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

Saad Alhumaid 1,*©, Muneera Alabdulqader 2©, Nourah Al Dossary 3, Zainab Al Alawi 4, Abdulrahman A. Alnaim 5, Koblan M. Al Mutared 6, Khalid Al Noaim 5 ©, Mohammed A. Al Ghamdi 7, Suha Jafar Albrahim 8, Abdulaziz A. Alahmari 7, Sarah Mahmoud Al Hajji Mohammed 9, Yameen Ali Almatawah 10, Omar Musa Bayameen 11, Ahmed Abdulwhab Alismaeel 11, Sherifah Khaled Alzamil 11, Samiah Ahmad Alturki 11, Zahra’a Radi Albrahim 11, Nasreen Ahmad Al Bagshi 11, Hesham Yousef Alshawareb 12, Jaafar Abdullah Alhudar 13, Qassim Abdulatif Alqurayhi 14, Samirah Mansour Alghadeer 15, Hassan Ali Alhadab 16, Taleb Nasser Aljubran 9, Yousif Ahmad Alabdulaly 17, Abbas Al Mutair 18,19,20,21 and Ali A. Rabaan 22,23,24©

Abstract: Background: Coinfection with bacteria, fungi, and respiratory viruses has been described as a factor associated with more severe clinical outcomes in children with COVID-19. Such coinfections in children with COVID-19 have been reported to increase morbidity and mortality. Objectives: To identify the type and proportion of coinfections with SARS-CoV-2 and bacteria, fungi, and/or respiratory viruses, and investigate the severity of COVID-19 in children. Methods: For this systematic review and meta-analysis, we searched ProQuest, Medline, Embase, PubMed, CINAHL, Wiley online resources for relevant studies. Results: A total of 103 studies were included in the systematic review and meta-analysis. The most common coinfection was with bacteria, followed by fungi and respiratory viruses. Conclusion: Coinfections with bacteria, fungi, and respiratory viruses in children with COVID-19 are common and may contribute to more severe clinical outcomes.
library, Scopus, and Nature through the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for studies on the incidence of COVID-19 in children with bacterial, fungal, and/or respiratory coinfections, published from 1 December 2019 to 1 October 2022, with English language restriction. Results: Of the 169 papers that were identified, 130 articles were included in the systematic review (57 cohort, 52 case report, and 21 case series studies) and 34 articles (23 cohort, eight case series, and three case report studies) were included in the meta-analysis. Of the 17,588 COVID-19 children who were tested for co-pathogens, bacterial, fungal, and/or respiratory viral coinfections were reported ($n = 1633, 9.3\%$). The median patient age ranged from 1.4 months to 144 months across studies. There was an increased male predominance in pediatric COVID-19 patients diagnosed with bacterial, fungal, and/or viral coinfections in most of the studies (male gender: $n = 204, 59.1\%$ compared to female gender: $n = 141, 40.9\%$). The majority of the cases belonged to White (Caucasian) ($n = 441, 53.3\%$), Asian ($n = 205, 24.8\%$), Indian ($n = 71, 8.6\%$), and Black ($n = 51, 6.2\%$) ethnicities. The overall pooled proportions of children with laboratory-confirmed COVID-19 who had bacterial, fungal, and respiratory viral coinfections were 4.73\% (95% CI 3.86 to 5.60, $n = 445, 34$ studies, $I^2 = 85\%, p < 0.01$), 0.98\% (95% CI 0.13 to 1.83, $n = 17$, six studies, $I^2 = 49\%, p < 0.08$), and 5.41\% (95% CI 4.48 to 6.34, $n = 441, 32$ studies, $I^2 = 87\%, p < 0.01$), respectively. Children with COVID-19 in the ICU had higher coinfections compared to ICU and non-ICU patients, as follows: respiratory viral (6.61\%, 95% CI 5.06–8.17, $I^2 = 0\%$ versus 5.31\%, 95% CI 4.31–6.30, $I^2 = 88\%$) and fungal (1.72\%, 95% CI 0.45–2.99, $I^2 = 0\%$ versus 0.62\%, 95% CI 0.00–1.55, $I^2 = 54\%$); however, COVID-19 children admitted to the ICU had a lower bacterial coinfection compared to the COVID-19 children in the ICU and non-ICU group (3.02\%, 95% CI 1.70–4.34, $I^2 = 0\%$ versus 4.91\%, 95% CI 3.97–5.84, $I^2 = 87\%$). The most common identified virus and bacterium in children with COVID-19 were RSV ($n = 342, 31.4\%$) and Mycoplasma pneumonia ($n = 120, 23.1\%$). Conclusion: Children with COVID-19 seem to have distinctly lower rates of bacterial, fungal, and/or respiratory viral coinfections than adults. RSV and Mycoplasma pneumonia were the most common identified virus and bacterium in children infected with SARS-CoV-2. Knowledge of bacterial, fungal, and/or respiratory viral coinfections has potential diagnostic and treatment implications in COVID-19 children.

**Keywords:** bacterial; children; co-infection; coinfection; concurrent; COVID-19; fungal; meta-analysis; pediatric; SARS-CoV-2; viral; systematic review

### 1. Introduction

Although most cases of coronavirus disease 2019 (COVID-19) in pediatric populations are mild or asymptomatic [1], the clinical spectrum of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children ranges from asymptomatic to life-threatening [2,3]. Similar to adults, coinfection with bacteria, fungi, and respiratory viruses has been described as a factor associated with more severe clinical outcomes in children with COVID-19 [4–11]. Such coinfections have been reported to increase morbidity and mortality, therefore, knowledge of bacterial, fungal, and/or respiratory viral coinfections has potential diagnostic and treatment implications in children infected with SARS-CoV-2. Many studies have shown that COVID-19 children may develop severe diseases, requiring intensive care admission and/or mechanical ventilation because patients rapidly develop acute respiratory distress syndrome and sepsis, leading to death from multiple organ failure [12–23]. SARS-CoV-2 is hypothesized to weaken the bodies of children to bacterial, fungal, and/or respiratory viral coinfections [24], yet the mechanism of coinfection has not been fully established, but represents a threat to the respiratory epithelium favoring bacteremia, fungaemia, and/or viraemia (see Figure 1).

