The Daily COVID-19 Literature Surveillance Summary

January 26, 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

- Immune thrombocytopenia was found in a 22-year-old post COIVD-19 vaccine: A hematologist from Advocate Aurora Health in Wisconsin presents the case of a 22-year-old male with no history of bleeding or autoimmune disease who presented with widespread petechiae and gum bleeding 3 days post-Pfizer-BioNTech vaccine. The patient had severe thrombocytopenia (2x10^9/L) and was given a platelet transfusion on admission followed by intravenous immunoglobulin and dexamethasone. He was discharged on day 6 with a platelet count of 28 x10^9/L, which normalized by day 11 (173x10^9/L) . Authors suggest this patient's autoimmune thrombocytopenia (ITP) may have been induced by vaccine administration, but recognize ITP is common and further studies are needed to better evaluate this potential side effect.

Silver Linings

- Stillbirths were not found to be correlated with the COVID-19 pandemic in England. Public health researchers from England compared data from a single London hospital with national and regional hospitalization data (annual Hospital Episode Statistics (HES) data, monthly data available as Secondary Uses Service and data from the Office for National Statistics (ONS) civil deaths registrations for stillbirths) to investigate whether the rate of stillbirths had increased during the COVID-19 pandemic. They found there were 2,825 stillbirths between April 1, 2019 and June 30, 2020, with the highest proportion of stillbirth deliveries reported in London (145/26 760; 0.54% [95% CI, 0.46%-0.64%]). Nationally, no evidence of any increase above baseline during the pandemic period was found. For individual regions, there was no significant difference between the rate of stillbirth deliveries between the lockdown period and the same period the year prior. They suggest that while it is important to continue monitoring pregnancy outcomes as the pandemic continues to unfold, these findings are reassuring in light of concerns over access to prenatal services for pregnant patients during the pandemic.

TABLE OF CONTENTS

EPIDEMIOLOGY

SEROPREVALENCE OF ANTI-SARS-COV-2 IGG ANTIBODIES IN CHILDREN WITH HOUSEHOLD EXPOSURE TO ADULTS WITH COVID-19: PRELIMINARY FINDINGS

Buonsenso D, Valentini P, De Rose C, Pata D, Sinatti D, Speziale D, Ricci R, Carfì A, Landi F, Ferrari V, De Maio F, Palucci I, Sanguinetti M, Sali M; Gemelli Against COVID-19 Post-Acute Care Study Group.. Pediatr Pulmonol. 2021 Jan 20. doi: 10.1002/ppul.25280. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

The Gemelli Against COVID-19 Post-Acute Care Study Group from Rome, Italy evaluated the seroprevalence of anti-SARS-CoV-2 IgG among 80 household contacts (53 children, 27 adults) from 30 families with documented COVID-19 index cases (time period unclear). They found 52.3% of children (28/53) and 59.3% of adults (16/27) had anti-SARS-CoV-2 IgG (p>0.05), with children aged 5 or younger equally likely to have antibodies as children older than 5 (7/14 [50%] vs. 21/39 [53.8%], p>0.05)(Figure 1). Given the similar seroprevalence between children and adults, authors suggest children are equally susceptible to COVID-19 as adults and emphasize the importance of public health measures designed to mitigate the spread of infection among children.

ABSTRACT

Weather and the susceptibility of children to SARS-CoV-2 infection is still a debated question and currently a hot topic, particularly in view of important decisions regarding opening schools. Therefore, we performed this prospective analysis of anti-SARS-CoV-2 IgG antibodies in children with known household exposure to SARS-CoV-2 and compared their IgG status with the other adults exposed to the index case in the same household. 30 families with a documented COVID-19 index case were included. A total of 44 out of 80 household contacts (55%) of index patients had anti SARS-CoV-2 IgG antibodies. In particular, 16/27 (59,3%) adult partners had IgG antibodies compared with 28/53 (52,3%) of pediatric contacts (P > 0.05). Among the pediatric population, children >= 5 years of age had a similar probability of having SARS-CoV-2 IgG antibodies (21/39, 53.8%) compared to those < 5 years old (7/14, 50%) (P > 0.05). Adult partners and children also had a similar probability of having SARS-CoV-2 IgG antibodies. Interestingly, 10/28 (35.7%) of children and 5/27 (18.5%) of adults with SARS-CoV-2 IgG antibodies were previously diagnosed as COVID-19 cases. Our study shows evidence of a high rate of IgG antibodies in children exposed to SARS-CoV-2. This report has public health implications, highlighting the need to establish appropriate guidelines for school openings and other social activities related to childhood. This article is protected by copyright. All rights reserved.

FIGURES

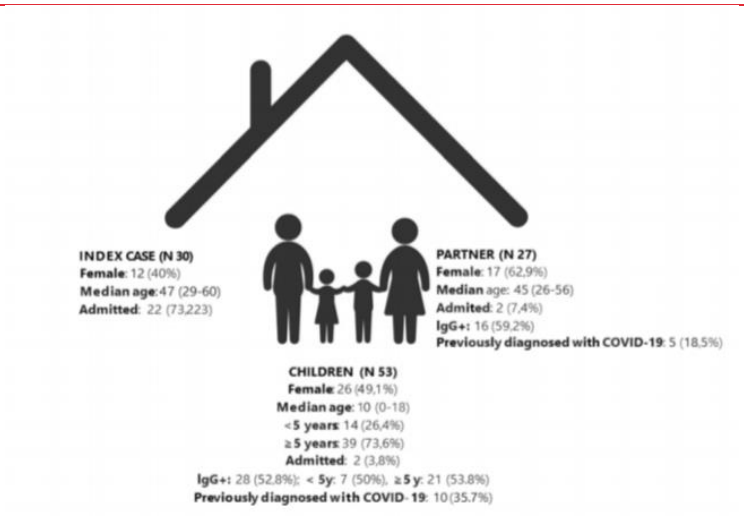

Figure 1: "Main epidemiological and microbiological characteristics of the study cohort".

COMPREHENSIVE ANALYSIS OF GENOMIC DIVERSITY OF SARS-COV-2 IN DIFFERENT GEOGRAPHIC REGIONS OF INDIA: AN ENDEAVOUR TO CLASSIFY INDIAN SARS-COV-2 STRAINS ON THE BASIS OF CO-EXISTING MUTATIONS

Sarkar R, Mitra S, Chandra P, Saha P, Banerjee A, Dutta S, Chawla-Sarkar M.. Arch Virol. 2021 Jan 19. doi: 10.1007/s00705-020-04911-0. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Virologists from the National Institute of Cholera and Enteric Diseases in West Bengal, India conducted a genomic analysis of 837 Indian SARS-CoV-2 samples collected between March and August 2020. They found 33 different mutations (18 unique to India), which they classified into 22 groups (Figure 1). Three clades were most prominent and had clear geographic distributions: the A2a clade (71.24% of samples) in East, West and Central India; both A3 (23.29%) and A2a in South and North India; and B (5.36%) in East and West India (Figure 3). Authors suggest these data provide important insight into the divergent evolution and strain distribution of SARS-CoV-2 strains that will inform vaccine and treatment development.

