The Daily COVID-19 Literature Surveillance Summary

August 25, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

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LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".

Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

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

EXECUTIVE SUMMARY

Epidemiology

- Australian systematic review and meta-analysis further confirms that patients with chronic disease are at higher risk for worse outcomes with COVID-19. The most common comorbidities were hypertension (22%), diabetes (14%), and cardiovascular diseases (13%). Crude case fatality rate (CFR) was 7% overall but increased significantly with increasing number of comorbidities.
- Patients with elevated C-reactive protein (CRP), older age (≥60 years), underlying comorbidities, and severe COVID-19 pneumonia were at a higher risk for cardiac involvement.

Understanding the Pathology

- A retrospective cross-sectional study by Chest Diseases specialists in Turkey enrolled 123 adult COVID-19 pneumonia patients with pulmonary infiltrates on CT chest (34 mild, 89 severe), comparing 91 BCG-vaccinated and 32 unvaccinated patients and found increased age ($p<0.001$) and low income ($p<0.001$) to be predictors for severe pneumonia, whereas BCG vaccination was not found to be associated with severe COVID-19 pneumonia.

- Researchers in clinical pharmacy, genomics, and cellular/organismic biology at Taipei Medical University in Taiwan utilized genome databases to analyze expression of transmembrane protease serine 2 (TMPRSS2) and identified four genetic variants associated with increased expression of TMPRSS2 particularly in lung tissue. American and European populations had the greatest frequency of these up-regulating variants and homozygosity for one particular allele (rs469390, missense mutation) yielded the highest expression of lung-associated TMPRSS2, suggesting that examining allelic frequency of TMPRSS2 variants may give epidemiological insight into populations with greater susceptibility to COVID-19.

Management

- A prospective study, conducted by fungal experts from the Center of Expertise in Mycology in the Netherlands, of 108 mechanically ventilated COVID-19 patients with ARDS to assess for prevalence of pulmonary aspergillosis found a 27.7% incidence of COVID-19 associated pulmonary aspergillosis (CAPA), with a 25% lower survival rate among this population than in the non-CAPA patients (19% vs 44%). A correlation between bronchoalveolar lavage (BAL) Galactomannan-index (GM) and odds of death was observed, justified by lower mortality, and reduced GM-index in 11/19 CAPA patients receiving voriconazole and indicated the importance of early identification of clinical and host risk factors for CAPA in critically-ill COVID-19 patients.

Adjusting Practice During COVID-19

- Cardiologists conducted a prospective cohort study at two referral centers (n=1,372 heart failure [HF] patients) in London, England from January 7th, 2020 to June 14th, 2020 and found HF hospitalizations decreased during the COVID-19 pandemic as compared to 2019 ($p<0.001$) but in-hospital HF mortality significantly increased ($p=0.015$) and hospitalization for HF in 2020 was independently associated with worse outcomes (hazard ratio: 2.25, $p=0.002$). Authors suggest patients hospitalized for HF may be at higher risk for adverse outcomes during the COVID-19 pandemic and further investigation of prognosis predictors is needed to inform on management within this population.

R&D: Diagnosis & Treatments

- A retrospective observational study conducted at Third Hospital in Wuhan, China involving 191 COVID-19 patients and 50 healthy controls investigated the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) discrepancies among the infected patients and controls. They found higher NLR, higher CRP, and lower lymphocyte% among the COVID-19 group than the controls ($p<0.001$), in addition to higher NLR, higher CRP, and lower lymphocyte % among patients with severe infection when compared to those with moderate disease ($p<0.05$). The authors believe these results highlight NLR, CRP, and lymphocyte % as independent risk factors and NLR+CRP can improve diagnostic efficiency.

Mental Health & Resilience Needs

- A survey study conducted by special education and child development experts from California and Oregon interviewed 77 primarily Hispanic parents of children aged 3-5 who have intellectual and developmental disabilities (IDD) to determine the impact of and challenges that the COVID-19 pandemic has brought upon their families and found the following: the biggest challenge for families is being stuck at home, a majority of child programs and services have decreased, a silver lining is being able to spend more time as a family, coping strategies include implementing routines and schedules, and a majority of families are concerned about long term economic challenges. The authors demonstrate the importance of

further research into the short-and-long-term impact of the pandemic on children with IDD and their families.

TABLE OF CONTENTS

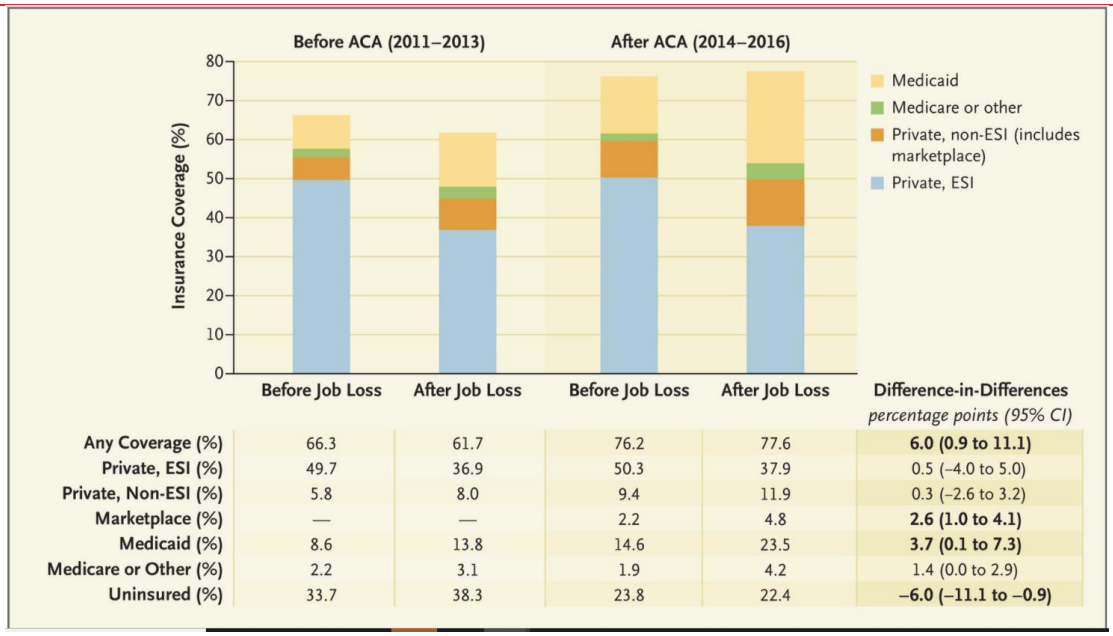
INSURANCE COVERAGE AFTER JOB LOSS - THE IMPORTANCE OF THE ACA DURING THE COVID-ASSOCIATED RECESSION

Agarwal SD, Sommers BD.. N Engl J Med. 2020 Aug 19. doi: 10.1056/NEJMp2023312. Online ahead of print.
Level of Evidence: Other - Expert Opinion

BLUF

Health policy and economics experts from Harvard reviewed rates of insurance coverage in adults who lost their jobs pre- and post-Affordable Care Act (ACA). Authors found the net reduction in coverage loss after job loss was 6% lower in the post-ACA period (Table 1), suggesting that the ACA will play a vital role in maintaining insurance coverage during the COVID-19 related recession in which the unemployment rate has reached 14.7%, a level that has not been seen since the Great Depression.

FIGURES



	Before ACA (2011–2013)		After ACA (2014–2016)		Difference-in-Differences
	Before Job Loss	After Job Loss	Before Job Loss	After Job Loss	*percentage points (95% CI)*
Any Coverage (%)	66.3	61.7	76.2	77.6	**6.0 (0.9 to 11.1)**
Private, ESI (%)	49.7	36.9	50.3	37.9	0.5 (–4.0 to 5.0)
Private, Non-ESI (%)	5.8	8.0	9.4	11.9	0.3 (–2.6 to 3.2)
Marketplace (%)	—	—	2.2	4.8	**2.6 (1.0 to 4.1)**
Medicaid (%)	8.6	13.8	14.6	23.5	**3.7 (0.1 to 7.3)**
Medicare or Other (%)	2.2	3.1	1.9	4.2	1.4 (0.0 to 2.9)
Uninsured (%)	33.7	38.3	23.8	22.4	**–6.0 (–11.1 to –0.9)**

Pre- and Post-ACA Health Insurance Coverage among Nonelderly Adults with Job Loss. Bold type indicates a differences-in-differences estimate that is significant at P<0.05 (see the Supplementary Appendix for details). Data are from the Medical Expenditure Panel Survey for 2011–2016. The sample included all adults 19 to 64 years of age who had any employment in the first round of the survey but had become unemployed by the final round (pre-ACA, N=1350; post-ACA, N=1103). Participants were interviewed in five rounds over 2 years. The mean age of the full population-weighted cohort was 39.7 years, and 57.5% of participants were female, 13.5% were Black, and 17.7% were Hispanic. Insurance types were mutually exclusive and were defined according to the following hierarchy: (1) employer-sponsored insurance (ESI), (2) Medicaid, (3) marketplace or nongroup insurance, (4) Medicare or other, and (5) uninsured. Percentages may not total 100 because of rounding. CI denotes confidence interval.

CORE OUTCOMES SET FOR TRIALS IN PEOPLE WITH CORONAVIRUS DISEASE 2019

Tong A, Elliott JH, Azevedo LC, Baumgart A, Bersten A, Cervantes L, Chew DP, Cho Y, Cooper T, Crowe S, Douglas IS, Evangelidis N, Flemyng E, Hannan E, Horby P, Howell M, Lee J, Liu E, Lorca E, Lynch D, Marshall JC, Matus Gonzalez A, McKenzie A, Manera KE, McLeod C, Mehta S, Mer M, Conway Morris A, Nseir S, Povoa P, Reid M, Sakr Y, Shen N, Smyth AR, Snelling T, Strippoli GF, Teixeira-Pinto A, Torres A, Turner T, Viecelli AK, Webb S, Williamson PR, Woc-Colburn L, Zhang J, Craig JC; COVID-19-Core Outcomes Set (COS) Workshop Investigators.. Crit Care Med. 2020 Aug 17. doi: 10.1097/CCM.0000000000004585. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

An international team of researchers and clinicians report a core set of outcomes that should be used in all clinical trials of people with COVID-19 (Figure 1). This core set of outcomes, which includes mortality, respiratory failure, multi-organ failure, shortness of breath, and recovery, was established across 4 workshops with adults who had confirmed or suspected COVID-19, their family members, the general public, and health professionals (n=9289 respondents from 111 countries), to address the heterogeneity of outcomes reported across trials conducted thus far and ensure that all stakeholders were represented.

ABSTRACT

OBJECTIVES: The outcomes reported in trials in coronavirus disease 2019 are extremely heterogeneous and of uncertain patient relevance, limiting their applicability for clinical decision-making. The aim of this workshop was to establish a core outcomes set for trials in people with suspected or confirmed coronavirus disease 2019. DESIGN: Four international online multistakeholder consensus workshops were convened to discuss proposed core outcomes for trials in people with suspected or confirmed coronavirus disease 2019, informed by a survey involving 9,289 respondents from 111 countries. The transcripts were analyzed thematically. The workshop recommendations were used to finalize the core outcomes set. SETTING: International. SUBJECTS: Adults 18 years old and over with confirmed or suspected coronavirus disease 2019, their family members, members of the general public and health professionals (including clinicians, policy makers, regulators, funders, researchers). INTERVENTIONS: None. MEASUREMENTS: None. MAIN RESULTS: Six themes were identified. "Responding to the critical and acute health crisis" reflected the immediate focus on saving lives and preventing life-threatening complications that underpinned the high prioritization of mortality, respiratory failure, and multiple organ failure. "Capturing different settings of care" highlighted the need to minimize the burden on hospitals and to acknowledge outcomes in community settings. "Encompassing the full trajectory and severity of disease" was addressing longer term impacts and the full spectrum of illness (e.g. shortness of breath and recovery). "Distinguishing overlap, correlation and collinearity" meant recognizing that symptoms such as shortness of breath had distinct value and minimizing overlap (e.g. lung function and pneumonia were on the continuum toward respiratory failure). "Recognizing adverse events" refers to the potential harms of new and evolving interventions. "Being cognizant of family and psychosocial wellbeing" reflected the pervasive impacts of coronavirus disease 2019. CONCLUSIONS: Mortality, respiratory failure, multiple organ failure, shortness of breath, and recovery are critically important outcomes to be consistently reported in coronavirus disease 2019 trials.