There is a lack of systematic reviews and meta-analyses on the type and frequency of coinfection by bacterial, fungal, and/or respiratory viral infections and associated clinical outcomes among COVID-19 children. We aimed to identify the type and proportion
of coinfections with SARS-CoV-2 and bacteria, fungi, and/or respiratory viruses, and investigate the severity of COVID-19 in these patients.

Figure 1. Monoinfection with SARS-CoV-2 results in less severe form of COVID-19 and better prognosis. In contrast, SARS-CoV-2 coinfection with bacteria, fungi, and/or respiratory viruses may intensify the severity of COVID-19 and increase the expression of macrophages, T and B defensive cells that may cause the elevation of inflammatory cytokines such as tumor necrosis factor-alpha, interleukin-1, and interleukin-6 in the infected organs, leading to a hyperinflammatory response by recruiting immune cells.

2. Methods

2.1. Design

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA) in conducting this systematic review and meta-analysis [25]. The following electronic databases were searched: PROQUEST, MEDLINE, EMBASE, PUBMED, CINAHL, WILEY ONLINE LIBRARY, SCOPUS, and NATURE with Full Text. We used the following keywords: (“COVID-19” OR “SARS-CoV-2” OR “Severe acute Respiratory Syndrome Coronavirus 2” OR “Coronavirus Disease 2019” OR “2019 novel coronavirus”) AND (“children” OR “child” OR “paediatric” OR “pediatric” OR “infant” OR “toddler” OR “adolescent” OR “newborn”) AND (“coinfection” OR “co-infection” OR “cocirculation” OR “co-circulation” OR “coinfected” OR “co-infected” OR “co-circulated” OR “mixed” OR “concurrent” OR “concomitant”). The search was limited to papers published in English between 1 December 2019 and 1 October 2022. Based on the title and abstract of each selected article, we selected
those discussing and reporting the occurrence of bacterial, fungal, and/or respiratory viral coinfection in children with COVID-19.

2.2. Inclusion–Exclusion Criteria

Inclusion criteria were as follows: (1) published case reports, case series, and cohort studies that focused on children infected with SARS-CoV-2 and bacteria, fungi, and/or respiratory viruses; (2) studies of experimental or observational design reporting the incidence of SARS-CoV-2 infection in pediatric patients with other co-pathogens; (3) language restricted to English. The exclusion criteria were as follows: (1) editorials, commentaries, case and animal studies, reviews, and meta-analyses; (2) studies that did not report data on COVID-19 in coinfected patients; (3) studies that never reported details on identified coinfected cases with SARS-CoV-2 infection; (4) studies that reported coinfection in adult COVID-19 patients; (5) studies that reported coinfection in patients with negative SARS-CoV-2 polymerase chain reaction (PCR) tests; (6) duplicate publications.

2.3. Data Extraction

Six authors (Saad Alhumaid, Muneera Alabdulqader, Nourah Al Dossary, Zainab Al Alawi, Abdulrahman A. Alnaim, and Koblan M. Al mutared) critically reviewed all of the studies retrieved and selected those judged to be the most relevant. Data were carefully extracted from the relevant research studies independently. Articles were categorized as case report, case series, or cohort studies. The following data were extracted from selected studies: authors; publication year; study location; study design and setting; number of SARS-CoV-2 children tested for co-pathogens; number of coinfected children; age; proportion of male children; patient ethnicity; number of children with bacterial, fungal, and/or respiratory viral coinfections; total organisms identified; antimicrobials prescribed; laboratory techniques for co-pathogen detection; number of children admitted to intensive care unit (ICU), placed on mechanical ventilation, and/or suffered acute respiratory distress syndrome (ARDS); assessment of study risk of bias; and final treatment outcome (survived or died). These data are noted in Table 1.

2.4. Quality Assessment

For many selected cohort studies, the Newcastle–Ottawa scale (NOS) was used to assess the risk of bias, a tool which measures quality in the three parameters of selection, comparability, and exposure/outcome, and allocates a maximum of 4, 2, and 3 points, respectively [26]. High-quality studies are scored greater than 7 on this scale, and moderate-quality studies between 5 and 7 [26]. Otherwise, quality assessment of the selected case report and case series studies was undertaken based on the modified NOS [27]. Items related to the comparability and adjustment were removed from the NOS, and items which focused on selection and representativeness of cases, and the ascertainment of outcomes and exposure, were kept [27]. Modified NOS consists of five items, each of which requires a yes or no response to indicate whether bias is likely, and these items were applied to single-arm studies [27]. Quality of the study was considered good if all five criteria were met, moderate when four were met, and poor when three or less were met. Quality assessment was performed by six authors (Khalid Al Noaim, Mohammed A. Al Ghamdi, Suha Jafar Albahrani, Abdulaziz A. Alahmari, Sarah Mahmoud Al HajjiMohammed, and Yameen Ali Almatawah) independently, with any disagreement to be resolved by consensus.

