The Daily COVID-19 Literature Surveillance Summary

November 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

Understanding the Pathology

- Truncation of orf3b in the circulating SARS-CoV-2 strains have been shown in one study. Microbiologists and Infectious Disease researchers from the University of Hong Kong analyze the genome of SAR-CoV-2 with a particular focus on the orf3b gene, which was found to antagonize type-I interferon activation. Using the sequence data from the GISAID depository, they report a steady increase and persistence of the truncated form of the orf3b gene in SARS-CoV-2 strains worldwide, particularly in countries with the highest confirmed number of COVID-19 cases. The authors note that further research on orf3b's truncation in context with COVID-19's transmissibility and infectivity could be beneficial for guiding future therapeutic and diagnostic developments.

R&D: Diagnosis & Treatments

- Convalescent plasma anti-SARS-CoV-2 spike protein ectodomain and receptor-binding domain IgG correlate with virus neutralization. Researchers primarily at Houston Methodist Hospital analyzed samples of plasma from 68 recovered COVID-19 patients, 2,814 asymptomatic patients, and 10 naive human plasma specimens to investigate the relationship between different neutralizing antibodies and possible ways to screen plasma samples for a virus neutralization (VN) titer ≥ 160. Analysis revealed a positive relationship among spike ectodomain (anti-ECD), anti–receptor-binding domain (anti-RBD) IgG titers, and SARS-CoV-2 virus neutralization (VN) titers, where probability of a VN titer of ≥160 was ≥80% when anti-RBD or anti-ECD titers were ≥1:1350. While no significant relationship was detected between symptom severity and VN titer level, an analysis of 2,814 asymptomatic adults found 14 individuals with sufficient VN titers, with all of those individuals having RBD titers of ≥1:1350. Based on this study's findings, screening for potential anti-SARS-CoV-2 convalescent plasma donors cannot be completed by analysis of symptom severity alone, but spike ectodomain and anti–receptor-binding domain IgG titers may provide a reasonable estimate of VN titer levels.

- There is lack of efficacy of standard doses of ivermectin in severe COVID-19 patients according to a retrospective controlled cohort study. Specialists in global health and infectious disease from Hospital Clinic-Universitat de Barcelona, Spain evaluated efficacy of standard doses of ivermectin in 13 patients with severe COVID-19 against 13 controls without ivermectin. They found no significant differences in clinical or microbiological outcomes between the two groups after 8-11 days of treatment ($p > 0.999$). Authors acknowledge the small sample size in this study, but suggest their results warrant further research involving high-dose ivermectin to better evaluate its efficacy in patients with severe COVID-19.

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EPIDEMIOLOGY

SARS-COV-2 SEROPREVALENCE AND ANTIBODY KINETICS AMONG HEALTH CARE WORKERS IN A SPANISH HOSPITAL AFTER THREE MONTHS OF FOLLOW-UP

Moncunill G, Mayor A, Santano R, Jiménez A, Vidal M, Tortajada M, Sanz S, Méndez S, Llupià A, Aguilar R, Alonso S, Barrios D, Carolis C, Cisteró P, Chóliz E, Cruz A, Fochs S, Jairoce C, Hecht J, Lamoglia M, Martínez MJ, Moreno J, Mitchell RA, Ortega N, Pey N, Puyol L, Ribes M, Rosell N, Figueroa-Romero A, Sotomayor P, Torres S, Williams S, Barroso S, Vilella A, Trilla A, Varela P, Dobaño C, Garcia-Basteiro AL.. J Infect Dis. 2020 Nov 11:jiaa696. doi: 10.1093/infdis/jiaa696. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A cohort study conducted by physicians at Universitat de Barcelona, Spain randomly selected healthcare workers (n=578) to assess for SARS-CoV-2 infection via rRT-PCR as well as IgM, IgA and IgG to the receptor-binding domain by spike protein. At one month follow-up they found infection measured by rRT-PCR and serology had risen from the initial rate of 11.2% to 14.9% with a seroprevalence of 14.5% while IgM, IgG and IgA levels declined at 3 months with reported antibody decay rates of 0.15, 0.66 and 0.12, respectively (Figures 1,3). These findings demonstrate the possibility of SARS-CoV-2 infections going undetected, and authors recommend further research on antibody decay rates to examine their role in protection from SARS-CoV-2.

ABSTRACT

BACKGROUND: At the COVID-19 pandemic peak in Spain, prevalence of SARS-CoV-2 infection in a cohort of 578 randomly selected health care workers (HCW) from Hospital Clinic de Barcelona was 11.2%. METHODS: A follow-up survey one month later (April-May 2020) measured infection by rRT-PCR and IgM, IgA, IgG to the receptor-binding domain of the spike protein by Luminex. Antibody kinetics, including IgG subclasses, was assessed till month 3. RESULTS: At month 1, the prevalence of infection measured by rRT-PCR and serology was 14.9% (84/565) and the seroprevalence 14.5% (82/565). We found 25 (5%) new infections in participants without previous evidence of infection (501). IgM, IgG and IgA levels declined in 3 months (antibody decay rates 0.15 (95% CI, 0.11; 0.19), 0.66 (95% CI, 0.54; 0.82), 0.12 (95% CI, 0.09; 0.16), respectively), and 68.33% of HCW had seroreverted for IgM, 3.08% for IgG, and 24.29% for IgA. The most frequent subclass responses were IgG1 (highest levels) and IgG2, followed by IgG3, and only IgA1 but no IgA2 was detected. CONCLUSIONS: Continuous and improved surveillance of SARS-CoV-2 infections in HCW remains critical, particularly in high-risk groups. The observed fast decay of IgA and IgM levels have implications for seroprevalence studies using these isotypes.

Figure 1

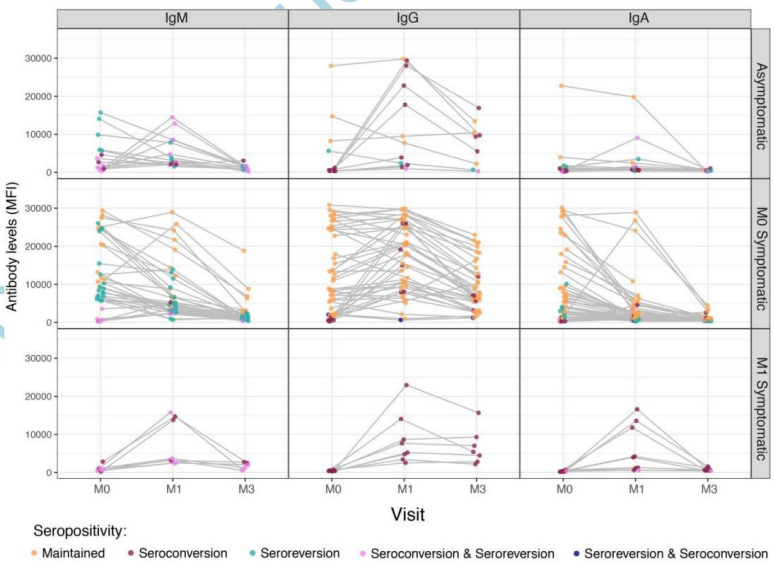


Figure 1. Kinetics of SARS-CoV-2 antibodies in seropositive individuals during the three months of follow-up. Levels (median fluorescence intensity, MFI) of IgM, IgG, and IgA against receptor-binding domain (RBD) of the SARS-CoV-2 spike glycoprotein stratified by asymptomatic participants and participants who reported COVID-19 compatible symptoms for the first time at recruitment (month 0, M0) or at month 1 (M1). No participants reported symptoms for the first time at month 3. Lines indicate paired samples. Yellow dots depict individuals (IgM N=12; IgG N=41, IgA N=35) who had detectable antibody levels at all study visits when antibody levels where measured ; burgundy dots show individuals who seroconverted for a particular isotype at M1 (IgM N=7; IgG N=21, IgA N=17); green dots, individuals who seroreverted between M0 and M1 (IgM N=3; IgG N=0, IgA N=4) or M1 and M3 (IgM N=21; IgG N=1, IgA N=6); pink dots, individuals who seroconverted from M0 to M1 and then seroreverted (IgM N=17; IgG N=1, IgA N=7); and blue dots, individuals who seroreverted and seroconverted again (IgM=0, IgG N=1, IgA=1).

Figure 3

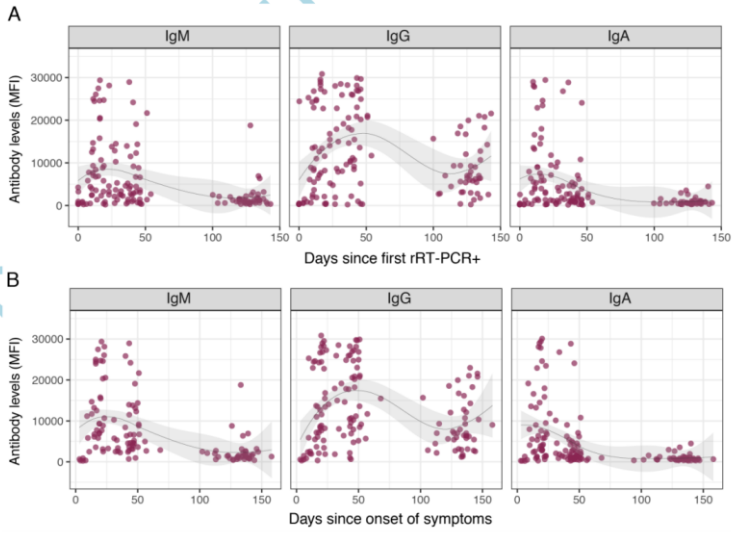


Figure 3. SARS-CoV-2 antibody levels by time since first rRT-PCR and onset of symptoms. Levels (median fluorescence intensity, MFI) of IgM, IgG, and IgA against receptor-binding domain (RBD) of the SARS-CoV-2 spike glycoprotein by (A) days since the first positive rRT-PCR, and (B) days since onset of any symptom. Graphs show pooled month 0, month 1 and month 3 data. Data in (A) are shown only for individuals with any rRT-PCR positive (N =142). Data in (B) are shown only for seropositive individuals at any visit since onset of any symptom compatible with COVID-19 (N =121 for IgM, 145 for IgG, and 149 for IgA). The fitting curve was calculated using the LOESS (locally estimated scatterplot smoothing) method. Shaded areas represent 95% confidence intervals.

ADULTS

DIAGNOSTIC AND PROGNOSTIC UTILITY OF WBC COUNTS AND CELL POPULATION DATA IN PATIENTS WITH COVID-19

Naoum FA, Ruiz ALZ, Martin FHO, Brito THG, Hassem V, Oliveira MGL.. Int J Lab Hematol. 2020 Nov 15. doi: 10.1111/ijlh.13395. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Investigators mainly from Ultra X Medical Diagnostic in São José do Rio Preto, Brazil retrospectively analyzed complete blood count (CBC; Table 1) and cell population data (CPD; Figure 1) of 100 COVID-19 patients presenting to the emergency department (49 discharged and recovered, 51 admitted, 22 of which deceased) compared with 47 healthy control subjects. Analysis of CBC results revealed decreased lymphocyte and eosinophils in COVID-19 patients, with increased severity corresponding to severity of disease, and CPD analysis revealed increased neutrophils volume with decreased conductivity in COVID-19 deceased patients. Results suggest that both baseline CBC and CPD can be used as practical, readily accessible biomarkers for disease severity, helping guide treatment and isolation protocols on individual patients.

