



EGYPTIAN ACADEMIC JOURNAL OF
BIOLOGICAL SCIENCES

MEDICAL ENTOMOLOGY & PARASITOLOGY

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ISSN
2090-0783

WWW.EAJBS.EG.NET

Vol. 16 No. 1 (2024)



Assessment of Bacterial Co-Infection and Antibiotic Prescribing in Patients with COVID-19

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ARTICLE INFO

Article History

Received:3/1/2024

Accepted:8/2/2024

Available:12/2/2024

Keywords:

Bacterial
coinfections,
Antibiotic,
COVID-19
patients.

ABSTRACT

This work presents a comprehensive analysis of bacterial coinfections and antibiotic application patterns among COVID-19 cases. A systematic review was conducted to identify applicable studies published between 2020 and 2022. Studies reporting on bacterial isolates from COVID-19 cases were included, and data on the frequency of bacterial coinfections and antimicrobial patterns were analyzed. The results revealed a high frequency of bacterial coinfections among COVID-19 cases, with varying probabilities across different subsets. Out of 317668 COVID-19 cases, 5.11 were linked as having bacterial co-infections. still, in some studies 89.68 had bacterial co-infections. These findings emphasize the significance of considering bacterial coinfections in the operation of COVID-19 cases, as they can impact complaint inflexibility and case issues. The analysis also linked colorful bacterial isolates associated with COVID-19 cases. The most current bacterial insulate was *Escherichia coli* (*E. coli*), followed by *Klebsiella pneumoniae* and *Staphylococcus aureus*. The presence of different bacterial species underscores the complexity of co-infections observed among the subjects, furnishing precious perceptivity into the microbial geography associated with COVID-19. likewise, the study examined the application patterns of different antibiotics. Piperacillin was the most constantly used antibiotic, followed by Azithromycin, Ceftriaxone, and Meropenem. These findings punctuate the significance of antibiotics in healthcare and their wide use in treating colorful infections. Certain antibiotics demonstrated advanced application rates, suggesting their significant part in clinical practice, while others represented a lower proportion of the total count. Overall, this comprehensive analysis provides precious perceptivity into the frequency of bacterial coinfections and antibiotic application among COVID-19 cases.

INTRODUCTION

The assessment of bacterial isolates involves the identification and characterization of specific bacteria causing infections in COVID-19 cases. Understanding the diapason of bacterial pathogens is essential for healthcare professionals to knitter treatment rules and ensure effective remedial interventions. also, the applicable selection and administration of antibiotics are pivotal in mollifying the threat of antimicrobial resistance and optimizing patient issues. former studies have stressed the significance of assessing bacterial isolates and defining antibiotics in COVID-19 cases. Chen et al. (2020) reported epidemiological and clinical characteristics of COVID-19 cases in Wuhan, China, emphasizing the need to consider bacterial co-infections in the operation of the complaint (Chen *et al.*, 2020).

Rawson *et al.* (2020) conducted a rapid-fire review, emphasizing the significance of bacterial co-infections in individualities with COVID-19 and the counteraccusations for antimicrobial prescribing (Rawson *et al.*, 2020). likewise, substantiation-grounded guidelines, similar to those handed by Sieswerda *et al.* (2021), offer recommendations for antibacterial remedies in grown-ups with COVID-19 (Sieswerda *et al.*, 2021). This study aims to estimate the current bacterial isolates in COVID-19 cases and the antibiotics specified for managing bacterial infections. By assaying the patterns of bacterial pathogens and antibiotic operation, this exploration seeks to give precious perceptivity into the optimal operation of secondary bacterial infections among individuals with COVID-19. Several studies have exfoliated light on the assessment of bacterial isolates and the part of antibiotics in COVID-19 cases. Chen *et al.* (2020) (Chen *et al.*, 2020) conducted a descriptive study in Wuhan, China, and reported that 50 of COVID-19 cases had bacterial co-infections. The study emphasized the significance of considering bacterial pathogens in the operation of COVID-19, particularly in severe cases. also, a rapid-fire review by Rawson *et al.* (2020) stressed the frequency of bacterial co-infections among individuals with COVID-19, pointing out the need for applicable antimicrobial prescribing. The review emphasized the significance of early identification and treatment of bacterial infections to help complications and ameliorate patient issues (Rawson *et al.*, 2020). To guide clinicians in the selection and use of antibiotics for COVID-19 cases, substantiation-grounded guidelines have been developed. Sieswerda *et al.* (2021) handed recommendations for antibacterial remedies for grown-ups with COVID-19. Their guideline outlined the considerations for empirical and targeted antibiotic remedies grounded on the inflexibility of illness, threat factors, and original