ABSTRACT

Accumulation of mutations within the genome is the primary driving force in viral evolution within an endemic setting. This inherent feature often leads to altered virulence, infectivity and transmissibility, and antigenic shifts to escape host immunity, which might compromise the efficacy of vaccines and antiviral drugs. Therefore, we carried out a genome-wide analysis of circulating SARS-CoV-2 strains to detect the emergence of novel co-existing mutations and trace their geographical distribution within India. Comprehensive analysis of whole genome sequences of 837 Indian SARS-CoV-2 strains revealed the occurrence of 33 different mutations, 18 of which were unique to India. Novel mutations were observed in the S glycoprotein (6/33), NSP3 (5/33), RdRp/NSP12 (4/33), NSP2 (2/33), and N (1/33). Non-synonymous mutations were found to be 3.07 times more prevalent than synonymous mutations. We classified the Indian isolates into 22 groups based on their co-existing mutations. Phylogenetic analysis revealed that the representative strains of each group were divided into various sub-clades within their respective clades, based on the presence of unique co-existing mutations. The A2a clade was found to be dominant in India (71.34%), followed by A3 (23.29%) and B (5.36%), but a heterogeneous distribution was observed among various geographical regions. The A2a clade was highly predominant in East India, Western India, and Central India, whereas the A2a and A3 clades were nearly equal in prevalence in South and North India. This study highlights the divergent evolution of SARS-CoV-2 strains and co-circulation of multiple clades in India. Monitoring of the emerging mutations will pave the way for vaccine formulation and the design of antiviral drugs.

FIGURES

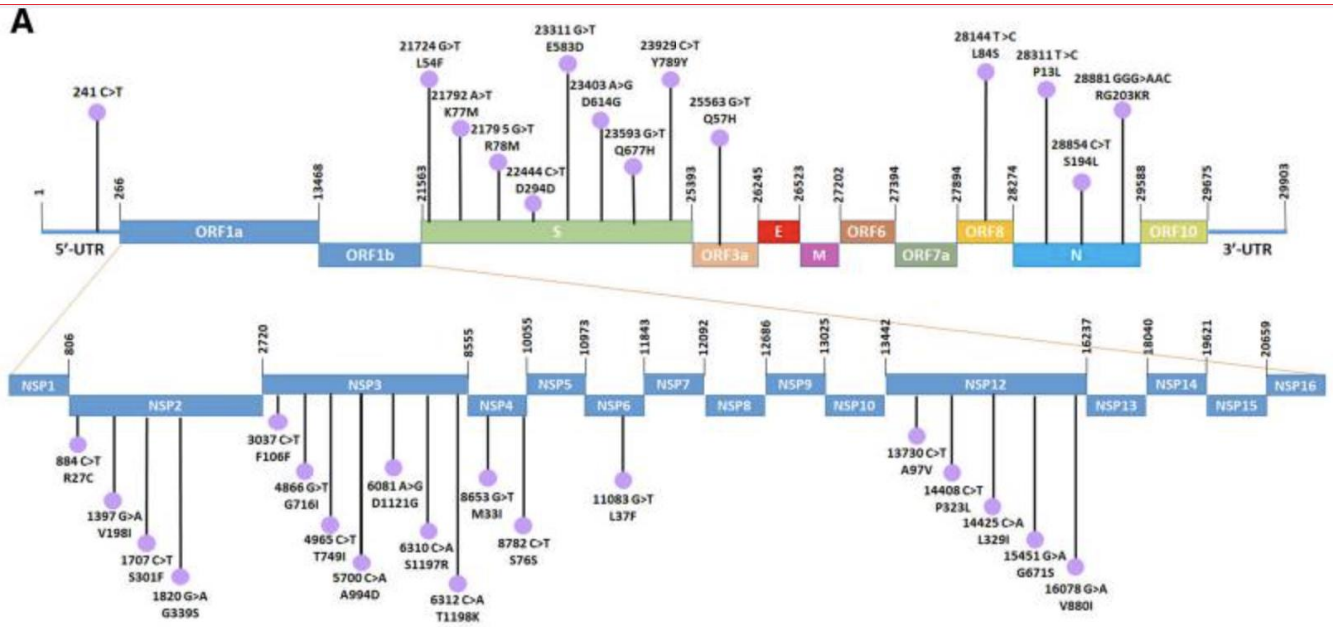

Figure 1A: Pictorial representation of 33 different mutations (at both the nucleotide and amino acid levels) found in different regions (coding and non-coding regions) of the SARS-CoV-2 genome.

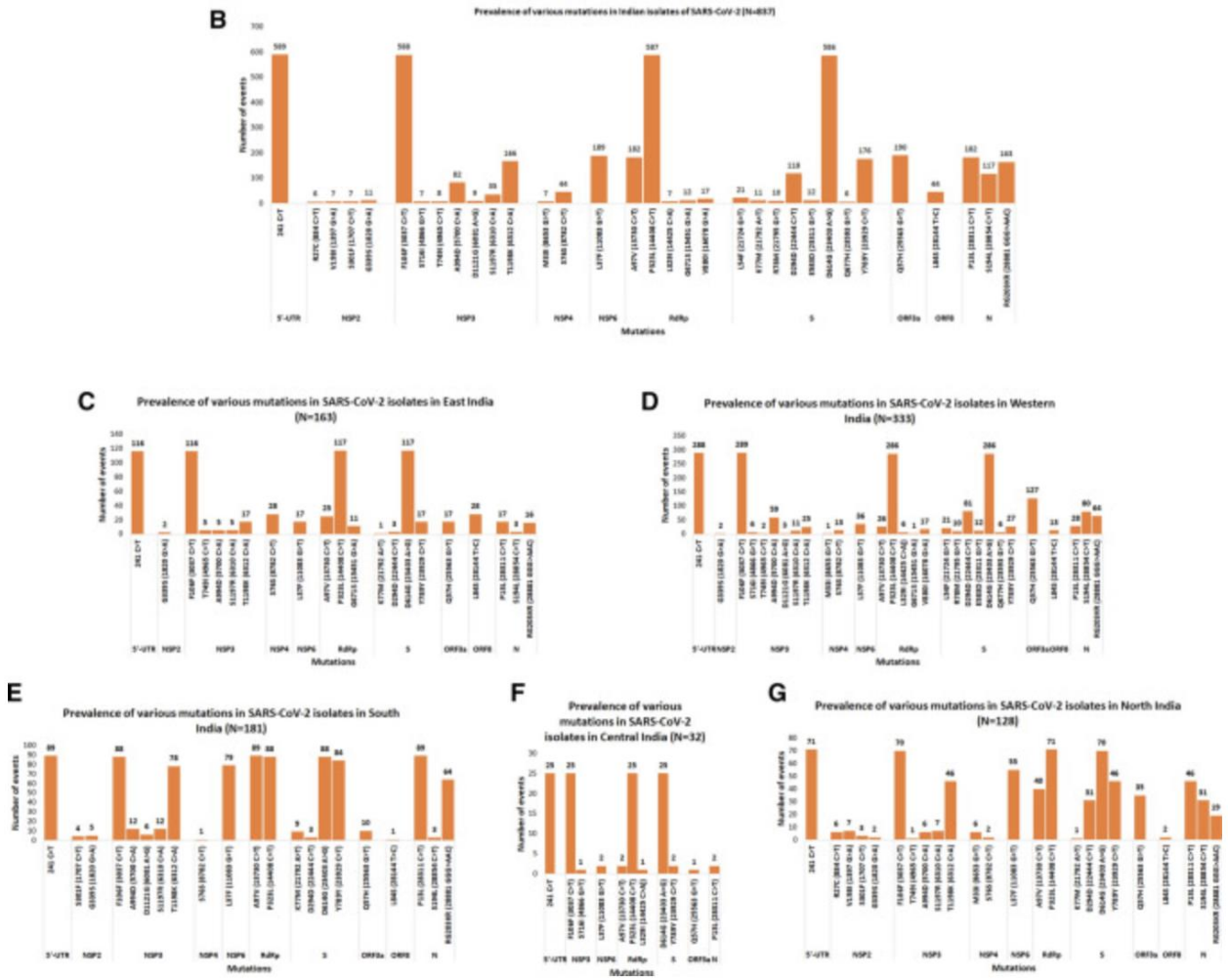

Figure 1(B) Relative frequencies of 33 different mutations in India. (C-G) Identification of various mutations present in the genome of SARS-CoV-2 circulating in different geographic regions in India. Relative frequencies of various mutations in (C) East India, (D) Western India, (E) South India, (F) Central India and (G) North India

