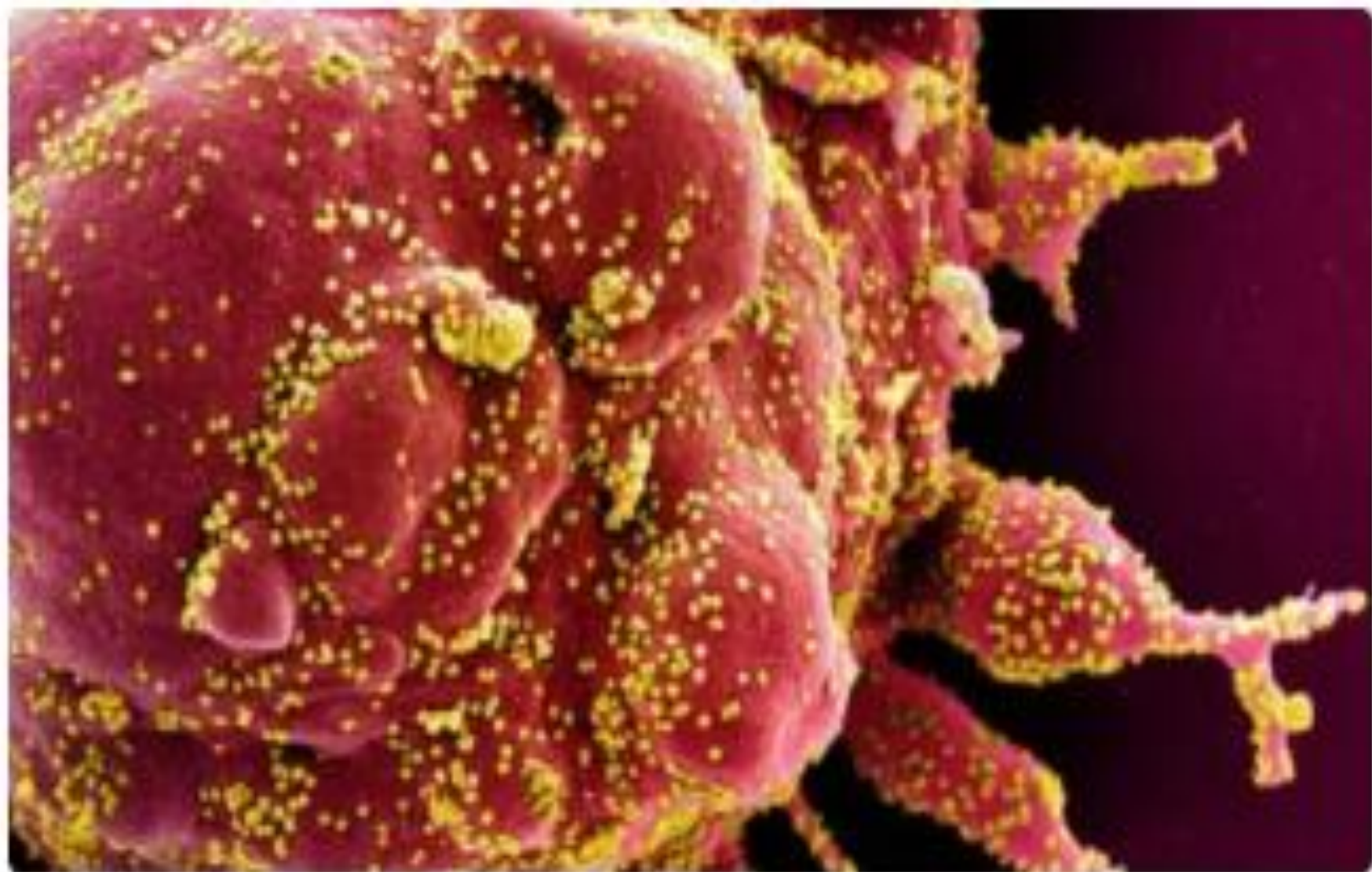


سُبْحَانَكَ اللَّهُمَّ رَبَّ السَّمَاوَاتِ السَّبْعِ وَالْأَرْضِ وَالْمَرْجِ وَالْحَمْدُ لَكَ يَا حَيُّ يَا قَيُّوْمُ

A 3D rendering of a COVID-19 virus particle, showing its characteristic spherical shape with a grey, textured surface and numerous red, crown-like spikes protruding from it. The text "COVID-19" is overlaid in large, white, bold, sans-serif capital letters across the center of the virus. The background is a solid black color.