FIGURES

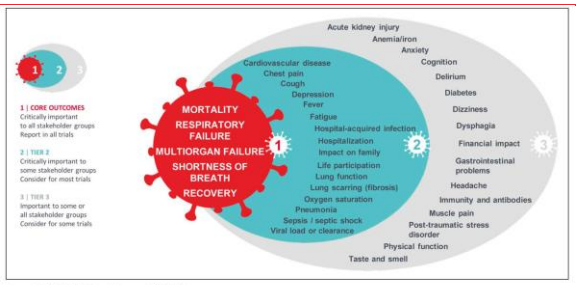


Figure 1. COVID-19-Core Outcomes Set (COS).

ADULTS

THE EPIDEMIOLOGICAL BURDEN OF AND OVERALL DISTRIBUTION OF CHRONIC COMORBIDITIES IN CORONAVIRUS DISEASE-2019 AMONG 202,005 INFECTED PATIENTS: EVIDENCE FROM A SYSTEMATIC REVIEW AND META-ANALYSIS

Mahumud RA, Kamara JK, Renzaho AMN.. Infection. 2020 Aug 19. doi: 10.1007/s15010-020-01502-8. Online ahead of print.
Level of Evidence: 2 - Systematic review of surveys that allow matching to local circumstances

BLUF

Epidemiologists in Australia conducted a systematic review and meta-analysis of 23 global studies published prior to April 10th, 2020 including 202,005 COVID-19 patients (Figure 1) and found 37% of patients had at least one comorbid condition (Figure 2) with the most common comorbidities being hypertension (22%), diabetes (14%), and cardiovascular diseases (13%). Crude case fatality rate (CFR) was 7% overall but increased significantly with increasing number of comorbidities (Figure 3). Authors suggest presence of chronic comorbidities in COVID-19 patients may be significant risk factors for worse outcomes.

SUMMARY

Additional study findings include:
- The most predominant symptoms of COVID-19 were fever (87.5%), cough (57.1%), and fatigue (32.7%). The CFR increased when multiple symptoms were reported ranging from 14% for four symptoms to 21% for seven or more symptoms.
- The CFR was 6% for one comorbid condition, 13% for two or three comorbid conditions, 12% for four comorbid conditions, 14% for five comorbid conditions, and 21% for six or more comorbid conditions (Figure 3).

ABSTRACT

PURPOSE: The main purpose of this study was to examine the overall distribution of chronic comorbidities in coronavirus disease-19 (COVID-19) infected populations and the risk of the underlying burden of disease in terms of the case fatality ratio (CFR). METHODS: We carried out a systematic review and meta-analysis of studies on COVID-19 patients published before 10th April 2020. Twenty-three studies containing data for 202,005 COVID-19 patients were identified and included in our study. Pooled effects of chronic comorbid conditions and CFR with 95% confidence intervals were calculated using random-effects models. RESULTS: A median age of COVID-19 patients was 56.4 years and 55% of the patients were male. The most prevalent chronic comorbid conditions were: any type of chronic comorbidity (37%; 95% CI 32-41%), hypertension (22%; 95% CI 17-27%), diabetes (14%; 95% CI 12-17%), respiratory diseases (5%; 95% CI 3-6%), cardiovascular diseases (13%; 95% CI 10-16%) and other chronic diseases (e.g., cancer) (8%; 95% CI 6-10%). Furthermore, 37% of COVID-19 patients had at least one chronic comorbid condition, 28% of patients had two conditions, and 19% of patients had three or more chronic conditions. The overall pooled CFR was 7% (95% CI 6-7%). The crude CFRs increased significantly with increasing number of chronic comorbid conditions, ranging from 6% for at least one chronic comorbid condition to 13% for 2 or 3 chronic comorbid conditions, 12% for 4 chronic comorbid conditions, 14% for 5 chronic comorbid conditions, and 21% for 6 or more chronic comorbid conditions. Furthermore, the overall CFRs also significantly increased with higher levels of reported clinical symptoms, ranging from 14% for at least four symptoms, to 15% for 5 or 6 symptoms, and 21% for 7 or more symptoms. CONCLUSIONS: The chronic comorbid conditions were identified as dominating risk factors, which should be considered in an emergency disease management and treatment choices. There is urgent need to further enhance systematic and real-time sharing of epidemiologic data, clinical results, and experience to inform the global response to COVID-19.

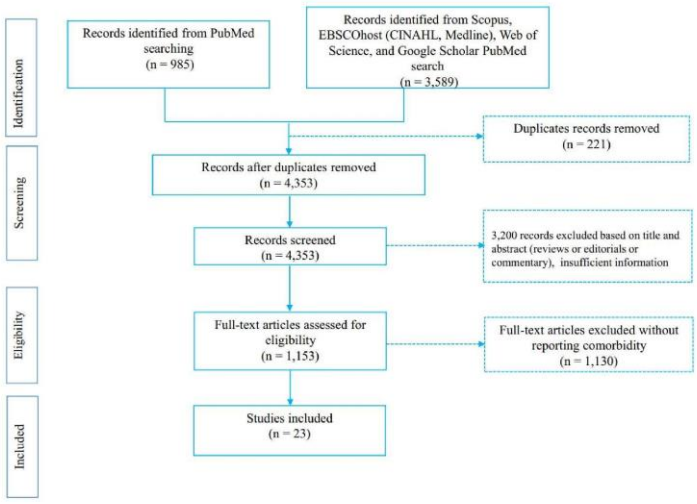


Figure 1. Steps of study selection procedures.

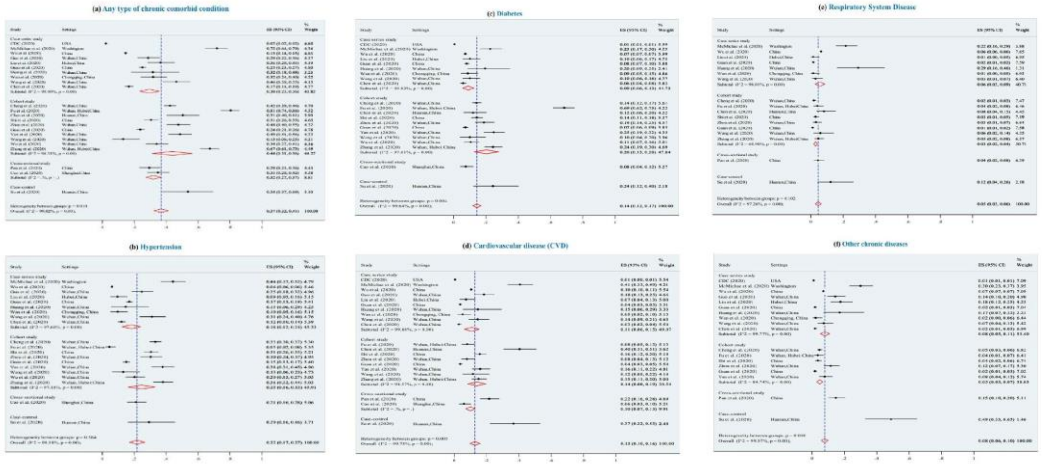


Figure 2. Meta-analysis of the proportion of comorbidities in COVID-19 infected populations.
a. Any type of chronic diseases. b. Hypertension. c. Diabetes. d. Cardiovascular disease (CVD). e. Respiratory system diseases. f. Other chronic diseases.

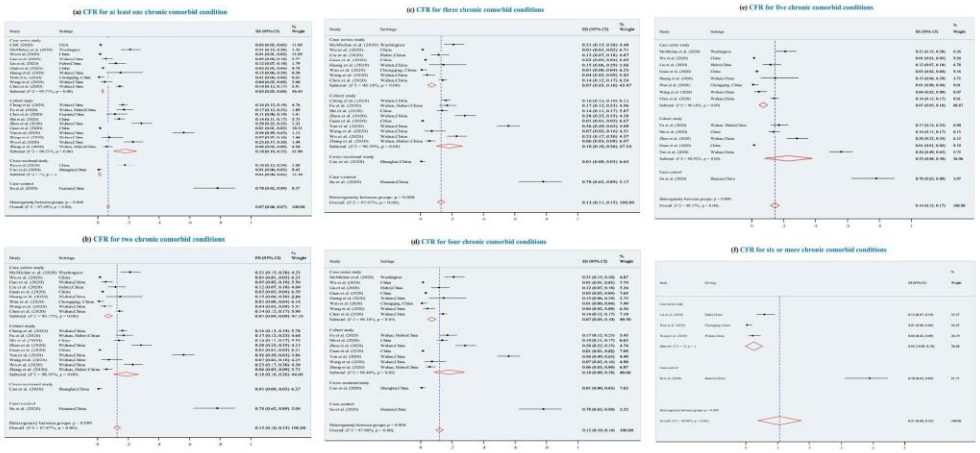


Figure 3. Association between case fatality ratio (CFR) and number of chronic comorbid conditions in COVID-19 infected populations. a. CFR for any type of chronic disease. b. CFR for 2 chronic comorbid conditions. c. CFR for 3 chronic comorbid conditions. d. CFR for 4 chronic comorbid conditions. e. CFR for 5 chronic comorbid conditions. f. CFR for 6 or more chronic comorbid conditions

CLINICAL CHARACTERISTICS AND RISK FACTORS OF CARDIAC INVOLVEMENT IN COVID-19

Xu H, Hou K, Xu R, Li Z, Fu H, Wen L, Xie L, Liu H, Selvanayagam JB, Zhang N, Yang Z, Yang M, Guo Y.. J Am Heart Assoc. 2020 Aug 18:e016807. doi: 10.1161/JAHA.120.016807. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective study of 102 COVID-19 patients hospitalized between January 2 and March 17, 2020 conducted by radiologists in China found 70.6% (n=72) of patients had at least one symptom suggesting cardiac involvement including tachycardia (n=20), elevated myocardial enzymes (n=55), cardiomyopathy (n=59), and acute coronary syndrome (n=9). Furthermore, patients with elevated C-reactive protein (CRP), older age (≥60 years), underlying comorbidities, and severe COVID-19 pneumonia were at a higher risk for cardiac involvement (Table 5). Authors suggest that common cardiovascular involvement in COVID-19 patients calls for early cardiac support during treatment (especially for patients with risk factors) to reduce morbidity and mortality.

ABSTRACT

Background Increasing studies demonstrated that the cardiac involvements are related to Coronavirus Disease 2019 (COVID-19). Thus, we investigated the clinical characteristics of COVID-19 patients and further determined the risk factors for cardiac involvements in them. Methods and Results We analyzed data from 102 consecutive laboratory-confirmed and hospitalized COVID-19 patients (52 women; age, 19-87 years). Epidemiological and demographic characteristics, clinical features, routine laboratory tests (including cardiac injury biomarkers), echocardiography, electrocardiography, chest imaging findings, management methods, and clinical outcomes were collected. Patients were divided into acute cardiac injury (ACI), with and without cardiac marker abnormities groups according to different level of cardiac markers. In this research, cardiac involvements were found in 72 of the 102 (70.6%) patients: tachycardia (n=20), electrocardiography abnormities (n=23), echocardiography abnormities (n=59), elevated myocardial enzymes (n=55), and acute myocardial injury (n=9). Eight ACI patients were aged >60 years; seven of them had two or more underlying comorbidities (hypertension, diabetes, cardiovascular diseases, chronic obstructive pulmonary disease and chronic kidney disease). Novel coronavirus pneumonia (NCP) was much more severe in the ACI patients than in patients with non-definite ACI (p<0.001). Multivariate analyses showed that C-reactive protein (CRP) levels, old age, NCP severity, and underlying comorbidities were the risk factors for cardiac abnormalities in COVID-19 patients. Conclusions Cardiac involvements are common in COVID-19 patients. Elevated CRP levels, old age, underlying comorbidities, and NCP severity are the main risk factors for cardiac involvement in COVID-19 patients. More attention should be given to cardiovascular protection during COVID-19 treatment for mortality reduction.