ABSTRACT

INTRODUCTION: Early diagnosis and identification of potential critical cases for timely treatment are crucial for COVID-19 patients. The aim of this study was to analyze the diagnostic and prognostic implications of WBC and cell population data (CPD) abnormalities related to COVID-19 at disease onset. METHODS: Baseline WBC counts and CPD data were analyzed in one hundred COVID-19 patients presenting to emergency department and subsequently discharged (n = 49), admitted (n = 51) or deceased (n = 22), and in 47 healthy subjects. RESULTS: Lymphopenia and eosinopenia were observed in all COVID-19 patients, with more intensity in the admitted and deceased groups, that also presented increased WBC and neutrophil counts. On CPD analysis, COVID-19 was associated with increased volume of neutrophils, lymphocytes, and monocytes, whereas conductivity was decreased for neutrophils and increased for lymphocytes. The ROC curve analysis showed good performance for lymphocyte counts in predicting COVID-19 diagnosis (AUC = 0.858), for neutrophil counts in predicting admission for COVID-19 (AUC = 0.744) and for monocytes volume in predicting COVID-19 diagnosis (AUC = 0.837). CONCLUSION: WBC counts and CPD parameters at disease onset in COVID-19 patients can improve diagnostic characterization and aid in the discrimination between severe and nonsevere presentations.

FIGURES

	Control (n = 47)	COVID outpatients (n = 49)	COVID admitted (n = 51)	COVID deceased (n = 22)
WBC ($\times 10^9$/L)	6.96 ± 1.65	7.06 ± 3.36	10.21 ± 5.62*,**	10.78 ± 6.9*,**
Neutrophils ($\times 10^9$/L)	4.36 ± 1.23	5.12 ± 3.10	8.71 ± 5.24*,**	9.35 ± 6.4*,**
Lymphocytes ($\times 10^9$/L)	1.90 ± 0.43	1.34 ± 0.70*	0.91 ± 0.47*,**	0.90 ± 0.62*,**
Monocytes ($\times 10^9$/L)	0.57 ± 0.18	0.57 ± 0.30	0.55 ± 0.35	0.48 ± 0.33
Eosinophils ($\times 10^9$/L)	0.18 ± 0.16	0.05 ± 0.07*	0.22 ± 0.37*,**	0.13 ± 0.24*,**
Basophils ($\times 10^9$/L)	0.32 ± 0.47	0.03 ± 0.02	0.30 ± 0.28	0.25 ± 0.23

*$P < .01$ vs control.

**$P < .05$ vs COVID outpatients.

Table 1. WBC counts in control and COVID-19 groups.

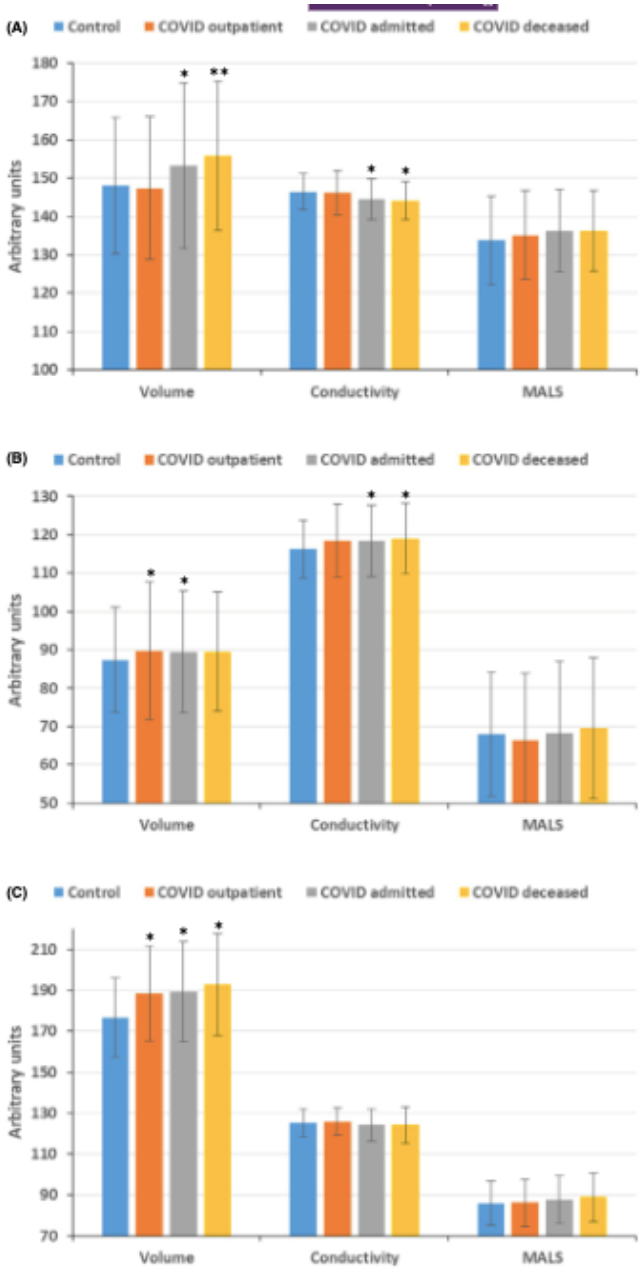


Figure 1. Cell population data of neutrophils (A), lymphocytes (B) and monocytes (C) in control and COVID groups. MALS, median angle light scatter. *P< .05 vs control group; **P< .05 vs control, COVID outpatient and COVID admitted groups.

ATTRIBUTES OF DYSGEUSIA AND ANOSMIA OF CORONAVIRUS DISEASE 2019 (COVID-19) IN HOSPITALIZED PATIENTS

Samaranayake LP, Fakhruddin KS, Mohammad OE, Panduwawala C, Bandara N, Ngo HC.. Oral Dis. 2020 Nov 11. doi: 10.1111/odi.13713. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A prospective survey study conducted by dental experts in China and UAE assessed hospitalized COVID-19 patients (n=149) and found 94.6% prevalence of dysgeusia and anosmia, with male predominance of chemosensory dysfunction (Table 1), correlation with presence of comorbidities (Table 2), and higher dysfunction prevalence with increased COVID-19 severity (Figure 3). These data suggest existing comorbidities, male gender, and severe COVID-19 may increase risk of chemosensory dysfunction in patients with SARS-CoV-2 infection.

ABSTRACT

OBJECTIVES: While chemosensory dysfunctions, dysgeusia and anosmia/hyposmia, are recognized as distinctive symptoms of COVID-19, their temporality of presentation, and association with the patient age, gender, disease severity, and co-morbidities have been sparsely studied. Hence we evaluated the latter associations of chemosensory dysfunction, in hospitalized COVID-19 patients in the United Arab Emirates (UAE). MATERIALS AND METHODS: Information on chemosensory dysfunction and history of chronic systemic co-morbidities, if any, were obtained from 149 COVID-19 patients in an infectious Disease Hospital in UAE. using their medical records, as well as from a face-to-face questionnaire survey. Additionally, a modified SNOT-22 questionnaire, that measures disease specific quality of life in patients with upper respiratory tract affections was also administered. RESULTS: Chemosensory dysfunction was reported by 94.6% of the cohort, and anosmia with dysgeusia were significantly more in males than females with severe COVID-19. Males with moderate COVID-19 and systemic comorbidities were more likely to present with chemosensory dysfunction in comparison to females. SNOT-22 questionnaire revealed that nasal blockage and runny nose were more prevalent in mild/moderate, than in the severe state of COVID-19. CONCLUSION: Our data confirm the commonality of chemosensory dysfunction during COVID-19 progression, and the significantly more pronounced combined dysfunction in males with severe COVID-19, and co-morbidities.

FIGURES

Table 1. The relationship between the temporality of the symptoms of chemosensory dysfunction, COVID-19 disease severity, and the gender of the study cohort (n=141)

	Mild (n=15)	Moderate (n=94)	Severe (n=32)
Loss of smell before fever/ blocked/runny nose/sore throat			
Male (94; 66.7%)	6 (6.4%)	47 (50%)	6 (6.4%)
Female (47; 33.3%)	7 (14.9%)	22 (46.8%)	4 (8.5%)
Change in taste before fever/ blocked/runny nose/sore throat			
Male (94; 66.7%)	0	2 (2.1%)	5 (5.4%)
Female (47; 33.3%)	2 (4.3%)	7 (14.9%) **	2 (4.3%)
Simultaneous loss of smell and taste			
Male (94; 66.7%)	0	2 (2.1%)	11 (11.7%) ^^
Female (47; 33.3%)	0	2 (4.3%)	4 (8.5%)
Loss of smell after hospital admission			
Male (94; 66.7%)	0	3 (3.2%)	0
Female (47; 33.3%)	0	1 (2.1%)	0
Loss of taste after hospital admission			
Male (94; 66.7%)	0	7 (7.4%)	0
Female (47; 33.3%)	0	3 (6.4%)	0

p-value= 0.001** between male vs. female; *p*-value= 0.001^^ between moderate vs. severe COVID-disease severities; *Obtained using Chi squared test and Fischer exact test.*

Table 1. The relationship between the temporality of the symptoms of chemosensory dysfunction, COVID-19 disease severity, and the gender of the study cohort (n=141)

Table 2. The relationship between the COVID-19 disease severity, chemosensory dysfunction, and any underlying, systemic co-morbidities of (n =96)

	Mild	Moderate	Severe
Hypertension/other Cardiac conditions			
Male (67; 68.4%)	2 (3%)	12 (18%) **	4 (6%)
Female (31; 31.6%)	1 (3.2%)	2 (6.5%)	1 (3.2%)
Diabetes (Type II)			
Male (67; 68.4%)	0	9 (13.4%)	7 (10.4%)
Female (31; 31.6%)	0	8 (25.8%)	0
Co-morbidities (Hypertension/Cardiac conditions and Diabetes)			
Male (67; 68.4%)	0	21 (31.3%) *	9 (13.4%)
Female (31; 31.6%)	0	8 (25.8%)	5 (16.1%)
Asthma/COPD			
Male (67; 68.4%)	0	1 (1.5%)	1 (1.5%)
Female (31; 31.6%)	0	3 (9.7%)	0
Renal ailments			
Male (67; 68.4%)	0	0	1 (1.5%)
Female (31; 31.6%)	0	0	0
Cancer survivors			
Male (67; 68.4%)	0	0	0
Female (31; 31.6%)	0	0	3 (9.7%)

p-value= 0.05*; 0.001** between moderate vs. severe COVID-disease severities; *Obtained using Chi squared test and Fischer exact test.*

Table 2. The relationship between the COVID-19 disease severity, chemosensory dysfunction, and any underlying, systemic co-morbidities of (n =96)

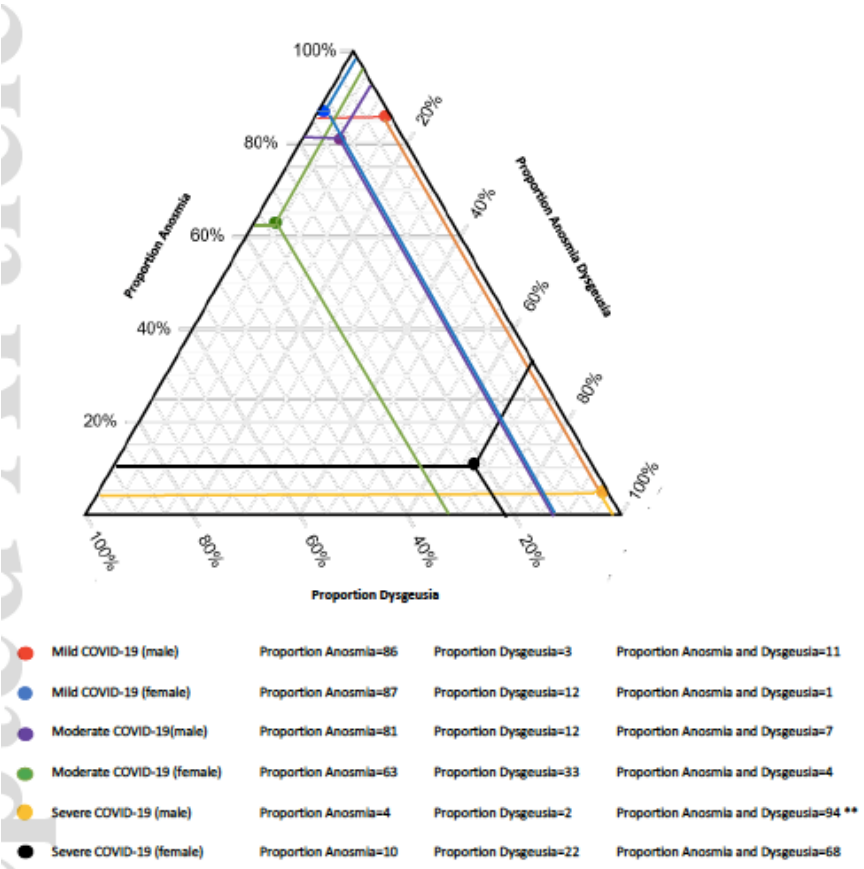


Figure 3. Proportion of Chemosensory dysfunction -symptoms in COVID-19 cases of varying disease severity. *p*-value= 0.001**; *Obtained using Chi squared test and Fischer exact test.*

Figure 3. Proportion of Chemosensory dysfunction -symptoms in COVID-19 cases of varying disease severity. p-value= 0.001**; Obtained using Chi squared test and Fischer exact test.