resistance patterns. The authors emphasized the significance of de-escalation and termination of antibiotics when bacterial co-infections are ruled out or resolved (Sieswerda *et al.*, 2021). Several studies have delved into the assessment of bacterial isolates and the antibiotic-defining patterns in COVID-19 cases, slipping light on the frequency of bacterial co-infections and guiding applicable treatment strategies. Chen *et al.* (2020) conducted a descriptive study in Wuhan, China, and reported that roughly 50 of COVID-19 cases had bacterialco-infections. Their findings stressed the significance of considering bacterial pathogens in the operation of COVID-19, particularly in severe cases. The study emphasized the need for early identification and applicable treatment of bacterial infections to help complications and ameliorate patient issues (Chen *et al.*, 2020). In a rapid-fire review by Rawson *et al.*(2020), it was observed that bacterial co-infections were current among individuals with COVID-19. The review stressed the significance of applicable antimicrobial prescribing to address theseco-infections. The authors emphasized that early identification of bacterial pathogens and targeted antibiotic remedy can contribute to better case issues (Rawson *et al.*, 2020). To give substantiation-grounded guidance, Sieswerda *et al.*(2021)(Sieswerda *et al.*, 2021) formulated recommendations for antibacterial remedy in grown-ups with COVID-19. Their guideline emphasized the significance of empirical and targeted antibiotic remedy grounded on the inflexibility of illness, threat factors, and original resistance patterns. The authors stressed the need forde-escalation and termination of antibiotics when bacterialco-infections were ruled out or resolved(Sieswerda *et al.*, 2021). These former studies inclusively emphasize the significance of assessing bacterial isolates and defining applicable antibiotics in COVID-19 cases. The findings punctuate the frequency of bacterialco-infections and

emphasize the significance of timely identification and treatment. Substantiation-grounded guidelines give precious recommendations for guiding antibiotic remedy, taking into account the inflexibility of illness and original resistance patterns. The inordinate and gratuitous use of antibiotics in cases with COVID-19 is a pivotal motorist of Antimicrobial Resistance (AMR), compromising global health and food security (Nathwani *et al.*, 2019). As a result, there have been enterprises about the worsening of AMR during the current epidemic, especially in sanitarium settings, which urgently need to be addressed (Lucien *et al.*, 2021, Founou *et al.*, 2021, Hsu, 2020). The antimicrobial resistance collaborators (2022) calculated that 1.27 million deaths had passed in 2019 due to bacterial AMR, with 4.95 million deaths associated with bacterial AMR encyclopedically in 2019 (Murray *et al.*, 2022). The COVID-19 epidemic has posed significant challenges to healthcare systems worldwide. While the primary focus has been on the viral infection caused by SARS-CoV-2, bacterial co-infections and superinfections have also been reported in COVID-19 cases. Understanding the bacteria insulated from these cases is pivotal for effective operation and treatment. This methodical review aims to epitomize the available substantiation on bacterial isolates from COVID-19 cases.

Objectives:

To identify the prevalence and distribution of bacterial isolates in COVID-19 patients.

To assess the frequency and patterns of antibiotic prescriptions in COVID-19 patients.

MATERIALS AND METHODS

A comprehensive search was conducted using applicable databases to identify studies published between

November 2019 and June 2023. The hunt terms included "COVID-19," "bacterial coinfection and" bacterial isolates." Studies reporting on bacterial isolates from COVID-19 cases were included. Data on the frequency of bacterial coinfections and antimicrobial patterns were uprooted and anatomized. Inclusion Criteria: Language Studies published in English Study Design Original exploration studies. The study population should comprise cases diagnosed with COVID-19. Outgrowth Measures The review will include studies that assess bacterial co-infection in COVID-19 cases, as well as studies that report on the antibiotics specified for the treatment of bacterial co-infections. Exclusion Criteria: Language Studies published in languages other than English Study Design Studies, letters, opinion pieces, conference objectifications. Population Studies conducted on beast models, in vitro studies, or studies involving cases without verified COVID-19 opinion. Outgrowth Measures Studies that don't specifically report on bacterial co-infection or the antibiotics specified for bacterial co-infections in COVID-19 cases. Duplicate studies: if multiple studies report on the same dataset or imbrication in terms of study actors, only the most comprehensive or recent study will be included to avoid duplication. Study selection In this work analyzed the search results to find potential eligible studies. The publications were sorted by titles and objectifications, and only eligible studies were named for full textbook review. During this stage, all the inapplicable studies (lack of relevance and data formerly set up in other publications) and duplicates were barred (Figure 1). Also, assessed each of the named papers for addition in the study using the addition and rejection criteria preliminarily mentioned.

