The Daily COVID-19 Literature Surveillance Summary

March 15, 2021

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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

Transmission & Prevention

- Mask wearing contributes to controlling community spread of SARS-CoV-2. A review article conducted by researchers from the Center for Disease Control and Prevention in Atlanta, Georgia discuss how widespread community masking has been shown in multiple studies to limit exhalation and inhalation of infectious virus, provide a barrier to large respiratory droplets to protect uninfected mask wearers, and is associated with decreased rates of infection and death from COVID-19 infection. Multilayer cloth masks have been shown to be more effective than single layer masks in some studies, however the prevalence of mask wearing outweighs the mask type. It is especially crucial to emphasize the importance of widespread masking and prevention efforts, especially with rising prevalence of more transmissible SARS-CoV-2 variants, until national vaccination administration reaches efficacious levels.

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ESTIMATION OF THE FRACTION OF COVID-19 INFECTED PEOPLE IN U.S. STATES AND COUNTRIES WORLDWIDE

Noh J, Danuser G.. PLoS One. 2021 Feb 8;16(2):e0246772. doi: 10.1371/journal.pone.0246772. eCollection 2021.
Level of Evidence: 5 - Modeling

BLUF

Biostatisticians from the University of Texas Southwestern Medical Center created a machine-based learning algorithm to better model actual daily COVID-19 case counts given the substantial number of undocumented infections (Figure 1). Using repository data from Johns Hopkins University and the COVID-19 Tracking Project, they produced similar estimates of cumulative incidences to those determined by seroprevalence surveys (i.e. 0.6%-1.9% vs 1.1-2.1% over 3 weeks in Washington state)(Figure 2A). They estimated daily cases in the United States in April 2020 approached 400,000 while only 30,000 were reported (Figure 3A), and authors suggest that their computerized model provides a more accurate daily infection ascertainment rate.

ABSTRACT

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, daily counts of confirmed cases and deaths have been publicly reported in real-time to control the virus spread. However, substantial undocumented infections have obscured the true size of the currently infected population, which is arguably the most critical number for public health policy decisions. We developed a machine learning framework to estimate time courses of actual new COVID-19 cases and current infections in all 50 U.S. states and the 50 most infected countries from reported test results and deaths. Using published epidemiological parameters, our algorithm optimized slowly varying daily ascertainment rates and a time course of currently infected cases each day. Severe under-ascertainment of COVID-19 cases was found to be universal across U.S. states and countries worldwide. In 25 out of the 50 countries, actual cumulative cases were estimated to be 5-20 times greater than the confirmed cases. Our estimates of cumulative incidence were in line with the existing seroprevalence rates in 46 U.S. states. Our framework projected for countries like Belgium, Brazil, and the U.S. that ~10% of the population has been infected once. In the U.S. states like Louisiana, Georgia, and Florida, more than 4% of the population was estimated to be currently infected, as of September 3, 2020, while in New York this fraction is 0.12%. The estimation of the actual fraction of currently infected people is crucial for any definition of public health policies, which up to this point may have been misguided by the reliance on confirmed cases.

FIGURES

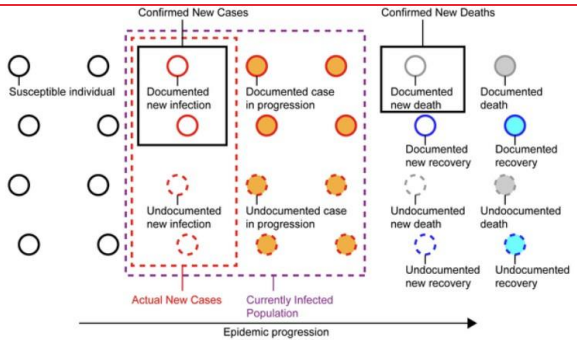

Figure 1. Undocumented COVID-19 cases.
In an epidemic process, a population is categorized into susceptible, infected, deceased, or recovered individuals. Counts of confirmed COVID-19 cases, deaths, and recoveries are insufficient to calculate the number of currently infected individuals (purple dotted box) because of substantial undocumented infections not captured by diagnostic tests. The input to the proposed framework is the daily counts of confirmed new cases and deaths (black boxes). Using pandemic parameters such as the Infection-Fatality-Rate and the mean duration periods from infection to death and recovery, the framework estimates the counts of actual new cases (red dotted box) and currently infected individuals.