2.5. Data Analysis

The proportion of confirmed COVID-19 children with bacterial, fungal, and/or respiratory viral coinfection were examined. This proportion was further classified based on initial presentation or during the course of the illness. A random effects DerSimonian–Laird model was used, which produces wider confidence intervals (CIs) than a fixed effect model [28]. Results are illustrated using a forest plot. The Cochran’s chi-square (χ²) and the I² statistic provided the tools for examining statistical heterogeneity [29]. An I² value
of >50% suggested significant heterogeneity [30]. To lower the source of heterogeneity, we conducted a subgroup analysis based on children’s admission to the ICU. To estimate publication bias, funnel plots and Egger’s correlation were used, and a p-value < 0.05 was considered to indicate statistical significance. All p-values were based on two-sided tests and significance was set at a p-value less than 0.05. R version 4.1.0 with the packages forestplot and forestplot was used for all statistical analyses. Figure 1 was created with BioRender.com (agreement no. NX24IV1VNB) (accessed on 14 October 2022).

3. Results

3.1. Study Characteristics and Quality

A total of 130 publications were identified (Figure 2). After scanning titles and abstracts, 67 duplicate articles were discarded. Another 33 irrelevant articles were excluded based on the titles and abstracts. The full texts of the 378 remaining articles were reviewed, and 248 irrelevant articles were excluded. As a result, we identified 130 studies that met our inclusion criteria and reported SARS-CoV-2 infection in pediatric patients with bacterial, fungal, and viral coinfection [4–23,31–140]. The detailed characteristics of the included studies are shown in Table 1. Among these, two articles were preprint versions [64,89]. There were 57 co-host [4–12,17,31,32,34–37,39,41,42,44,49,53,58,66,69,71,73,78–84,89,90,95,98,99,102,105,108, 109,115,116,118,119,123,125,127,129,131,133,134,137–139], 52 case report [13–16,18,19,21–23, 33,38,40,43,45,46,48,50–52,55,56,59,64,65,67,68,70,72,74–77,86,87,91,93,94,97,104,106,107,110, 111,113,114,121,122,124,126,128,130,140], and 21 case series [20,47,54,57,60–63,85,88,92,96, 109,115,116,118,119,123,125,127,129–132,135–139], 23 that used antibody tests (immunoglobulins M and/or G) [5,8,22,23,45,52,54,56,70,72,77,80,81,85,98,100,104,108, 111,120,122,133,140], 42 that used cultures (blood, urine, cerebrospinal fluid, tracheal, nasal...
discharge, pharyngeal swabs, wound, respiratory secretions, bronchoalveolar lavage, alveolar fluid, sputum, and pleural fluid) [5,6,11–13,15,16,20,21,23,38,40,42,50,51,53,55,60,63, 64,74,75,84,85,87,88,90,92,96,97,105–107,109,112,114,118,121,124,126,128,134], 29 that used two or more laboratory methods (RT-PCR, antibody tests, and/or culture) [4–8,12,20,23,36, 39,42,50,52,53,57,58,63,72,77,78,81,84,85,98,105,109,124,126,133], and two that did not specify their testing method [32,33]. Among the 130 included studies, 57 cohort studies were assessed using the NOS: 52 studies were found to be moderate-quality studies (i.e., NOS scores were between 5 and 7) and five studies demonstrated a relatively high quality (i.e., NOS scores > 7). All case reports and case series studies were assessed for bias using the modified NOS. Forty-nine studies were deemed to have high methodological quality, and three exhibited moderate methodological quality; Table 1.

Figure 2. Flow diagram of literature search and data extraction from studies included in the systematic review and meta-analysis.
Table 1. Summary of the characteristics of the included studies with evidence on SARS-CoV-2 and bacterial, fungal, and/or respiratory viral coinfections in children (n = 130), 2020–2022.