COVID-19



تجویز منطقی آنتی بیوتیک در بیماران سرپایی مبتلا به COVID-19

F. MANSOURI

1399/6/13

COVID-19 presents antibiotic stewardship with challenges

- In the months since the novel coronavirus emerged in China and began spreading around the globe,
 - reports of bacterial co-infections
 - and widespread antibiotic use in COVID-19 patients has prompted concerns that
 - ✓ the unprecedented viral pandemic,
 - ✓ on top of the devastation it has already caused,
 - could have the downstream effect of
 - diminishing antibiotic supplies and further
 - fueling rates of antibiotic resistance.

COVID-19 presents antibiotic stewardship with challenges

- Even though COVID-19 is caused by a virus—SARS-CoV-2—and antibiotics should have no effect on it,
 - those concerns aren't unfounded .

COVID-19 presents antibiotic stewardship with challenges

- Even though COVID-19 is caused by a virus—SARS-CoV-2—and antibiotics should have no effect on it,
 - those concerns aren't unfounded .

COVID-19 presents antibiotic stewardship with challenges

- Clinicians have frequently had to resort to antibiotics for COVID-19 patients because of
 - clinical uncertainty,
 - the risk of secondary bacterial infections in patients with underlying conditions
 - and lengthy hospitalizations,
 - and most of all, **a lack of any other proven treatment.**

COVID-19 presents antibiotic stewardship with challenges

- To date, the picture on antibiotic use in COVID-19 patients is
 - incomplete
 - but worrisome.
- An early study from Wuhan, China, where the pandemic originated, indicated nearly all hospitalized patients were receiving antibiotics.

COVID-19 presents antibiotic stewardship with challenges

- A [recent review](#) of COVID-19 studies published since the pandemic began found that
 - while only 8% of COVID-19 patients had documented bacterial co-infections,
 - 72% had received antibiotic therapy.

COVID-19 presents antibiotic stewardship with challenges

- **"I think the hardest thing to do as a doctor is nothing, even if nothing is the right answer,"** says Valerie Vaughn, MD, a hospitalist at the University of Michigan's academic medical center, also in Ann Arbor.

Data will aid stewardship going forward

- For Debbie Goff, PharmD, a pharmacist who specializes in infectious diseases and antibiotic stewardship at The Ohio State University Wexner Medical Center in Columbus,
the amount of antibiotic prescribing occurring in COVID-19 patients
 - **is understandable**
 - **but frustrating.**

**What is the evidence for
using macrolide antibiotics
to treat COVID-19?**

What is the evidence for using macrolide antibiotics to treat COVID-19?

What is the evidence for using macrolide antibiotics to treat COVID-19?



There is currently insufficient evidence to recommend treatment with macrolide antibiotics for COVID-19, alone or combined with hydroxychloroquine, outside of research. There remains potential for harm. Clinicians may wish to use macrolides to treat a bacterial super-infection that has complicated COVID-19

#EvidenceCOVID

Kome Gbinigie and Kerstin Frie
28th April 2020

What is the evidence for using macrolide antibiotics to treat COVID-19?

- **VERDICT**

- We identified three studies, two *in vitro* and one *in vivo*, assessing the use of macrolide antibiotics for the treatment of COVID-19.
- Each of these studies assessed treatment with azithromycin.
- The evidence from the *in vivo* study and one *in vitro* study
 - suggest a **possible synergy** between azithromycin and hydroxychloroquine.

What is the evidence for using macrolide antibiotics to treat COVID-19?

- However, the *in vivo* study
 - had a small number of participants
 - and was methodologically flawed; the findings must therefore be treated with caution.

What is the evidence for using macrolide antibiotics to treat COVID-19?