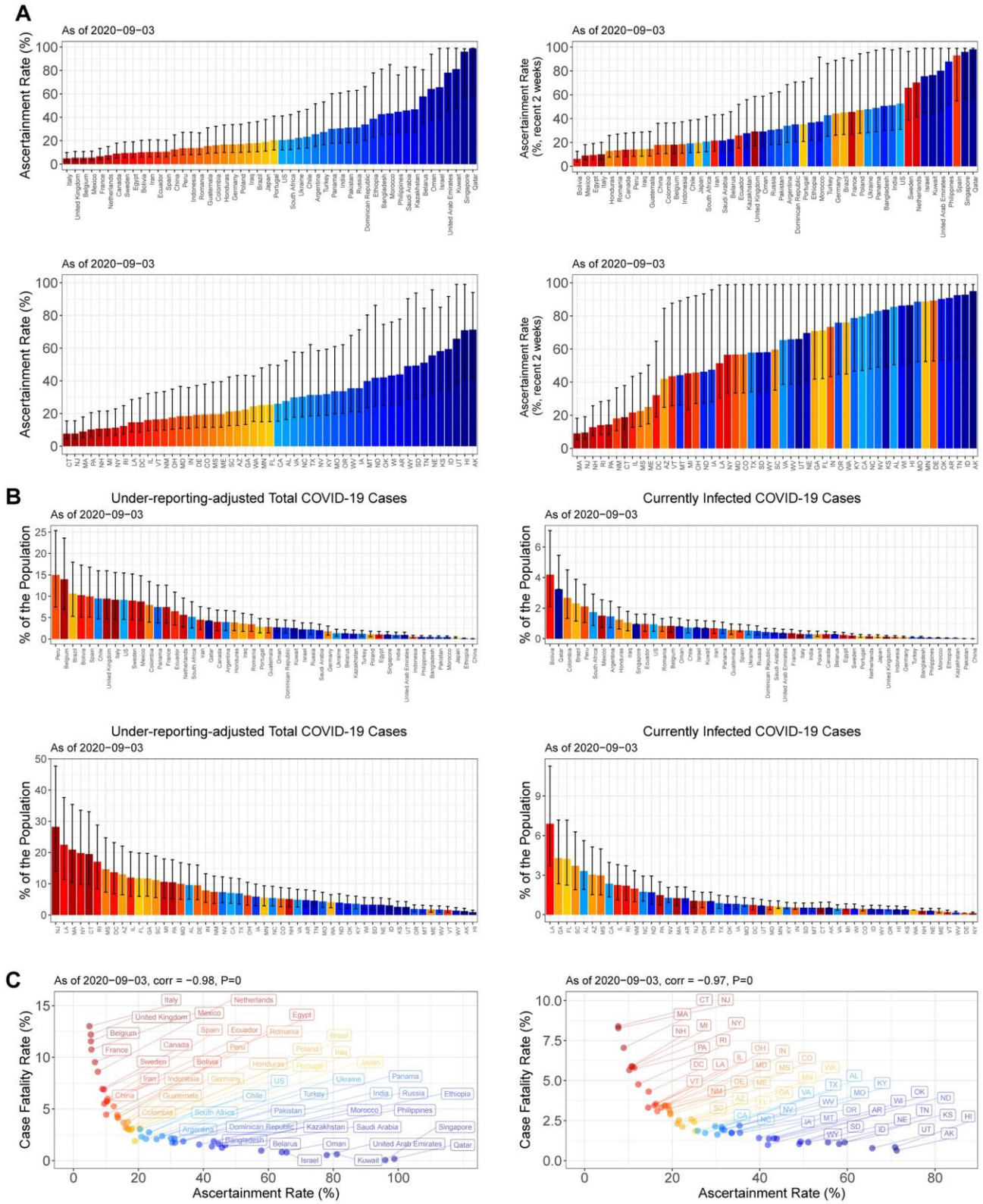

Figure 4. Estimates of ascertainment rates, cumulative incidence rates, and actual fractions of current infections in 50 countries and 50 U.S. states.

(A) Estimates of ascertainment rates for the whole period until September 3, 2020 (left), and recent ascertainment rates (August 21–September 3, 2020) (right), in 50 countries with the most confirmed cases (upper) and 50 U.S. states (lower). (B) Cumulative incidence rates (left), and percentages of currently infected individuals in each population (right) in the 50 countries (upper) and 50 U.S. states (lower). Error bars indicate 95%-confidence intervals. (C) Scatter plots between the crude case-fatality-rates and the ascertainment rates for the 50 countries (left) and 50 U.S. states (right). Spearman rank correlations and their P-values are shown.