| Author, Year, Study Location | Study Design, Setting | Number of SARS-CoV-2 Patients Tested for Co-Pathogens, n | Co-infecting Patients, n | Age (Month) | Male, n (%) AND Ethnicity, n | Bacterial Coinfection, n | Fungal Coinfection, n | Respiratory Viral Coinfection, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for Co-Pathogen Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Tool Used, Final Score and Treatment Outcome) |
|-----------------------------|-----------------------|--------------------------------------------------------|--------------------------|-------------|--------------------------------|------------------------|------------------------|-------------------------------|----------------|------------------------|-----------------------------------------------|----------------|-----------------------|--------|--------------------------------------------------|
| Aggarwal et al. 2020[21], India | Retrospective cohort, multicenter | 770 | 4 | 12, 18, 96, and 72 | 2 (7%) AND 4 Indian | 0 | 0 | 6 | 3 Influenza A virus AND 3 Adenovirus | 0 | RT-PCR for respiratory specimens (viruses) | 0 | 0 | 0 | (NOS, 7, 4 survived) |
| Al Mansouri et al. 2021[22], United Arab Emirates | Retrospective cohort, single-center | 17 | 7 | Median (IQR), 84 (50–128) | Gender (not-reported) AND Ethnicity (not reported) | 2 | 0 | 5 | 3 Respirovirus AND 2 Group A Streptococcus AND 1.5 SARS-CoV-2 | 7 Not reported | RT-PCR for respiratory specimens (viruses) | 0 | 0 | 0 | (NOS, 6, Treatment outcome not reported) |
| Allen-Manzur et al. 2021[23], Mexico | Retrospective case report, single-center | 1 | 1 | 6 | 0 (0%) AND 1 Hispanic | 1 | 0 | 0 | 1 Mucoraceae | 1 Not reported | RT-PCR for respiratory specimens (viruses) | 0 | 0 | 0 | (NOS, 7, 4 survived) |
| Aykac et al. 2021[39], Turkey | Retrospective cohort, single-center | 32 | 6 | Median (IQR), 6 | 2 (6.25%) AND 6 Hispanic | 0 | 0 | 6 | 6 RSV | 1 Not reported | Chemiluminescence for RSV | 1 | 1 | 0 | (NOS, 6, 4 survived) |
| Aykac et al. 2021[40], Turkey | Retrospective cohort, single-center | 125 | 59 | Two patients <12 months to <10 months; Six patients <10 months to <24 months | Gender (not-reported) AND Ethnicity (not reported) | 0 | 0 | 59 | 32 Influenza A virus AND 16 Influenza B virus AND 1 Respirovirus | 59 Not reported | RT-PCR for respiratory specimens (viruses) | 59 Not reported | 59 Not reported | 59 Not reported | (NOS, 6, Treatment outcome not reported) |
| Aykac et al. 2021[39], Turkey | Retrospective cohort, single-center | 115 | 37 | Median (IQR), 48 (12–132) | Gender (not-reported) AND Ethnicity (not reported) | 37 | 0 | 4 | 37 Streptococcus pneumoniae AND 1 RSV AND 1.5 SARS-CoV-2 | 7 Cefuroxime AND 7 Ampicillin | RT-PCR for respiratory specimens (viruses) AND PCR assays (Streptococcus pneumoniae) | 1 | 1 | 1 | (NOS, 6, Treatment outcome not reported) |
| Ayubzadeh et al. 2021[41], Canada | Retrospective cohort, single-center | 1 | 1 | 108 | 1 (9%) AND 1 Pakistani | 1 | 0 | 0 | 1 Gram-negative bacilli AND 1 Staphylococcus | 1 Metronidazol AND 1 Ciprofloxacin | Blood culture (bacteria) | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
### Table 1. Cont.

| Author(s), Year, Study Location | Study Design, Setting | Number of SARS-CoV2 Patients n | Confirmed Patients, n | Age (Months) a | Male, n (%H, AND Ethnicity, n) | Bacterial Coinfection, n | Fungal Coinfection, n | Respiratory Viral Coinfection, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for Co-Pathogens Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Tool) | Treatment Outcome |
|--------------------------------|----------------------|-------------------------------|-----------------------|----------------|--------------------------------|------------------------|-----------------------|-------------------------------|-----------------|-------------------|--------------------------------|----------------|-------------------|----------|---------------------------------|----------------|
| Berkouk et al. 2021 [31], Turkey | Retrospective cohort, single-center | 128 | 21 | 1 patient: 5 Other patients: not reported | Gender (not reported) AND 21 White (Caucasian) | 0 | 0 | 23 | 9. Enterovirus 5. Adenovirus 4. RSV 5. Influenza | 21 Not reported | RT-PCR for respiratory specimens (viruses) c | 21 Not reported | 0 | 21 Not reported | (NOS, 6) Treatment outcome (not reported) |
| Besidesi et al. 2020 [49], United States | Retrospective case report, single-center | 27 | 2 | 1 and 3 | Gender (not reported) AND 27 White (Caucasian) | 3 | 0 | 0 | 1 Streptococcus 1 Escherichia 1 Enterobacter cloacae | 2. AngiMann 1 Gonococcus 1 3rd generation cephalosporins | RT-PCR for respiratory specimens (viruses) c | Blood culture (bacteria) Urine culture (bacteria) | 1 | 1 | 1 | (NOS, 7), 2 survived |
| Berkouk et al. 2021 [31], France | Retrospective case report, single-center | 1 | 1 | 156 | 0 (0) AND 1 White (Caucasian) | 0 | 0 | 1 | EBV | 0 | RT-PCR for respiratory specimens (viruses) c | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
| Canno et al. 2020 [4], Italy | Retrospective cohort, single-center | 64 | 17 | Age group <24 was the most frequent | Gender (not reported) AND 17 White (Caucasian) | 0 | 0 | 19 | 1 Other coronaviruses (22e, NL63, and OC43) 12 Bacteroides 2 Adenovirus | 17 Not reported | RT-PCR for respiratory specimens (viruses) c | 17 Not reported | 17 Not reported | 17 Not reported | (NOS, 6) Treatment outcome (not reported) |
| Chacón-Cruz et al. 2021 [34], Mexico | Retrospective case report, single-center | 1 | 1 | 84 | 1 (0) AND 1 Hispanic | 1 | 0 | 0 | 1 Neisseria meningitidis | 1. Aminocillin 1 Cephalosporin 1 Doxycycline | PCR assays (Neisseria meningitidis) | 1 Not reported | 1 Not reported | 1 | (Modified NOS, high) 1 died |
| Chen et al. 2020 [35], China | Retrospective case report, single-center | 1 | 1 | 144 | 1 (0) AND 1 White (Caucasian) | 2 | 0 | 0 | 1. Mycoplasma pneumoniae 1 Chlamydia pneumoniae | 1. Metocloprazine 1 Colistin 1 Dayealamic acid | Serum antibody tests (lgM, lgG) | 0 | 0 | 1 | (Modified NOS, high) 1 survived |
| Choudhary et al. 2022 [22], India | Retrospective cohort, multicenter | 947 | 235 | Age group <60: 101 (33.9%) patients (viral coinfection) Age group <60: 50 (16.8%) patients (bacterial coinfection) | Gender (not reported) AND Ethnicity (not reported) | 123 | 7 | 113 | 75 RSV 114 Virus 122 Bacterial 7 Fungal | 123 Antibiotics | RT-PCR for respiratory specimens (viruses) c | Blood culture (bacteria) Serum antibody tests (lgM, lgG) | 33 | 14 | 235 Not reported | (NOS, 8), 235 survived 2 died |
| Cichota et al. 2021 [36], Italy | Retrospective case report, single-center | 1 | 1 | 72 | 1 (0) AND 1 Black | 0 | 0 | 1 | 1. Parvovirus B19 | 1 Antibiotics | PCR assays (Parvovirus B19) | 1 | 1 | 1 | (Modified NOS, high) 1 survived |
| Danis et al. 2020 [37], France | Retrospective case report, single-center | 12 | 1 | 109 | 1 (0) AND 1 White (Caucasian) | 0 | 0 | 2 | 1 Influenza A virus 1 Rhinovirus | 0 | RT-PCR for respiratory specimens (viruses) c | 0 | 0 | 0 | (NOS, 7), 1 survived |
| Darley and Kent 2020 [40], United States | Retrospective case report, single-center | 1 | 1 | 4 | 1 (0) AND 1 White (Caucasian) | 0 | 0 | 1 | 1. Adenovirus | 0 | RT-PCR for respiratory specimens (viruses) c | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
| Duffie et al. 2020 [41], United States | Retrospective case report, single-center | 65 | 4 | Median, 115.2 | Gender (not reported) AND Ethnicity (not reported) | 0 | 0 | 5 | 2 Enterovirus 2 RSV 1 Other coronaviruses (22e, NL63, and OC43) | 4 Not reported | RT-PCR for respiratory specimens (viruses) c | 4 Not reported | 4 Not reported | 4 Not reported | (NOS, 6) Treatment outcome (not reported) |
| Dursun et al. 2021 [42], Turkey | Retrospective case report, single-center | 2 | 2 | 84 and 156 | 0 (0) AND 2 White (Caucasian) | 0 | 2 | 0 | 2 Fungal bacteria | 2 Mannopot 2 Fluconazole | RT-PCR for respiratory specimens (viruses) c | Blood culture (bacteria) | 0 | 0 | 0 | (Modified NOS, high) 2 survived |
| Dharavade et al. 2021 [43], India | Retrospective case report, single-center | 1 | 1 | 48 | 0 (0) AND 1 Indian | 1 | 0 | 0 | 1. Mycobacterium tuberculosis | 1 Ceftriaxone 1 Isoniazid 1 Rifampin 1 Pyrazinamide 1 Ethambutol | CSF culture (bacteria) | 1 | 1 | 1 | (Modified NOS, high) 1 survived |
### Table 1. Cont.