UNDERSTANDING THE PATHOLOGY

LOSS OF ORF3B IN THE CIRCULATING SARS-COV-2 STRAINS

Lam JY, Yuen CK, Ip JD, Wong WM, To KK, Yuen KY, Kok KH.. Emerg Microbes Infect. 2020 Nov 18:1-678. doi: 10.1080/22221751.2020.1852892. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Microbiologists and Infectious Disease researchers from the University of Hong Kong analyze the genome of SAR-CoV-2 with a particular focus on the orf3b gene, which was found to antagonize type-I interferon activation. Using the sequence data from the GISAID depository, the authors report a steady increase and persistence of the truncated form of the orf3b gene in SARS-CoV-2 strains worldwide (Figure 1), particularly in countries with the highest confirmed number of COVID-19 cases. The authors note that further research on orf3b's truncation in context with COVID-19's transmissibility and infectivity could be beneficial for guiding future therapeutic and diagnostic developments.

SUMMARY

The genotypes with the full length orf3b (57a.a.) vs. the truncated orf3b (13a.a) give rise to two drastically different isoforms of the the viral protein. The SARS-CoV-2 orfb3 gene has been identified as an interferon antagonist, and the truncated mutation leads to a loss of function for that gene (Figure 2). However, all viruses with this mutations also carry the spike G614 genotype which has been shown to enhance the virus transmissibility and infectivity. This implies that the viruses with the truncated orf3b gene has reduced disease severity but are more infectious as compared to the wild-type.

ABSTRACT

The newly emerged betacoronavirus, SARS-CoV-2, causes the COVID-19 pandemic since December 2019 with more than 35 million laboratory confirmed human infections and over one million deaths within nine months. The genome of SARS-CoV-2 continues to evolve during the global transmission with the notable emergence of the spike D614G substitution that enhances infectivity. Some of these viral adaptations may alter not only the infectivity but also viral pathogenesis. Continuous phylogenomic analysis of circulating viral strains and functional investigation of new non-synonymous substitutions may help to understand the evolution of virus, its virulence and transmissibility. Here we describe a loss of an accessory protein orf3b (57 amino acids) in current circulating SARS-CoV-2 strains, contributing around 24% of more than 100,000 complete viral genomes analyzed. The loss of 3b is caused by the presence of an early stop codon which is created by an orf3a Q57H substitution. There is an increasing trend in the loss of orf3b which has reached 32% in May 2020. Geographically, loss of 3b is more prevalent in certain countries including Colombia (46%), USA (48%), South Korea (51%), France (66%), Saudi Arabia (72%), Finland (76%) and Egypt (77%). Interestingly, the loss of 3b coincides with the emergence of spike D614G substitution. In addition, we found that truncated orf3b has lost the interferon antagonism compared to the full-length orf3b, suggesting a loss of function by the newly adapted virus. Further investigation of orf3b deletion and spike D614G substitution on virulence and infectivity respectively will provide important insights into SARS-CoV-2 evolution.

A **Relative percentage of Δ3b genotype.**

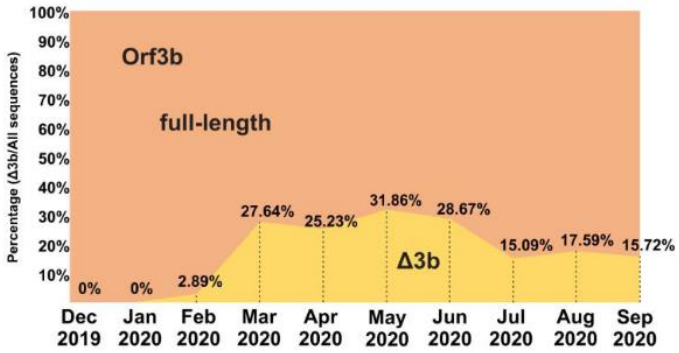
Sequence data (n = 150,198) were downloaded from GISAID and NextStrain.org.

3b/All	114381/150198 (76.15%)
Δ3b/All	35771/150198 (23.82%)
Spike D614/All	19529/150198 (13.00%)
Spike G614/All	130666/150198 (87.00%)
Δ3b with Spike D614/Total Δ3b	108/35771 (0.302%)
Δ3b with Spike G614/Total Δ3b	35663/35771 (99.69%)

B **Recent circulation (Dec 2019 to Sep 2020, n = 150,198) of the Δ3b genotype**

	Dec 2019	Jan 2020	Feb 2020	Mar 2020	Apr 2020	May 2020	Jun 2020	Jul 2020	Aug 2020	Sep 2020	Total
Δ3b (No. of strains)	0	0	35	10355	8283	4741	4950	2134	2455	2818	35771
3b (No. of strains)	23	509	1174	27092	24535	10139	12303	12001	11495	15110	114381
Percentage (Δ3b/Month total)	0%	0%	2.89%	27.64%	25.23%	31.86%	28.67%	15.09%	17.59%	15.72%	
Spike D614 (No. of strains)	23	495	957	11452	5012	981	401	134	53	21	19529
Spike G614 (No. of strains)	0	14	252	26006	27814	13902	16865	14003	13902	17908	130666
Percentage (G614/Month total)	0%	2.75%	20.84%	69.43%	84.73%	93.41%	97.68%	99.03%	99.62%	99.97%	

C **Emergence of Δ3b genotype from Dec 2019 to Sep 2020 (n = 150,198)**



D **Emergence of Spike D614G genotype from Dec 2019 to Sep 2020 (n = 150,198)**

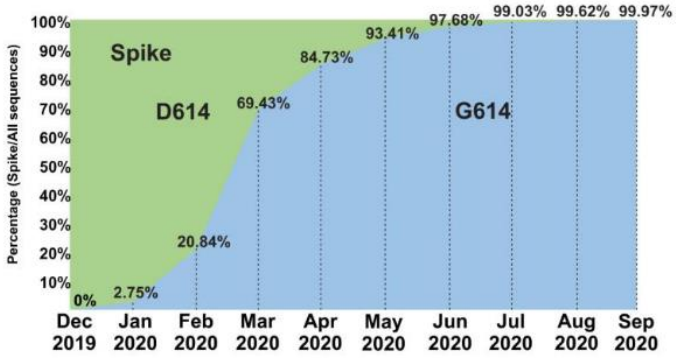


Figure 1. Increasing circulation of SARS-CoV-2 strains with Δ3b

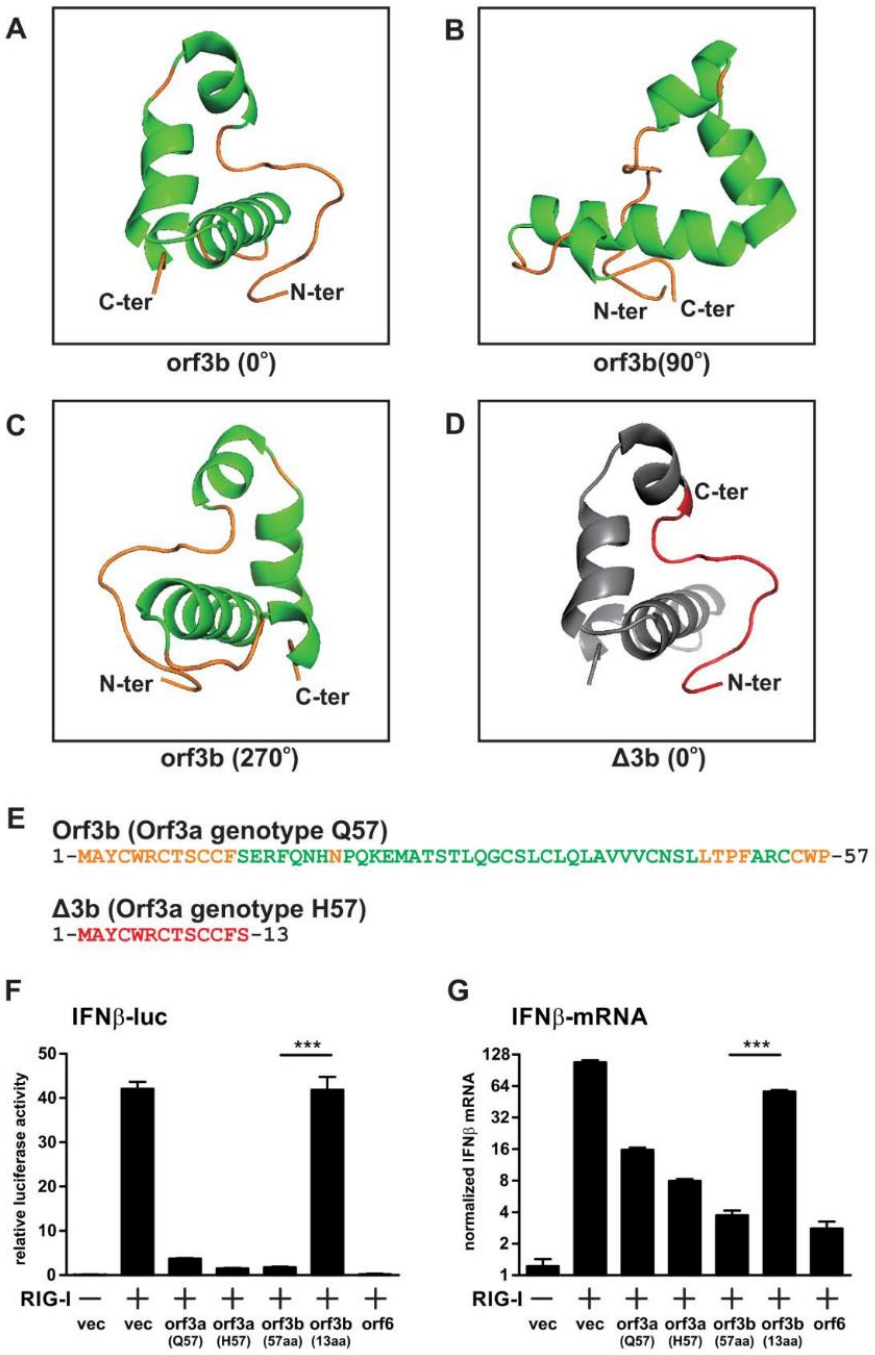


Figure 2. Structure prediction and interferon antagonism of SARS-CoV-2 orf3b and Δ3b

MECHANISMS OF COVID-19-INDUCED HEART FAILURE: A SHORT REVIEW

Adeghate EA, Eid N, Singh J.. Heart Fail Rev. 2020 Nov 16. doi: 10.1007/s10741-020-10037-x. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Investigators from the United Arab Emirates University and the University of Central Lancashire reviewed mechanisms through which COVID-19 can lead to heart failure. They found that this process is multifactorial and includes processes such as tissue inflammation (Figure 2), cytokine storm (including interleukin-1beta, tumor necrosis factor-alpha, etc.), endothelial injury and micro-thrombosis, and acute respiratory distress syndrome (ARDS, Figure 3). These findings provide a foundation to understanding the mechanisms behind heart failure in COVID-19 and cautions healthcare workers to monitor markers (Troponin T, CK-MB, etc.) of cardiac function in COVID-19 patients.

