
بسم الله الرحمن الرحیم

Bacterial co-infection in COVID

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IUMS

Introduction

- Is it important?
- Prevalence?
- Our practice?

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Introduction

- In severe COVID-19 Lung pathology reflects
  - ✓ viral injury
  - ✓ Immune-mediated injury
  - ✓ Bacterial superinfection
- Bacterial coinfection increased SARS-CoV-2 patients
  - ✓ Hospital length of stay
  - ✓ Need for ventilatory support
  - ✓ ARDS
  - ✓ Shock
  - ✓ multi-organ injury
  - ✓ more severe COVID-19 disease

Conflict

- Overlap symptom
- Sampling is necessary
- Time of sampling
- Colonization or infection
- Sampling lead to infection spread
- Lack of enough accuracy
- Is it super infection or co infection?

Introduction

- Limited information exists about the frequency and microbiology of pulmonary coinfections and superinfections in patients with COVID-19, such as hospital-acquired pneumonia (HAP) and ventilator associated pneumonia (VAP).

- Some studies from China emphasize the lack of bacterial coinfections in patients with COVID-19, while other studies suggest that these patients experience frequent bacterial complications.

Introduction

- There is appropriate concern about performing pulmonary diagnostic procedures such as bronchoscopy or other airway sampling procedures that require disruption of a closed airway circuit in patients with COVID-19.

- Thus, while some clinicians do not routinely start empiric broad-spectrum antimicrobial therapy for patients with severe COVID-19 disease, other experienced clinicians routinely use such therapy.

NIH

- However, empiric broad-spectrum antimicrobial therapy is the standard of care for the treatment of shock.

But :

- Antibiotic stewardship is critical to avoid reflexive or continued courses of antibiotics.

Incidence

pathogens

MDPI

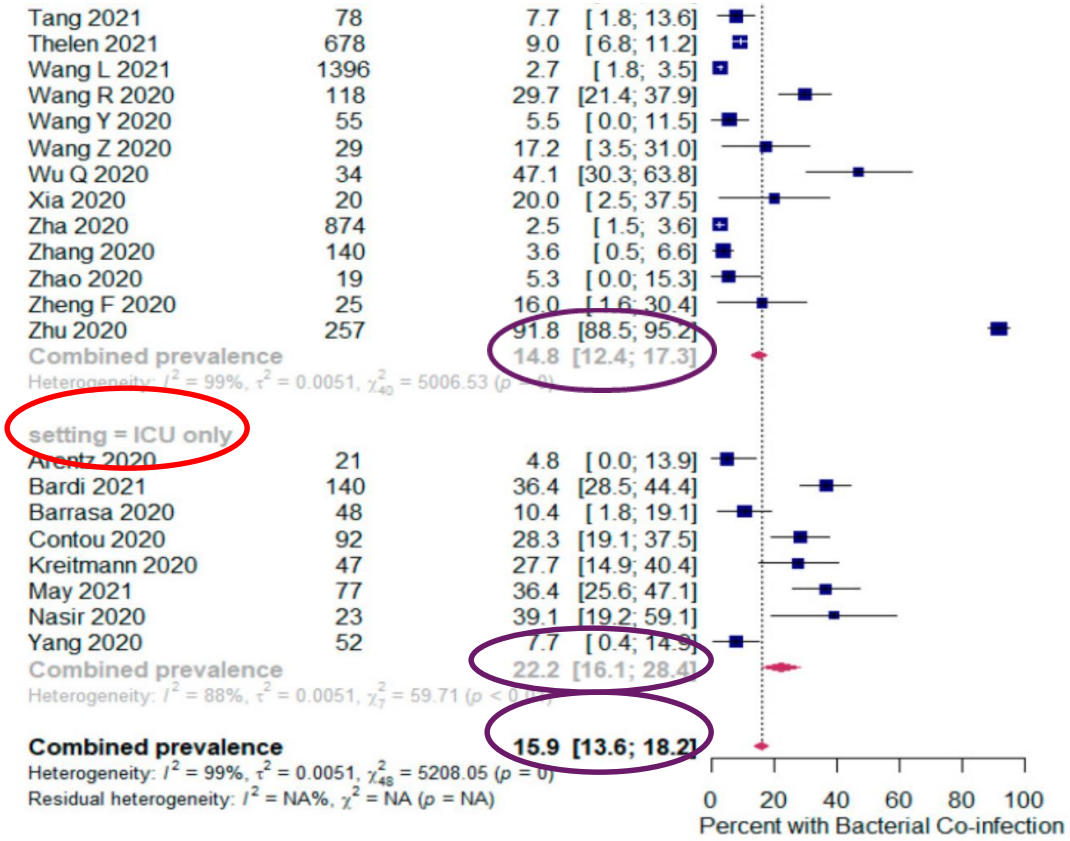
Systematic Review

Coinfections with Bacteria, Fungi, and Respiratory Viruses in Patients with SARS-CoV-2: A Systematic Review and Meta-Analysis