FIGURES

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.1(1.0-1.1)	p<0.001	1.1(1.0-1.1)	0.04
Sex	1.1(0.5-2.3)	0.848	N. A	N.A
Days from illness onset to admission	1.1(1.0-1.2)	0.125	N. A	N.A
NCP type	6.1(2.32-15.9)	p<0.001	4.9(1.8-13.7)	0.002
Comorbidities	3.2(1.5-6.6)	0.002	2.4(1.0-5.4)	0.042
Complication	10.1(2.2-46.3)	0.003	3.6(0.6-20.9)	0.148
CRP	1.1 (1.0-1.2)	p<0.001	1.1(1.0-1.2)	0.001
D-dimer	2.3(0.9-5.9)	0.093	N. A	N. A

Table 5. Risk factors for cardiac involvements according to logistic regression. NCP, novel coronavirus pneumonia; CRP, C-reactive protein; OR, odd ratio; CI, confidence interval.

FACTORS DETERMINING COVID-19 PNEUMONIA SEVERITY IN A COUNTRY WITH ROUTINE BCG VACCINATION

Aksu K, Naziroğlu T, Özkan P.. Clin Exp Immunol. 2020 Aug 19. doi: 10.1111/cei.13507. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A retrospective cross-sectional study by Chest Diseases specialists in Turkey from March 11 - June 10, 2020 investigating the relationship between BCG vaccination and COVID-19 pneumonia severity enrolled 123 adult COVID-19 pneumonia patients with pulmonary infiltrates on CT chest (34 mild, 89 severe), comparing 91 BCG-vaccinated and 32 unvaccinated patients. They found increased age (p<0.001) and low income (p<0.001) to be predictors for severe pneumonia (Tables 2, 3), whereas BCG vaccination was not found to be associated with severe COVID-19 pneumonia (Table 4).

SUMMARY

Among 123 COVID-19 pneumonia patients in this study, 34 had mild and 89 had severe disease. These patients were divided into BCG vaccinated(91) and unvaccinated(32) groups. Age, gender, BMI, smoking history, diabetes, hypertension, income were compared. They found:
- Increased age (p<0.001) and low income (p=0.001) were significantly higher in unvaccinated than the BCG-vaccinated group (Table 2).
- Increased age (54.0 ± 11.5 vs 38.3 ± 10.7 years, p<0.001), diabetes (32.6% vs 5.9%, p=0.002), and low income (84.3% vs 52.9%, p<0.001) were significantly higher in severe than mild COVID-19 pneumonia patients (Table 3).
- Logistic regression analysis revealed age (OR 1.119,p<0.001) and low income (OR 3.209, p=0.049) to be the independent factors predicting disease severity while BCG-vaccination status is not associated with severe COVID-19 pneumonia (Table 4).

ABSTRACT

BACKGROUND: The impact of countries' Bacillus Calmette-Guerin (BCG) vaccination policies on the course of coronavirus disease (COVID-19) outbreak is a curiosity. In this study, the relationship between BCG vaccination status and severity of COVID-19 pneumonia and the factors affecting disease severity were investigated. METHODS: A retrospective cross-sectional study was conducted between March-June 2020 in patients diagnosed with COVID-19 pneumonia, confirmed by severe acute respiratory syndrome coronavirus-2 polymerase chain reaction positivity in a nasopharyngeal sample and pulmonary infiltrates in computed chest tomography, in a state hospital in Istanbul, Turkey. Sociodemographic features, body mass index, smoking status, concomitant diseases, income rates, and BCG vaccination status of subjects were analyzed. RESULTS: Study population consisted of 123 adults with COVID-19 pneumonia (mean age, 49.7 years [standard deviation, 13.3 years]; 82 (66.7%) male). While the rate of cases vaccinated with BCG is lower (68.5% vs 88.2%; p=.026), the mean age (54.0 +- 11.5 years vs 38.3 +-10.7 years; p <.001), diabetes (32.6% vs 5.9%; p=.002) and low income (84.3% vs 52.9% p<.001) are higher in patients with severe disease compared to those with mild disease. According to multivariate analysis increasing age (odds ratio [OR], 1.119; 95% confidence interval [CI], 1.062 - 1.178; p<.001) and low income (OR, 3.209; 95% CI, 1.008 - 10.222; p =.049) are associated with severe disease in COVID-19 pneumonia. CONCLUSION: This study reveals that BCG vaccination is not associated with disease severity in COVID-19 pneumonia. Age and low income are the main determinants of severe COVID-19 pneumonia.

	BCG-unvaccinated cases (n=32)	BCG-vaccinated cases (n=91)	p
Age; years (mean ±SD)	58.2 ±13.2	46.7 ± 12.1	<.001
Male gender	23 (71.9)	59 (64.8)	.467
Body-mass index; kg/m^2 (mean ±SD)	26.6 ± 2.6	27.3 ± 4.7	.437
Low income	31 (96.9)	62 (68.1)	.001
Current smoker	3 (9.4)	11 (12.1)	.678
Diabetes	10 (31.3)	21 (23.1)	.360
Hypertension	9 (28.1)	14 (15.4)	.112
Coronary artery disease	1 (3.1)	3 (3.3)	N/A†
Severe clinical condition	28 (87.5)	61 (67.0)	.026

Data are expressed as n (%), unless otherwise stated. *BCG* Bacillus Calmette-Guerinn. †Statistical analysis could not be performed due to a small number of subjects.

Table 2: Comparison of characteristics of BCG-vaccinated and -unvaccinated cases with COVID-19 pneumonia (n=123).

	Mild (n=34)	Severe (n=89)	p
Age; years (mean ±SD)	38.3 ±10.7	54.0 ± 11.5	<.001
Male gender	22 (64.7)	60 (67.4)	.776
Body-mass index; kg/m^2 (mean ±SD)	26.8 ± 5.3	27.2 ± 3.7	.601
Low income	18 (52.9)	75 (84.3)	<.001
BCG-vaccinated	30 (88.2)	61 (68.5)	.026
Current smoker	3 (8.8)	11 (12.4)	.756
Diabetes	2 (5.9)	29 (32.6)	.002
Hypertension	3 (8.8)	20 (22.5)	.083
Coronary artery disease	1 (2.9)	3 (3.4)	N/A†

Table 3: Comparison of characteristics of COVID-19 subjects with mild and severe disease(n=123).

	Exp (B)	95% CI for Exp (B)	p
Increased age	1.119	1.062 – 1.178	<.001
Gender	.510	.164-1.591	.246
Low income	3.209	1.008 – 10.222	.049
BCG-unvaccinated	.995	.224 – 4.417	.994
Smoking	2.777	.533 – 14.478	.225
Diabetes	.287	.052 - 1.577	.151
Hypertension	2.227	.441 – 11.237	.332

BCG Bacillus Calmette-Guerinn.

Table 4: Results of binomial logistic regression.

TASTE AND SMELL DISORDERS IN COVID-19 PATIENTS: ROLE OF INTERLEUKIN-6

Cazzolla AP, Lovero R, Lo Muzio L, Testa NF, Schirinzi A, Palmieri G, Pozzessere P, Procacci V, Di Comite M, Ciavarella D, Pepe M, De Ruvo C, Crincoli V, Di Serio F, Santacroce L.. ACS Chem Neurosci. 2020 Aug 19. doi: 10.1021/acschemneuro.0c00447. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

A cohort study by clinical researchers in Italy compared IL-6 levels to smell and taste scores (via patient survey) of 67 COVID-19 patients with smell or taste dysfunction at the time of hospital admission and at the time of swab negativization. They found IL-6 levels, smell scores, and taste scores to be statistically higher at initial evaluation compared to the second (Figure 2, Table 3), as well as statistically significant correlations between decreased IL-6 and improved smell score ($p<0.05$), and decreased IL-6 and improved taste score ($p=0.047$) (Table 3), demonstrating that high levels of IL-6 may be related to smell and taste disorders in COVID-19 patients.

ABSTRACT

The rapid recovery of smell and/or taste functions in COVID-19 patients could be attributed to a decrease in Interleukin-6 levels rather than central nervous system ischemic injury or viral damage to neuronal cells. To correlate Interleukin-6 levels in COVID-19 patients with olfactory and/or gustatory dysfunctions and to investigate the role of IL-6 in the onset of these disorders. This observational study investigated 67 COVID-19 patients with taste and/or smell disorders, who did not require intensive care admission, admitted at COVID Hospital of Policlinico of Bari from March to May 2020. Interleukin-6 was assayed to COVID-19 patients with taste and/or smell disturbances at the time of admission and at the time of swab negativization. At the same time, patients have been given a specific survey to evaluate the severity of taste and/or smell disturbances. Of 125 patients with smell and/or taste dysfunctions at onset of disease, 67 fulfilled the inclusion criteria, while 58 were excluded because 35 of them required intensive care admission, 5 were unable to answer, 5 deceased, 7 had finished chemotherapy recently and 5 refused. The evaluation of taste and/or smell disorders was carried out using a survey performed at the time of admission and at the time of swab negativization. Sino-nasal outcome test 22 (SNOT-22) was used as a reference for olfactory function assessment and Taste and Smell Questionnaire Section of the US NHANES 2011-2014 protocol (CDC 2013b) was used as reference for gustatory function assessment. A venous blood sample was taken for each patient to measure IL-6 levels upon entry and at swab negativization. Interleukin-6 levels in COVID-19 patients in relation with olfactory and/or gustatory disorders from the time of their admission to the time of swab negativization. Statistically significant correlations were obtained between the decrease of Interleukin-6 levels and the improvement of smell (p value<0,05) and taste (p=0,047) functions at swab negativization. The acquired results demonstrate the key role of Interleukin-6 in the pathogenesis of chemosensitive disorders in COVID-19 patients.

FIGURES

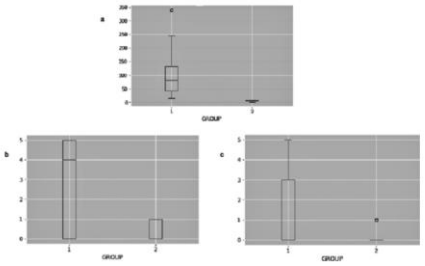


Figure 2. (a) IL-6 and (b) smell and (c) taste score distributions in COVID-19 patients at first and second evaluation.

Table 3. Values of the (a) Wilcoxon Test and (b) Pearson's Correlation Coefficients between All the Variables of the Dataset Considered

(a) Wilcoxon Signed-Rank Test			
variable		Wilcoxon test	*p* value
IL-6 level (first evaluation) vs IL-6 level (second evaluation)		2278	<0.05
score smell dysfunction (first evaluation) vs score smell dysfunction (second evaluation)		1225	<0.05
score taste dysfunction (first evaluation) vs score taste dysfunction (second evaluation)		325	<0.05
(b) Pearson's Linear Correlation Coefficients			
variable	**Pearson coefficient (*r*)**	**95% confidence intervals**	***p* value**
delta IL-6 vs delta score smell	0.58	0.33 to 0.68	<0.05
delta IL-6 vs delta score taste	0.24	0.003 to 0.45	0.047
delta score taste vs delta score smell	−0.38	−0.567 to −0.15	<0.05

POST-MORTEM VIRAL DYNAMICS AND TROPISM IN COVID-19 PATIENTS IN CORRELATION WITH ORGAN DAMAGE

Skok K, Stelzl E, Trauner M, Kessler HH, Lax SF.. Virchows Arch. 2020 Aug 20. doi: 10.1007/s00428-020-02903-8. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

Austrian physicians conducted a series of 19 post-mortem swab analyses of COVID-19 patients to investigate the quantity of SARS-CoV-2 RNA and protein found in various organs and correlated it to their pathology on autopsy (Table 1). The study findings included:

1) high levels of viral RNA in the throat and lungs, and low levels in the intestines (Figure 1)
2) no evidence of viral RNA in other tissues studied (ie., blood, bile, and brain; Figure 1)
3) a lack of correlation between RNA load and level of organ pathology within and between organ groups (Figure 2).

This study builds on existing literature that suggests the course of pathology in COVID-19 is likely heavily driven by the host response to infection rather than viral load itself since RNA load does not necessarily correlate with organ pathology.

