COVID-19 in children reveals molecular checkpoints gating pathogenesis illuminating potential therapeutics
www.pnas.org/cgi/doi/10.1073/pnas.2012358117