Saad Alhumaid [1,*], Abbas Al Mutair [2,3,4], Zainab Al Alawi [5], Abeer M. Alshawi [6], Salamah A. Alomran [6], Mohammed S. Almuhanna [7], Anwar A. Almuslim [7], Ahmed H. Bu Shafia [8], Abdullah M. Alotaibi [9], Gasmelseed Y. Ahmed [2], Ali A. Rabaan [10], Jaffar A. Al-Tawfiq [11,12,13] and Awad Al-Omari [14,15]

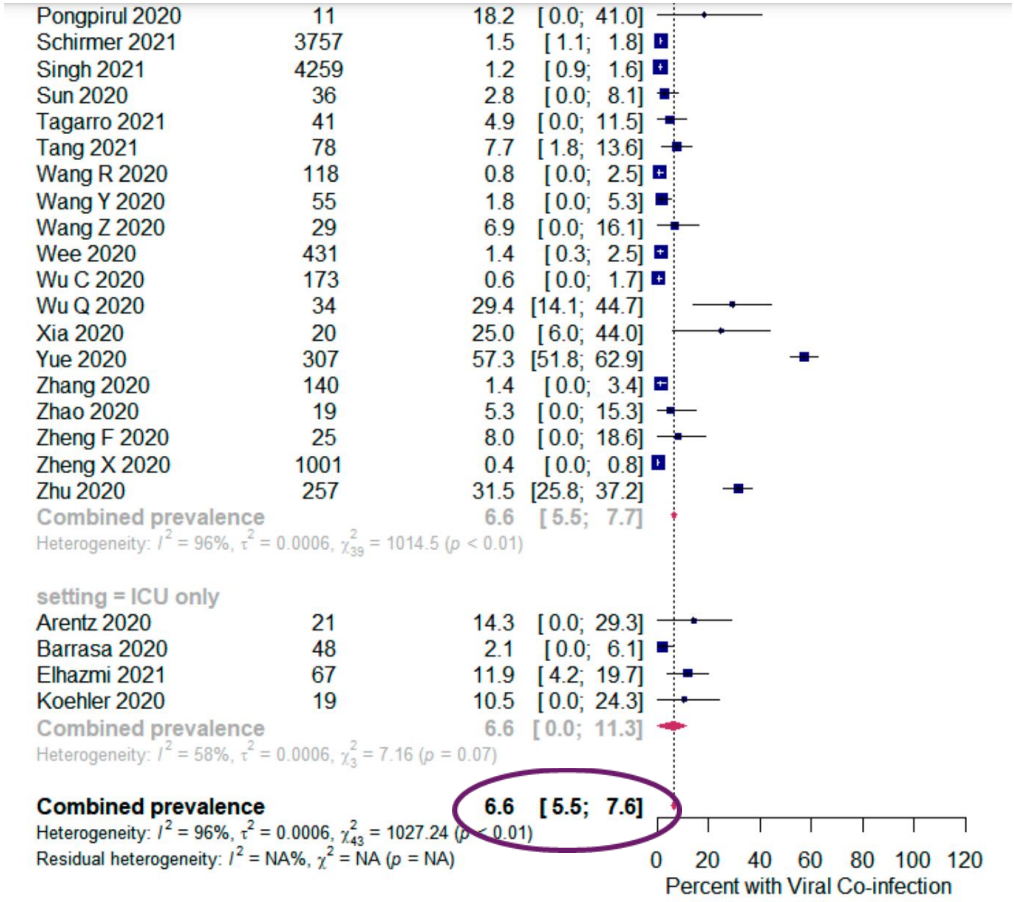
Pathogens **2021**, *10*, 809.