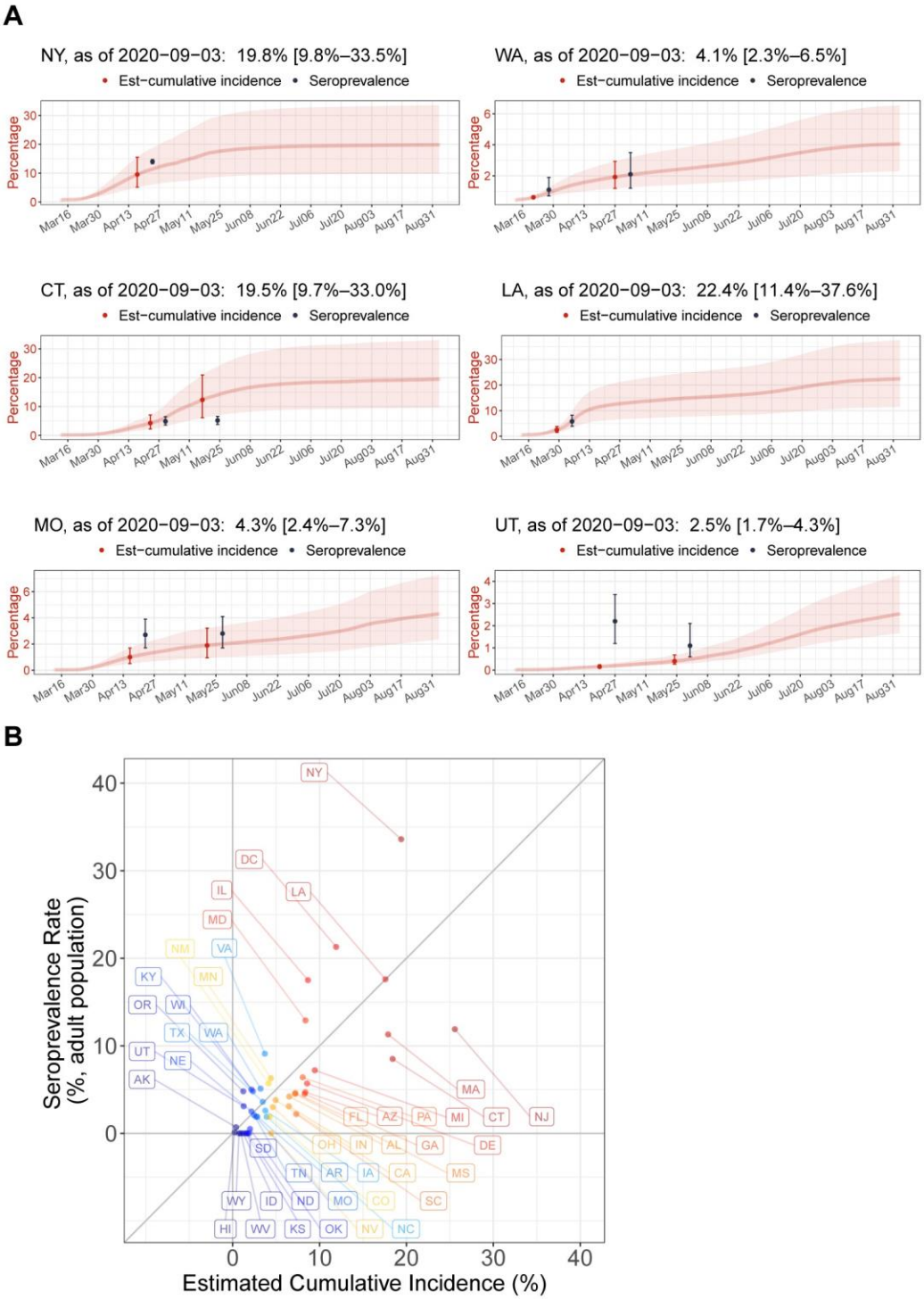

Fig 2. Validation of prediction framework using seroprevalence rates in U.S. states.

(A) Seroprevalence rates in six U.S. states (black) surveyed until May 2020, are overlaid on computationally estimated time courses of cumulative incidence rates (red) from March 13 to September 3, 2020, for New York, Washington state, Connecticut, Louisiana, Missouri, and Utah from upper-left to lower-right. The indicated date of the seroprevalence rate is the mid-point of the serum collection period. The corresponding cumulative incidence estimate is on the date one-week prior to the date of the seroprevalence rate to account for time delays from infection to antibody detection. Error bars and shaded bands indicate 95% confidence intervals. (B) The Y-axis shows the seroprevalence rates in adult (≥18 years) populations of 45 U.S. states and Washington D.C. estimated from a nationwide plasma sample (n = 28,503) of patients on dialysis during July 2020. The X-axis shows the computationally estimated cumulative incidence rates for the states on July 8, 2020, that is one week prior to the mid-point of the plasma sample collection period, July 2020.

ADULTS

INCIDENCE AND CLINICAL OUTCOME OF CORONAVIRUS DISEASE 2019 IN A COHORT OF 11,560 BRAZILIAN PATIENTS WITH MULTIPLE SCLEROSIS

REDONE.br – Neuroimmunology Brazilian Study Group Focused on COVID-19 and MS.. Mult Scler. 2021 Feb 2:1352458520978354. doi: 10.1177/1352458520978354. Online ahead of print.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

An observational cohort study in Brazil from March 13 to June 4, 2020 by the Neuroimmunology Brazilian Study Group found that, in 11,560 patients with multiple sclerosis (pwMS) there was an incidence rate of 27.7/10,000 patients, which nearly matched that of the general population: 29.2/10,000 (Figure 1). 87% of pwMS with COVID-19 developed only mild symptoms, with atypical symptoms including headache (54%) and anosmia (46%), and almost all continued receiving disease-modifying treatment (DMT) during the COVID-19 pandemic (Table 1). More research is needed to define how MS and DMTs modify the outcome of infections.

ABSTRACT

BACKGROUND: Little information is available regarding the incidence and clinical outcome of the SARS-CoV2 infection in patients with multiple sclerosis (pwMS). OBJECTIVE: To determine the incidence, clinical outcome, and impact of COVID-19 on pwMS. METHODS: This observational study was prospectively performed on a cohort of pwMS (N = 11,560) followed up by 47 out of 51 Brazilian MS referral centers that registered pwMS with COVID-19 at the REDONE platform from 13 March to 4 June 2020. RESULTS: The incidence of COVID-19 for pwMS patients was 27.7/10,000 patients and for the general population was 29.2/10,000 inhabitants. A total of 94 (77 women) pwMS patients, aged 40 +- 10.25 years, presenting 9.9 +- 8.6 years of MS disease duration, developed the COVID-19, most of them (87%) exhibited the mild form of the disease. Eighty (96%) patients maintained the use of MS disease-modifying treatment (DMT) during COVID-19 pandemic and 14 patients were not in use of DMTs. CONCLUSION: Incidence of COVID-19 in Brazilian pwMS was not different from those observed for the general Brazilian population. Most pwMS exhibited mild COVID-19, despite the maintenance of the underlying MS treatment.

FIGURES

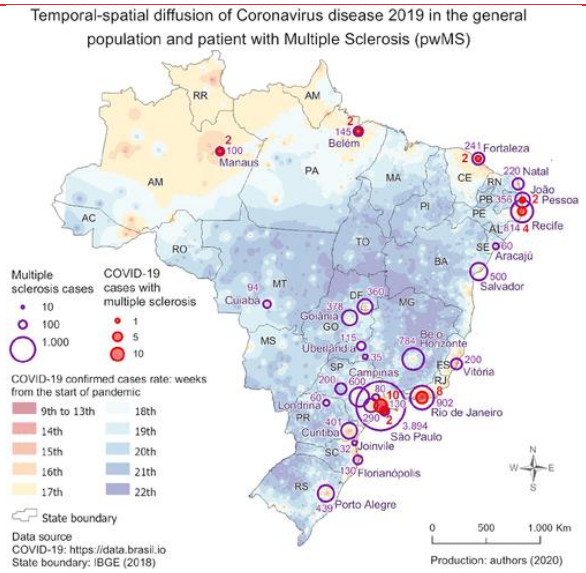

Figure 1. Mapping of COVID-19 in the general Brazilian population and in Brazilian patients with multiple sclerosis (pwMS)

Table 1. Demographic and clinical characteristics of all patients with multiple sclerosis (pwMS) presenting Coronavirus Disease 2019, as informed at REDONE-COVID19 Brazilian Registry.

