The Daily COVID-19 Literature Surveillance Summary

March 22, 2021

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

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

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

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

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

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

EXECUTIVE SUMMARY

Transmission & Prevention

- Age <10 may have lower risks of transmission while age >60 may have higher risks of transmission of SARS-CoV-2 in public areas. Three Public Health experts from Harvard University and University of St. Andrew's wrote a review article on the effect of age on transmission of SARS-CoV-2 after reviewing current literature on detection of SARS-CoV-2 in contacts of COVID-19 cases, serological studies, and studies of infections in schools. They found that susceptibility to infection for children under 10 years old is significantly lower, while in adults older than 60 is higher. Also, serological studies suggest that younger adults (<35 years) often have high incidence of infection in the community, and there is also evidence that the virus may spread robustly in secondary/high schools and spread less in primary schools, with class size possibly affecting spread. This review is helpful in establishing guidelines to re-open schools during the pandemic, particularly secondary/high schools, and shows that efforts should be taken to diminish mixing in individuals aged 18–35 years.

TABLE OF CONTENTS

CLIMATE

GLOBAL

YEARS OF LIFE LOST TO COVID-19 IN 81 COUNTRIES

Pifarré I Arolas H, Acosta E, López-Casasnovas G, Lo A, Nicodemo C, Riffe T, Myrskylä M.. Sci Rep. 2021 Feb 18;11(1):3504. doi: 10.1038/s41598-021-83040-3.
Level of Evidence: 1 - Local and current random sample surveys (or censuses)

BLUF

This study from the Universitat Pompeu Fabra, Spain studies years of life lost (YLL) secondary to COVID-19 attributable deaths in 81 countries using the Human Mortality Database and the World Population Prospects. Results show over 20.5 million YLL globally, with 44.9% of total YLL attributed to ages between 55-75 (Figure 2), and gender stratification revealing that men lost 45% more years than women. While this data is in concordance with the previously held belief that COVID-19 disproportionately affects the elderly, the authors suggest that new policies targeting the protection of these vulnerable groups should also consider gender disparities.

ABSTRACT

Understanding the mortality impact of COVID-19 requires not only counting the dead, but analyzing how premature the deaths are. We calculate years of life lost (YLL) across 81 countries due to COVID-19 attributable deaths, and also conduct an analysis based on estimated excess deaths. We find that over 20.5 million years of life have been lost to COVID-19 globally. As of January 6, 2021, YLL in heavily affected countries are 2-9 times the average seasonal influenza; three quarters of the YLL result from deaths in ages below 75 and almost a third from deaths below 55; and men have lost 45% more life years than women. The results confirm the large mortality impact of COVID-19 among the elderly. They also call for heightened awareness in devising policies that protect vulnerable demographics losing the largest number of life-years.