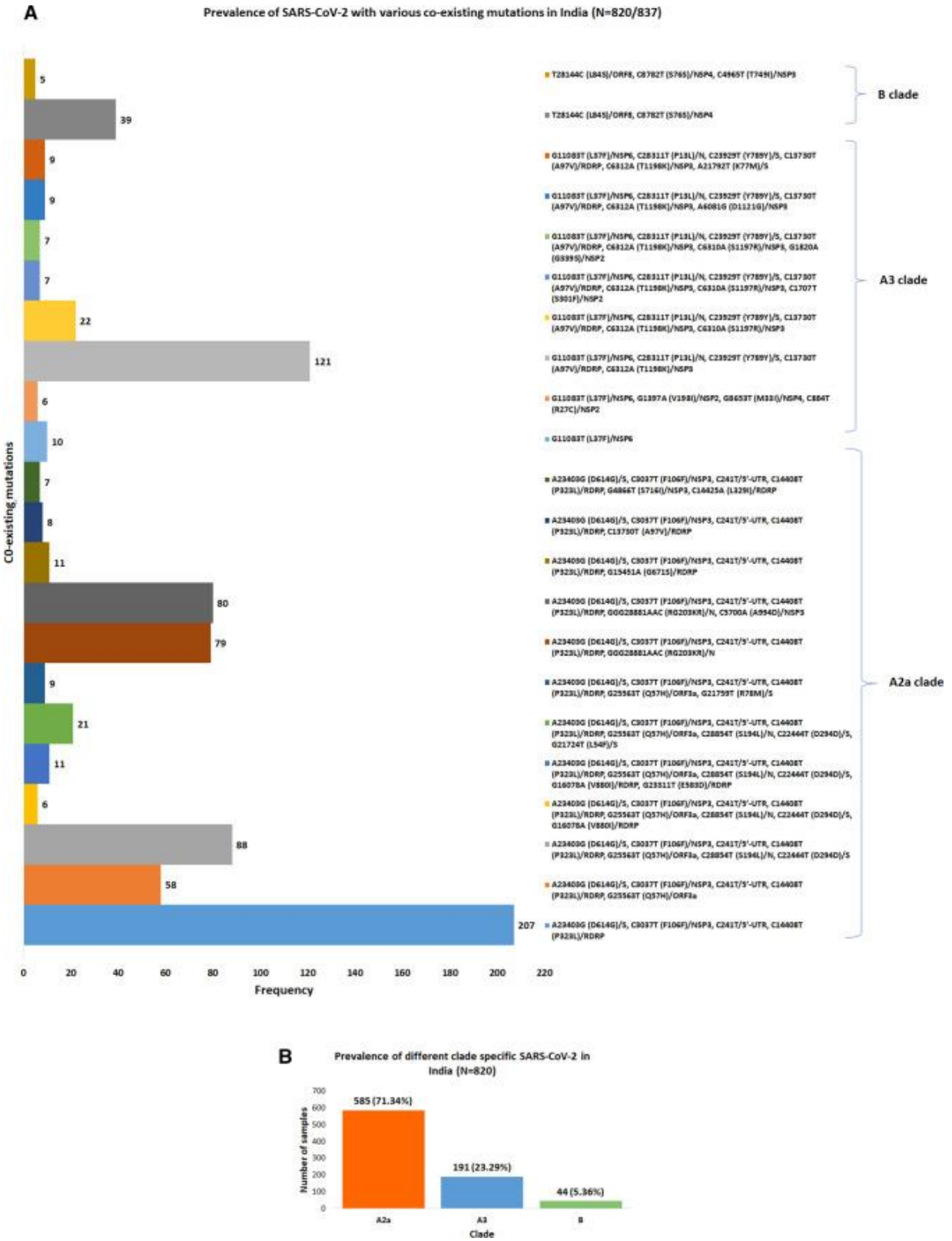

Figure 3: Grouping of SARS-CoV-2 strains on the basis of co-existing mutations and analysis of their prevalence. (A) Analysis of mutations revealed the presence of the clades (A2a, A3 and B) of SARS-CoV-2 strains in India. The accumulation of novel mutations in addition to clade-specific variations allowed us to classify A2a clade strains into 12 groups, A3 clade strains into eight groups, and B clade strains into two groups. We also show the number of strains belonging to each group. (B) Prevalence of three clade-specific mutations in India. The A2a clade (71.34%) was found to be the most prevalent in India, followed by A3 (23.29%) and B (5.36%).

COVID-19: DISEASE, OR NO DISEASE? - THAT IS THE QUESTION. IT'S THE DOSE STUPID!

Sehrawat S, Rouse BT.. Microbes Infect. 2021 Jan 12:104779. doi: 10.1016/j.micinf.2021.104779. Online ahead of print.
Level of Evidence: 5 - Opinion

BLUF

Immunologists from the Indian Institute of Science Education in Punjab and the University of Tennessee argue that the infectious load of SARS-CoV-2 is correlated to symptomatic severity (Figure 1) and suggest disease course severity can be minimized by lowering the initial dose of viral exposure. They recommend social distancing, neutralizing monoclonal antibodies, BCG vaccination, and infusion of S-type lectins as possible methods to improve the chances of a milder disease course.

ABSTRACT

The COVID-19 pandemic has raised many issues not the least of which is the reason for its high variability in consequences to the infected person. In this opinion letter, we advocate that the dose and presentation of the infecting virus is a major factor that affects whether the outcome is subclinical, tissue damaging or even lethal following infection. We briefly describe the known effects of virus dose on the course COVID-19 and discuss practical maneuvers as well as largely untested procedures that can raise the threshold dose needed to break through barriers of resistance.

FIGURES

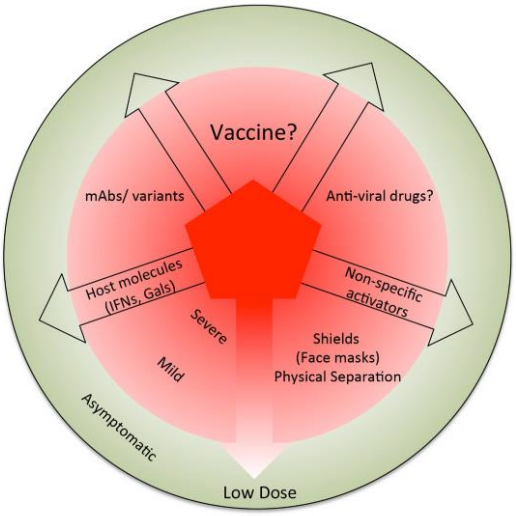

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Fig 1. **A cartoon demonstrating the influence of dose of infection on COVID-19 induced disease and some potential maneuvers to limit the infecting dose.** Depending on the infecting dose the spectrum of COVID-19 disease ranges from asymptomatic to mild and severe disease. While the mild infections resolve with favorable outcome severe disease invariably require intensive care and some individuals eventually succumb to the infection. Interventions such as shielding devices and social behavior, promotion of innate immune function, infusion of host derived or recombinant molecules such as type I IFNs, galectins, high affinity monoclonal antibodies or their variants as well as effective anti-viral drugs could reduce the initial dose of virus infection. Question mark represents uncertain efficacy of currently used drugs or a lack of vaccines.