Prevalence of bacterial coinfection



Alhumaid, S: Pathogens2021, 10 ,809

Viral co infection



Alhumaid, S: Pathogens2021, 10 ,809

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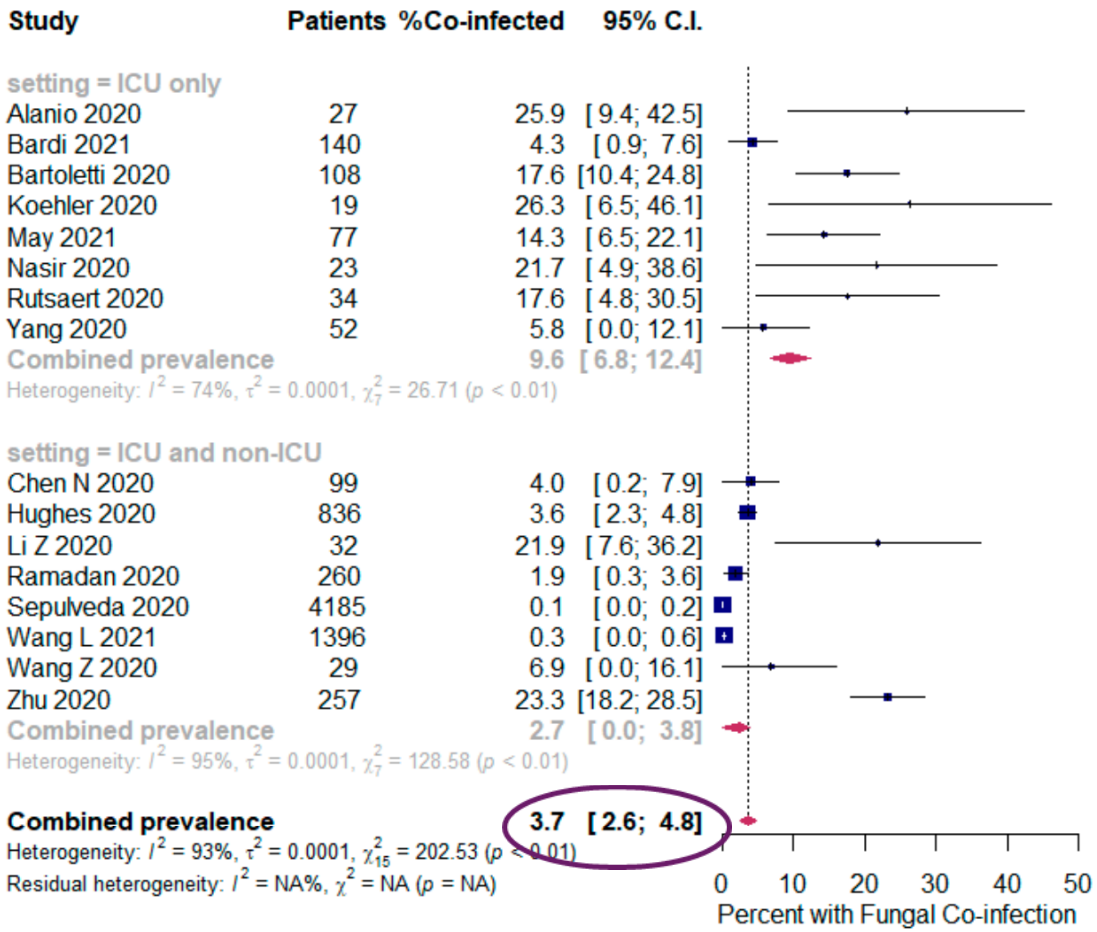
Fungal co infection



Alhumaid, S: Pathogens2021, 10 ,809

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Co-infection

- Seventy-eight studies reported data on specific organisms associated with co-infection or superinfection in COVID-19 patients

- Bacterial Co-infections:
  - ✓ *Klebsiella pneumonia* (9.9%)
  - ✓ *Streptococcus pneumonia* (8.2%)
  - ✓ *Staphylococcus aureus* (7.7%)

- Virus co-infections:
  - ✓ influenza type A (22.3%)
  - ✓ influenza type B (3.8%)
  - ✓ respiratory syncytial virus (3.8)

Alhumaid, S: Pathogens2021, 10 ,809

Superinfections

- Bacteria
  - ✓ *Acinetobacter spp*. (22.0%)
  - ✓ *Pseudomonas* (10.8%)
  - ✓ *Escherichia coli* (6.9%)
- Viruses
  - ✓ Rhinovirus
- Fungi
  - ✓ *Candida sp*. (18.8%).