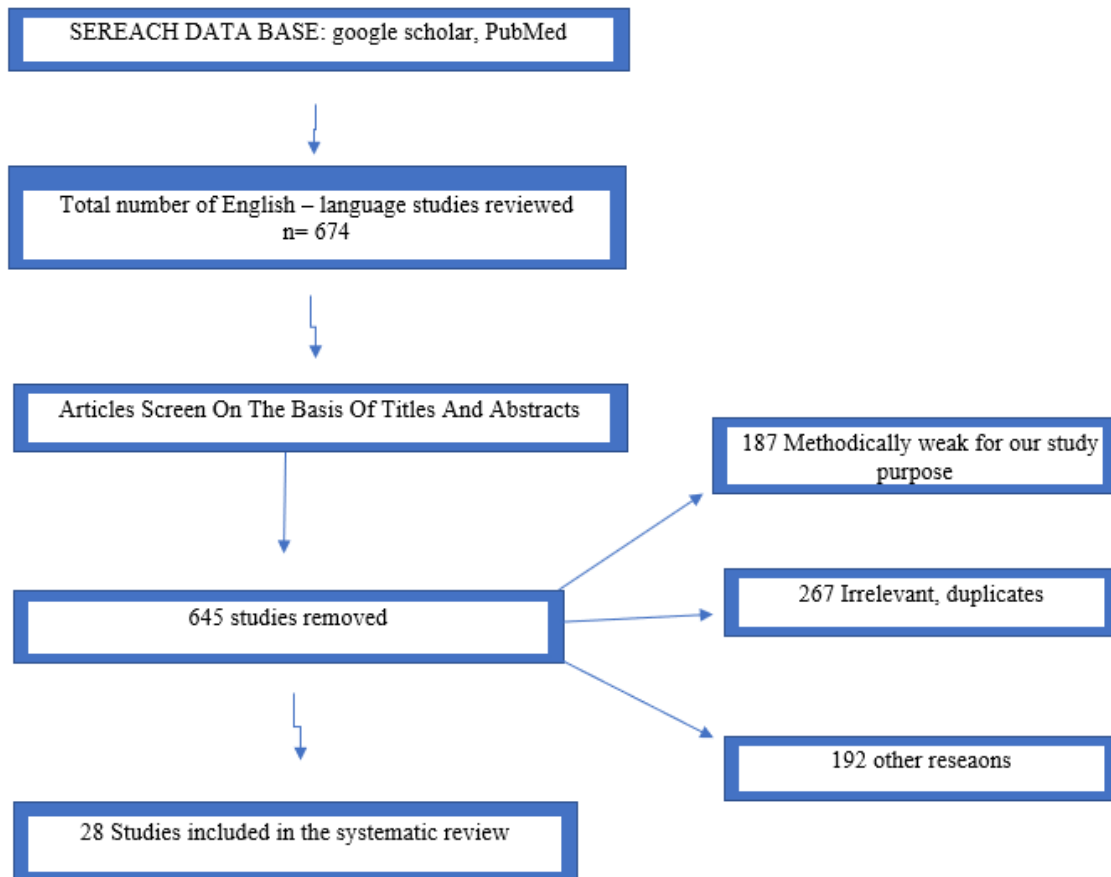


Fig. 1: Flow of information through the different stages of the systematic review

RESULTS AND DISCUSSION

Table (1), provides information on the total number of COVID-19 patients and the occurrence of bacterial co-infection in these patients. It also includes the corresponding co-infection percentages.

In total out of 317668 COVID-19 patients, only 16230 (5.11%) were identified as having bacterial co-infections, but still, there are some studies conducted in different areas revealed a high prevalence of bacterial co-infection among COVID-19 patients such as a study performed by Ramzan et al., 2022, present out of 3371 COVID-19 patients, 2922(89.68%) were identified as having bacterial co-infections.