| Author, Year, Study Location | Study Design, Setting | Number of SARS-CoV-2 Patients Cohort, n | Confirmed Patients, n | Age (Months) a | Male, n (%) AND Ethnicity, n b | Bacterial Coinfection, n | Fungal Coinfection, n | Respiratory Viral Coinfection, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for CoPathogens Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias Risk of Treatment Outcome |
|-----------------------------|-----------------------|----------------------------------------|-----------------------|----------------|--------------------------------|-------------------------|-------------------------|--------------------------|----------------|------------------------|--------------------------------------------|---------------|--------------------------|---------|----------------------------------------------------------|
| Di Noto et al. 2022 [11], Italy | Retrospective case report, single-center | 1 | 1 | 24 | 1 (0%) AND 1 White (Caucasian) | 0 | 0 | 1 | 1 Human Herpesvirus 6 | 1 Acyclovir 1 Ganciclovir | CSF PCR assay (viruses) Serum antibody test (lgM) | 0 | 0 | 0 | (Modified NOS, high) Survived |
| Dikranian et al. 2022 [11], Multicountry | Retrospective cohort, multicenter | 422 | 31 | Age group ≤6 | 126/420 (64.6%) | Age group >20 to 100 | 165/380 (43.8%) | Age group >100 to 216 | 188/820 (23.9%) | Gender (not reported) AND Ethnicity (not reported) | 0 | 0 | 30 | 11 Influenza B 2 Influenza A 1 Coronavirus NL63 1 Coronavirus SARS-CoV-2 1 Parainfluenza 3 1 Parainfluenza 1 1 M. pneumoniae 8 Unspecified viruses | 35 Not reported | RT-PCR for respiratory specimens (viruses) 6 Blood culture (bacteria) 1 Spectrum (bacteria) | 22 | 31 Not reported | 31 Not reported | (NOS, 6) Treatment outcome (not reported) |
| Ducru et al. 2020 [13], United States | Prospective cohort, single-center | 24 | 7 | Median (IQR), 60 (30–102) | 3 White (Caucasian) 1 Hispanic 1 Black | 4 | 0 | 5 | 1 Parainfluenza 1 1 Parainfluenza 4 2 RSV | 1 Staphylococcus 1 Mycobacteriaceae 1 Unknown 1 Salmonella typhimurium | 7 Not reported | RT-PCR for respiratory specimens (viruses) 6 Blood culture (bacteria) 1 Sputum (culture) | 1 | 1 | 1 | (NOS, 6) Survived 1 Died |
| Dong et al. 2020 [16], China | Retrospective case report, single-center | 11 | 1 | 28 | 1 (0%) AND 1 Asian | 0 | 0 | 1 | 1 Cytomegalovirus | 0 | Serum antibody test (lgM) | 0 | 0 | 0 | (Modified NOS, high) Survived |
| Escaño et al. 2020 [17], South Africa | Retrospective case report, multicenter | 1 | 1 | 31 | 0 (0%) AND 1 Black | 1 | 0 | 0 | 1 Mycobacteriaceae | 1 Anthracobacter 1 Pneumococcus 1 Pseudomonas 1 Enfermentol | Blood culture (bacteria) | 0 | 0 | 0 | (Modified NOS, high) Survived |
| Fernandez et al. 2021 [18], Bangladesh | Retrospective case report, single-center | 1 | 1 | 96 | 0 (0%) AND 1 Bangladesh | 0 | 0 | 1 | 1 Dengue virus | 1 Anthracobacter 1 Dengue NS1 antigen | 1 | 1 | 1 | (Modified NOS, high) Survived |
| Freij et al. 2020 [19], United States | Retrospective case report, single-center | 1 | 1 | 60 | 0 (0%) AND 1 Black | 2 | 0 | 0 | 1 Mycobacteriaceae 1 Staphylococcus 1 Group A Streptococci 1 Amoxicillin 1 Amoxicillin | CSF culture (bacteria) | 1 | 1 | 0 | (Modified NOS, high) Died |
| Frost et al. 2021 [20], United States | Retrospective case report, single-center | 7 | 6 | Median (IQR), 16 (7–30) | 5 White 1 Hispanic | 14 | 0 | 5 | 1 Adenovirus 1 M. pneumoniae 2 RSV 1 Enterovirus 1 Streptococcus | 2 Hemophilius influenzae 3 Moraxella catarrhalis 2 Staphylococcus aureus | 7 Not reported | RT-PCR for respiratory specimens (viruses) 6 PCR assay (bacteria) | 0 | 0 | 0 | (Modified NOS, high) Survived 6 Died |
| Gazzarini et al. 2021 [21], Italy | Retrospective cohort, multicenter | 515 | 69 | Median (IQR), 87 (57–149) | Gender (not reported) AND 69 White (Caucasian) | 32 | 0 | 45 | 45 Unspecified viruses 22 Unspecified bacteria | 69 Not reported | RT-PCR for respiratory specimens (viruses) 6 PCR assay (bacteria) | 3 | 3 | 2 | (NOS, 7) 67 survived 2 Died |
| Gazzarini et al. 2020 [38], Italy | Retrospective cohort, multicenter | 168 | 10 | Median (IQR), 28 (4–115) | Gender (not reported) AND 10 White (Caucasian) | 1 | 0 | 10 | 3 RSV 3 Influenza A 1 Influenza A virus 1 Other coronaviruses (229E, NL63, and OC43) 1 Streptococcus pyogenes | 10 Not reported | RT-PCR for respiratory specimens (viruses) 6 PCR assay (bacteria) | 2 | 2 | 2 | (NOS, 6) Treatment outcome (not reported) |
| Gauvard et al. 2020 [39], South Africa | Retrospective case report, single-center | 1 | 1 | 29 | 1 (0%) AND 1 Black | 1 | 0 | 0 | 1 Rifampicin-sensitive Mycobacteriaceae | 1 Anthracobacter 1 Rifampicin 1 Erythromycin 1 Amoxicillin | PCR assay for gastric aspirate (mycobacterium isolation) | 0 | 0 | 0 | (Modified NOS, high) Survived |