ABSTRACT

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes coronavirus disease 2019 (COVID-19) has infected more than 42.5 million people globally resulting in the death of over 1.15 million subjects. It has inflicted severe public health and economic hardships across the world. In addition to acute respiratory distress syndrome, respiratory failure, sepsis, and acute kidney injury, COVID-19 also causes heart failure (HF). COVID-19-induced HF is manifested via different mechanisms, including, but not limited to, (1) virus-induced infiltration of inflammatory cells, which could impair the function of the heart; (2) pro-inflammatory cytokines (monocyte chemoattractant protein-1, interleukin-1beta; interleukin-6; tumor necrosis factor-alpha) that could cause necrosis and death of the myocardium; (3) endothelial injury coupled with micro-thrombosis which could damage the endocardium; and (4) acute respiratory distress syndrome and respiratory failure that could lead to heart failure due to severe hypoxia. It is concluded that the etiology of COVID-19-induced HF is multifactorial and mitigation of the development of HF in patients with COVID-19 will require different approaches such as social distancing, drug therapy, and the urgent development of a vaccine to eradicate the disease.

FIGURES

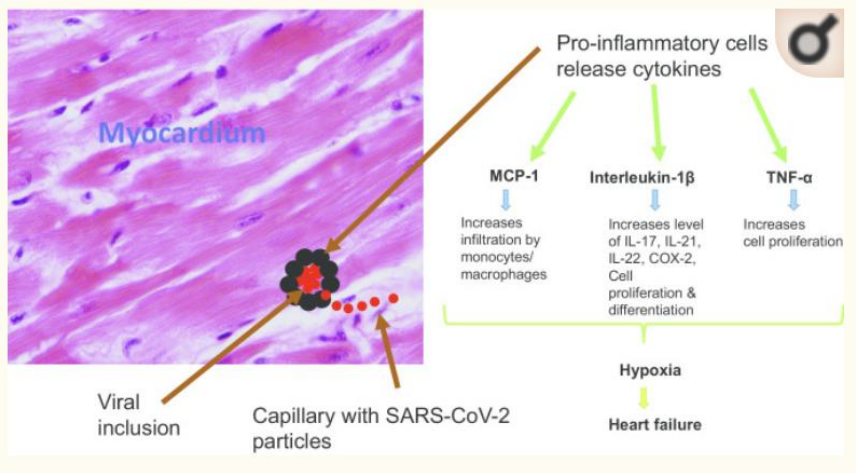


Figure 2. This schematic diagram depicts the inclusion of SARS-CoV-2 in the myocardium. Pro-inflammatory cells initially surround SARS-CoV-2 particles to form an inclusion. Thereafter, the inflammatory cells around viral particles release cytokines such as monocyte chemoattractant protein-1 (MCP-1), interleukin-1β, and tumor necrosis factor-α (TNF-α) which act as noxious factors to the heart resulting in hypoxia and if severe, sudden cardiac death

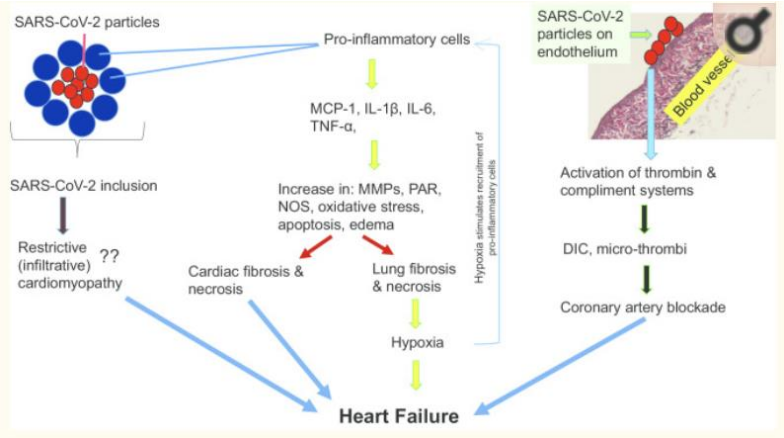


Figure 3. This schematic diagram illustrates the putative mechanisms by which COVID-19 induces heart failure (HF). SARS-CoV-2 inclusions within the myocardium may cause infiltrative restrictive cardiomyopathy leading to HF. Moreover, pro-inflammatory cells surrounding SARS-CoV-2 inclusions release cytokines such as tumor necrosis alpha (TNF-α), monocyte chemoattractant protein-1 (MCP-1), interleukin-1β (IL-1β), interleukin-6 (IL-6) and many others. These cytokines increase the tissue levels of matrix metalloproteinases (MMPs), protease-activated receptor (PAR), nitric oxide synthase (NOS), severe oxidative stress, apoptosis, and edema in both the heart and lungs. All of these could lead to cardiac and pulmonary fibrosis and necrosis, eventually resulting in HF. In addition, SARS-CoV-2-induced lesion of the cardiovascular endothelium leads to the activation of thrombin and the complement systems. This activation causes disseminated intravascular coagulopathy (DIC) and many thrombi, which could block coronary arteries resulting in myocardial infarction and subsequently HF. Lung fibrosis and hypoxia stimulate further recruitment of pro-inflammatory cells, thereby initiating a vicious cycle

COVID-19 CORONAVIRUS VACCINE T CELL EPITOPE PREDICTION ANALYSIS BASED ON DISTRIBUTIONS OF HLA CLASS I LOCI (HLA-A, -B, -C) ACROSS GLOBAL POPULATIONS

Cun Y, Li C, Shi L, Sun M, Dai S, Sun L, Shi L, Yao Y.. Hum Vaccin Immunother. 2020 Nov 11:1-12. doi: 10.1080/21645515.2020.1823777. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

A T-cell epitope prediction analysis by medical biologists and vaccine researchers in Kunming, China used SARS-CoV-2 protein sequences from the NCBI database and distribution of 70 HLA alleles (which occur in >1% of human population) to predict T-cell epitope combinations for vaccine production (Figure 1) and found a 14 epitope combination (Table 8) of N and S proteins that in theory could effectively vaccinate 89.6% people worldwide (Table 9). Authors propose these results to aid in further exploration of these epitopes as candidates for an effective SARS-CoV-2 vaccine.

ABSTRACT

T cell immunity, such as CD4 and/or CD8 T cell responses, plays a vital role in controlling the virus infection and pathological damage. Several studies have reported SARS-CoV-2 proteins could serve as ideal vaccine candidates against SARS-CoV-2 infection by activating the T cell responses. In the current study, based on the SARS-CoV-2 sequence and distribution of host human leukocyte antigen (HLA), we predicted the possible epitopes for the vaccine against SARS-CoV-2 infections. Firstly, the current study retrieved the SARS-CoV-2 S and N protein sequences from the NCBI Database. Then, using the Immune Epitope Database Analysis Resource, we predicted the CTL epitopes of the SARS-CoV-2 S and N proteins according to worldwide frequency distributions of HLA-A, -B, and -C alleles (>1%). Our results predicted 90 and 106 epitopes of N and S proteins, respectively. Epitope cluster analysis showed 16 and 34 respective clusters of SARS-CoV-2 N and S proteins, which covered 95.91% and 96.14% of the global population, respectively. After epitope conservancy analysis, 8 N protein epitopes and 6 S protein epitopes showed conservancy within two SARS-CoV-2 types. Of these 14 epitopes, 13 could cover SARS coronavirus and Bat SARS-like coronavirus. The remaining epitope (KWPWYIWLGF1211-1220) could cover MERS coronavirus. Finally, the 14-epitope combination could vaccinate 89.60% of all individuals worldwide. Our results propose single or combined CTL epitopes predicted in the current study as candidates for vaccines to effectively control SARS-CoV-2 infection and development.

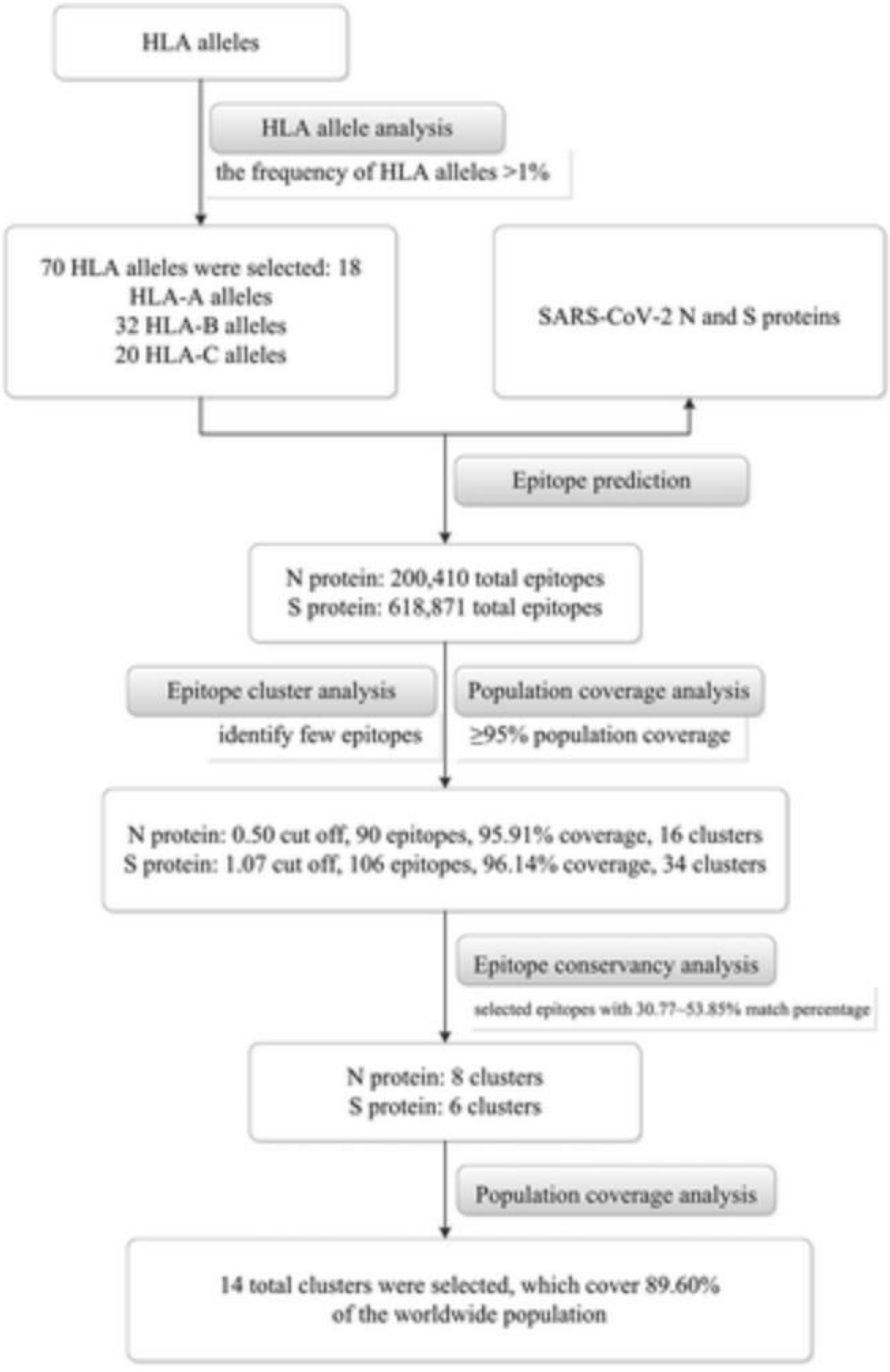


Figure 1. The flow chart of epitope prediction analysis and results

Description	Total Score	Population Coverage		
		Coverage[a]	Average hit[b]	PC90[c]
8 epitopes in N protein	0.50	0.8413	1.93	0.63
5 epitopes in S protein	1.07	0.5312	1.02	0.21
8 epitopes in N protein and 5 clusters in S protein	-	0.8494	2.95	0.66
14 epitopes for SARS-CoV-2 (NC_045512.2 and MT007544.1)	-	0.8960	3.22	0.96
13 epitopes for SARS-CoV (FJ882944.1 and NC_004718.3)	-	0.8494	2.95	0.66
13 epitopes for SARS-like coronavirus (KT444582.1)	-	0.8494	2.95	0.66
12 epitopes for Bat SARS-like coronavirus (KY417144.1)	-	0.8191	2.53	0.55
11 epitopes for Bat SARS-like coronavirus (MG772934.1)	-	0.8494	2.79	0.66