Alhumaid, S: Pathogens2021, 10 ,809

Prevalence of pathogens

Pathogen type	Co-infection (N = 1910) No. (%)	Superinfection (N = 480) No. (%)
Bacteria		
Staphylococcus aureus	148 (7.7)	13 (2.7)
Haemophilus influenza	127 (6.6)	6 (1.3)
Mycoplasma pneumoniae	82 (4.3)	6 (1.3)
Acinetobacter spps	78 (4.1)	107 (22.3)
Escherichia coli	73 (3.8)	33 (6.9)
Stenotrophomonas maltophilia	10 (0.5)	18 (3.8)
Klebsiella pneumoniae	189 (9.9)	28 (5.8)
Streptococcus pneumoniae	156 (8.2)	4 (0.8)
Chlamydia pneumoniae	29 (1.5)	0 (0)
Bordetella	3 (0.2)	0 (0)
Moraxella catarrhalis	32 (1.7)	2 (0.4)
Pseudomonas	67 (3.5)	52 (10.8)
Enterococcus faecium	14 (0.7)	22 (4.6)
Viruses		
Non-SARS-CoV-2[a] coronavirus strains	38 (2.0)	9 (1.9)
Human influenza A	426 (22.3)	0 (0)
Human influenza *B*	73 (3.8)	0 (0)
Respiratory syncytial virus	72 (3.8)	2 (0.4)
Parainfluenza	17 (0.9)	0 (0)
Human metapneumovirus	20 (1.0)	9 (1.9)
Rhinovirus	68 (3.6)	11 (2.3)
Adenovirus	35 (1.8)	2 (0.4)
Fungi		
Mucor	6 (0.3)	1 (0.2)
Candida spp.	19 (1.0)	90 (18.8)
Aspergillus	128 (6.7)	65 (13.5)

Alhumaid, S: Pathogens2021, 10 ,809

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Risk factor

Viruses can facilitate the attachment and colonization of the bacteria in the respiratory tract

- Older Age
- Obesity
- Cancer
- kidney disease

Other factors:

- ✓ ICU type
- ✓ Used equipment rate
- ✓ Admission or discharge criteria
- ✓ High workload or nurse ratio


RISK FACTOR


16


Radix
RADIX AL
HAND ANTISEPTIC

Laboratory

- Laboratory abnormalities that have been described in SARS-CoV-2 patients with bacterial and respiratory viral coinfections:

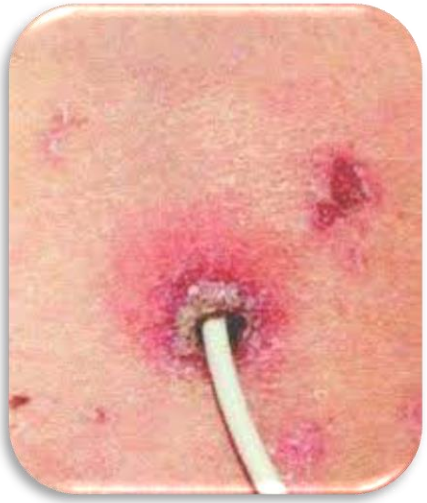
  - ✓ Procalcitonin
  - ✓ D-dimer
  - ✓ WBC
  - ✓ LDH

Timing

- The data on the timing of the occurrence of co-infection was variable.
- The occurrence of co-infections has a median time of 4–11.5 days (IQR 2–42) of ICU admission
- Bacterial co-infection was infrequent within 2–4 days of hospital admission

site of infection

- Pneumonia
- Bacteremia
- Catheter induced
- UTI
- Sinusitis



retrospective cohort study in a UK secondary-care setting

Table 1
Characteristics and microbiologic investigations on SARS-CoV-2 cohort and comparator influenza A/B cohort, London 2020

Characteristic	SARS-CoV-2 ($n = 836$)	Influenza A/B ($n = 216$)	p
Date range of study	25/2/20–30/4/20	1/9/19–30/4/20	
Age (years), median (interquartile range)	69 (55–81)	36 (22–65)	<0.0001
Gender			
Male	519 (62)	91 (42)	<0.0001
Female	317 (38)	125 (58)	<0.0001
Microbiologic investigations undertaken			
Blood culture	643 (77)	141 (65)	0.0006
Respiratory (sputum)	110 (13)	38 (18)	0.1185
Respiratory (BAL)	13 (2)	—	0.1340
Pneumococcal urinary antigen	249 (30)	19 (9)	<0.0001
Legionella urinary antigen	246 (29)	21 (10)	<0.0001
Respiratory viruses (influenza A/B, RSV)	250 (30)[a]	—	NA

S. Hughes et al. Clinical Microbiology and Infection 26 (2020)

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retrospective cohort study in a UK secondary-care setting

Microbiologic culture results from SARS-CoV-2 cohort and comparator influenza A/B cohort, London, 2020