FIGURES

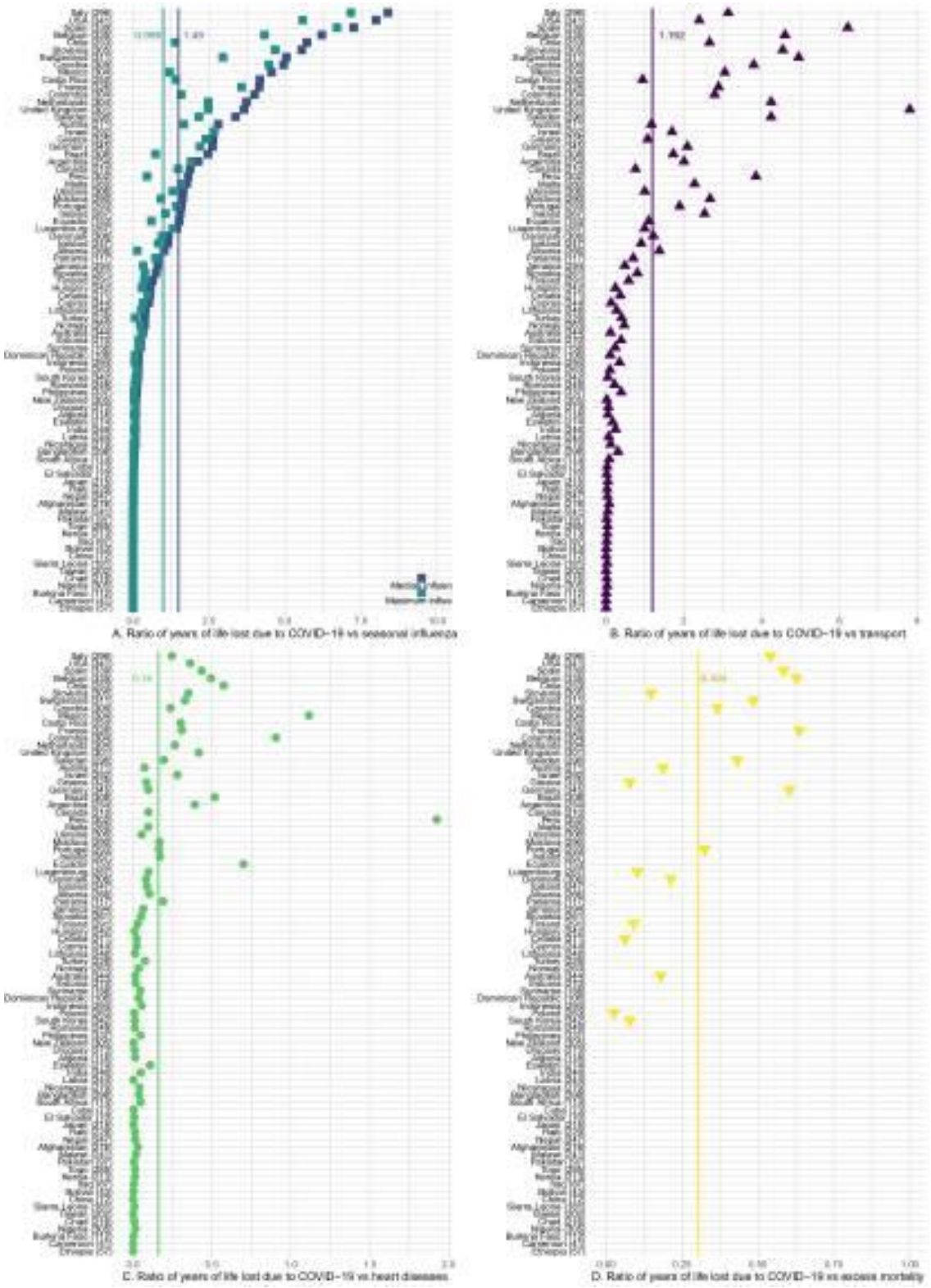


Figure 2. Panel A displays the country-specific proportions of YLL traced back to each age group. The global average proportion is presented at the top, and countries are in decreasing proportion of YLL in the under 55 age bracket. Panel B reports the ratio of male YLL rates to female YLL rates for countries with available gender specific COVID-19 death counts. Countries with genders equally affected by YLL rate are closer to the parity line at 1, while countries with women more affected have points lying on the left; countries with men more severely affected display points lying to the right. Global average and global weighted average of male to female YLL are presented at the top.

ON THE EFFECT OF AGE ON THE TRANSMISSION OF SARS-COV-2 IN HOUSEHOLDS, SCHOOLS, AND THE COMMUNITY

Goldstein E, Lipsitch M, Cevik M.. J Infect Dis. 2021 Feb 13;223(3):362-369. doi: 10.1093/infdis/jiaa691.
Level of Evidence: 3 - Local non-random sample

BLUF

Three Public Health experts from Harvard University and University of St. Andrew's wrote a review article on the effect of age on transmission of SARS-CoV-2 after reviewing current literature on detection of SARS-CoV-2 in contacts of COVID-19 cases, serological studies, and studies of infections in schools. They found that susceptibility to infection for children under 10 years old is significantly lower, while in adults older than 60 is higher (Figure 1). Also, serological studies suggest that younger adults (<35 years) often have high incidence of infection in the community, and there is also evidence that the virus may spread robustly in secondary/high schools and spread less in primary schools, with class size possibly affecting spread. This review is helpful in establishing guidelines to re-open schools during the pandemic, particularly secondary/high schools, and shows that efforts should be taken to diminish mixing in individuals aged 18–35 years.

ABSTRACT

BACKGROUND: There is limited information on the effect of age on the transmission of SARS-CoV-2 infection in different settings. METHODS: We reviewed published studies/data on detection of SARS-CoV-2 infection in contacts of COVID-19 cases, serological studies, and studies of infections in schools. RESULTS: Compared to younger/middle aged adults, susceptibility to infection for children aged under 10y is estimated to be significantly lower, while estimated susceptibility to infection in adults aged over 60y is higher. Serological studies suggest that younger adults (particularly those aged under 35y) often have high cumulative incidence of SARS-CoV-2 infection in the community. There is some evidence that given limited control measures, SARS-CoV-2 may spread robustly in secondary/high schools, and to a lesser degree in primary schools, with class size possibly affecting that spread. There is also evidence of more limited spread in schools when some mitigation measures are implemented. Several potential biases that may affect these studies are discussed. CONCLUSIONS: Mitigation measures should be implemented when opening schools, particularly secondary/high schools. Efforts should be undertaken to diminish mixing in younger adults, particularly individuals aged 18-35y to mitigate the spread of the epidemic in the community.