ABSTRACT

The persistence of SARS-CoV-2 after death of infected individuals is unclear. The aim of this study was to investigate the presence of SARS-CoV-2 RNA in different organs in correlation with tissue damage and post-mortem viral dynamics in COVID-19 deceased. Twenty-eight patients (17 males, 11 females; age 66-96 years; mean 82.9, median 82.5 years) diagnosed with COVID-19 were studied. Swabs were taken post-mortem during autopsy (N = 19) from the throat, both lungs, intestine, gallbladder, and brain or without autopsy (N = 9) only from the throat. Selective amplification of target nucleic acid from the samples was achieved by using primers for ORF1a/b non-structural region and the structural protein envelope E-gene of the virus. The results of 125 post-mortem and 47 ante-mortem swabs were presented as cycle threshold (Ct) values and categorized as strong, moderate, and weak. Viral RNA was detected more frequently in the lungs and throat than in the intestine. Blood, bile, and the brain were negative. Consecutive throat swabs were positive up to 128 h after death without significant increase of Ct values. All lungs showed diffuse alveolar damage, thrombosis, and infarction and less frequently bronchopneumonia irrespective of Ct values. In 30% the intestine revealed focal ischemic changes. Nucleocapsid protein of SARS-CoV-2 was detected by immunohistochemistry in bronchial and intestinal epithelium, bronchial glands, and pneumocytes. In conclusion, viral RNA is still present several days after death, most frequently in the respiratory tract and associated with severe and fatal organ damage. Potential infectivity cannot be ruled out post-mortem.

FIGURES

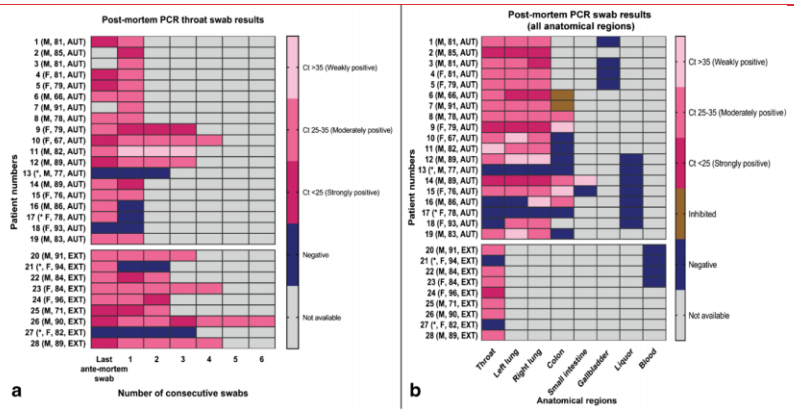


Figure 1: Distribution of qPCR results (according to Ct values) of the collected samples. The post-mortem swab qPCR results from throat (a) and all organs (b) are shown as heatmaps. qPCR results are grouped as weakly, moderately and strongly positive, negative, and inhibited. M, male; F, female; AUT, autopsy; EXT, external examination. *Patients with exclusively negative post-mortem results

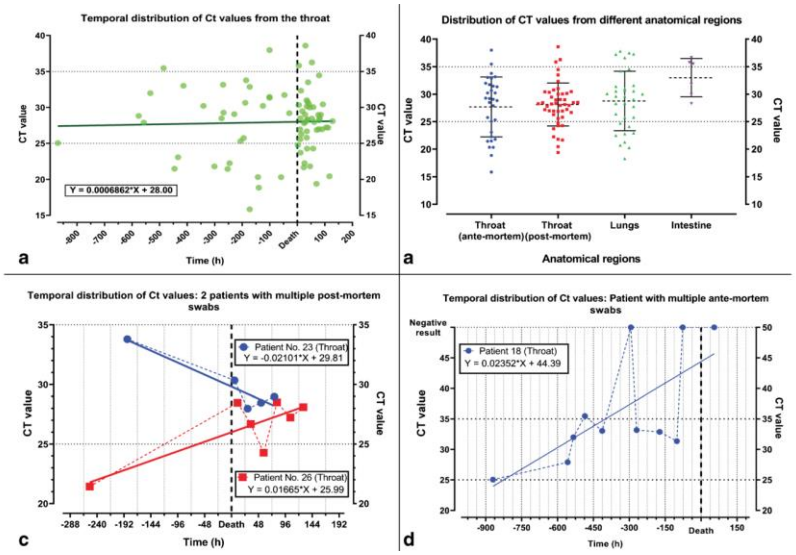


Figure 2: Temporal distribution of Ct values of all pharyngeal swabs from 24 post-mortem positive patients (a) and numeric distribution of all swabs (b). Temporal distribution of the Ct values in two patients with multiple post-mortem swabs (c) and in a patient with 10 ante-mortem and one post-mortem swabs (d)

Table 1 Clinical and viral data of 19 patients with autopsy in correlation with organ damage

Patient number	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
Clinical data																			
Age	81	85	81	81	79	66	91	78	79	67	82	89	77	89	76	86	78	93	83
Gender	M	M	M	F	F	M	M	M	F	F	M	M	M	M	F	M	F	F	M
Onset of symptoms to death (days)	11	11	10	4	6	5	10	18	8	20	8	13	15	9	14	9	36	36	12
Duration of hospitalization (days)	7	6	8	4	5	6	9	11	8	20	8	12	14	8	13	8	35	34	11
Ct values of swabs																			
Throat: First a.m.	15.84	Pos., Ct nav	Pos., Ct nav	18.85	20.33	30.22	Pos., Ct nav	21.47	25.75	22.24	30.22	23.07	32.8	29.07	37.97	28.83	26.55	25.04	31.73
Throat: Last a.m.	Same	Pos., Ct nav	Pos., Ct nav	Same	Same	Same	Pos., Ct nav	31.46	Same	Same	Same	Same	Neg	Same	29.21	Same	33.41	Neg	Same
Throat: First p.m.	33.5	22.25	34.47	29.02	28.26	28.21	30	30.43	21.65	29.48	35.83	26.95	Neg	20.44	26.98	Neg	Neg	Neg	30.13
Right lung	26.39	22.94	24.7	29.04	30.56	22.79	25.76	31.59	21.27	30.03	30.99	37.21	Neg	18.28	34.21	37.26	Neg	31.41	30.55
Left lung	25.80	24.12	29.62	29.61	28.35	22.49	27.76	30.08	20.70	36.60	28.29	37.46	Neg	20.25	34.57	Neg	Neg	30.68	37.79
Colon	NA	NA	NA	NA	NA	Inhib	Inhib	29.95	35.51	Neg	Neg	Neg	Neg	31.84	36.63	28.29	Neg	NA	Neg
Organ damage																			
Lungs																			
Edema	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Hyaline membranes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Proliferation	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pulmonary artery thrombosis	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Infarction	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Bronchopneumonia	No	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Fibrosis	No	Yes	Yes	No	Yes	No	Yes	Yes	No	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Degree of organ damage	Sev	Sev	Mod	Mod	Mod	Sev	Sev	Sev	Sev	Sev	Sev	Sev	Sev	Mod	Mod	Mod	Sev	Mod	Sev
Bowel																			
Ischemic changes	No	No	No	No	No	No	No	Yes	No	No	No	Yes	Yes	Yes	No	No	Yes	Yes	No

a.m. ante mortem; *p.m.* post-mortem; *NA* not assessed; *Neg* negative; *Inhib* inhibited (detection of the internal control failed due to inhibitory agents); Pos. *Ct nav* test positive but Ct values were not available (tests were performed in other labs); *Same* data from only one ante-mortem swab were available; *Sev* severe; *Mod* moderate; *M* male; *F* female

IN SILICO

GENETIC VARIANTS THAT INFLUENCE SARS-COV-2 RECEPTOR TMPRSS2 EXPRESSION AMONG POPULATION COHORTS FROM MULTIPLE CONTINENTS

Irham LM, Chou WH, Calkins MJ, Adikusuma W, Hsieh SL, Chang WC.. Biochem Biophys Res Commun. 2020 Aug 20;529(2):263-269. doi: 10.1016/j.bbrc.2020.05.179. Epub 2020 Jun 8.
Level of Evidence: Other - Mechanism-based reasoning

BLUF

Researchers in clinical pharmacy, genomics, and cellular/organismic biology at Taipei Medical University in Taiwan utilized genome databases to analyze expression of transmembrane protease serine 2 (TMPRSS2), a protein that facilitates cellular uptake of SARS-CoV-2, and identified four genetic variants associated with increased expression of TMPRSS2 particularly in lung tissue (Table 1, Figure 3). American and European populations had the greatest frequency of these up-regulating variants (Figure 4), and homozygosity for one particular allele (rs469390, missense mutation) yielded the highest expression of lung-associated TMPRSS2. These findings suggest that examining allelic frequency of TMPRSS2 variants may give epidemiological insight into populations with greater susceptibility to COVID-19.

ABSTRACT

The World Health Organization recently announced that pandemic status has been achieved for coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Exponential increases in patient numbers have been reported around the world, along with proportional increases in the number of COVID-19-related deaths. The SARS-CoV-2 infection rate in a population is expected to be influenced by social practices, availability of vaccines or prophylactics, and the prevalence of susceptibility genes in the population. Previous work revealed that cellular uptake of SARS-CoV-2 requires Angiotensin Converting Enzyme 2 (ACE-2) and a cellular protease. The spike (S) protein on SARS-CoV-2 binds ACE-2, which functions as an entry receptor. Following receptor binding, transmembrane protease serine 2 (encoded by TMPRSS2) primes the S protein to allow cellular uptake. Therefore, individual expression of TMPRSS2 may be a crucial determinant of SARS-CoV-2 infection susceptibility. Here, we utilized multiple large genome databases, including the GTEx portal, SNP nexus, and Ensembl genome project, to identify gene expression profiles for TMPRSS2 and its important expression quantitative trait loci. Our results show that four variants (rs464397, rs469390, rs2070788 and rs383510) affect expression of TMPRSS2 in lung tissue. The allele frequency of each variant was then assessed in regional populations, including African, American, European, and three Asian cohorts (China, Japan and Taiwan). Interestingly, our data shows that TMPRSS2-upregulating variants are at higher frequencies in European and American populations than in the Asian populations, which implies that these populations might be relatively susceptible to SARS-CoV-2 infection.

FIGURES

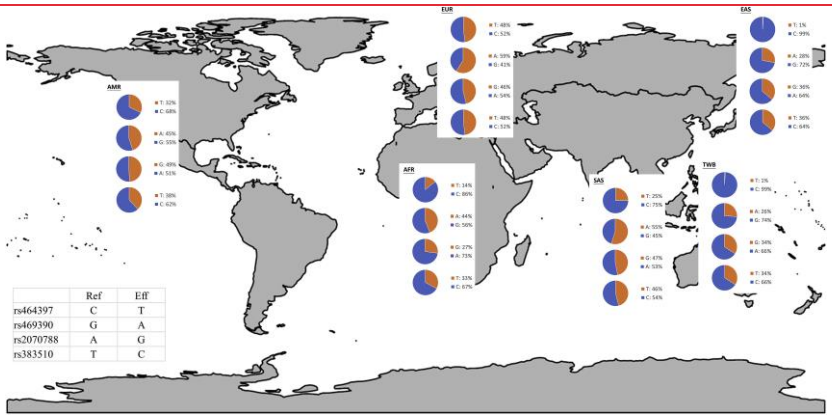


Figure 4: The distribution of allele frequencies that influences TMPRSS2 expression among different populations. Pie charts show the distributions of four variants (rs464397, rs469390, rs2070788 and rs383510) in various populations. EUR, European; AFR, African; AMR, American; EAS, East Asian; SAS, Southeast Asian and TWB, Taiwan Biobank. The alleles associated with higher expression of TMPRSS2 in lung tissue are shown in orange in the pie charts. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Cis-expression of quantitative trait loci results for the transmembrane serine protease 2 (*TMPRSS2*) SNPs from genotype-tissue expression database.