Fig 1. A cartoon demonstrating the influence of dose of infection on COVID-19 induced disease and some potential maneuvers to limit the infecting dose. Depending on the infecting dose the spectrum of COVID-19 disease ranges from asymptomatic to mild and severe disease. While the mild infections resolve with favorable outcome severe disease invariably require intensive care and some individuals eventually succumb to the infection. Interventions such as shielding devices and social behavior, promotion of innate immune function, infusion of host derived or recombinant molecules such as type I IFNs, galectins, high affinity monoclonal antibodies or their variants as well as effective anti-viral drugs could reduce the initial dose of virus infection. Question mark represents uncertain efficacy of currently used drugs or a lack of vaccines.

ADULTS

OLFACTORY FUNCTION AND VIRAL RECOVERY IN COVID-19

Mazzoli M, Molinari MA, Tondelli M, Giovannini G, Ricceri R, Ciolli L, Picchetto L, Meletti S.. Brain Behav. 2021 Jan 19:e02006. doi: 10.1002/brb3.2006. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Italian neurologists assessed the olfactory function of 51 hospitalized COVID-19 patients between April 15-30, 2020 using the Smell Identification subtest of the Sniffin' Sticks Test (SI-SST). They found 45% of patients had objective evidence of olfactory dysfunction by SI-SST, with patients without viral recovery (see summary for definition) more likely to be hyposmic (RR: 10.323, (p<0.0001). Logistic regression showed a positive correlation between SI-SST score (where higher scores correspond to better olfactory function) and odds of viral clearance (p<0.003, OR 2.242)(Figure 1, Table 2). Authors suggest objectively assessed improvement in olfactory function via SI-SST is associated with viral recovery and may be a safe, cost-effective, alternative to RT-PCR for detecting viral clearance in COVID-19 patients.

SUMMARY

"Viral recovery was defined as negative SARS-CoV-2 RT-PCR assays on two consecutive rhinopharyngeal swabs at least 24 hr apart."

ABSTRACT

BACKGROUND: Olfactory and taste disorders were reported in up to 30%-80% of COVID-19 patients. The purpose of our study was to objectively assess smell impairment in COVID-19 patients and to correlate olfactory function with viral recovery. METHODS: Between 15 and 30 April 2020, hospitalized patients with confirmed SARS-CoV-2 infection underwent an objective assessment of olfactory function with the Smell Identification subtest of the Sniffin' Sticks Test (SI-SST). Association between viral recovery and SI-SST performance was evaluated. RESULTS: 51 patients were enrolled (49% males, mean age 66.2 +- 14.6 years). At the time of test administration, 45% were clinically recovered and 39% were virus-free. Objective hyposmia/anosmia was found in 45% of the patients. Subjective olfactory disorders showed no association with the clinical or viral recovery status of the patients. On the contrary, none of the patients with anosmia and the 5% of hyposmic patients at test had viral recovery. The relative risk for hyposmic patients to be still positive at swab test was 10.323 (95% CI 1.483-71.869, p < .0001). Logistic regression analysis showed an independent and significant correlation between viral clearance and SI-SST scores (OR = 2.242; 95% CI 1.322-3.802, p < .003). ROC curve analysis confirmed that a SI-SST > 10.5 predicts viral clearance with 79% sensitivity and 87% specificity (AUC = 0.883). CONCLUSION: Hyposmia is part of COVID-19 symptoms; however, only objectively assessed olfactory function is associated with viral recovery. SI-SST is an easy and safe instrument, and further large multicentric studies should assess its value to predict infection and recovery.

FIGURES

		Subjective hyposmia			Clinical recovery			Viral recovery		
SI-SST performance	Overall sample (*N* = 51)	Present (*N* = 13)	Absent (*N* = 38)	*p*	Present (*N* = 23)	Absent (*N* = 28)	*p*	Present (*N* = 20)	Absent (*N* = 31)	*p*
Mean score (±*SD*)	10.0 (±2.5)	10.8 (±2.5)	9.8 (±2.5)	.226	10.8 (±2.5)	9.4 (±2.5)	.059	12.0 (±2.5)	8.8 (±2.5)	**<.001**
Range	5–15	7–15	5–14		5–15	5–14		9–15	5–14	
Hyposmia, *n* (%)[a]	17 (33%)	4 (31%)	13 (34%)	.820	6 (26%)	11 (39%)	.320	1 (5%)	16 (52%)	**.001**
Functional anosmia, *n* (%)[b]	13 (26%)	3 (23%)	10 (26%)	.817	4 (17%)	9 (32%)	.229	0 (0%)	13 (42%)	**.001**
Combined hyposmia and anosmia, *n* (%)[c]	23 (45%)	5 (38%)	18 (47%)	.577	8 (35%)	15 (54%)	.180	1 (5%)	22 (71%)	**<.001**

Note: Groups were compared using chi-square test for dichotomous variables. Significance: $p < .05$, two-tailed (in bold).

[a]Hyposmia: defined as SI-SST score < 10th percentile, adjusted for age and sex.

[b]Functional anosmia: defined as SI-SST score < 8 points.

[c]Combined hyposmia and anosmia: defined as SI-SST score < 10th percentile, adjusted for age and sex, or SI-SST raw score < 8 points.

Table 2: "Supporting information: SI-SST performance in relation to subjective hyposmia, clinical recovery and viral recovery (group comparison analysis)".

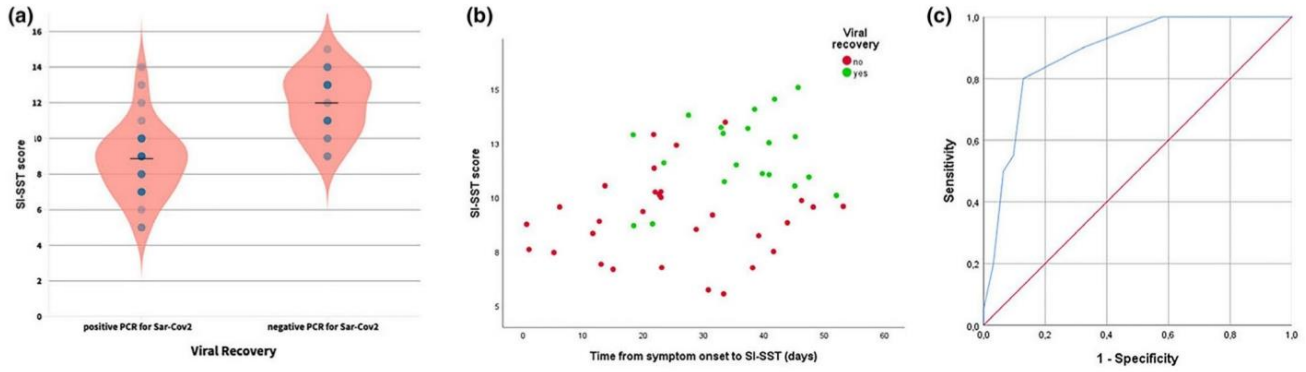


Figure 1: "(a)Violin plots showing SI-SST score distribution in patients with or without viral recovery (negative at 2 consecutive 24 hr apart nasopharyngeal swabs). The black line represents the mean score of each group. (b) Scatterplot showing SI-SST score distribution as a function of time from symptom onset and viral recovery. (c) Receiver operating characteristic (ROC) curve for prediction of viral recovery based on SI-SST score".