a: Mean (IQR) or median (IQR) or range (min–max); b: Male, n (%) AND Ethnicity, n; b: White, n (%) AND Ethnicity, n; b: Other, n (%) AND Ethnicity, n; b: Asian, n (%) AND Ethnicity, n; b: Black, n (%) AND Ethnicity, n; |
| Study Design, Setting | Number of SARS-CoV2 Patients | Male, n (%) AND Ethnicity, n | Age (Months) | Bacterial Coinfection, n | Fungal Coinfection, n | Respiratory Viral Coinfection, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for Co-Pathogens Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Tool and Findings) and Treatment Outcome |
|-----------------------|------------------------------|-----------------------------|--------------|-------------------------|------------------------|-------------------------------|----------------|----------------------|--------------------------------|----------------|----------------|-------------|------------------------------------------------|
| Hamzavi et al. 2020 [18], Iran | Retrospective case series, single-center | 6 | 3 (50) AND 2 White (Caucasian) | 1 0 0 | 0 | 0 | 0 | 4 Penicillin | Nasal discharge (culture) | 0 | 0 | 0 | (Modified NOS, high) 6 survived |
| Hare et al. 2021 [62], United Kingdom | Retrospective case series, single-center | 1 | 1 168 | 1 (0.6) AND 1 Persian | 1 | 0 | 0 | 1 Staphylococcus aureus | 1 Vancomycin Blood (culture) | 1 | 1 | 1 | (Modified NOS, high) 1 dead |
| Hassoun et al. 2021 [63], United States | Retrospective case reports, multicenter | 3 | 3 13, 72, and 72 | 0 0 | 0 | 3 | 3 Adenovirus | 3 | 3 | 3 (Modified NOS, high) 3 dead |
| He et al. 2020 [15], China | Retrospective cohort, multicenter | 15 | 4 Medium (IQR), 72 (26–64) | 0 (25) AND 4 Asian | 2 2 | 0 | 2 Uropathogenic bacteria 2 Unspecified fungi | 4 Antibiotics | 0 | 0 | 0 | (Modified NOS, high) 6 survived |
| Hetzberg et al. 2020 [64], United States | Retrospective case reports, single-center | 3 | 3 2, 24, and 60 | 2 (66.7) AND Ethnicity (not reported) | 1 | 0 | 2 | 2 Rhinovirus 1 Bordetella pertussis | 1 Azithromycin | 0 | 0 | 0 | (Modified NOS, high) 3 survived |
| Jarmolinski et al. 2021 [65], Poland | Retrospective case report, single-center | 1 | 1 108 | 0 (0) AND 1 White (Caucasian) | 0 | 0 | 2 | 1 Adenovirus 1 RSV | 1 Reovirus | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
| Jiang et al. 2020 [66], China | Retrospective case reports, single-center | 161 | 2 80 and 42 | 0 (0) AND 2 Asian | 1 | 0 | 3 | 2 Adenovirus 1 Measles virus | 2 Antibiotics | 1 | 1 | 1 | (Modified NOS, high) 1 survived |