FIGURES

	Age Group 1		Age Group 2		Age Group 3		Age Group 4		Age Group 5	
Study [Reference]	Age, y	OR (95% CI)	Age, y	OR (95% CI)	Age, y	OR (95% CI)	Age, y	OR (95% CI)	Age, y	OR (95% CI)
PCR, H+C [3]	<15	0.34 (.24–.49)	15–64	1 (ref.)	> 65	1.67 (1.12–1.92)	…	…	…	…
PCR, H+C [2]	<20	0.23 (.11–.46)	20–59	0.64 (.43–.97)	> 60	1 (ref.)	…	…	…	…
PCR, H+C [12]	0–14	0.58 (0.34, 0.98)	15–64	1 (ref.)	> 65	1.64 (1.02–2.63)	…	…	…	…
PCR, H [11]	0–3	1.13 (.29–4.48)	4–18	0.09 (.01–.73)	19–60	1 (ref.)	> 60	1.23 (.51–2.98)	…	…
PCR, H [14]	<18	0.41 (.17–.99)	18–29	1 (ref.)	30–49	1.74 (.70–4.32)	50–64	2.23 (.87–5.75)	> 65	1.99 (.67–6.0)
PCR, H [10]	<18	0.18 (.06–.54)	> 18	1 (ref.)	…	…	…	…	…	…
PCR, H [13]	<20	Suscept. 0.45 (.40–.55)	> 20	Suscept. 1 (ref.)	…	…	…	…	…	…
PCR, H+C [17]	0–17	0.78 (.41–1.50)	18–44	1 (ref.)	45–59	1.16 (.70–1.92)	> 60	2.34 (1.39–3.97)	…	…
PCR, H [18]	0–17	0.96 (.71–1.29)	18–39	1 (ref.)	40–64	0.89 (.67–1.19)	> 65	1.31 (.75–2.19)	…	…
PCR, H [15]	0–18	0.88 (.37–2.02)	18–49	1 (ref.)	> 50	1.86 (.73–4.65)	…	…	…	…
PCR, H+C [16]	No age-related differences in susceptibility were found									
PCR, H [19]	<18	1.69 (.7–4.2)	> 18	1 (ref.)	…	…	…	…	…	…
Serology, H [20]	<18	0.77 (.27–2.17)	> 18	1 (ref.)	…	…	…	…	…	…
Serology, H [21]	<18	1.39 (.55–3.53)	> 18	1 (ref.)	…	…	…	…	…	…

See the caveats in the "Potential biases for the estimates of susceptibility in children versus adults" section.

Abbreviations: CI, confidence interval; H, household contacts; H+C, household plus community contacts (multivariable analysis adjusting for contact setting, etc.); OR, odds ratio; PCR, study based on polymerase chain reaction testing of close contacts; ref., reference; serology, study based on serological testing of close contacts; suscept, susceptibility.

Figure 1. Odds Ratios (or Relative Susceptibility) for Infection in Close Contacts of an Infected Person by Age Group Relative to the Reference Age Group in 14 Studies

RHEUMATOLOGY

POST-COVID-19 ARTHRITIS: A CASE REPORT AND LITERATURE REVIEW

Gasparotto M, Framba V, Piovella C, Doria A, Iaccarino L.. Clin Rheumatol. 2021 Feb 15. doi: 10.1007/s10067-020-05550-1. Online ahead of print.
Level of Evidence: 5 - Case report

BLUF

A case report article conducted by researchers at the University of Padova in Italy involved a 60-year-old Caucasian male who was hospitalized for severe COVID-19 interstitial pneumonia in April 2020 (See Table 1), who was found to have acute oligoarthritis (See Table 2) 13 days post-discharge requiring subsequent hospitalization. A literature search (See Table 3) was performed on viral-associated arthritis, which is hypothesized to be due to activation of inflammatory response with molecular mimicry that may be involved in both acute systemic and post-infective viral-related immunologic consequences. The pathogenesis of inflammatory joint manifestations, most commonly presenting in the lower extremities and more prevalent in males, may be confounded by use of hydroxychloroquine and corticosteroids, is a diagnosis of exclusion given need for extensive diagnostic testing to rule out other conditions. There are increasing reports of COVID-19-related arthritis; however, further studies are needed to better characterize post-infectious related consequences especially pertaining to inflammatory joint involvement.