SNP ID	Gencode ID (ENSG00000-)	Gene symbol	*p*-value	Effect size	Tissue	Actions
rs464397	184012.11	*TMPRSS2*	0.000010	−0.08	**Lung**	TT > TC > CC
	157601.13	*MX1*	2.1e-13	−0.31	Thyroid	TT > TC > CC
rs469390	184012.11	*TMPRSS2*	0.0000068	0.091	**Lung**	AA > AG > GG
	157601.13	*MX1*	1.40E-13	0.32	Thyroid	AA > AG > GG
	157601.13	*MX1*	4.50E-12	0.27	Nerve - Tibial	AA > AG > GG
	157601.13	*MX1*	9.00E-08	0.25	**Lung**	AA > AG > GG
	157601.13	*MX1*	5.60E-07	0.2	Artery - Tibial	AA > AG > GG
	157601.13	*MX1*	8.60E-07	0.21	Breast - Mammary Tissue	AA > AG > GG
	157601.13	*MX1*	1.1E-06	0.18	Muscle - Skeletal	AA > AG > GG
	157601.13	*MX1*	1.5E-06	0.2	Skin - Not Sun Exposed (Suprapubic)	AA > AG > GG
	157601.13	*MX1*	3.3E-06	0.18	Esophagus - Mucosa	AA > AG > GG
	157601.13	*MX1*	3.8E-06	0.19	Esophagus - Muscularis	AA > AG > GG
	157601.13	*MX1*	4.8E-06	0.21	Testis	AA > AG > GG
	157601.13	*MX1*	0.000013	0.22	Colon - Transverse	AA > AG > GG
	157601.13	*MX1*	0.000014	0.24	Esophagus - Gastroesophageal Junction	AA > AG > GG
	157601.13	*MX1*	0.000023	0.16	Skin - Sun Exposed (Lower leg)	AA > AG > GG
	157601.13	*MX1*	0.000043	0.21	Artery - Aorta	AA > AG > GG
rs2070788	184012.11	*TMPRSS2*	8.9e-9	−0.11	**Lung**	GG > AG > AA
	157601.13	*MX1*	0.000012	−0.18	Thyroid	GG > AG > AA
rs383510	184012.11	*TMPRSS2*	1.2e-8	−0.11	**Lung**	TT > TC > CC

Source: Expression Quantitative trail loci (eQTL) obtained from https://gtexportal.org/home.

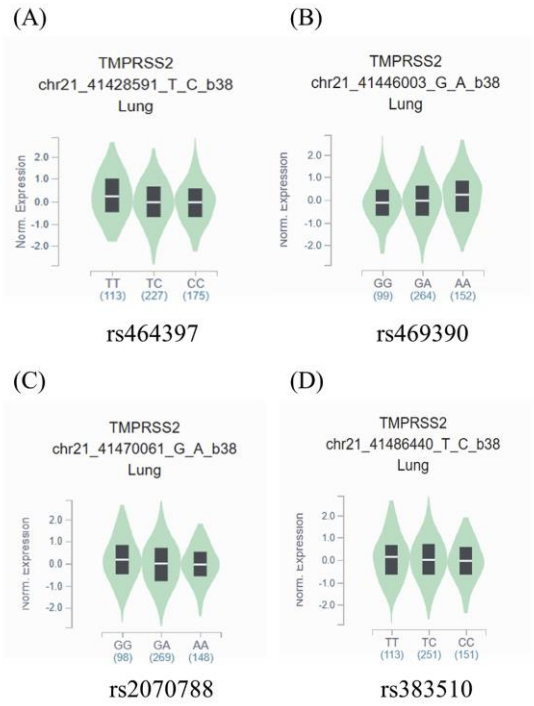


Fig. 3. *Cis*-expression of quantitative trait loci results for transmembrane serine protease 2 (*TMPRSS2*) in lung tissue. Plots show the expression of *TMPRSS2* for each genotype of the four SNPs: rs464397 (A), rs469390 (B), rs2070788 (C) and rs383510 (D).

COVID-19 AND SALIVA: A PRIMER FOR DENTAL HEALTH CARE PROFESSIONALS

Srinivasan M, Thyvalikakath TP, Cook BN, Zero DT.. Int Dent J. 2020 Aug 23. doi: 10.1111/idj.12606. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A literature review conducted at the Indiana University School of Dentistry in Indianapolis discusses how previous research has shown saliva to be more sensitive in detection of COVID-19 than nasopharyngeal swabs, possibly due to the increased number of ACE2 receptors in oral epithelial cells (Figure 1) in addition to possible presence of oral-fecal transmission. This article explores that while this may benefit diagnostics, it may place dental professionals at increased risk for contracting COVID-19 from saliva on instruments and surfaces, suggesting that PPE be changed between patients and antimicrobial mouth rinses be utilized to reduce risk of transmission.

FIGURES

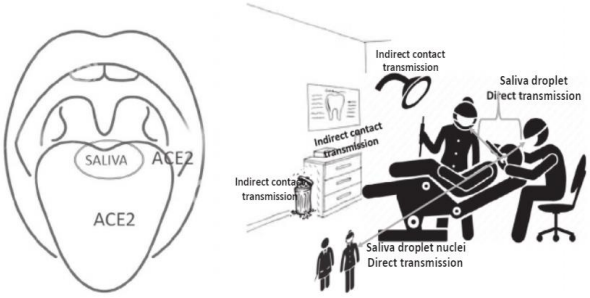


Figure 1. Saliva and COVID-19. The COVID-19 virus is detected in saliva of severely ill patients at higher sensitivity, as well as in asymptomatic carriers.The oral epithelial cells and the salivary gland ductal epithelial cells that express ACE2, the receptor for the COVID-19 virus, could function as cellular reservoirs for the virus. Dental healthcare professionals and co-workers are at risk for direct transmission of COVID-19 virus. The virus remains stable on inanimate surfaces for variable periods of time ranging from a few minutes to few days. Inadvertent transmission can occur by contaminating the instruments, work-surfaces and cabinets by hands soiled with saliva that repeatedly contact equipment in the operatory.

TRACHEAL STENOSIS AFTER TRACHEOSTOMY FOR MECHANICAL VENTILATION IN COVID-19 PNEUMONIA - A REPORT OF 2 CASES FROM NORTHERN ITALY

Gervasio CF, Averono G, Robiolio L, Bertoletti M, Colageo U, De Col L, Bertone F.. Am J Case Rep. 2020 Aug 14;21:e926731. doi: 10.12659/AJCR.926731.
Level of Evidence: Other - Case Report

BLUF

Two case reports by physicians from the Nuovo Ospedale Degli Infermi (New Hospital for the Sick), Biella, Italy observed delayed tracheal stenosis in patients with severe COVID-19 pneumonia who underwent tracheostomy with a prolonged endotracheal intubation period. Their reports suggest that tracheal stenosis is a complication that should be followed-up closely following prolonged intubation, even in patients who recover from severe COVID-19.

SUMMARY

Case 1: A 54 year-old male with a past medical history significant for hypertension, obesity, disc herniation who presented with COVID-19 severe respiratory distress requiring orotracheal intubation. The patient required a surgical tracheostomy 7 days later and was discharged stably after a 20-day hospital course. The patient then returned 5 days later after discharge with respiratory distress from tracheal stenosis, and was consequently treated with IV corticosteroids.

Case 2: A 43 year-old male with a past medical history significant for obesity and type 2 diabetes mellitus who presented with COVID-19 severe respiratory distress requiring orotracheal intubation. The patient required a surgical tracheostomy 9 days later and was discharged stably after a 25-day hospital course. The patient then returned 18 days later after discharge with respiratory distress from tracheal stenosis and was consequently treated with IV corticosteroids; however, the symptoms did not improve and the patient required a tracheal resection.

ABSTRACT

BACKGROUND The role of tracheostomy during the coronavirus disease 2019 (COVID-19) pandemic is still to be determined, and the complication rate of the tracheostomy in COVID-19 patients is still unknown. Postintubation tracheal stenosis is a well-known risk of prolonged endotracheal intubation, but it is too early to define the existence of any difference among the COVID-19 cohort of patients and non-COVID-19 patients. This report is of 2 cases of COVID-19 pneumonia that required tracheostomy and prolonged endotracheal intubation, which were followed by delayed tracheal stenosis. CASE REPORT Case 1. A 54-year-old male was admitted to our hospital (Biella, Italy) for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. The patient underwent orotracheal intubation, progressively improving his breathing function, and was discharged after 20 days. Ten days later, the patient presented with severe respiratory distress. Computed tomography (CT) scan and bronchoscopy showed signs of tracheal stenosis. We administered intravenous steroids for 10 days. The patient showed increasing improvement in his breathing function and was discharged with no other signs of respiratory distress. Case 2. A 43-year-old male was admitted to our hospital for SARS-CoV-2 infection. The patient underwent orotracheal intubation, progressively improving his breathing function, and was discharged after 25 days. Eighteen days later, the patient came to our emergency room with severe respiratory distress. CT scan and bronchoscopy showed signs of tracheal stenosis. The patient had to undergo tracheal resection. CONCLUSIONS The 2 cases presented in this report have shown that even when patients recover from severe COVID-19 pneumonia requiring tracheostomy and mechanical ventilation, tracheal stenosis should be recognized as a potential complication and careful follow-up is required.

CRITICAL CARE

THE CHALLENGE OF MANAGING COVID-19 ASSOCIATED PULMONARY ASPERGILLOSIS

Brüggemann RJ, van de Veerdonk FL, Verweij PE.. Clin Infect Dis. 2020 Aug 18:ciaa1211. doi: 10.1093/cid/ciaa1211. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A prospective study, conducted by fungal experts from the Center of Expertise in Mycology in the Netherlands, of 108 mechanically ventilated COVID-19 patients with ARDS involved collecting bronchoalveolar lavage (BAL) samples through systematic bronchoscopy to assess for prevalence of pulmonary aspergillosis. They found 27.7% incidence of COVID-19 associated pulmonary aspergillosis (CAPA), with a 25% lower survival rate among this population than in the non-CAPA patients (19% vs 44%). A correlation between BAL Galactomannan-index (GM) and odds of death was observed, justified by lower mortality and reduced GM-index in 11/19 CAPA patients receiving voriconazole. These results indicate the importance of early identification of clinical and host risk factors for CAPA in critically-ill COVID-19 patients.

SUMMARY

This study involved a cohort of 108 COVID-19 patients with ARDS who were mechanically ventilated and were treated with corticosteroids and tocilizumab. BAL samples were collected by bronchoscopy. The authors hypothesize CAPA in these patients may be due to:
- Corticosteroid use in mechanically ventilated patients leading to inhibition of LC3-associated phagocytosis (LAP).
- Tocilizumab (anti-IL-6 antibody) inhibiting STAT3 leading to inactivation of TH17, thereby increasing susceptibility to CAPA.
Also, the uncertainty of Invasive pulmonary aspergillosis (IPA) in these patients may be due to:
- Detection of aspergillus in sputum and tracheal aspirates representing upper airway colonization and limited availability of BAL samples.
- Increased number of negative serum GM levels, including CAPA patients.
The authors found a "significant association between CAPA diagnosis and mortality" proven by lower deaths and reduced GM-index in voriconazle treated CAPA patients.

MEDICAL SUBSPECIALTIES

ENDOCRINOLOGY

NEW-ONSET DIABETES IN COVID-19

Rubino F, Amiel SA, Zimmet P, Alberti G, Bornstein S, Eckel RH, Mingrone G, Boehm B, Cooper ME, Chai Z, Del Prato S, Ji L, Hopkins D, Herman WH, Khunti K, Mbanya JC, Renard E.. N Engl J Med. 2020 Aug 20;383(8):789-790. doi: 10.1056/NEJMc2018688. Epub 2020 Jun 12.
Level of Evidence: Other - Expert Opinion

BLUF

A letter to the editor written by an international group of leading diabetes researchers highlights the creation of a global registry of patients who have COVID-19-related diabetes as part of the CoviDIAB Project, which aims to understand how SARS-CoV-2 alters glucose metabolism and contributes to worsening of pre-existing and induction of new diabetes. Authors suggest this registry is critical to understand this pathophysiology and to better care for COVID-19 patients.

SEVERE DIABETIC KETOACIDOSIS AND CORONAVIRUS DISEASE 2019 (COVID-19) INFECTION IN A TEENAGE PATIENT WITH NEWLY DIAGNOSED DIABETES

Rabizadeh S, Hajmiri M, Rajab A, Emadi Kouchak H, Nakhjavani M.. J Pediatr Endocrinol Metab. 2020 Aug 18:/j/jpem.ahead-of-print/jpem-2020-0296/jpem-2020-0296.xml. doi: 10.1515/jpem-2020-0296. Online ahead of print.
Level of Evidence: Other - Case Report

BLUF

A case report by physicians from the Tehran University of Medical Sciences, Iran found COVID-19 in a teenage patient with diabetes newly diagnosed from a severe diabetic ketoacidosis (DKA) episode. The report highlights how patients with diabetes may be at greater risk of contracting COVID-19 and that COVID-19 may exacerbate complications, such as DKA, in patients with diabetes.