AXIAL PRESENTATION OF REACTIVE ARTHRITIS SECONDARY TO COVID-19 INFECTION

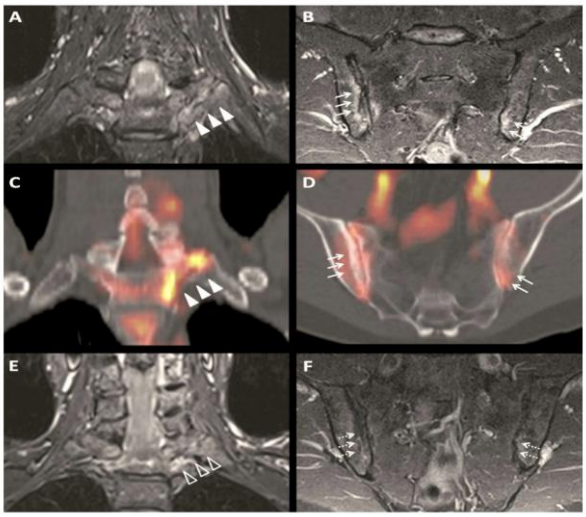
Coath FL, Mackay J, Gaffney JK.. Rheumatology (Oxford). 2021 Jan 20:keab009. doi: 10.1093/rheumatology/keab009. Online ahead of print.
Level of Evidence: 5 - Case report

BLUF

Rheumatologists and radiologists from the United Kingdom present the case of an adult male patient who presented in April 2020 with back pain and a positive SARS-CoV-2 antibody test (no PCR was obtained) after experiencing fever, night sweats, malaise, weight loss, and anosmia in the weeks prior. He was found to have elevated CRP, positive HLA-B27, and joint edema on MRI and PET-CT (Figure 1). Authors suggest the timing of his presentation relative to COVID-19 like symptoms suggest a viral induced reactive arthritis, a possibly novel presentation of SARS-CoV-2 that warrants further exploration.

FIGURES

FIGURE LEGEND:
Figure 1.
Baseline coronal STIR MRI (A) and fused PET-CT (C) images showing left 1st costovertebritis and costotransversitis (arrowheads); Baseline coronal oblique STIR MRI (B) and fused PET-CT (D) images showing bilateral asymmetrical sacroiliitis (arrows); Follow-up MRI demonstrates partial resolution of left 1st costovertebritis and costotransversitis (E; arrowhead outlines) and near complete resolution of sacroiliitis (F; dashed arrows).



EARLY DIFFERENCES IN CYTOKINE PRODUCTION DISTINGUISH SEVERITY OF COVID-19

Tjan LH, Furukawa K, Nagano T, Kiriu T, Nishimura M, Arii J, Hino Y, Iwata S, Nishimura Y, Mori Y.. J Infect Dis. 2021 Jan 7:jiab005. doi: 10.1093/infdis/jiab005. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Virologists and pulmonologists from Kobe University Graduate School of Medicine and the Hyogo Prefectural Kakogawa Medical Center in Japan evaluated the innate immune response of 95 COVID-19 patients with different disease severities (see summary for definition). They found cytokines IL-2 and IL-12 were higher in the acute phase of infection in asymptomatic and mild disease severity compared to those with moderate or severe disease (Figure 1), while cytokines IL-6 and IL-18 levels progressively increased with disease severity (Figure 2). Authors propose IL-12 and IL-2 maintain NK cells and allow the body to stave off viral spread, while cytokines IL-18 and IL-6 may promote severe disease by inducing acute respiratory distress syndrome and plasminogen activator inhibitor-1 in vascular endothelial cells.

SUMMARY

Authors defined disease severity categories as follows:
1. Mild: "COVID-19 patients without evidence of pneumonia or hypoxia"
2. Moderate: "clinical signs of pneumonia" with SpO2 >90% on room air
3. Severe: "clinical signs of pneumonia" with respiratory rate >30 breaths/min, severe respiratory distress, or SpO2 <90% on room air

All SARS-CoV-2 diagnoses were made via PCR of a nasopharyngeal swab sample.

ABSTRACT

Most COVID-19 patients experience asymptomatic/mild symptoms, but some suffer critical symptoms requiring intensive care. It is important to determine how asymptomatic/mild patients react to SARS-CoV-2 infection and suppress virus spread. Innate immunity is important for evasion from the first virus attack, and it may play an important role in the pathogenesis in these patients. We measured serum cytokine levels of 95 COVID-19 patients during the infection's acute phase and are first to report that significantly higher IL-12 and IL-2 levels were induced in asymptomatic/mild patients versus those in the moderate/severe patients, indicating these cytokines' key roles in asymptomatic/mild infections' pathogenesis.

FIGURES

Figure 1

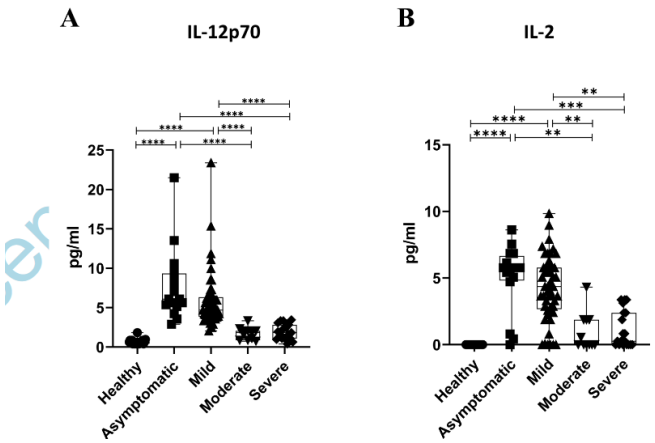


Figure 1. Serum IL-12p70(A) and IL-2(B) levels in asymptomatic and symptomatic (mild, moderate, severe) COVID-19 patients and healthy controls. The box plots shows median (middle line) with the first and third quartiles (boxes), and the whiskers show maximum and minimum values. **p<0.005; ***p<0.001; ****p<0.0001.

Figure 2

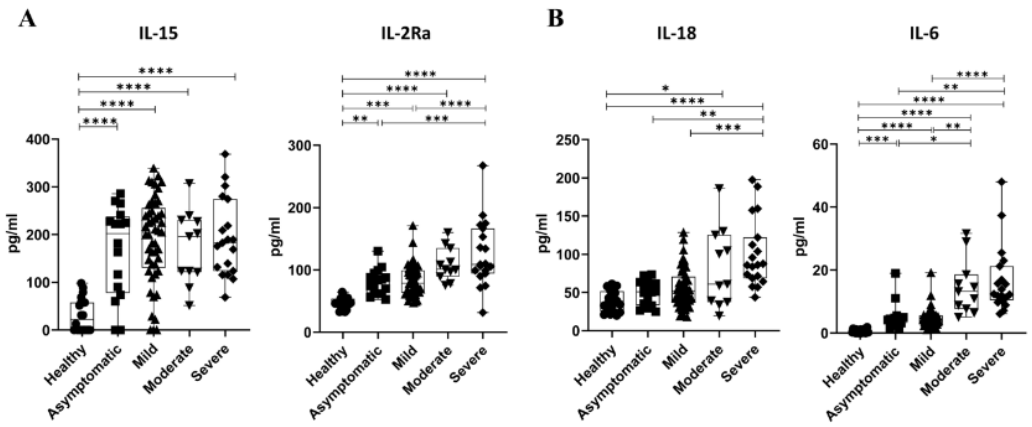


Figure 2. The serum levels of interleukins induced in asymptomatic and symptomatic (mild, moderate, severe) COVID-19 patients.A:The serum levels of interleukin (IL)-15 and IL-2Ra were increased in the COVID-19 patients, but they were not correlated with the disease severities. B:The serum levels of IL-18 and IL-6 were increased in the COVID-19 patients and correlated with the disease severities. The box plots shows median (middle line) with the first and third quartiles (boxes), and the whiskers show maximum and minimum values. *p<0.05; **p<0.005; ***p<0.001; ****p<0.0001.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