- The two *in vitro* studies provided conflicting results regarding the activity of azithromycin alone against SARS-CoV-2;
 - one found that **azithromycin** alone had activity against the virus,
 - whilst the other found anti-SARS-CoV-2 activity only when **azithromycin** was combined with **hydroxychloroquine**.

What is the evidence for using macrolide antibiotics to treat COVID-19?

- At present, **there is insufficient evidence** to recommend treatment with macrolides,
 - alone
 - or combined with hydroxychloroquine, for COVID-19 outside of research.
- Both **macrolide antibiotics** and **hydroxychloroquine** can **increase the QT interval**;
 - combining these drugs may therefore result in cardiovascular harms.

What is the evidence for using macrolide antibiotics to treat COVID-19?

- Clinicians may wish to use macrolide antibiotics to treat a bacterial super-infection that has complicated COVID-19,
 - in line with **local/national** treatment protocols.

> [JAMA](#). 2020 May 11;323(24):2493-2502. doi: 10.1001/jama.2020.8630. Online ahead of print.

Association of Treatment With Hydroxychloroquine or Azithromycin With In-Hospital Mortality in Patients With COVID-19 in New York State

Eli S Rosenberg ¹, Elizabeth M Dufort ², Tomoko Udo ¹, Larissa A Wilberschied ², Jessica Kumar ², James Tesoriero ², Patti Weinberg ³, James Kirkwood ², Alison Muse ², Jack DeHovitz ³ ⁴, Debra S Blog ², Brad Hutton ², David R Holtgrave ¹, Howard A Zucker ²

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PMID: 32392282 PMCID: [PMC7215635](#) DOI: [10.1001/jama.2020.8630](#)

[Free PMC article](#)

Abstract

- **Importance:**
- Hydroxychloroquine, with or without azithromycin, has been considered as a possible therapeutic agent for patients with coronavirus disease 2019 (COVID-19).
- However, there are limited data on efficacy and associated adverse events.
- **Objective:**
- To describe the association between use of hydroxychloroquine, with or without azithromycin, and clinical outcomes among hospital inpatients diagnosed with COVID-19.

- **Design, setting, and participants:**
- Retrospective multicenter cohort study of patients from a random sample of all admitted patients with laboratory-confirmed COVID-19 in **25 hospitals**, representing 88.2% of patients with COVID-19 in the New York metropolitan region.
- Eligible patients were admitted for at least 24 hours between March 15 and 28, 2020.
- Medications, preexisting conditions, clinical measures on admission, outcomes, and adverse events were abstracted from medical records.
- The date of final follow-up was April 24, 2020.

- **Exposures:**

- Receipt of both hydroxychloroquine and azithromycin,
- hydroxychloroquine alone,
- azithromycin alone,
- or neither.

- **Main outcomes and measures:**

- Primary outcome was in-hospital mortality.
- Secondary outcomes were cardiac arrest and abnormal electrocardiogram findings (arrhythmia or QT prolongation).

- **Results:**

- Among **1438 hospitalized patients** with a diagnosis of COVID-19 (858 [59.7%] male, median age, 63 years), those receiving hydroxychloroquine, azithromycin, or both were more likely than those not receiving either drug to have diabetes, respiratory rate >22/min, abnormal chest imaging findings, O₂ saturation lower than 90%, and aspartate aminotransferase greater than 40 U/L.

- Overall in-hospital mortality was 20.3% (95% CI, 18.2%-22.4%).
- **The probability of death** for patients receiving
 - **hydroxychloroquine + azithromycin** was 189/735 (**25.7%** [95% CI, 22.3%-28.9%]),
 - **hydroxychloroquine alone**, 54/271 (**19.9%** [95% CI, 15.2%-24.7%]),
 - **azithromycin alone**, 21/211 (**10.0%** [95% CI, 5.9%-14.0%]),
 - and **neither drug**, 28/221 (**12.7%** [95% CI, 8.3%-17.1%]).