SUMMARY

A 16 year-old male presented with a 7-day history of polyuria, polydipsia, fatigue, abdominal pain, and nausea. The laboratory work-up revealed diabetic ketoacidosis (DKA): 512 mg/dL, venous blood gas: pH = 6.9, HCO3- = 8 meq/L, urine proteinuria and ketonuria. The patient was admitted to the ICU and treated with fluid resuscitation. He tested positive for COVID-19 on day 3 of the hospital course and the patient received hydroxychloroquine and Kaletra. The patient subsequently recovered (no fever or dyspnea) and was discharged home with a basal-bolus insulin regimen.

ABSTRACT

Objectives Recently, World Health Organization has declared coronavirus disease 2019 (COVID-19) infection a pandemic. Patients with diabetes may be at an increased risk of developing COVID-19 infection, as well as increased risk of morbidity and mortality. Although the current data have shown that the coronavirus infection generally has a milder course in children. Case presentation In this case report, we present a teenage patient with severe diabetic ketoacidosis (DKA) as the first manifestation of his diabetes and COVID-19 infection. Conclusions He was treated for DKA and COVID-19 infection, and fortunately, had a good response to the treatment.

HOSPITAL PREPAREDNESS FOR COVID-19: THE KNOWN AND THE KNOWN UNKNOWN

Kaito D, Matsumura K, Yamamoto R.. Keio J Med. 2020 Aug 22. doi: 10.2302/kjm.2020-0011-OA. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

Emergency and critical care physicians from Keio University School of Medicine in Tokyo, Japan summarized the recent related literature on hospital preparedness, initial management of COVID-19, and the surveillance of healthcare workers (HCWs) to provide potential clinical guidelines for physicians who will encounter COVID-19.

SUMMARY

Preparing for the First COVID-19 Case
- Organizational reconstruction was recommended by establishing a multidisciplinary designated team to create an incident management system (IMS) for COVID-19 and organizing hospital emergency response plans (Figure 1).
- Optimizing the use of key equipment used for droplet, contact, or airborne precautions should be prioritized. Reuse and/or extending the use of PPE was also recommended (Table 1).

Suspecting and Diagnosing a COVID-19 Case
- COVID-19 should be suspected based on signs and symptoms. Signs include but are not limited to: contact with patients with COVID-19 or travel to epidemic areas. Symptoms vary but include fever, cough, fatigue, loss of appetite, and shortness of breath, and some patients also show myalgia, sore throat, and headache.
- Viral testing with RT-PCR analysis for SARS-CoV-2 is recommended, although other laboratory and imaging findings such as a chest x-ray or chest CT can provide support for the diagnosis.

Initial Management of COVID-19
- Stratifying designated teams who will care for patients with COVID-19 should be based on disease severity.
- Adult COVID-19 patients should be started on supplemental oxygen by nasal cannula when the peripheral oxygen saturation is <92%. High-flow nasal cannula is recommended since it has been shown to lead to decreased intubation, although there is a risk of HCW transmission.
- There are limited studies regarding the best hemodynamic support for patients but immediate resuscitation by crystalloids or norepinephrine is recommended.
- Only remdesivir and dexamethasone have been shown to decrease morbidity and mortality of patients with COVID-19, although it should be selected carefully in discussion with other providers.

Dealing with the Aftermath
- Contact tracing immediately or within 24 hours is recommended following a detection of a confirmed COVID-19 case. The degree of exposure needs to be assessed as well (Table 2).
- Surgical masks and proper hand hygiene is recommended for HCWs to prevent nosocomial infection of COVID-19.
- Quarantine is recommended following contact tracing and is effective in preventing the generation of new clusters of patients with COVID-19. Medical surveillance for at least 14 days from the last contact is recommended.
- An ongoing COVID-19 outbreak brings both physical and psychological stress to HCWs so providing strategies to deal with these such as counseling are recommended.

ABSTRACT

In late March 2020, we faced a nosocomial outbreak of novel coronavirus disease 2019 (COVID-19) at Keio University Hospital, Tokyo, Japan. Presently, COVID-19 is an unprecedented worldwide biohazard, and a nosocomial outbreak can occur in any hospital at any time. Therefore, we reviewed the literature regarding hospital preparedness, the initial management of COVID-19, and the surveillance of healthcare workers (HCWs) to find information that would be generally useful for physicians when confronted with COVID-19. In terms of hospital preparedness, each hospital should develop an incident management system and establish a designated multidisciplinary medical team. To initiate case management, COVID-19 should be suspected based on patient symptoms and/or high-risk history and then should be confirmed by viral testing, such

as reverse transcription polymerase chain reaction (RT-PCR) analysis. Although some patients will become critically ill, the guidelines for respiratory failure and septic shock for non-COVID-19 cases can be followed for supportive treatment. Antiviral medications should be carefully selected because the available information is confused by the large volume of preprint literature and unreliable data. HCWs who have come into contact with patients with COVID-19 can generate new in-hospital clusters of COVID-19 cases. Quarantine following contact tracking with risk stratification is effective in preventing transmission, and the essentials of medical surveillance include monitoring different types of symptoms, delegation of supervision, and continuation of surveillance regardless of the RT-PCR results. Preparation for COVID-19 is recommended before the first COVID-19 case is encountered.

FIGURES

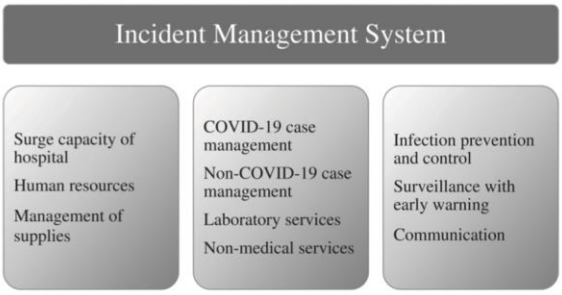


Figure. 1. Incident management system (IMS) with ten components structured for COVID-19.4 A multidisciplinary IMS should be developed for tackling in-hospital COVID-19 crises.

	Demands	Difficulties	Potential solutions
Stuff	PPE (e.g., N95 masks, face shields, gowns, gloves) Devices (e.g., ventilators, monitors, CRRT, ECMO)	Lack of PPE and devices Overuse of PPE Hard to predict demand and supply	Communication with authorities Relocation of PPE and devices Rational use of PPE
Staff	Physicians (e.g., emergency, intensivists, respiratory, infection control) Nurses and support staff	Heavy workload, lack of manpower Risk of nosocomial infection, lack of knowledge on infection control and treatment	Shift working and psychological support Emergency response plan Education and training on IPC and treatment
Space	Beds in intensive care units and infectious disease wards Triage space	Lack of infection preventive systems (e.g., negative-pressure isolation)	Conversion of ORs to ICUs New triage location and alternative facilities (e.g., hotels, gyms)

PPE, personal protective equipment; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; IPC, infection prevention and control; OR, operation room; ICU, intensive care unit.

Table 1. "Stuff, staff, and space" optimization for the COVID-19 crisis.

	WHO[64]	CDC[65]	PHE[66]	ECDC[67]
Distance and duration of contact	Face-to-face contact within 1 m and for >15 min	Being within 6 ft for ≥15 min or any duration for AGP	Face-to-face contact or being within 2 m and for >15 min	Face-to-face contact or being within 2 m and for >15 min
Type of contact	Direct care for patients with COVID-19 without proper PPE	Unprotected direct contact		Direct physical contact, unprotected direct contact
PPE		No respirator/facemask, no eye protection, inappropriate PPE for AGP		HCWs or laboratory workers without recommended PPE
Management	Monitoring for 14 days from last contact	Work exclusion and surveillance for 14 days from last contact	Work exclusion and home quarantine for 14 days from last contact	Work exclusion and surveillance for 14 days from last contact

ECDC, European Centers for Disease Prevention and Control; PPE, personal protective equipment; AGP, aerosol-generating procedure.

Table 2. High-risk contacts for COVID-19 cases.

MEDICAL SUBSPECIALTIES

CARDIOLOGY

TEMPORAL TRENDS IN DECOMPENSATED HEART FAILURE AND OUTCOMES DURING COVID-19: A MULTISITE REPORT FROM HEART FAILURE REFERRAL CENTRES IN LONDON

Cannata A, Bromage DI, Rind IA, Gregorio C, Bannister C, Albarjas M, Piper S, Shah AM, McDonagh TA.. Eur J Heart Fail. 2020 Aug 18. doi: 10.1002/ejhf.1986. Online ahead of print.
Level of Evidence: 3 - Cohort study or control arm of randomized trial

BLUF

Cardiologists conducted a prospective cohort study at two referral centers (n=1,372 heart failure [HF] patients) in London, England from January 7th, 2020 to June 14th, 2020 and found HF hospitalizations decreased during the COVID-19 pandemic as compared to 2019 (p<0.001) but in-hospital HF mortality significantly increased (p=0.015) and hospitalization for HF in 2020 was independently associated with worse outcomes (hazard ratio: 2.25, p=0.002). Authors suggest patients hospitalized for

HF may be at higher risk for adverse outcomes during the COVID-19 pandemic and further investigation of prognosis predictors is needed to inform on management within this population.

ABSTRACT

AIMS: Admission rates for acute decompensated heart failure declined during COVID-19. However, the impact of this reduction on hospital mortality is unknown. We describe temporal trends in the presentation of patients with acute heart failure (HF) and their in-hospital outcomes from two referral centres in London during the COVID-19 pandemic. METHODS AND RESULTS: A total of 1372 patients hospitalized for HF in two referral centres in South London between 7th January and 14th June 2020, were included in the study and compared to the same time period in 2019. The primary outcome was all-cause in-hospital mortality. HF hospitalizations were significantly reduced during the COVID-19 pandemic, compared to 2019 ($p<0.001$). Specifically, we observed a temporary reduction in hospitalizations during the COVID-19 peak, followed by a return to 2019 levels. Patients admitted during the COVID-19 pandemic had similar demographic characteristics compared to the same period in 2019. However, in-hospital mortality was significantly higher in 2020 compared to 2019 ($p=0.015$). Hospitalization in 2020 was independently associated with worse in-hospital mortality (hazard ratio [HR] 2.23, 95% Confidence Interval [CI] 1.34 - 3.72; $p=0.002$). CONCLUSION: During the COVID-19 pandemic there was a reduction in HF hospitalizations and higher in-hospital mortality. Hospitalisation for HF in 2020 is independently associated with more adverse outcomes. Further studies are required to investigate the predictors of these adverse outcomes to help inform potential changes to the management of HF patients while some constraints to usual care remain. This article is protected by copyright. All rights reserved.

MANAGING SEVERE AORTIC STENOSIS IN THE COVID-19 ERA

Tanguturi VK, Lindman BR, Pibarot P, Passeri JJ, Kapadia S, Mack MJ, Inglessis I, Langer NB, Sundt TM, Hung J, Elmariah S.. JACC Cardiovasc Interv. 2020 Aug 24;13(16):1937-1944. doi: 10.1016/j.jcin.2020.05.045. Epub 2020 Jun 1.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

A review conducted by cardiologists from Massachusetts General Hospital and various medical schools and affiliated hospitals investigated strategies to mitigate the risks of delayed treatment in severe symptomatic aortic stenosis (AS) during the COVID-19 pandemic due to high mortality associated with contracting COVID-19 in individuals with severe preexisting conditions (Figure 1). Table 1 illustrates the difference in typical AS care compared to COVID-19 era of patient care, leading to proposals for treatment workup and strategies in Figure 2, highlighting the importance of being mindful of maintenance of preexisting conditions throughout the COVID-19 pandemic.

ABSTRACT

The novel coronavirus-19 (COVID-19) pandemic has created uncertainty in the management of patients with severe aortic stenosis (AS). This population experiences high mortality from delays in treatment of valve disease but is largely overlapping with the population of highest mortality from COVID-19. We present strategies for managing patients with severe AS in the COVID-era. We suggest transitions to virtual assessments and consultation, careful pruning and planning of necessary testing, as well as fewer and shorter hospital admissions. These strategies center on minimizing patient exposure to COVID-19 and expenditure of human and health-care resources without significant sacrifice to patient outcomes during this public health emergency. Areas of innovation to improve our care during this time include increased use of wearable and remote devices to assess patient performance and vital signs, devices for facile cardiac assessment, and widespread use of clinical protocols for expedient discharge with virtual physical therapy and cardiac rehabilitation options.