Characteristic	SARS-CoV-2 ($n = 836$)	Influenza A/B ($n = 216$)
Blood culture results, respiratory source		
Enterobacterales (CA/HCAI)	1/1	—
Streptococcus spp.[a]	—	1
Staphylococcus aureus (CA/HCAI)	—	1/0
Blood culture results, nonrespiratory source		
Coagulase-negative staphylococci	36	6
Enterobacterales (CA/HCAI)	5/1	—
Streptococcus spp.[a]	4/0	—
Staphylococcus aureus (CA/HCAI)	1/0	—
Enterococcus spp. (CA/HCAI)	1/3	—
Candida albicans (CA/HCAI)	0/3	
Pseudomonas aeruginosa	0/1	
Other	5[b]	—
Blood cultures, no growth	583	133
Respiratory culture results		
No growth	64	22
S. aureus (CA/HCAI)	4/2	—
Pseudomonas spp. (CA/HCAI)	3/9	0/4
Enterobacter spp. (CA/HCAI)	2/3	—
Klebsiella spp. (CA/HCAI)	2/4	—
Serratia spp. (CA/HCAI)	1/1	1/0
Candida spp./yeast (CA/HCAI)	10/14	0/7
Aspergillus spp. (CA/HCAI)	1/2	0/1
Other pathogens		
CA (n)	*Haemophilus influenzae* (1)	*Moraxella* spp. (1), *Streptococcus pneumoniae* (2)
HCAI (n)	*Hafnia* spp. (1), *Morganella* spp. (1), *Providencia* spp. (1), *Stenotrophomonas maltophilia* (2)	—
Pneumococcal antigen (detected/tested)	0/249	1/19
Legionella antigen (detected/tested)	0/246	0/21
Influenza A/B, RSV (detected/tested)	0/250	—

S. Hughes et al. Clinical Microbiology and Infection 26 (2020)

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Antibiotic

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Empiric Antimicrobials in Critically Ill Patients

C

There are inadequate data regarding the use of empiric antibacterial agents in patients with severe COVID-19. Cohort studies...

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Empiric Antibacterial Therapy and Community-onset Bacterial Coinfection in Patients Hospitalized With Coronavirus Disease 2019 (COVID-19)

Recently moved from Do

WHO | CDC | SCCM | ESICM | IDSA

NIH | UCSF | BWH | AIIMS

Empiric Antimicrobials in Non-Critically Ill Patients

C

There are inadequate data regarding the use of empiric antibacterial agents in patients with mild or moderate COVID-19. Most...

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Bacterial Co-Infection and Secondary Infection in Patients with COVID-19 (CIMI July 2020)

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Empiric Broad-Spectrum Antimicrobial Therapy

Recommendations

- In patients with severe or critical COVID-19, there is insufficient evidence for the Panel to recommend either for or against empiric broad-spectrum antimicrobial therapy in the absence of another indication.
- If antimicrobials are initiated, the Panel recommends that their use should be reassessed daily to minimize the adverse consequences of unnecessary antimicrobial therapy **(AIII)**.

Rationale

At this time, there are no reliable estimates of the incidence or prevalence of copathogens with SARS-CoV-2.

Some experts routinely administer broad-spectrum antibiotics as empiric therapy for bacterial pneumonia to all patients with COVID-19 and moderate or severe hypoxemia. Other experts administer antibiotics only for specific situations, such as the presence of a lobar infiltrate on a chest X-ray, leukocytosis, an elevated serum lactate level, microbiologic data, or shock.

CDC

Drugs and Investigational Therapies

Are empiric antibiotics recommended for patients suspected of having COVID-19?

Several patients with COVID-19 have been reported to present with concurrent community-acquired bacterial pneumonia. Decisions to administer antibiotics to COVID-19 patients should be based on the likelihood of bacterial infection (community-acquired or hospital-acquired), illness severity, and antimicrobial stewardship issues. For more information, see Diagnosis and

Spanish study

- Administer empiric antibiotic therapy solely to patients who were admitted for COVID-19 and who presented with
  1. chest X-ray suggestive of bacterial infection or
  2. need for direct ICU admission or
  3. severe immunocompromised condition.

- Our results support the avoidance of antibiotic therapy in most patients hospitalized for COVID-19