- **Conclusions and relevance:**

- Among patients hospitalized in metropolitan New York with COVID-19, treatment with

- **hydroxychloroquine,**

- **azithromycin,**

- **or both,**

- **compared with neither treatment,**

- was not significantly associated with differences in**

- hospital mortality.**

- However, the interpretation of these findings may be limited by the observational design.

Review

> [Int J Antimicrob Agents](#). 2020 Aug;56(2):106053.

doi: [10.1016/j.ijantimicag.2020.106053](https://doi.org/10.1016/j.ijantimicag.2020.106053). Epub 2020 Jun 10.

Macrolides and viral infections: focus on azithromycin in COVID-19 pathology

[Arianna Pani](#)¹, [Marinella Lauriola](#)², [Alessandra Romandini](#)¹, [Francesco Scaglione](#)³

Affiliations + expand

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[Free PMC article](#)

Abstract

- The emergence of the new COVID-19 virus is proving to be
➤ **a challenge in seeking effective therapies.**
- Since the most severe clinical manifestation of COVID-19 appears to be a **severe acute respiratory syndrome**, **azithromycin** has been proposed as a potential treatment.

Macrolides and viral infections: focus on azithromycin in COVID-19 pathology

- Azithromycin is known to have
 - ✓ immunomodulating
 - ✓ and antiviral properties.
- In vitro studies have demonstrated the capacity of azithromycin in reducing production of pro-inflammatory cytokines such as
 - IL-8, IL-6, TNF alpha,
 - reduce oxidative stress,
 - and modulate T-helper functions.

Macrolides and viral infections: focus on azithromycin in COVID-19 pathology

- At the same time there are multiple clinical evidences of the role of azithromycin in acute respiratory distress syndrome and against Middle East Respiratory syndrome (MERS).
- Some preliminary evidence has demonstrated controversial results regarding efficacy of azithromycin in combination with hydroxychloroquine in COVID-19.

- First, a French trial demonstrated 100% virological negativizing of six patients treated with
 - azithromycin plus hydroxychloroquine
 - vs. 57.1% of patients treated with only hydroxychloroquine
 - and 12.5% of the control group ($P < 0.05$).

- On the other hand, another case series revealed
 - **no efficacy at all on 11 patients treated with the same combination and doses.**
- Furthermore, there are some concerns regarding the association of azithromycin and hydroxychloroquine because of potential QT prolongation.
- In fact, both drugs have this as a potential side effect and evidence regarding the safe use of this combination is controversial.

ORIGINAL ARTICLE

Hydroxychloroquine with or without Azithromycin in Mild-to-Moderate Covid-19

A.B. Cavalcanti, F.G. Zampieri, R.G. Rosa, L.C.P. Azevedo, V.C. Veiga, A. Avezum, L.P. Damiani, A. Marcadenti, L. Kawano-Dourado, T. Lisboa, D.L.M. Junqueira, P.G.M. de Barros e Silva, L. Tramujas, E.O. Abreu-Silva, L.N. Laranjeira, A.T. Soares, L.S. Echenique, A.J. Pereira, F.G.R. Freitas, O.C.E. Gebara, V.C.S. Dantas, R.H.M. Furtado, E.P. Milan, N.A. Golin, F.F. Cardoso, I.S. Maia, C.R. Hoffmann Filho, A.P.M. Kormann, R.B. Amazonas, M.F. Bocchi de Oliveira, A. Serpa-Neto, M. Falavigna, R.D. Lopes, F.R. Machado, and O. Berwanger, for the Coalition Covid-19 Brazil I Investigators*

This article was published on July 23, 2020, at NEJM.org.

ABSTRACT

BACKGROUND

Hydroxychloroquine and azithromycin have been used to treat patients with coronavirus disease 2019 (Covid-19). However, evidence on the safety and efficacy of these therapies is limited.

METHODS

We conducted a multicenter, randomized, open-label, three-group, controlled trial involving hospitalized patients with suspected or confirmed Covid-19 who were receiving either no supplemental oxygen or a maximum of 4 liters per minute of supplemental oxygen. Patients were randomly assigned in a 1:1:1 ratio to receive standard care, standard care plus hydroxychloroquine at a dose of 400 mg twice daily, or standard care plus hydroxychloroquine at a dose of 400 mg twice daily plus azithromycin at a dose of 500 mg once daily for 7 days. The primary outcome was clinical status at 15 days as assessed with the use of a seven-level ordinal scale (with levels ranging from one to seven and higher scores indicating a worse condition) in the modified intention-to-treat population (patients with a confirmed diagnosis of Covid-19). Safety was also assessed.