FIGURES

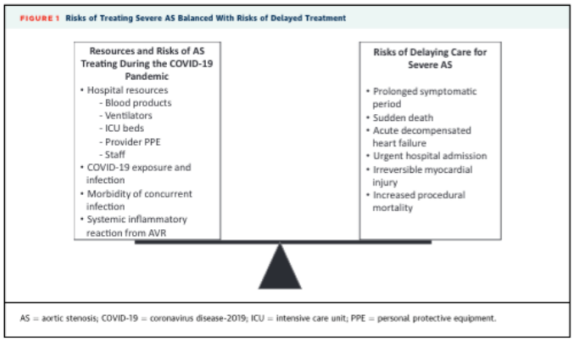


Figure 1: Risks of Treating Severe AS Balanced With Risks of Delayed Treatment

TABLE 1 Typical Versus COVID-19-Era Care of a Patient With Symptomatic Severe AS

Typical Care	COVID-19-Era Care
Patient assessment by primary cardiologist	
• In-person detailed assessment and physical examination • Routine outpatient echocardiography	• Virtual or telephone assessment to screen for symptoms. • Outpatient TTE only if uncertain about AS severity or other cardiac concerns
Patient assessment by consulting providers	
• In-person consultation with cardiac surgery, interventional cardiology, and/or other heart team providers • Heart team discussion	• Virtual or telephone assessment by cardiac surgery, interventional cardiology, and/or other heart team providers • Virtual heart team discussion
Testing	
• Dental panorex radiography and clearance • Pulmonary function test • Carotid Doppler ultrasound • Invasive coronary angiography • TAVR-protocol CTA of chest, abdomen, and pelvis (if TAVR candidate)	• Dental panorex radiography only for known dental pathology/caries • Defer pulmonary function test unless required for decision making • Defer carotid Doppler ultrasound • Coronary angiography performed in the same admission pre-SAVR or during TAVR • TAVR-protocol CTA extended to include neck, chest, abdomen, and pelvis and coronary screen (if TAVR candidate)
Post-procedurally	
• Rapid mobilization • Patient observed for 24-72 h post-TAVR • Patient observed inpatient for 5 to 7 days post-SAVR • Home PT and/or inpatient rehabilitation • Outpatient cardiac rehabilitation	• Rapid mobilization • Emphasis on discharge within 24-48 h post-TAVR • Expedited discharge post-SAVR if feasible • Avoid home PT and inpatient rehabilitation • Virtual outpatient physical therapy and cardiac rehabilitation.

AS = aortic stenosis; COVID-19 = coronavirus disease-2019; CTA = computed tomographic angiography; PT = physical therapy; SAVR = surgical aortic valve replacement; TAVR = transcatheter aortic valve replacement; TTE = transthoracic echocardiography.

Table 1: Typical Versus COVID-19 Era Care of a Patient with Symptomatic Severe AS

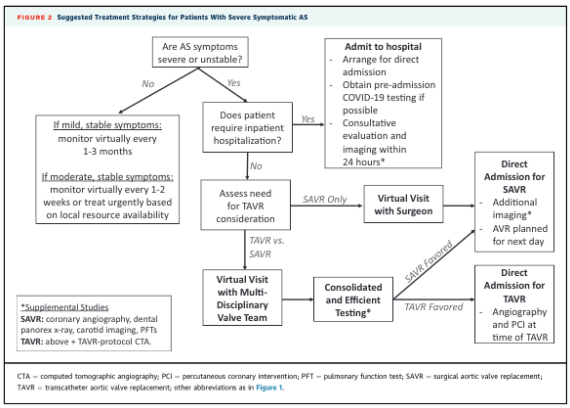


Figure 2: Suggested Treatment Strategies for Patients With Severe Symptomatic AS

UTILITY OF THE NEUTROPHIL-TO-LYMPHOCYTE RATIO AND C-REACTIVE PROTEIN LEVEL FOR CORONAVIRUS DISEASE 2019 (COVID-19)

Yufei Y, Mingli L, Xuejiao L, Xuemei D, Yiming J, Qin Q, Hui S, Jie G.. Scand J Clin Lab Invest. 2020 Aug 17:1-5. doi: 10.1080/00365513.2020.1803587. Online ahead of print.
Level of Evidence: 4 - Case-control studies, or "poor or non-independent reference standard

BLUF

A retrospective observational study conducted at Third Hospital in Wuhan, China involving 191 COVID-19 patients and 50 healthy controls from Jan. 21 - Feb. 20, 2020 investigated the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein (CRP) discrepancies among the infected patients and controls.They found higher NLR, higher CRP, and lower lymphocyte% among the COVID-19 group than the controls ($p<0.001$), in addition to higher NLR, higher CRP, and lower lymphocyte % among patients with severe infection when compared to those with moderate disease ($p<0.05$; Table 2). The authors believe these results highlight NLR, CRP, and lymphocyte % as independent risk factors (Table 3) and NLR+CRP can improve diagnostic efficiency (Table 4).

SUMMARY

A retrospective observational study enrolled 191 COVID-19 patients (108 males and 83 females) and 50 healthy volunteers. Clinical and laboratory data were extracted from medical records. The COVID-19 patients were divided into moderate, severely ill (severe, critical, and death) groups. They found the following:
- NLR, CRP was higher with lower lymphocyte % in the COVID-19 group than healthy volunteers (Table 2).
- The moderate COVID-19 group had lower NLR, CRP levels ($p<0.05$) than severely ill patients, and higher lymphocyte % than critical and death groups ($p<0.05$).
- No statistically significant difference in WBC counts.
- Logistic regression analysis shows NLR, lymphocyte % ($p<0.001$), CRP ($p<0.041$) as an independent risk factor of COVID-19 (Table 3).
- ROC curves exhibit combined NLR+CRP (AUC=0.863) with higher diagnostic accuracy than the individual parameters i.e. NLR, CRP, lymphocyte %, WBC (AUC= 0.835, 0.775, 0.749, 0.416 respectively) as in Table 4.

ABSTRACT

To investigate the value of the combined detection of the neutrophil-to-lymphocyte ratio (NLR) and C-reactive protein level (CRP) in the diagnosis of COVID-19. A total of 191 patients with COVID-19 were recruited at the Third Hospital of Wuhan from 21 January 2020 to 20 February 2020. Fifty healthy volunteers were randomly selected as the control group. Age, gender, white blood cell count (WBC), CRP, lymphocyte percentage, and NLR were extracted. Quantitative clinical characteristics and laboratory values were compared between groups. Risk factors and receiver operating characteristic (ROC) curves for COVID-19 were analyzed. We found that the NLR and CRP were higher, while the lymphocyte percentage was lower in patients with COVID-19 than in healthy controls. Among patients confirmed to have COVID-19, the NLR and CRP of the moderate group were lower than those of severely ill patients (severe, critical and death groups), and the lymphocyte percentage of the moderate group was higher than that of the critical and death group. There were no significant differences in WBC among all groups. Logistic regression analysis showed that the NLR, CRP, and lymphocyte percentage were independent risk factors for COVID-19. The AUC of the combined determination of NLR and CRP was 0.863, which was higher than that of NLR, CRP, WBC, and lymphocyte percentage (AUC: 0.835, 0.775, 0.416, and 0.749, respectively). Our results showed that the NLR and CRP were independent risk factors for COVID-19, and the combined detection of the NLR and CRP showed improved diagnostic performance for COVID-19.

FIGURES

Group	Case number	NLR	CRP (mg/L)	WBC ($\times 10^9$/L)	LY (%)
Death	45	6.97 (9.19–12.87)*	113.21 (111.53–142.75)*	6.60 (6.78–8.28)	11.50 (16.29–24.40)*
Critical	43	6.04 (10.86–17.43)*	80.37 (80.85–111.55)*	6.60 (7.01–8.58)	13.10 (12.66–17.95)*
Severe	20	4.94 (6.44–11.88)*	76.45 (61.92–97.18)*	5.80 (6.13–7.71)	14.90 (16.69–27.97)*
Moderate	83	3.22 (3.97–5.02)*#△o	7.01 (19.90–34.21)*#△o	6.10 (6.45–7.19)	21.40 (29.60–35.58)*#△
Healthy controls	50	1.95 (1.96–2.17)	5.00 (4.81–5.30)	7.20 (7.02–7.46)	29.96 (29.19–31.13)
p Value		<0.001	<0.001	0.423	<0.001

*: Compared with the healthy control group, $p < 0.05$; #: compared with the death group, $p < 0.05$; △: compared with the critical group, $p < 0.05$; O: compared with the severe group, $p < 0.05$.

Table 2: Comparison of laboratory tests among different groups of COVID-19 patients divided according to disease severity and healthy controls.

	β value	SE	Wald	*p* Value	OR (95% CI)
NLR	3.069	0.659	21.676	<.001	21.517 (5.912–78.317)
CRP	0.105	0.051	4.161	.041	1.111 (1.004–1.229)
WBC	−0.164	0.163	1.013	.314	0.848 (0.616–1.169)
LY%	0.211	0.058	14.430	<.001	1.248 (1.113–1.399)
Gender	0.861	0.607	2.015	.156	2.366 (0.720–7.770)
Age	0.033	0.021	2.496	.114	1.034 (0.992–1.078)

Table 3: Logistic regression analysis of factors that affect SARS-CoV2 infection.

Table 4. Comparison of the diagnostic efficacy of WBC, lymphocyte percentage, CRP, NLR, and combined CRP and NLR for COVID-19.

	AUC (95% CI)	Youden index	Sensitivity (%)	Specificity (%)	Cut-off value
NLR	0.835 (0.786–0.884)	0.662	70.2	96.0	3.17
CRP	0.775 (0.717–0.832)	0.668	72.8	94.0	8.55
WBC	0.416 (0.347–0.485)	0.184	20.4	68.0	9.85
LY%	0.749 (0.690–0.809)	0.650	67.0	98.0	21.34
NLR and CRP	0.863 (0.818–0.909)	0.755	77.5	98.0	0.71

Table 4: Comparison of the diagnostic efficacy of WBC, lymphocyte percentage, CRP, NLR, and combined CRP and NLR for COVID-19.

DEVELOPMENTS IN TREATMENTS

AIRWAY HYGIENE IN COVID-19 PNEUMONIA: TREATMENT RESPONSES OF 3 CRITICALLY ILL CRUISE SHIP EMPLOYEES

Farooqi FI, Morgan RC, Dhawan N, Dinh J, Yatzkan G, Michel G.. Am J Case Rep. 2020 Aug 18;21:e926596. doi: 10.12659/AJCR.926596.

Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

A case series conducted in Florida involved 3 cruise ship employees (See Table 1 for patient characteristics) with severe COVID-19 infection who required supportive mechanical ventilation. They were treated with a regimen including hydroxychloroquine, azithromycin, and dexamethasone along with pulmonary hygiene consisting of a daily regimen of heparin, azithromycin, dexamethasone, vitamin C, guaifenesin, levalbuterol, ipratropium, n-acetylcystine, and tracheal suctioning. Imaging studies monitored for improvement (Figure 2) make a case for the use of pulmonary hygiene regimen as treatment for mucus accumulation due to COVID-19-related ARDS, as all 3 patients were subsequently extubated, downgraded from ICU, and achieved 30-day survival.