Table 9. The population coverage results (%) of the 14 combination epitopes

Protein	Epitope sequence	HLA Alleles
N protein	$IAQFAPSASAFF_{304-315}$ [a]	A*23:01, B*15:01, B*15:02, B*15:25, B*35:01, C*03:02, C*03:03, C*03:04, C*12:03, C*14:02, C*16:01
	$MSRIGMEVTPSGTWLTY_{317-333}$	A*29:02, A*30:02, B*18:01, B*35:01, B*44:02, B*44:03, B*53:01, B*58:01
	$LPQGTTLPKGFY_{161-172}$	A*30:02, B*35:01
	$ILLNKHIDAY_{351-360}$	B*15:25, B*15:01, B*15:02
	$NTASWFTAL_{48-56}$	A*68:02
	$LPNNTASWF_{45-53}$	B*35:01, B*53:01
	$LLLDRLNQL_{222-230}$	A*02:01, A*02:06
	$IGYYRRATR_{84-92}$	A*31:01
S protein	$LQIPFAMQMAYRF_{894-906}$	A*23:01, A*29:02, B*15:01, B*15:25, B*35:01, B*53:01, B*58:01, C*03:02, C*03:03, C*03:04
	$KRSFIEDLLF_{814-823}$	B*58:01, B*57:01
	$YEQYIKWPWY_{1214-1223}$	B*18:01
	$FPNITNLCPF_{337-346}$	B*35:01
	$WTFGAGAAL_{894-902}$	C*03:04, C*03:03
	$KWPWYIWLGF_{1211-1220}$	A*23:01, A*24:02

[a]Amino-acid position

Table 8. The epitope sequences and its presented HLA alleles of the 14 combination epitopes

IN SILICO

LARGE SCALE GENOMIC ANALYSIS OF 3067 SARS-COV-2 GENOMES REVEALS A CLONAL GEO-DISTRIBUTION AND A RICH GENETIC VARIATIONS OF HOTSPOTS MUTATIONS

Laamarti M, Alouane T, Kartti S, Chemao-Elfihri MW, Hakmi M, Essabbar A, Laamarti M, Hlali H, Bendani H, Boumajdi N, Benhrif O, Allam L, El Hafidi N, El Jaoudi R, Allali I, Marchoudi N, Fekkak J, Benrahma H, Nejjari C, Amzazi S, Belyamani L, Ibrahimi A.. PLoS One. 2020 Nov 10;15(11):e0240345. doi: 10.1371/journal.pone.0240345. eCollection 2020.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Medical biotechnologists affiliated with Rabat Medical & Pharmacy School in Morocco analyzed SARS-CoV-2 genomes (n=3067; see summary) isolated from 55 countries using a mutational frequency analysis and found >500 non-synonymous mutations, with 68 having a frequency >0.06% (Figure 2). The highest number of unique mutations were located in China and USA, which accumulated over 3 months (Figure 1). Authors suggest their findings inform on genetic haplotypes by geographic location worldwide, which could provide a better understanding of SARS-CoV-2 genetic diversity and evolution during the pandemic.

SUMMARY

Analysis of 3067 unique SARS-CoV-2 genomes collected from GISAID EpiCovTM database:
- Unique strains were identified across 55 countries over 3 months.
- Most mutations were found in the orf1ab gene, along with many located in the spike protein.
- 68 mutations were found to be present in 20/3067 genomes (0.06%).
- 10 hyper-variable genomic hotspots were also identified with a frequency >0.10 (Figure 2).

ABSTRACT

In late December 2019, an emerging viral infection COVID-19 was identified in Wuhan, China, and became a global pandemic. Characterization of the genetic variants of SARS-CoV-2 is crucial in following and evaluating it spread across countries. In this study, we collected and analyzed 3,067 SARS-CoV-2 genomes isolated from 55 countries during the first three months after the onset of this virus. Using comparative genomics analysis, we traced the profiles of the whole-genome mutations and compared the frequency of each mutation in the studied population. The accumulation of mutations during the epidemic period with their geographic locations was also monitored. The results showed 782 variants sites, of which 512 (65.47%) had a non-synonymous effect. Frequencies of mutated alleles revealed the presence of 68 recurrent mutations, including ten hotspot non-synonymous mutations with a prevalence higher than 0.10 in this population and distributed in six SARS-CoV-2 genes. The distribution of these recurrent mutations on the world map revealed that certain genotypes are specific to geographic locations. We also identified co-occurring mutations resulting in the presence of several haplotypes. Moreover, evolution over time has shown a mechanism of mutation co-accumulation which might affect the severity and spread of the SARS-CoV-2. The phylogentic analysis identified two major Clades C1 and C2 harboring mutations L3606F and G614D, respectively and both emerging for the first time in China. On the other hand, analysis of the selective pressure revealed the presence of negatively selected residues that could be taken into considerations as therapeutic targets. We have also created an inclusive unified database (http://covid-19.medbiotech.ma) that lists all of the genetic variants of the SARS-CoV-2 genomes found in this study with phylogeographic analysis around the world.

FIGURES

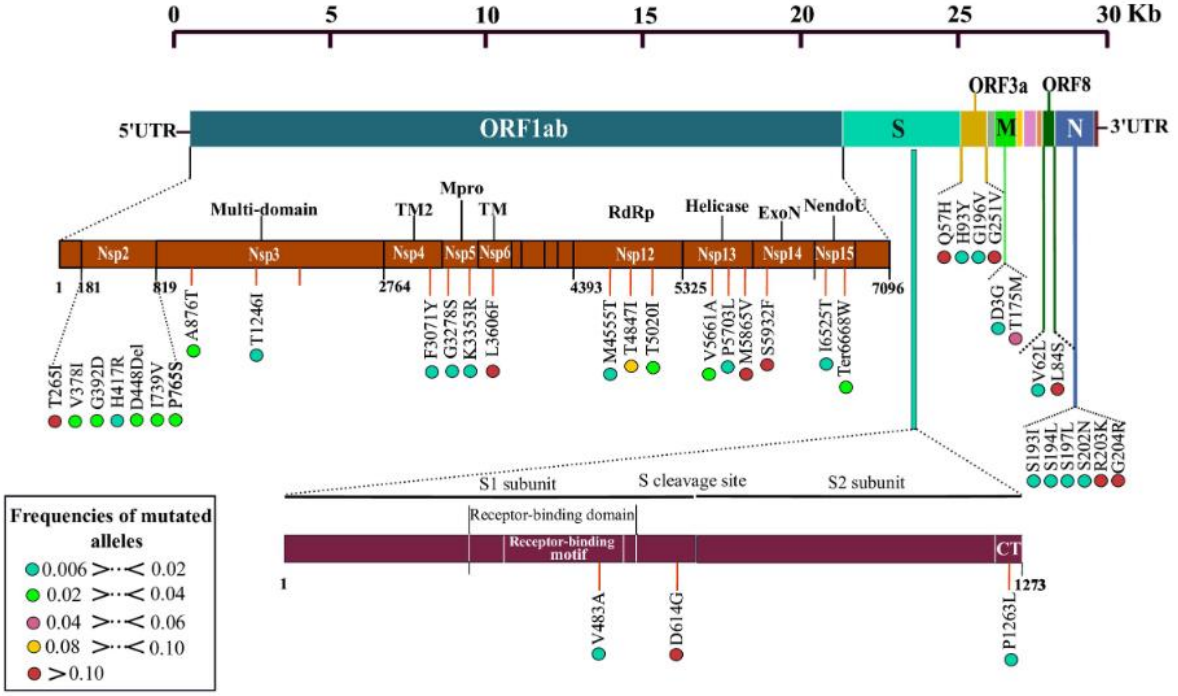


Figure 2. Schematic representation illustrating the distribution of recurrent non-synonymous mutations along the SARS-CoV-2 genome.

The brown and garnet diagrams illustrate the non-structural proteins (nsp1 to nsp 16) of the orf1ab protein and the two subunits of the spike protein, respectively. Recurrent mutations represented by vertical lines. The frequency of each mutation in the population is presented by color coded circles. Abbreviations: S, spike; E, enveloppe; M, membrane protein; N, nucleocapsid protein; CT, Cytoplasmic chail.

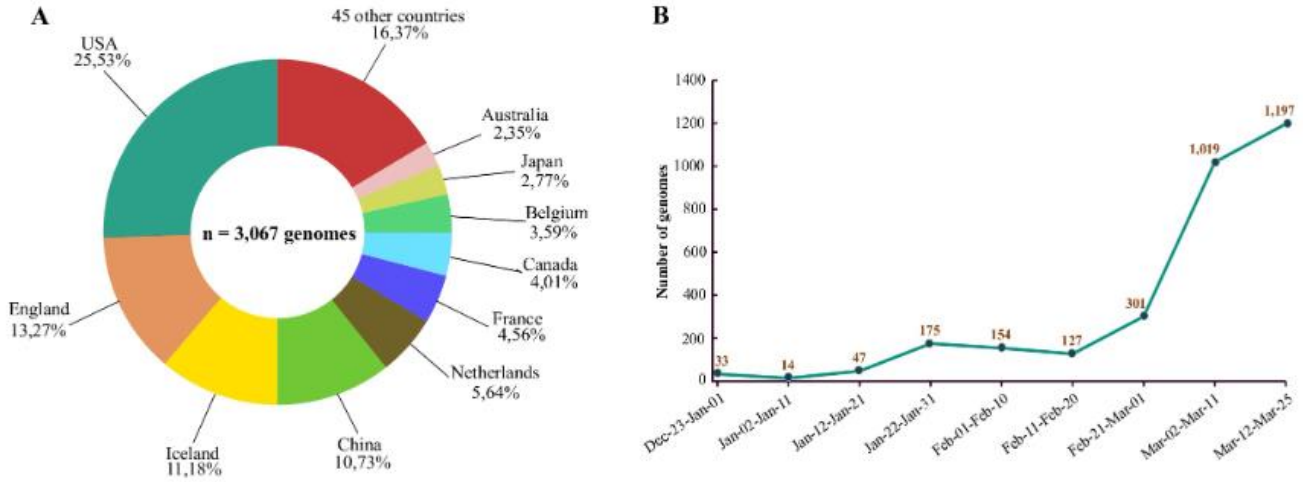


Figure 1. Distribution of the 3,067 genomes used in this study by country and date of isolation. A) The pie chart represents the percentage of genomes used in this study according to their geographic origins. The colors indicate different countries. B) Number of genomes of complete pathogens, distributed over a period of 3 months from the end of December to the end of March.