Incidence on 4 June 2020	27.7/10,000
COVID-19/pwMS	32
MS Cohort	11,560
Total number	$N = 94$ (%)
Age (mean ± SD)	40.59 (± 10.25)
Age ⩽ 50	77 (83%)
Age > 50	15 (16%)
Missing	2 (1%)
Gender	
Women	73 (78%)
Men	21 (22%)
MS onset age (mean ± SD years)	31.81 (± 8.40)
MS disease duration (mean ± SD years)	9.93 (± 8.61)
Skin color	
White	58 (62%)
Non-White	31 (33%)
Severity	
Mild	82 (87%)
Moderate	10 (11%)
Severe	2 (2%)
Symptoms	
Fever	68 (72%)
Cough	55 (58%)
Myalgia	55 (58%)
Coryza	39 (41%)
Asthenia/fatigue	43 (46%)
Dyspnea	36 (38%)
Odynophagia	41 (44%)
Chills	21 (22%)
Diarrhea	17 (18%)
Headache	51 (54%)
Hyposmia or dysgeusia	43 (46%)
Comorbidity	
No comorbidity	75 (80%)
Hypertension	8 (8%)
Diabetes	1 (1%)
Dyslipidemia	6 (6%)
Cardiac disease	1 (1%)
Lung disease	1 (1%)
Asthma	2 (2%)
Obesity	2 (2%)
Thyroid disease	2 (2%)
Neoplasm	2 (2%)
Smoker	9 (10%)
Disease-modifying therapy (DMT)	
No therapy	13 (14%)
Interferon beta	9 (10%)
Glatiramer acetate	5 (5%)
Natalizumab	20 (21%)
Teriflunomide	5 (5%)
Fumarate dimethyl	17 (18%)
Fingolimod	16 (16%)
Ocrelizumab	5 (5%)
Rituximab	2 (2%)
Alemtuzumab	1 (1%)

(Continued)

Table 1. (Continued)

MS: multiple sclerosis; SD: standard deviation; RT-PCR: reverse transcription polymerase chain reaction.
The incidence of COVID-19 in the general Brazilian population and in pwMS was calculated using the same criterion considering SARS-CoV2 infection by RT-PCR or serology.

Table 1. Demographic and clinical characteristics of all patients with multiple sclerosis (pwMS) presenting Coronavirus Disease 2019, as informed at REDONE-COVID19 Brazilian Registry.

TRANSMISSION & PREVENTION

DEEP VEIN THROMBOSIS (DVT) OCCURRING SHORTLY AFTER THE SECOND DOSE OF MRNA SARS-COV-2 VACCINE

Carli G, Nichele I, Ruggeri M, Barra S, Tosetto A.. Intern Emerg Med. 2021 Mar 9. doi: 10.1007/s11739-021-02685-0. Online ahead of print.
Level of Evidence: 5 - Case Report

BLUF

Hematologists from Bortolo Hospital in Vicenza, Italy present the case of an otherwise healthy 66-year-old woman who developed deep vein thrombosis (DVT) involving the right peroneal vein and extending up to the popliteal vein after receiving the second dose of a mRNA Covid-19 vaccine (BNT162b2, Comirnaty, Pfizer/BioNTech)(summary). Symptoms resolved after one week of apixaban treatment. Authors suggest further investigation into DVT as a possible vaccine side-effect.

SUMMARY

The woman received the first dose of the vaccine subcutaneously on January 4th, 2021, without any reported clinical problem. She received the second dose on January 25th, and 24 hours later she developed persistent fever with chills, fatigue, malaise, and muscle pain. Two days after developing those symptoms, she had persistent pain and was unable to walk - this is when she was diagnosed with DVT. Physical examination was normal apart from mild edema in the right calf. Thrombophilia workup was negative, apart from a heterozygous FV Leiden mutation.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

THE PRICE OF SUCCESS-HOW TO EVALUATE COVID-19 VACCINES WHEN THEY'RE AVAILABLE OUTSIDE OF CLINICAL TRIALS

Rubin R.. JAMA. 2021 Mar 9;325(10):918-921. doi: 10.1001/jama.2021.0641.
Level of Evidence: 5 - Expert Opinion

BLUF

In this perspective article, the JAMA affiliated author compares the current ethical dilemmas against practicality and validity regarding COVID-19 vaccine trials, given the unprecedented pandemic altering the pervious normal course of pharmaceutical trials. Difficulty lies in the decision for un-blinding current trials so that those given placebo doses have the chance to get vaccinated, reducing their risk of contracting SARS-CoV-2 but decreasing study validity in the long term. Some researchers have looked into alternative protocols for future trials to avoid such issues, suggesting to get rid of placebos all together and relying on observational data comparing groups vaccinated at different times.