IMMUNE THROMBOCYTOPENIA IN A 22-YEAR-OLD POST COVID-19 VACCINE

Tarawneh OH, Tarawneh HS.. Am J Hematol. 2021 Jan 21. doi: 10.1002/ajh.26106. Online ahead of print.
Level of Evidence: 5 - Case Report

BLUF

A hematologist from Advocate Aurora Health in Wisconsin presents the case of a 22-year-old male with no history of bleeding or autoimmune disease who presented with widespread petechiae (Figure 1) and gum bleeding 3 days post-Pfizer-BioNTech vaccine. The patient had severe thrombocytopenia (2x10^9/L) and was given a platelet transfusion on admission followed by intravenous immunoglobulin and dexamethasone (see summary). He was discharged on day 6 with a platelet count of 28 x10^9/L, which normalized by day 11 (173x10^9/L) . Authors suggest this patient's autoimmune thrombocytopenia (ITP) may have been induced by vaccine administration, but recognize ITP is common and further studies are needed to better evaluate this potential side effect.

SUMMARY

The patient had a normal platelet count two months prior to presentation (145x10^9/L).

Admission Labs:
- Severe thrombocytopenia (2x10^9/L)
- Mildly elevated AST, ALT
- Normal Hb, WBC, PT, PTT, fibrinogen levels

Treatment:
- Platelet transfusion on admission
- Intravenous immunoglobulin 1g/kg for 2 days
- Dexamethasone 40mg/day for 4 days

Discharge Labs:
- platelet count: 28 x10^9/L
- Sjogren's Syndrome A (SSA) antibody: 2.8 (normal<1 AI)
- Normal Rheumatoid factor, antibodies for Cyclic Citrullinated Peptide, Anti Centromere, Chromatin IgG, dsDNA, Jo1, Ribosomal P Protein, Ribonucleoprotein, Scleroderma, Smith, Sjogren's Syndrome B, Sm/Rnp IgG, Antinuclear Antibody (<1:80, normal <1:80)

Notable Follow-up Labs on Day 11:
- normal platelet count (173x10^9/L)
- positive platelet IIb/IIIa, Ia/IIa autoantibodies
- mildly elevated SSA Ab (1.5, normal<1 AI)
- low complement C4 (10.9, reference range: 16-38 mg/dL)
- complement C3 (94) was normal (reference range: 79-152 mg/dL)

Figure 1: "Purpuric lesions on the patient's upper extremity".

NEUROLOGY

STROKE ADMISSION RATES BEFORE, DURING AND AFTER THE FIRST PHASE OF THE COVID-19 PANDEMIC

Kristoffersen ES, Jahr SH, Faiz KW, Thommessen B, Rønning OM.. Neurol Sci. 2021 Jan 11. doi: 10.1007/s10072-021-05039-y. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Investigators from the University of Oslo, Norway conducted a retrospective cross-sectional study of 680 patients who were admitted to Akershus University Hospital in Lørenskog, Norway with TIA or acute stroke (both ischemic and hemorrhagic) from January 3 - September 24, 2020. They found a significant decrease in admissions (15/week, $p < 0.011$) during the strictest period of lockdown (March 13 - April 30) compared to pre- and post-lockdown periods in 2020, as well as a decrease in admissions from January - September, 2020 compared to the same time period in 2015 - 2019 (Figure 1). These results highlight the potential negative complications from delayed care in patients suffering from strokes due to the pandemic.

ABSTRACT

BACKGROUND: There was a significant decrease in stroke admissions during the first phase of the COVID-19 pandemic. There are concerns that stroke patients have not sought medical attention and in the months after the lockdown suffer recurrent severe strokes. The aims of this study were to investigate how stroke admission rates and distributions of severity varied before, during and after the lockdown in a representative Norwegian hospital population. METHODS: All patients discharged from Akershus University Hospital with a diagnosis of transient ischemic attack (TIA) or acute stroke from January to September 2020 were identified by hospital chart review. RESULTS: We observed a transient decrease in weekly stroke admissions during lockdown from an average of 21.4 (SD 4.7) before to 15.0 (SD 4.2) during and 17.2 (SD 3.3) after ($p < 0.011$). The proportion of mild ischemic and haemorrhagic strokes was also lower during lockdown with 66% before, 57% during and 68% after ($p = 0.011$). CONCLUSION: The period of COVID-19 lockdown was associated with a temporary reduction in total admissions of strokes. In particular, there were fewer with TIA and mild stroke. Given the need to prevent the worsening of symptoms and risk of recurrence, it is necessary to emphasise the importance to seek medical care even in states of emergency.

FIGURES

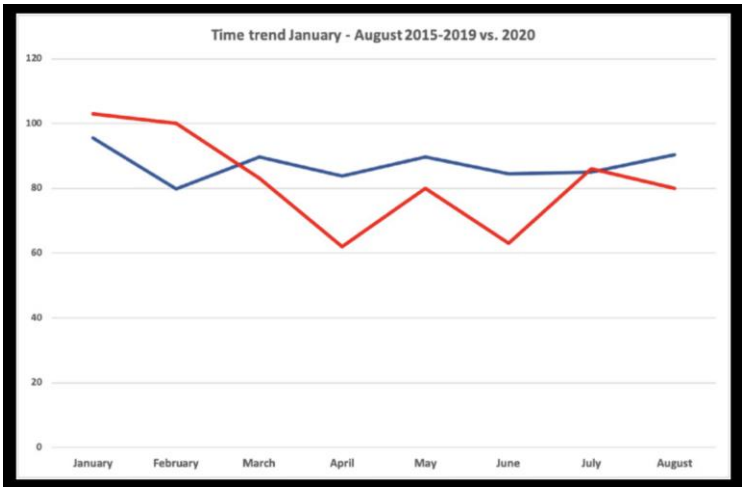


Figure 1. Month by month trend (January–August) for admissions due to acute stroke and transient ischemic attacks. Blue line: 2015–2019 (average). Red line: 2020.

RECENT DEVELOPMENTS ON THERAPEUTIC AND DIAGNOSTIC APPROACHES FOR COVID-19

Majumder J, Minko T.. AAPS J. 2021 Jan 5;23(1):14. doi: 10.1208/s12248-020-00532-2.
Level of Evidence: 5 - Review / Literature Review

BLUF

A literature review conducted by a multidisciplinary group associated with the State University of New Jersey and Rutgers Cancer Institute summarize recent literature on diagnostics and therapeutics for COVID-19. They discuss developments in antiviral drugs (Figure 3), monoclonal antibodies, vaccines (Figure 6), immunotherapy, computer-aided designed antivirals, nanotechnology-based drug delivery, and diagnostic approaches (Figure 8) (see summary). The authors suggest promising conventional and novel research continues to emerge and offers hope in the fight against COVID-19.