HEAVY EXPOSURE OF CHILDREN AGED 9-12 YEARS WITH SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 DID NOT LEAD TO INFECTION

Schmidt E, Steinhagen K, Rupp J.. J Pediatric Infect Dis Soc. 2020 Nov 10;9(5):620-621. doi: 10.1093/jpids/piaa116.
Level of Evidence: 5 - Case report

BLUF

A case report by experimental dermatology and immunology specialists from University of Lübeck, Germany discussed 4 siblings of the same household (ages 9, 9, 10, and 12) that had prolonged contact with their parents who both tested positive for SARS-CoV-2 via PCR. The children remained asymptomatic with negative SARS-CoV-2 RNA nasopharyngeal swabs at 1 and 2 weeks after exposure, as well as negative serum immunoglobulins (IgA, IgG, and IgM) to viral proteins at 3 weeks after exposure (Figure 1). Authors suggest there may be an absence of transmission to children in some instances despite heavy exposure, which requires further investigation as it could inform on preventive measures such as school closures and social distancing.

ABSTRACT

The reason for the apparently lower infection rate of children with SARS-CoV-2 compared to adults is still unclear. Here, we report on four school children with heavy exposure to SARS-CoV-2 with no clinical signs of COVID-19, repeated negative nasopharyngeal swabs for SARS-CoV-2 RNA, and no seroconversion.

FIGURES

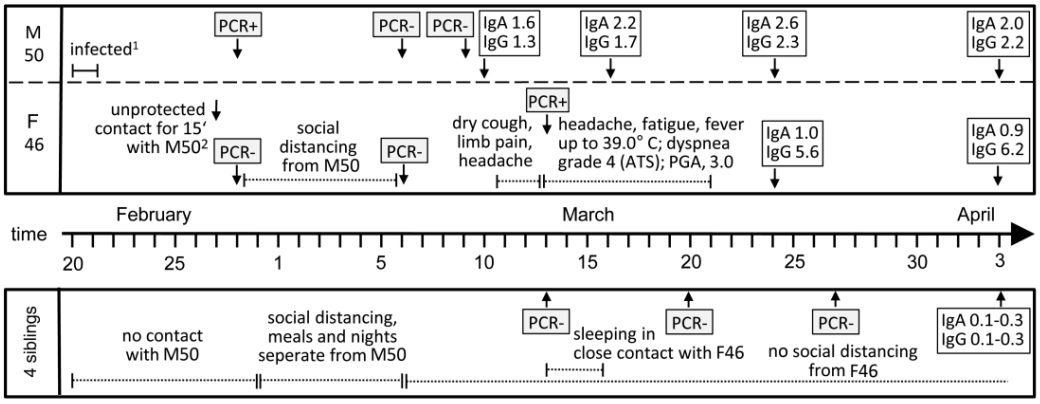


Figure 1. Clinical data and results of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA polymerase chain reaction (PCR) of nasopharyngeal swabs and anti–SARS-CoV-2 enzyme-linked immunosorbent assay (ELISA) over time. PCR results of nasopharyngeal swabs for detection of SARSCoV-2 RNA are shown in gray boxes. ELISA values for serum immunoglobulin A and immunoglobulin G (both positive ≥1.1) against the recombinant S1 domain of structural protein of SARS-CoV-2 are indicated in white boxes. 1 During a scientific meeting in Munich, Germany. 2 Returning from a scientific meeting in Southeast Asia, just before Lübeck Public Health Department informed M50 to be a coronavirus disease 2019 contact person during the Munich meeting [5]. The 4 siblings included 3 girls and 1 boy aged 12, 10, 9, and 9 years. Abbreviations: ATS, American Thoracic Society; F46, 46-year-old mother; IgA, immunoglobulin A; IgG, immunoglobulin G; M50, 50-year-old father; PCR, polymerase chain reaction; PGA, patient global assessment (0–10).

AN EYE ON THE FUTURE OF COVID'19: PREDICTION OF LIKELY POSITIVE CASES AND FATALITY IN INDIA OVER A 30 DAYS HORIZON USING PROPHET MODEL

Tulshyan V, Sharma D, Mittal M.. Disaster Med Public Health Prep. 2020 Nov 18:1-20. doi: 10.1017/dmp.2020.444. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

Investigators from various departments of computer science and engineering in India used Python programing and Prophet Model time series analysis to estimate COVID-19 positive cases and case fatality rate (reported as 2-3%) in India from March 24 through May 24, 2020. The results were divided into three categories:

1) Prediction of 92,594 total cases during the lockdown phase (Figure 2)
2) Prediction of 200,000 total cases after the relaxation of the lockdown, with an increased predicted growth rate from 0.8% to 1.6% (Figure 3)
3) Prediction of 1,913 total deaths; however, this number has a low accuracy rate as the data used was continuously changing (Figure 4)

These results suggest that the degree of lockdown, self-quarantining, and strict norms of social distancing are all relevant factors in controlling the spread of this highly infectious virus, especially in heavily populated regions.

SUMMARY

India was chosen as an ideal model for this analysis due to its high population density per square kilometer, making the algorithm outcomes more accurate.

ABSTRACT

BACKGROUND: The coronavirus disease pandemic was initiated in Wuhan province of mainland China in December 2019 and has spread over the world. OBJECTIVE: This study analyses the effects of COVID 19 based on Likely Positive Cases and fatality in India during and after the lockdown period from 24 March 2020 to 24 May 2020. METHODS: Python has been used as the main programming language for data analysis and forecasting using the Prophet Model, a time series analysis model. The dataset has been preprocessed by grouping together the days for total numbers of cases and deaths on few selected dates and removed missing values present in some states. RESULTS: The Prophet model performs better in terms of precision on the real data. Prediction depicts that during the lockdown, the total cases were rising but in a controlled manner with an accuracy of 87%. After the relaxation of lockdown rules, the predictions have shown an obstreperous situation with an accuracy of 60%. CONCLUSION: The resilience could have been better if the lockdown with strict norms was continued without much relaxation. The situation after lockdown has been found to be uncertain as observed by the experimental study conducted in this work.

FIGURES

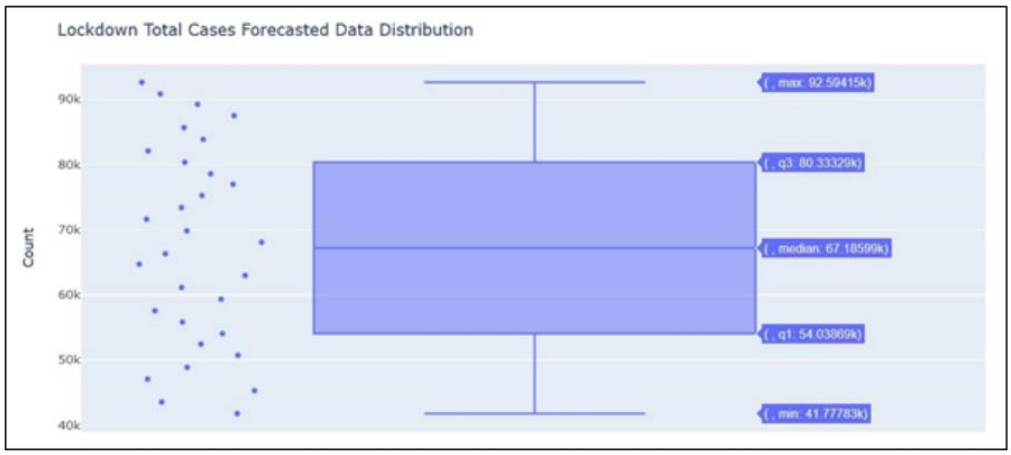


Figure 2. Total Cases (Lockdown) Forecasted Data Distribution.

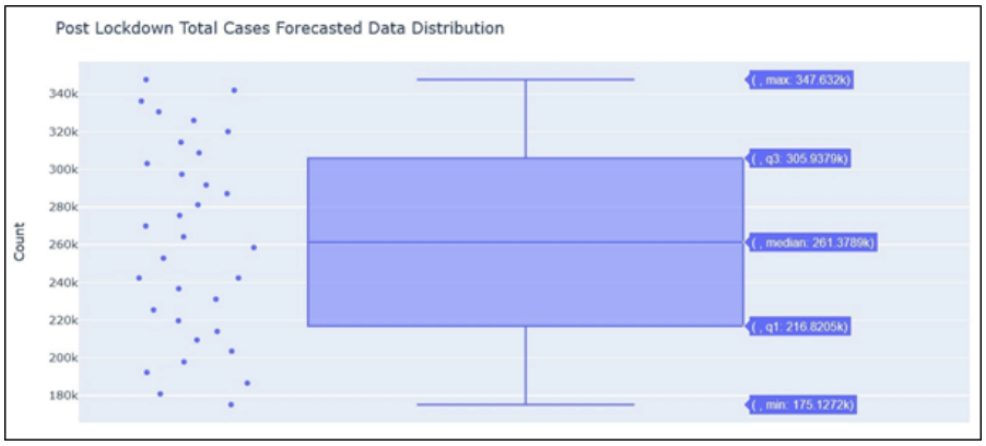


Figure 3. Total Cases (Post-Lockdown) Forecasted Data Distribution.

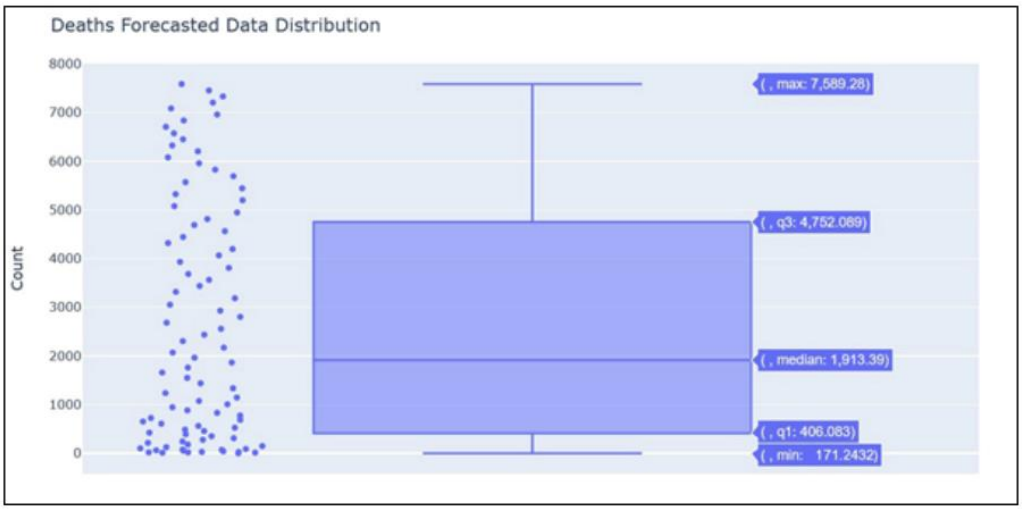


Figure 4. Deaths Forecasted Data Distribution.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

MULTI-SPECIES ELISA FOR THE DETECTION OF ANTIBODIES AGAINST SARS-COV-2 IN ANIMALS

Wernike K, Aebischer A, Michelitsch A, Hoffmann D, Freuling C, Balkema-Buschmann A, Graaf A, Müller T, Osterrieder N, Rissmann M, Rubbenstroth D, Schön J, Schulz C, Trimpert J, Ulrich L, Volz A, Mettenleiter T, Beer M.. Transbound Emerg Dis. 2020 Nov 15. doi: 10.1111/tbed.13926. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

A mechanism-based study, completed at Friedrich-Loefller-Institut (Germany), examined the efficacy of an in-house developed multi-species ELISA to detect SARS-CoV-2 receptor-binding domain (RBD) with 59 sera samples of experimentally infected animals (including ferrets, raccoon dogs, hamsters, rabbits, chickens, cattle and a cat) and 220 antibody-negative sera of the same animal species. This study revealed that the ELISA had a specificity of 100% and sensitivity of 98.31%, as experimentally infected animals consistently tested positive (Figure 3). Beyond uncovering an ELISA effective at detecting SARS-CoV-2 from sera across species, this study demonstrates that SARS-CoV-2 is capable of infecting many different species, demonstrating potential sources of viral spread for further investigation.