Table 1. Cont.
### Table 1. Cont.

| Author, Year, Study Location | Study Design, Setting | Number of SARS-CoV-2 Patients | Co-Pathogens, n | Male, n (%) AND Ethnicity, n | Bacterial Co-infections, n | Fungal Co-infections, n | Respiratory Virus Co-infections, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for Co-Pathogen Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Tool) | Treatment Outcome |
|-----------------------------|-----------------------|-------------------------------|-----------------|----------------------------|---------------------------|-------------------------|-------------------------------|-----------------|----------------------|-----------------------------------------------|----------------|--------------------------|---------|----------------------------------------|------------------|
| Kakuya et al. 2020 [75], Japan | Retrospective cohort, single-center | 3 | 2159 | 152 and 40 | 2 (0.03) AND 2 Asian | 0 | 0 | 2 | 1 Influenza A virus 1 Metapneumovirus | 1 Ceftriaxone | RT-PCR for respiratory specimen (virus) 6 | 0 | 0 | 0 | (Modified NOS, high) 2 survived |
| Kandhasamythan et al. 2021 [76], Kingdom of Thailand | Retrospective cohort, multicenter | 75 | 17 | Median (IQR), 120 (52–156) | Gender (not reported) AND 6 White (Caucasian) 5 Asian 4 Black | 6 | 4 | 14 | 5 Parainfluenza 3 2 Adenovirus 1 Mycoplasma 1 Rhinovirus 4 Coronavirus 4 Unspecified fungi | 3 Amoxicillin/clavulanic acid 1 Azithromycin | RT-PCR for respiratory specimen (virus) 6 | 17 | 7 | 10 | (NOS, 8) 16 survived 1 died |
| Kasahan et al. 2021 [77], Turkey | Retrospective cohort, single-center | 95 | 7 | Mean ± SD, 10 ± 4 ± 4.44 | 5 (7.4%) AND 7 White (Caucasian) | 1 | 0 | 7 | 2 Rhinovirus 2 Coronavirus NL63 1 Mycoplasma pneumoniae 1 RSV 1 Adenovirus 7 Antimicrobials | RT-PCR for respiratory specimen (virus) 6 | 0 | 0 | 0 | (NOS, 7) 7 survived |
| Kamizi et al. 2020 [78], Iran | Retrospective case report, single-center | 1 | 1 | 144 | 1 (0.05) AND 1 Persian | 0 | 0 | 1 | 1 Varicella zoster virus 1 Azithromycin | RT-PCR for respiratory specimen (virus) 6 | 2 Not reported | 2 Not reported | 2 Not reported | (NOS, 6) Treatment outcome (not reported) |
| Katz et al. 2022 [79], United States | Retrospective cohort, multicenter | 16 | 2 | 72 and 120 | 1 (65) AND 2 White (Caucasian) | 0 | 0 | 2 | 2 Herpes simplex virus 2 Not reported | RT-PCR for respiratory specimen (virus) 6 | 0 | 0 | 0 | (NOS, 6) Treatment outcome (not reported) |
| Katz et al. 2021 [80], India | Retrospective case report, single-center | 1 | 1 | 9 | 0 (0) AND 1 Indian | 0 | 0 | 1 | 1 Dengue virus | Ceftriaxone 1 Vancomycin 1 Dorsirimite | RT-PCR for respiratory specimen (virus) 6 | 1 | 1 | 1 | (Modified NOS, high) 1 survived |
| Keshtavar Valamer et al. 2022 [81], Iran | Retrospective cohort, single-center | 25 | 2 | Mean ± SD, 50.8 ± 51.8 | Gender (not reported) AND 2 Persian | 0 | 0 | 2 | 2 Human coronavirus OC43 | RT-PCR for respiratory specimen (virus) 6 | 2 Not reported | 2 Not reported | 2 Not reported | (NOS, 6) Treatment outcome (not reported) |
| Khatarwar et al. 2021 [82], India | Retrospective case report, single-center | 1 | 1 | 166 | 1 (0.05) AND 1 Indian | 0 | 0 | 0 | 1 Mycobacterium tuberculosis | 1 Meropenem 1 Vancomycin 1 Ceftriaxone 1 Amoxicillin 1 Gentamicin 1 Rifampicin 1 Metronidazol 1 Micafungin | CSF culture (bacteria) | 1 | 1 | 1 | (Modified NOS, high) 1 survived |
| Lambropoulou et al. 2021 [83], Greece | Retrospective cohort, single-center | 1 | 1 | 36 | 0 (0) AND 1 White (Caucasian) | 0 | 0 | 0 | 1 Escherichia fergusonii | 1 Piperacillin/tazobactam 1 Ampicillin 1 Imipenem 1 Meropenem 1 Miconazol | Blood (culture) | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
| Le Clerc et al. 2021 [84], France | Retrospective cohort, multicenter | 2159 | 58 | Age group <180 23 (43.1%) patients (rhinovirus co-infection) | 2 (0.04) AND Ethnicity (not reported) | 56 Not reported | 56 Not reported | 58 | 58 Rhinovirus 93 Not reported | RT-PCR for respiratory specimen (virus) 6 | 58 Not reported | 56 Not reported | 58 Not reported | (NOS, 6) 57 survived 1 died |
| Le Roux et al. 2020 [85], France | Retrospective case report, single-center | 1 | 1 | 10 | 1 (0.05) AND 1 White (Caucasian) | 0 | 0 | 2 | 1 Varicella zoster virus 1 Adenovirus | 1 Amoxicillin/clavulanic acid 1 Azithromycin 1 Acyclovir | PCR | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