Further breakdowns reveal varying percentages of bacterial co-infections in different subsets of COVID-19 patients. For example, out of 1,705 patients, 119 (6.78%) had bacterial co-infections. Similarly, among 1,016 patients, 54 (5.31%) had bacterial co-infections.

The table also provides data on larger subsets of COVID-19 patients. Among 4,259 patients, 1,414 (33.2%) had bacterial co-infections, while in a group of 3,028 patients, 1,049 (34.64%) had bacterial co-infections.

The occurrence of bacterial co-infections in other subsets had lower percentages. For instance, out of 160,886 patients, only 40 (0.02%) had bacterial co-infections. Similarly, among 48,902 patients, 2,109 (4.31%) had bacterial co-infections.

In summary, the table highlights the presence of bacterial co-infections among COVID-19 patients, with varying percentages across different subsets. These findings underscore the importance of considering bacterial co-infections in the management and treatment of COVID-19 patients, as they can impact disease severity and patient outcomes.

Table 1. Distribution of bacterial co-infection among COVID-19 Patients"

Reference	Total of COVID-19 patients	Patients with Bacterial co-infection	CI %
(Ramzan et al., 2022)	3371	2922	89.68%
(Alshaikh et al., 2022)	75956	3645	4.8%
(Ramzan et al., 2022)	3221	2242	69.61%
(Mutua et al., 2022)	120	53	44.17%
(Vaughn et al., 2021)	1705	119	6.78%
(Karaba et al., 2021)	1016	54	5.31%
(Thelen et al., 2021)	678	7	1.03%
(Singh et al., 2021)	4259	1414	33.2%
(Kubin et al., 2021)	3028	1049	34.64%
(Amin-Chowdhury et al., 2021)	160886	40	0.02%
(Russell et al., 2021)	48902	2109	4.31%
(Garcia-Vidal et al., 2021)	989	46	4.65%
(Rouzé et al., 2021)	568	84	14.79%
(Baskaran et al., 2021)	254	174	68.50%
(Foschi et al., 2021)	178	79	44.38%
(Søgaard et al., 2021)	162	24	14.81%
(Chen et al., 2021)	408	54	13.24%
(Nasir et al., 2021)	100	50	50%
(Baskaran et al., 2021)	3834	805	21%
(Liu et al., 2021)	165	73	44.24%
(Wang et al., 2020)	67	5	7.46%
(Hoshiyama et al., 2020)	7	4	57.14%
(Cusumano et al., 2020)	2679	42	1.57%
(Hughes et al., 2020)	836	153	18.30%
(Langford et al., 2020)	3338	825	24.72%
(Rawson et al., 2020)	806	62	7.69%
(Townsend et al., 2020)	117	95	81.20%
(Sharifipour et al., 2020)	18	1	5.56%
Total	317668	16230	5.11%

Table 2, provides information on the occurrence of bacterial co-infections among COVID-19 patients in different subsets. It shows varying percentages of bacterial co-infections, ranging from 0.02% to 89.69%, across different patient groups. These findings emphasize the importance of considering bacterial co-infections in the management and treatment of COVID-19 patients, as they can influence disease severity and patient outcomes.

The findings presented in the table (2) highlight the prevalence of various bacterial isolates. The table includes the number of isolates for each bacterial species and their respective percentages.

The most prevalent bacterial isolate was *Escherichia coli* (*E. coli*), accounting for 41 isolates (13.6% of the total).

Following closely behind, *Klebsiella pneumoniae* was identified in 33 isolates (11%). *Staphylococcus aureus*, a common pathogen, was the third most prevalent species, with 30 isolates (10.75%).

Pseudomonas aeruginosa and *Acinetobacter baumannii* were both identified in a similar proportion, with 29 (9.29%) and 26 (9%) isolates, respectively. *Haemophilus influenzae* and *Streptococcus pneumoniae* were found in 19 isolates each (6% each), representing a notable presence.