SUMMARY

The authors review the following new developments in:
- Antiviral Drugs : Including ACE 2 receptor blockers, those blocking viral replication in the cell (Fig. 3), nucleotide analogs like Remdesivir, indole-based antivirals like Umifenovir, pyrazine class antivirals like Favipiravir, aminoquinolines such as Chloroquine.
- Monoclonal Antibodies: Such as anti-SARS-CoV-2 RBD-hACE2 blocking monoclonal antibodies (mAbs)
- Vaccines: including repurposed live vaccines such as oral polio, MMR, BCG, as well as mRNA such as Moderna mRNA-1273, DNA plasmid encoding S protein such as Inovio Pharma (INO-4800) and CanSino Biologics (Ad5-nCoV) (Fig. 6)
- Immunotherapy: monoclonal antibodies such as tocilizumab, sirukumab, olokizumab, clazakizumab
- Computer-aided Designed Antivirals: RNA-dependent-RNA polymerase (RdRp) inhibitors, such as galidesivir, favipiravir, and penciclovir, viral 3-chymotrypsin-like cysteine protease (3CLpro) enzyme inhibitors, endopeptidase binders such as lopinavir and ritonavir
- Nanotechnology-Based Drug Delivery: There are no nanoparticle-based therapeutics for the treatment of COVID-19 currently but ongoing research is occurring based on nanotherapeutics research of SARS-CoV and MERS-CoV.
- Combinatorial Nanotechnology-Based Treatment: Current testing is happening in regards to a complex delivery system of drugs targeted to ARDS in COVID-19 patients.
- Diagnostic Approaches: PCR (including rt-PRC), serologic testing (Fig. 8), nanoparticle-based screening (AuNP-LF colorimetric bioassay), CT Imaging

ABSTRACT

The ongoing pandemic of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has made a serious public health threat worldwide with millions of people at risk in a growing number of countries. Though there are no clinically approved antiviral drugs and vaccines for COVID-19, attempts are ongoing for clinical trials of several known antiviral drugs, their combination, as well as development of vaccines in patients with confirmed COVID-19. This review focuses on the latest approaches to diagnostics and therapy of COVID-19. We have summarized recent progress on the conventional therapeutics such as antiviral drugs, vaccines, anti-SARS-CoV-2 antibody treatments, and convalescent plasma therapy which are currently under extensive research and clinical trials for the treatment of COVID-19. The developments of nanoparticle-based therapeutic and diagnostic approaches have been also discussed for COVID-19. We have assessed recent literature data on this topic and made a summary of current development and future perspectives.

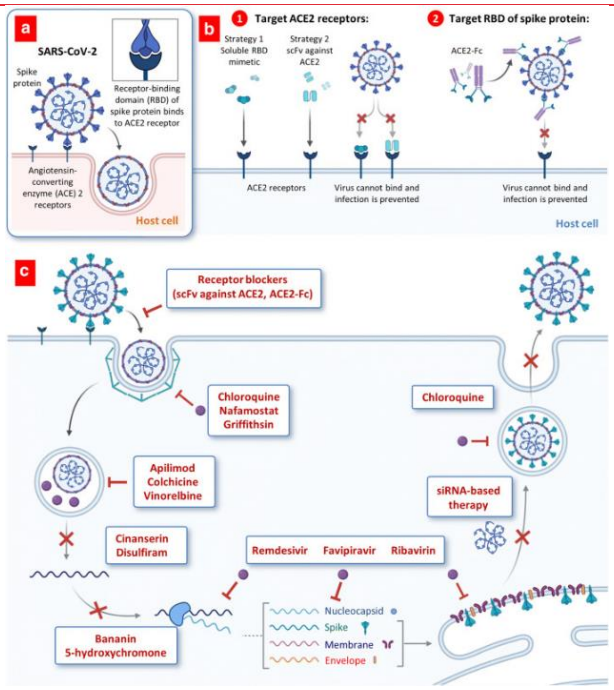


Fig. 3 Proposed therapeutic treatments for COVID-19. a, b Targeting viral entry mechanism. a Viral entry mechanism of SARS-CoV-2. b Possible approaches for blocking ACE2 receptors. c Antiviral drugs targeting the coronavirus replication cycle (simplified). Abbreviations: ACE2, angiotensin-converting enzyme 2; scFvs, recombinant human single-chain variable region fragments against the S1 domain of spike (S) protein of the SARS-CoV; ACE2-Fc, immunoglobulin fragment (Fc)-ACE2 fusion protein

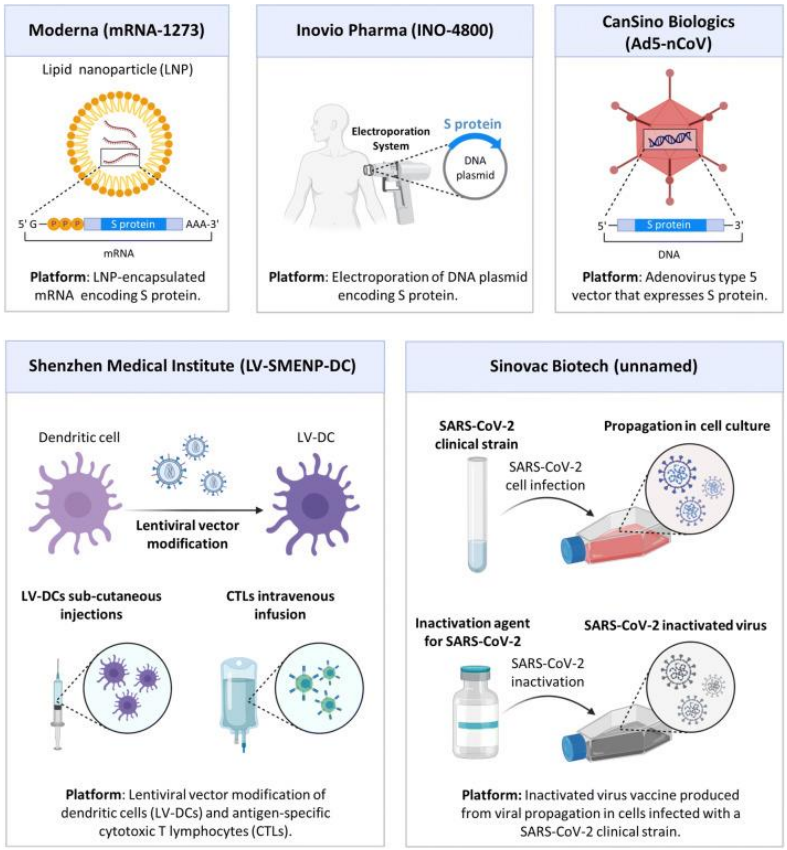


Fig.6 Clinical phase vaccine candidates for COVID-19 (as of April, 2020). Based on data from (36)