SUMMARY

60-year-old Caucasian male with no comorbidities was hospitalized for COVID-19 interstitial pneumonia with significant inflammatory markers requiring intubation, antibiotics, anticoagulation therapy and was discharged after 19 days. Thirteen days post-discharge, he had onset of tenderness of right ankle, knee and hip with low-grade fever, which revealed highly inflammatory infiltrate on arthrocentesis resulting in subsequent hospitalization, where he was found to have SARS-CoV-2 seroconversion. Antinuclear antibodies, extractable antinuclear antibodies, rheumatoid factor, anti-citrullinated peptide, HLA-B27 typing were all negative, likely supporting this diagnosis of post-SARS-CoV-2 viral acute arthritis, which resolved after 3 weeks of NSAID therapy.

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) is the novel pathogen responsible for the coronavirus disease 19 (COVID-19) outbreak. Researchers and clinicians are exploring the pathogenetic mechanisms of the viral-induced damage and growing interest is focusing on the short-term and long-term immune-mediated consequences triggered by the infection. We will focus on post-SARS-CoV2 infection arthritis which may arise as a new pathological condition associated with COVID-19. In this article, we describe a case of acute oligoarthritis occurring 13 days after a SARS-CoV2 severe pneumonia in a middle-aged Caucasian man and we go over a brief review of the current available literature. We hypothesize that molecular mimicry might be the basic immunological mechanism responsible for the onset of COVID-19-related arthritis based on the current knowledge of SARS-CoV2 and on the known pathogenetic mechanism of viral-induced arthritis.

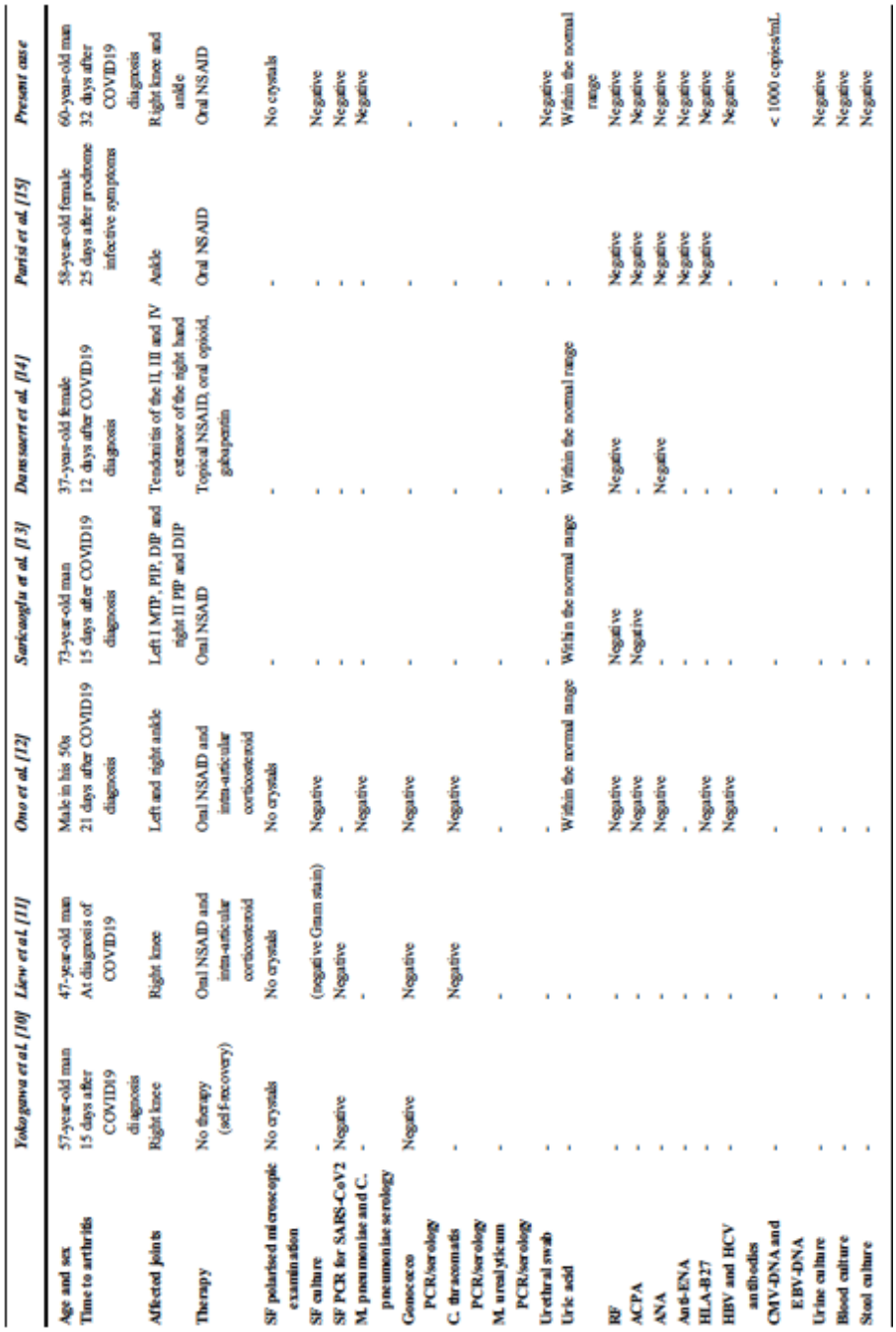
Table 3 Case reports of arthritis reactive to SARS-Co V2 infection, clinical characteristics and diagnostic workup