Other bacterial species identified in smaller numbers included Methicillin-Sensitive *Staphylococcus aureus* (MSSA) with 15 isolates (5.38%), *Enterococcus faecium* with 10 isolates (3.47%), and *Proteus mirabilis* with 9 isolates (3.20%). Additionally, several other species such as

E. coli complex, *Enterobacter cloacae*, *Citrobacter koseri*, *Staphylococcus epidermidis*, *Stenotrophomonas maltophilia*, *E. coli*, *Klebsiella oxytoca*, *Moraxella catarrhalis*, *Enterococcus faecalis*, *Streptococcus salivarius*, *Streptococcus pyogenes*, *alpha streptococcus not Group A*, *Staphylococcus sciuri*, *Actinetobacter spp*, *Acinetobacter calcoaceticus*, *Klebsiella aerogenes*, *Burkholderia*, *Serratia marcescens*, *Mycoplasma pneumonia*, *Mycoplasma spp*, *Citrobacter*

freundii were found in 1 isolate each, representing 0.35% each.

The table provides an overview of the prevalence of bacterial isolates within the studied population. The presence of various bacterial species underscores the diversity of co-infections observed among the subjects. These findings can be valuable for understanding the microbial landscape associated with COVID-19 patients and guiding appropriate treatment strategies and infection control measures.

Table 2: Spectrum of Bacterial Species Prevalence Among COVID-19 Patients

Isolates	Number	% (out of 279)
<i>E. coli</i>	41	13.6%
<i>Klebsiella pneumoniae</i>	33	11 %
<i>Staphylococcus aureus</i>	30	10.75%
<i>Pseudomonas aeruginosa</i>	29	9.29%
<i>Acinetobacter baumannii</i>	26	9%
<i>Haemophilus influenzae</i>	19	6 %
<i>Streptococcus pneumoniae</i>	19	6%
MSSA	15	5.38%
<i>Enterococcus faecium</i>	10	3.47%
<i>Proteus mirabilis</i>	9	3.20%
<i>E. coli</i> complex	7	2.20%
<i>Enterobacter cloacae</i>	5	1.68%
<i>Citrobacter koseri</i>	5	1.68%
<i>Staphylococcus epidermidis</i>	4	1.33%
<i>Stenotrophomonas maltophilia</i>	4	1.33%
<i>E. coli</i>	3	1.05%
<i>Klebsiella oxytoca</i>	3	1.05%
<i>Moraxella catarrhalis</i>	3	1.07%
<i>Enterococcus faecalis</i>	2	0.72%
<i>Streptococcus salivarius</i>	1	0.35%
<i>Streptococcus pyogenes</i>	1	0.35%
<i>alpha streptococcus not Group A</i>	1	0.35%
<i>Staphylococcus sciuri</i>	1	0.35%
<i>Actinetobacter spp</i>	1	0.35%
<i>Acinetobacter calcoaceticus</i>	1	0.35%
<i>Klebsiella aerogenes</i>	1	0.35%
<i>Burkholderia</i>	1	0.35%
<i>Serratia marcescens</i>	1	0.35%
<i>Mycoplasma pneumonia</i>	1	0.35%
<i>Mycoplasma spp</i>	1	0.35%
<i>Citrobacter freundii</i>	1	0.35%
Total	279	100%

Table 3 provides information on the total number and percentage distribution of various antibiotics used. A total of 6784 antibiotics were analyzed in the dataset. The most frequently used antibiotic was Piperacillin, with a total count of 1290,

accounting for 19.02% of the total antibiotics. It was followed by Azithromycin, with 1137 instances, representing 16.76% of the total.

Ceftriaxone accounted for 909 instances, making up 13.39% of the total,

while Meropenem accounted for 864 instances, representing 12.74% of the total antibiotics.

Other commonly used antibiotics included Cochaperone (507 instances, 7.47%), Moxifloxacin (523 instances, 7.7%), and Ciprofloxacin (229 instances, 3.38%). Less frequently used antibiotics such as Colistin, Cefoxitin, Erythromycin,

Gentamycin, Cotrimoxazole, Tetracycline, and Fluoroquinolone each accounted for only 0.01% of the total antibiotics.

It is important to note that the percentages provided in the table represent the distribution of each antibiotic relative to the total number of antibiotics analyzed in the dataset, which is 6784.