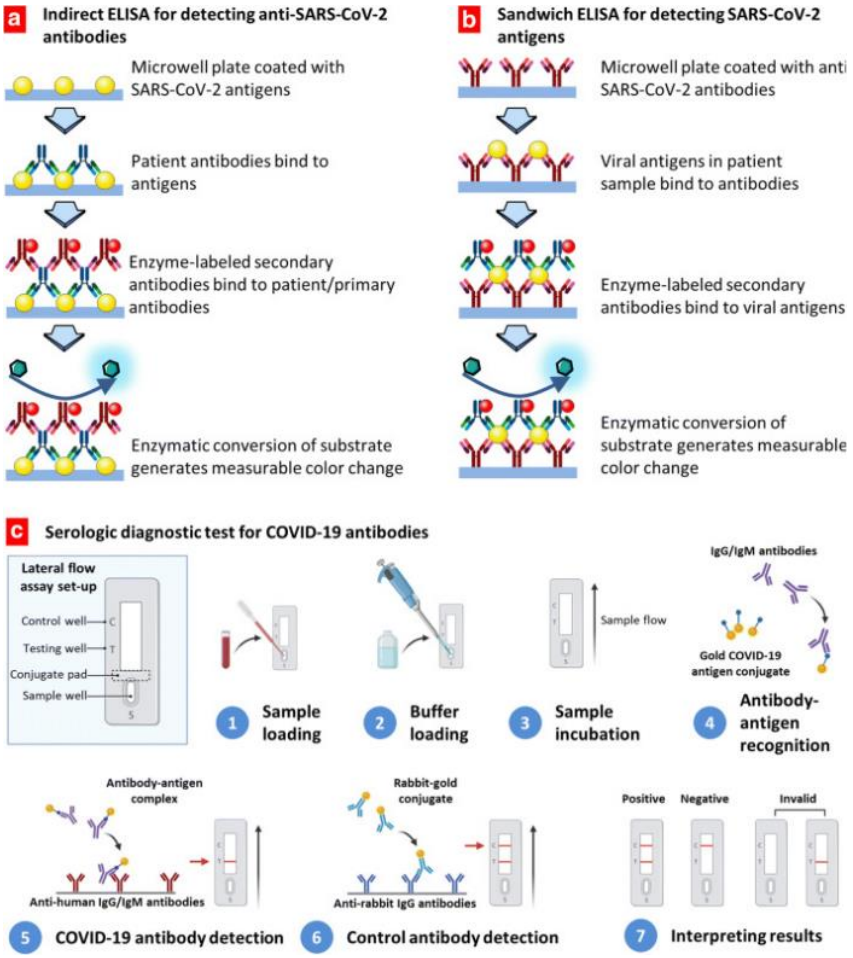


Fig. 8 Assay techniques and tests for COVID-19 diagnosis. a, b The enzyme-linked immunosorbent assays (ELISA) detecting COVID-19 antibodies (a) or antigens (b). Redrawn with permission from (155). c Serologic diagnostic tests for COVID-19 antibodies

CURRENT DIAGNOSTICS

HEALTH WORKERS' ANTIBODY LEVELS WANE AFTER SARS-COV-2 INFECTION

Kuehn BM.. JAMA. 2021 Jan 12;325(2):122. doi: 10.1001/jama.2020.25457.
Level of Evidence: 5 - Review / Literature Review

BLUF

In this review article, the author details the current knowledge on the duration of antibodies against SARS-CoV-2 after recovery of infection, citing a study of 3248 health care workers who had documented infection and subsequent recovery from COVID-19. 194 of participants had detectable antibodies immediately following infection, of those 80% returned for follow up testing 2 months later, finding a decrease in antibodies in 95%. The results suggest antibody testing for prevalence of previous disease will likely underestimate the number of infections, as well as viable duration of convalescent plasma used for treatment.

STILLBIRTHS DURING THE COVID-19 PANDEMIC IN ENGLAND, APRIL-JUNE 2020

Stowe J, Smith H, Thurland K, Ramsay ME, Andrews N, Ladhani SN.. JAMA. 2021 Jan 5;325(1):86-87. doi: 10.1001/jama.2020.21369.
Level of Evidence: 3 - Local non-random sample

BLUF

Public health researchers from England compared data from a single London hospital with national and regional hospitalization data (annual Hospital Episode Statistics (HES) data, monthly data available as Secondary Uses Service and data from the Office for National Statistics (ONS) civil deaths registrations for stillbirths) to investigate whether the rate of stillbirths had increased during the COVID-19 pandemic. They found there were 2825 stillbirths between April 1, 2019 and June 30, 2020, with the highest proportion of stillbirth deliveries reported in London (145/26 760; 0.54% [95% CI, 0.46%-0.64%]). Nationally, no evidence of any increase above baseline during the pandemic period was found (Figure 1). For individual regions, there was no significant difference between the rate of stillbirth deliveries between the lockdown period (defined as April 1, 2020 - June 30, 2020) and the same period the year prior (Table 1). They suggest that while it is important to continue monitoring pregnancy outcomes as the pandemic continues to unfold, these findings are reassuring in light of concerns over access to prenatal services for pregnant patients during the pandemic.

FIGURES

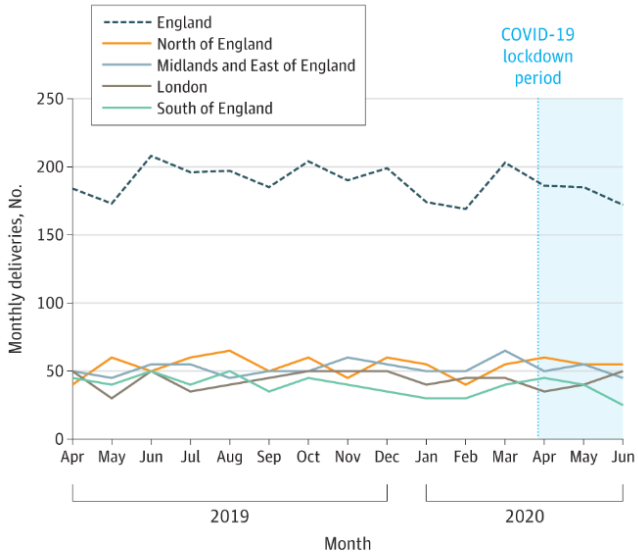


Figure 1. Monthly Count of Deliveries With a Record of Stillbirth in England and Its Regions, April 2019 to June 2020

Table. Count and Proportion of Deliveries With a Recorded Stillbirth and Rate Ratio of Periods Before Lockdown and in Lockdown Adjusted by Calendar Month[a]

	Prelockdown comparison period (April 2019 to June 2019)			Lockdown period (April 2020 to June 2020)			Incidence rate ratio (95% CI)	P value[b]
	No. of stillbirths	Total No. with a delivery outcome	Stillbirth rate, % (95% CI)	No. of stillbirths	Total No. with a delivery outcome	Stillbirth rate, % (95% CI)		
All England	565	139 745	0.40 (0.37-0.44)	543	131 218	0.41 (0.38-0.45)	1.02 (0.91-1.15)	.69
North of England	150	38 165	0.39 (0.33-0.46)	170	35 400	0.48 (0.41-0.56)	1.22 (0.98-1.52)	.07
Midlands and East of England	150	42 220	0.36 (0.30-0.42)	150	39 295	0.38 (0.32-0.45)	1.07 (0.86-1.35)	.53
London	130	25 960	0.50 (0.42-0.59)	125	24 640	0.51 (0.42-0.60)	1.02 (0.79-1.30)	.90
South of England	135	33 390	0.40 (0.34-0.48)	110	31 880	0.35 (0.28-0.42)	0.85 (0.66-1.10)	.21

[a] Subnational figures have been rounded to the nearest 5; percentages calculated using rounded counts. Sources: April 2019-March 2020: Hospital Episode Statistics, NHS Digital. Copyright 2020, reused with the permission of NHS Digital. All rights reserved (provisional data). April 2020-June 2020: Secondary Uses Service, NHS Digital. Copyright 2020, reused with the permission of NHS Digital. All rights reserved.
[b] Significance test at the .05 level.

Table 1. Count and Proportion of Deliveries With a Recorded Stillbirth and Rate Ratio of Periods Before Lockdown and in Lockdown Adjusted by Calendar Montha

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