	Yokogawa et al. [10]	*Liew et al. [11]*	*Ono et al. [12]*	*Saricaoglu et al. [13]*	*Damsaert et al. [14]*	*Parisi et al. [15]*	*Present case*
Age and sex	57-year-old man	47-year-old man	Male in his 50s	73-year-old man	37-years-old female	58-year-old female	60-year-old man
Time to arthritis	15 days after COVID19 diagnosis	At diagnosis of COVID19	21 days after COVID19 diagnosis	15 days after COVID19 diagnosis	12 days after COVID19 diagnosis	25 days after prodrome infective symptoms	32 days after COVID19 diagnosis
Affected joints	Right knee	Right knee	Left and right ankle	Left I MTP, PIP, DIP and right II PIP and DIP	Tendonitis of the II, III and IV extensor of the right hand	Ankle	Right knee and ankle
Therapy	No therapy (self-recovery)	Oral NSAID and intra-articular corticosteroid	Oral NSAID and intra-articular corticosteroid	Oral NSAID	Topical NSAID, oral opioid, gabapentin	Oral NSAID	Oral NSAID
SF polarised microscopic examination	No crystals	No crystals	No crystals	-	-	-	No crystals
SF culture	-	(negative Gram stain)	Negative	-	-	-	Negative
SF PCR for SARS-CoV2	Negative	Negative	-	-	-	-	Negative
M. pneumoniae and C. pneumoniae serology	-	-	Negative	-	-	-	Negative
Gonococo PCR/serology	Negative	Negative	Negative	-	-	-	-
C. thracomatis PCR/serology	-	Negative	Negative	-	-	-	-
M. ureolyticum PCR/serology	-	-	-	-	-	-	-
Urethral swab	-	-	-	-	-	-	Negative
Uric acid	-	-	Within the normal range	Within the normal range	Within the normal range	-	Within the normal range
RF	-	-	Negative	Negative	Negative	Negative	Negative
ACPA	-	-	Negative	Negative	-	Negative	Negative
ANA	-	-	Negative	-	Negative	Negative	Negative
Anti-ENA	-	-	-	-	-	Negative	Negative
HLA-B27	-	-	Negative	-	-	Negative	Negative
HBV and HCV antibodies	-	-	Negative	-	-	-	Negative
CMV-DNA and EBV-DNA	-	-	-	-	-	-	< 1000 copies/mL
Urine culture	-	-	-	-	-	-	Negative
Blood culture	-	-	-	-	-	-	Negative
Stool culture	-	-	-	-	-	-	Negative

Table 1: Laboratory findings during clinical course in our patient
WBC white blood cell, Hb hemoglobin, PLT platelet, ESR erythrocyte sedimentation rate, CRP C-reactive protein, LAD lactate dehydrogenase, SARSCoV2 severe acute respiratory syndrome coronavirus 2

Aspect	Yellow turbid
Differential count of WBC	WBC 20.000/mmc, PMN 90%, M 10%
Polarized light microscopy	No crystals
SARS-Cov2 RT-PCR	Negative
Culture	Negative

Table 2: Synovial fluid analysis WBC white blood cell, PMN polymorphonucleate, Monocyte, RT-PCR real-time polymerase chain reaction