ABSTRACT

BACKGROUND COVID-19, the disease entity caused by the novel severe acute respiratory coronavirus 2 (SARS-CoV-2), continues to pose a major therapeutic challenge for clinicians. At present, an effective treatment regimen and vaccination has not been established. Many patients develop severe symptoms requiring endotracheal intubation and a prolonged stay in the Intensive Care Unit (ICU). In early postmortem examinations of COVID-19 patients, profuse viscous secretions were observed throughout the respiratory tract. Thus, oxygen supplementation without aggressive pulmonary hygiene management may be suboptimal. In the present case series, pulmonary hygiene management encompassed mucolytics, bronchodilators, and tracheal suctioning. We report 3 severe cases of COVID-19 pneumonia in cruise ship employees who were admitted to the ICU and responded to supportive mechanical ventilation and pulmonary hygiene management. CASE REPORT Three cruise ship employees with COVID-19 underwent endotracheal intubation and were admitted to the ICU for acute hypoxemic respiratory failure. Initial chest X-rays suggested multifocal pneumonia with superimposed acute respiratory distress syndrome (ARDS). A

regimen of hydroxychloroquine, azithromycin, and dexamethasone was initiated on admission in all cases. Additionally, medications used for pulmonary hygiene were administered through a metered-dose inhaler (MDI) in line with the ventilator circuit. Endotracheal suctioning was performed prior to medication administration. The duration from endotracheal intubation to extubation ranged from 9 to 24 days. All 3 patients reached 30-day survival. CONCLUSIONS The cases reported highlight the importance of the use of airway hygiene with mucolytics, bronchodilators, and tracheal suctioning for patients with COVID-19 pneumonia requiring ventilatory support.

FIGURES

Table 1. Patient characteristics and prognostic factors.

Case #	Age (yrs)	Gender	BMI (kg/m²)	Comorbidities	Symptoms	Duration of symptoms prior to hospitalization (days)	Sofa score* (pts)
1	72	Male	28.4	1. Coronary artery disease 2. Diabetes mellitus type II 3. Chronic kidney disease 4. Hypertension	1. Fever 2. Dry cough 3. Shortness of breath	5	11
2	65	Male	18.2	Diabetes mellitus type II	1. Shortness of breath 2. Chest tightness 3. Fever 4. Diarrhea	3	10
3	48	Male	23.5	None	1. Shortness of breath 2. Dry cough 3. Fever	7	9

Case #	Wbc (×10)	% Lymph	D-dimer (ng/ml)	Ferritin (ng/ml)	Crp (mg/dl)	X-ray findings	Duration of mechanical ventilation (days)	Death within 30 days from admission (yes/no)
1	13.1	5.3	676	916	16	Diffuse bilateral interstitial and airspace opacification	24	No
2	12.5	6.3	15335	7282	19.36	Diffuse interstitial prominence with bibasilar consolidation	10	No
3	7.6	4.9	785	3456.5	20.4	Bilateral multifocal airspace opacities	9	No

WBC – white blood cell count; %LYMPH – percentage of lymphocytes; CRP – C-reactive protein. * Sequential Organ Failure Assessment (SOFA) score within 24 hours of hospital admission. The SOFA score is used to predict mortality in critically-ill patients. A higher SOFA score is associated with a greater mortality rate. Interpretation of SOFA score, (Points) Mortality: (0–9) ≤33%, (10–11) 50%, (12+) 95.2%.

Table 1: Patient characteristic and prognostic factors.

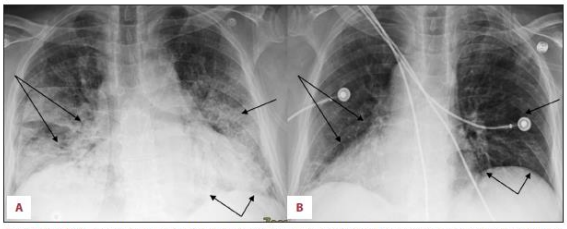


Figure 2. CXR (A) at presentation demonstrated diffuse interstitial prominence with bibasilar consolidations. Improving interstitial and airspace opacities (B) on day 14 of treatment.

Figure 2. CXR (A) at presentation demonstrated diffuse interstitial prominence with bibasilar consolidations. Improving interstitial and airspace opacities (B) on day 14 of treatment.

EXAMINING THE IMPACT OF COVID-19 IN ETHNICALLY DIVERSE FAMILIES WITH YOUNG CHILDREN WITH INTELLECTUAL AND DEVELOPMENTAL DISABILITIES

Neece C, McIntyre LL, Fenning R.. J Intellect Disabil Res. 2020 Aug 18. doi: 10.1111/jir.12769. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

A survey study conducted by special education and child development experts from California and Oregon interviewed 77 primarily Hispanic parents of children aged 3-5 who have intellectual and developmental disabilities (IDD) to determine the impact of and challenges that the COVID-19 pandemic has brought upon their families. They found the following: the biggest challenge for families is being stuck at home (Table 2), a majority of child programs and services have decreased, a silver lining is being able to spend more time as a family (Table 3), coping strategies include implementing routines and schedules, and a majority of families are concerned about long term economic challenges (Table 5). The authors demonstrate the importance of further research into the short-and-long-term impact of the pandemic on children with IDD and their families.

ABSTRACT

BACKGROUND: The COVID-19 pandemic introduced challenges to families with young children with developmental delays. Beyond the widespread concerns surrounding illness, loss of employment and social isolation, caregivers are responsible for overseeing their children's educational and therapeutic programmes at home often without the much needed support of professionals. METHOD: The present study sought to examine the impact of COVID-19 in 77 ethnically, linguistically and socioeconomically diverse families with young children with intellectual and developmental disabilities (IDDs) in California and Oregon, who were participating in larger intervention studies. Parents responded to five interview questions about the impact of the pandemic, services for their child, silver linings or positive aspects, coping and their concerns about the long-term impact of the pandemic. RESULTS: Parents reported that their biggest challenge was being at home caring for their children with the loss of many essential services. Parents reported some positive aspects of the pandemic, especially being together as a family. Although there were positive aspects of the situation, many parents expressed concern about long-term impacts of the pandemic on their children's development, given the loss of services, education and social engagement opportunities. CONCLUSION: Results suggest that parents of young children with IDD report significant challenges at home during the pandemic. Professional support, especially during the reopening phases, will be critical to support family well-being and child developmental outcomes.

FIGURES

Table 2 Frequencies of parent challenges

Type of challenge	*n*	%	Illustrative quote	Translation of quote if applicable
Primary challenge ($N = 77$)				
Difficulty being home	43	55.8	'Lo mas difícil ha sido para los ninos que no pueden salir, que se d esesperan, y se aburren de lo mismo.'	'The hardest thing has been for my children because they cannot go out, they are starting to go crazy, and are bored of doing the same things.'
Finances	9	11.7	'Es que mi pareja le descansaron de trabajo. Ya a veces estamos pensando que hacer con la renta y el pago del carro. Son las más estresantes.'	'It's that my partner was laid off from work. So now we are thinking about what to do with the rent and the car payment. Those are the most stressful.'
Lack of services and unmet needs	9	11.7	'Definitely loss in access to services that includes social interaction for my children, especially my kid with special needs. That's kind of the big one.'	
Health concerns	8	10.4	'Lo mas difícil ha sido saber que mis hijos mayores han tenido que seguir trabajando porque son trabajadores esenciales, y me preocupa saber que anden en la calle. Pido a Dios que me los cuide y que me los protege del virus.'	'The most difficult thing has been knowing that my older children have had to continue working because they are essential workers, and I am worried knowing they are out on the street. I ask God to take care of them and protect them from the virus.'
Child behaviour problems	8	10.4	'Esta semana [mi hija] tuvo más comportamientos porque ya no tiene su rutina y en ratos no quiere hacer nada.'	'This week [my daughter] had more behaviours because she does not have her routine anymore and has moments where she does not want to do anything.'
Secondary challenge ($N = 19$)				
Child behaviour problems	6	31.6		
Lack of services and unmet needs	4	21.1		
Difficulty being home	4	21.1		
Finances	4	21.1		
Health concerns	1	5.3		

Table 3 Parent-reported benefits and silver linings of the pandemic

Benefits and silver linings variables	*n*	%	Illustrative quote	Translation of quote if applicable
More family time and improved family relationships	32	49.2	'Nos hemos integrados mas como familia. Antes, [hija] estaba en la escuela y yo estaba esperando en casa… Estamos valorando estar juntos.'	'We have become more integrated as a family. Before, [daughter] was at school and I was waiting at home… We are valuing being together.'
No benefits or silver linings	9	13.8	'Beneficios? No creo. Ha sido muy dificil durante este tiempo.'	'Benefits? I do not think so. It has been very difficult during this time.'
Child has made some developmental gains during quarantine	7	10.8	'[Hijo] no habla nada, no diga palabras… ultimamente he escuchado que el anda cantando como los ABC, los numeros, y estoy escuchando mas sonidos que él está tratando de hacer.'	'[Son] does not speak at all, he does not say words… but lately I've heard him singing things like ABCs, numbers, and I'm hearing more sounds that he's trying to make.'
Slower pace of life, able to try new things, more present/mindful	6	9.2	'Habian muchas terapias, por aca, por allá, recogieranlos, hacer la comida. Ahora tengo el tiempo para dejar lo que estoy haciendo para ponerme en el piso a jugar. No se podría hacer antes.'	'There were many therapies, over here, over there, I had to pick them up, make food. Now I have the time to stop what I'm doing and get on the floor to play. That wasn't possible before.'
Observe resilience in child and community at large	6	9.2	'Creo que esa, la resilencia de mi hijo. Si, afectó un poco el cambio pero esta feliz. Esta contento en casa. No me pide salir.'	'I think it's that, the resilience of my son. Yes, he was affected by the change a little, but he is happy. He is happy at home. He does not ask me to leave.'
Able to get government assistance to meet basic needs	2	3.1	'Me aprobaron el beneficio de la comida.'	'My foodstamps were approved.'
Continued to stay healthy and safe	2	3.1	'No nos hemos enfermado. Antes [hijo] estaba enfermo pero creo que ha ayudado esa de no poder salir a la calle.'	'That we have not gotten sick. Before [son] was sick but I think it has helped him to not be able to go outside.'
More patience	1	1.5	'He aprendido a tener mas paciencia con [hijo].'	'I've learned to be more patient with [son].'

N = 65.

Table 5 Potential long-term impact of the pandemic on families

Long-term impact	*n*	%	Illustrative quote	Translation of quote if applicable
Economic challenges	18	28.6	'Lo único que me preocupa es los pagos que se tiene que hacer: la renta, los carros, la comida. Me preocupa que no haya mucho ingreso.'	'The only thing that worries me is the payments that have to be made: rent, the cars, food. I am concerned that there will not be much income.'
No impact	11	17.5	'Honestamente, no creo que nos afecta mucho.'	'Honestly, I do not think it will affect us much.'
Lack of child educational and developmental progress	10	15.9	'Creo que en la escuela, porque como no se mucho de internet, y las maestras no me contestan, no puedo acesar las clases de su escuela… y me preocupa a largo plazo sus estudios y en el desarrollo porque es mucho tiempo de estar sin clases.'	'I think that in school, because I do not know much about the internet, and the teachers do not answer me, I cannot access his classes… and I'm concerned long term about his studies and development because it's a long time to be without classes.'
Social changes (e.g. wearing masks, not seeing people)	8	12.7	'En la cuestion de socializar, eso es lo que está afectando todo nosotros. Nos afecta no poder salir a las compras, llevar a los niños a la escuela o al parque. Esas son las cosas que nos estan afectando.'	'In the issue of socialising, that is what is affecting all of us. It affects us not being able to go shopping, take the children to school or to the park. Those are the things that are affecting us.'
Positive impact	6	9.5	'You know what it's an eye opener for sure … being at home you appreciate what you normally do not. We do a lot more family activities, you know, boards games, things like that, then we did before.'	
Emotional impact (e.g. anxiety, fear, boredom)	5	7.9	'Va a afectar demasiado, porque yo ya no estoy tranquila. Porque dicen tantas cosas en las noticias. Un dia dicen una cosa, otro dia dicen otra. Como ahora estan diciendo que la pandemia puede venir igual en invierno, y ya estoy pensando en invierno, que pasa otra vez lo mismo. Y pienso que ya las cosas no van a ser igual. Para mi, cambió todo todo todo.'	'It will affect everything, because I am no longer calm. Because they say so many things on the news. One day they say one thing, another day they say another. Like now they are saying that the pandemic can come back the same in winter, and I am already thinking of winter, that the same thing happens again. And I think that things are not going to be the same. For me, it changed everything, everything, everything.'
Unsure	5	7.9	'Ay dios mio. Creo que no lo sé, de verdad. Espero que no. Si no, nos daña mucho de esto.'	'Oh my god. I think I do not know, really. I hope not. If not, it will hurt us a lot.'

N = 63.

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