PREVENTION IN THE COMMUNITY

EFFECTIVENESS OF MASK WEARING TO CONTROL COMMUNITY SPREAD OF SARS-COV-2

Brooks JT, Butler JC.. JAMA. 2021 Mar 9;325(10):998-999. doi: 10.1001/jama.2021.1505.
Level of Evidence: 5 - Review / Literature Review

BLUF

A review article conducted by researchers from the Center for Disease Control and Prevention in Atlanta, Georgia discuss how widespread community masking has been shown in multiple studies to limit exhalation and inhalation of infectious virus, provide a barrier to large respiratory droplets to protect uninfected mask wearers, and is associated with decreased rates of infection and death from COVID-19 infection (See Table). Multilayer cloth masks have been shown to be more effective than single layer masks in some studies, however the prevalence of mask wearing outweighs the mask type. It is especially crucial

to emphasize the importance of widespread masking and prevention efforts, especially with rising prevalence of more transmissible SARS-CoV-2 variants, until national vaccination administration reaches efficacious levels.

FIGURES

Table. Studies of the Effect of Mask Wearing on SARS-CoV-2 Infection Risk*

Source	Location	Population studied	Intervention	Outcome
Hendrix et al	Hair salon in Springfield, Missouri	139 Patrons at a salon with 2 infected and symptomatic stylists	Universal mask wearing in salon (by local ordinance and company policy)	No COVID-19 infections among 67 patrons who were available for follow-up
Payne et al	USS Theodore Roosevelt, Guam	382 US Navy service members	Self-reported mask wearing	Mask wearing reduced risk of infection by 70% (unadjusted odds ratio, 0.30 [95% CI, 0.17-0.52])
Wang Y et al	Households in Beijing, China	124 Households of diagnosed cases comprising 335 people	Self-reported mask wearing by index cases or ≥1 household member prior to index case's diagnosis	Mask wearing reduced risk of secondary infection by 79% (adjusted odds ratio, 0.21 [95% CI, 0.06-0.79])
Doung-ngern et al	Bangkok, Thailand	839 Close contacts of 211 index cases	Self-reported mask wearing by contact at time of high-risk exposure to case	Always having used a mask reduced infection risk by 77% (adjusted odds ratio, 0.23 [95% CI, 0.09-0.60])
Gallaway et al	Arizona	State population	Mandatory mask wearing in public	Temporal association between institution of mask wearing policy and subsequent decline in new diagnoses
Rader et al	US	374 021 Persons who completed web-based surveys	Self-reported mask wearing in grocery stores and in the homes of family or friends	A 10% increase in mask wearing tripled the likelihood of stopping community transmission (adjusted odds ratio, 3.53 [95% CI, 2.03-6.43])
Wang X et al	Boston, Massachusetts	9850 Health care workers (HCWs)	Universal masking of HCWs and patients in the Mass General Brigham health care system	Estimated weekly decline in new diagnoses among HCWs of 3.4% after full implementation of the mask wearing policy
Mitze et al	Jena (Thuringia), Germany	City population aged ≥15 y	Mandatory mask wearing in public spaces (eg, public transport, shops)	Estimated daily decline in new diagnoses of 1.32% after implementation of the mask mandate
Van Dyke et al	Kansas	State population	Mandatory mask wearing in public spaces	Estimated case rate per 100 000 persons decreased by 0.08 in counties with mask mandates but increased by 0.11 in those without
Lyu and Wehby	15 US states and Washington, DC	State populations	Mandatory mask wearing in public	Estimated overall initial daily decline in new diagnoses of 0.9% grew to 2.0% at 21 days following mandates
Karaivanov et al	Canada	Country population	Mandatory mask wearing indoors	Estimated weekly 25%-40% decline in new diagnoses following mask mandates

Table. Studies of the Effect of Mask Wearing on SARS-CoV-2 Infection Risk

ENDOCRINOLOGY

THYROID DYSFUNCTION IN RELATION TO IMMUNE PROFILE, DISEASE STATUS, AND OUTCOME IN 191 PATIENTS WITH COVID-19

Lui DTW, Lee CH, Chow WS, Lee ACH, Tam AR, Fong CHY, Law CY, Leung EKH, To KKW, Tan KCB, Woo YC, Lam CW, Hung IFN, Lam KSL.. J Clin Endocrinol Metab. 2021 Jan 23;106(2):e926-e935. doi: 10.1210/clinem/dgaa813.
Level of Evidence: 3 - Local non-random sample

BLUF

Investigators from the University of Hong Kong and Queen Mary Hospital, Hong Kong, China conducted a prospective cohort study of 191 SARS-CoV-2 positive patients with no previous thyroid dysfunction presenting to Queen Mary Hospital between July 21 - August 21, 2020, in order to determine thyroid function in the setting of mild to moderate COVID-19. The results reveled 13.1% had abnormal thyroid function tests (TSH, free T3, or free T4), with systemic inflammation more associated with lower free T3 levels, suggesting the need for thyroid evaluation and surveillance in the setting of COVID-19.

SUMMARY

Along with levels of TSH, free T4, and free T3, the study researchers also analyzed anti-thyroglobulin antibody (anti-Tg) titer, anti-thyroid peroxidase antibody (anti-TPO) titer, and AntiTSH receptor antibody (anti-TSHR) titer all through ELISA. Patient demographics, comorbidities, basic hematological values, serum chemistries, CRP, ESR, viral Ct values, and chest x-rays were also analyzed. The results reviled a statistically significant correlation of lower free T3 values with increased inflammation markers, such as CRP and ESR (Table 3), and prolonged hospital stay (>14 days). There were also 7 patients that had lab values suggestive of autoimmune thyroiditis, with only one thought to have Graves disease as preexisting and undiagnosed conditions prior to SARS-CoV-2 infection, highlighting the importance of thyroid observation in COVID-19 patients.