	Yokogawa et al. [10]	Liew et al. [11]	Ono et al. [12]	Saricaoglu et al. [13]	Damsaert et al. [14]	Parisi et al. [15]	Present case
Age and sex	57-year-old man	47-year-old man	Male in his 50s	73-year-old man	37-year-old female	58-year-old female	60-year-old man
Time to arthritis	15 days after COVID19 diagnosis	At diagnosis of COVID19	21 days after COVID19 diagnosis	15 days after COVID19 diagnosis	12 days after COVID19 diagnosis	25 days after prodrome infective symptoms	32 days after COVID19 diagnosis
Affected joints	Right knee	Right knee	Left and right ankle	Left I MTP, PIP, DIP and right II PIP and DIP	Tenodinitis of the II, III and IV extensor of the right hand	Ankle	Right knee and ankle
Therapy	No therapy (self-recovery)	Oral NSAID and intra-articular corticosteroid	Oral NSAID and intra-articular corticosteroid	Oral NSAID	Topical NSAID, oral opioid, gabapentin	Oral NSAID	Oral NSAID
SF polarised microscopic examination	No crystals	No crystals	No crystals	-	-	-	No crystals
SF culture	-	(negative Gram stain)	Negative	-	-	-	Negative
SF PCR for SARS-CoV2	Negative	Negative	-	-	-	-	Negative
M. pneumoniae and C. pneumoniae serology	-	-	Negative	-	-	-	Negative
Gonococo PCR/serology	Negative	Negative	Negative	-	-	-	-
C. thracomatis PCR/serology	-	Negative	Negative	-	-	-	-
M. ureolyticum PCR/serology	-	-	-	-	-	-	-
Urethral swab	-	-	-	-	-	-	Negative
Uric acid	-	-	Within the normal range	Within the normal range	Within the normal range	-	Within the normal range
RF	-	-	Negative	Negative	Negative	Negative	Negative
ACPA	-	-	Negative	Negative	-	Negative	Negative
ANA	-	-	Negative	-	Negative	Negative	Negative
Anti-ENA	-	-	-	-	-	Negative	Negative
HLA-B27	-	-	Negative	-	-	Negative	Negative
HBV and HCV antibodies	-	-	Negative	-	-	-	Negative
CMV-DNA and EBV-DNA	-	-	-	-	-	-	< 1000 copies/mL
Urine culture	-	-	-	-	-	-	Negative
Blood culture	-	-	-	-	-	-	Negative
Stool culture	-	-	-	-	-	-	Negative

Table 3: Case reports of arthritis reactive to SARS-CoV2 infection, clinical characteristics and diagnostic workup COVID19, Coronavirus disease 19; MTP, metatarsophalangeal, PIP, proximal interphalangeal; DIP, distal interphalangeal; NSAID, non-steroidal anti-inflammatory drug; SF, synovial fluid; PCR, polymerase chain reaction; SARS-CoV2, severe acute respiratory syndrome coronavirus 2; RE, rheumatoid factor; ACPA, anti-citrullinated peptide antibodies; ANA, anti-nuclear antibodies; ENA, Extractable nuclear antibodies; HLA, human leukocyte antigen, HBV, hepatitis B virus; HCV, hepatitis C virus

R&D: DIAGNOSIS & TREATMENTS

DEVELOPMENTS IN DIAGNOSTICS

AUTOANTIBODIES IN SEVERE COVID-19-RELATED ACUTE RESPIRATORY DISTRESS SYNDROME: JUST INNOCENT BYSTANDERS?

Umbrello M, Nespoli S, Pisano E, Bonino C, Muttini S.. Int J Rheum Dis. 2021 Feb 4. doi: 10.1111/1756-185X.14077. Online ahead of print.
Level of Evidence: 3 - Non -randomized controlled cohort/follow-up study

BLUF

An observational study conducted by intensivists from Polo Universitario, Milan, Italy of 28 consecutive ICU patients admitted to Ospedale San Carlo Borromeo with confirmed SARS-CoV-2 infection found that 15 patients (53.6%) had autoantibodies, including anti-mitochondrial, anti-nuclear, anti-smooth muscle cell, and anti-neutrophil cytoplasmic antibodies. Compared to the ICU patients without antibodies, the patients with antibodies had higher organ failure scores but no difference in hospital mortality, duration of mechanical ventilation, or ICU and hospital length of stay, suggesting that autoimmunity cannot yet be considered a hallmark of COVID-19 infections (Table 1). The small-size of the study warrants larger, more controlled analysis of the relationship between specific autoantibodies and COVID-19 prognosis.

FIGURES

TABLE 1. Clinical outcomes in patients with and without autoantibodies[a]

	No autoantibodies (N = 13)	Autoantibodies (N = 15)	*P*
ICU mortality	7 (53.9)	6 (40)	.464
Duration of mechanical ventilation (days)	13 (4; 26)	10 (8; 17)	.7119
Duration of pressure support ventilation (days)	2 (1; 5)	3 (1; 6)	.9815
ICU length of stay (days)	17 (5; 26)	11 (8; 23)	.6280
Hospital length of stay (days)	27 (23; 37)	26 (21; 35)	.7967
Ventilator-free days (days)	0 (0; 24)	11 (0; 20)	.7891
Patients who developed VAP	7 (53.9)	8 (53.3)	.978
Number of VAP per patient	2 (1; 4)	2 (1; 2)	.4579
Patients who developed bacteremia (%)	6 (46.2)	7 (46.7)	.978
Number of bacteremias per patient	1 (1; 2)	1 (1; 2)	.8053

TABLE 1. Clinical outcomes in patients with and without autoantibodies

DEVELOPMENTS IN TREATMENTS

DEXAMETHASONE USE AND MORTALITY IN HOSPITALIZED PATIENTS WITH CORONAVIRUS DISEASE 2019: A MULTICENTER RETROSPECTIVE OBSERVATIONAL STUDY