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused a pandemic with millions of infected humans and hundreds of thousands of fatalities. As the novel disease - referred to as COVID-19 - unfolded, occasional anthropozoonotic

infections of animals by owners or caretakers were reported in dogs, felid species and farmed mink. Further species were shown to be susceptible under experimental conditions. The extent of natural infections of animals, however, is still largely unknown. Serological methods will be useful tools for tracing SARS-CoV-2 infections in animals once test systems are evaluated for use in different species. Here, we developed an indirect multi-species ELISA based on the receptor-binding domain (RBD) of SARS-CoV-2. The newly established ELISA was evaluated using 59 sera of infected or vaccinated animals including ferrets, raccoon dogs, hamsters, rabbits, chickens, cattle and a cat, and a total of 220 antibody-negative sera of the same animal species. Overall, a diagnostic specificity of 100.0% and sensitivity of 98.31% was achieved, and the functionality with every species included in this study could be demonstrated. Hence, a versatile and reliable ELISA protocol was established that enables high-throughput antibody detection in a broad range of animal species, which may be used for outbreak investigations, to assess the seroprevalence in susceptible species or to screen for reservoir or intermediate hosts.

FIGURES

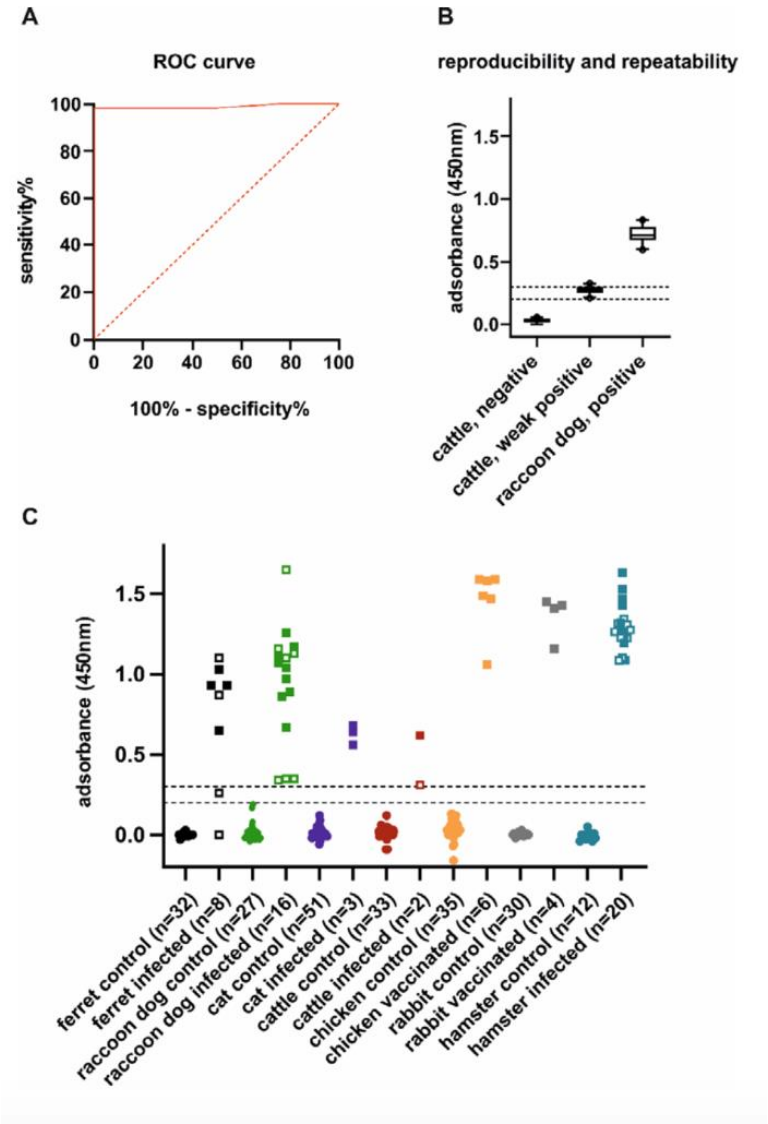


Figure 3: Assay validation and diagnostic performance. A) Receiver operating characteristic (ROC) analyses of the SARS-CoV-2 ELISA using the RBD domain as antigen and 220 negative animal sera (ferret, raccoon dog, cat, cattle, chicken, rabbit and hamster) and 59 sera of infected or vaccinated animals. B) Reproducibility and repeatability of the ELISA. A negative and a very weak positive cattle serum, as well as a positive sample collected from a raccoon dog were tested in five replicates each in five independent approaches. The box plots represent the results of all 25 respective replicates. Each outlier is marked by a circle. C) Performance of the SARS-CoV-2 ELISA for animals era from clinical trials. Samples taken on day 8 or 12 after infection are shown by open squares. Sera that were collected from day 15 on wards after an experimental infection (ferret, raccoon dog, cattle, hamster) or immunization (chicken, rabbit), or after the first RT-PCR positive throat swab sample (cat) are indicated by filled squares. Negative control samples are shown by circles. The total number of sera per group is given in brackets.

ADHERENCE OF THE GENERAL PUBLIC TO SELF-PROTECTION GUIDELINES DURING THE COVID-19 PANDEMIC

Jabbari P, Taraghikhah N, Jabbari F, Ebrahimi S, Rezaei N.. Disaster Med Public Health Prep. 2020 Nov 18:1-12. doi: 10.1017/dmp.2020.445. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A cross-sectional survey-based study, conducted in 2 public places in Tehran, Iran during June 2020, investigated the public's knowledge and use of PPE and self-protection against SARS-CoV-2 through a survey of 431 participants. The survey found that half of the participants did not ensure hand hygiene, while use of respiratory protection was greater (Figure 1). There was also some lack in knowledge of how to properly use respiratory protection and engage in other preventative practices, such as social distancing and disinfectant use (Table 1). While this study may not accurately represent Tehran's whole population due to selection bias, this study demonstrates the need for an effective channel of communication to the public about COVID-19 in order to help decrease its rate of spread.

ABSTRACT

BACKGROUND: Novel coronavirus disease (COVID-19) pandemic is rapidly growing due to high level of contagiousness. Different measures have been taken to slow the spread of the virus. Appropriate use of personal protective equipment (PPE) is one of these key measures. In this cross-sectional study, we investigated adherence of the general public to use of PPE and their knowledge regarding the rationale behind their use. METHODS: Two samples were chosen from public places (a subway station and a city store) in Tehran, Iran, one of the countries affected by COVID-19. Individuals were observed for appropriate use of PPE and interviewed regarding their knowledge on some basic self-protection information. RESULTS: Approximately, half of the 431 participants did not take any measures to ensure hand hygiene, while those who did not use respiratory protection were far fewer. A considerable number of individuals, however, did not use these PPE correctly. On the other hand, there was a gap in the knowledge of the general public regarding different aspects of protective measures. The majority of the participants were receptive towards education on preventive measurements through public media. CONCLUSION: Education is an important aspect in containing the COVID-19 pandemic, as it directly increases adherence of the general public to protective measures.

FIGURES

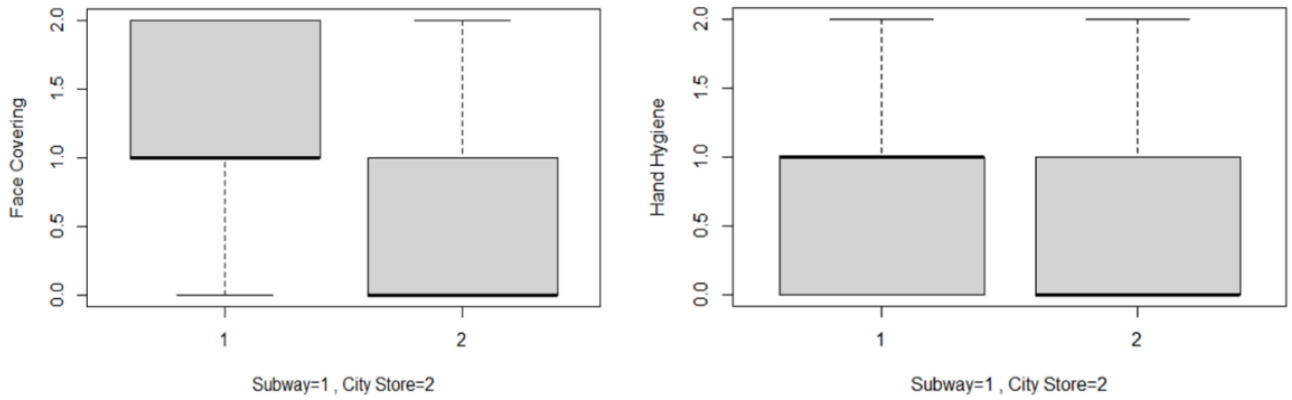


Figure 1- Use of PPE among two study samples. Face covering: Score 0= no PPE, score 1= incorrect use, score 2= appropriate use. Hand hygiene: score zero: no measure, score 1= glove OR hand sanitizer, score 2= glove AND hand sanitizer.

Subway (N=268)			
Hand hygiene	Gloves	N=73	
	Disinfectant	N=119	
Face covering	Cloths	Correct	N=0
		Incorrect	N=67
	Surgical	Correct	N=91
		Incorrect	N=52
	Shields	Only	N=2
		+ mask	N=9
City Store (N=163)			
Hand hygiene	Gloves	N=45	
	Disinfectant	N=44	
Face covering	Cloths	Correct	N=0
		Incorrect	N=25
	Surgical	Correct	N=25
		Incorrect	N=25
	Shields	Only	N=3
		+ mask	N=1
General Awareness (N=431)			
Social distancing	No awareness	N=28	
	Incorrect	N=26	
	Correct	N=377	
Standard disinfectant	No awareness	N=197	
	Incorrect	N=66	
	Correct	N=163	
Preferred education platform	Public media	N=265	
	Online platforms	N=111	
	Person-to-person	N=48	
	No preference	N=7	

Table 1- Summary of the study interviews and observations.

RAPIDLY DEPLOYABLE MOUSE MODELS OF SARS-COV-2 INFECTION ADD FLEXIBILITY TO THE COVID-19 TOOLBOX

Harker JA, Johansson C.. Am J Respir Cell Mol Biol. 2020 Nov 10. doi: 10.1165/rcmb.2020-0456ED. Online ahead of print.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Immunologists from the Imperial College London, United Kingdom describe the use of genetically-engineered mice to replicate and model SARS-CoV-2 infection, as hACE2 expression under various promoters has been linked to several unique pathways in mice (Figure 1). They propose Ad-hACE2 (adenovirus-human ACE2) and AAV-hACE2 (adenovirus-associated) models may be particularly effective for anti-viral drug screening, whereas K18-hACE2 (human keratin 18) mouse models may be most helpful for testing vaccines. Authors advocate for the use of mouse models to fill SARS-CoV-2 mechanistic knowledge gaps, suggesting they have potential utility in determining disease severity via interferon effects and providing insight on "long-COVID" in those recovering from SARS-CoV-2 infection.