ABSTRACT

OBJECTIVE: SARS-CoV-2-related thyroiditis is increasingly recognized. The role of thyroid autoimmunity and SARS-CoV-2 viral load in SARS-CoV-2-related thyroid dysfunction is unclear. We evaluated the thyroid function of a cohort of COVID-19 patients, in relation to their clinical features, biochemical, immunological and inflammatory markers. METHODS: Consecutive adult patients, without known thyroid disorders, admitted to Queen Mary Hospital for COVID-19 from 21 July to 21 August, 2020 were included. Serum levels of thyroid-stimulating hormone (TSH), free thyroxine, free triiodothyronine (fT3) and anti-thyroid antibodies were measured on admission. RESULTS: Among 191 patients with COVID-19 (mean age 53.5 +- 17.2 years; 51.8% male), 84.3% were mild, 12.6% were moderate, and 3.1% were severe. 13.1% had abnormal thyroid function. Ten patients had isolated low TSH, suggestive of subclinical thyrotoxicosis due to thyroiditis, although the contribution of autoimmunity was likely in two of them. Autoimmune thyroiditis probably also contributed to subclinical hypothyroidism in another patient. Ten patients had isolated low fT3, likely representing non-thyroidal illness syndrome. Lower SARS-Cov-2 PCR cycle threshold values and elevated C-reactive protein were independently associated with occurrence of low TSH (p=0.030) and low fT3 (p=0.007) respectively. A decreasing trend of fT3 with increasing COVID-19 severity (p=0.032) was found. Patients with low fT3 had more adverse COVID-19-related outcomes. CONCLUSION: Around 15% of patients with mild to moderate COVID-19 had thyroid dysfunction. There may be a direct effect of SARS-CoV-2 on thyroid function, potentially leading to exacerbation of pre-existing autoimmune thyroid disease. Low fT3, associated with systemic inflammation, may have a prognostic significance.

FIGURES

Table 3. Comparison between patients with normal fT3 and low fT3

Variables	Normal fT3 (n=166)	Low fT3 (n=12)	P-value
TSH (mIU/L)	1.20 (0.81–1.70)	0.92 (0.55–1.50)	0.133
fT4 (pmol/L)	18.3 ± 2.3	16.1 ± 3.1	**0.002**
fT3 (pmol/L)	4.21 ± 0.63	2.79 ± 0.29	**<0.001**
fT3/fT4 ratio	0.232 ± 0.041	0.178 ± 0.034	**<0.001**
Age (years)	52.7 ± 17.3	60.4 ± 13.5	0.132
Male	85 (51.2%)	8 (66.7%)	0.300
COVID-19 severity			0.434
Mild	141 (84.9%)	9 (75.0%)	
Moderate	20 (12.0%)	2 (16.7%)	
Severe	5 (3.0%)	1 (8.3%)	
Symptomatic	124 (74.7%)	11 (91.7%)	0.298
Baseline oxygen saturation (%)	98 (97–99)	98 (95–98)	0.419
Oxygen required on admission (%)	5 (3.0)	1 (8.3)	0.346
Fever	78 (47.0%)	10 (83.3%)	**0.015**
Anti-Tg/TPO positivity	36 (21.7%)	3 (25.0%)	0.730
Creatinine (umol/L)	71 (56–84)	84 (70–93)	0.065
AST (U/L)	26 (21–38)	32 (26–53)	**0.042**
Creatine kinase (U/L)	93 (65–137)	143 (97–168)	0.055
Lactate dehydrogenase (U/L)	223 (185–262)	299 (257–333)	**<0.001**
CRP (mg/dL)	0.43 (0.31–1.51)	6.29 (1.93–9.48)	**<0.001**
ESR (mm/hr)	34.0 (20.0–53.5)	73.0 (39.3–97.0)	**0.005**
SARS-CoV-2 PCR Ct value	26.03 ± 7.04	25.12 ± 4.69	0.542

Data are presented as mean±SD, median (IQR), number (%) as appropriate.

Abbreviations: TSH, thyroid-stimulating hormone; fT4, free thyroxine; fT3, free triiodothyronine; anti-TPO, anti-thyroid peroxidase; anti-Tg, anti-thyroglobulin; AST, aspartate aminotransferase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Ct, cycle threshold.

Interval from symptom onset to thyroid function testing, and comorbidities, were comparable between the two groups.

Accepted Manuscript

Table 3. Comparison between patients with normal fT3 and low fT3.

PSYCHIATRY

PREVALENCE AND CORRELATES OF CHRONIC FATIGUE SYNDROME AND POST-TRAUMATIC STRESS DISORDER AFTER THE OUTBREAK OF THE COVID-19

Simani L, Ramezani M, Darazam IA, Sagharichi M, Aalipour MA, Ghorbani F, Pakdaman H.. J Neurovirol. 2021 Feb 2. doi: 10.1007/s13365-021-00949-1. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A group of physicians from Tehran, Iran assessed the presence of chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and post-traumatic stress disorder (PTSD) among 120 patients diagnosed with COVID-19 between February 20 - April 20, 2020 over a 6 month follow up period, using the Fukuda guidelines for CFS and the DSM-5/PCL-5 checklist for PTSD. They found that the prevalence of fatigue symptoms was 17.5% while the prevalence rate of PTSD was 5.8%, and 10% screened positive for chronic idiopathic fatigue (CIF), 5% for CFS-like with insufficient fatigue syndrome (CFSWIFS), and 2.5% for CFS (Figure 2), highlighting the need for awareness of potential psychiatric complications of COVID-19.

SUMMARY

The study also found that there was no association between CFS and PTSD, gender, co-morbidities, and chloroquine phosphate administration. They also found that the prevalence of CFS was similar between patients with COVID and those without COVID, and COVID patients who suffered from PTSD were not at increased risk of CFS.