Hoertel N, Sánchez-Rico M, Vernet R, Beeker N, Neuraz A, Alvarado JM, Daniel C, Paris N, Gramfort A, Lemaitre G, Salamanca E, Bernaux M, Bellamine A, Burgun A, Limosin F.. Br J Clin Pharmacol. 2021 Feb 19. doi: 10.1111/bcp.14784. Online ahead of print.
Level of Evidence: 2 - Inception cohort studies

BLUF

A multicenter retrospective observational study conducted at 36 AP-HP Greater Paris University hospitals by researchers from multiple medical institutions in Paris involving 12,217 patients with COVID-19 admitted from January 24 to May 20, 2020 found 63/178 (35%) patients who received dexamethasone needed respiratory support compared to 1129/12039 (9%) patients who didn't receive dexamethasone (See Figure 1). Administration of a cumulative dose between 60-150 mg is significantly associated with reduced mortality only when patients require respiratory support (See Figure 2 and 3). These findings suggest higher efficacy of dexamethasone in severely ill COVID-19 patients and serves to inform future randomized control trials.

ABSTRACT

AIM: To examine the association between dexamethasone use and mortality among patients hospitalized for COVID-19. METHODS: We examined the association between dexamethasone use and mortality at AP-HP Greater Paris University hospitals. Study baseline was defined as the date of hospital admission. The primary endpoint was time to death. We compared this endpoint between patients who received dexamethasone and those who did not in time-to-event analyses adjusted for patient characteristics (such as age, sex, and comorbidity) and clinical and biological markers of clinical severity of COVID-19, and stratified by the need for respiratory support, i.e. mechanical ventilation or oxygen. The primary analysis was a multivariable Cox regression model. RESULTS: Of 12,217 adult patients hospitalized with a positive COVID-19 PT-PCR test, 171 (1.4%) received dexamethasone orally or by intravenous perfusion during the visit. Among patients who required respiratory support, the end-point occurred in 10/63 (15.9%) patients who received dexamethasone and 298/1,129 (26.4%) patients who did not. In this group, there was a significant association between dexamethasone use and reduced mortality in the primary analysis (HR, 0.46; 95%CI, 0.22 to 0.96, p=0.039). Among patients who did not require respiratory support, there was no significant association between dexamethasone use and the endpoint. CONCLUSIONS: In this multicenter observational study, dexamethasone use administered either orally or by intravenous injection at a cumulative dose between 60 mg and 150 mg was associated with reduced mortality among patients with COVID-19 requiring respiratory support.