C. Garcia-Vidal et al. / Clinical Microbiology and Infection 27 (2021)

Spanish study

Main characteristic of patients hospitalized for COVID-19 for ≥48 hours

Characteristic	No infection (n = 917)	Community-acquired co-infection (n = 31)		Hospital-acquired superinfection (n = 43)	
		Value	p[a]	Value	p[b]
Age (years)	61 (48–74)	63 (54.5–74)	0.671	67 (55.75–74.25)	0.006
Male sex	510 (55.6)	18 (58.1)	0.956	26 (60.5)	0.822
Comorbidities					
Hypertension	167 (18.2)	7 (22.6)	0.537	7 (16.3)	0.748
Diabetes mellitus	89 (9.7)	7 (22.6)	0.019	7 (16.3)	0.160
Chronic heart disease	122 (13.3)	9 (29)	0.013	7 (16.3)	0.576
Chronic lung disease	95 (10.4)	6 (19.4)	0.110	7 (16.3)	0.218
Chronic renal disease	47 (5.1)	8 (25.8)	<0.001	6 (14)	0.013
Cancer	77 (8.4)	1 (3.2)	0.259	8 (18.6)	0.021
Inflammatory markers at onset					
C-reactive protein	7.06 (3.31–13.29)	6.76 (3.20–9.79)	0.714	11.78 (5.55–17.87)	0.012
Ferritin	544 (249.5–1100)	208 (154–431.5)	0.042	797 (296–1743)	0.575
Lymphocyte count	0.9 (0.6–1.2)	0.8 (0.6–1.1)	0.892	0.783 (0.5–1.1)	0.088
Lactate dehydrogenase	287 (233–372)	264 (221–377.5)	0.477	311.5 (247.5–471–8)	0.193
Treatment at onset					
Lopinavir/ritonavir	732 (79.8)	27 (87.1)	0.227	35 (81.4)	0.802
Hydroxychloroquine	799 (87.1)	29 (93.5)	0.225	40 (93)	0.186
Azithromycin	751 (81.9)	26 (83.9)	0.779	36 (83.7)	0.761
Remdesivir	39 (4.3)	0 (0)	0.226	2 (4.7)	0.559
Ceftriaxone	528 (57.6)	24 (77.4)	0.028	32 (74.4)	0.029
Ceftaroline	26 (2.8)	2 (6.5)	0.232	5 (11.6)	0.001
Immunomodulatory treatment					
Tocilizumab	200 (21.8)	5 (16.1)	0.450	16 (37.2)	0.018
Methylprednisolone	238 (26)	9 (29)	0.701	25 (58.1)	<0.001
Dexamethasone	23 (2.5)	4 (12.9)	0.01	8 (18.6)	<0.001
Length of hospital stay	9 (5–15)	8 (4.5–11.5)	0.565	20 (11–27.75)	<0.001
ICU admission	109 (11.9)	8 (25.8)	0.02	29 (67.4)	<0.001
Length of ICU admission	3 (1–10)	3 (0–9)	0.888	5 (0.5–20)	0.095
Death	86 (9.4)	5 (16.1)	0.21	8 (18.6)	0.047

C. Garcia-Vidal et al. / Clinical Microbiology and Infection 27 (2021)

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Pt age, sex	Admit from	Med risk factors	Prior hosp[a]antibx[b]	Organism	Resistance acquired	Episode type and number[c]	Days post-adm/intubation
49 M	Home	DM	No, No	Ps. a	Aztreonam	Late PNA	37/28
					Ceftazidime	third	
					pip/tazo		
60 F	Home	DM	No, No	Ps. a	Imipenem	Late PNA	39/38
		fmr smoker				second	
73 F	Home	CVA	No, Yes	Ps. a	Aztreonam	Late PNA	23/20
		endomet CA	(amox/clav)		ticar/clav	second	
					meropenem		
75 M	NH	asthma	Yes, No	MSSA	Replaced by MRSA	Late PNA	12/12
		dementia				first	
		aspiration					
		EtOH abuse					
74 M	Home	OSA	No, No	Ps. a	ticar/clav	Late PNA	45/40
		AVMs				first	
74 F	Home	fmr smoker	No, Yes	Ps. a	Ceftazidime	Late PNA	11/10
			(oseltam)		then carba	first	
54 M	Home	DM	No, Yes	MSSA	Replaced by MRSA	Late PNA	23/20
		fmr smoker	(azithro)			second	
66 F	Home	OSA	No, No	Ps. a	ticar/clav	Late PNA	30/27
		seizures			then aztreo	first	
		inter lung dis			pip/tazo		
60 M	Home	DM	No, No	Enter a	Aztreonam	Late PNA	58/54

C. Garcia-Vidal et al. / Clinical Microbiology and Infection 27 (2021)

United state

Based on our findings in severe COVID-19 pneumonia, we recommend:

- Empiric antibacterial should be used sparingly in patients presenting
  - ✓ without sputum production and
  - ✓ with a radiographic ground glass interstitial pattern suggestive of viral etiology

- consider discontinuation of empiric antibiotics after 48 h in patients *without sputum* to culture despite adequate access or who have no growth or “normal flora/yeast

Liu HH, Ann Clin Microbiol Antimicrob. 2021 Sep 25

United state

- With longer duration of hospitalisation, sputum cultures increasingly reflect hospital-acquired microbial flora so length of stay and “clinical trajectory” are critical in deciding to use antibiotics and selection of agents

- Culture results, antibiotic use, and clinical outcomes in COVID-19 patients should be reviewed periodically with changes guided by principles of antimicrobial stewardship.