RESULTS

A total of 667 patients underwent randomization; 504 patients had confirmed Covid-19 and were included in the modified intention-to-treat analysis. As compared with standard care, the proportional odds of having a higher score on the seven-point ordinal scale at 15 days was not affected by either hydroxychloroquine alone (odds ratio, 1.21; 95% confidence interval [CI], 0.69 to 2.11; $P=1.00$) or hydroxychloroquine plus azithromycin (odds ratio, 0.99; 95% CI, 0.57 to 1.73; $P=1.00$). Prolongation of the corrected QT interval and elevation of liver-enzyme levels were more frequent in patients receiving hydroxychloroquine, alone or with azithromycin, than in those who were not receiving either agent.

CONCLUSIONS

Among patients hospitalized with mild-to-moderate Covid-19, the use of hydroxychloroquine, alone or with azithromycin, did not improve clinical status at 15 days as compared with standard care. (Funded by the Coalition Covid-19 Brazil and EMS Pharma; ClinicalTrials.gov number, NCT04322123.)

WHO warns overuse of antibiotics for Covid-19 will cause more deaths

- The increased use of antibiotics to combat the Covid-19 pandemic will strengthen
 - **bacterial resistance** and
 - **ultimately lead to more deaths**during **the crisis** and **beyond**,
the World Health Organization (WHO)
has warned.

No, antibiotics do not work against viruses, only bacteria.

The new coronavirus (2019-nCoV) is a virus and, therefore, antibiotics should not be used as a means of prevention or treatment.

However, if you are hospitalized for the 2019-nCoV, you may receive antibiotics since bacterial co-infection is possible.



#Coronavirus

Are antibiotics effective in preventing and treating the new coronavirus?



Community Acquired Pneumonia	
Patient Population	Outpatient Antibiotic Regimen
Well-appearing patients with no comorbidities and no recent antibiotic use in an area without significant macrolide resistance	a macrolide ¹ (e.g., azithromycin 500 mg followed by 250 mg for four days; clarithromycin 500 mg BID) OR doxycycline ² (100 mg BID)
Well-appearing patients with no comorbidities and no recent antibiotic use in an area with significant macrolide resistance	a beta-lactam (e.g., amoxicillin 1 g TID; amoxicillin-clavulanate XR 2 g BID) plus a macrolide or doxycycline OR a respiratory fluoroquinolone (e.g., levofloxacin 750 mg daily)
Well-appearing patients with significant medical comorbidities ⁴ or with recent antibiotic use ⁵	a beta-lactam plus a macrolide or doxycycline OR a respiratory fluoroquinolone
1. Patients with a history of prolonged QTc interval should not receive macrolides. 2. Doxycycline is contraindicated for pregnant patients. 3. Fluoroquinolones may carry a higher risk for <i>Clostridium difficile</i> infection, and carry a black box warning for tendon rupture, although rare. 4. This includes COPD, DM, CHF, ESRD, alcoholism, liver failure, cancer or any other history of immunosuppression. Based on guidelines and recommendations from the ATS and IDSA. 5. Within the last 90 days.	

Activate Windows
Go to PC settings to activate Windows.

Critical drug shortages caused by COVID-19

Azithromycin

- There's currently a shortage of azithromycin tablets and injections, according to the FDA and ASHP.
- Azithromycin is indicated for treating a wide range of bacterial infections, but it's also been used in patients with respiratory infections because of its potential immunomodulatory effects.

Critical drug shortages caused by COVID-19

Azithromycin

- As noted above, azithromycin has been used in conjunction with hydroxychloroquine for treating COVID-19.
- Between February and March 2020, the number of patients who received both hydroxychloroquine and azithromycin prescriptions skyrocketed a staggering 1044%.



خسته نباشید