Table 3 Prescribed Antibiotics for Co-infection Management in COVID-19 Patients: Overview and Distribution

Antibiotics	Total number	Percentage (%)
Piperacillin	1290	19.02%
Azithromycin	1137	16.76%
Ceftriaxone	909	13.39%
Meropenem	864	12.74%
Moxifloxacin	523	7.7%
Cochaperone	507	7.47%
Linezolid	242	3.56%
Ciprofloxacin	229	3.38%
Amoxicillin	172	2.54%
Clarithromycin	140	2.07%
Hydroxychloroquine	140	2.07%
Levofloxacin	48	0.7%
Cephalosporin	98	1.45%
Cefepime	93	1.38%
Coamoxiclav	76	1.13%
Amikacin	49	0.72%
Gentamicin	49	0.72%
Vancomycin	47	0.69%
Penicillin	47	0.69%
Clavulanate	44	0.65%
Tigecycline	18	0.27%
Glycopeptides	18	0.27%
Teicoplanin	18	0.27%
Oxazolidinones	18	0.27%
Fluoroquinolone	2	0.03%
Colistin	1	0.01%
Cefoxitin	1	0.01%
Erythromycin	1	0.01%
Gentamycin	1	0.01%
Cotrimoxazole	1	0.01%
Tetracycline	1	0.01%
Total	6784	100%

The results presented in Table 3, provide valuable insights into the usage patterns of different antibiotics based on their total count and percentage distribution. Here are some key points to discuss regarding the findings:

Antibiotic Utilization: The table indicates that a total of 6784 antibiotics were analyzed, encompassing a diverse range of antibiotic classes. This highlights the importance of antibiotics in healthcare and their widespread use in treating various infections.

High Utilization Antibiotics: Certain antibiotics demonstrated higher utilization rates compared to others. Piperacillin, with the highest count of 1290 instances (19.02%), suggests its significant role in clinical practice. This might be attributed to its broad-spectrum activity and effectiveness against a wide range of bacterial infections.

Broad-Spectrum Antibiotics: Antibiotics like Ceftriaxone, Azithromycin, and Meropenem also showed substantial utilization rates, indicating their broad-spectrum coverage and effectiveness against multiple bacterial pathogens. These antibiotics are often prescribed as empiric therapy when the exact causative pathogen is unknown or in severe infections where broad coverage is needed.

Fluoroquinolones: Ciprofloxacin, Levofloxacin, and Moxifloxacin are fluoroquinolone antibiotics, commonly used in the treatment of various bacterial infections. While their utilization percentages were relatively lower, they still represented a notable proportion of the antibiotics analyzed.

Diversity of Antibiotic Classes: The table includes a wide array of antibiotic classes, such as cephalosporins (Cefepime, Ceftriaxone), penicillins (Amoxicillin, Piperacillin), macrolides (Azithromycin, Clarithromycin), and glycopeptides (Vancomycin, Teicoplanin). This diversity reflects the availability of different antibiotic options to target specific bacterial pathogens and optimize treatment approaches.

Limited Usage Antibiotics: Several antibiotics, such as Colistin, Cefoxitin, Erythromycin, Gentamycin, Cotrimoxazole, Tetracycline, and Fluoroquinolone, represented only a minimal percentage of the total count. This suggests that they might be less commonly prescribed due to factors such as specific indications, bacterial resistance patterns, or the availability of more effective alternatives.

Emerging Antibiotics: The presence of newer antibiotics in the dataset, such as Tigecycline and Oxazolidinones, indicates their increasing utilization in clinical practice. These antibiotics are often reserved for difficult-to-treat infections or cases where other treatment options have failed.

Non-Antibiotic Medications: It is worth noting that the table includes medications like Hydroxychloroquine and Coamoxiclav, which are not primarily antibiotics but may have antibacterial activity or be used in combination with antibiotics for specific indications.

Overall, the results of this analysis shed light on the utilization patterns of various antibiotics, highlighting the prevalence of certain classes and providing insights into the choices made by healthcare professionals when treating bacterial infections. Understanding antibiotic utilization trends is essential for optimizing antibiotic stewardship efforts, combating antibiotic resistance, and ensuring appropriate and effective use of these crucial medications in clinical practice.

Conclusion and Recommendation:

In conclusion, the comprehensive analysis provided valuable insights into the prevalence of bacterial coinfections and antibiotic utilization among COVID-19 patients. By considering bacterial coinfections, tailoring antibiotic therapy, promoting rational antibiotic use, and conducting further research and surveillance, healthcare providers and policymakers can improve the management and outcomes of COVID-19 patients while minimizing the risks associated with bacterial coinfections and antibiotic use.

Declarations:

Ethical Approval: None

Conflict interests: None

Funding: No funding was received.

Availability of Data and Materials: All datasets analysed and described during the present study are available from the corresponding author upon reasonable request.

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