ABSTRACT

As the SARS-COV-2 becomes a global pandemic, many researchers have a concern about the long COVID-19 complications. Chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) is a persistent, debilitating, and unexplained fatigue disorder. We investigated psychological morbidities such as CFS and post-traumatic stress disorder (PTSD) among survivors of COVID-19 over 6 months. All COVID-19 survivors from the university-affiliated hospital of Tehran, Iran, were assessed 6 months after infection onset by a previously validated questionnaire based on the Fukuda guidelines for CFS/EM and DSM-5 Checklist for PTSD (The Post-traumatic Stress Disorder Checklist for DSM-5 or PCL-5) to determine the presence of stress disorder and chronic fatigue problems. A total of 120 patients were enrolled. The prevalence rate of fatigue symptoms was 17.5%. Twelve (10%) screened positive for chronic idiopathic fatigue (CIF), 6 (5%) for CFS-like with insufficient fatigue syndrome (CFSWIFS), and 3 (2.5%) for CFS. The mean total scores in PCL-5 were 9.27 +- 10.76 (range:0-44), and the prevalence rate of PTSD was 5.8%. There was no significant association after adjusting between CFS and PTSD, gender, comorbidities, and chloroquine phosphate administration. The obtained data revealed the prevalence of CFS among patients with COVID-19, which is almost similar to CFS prevalence in the general population. Moreover, PTSD in patients with COVID-19 is not associated with the increased risk of CFS. Our study suggested that medical institutions should pay attention to the psychological consequences of the COVID-19 outbreak.

FIGURES

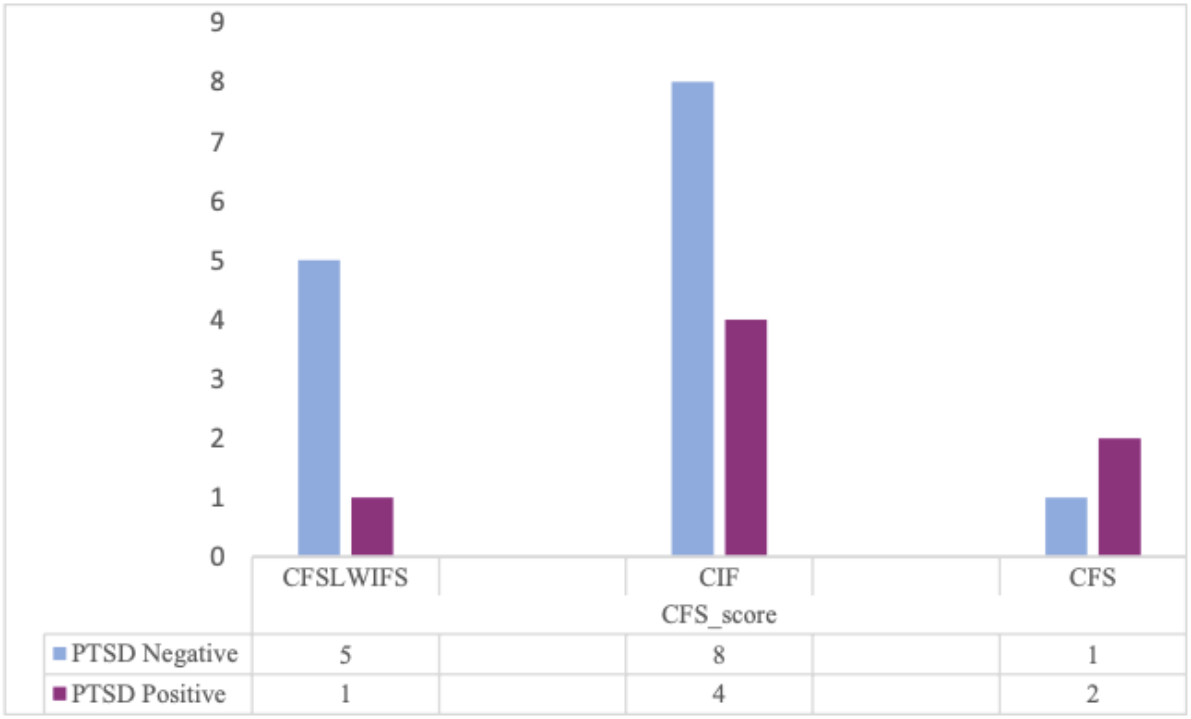

Figure 2. Number of participants experiencing PTSD and CFS

PROTEOMIC APPROACHES TO STUDY SARS-COV-2 BIOLOGY AND COVID-19 PATHOLOGY

Haas P, Muralidharan M, Krogan NJ, Kaake RM, Hüttenhain R.. J Proteome Res. 2021 Jan 19. doi: 10.1021/acs.jproteome.0c00764. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Researchers from various institutions in San Francisco and New York detail the contribution that current proteomic technology provides to the understanding of SARS-CoV-2 with regards to the structure, replication, modifications, biomarkers, and possible treatments (Figure 1). Utilization of proteomic technology is not only beneficial during the current pandemic, but can also be used in settings of other disease states.

SUMMARY

The current proteomic technology applications and contributions in the setting of SARS-CoV-2 include:

1. Understanding the dynamic structural changes the virus undergoes by overcoming limitations of traditional structural techniques with mass spectrometry based proteomic research.
2. Mapping the cellular machinery for viral replication and host interaction important for infection and transmission
3. Post-translational modifications that induce signaling pathways important for pathogenies
4. Identification of biomarkers, diagnostics, and pharmacology developments to help treat those with severe disease

The authors suggest these large-scale technology based proteomic resources can be beneficial not only to help fight the current pandemic, but also contribute to the understanding and treatment of additional viral diseases with high morbidity and mortality such as HIV.