FIGURES

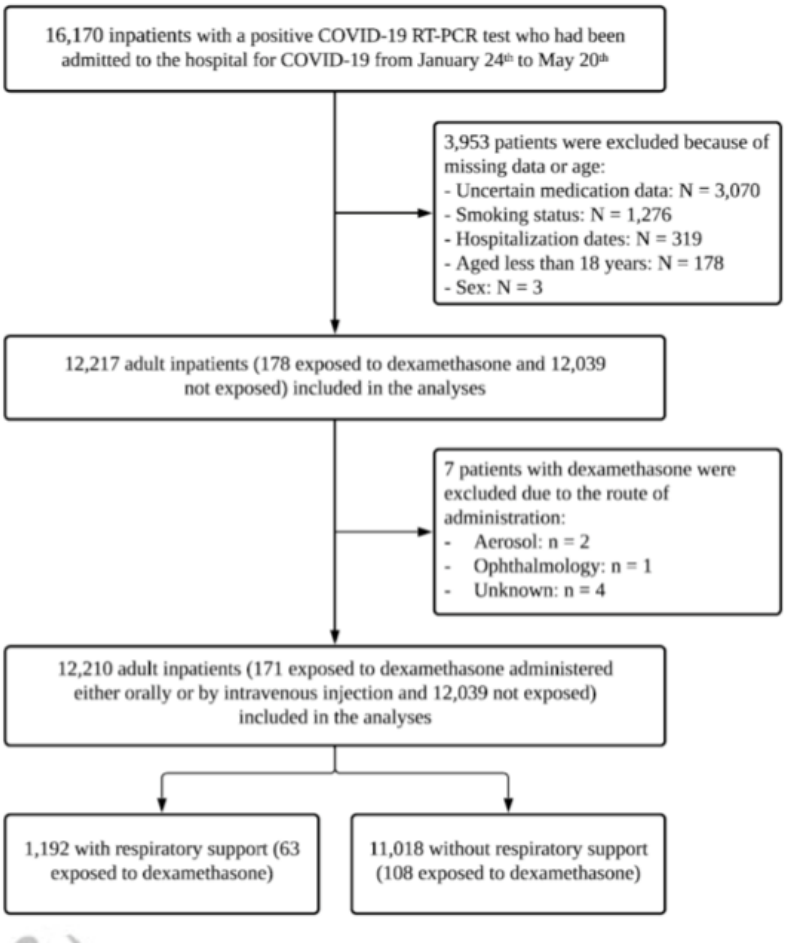


Figure 1: Study cohort

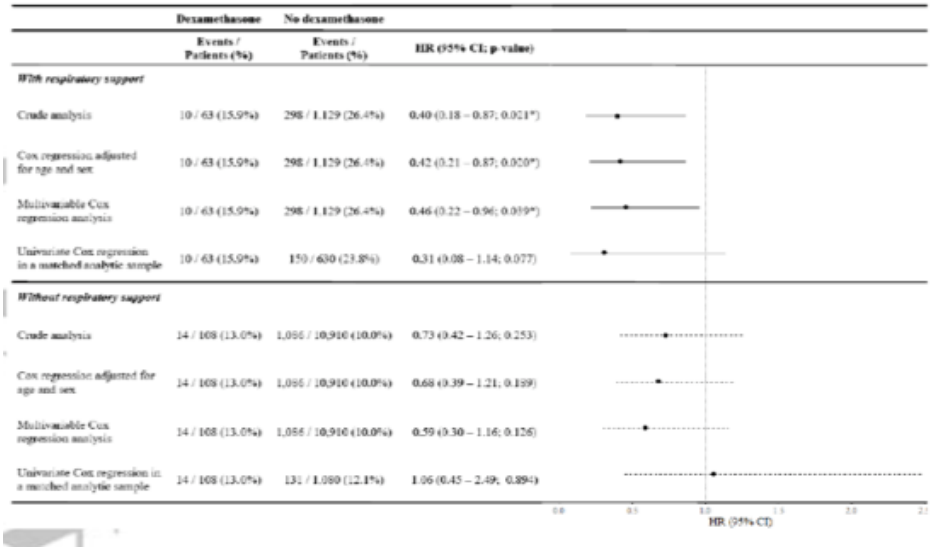


Figure 2. Association between dexamethasone use and time to death in the full sample and in the matched analytic sample. * p-value is significant (p<0.05). Abbreviations: HR, hazard ratio; CI, confidence interval

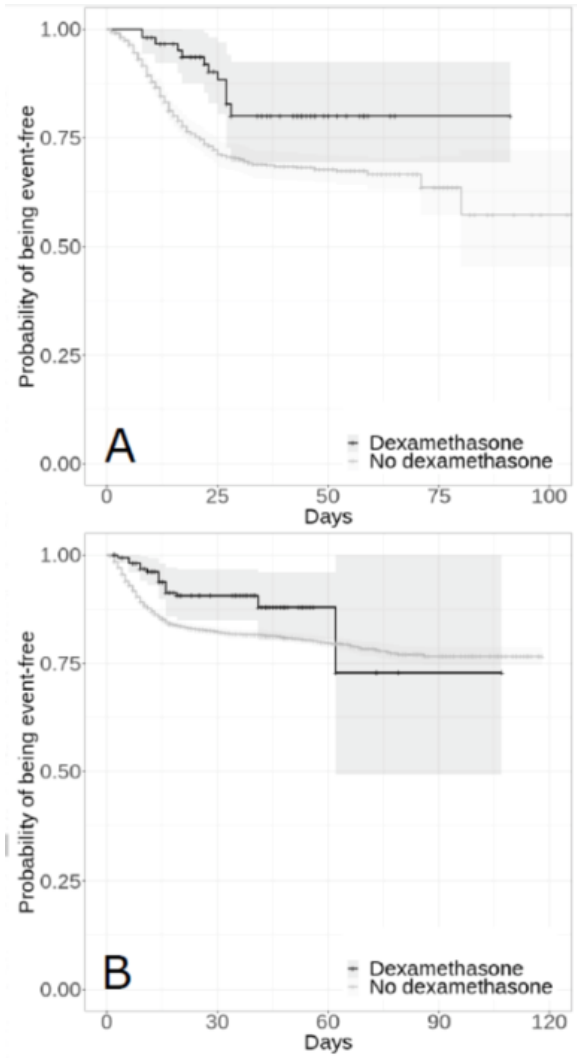


Figure 3. Kaplan-Meier curves for time to death in the full samples of patients hospitalized for COVID-19 who required respiratory support (i.e., mechanical ventilation or oxygen) (N=1,192) (A), and of those who did not (N=11,018) (B), according to dexamethasone use. The shaded areas represent pointwise 95% confidence intervals.

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