Liu HH, Ann Clin Microbiol Antimicrob. 2021 Sep 25

Antibiotic as a treatment of COVID

- The use of antibiotics follows the intention-to-treat the viral disease and not primarily to treat bacterial co-infections of individuals with COVID-19

Review > Cochrane Database Syst Rev. 2021 Oct 22;10(10):CD015025.
doi: 10.1002/14651858.CD015025.

Antibiotics for the treatment of COVID-19

Maria Popp [1], Miriam Stegemann [2], Manuel Riemer [1], Maria-Inti Metzendorf [3], Carolina S Romero [4], Agata Mikolajewska [2], Peter Kranke [1], Patrick Meybohm [1], Nicole Skoetz [5], Stephanie Weibel [1]

Affiliations + expand

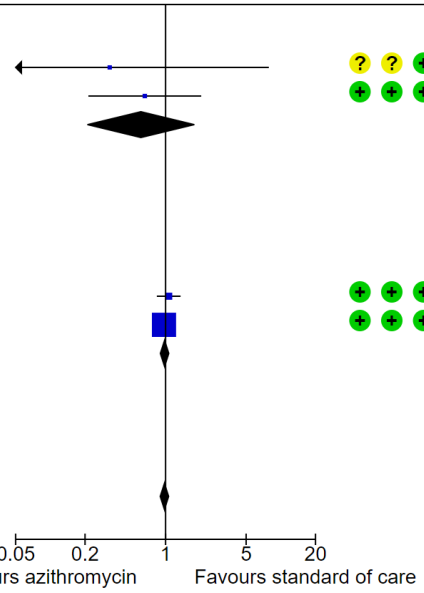
PMID: 34679203 PMCID: PMC8536098 (available on 2022-10-22)
DOI: 10.1002/14651858.CD015025

Abstract

Background: The effect of antibiotics with potential antiviral and anti-inflammatory properties are being investigated in clinical trials as treatment for COVID-19. The use of antibiotics follows the intention-to-treat the viral disease and not primarily to treat bacterial co-infections of individuals with COVID-19. A thorough understanding of the current evidence regarding effectiveness and safety of antibiotics as anti-viral treatments for COVID-19 based on randomised controlled trials (RCTs) is required.

Antibiotic as a treatment of COVID

Study or Subgroup	Azithromycin Events	Total	Standard of care Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
1.1.1 Moderate disease (WHO 4 to 5)						
Sekhavati 2020 (1)	0	56	1	55	0.1%	0.33 [0.01 , 7.87]
Cavalcanti 2020 (2)	5	172	7	159	0.5%	0.66 [0.21 , 2.04]
Subtotal (95% CI)		**228**		**214**	**0.6%**	**0.61 [0.21 , 1.77]**
Total events:	5		8			
Heterogeneity: Tau² = 0.00; Chi² = 0.17, df = 1 (P = 0.68); I² = 0%						
Test for overall effect: Z = 0.91 (P = 0.36)						
1.1.2 Moderate to severe disease (WHO 4 to 9)						
Furtado 2020 (3)	90	212	73	183	12.3%	1.06 [0.84 , 1.35]
RECOVERY 2021 (4)	561	2582	1162	5181	87.1%	0.97 [0.89 , 1.06]
Subtotal (95% CI)		**2794**		**5364**	**99.4%**	**0.98 [0.90 , 1.07]**
Total events:	651		1235			
Heterogeneity: Tau² = 0.00; Chi² = 0.53, df = 1 (P = 0.47); I² = 0%						
Test for overall effect: Z = 0.47 (P = 0.64)						
Total (95% CI)		**3022**		**5578**	**100.0%**	**0.98 [0.90 , 1.06]**
Total events:	656		1243			
Heterogeneity: Tau² = 0.00; Chi² = 1.46, df = 3 (P = 0.69); I² = 0%						
Test for overall effect: Z = 0.54 (P = 0.59)						
Test for subgroup differences: Chi² = 0.76, df = 1 (P = 0.38), I² = 0%						



inpatients with confirmed moderate to severe COVID-19

All-cause mortality at day 28

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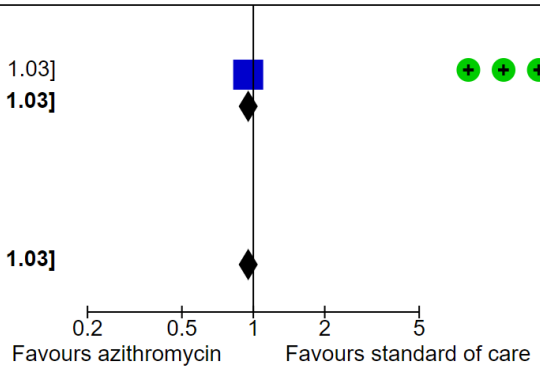
Antibiotic as a treatment of COVID