ABSTRACT

The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19), was declared a pandemic infection in March 2020. As of December 2020, two COVID-19 vaccines have been authorized for emergency use by the U.S. Food and Drug Administration, but there are no effective drugs to treat COVID-19, and pandemic mitigation efforts like physical distancing have had acute social and economic consequences. In this perspective, we discuss how the proteomic research community can leverage technologies and expertise to address the pandemic by investigating four key areas of study in SARS-CoV-2 biology. Specifically, we discuss how (1) mass spectrometry-based structural techniques can overcome limitations and complement traditional structural approaches to inform the dynamic structure of SARS-CoV-2 proteins, complexes, and virions; (2) virus-host protein-protein interaction mapping can identify the cellular machinery required for SARS-CoV-2 replication; (3) global protein abundance and post-translational modification profiling can characterize signaling pathways that are rewired during infection; and (4) proteomic technologies can aid in biomarker identification, diagnostics, and drug development in order to monitor COVID-19 pathology and investigate treatment strategies. Systems-level high-throughput capabilities of proteomic technologies can yield important insights into SARS-CoV-2 biology that are urgently needed during the pandemic, and more broadly, can inform coronavirus virology and host biology.

FIGURES

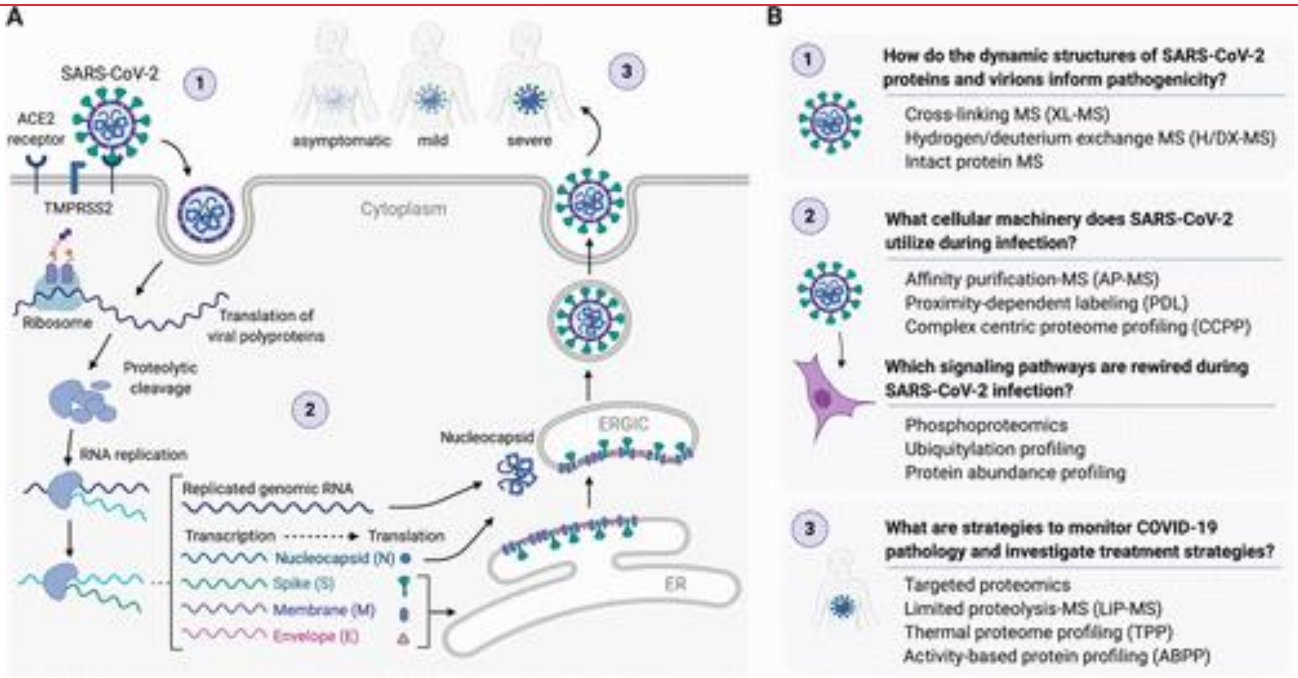

Figure 1. (A) SARS-CoV-2 life cycle. (B) Open questions to further our understanding of SARS-CoV-2 biology and proteomic techniques that can be leveraged to address these questions.

DEVELOPMENTS IN DIAGNOSTICS

COVID-19 "LIQUID BIOPSY" COULD OFFER MONITORING, PROGNOSTIC TOOL

Abbasi J.. JAMA. 2021 Mar 9;325(10):924. doi: 10.1001/jama.2021.2496.
Level of Evidence: 5 - Review / Literature Review

BLUF

An opinion piece penned by a health and science journalist briefly discusses recent research into using a “liquid biopsy” which is a cell-free DNA (cfDNA) profiling technique that triages COVID-19 patients with its ability to detect internal organ injury. According to the author, the research shows that the cfDNA profiles correlate with World Health Organization clinical progression scores of COVID-19 patients, the implication being that using cfDNA profiling could help help assess severity of disease and determine the likely progression of severity in COVID-19 patients.

SUMMARY

- Cornell University researchers are developing a “liquid biopsy” which can detect and quantify injury to organs due to COVID-19 infection via profiling epigenetic changes in cell-free DNA (cfDNA) from dead cells
- These profiles are specific to cells, tissues, and organs
- A recent study showed that cell-free DNA in the lung, liver, kidney and erythroblasts were increased in COVID-19 patients

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