FIGURES

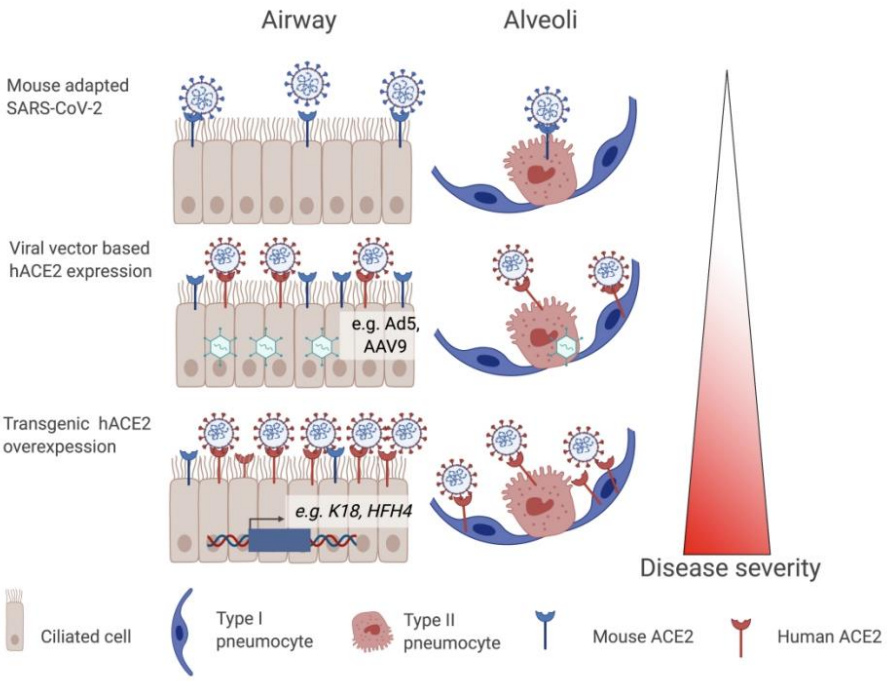


Figure 1. Mouse models of SARS-CoV-2 infection provide a broad range of disease phenotypes and pathologies for the study of COVID19. As summarized in this schematic use of mouse adapted, adenoviral induced and genetically overexpressed strategies, including Ad5-hACE2 overexpressed described in this Journal by Han et al, for promoting SARS-CoV-2 binding to ACE2 within the respiratory tract facilitate viral replication and provide a range of viral tropisms and disease severity with which to study pathogenesis. Figure created using Biorender.

CONVALESCENT PLASMA ANTI-SARS-COV-2 SPIKE PROTEIN ECTODOMAIN AND RECEPTOR-BINDING DOMAIN IGG CORRELATE WITH VIRUS NEUTRALIZATION

Salazar E, Kuchipudi SV, Christensen PA, Eagar T, Yi X, Zhao P, Jin Z, Long SW, Olsen RJ, Chen J, Castillo B, Leveque C, Towers D, Lavinder J, Gollihar J, Cardona J, Ippolito G, Nissly R, Bird I, Greenawalt D, Rossi RM, Gontu A, Srinivasan S, Poojary I, Cattadori IM, Hudson PJ, Josleyn NM, Prugar L, Huie K, Herbert A, Bernard DW, Dye JM, Kapur V, Musser JM.. J Clin Invest. 2020 Nov 16:141206. doi: 10.1172/JCI141206. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

A cohort study, conducted by researchers primarily at Houston Methodist Hospital, analyzed samples of plasma from 68 recovered COVID-19 patients, 2,814 asymptomatic patients, and 10 naive human plasma specimens to investigate the relationship between different neutralizing antibodies and possible ways to screen plasma samples for a virus neutralization (VN) titer ≥ 160 (the FDA-recommended level for COVID-19 treatment). Based on this study's findings (illustrated below), screening for potential anti-SARS-CoV-2 convalescent plasma donors cannot be completed by analysis of symptom severity alone, but spike ectodomain (anti-ECD) and anti– receptor-binding domain (anti-RBD) IgG titers may provide a reasonable estimate of VN titer levels.

SUMMARY

Analysis of the sera of 68 COVID-19 patients revealed a positive relationship among spike ectodomain (anti-ECD), anti–receptor-binding domain (anti-RBD) IgG titers, and SARS-CoV-2 virus neutralization (VN) titers, where probability of a VN titer of ≥160 was ≥80% when anti-RBD or anti-ECD titers were ≥1:1350 (Figure 2). While no significant relationship was detected between symptom severity and VN titer level (Figure 3), an analysis of 2,814 asymptomatic adults found 14 individuals with sufficient VN titers, with all of those individuals having RBD titers of ≥1:1350.

ABSTRACT

The newly emerged severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) highlights the urgent need for assays that detect protective levels of neutralizing antibodies. We studied the relationship between anti-spike ectodomain (ECD), anti-receptor binding domain (RBD) IgG titers, and SARS-CoV-2 virus neutralization (VN) titers generated by two in vitro assays using convalescent plasma samples from 68 COVID-19 patients. We report a strong positive correlation between both plasma anti-RBD and anti-ECD IgG titers and in vitro VN titer. The probability of a VN titer >=160, the FDA-recommended level for convalescent plasma used for COVID-19 treatment, was >=80% when anti-RBD or anti-ECD titers were >=1:1350. Of all donors, 37% lacked VN titers >=160. Dyspnea, hospitalization, and disease severity were significantly associated with higher VN titer. Frequent donation of convalescent plasma did not significantly decrease VN or IgG titers. Analysis of 2,814 asymptomatic adults found 73 individuals with anti-ECD IgG titers of >=1:50 and strong positive correlation with anti-RBD and VN titers. Fourteen of these individuals had VN titers >=1:160, all of which had anti-RBD titer >=1:1350. We conclude that anti-RBD or anti-ECD IgG titers can serve as a surrogate for VN titers to identify suitable plasma donors. Plasma anti-RBD or anti-ECD titers of >=1:1350 may provide critical information about protection against COVID-19 disease.

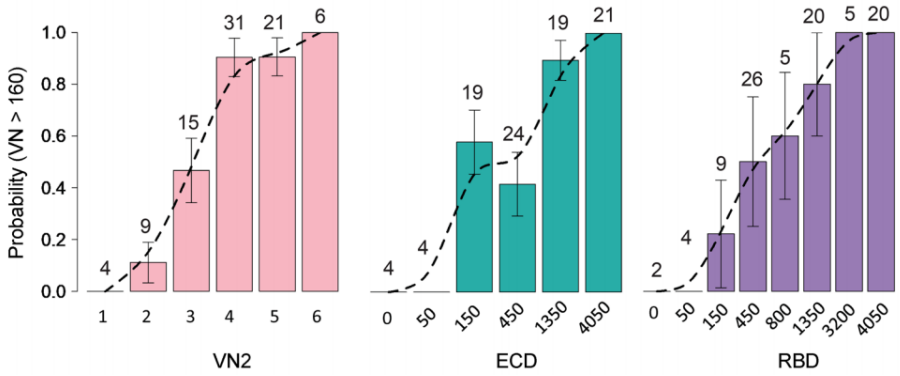


Figure 2. Prevalence of donors with VN >160 for VN2, ECD, and RBD. Probabilities of VN ≥160 were plotted for 6 range classes, with an interclass interval of 1.8 log2 IC50 values (class 1, <2; class 2, 2–12; class 3, 12–42; class 4, 42–147; class 5, 147–512; and class 6, >512) or observed classes for ECD (n = 6) and RBD (n = 8) reciprocal ELISA titers. A spline curve (dotted line, smoothness shape = 1) has been fitted to the probability values and standard errors (bars) are reported. The numbers of donor samples are shown above the bars.

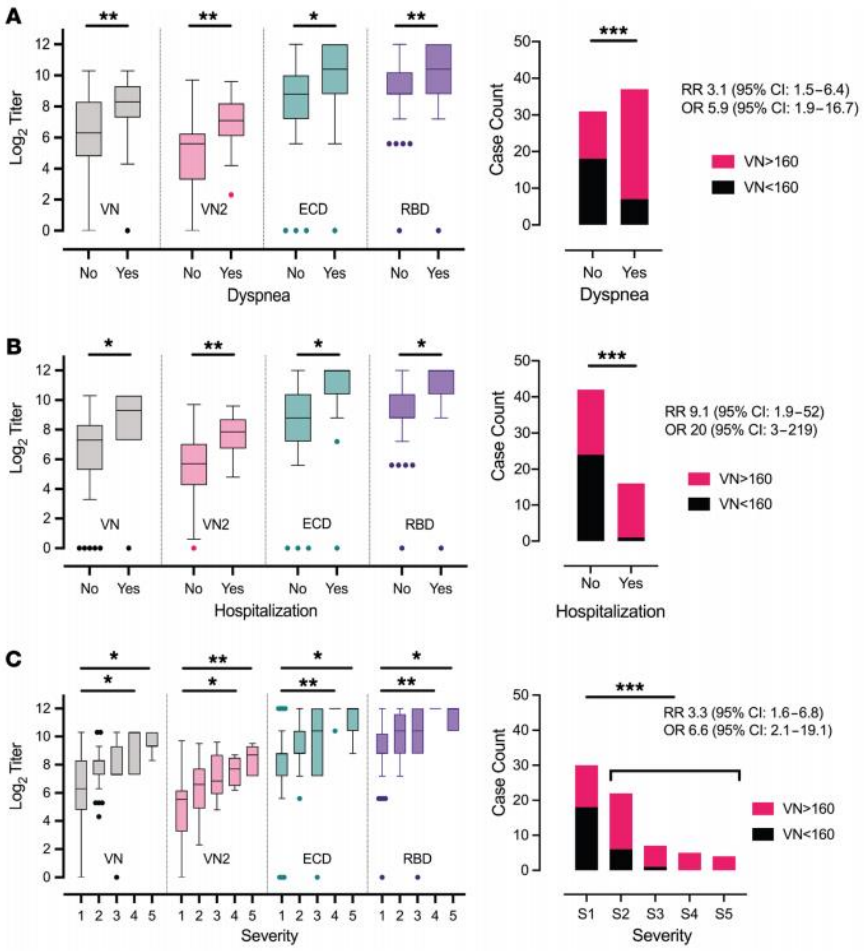


Figure 3. Distributions of VN, VN2, anti-ECD, and anti-RBD titers based on convalescent plasma donor self-reported clinical characteristics. Box plots of VN, VN2, anti-ECD and anti RBD titers by (A) dyspnea, (B) hospitalization, and (C) disease severity (1, low severity; 5, high severity) at initial plasma donation from the 68 individual donors. The median, minimum, maximum, first and third quartile, and extreme values are reported. Case counts of donors above and below the VN ≥160 threshold were stratified by whether they self-reported (A) occurrence of dyspnea during symptomatic phase of disease, (B) hospitalization, and (C) disease severity. Pairwise t test (*P < 0.05, **P < 0.01, ***P < 0.001), OR, and relative risk (RR) with CI are also reported.

LACK OF EFFICACY OF STANDARD DOSES OF IVERMECTIN IN SEVERE COVID-19 PATIENTS

Camprubí D, Almuedo-Riera A, Martí-Soler H, Soriano A, Hurtado JC, Subirà C, Grau-Pujol B, Krolewiecki A, Muñoz J.. PLoS One. 2020 Nov 11;15(11):e0242184. doi: 10.1371/journal.pone.0242184. eCollection 2020.
Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

This retrospective controlled cohort study by specialists in global health and infectious disease from Hospital Clinic-Universitat de Barcelona, Spain evaluated efficacy of standard doses of ivermectin in patients with severe COVID-19 (n=13) against controls without ivermectin (n=13). They found no significant differences in clinical or microbiological outcomes between the two groups after 8-11 days of treatment ($p > 0.999$). Authors acknowledge the small sample size in this study, but suggest their results warrant further research involving high-dose ivermectin to better evaluate its efficacy in patients with severe COVID-19.

ABSTRACT

Ivermectin has recently shown efficacy against SARS-CoV-2 in-vitro. We retrospectively reviewed severe COVID-19 patients receiving standard doses of ivermectin and we compared clinical and microbiological outcomes with a similar group of patients not receiving ivermectin. No differences were found between groups. We recommend the evaluation of high-doses of ivermectin in randomized trials against SARS-CoV-2.

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