Study or Subgroup	Azithromycin Events	Azithromycin Total	Standard of care Events	Standard of care Total	Weight	Risk Ratio M-H, Random, 95% CI
1.2.1 Moderate to severe disease (WHO 4-9)						
RECOVERY 2021 (1)	603	2430	1273	4881	100.0%	0.95 [0.87 , 1.03]
Subtotal (95% CI)		**2430**		**4881**	**100.0%**	**0.95 [0.87 , 1.03]**
Total events:	603		1273			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.16 (P = 0.24)						
Total (95% CI)		**2430**		**4881**	**100.0%**	**0.95 [0.87 , 1.03]**
Total events:	603		1273			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.16 (P = 0.24)						
Test for subgroup differences: Not applicable						



Worsening of clinical status: participants with clinical deterioration (new need for invasive mechanical ventilation) or death at day 28

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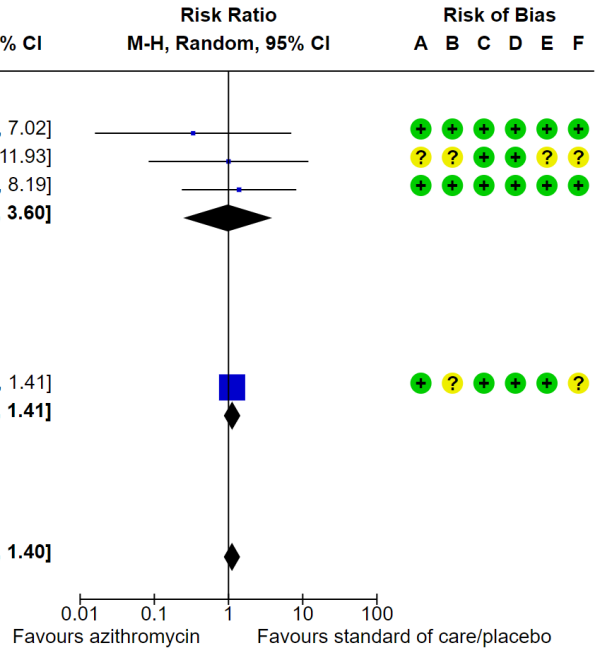
Antibiotic as a treatment of COVID

Study or Subgroup	Azithromycin Events	Azithromycin Total	Standard of care/placebo Events	Standard of care/placebo Total	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 Moderate disease (WHO 4-5)						
CJWT629A12301 (1)	0	7	1	7	0.6%	0.33 [0.02 , 7.02]
NCT04335552 (2)	1	5	1	5	0.8%	1.00 [0.08 , 11.93]
Cavalcanti 2020 (3)	3	172	2	159	1.6%	1.39 [0.23 , 8.19]
Subtotal (95% CI)		**184**		**171**	**3.0%**	**0.98 [0.26 , 3.60]**
Total events:	4		4			
Heterogeneity: Tau² = 0.00; Chi² = 0.63, df = 2 (P = 0.73); I² = 0%						
Test for overall effect: Z = 0.04 (P = 0.97)						
1.4.2 Moderate to severe disease (WHO 4-9)						
Furtado 2020 (4)	102	241	75	198	97.0%	1.12 [0.89 , 1.41]
Subtotal (95% CI)		**241**		**198**	**97.0%**	**1.12 [0.89 , 1.41]**
Total events:	102		75			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.94 (P = 0.35)						
Total (95% CI)		**425**		**369**	**100.0%**	**1.11 [0.89 , 1.40]**
Total events:	106		79			
Heterogeneity: Tau² = 0.00; Chi² = 0.67, df = 3 (P = 0.88); I² = 0%						
Test for overall effect: Z = 0.92 (P = 0.36)						
Test for subgroup differences: Chi² = 0.04, df = 1 (P = 0.84), I² = 0%						



Serious adverse events during the study period, defined as number of participants with any event

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Conclusion

- Incidence 15%
- Avoid from empiric treatment in typical pt
- Discontinue AB asap