| Author, Year, Study Location | Study Design, Setting | Number of SARS-CoV-2 Patients | Confirmed Patients, n | Age (Months) a | Male, n (%) AND Ethnicity, n b | Bacterial Coinfection, n | Fungal Coinfection, n | Respiratory Viral Coinfection, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for Co-Pathogen Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Tool and Finding) Treatment Outcome |
|-----------------------------|-----------------------|-----------------------------|---------------------|--------------|-------------------------------|-----------------------|-----------------|-------------------------------|-----------------|---------------------|---------------------------------|----------------|------------------------|---------|-------------------------------------------------------------|
| Lechertq et al. 2021[77], Switzerland | Retrospective case report, single-center | 1 | 1 | 96 | (1(88)) AND 1 White (Caucasian) | 1 | 0 | 1 | 1: EBV 1 Group A Streptococcus | 1 Aztreonam 1 Cefepime | RT-PCR for respiratory specimens (viruses) c Serum antibody tests (IgM, IgG) | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
| Lee et al. 2020[78], United States | Retrospective cohort, single-center | 1625 | 92 | Not reported | Gender (not reported) AND Ethnicity (not reported) | 0 | 0 | 111 | 36 RSV 38 Influenza A virus 1 Parainfluenza 2 B virus 2 Adenovirus 2 Parainfluenza 2 | Not reported | RT-PCR for respiratory specimens (viruses) c Serum antibody tests (IgM, IgG) | Not reported | Not reported | Not reported | (NOS, 7) Treatment outcome (not reported) |
| Leuninger et al. 2020[79], Switzerland | Retrospective cohort, single-center | 16 | 4 | Age group ≤0 2 (14.3%) patients (total coinfection) Age group >3 2 (14.3%) patients | Gender (not reported) AND 4 White (Caucasian) | 0 | 0 | 8 | 4 Rhinovirus 2 RSV 2 Parainfluenza virus (types 1–4) | 4 Not reported | RT-PCR for respiratory specimens (viruses) c | 4 Not reported | 4 Not reported | 4 Not reported | 135 survived |
| Li et al. 2020[80], China | Retrospective cohort, single-center | 40 | 15 | Mean ± SD: 61 ± 56 | Gender (not reported) AND 15 Asian | 14 | 0 | 4 | 3 Mycoplasma pneumoniae 3 Influenza A or B virus 1 Adenovirus 1 Streptococcus pyogenes | 13 Streptococcus 1 Moraxella catarrhalis | RT-PCR for respiratory specimens (viruses) c | 1 | 1 | 1 | (NOS, 7) 135 survived |
| Li et al. 2020[81], China | Retrospective cohort, single-center | 81 | 27 | Mean ± SD: 76.5 ± 9.6 | Gender (not reported) AND 27 Asian | 24 | 0 | 6 | 20 Mycoplasma pneumoniae 1 Influenza A virus 1 RSV 1 Adenovirus | 27 Not reported | RT-PCR for respiratory specimens (viruses) c Serum antibody tests (IgM, IgG) | 1 | 1 | 1 | (NOS, 7) 27 survived |
| Lin et al. 2020[82], China | Retrospective cohort, single-center | 92 | 1 | 36 | Gender (not reported) AND 1 Asian | 0 | 0 | 1 | 3 Streptococcus pyogenes | 1 Not reported | RT-PCR for respiratory specimens (viruses) c | 1 Not reported | 1 Not reported | 1 No reported | (Modified NOS, high) Treatment outcome (not reported) |
| Ma et al. 2020[83], China | Retrospective cohort, single-center | 45 | 4 | 4 | Gender (not reported) AND 4 Asian | 0 | 0 | 7 | 4 Mycoplasma pneumoniae 2 Parainfluenza virus 1 Adenovirus | 4 Not reported | RT-PCR for respiratory specimens (viruses) c | 3 | 3 | 3 | (NOS, 6) Treatment outcome (not reported) |
| Maria et al. 2020[84], Poland | Retrospective cohort, multicenter | 1285 | 135 | Median (IQR): 72 (52–156) | Gender (not reported) AND 135 White (Caucasian) | 15 | 0 | 37 | 11 Streptococcus pneumoniae 2 Influenza A virus 2 Escherichia coli 1 Adenovirus 1 Parainfluenza 1 Mycoplasma pneumoniae 1 Klebsiella pneumoniae 1 Mycoplasma catarrhalis 22 Rotavirus, adenoavirus, and parovirus | 135 Not reported | RT-PCR for respiratory specimens (viruses) c Blood, urine, and pharyngeal swabs (culture) | 3 | 0 | 2 | (NOS, 7) 135 survived |
| Marchiini et al. 2020[85], United States | Retrospective case series, single-center | 10 | 4 | Median (IQR): 132 (88–132) | Gender (not reported) AND Ethnicity (not reported) | 2 | 0 | 4 | 1 Mycoplasma pneumoniae 2 Adenovirus 1 Parainfluenza 1 Histoplasma capsulatum | 4 Not reported | RT-PCR for respiratory specimens (viruses) c Serum antibody tests (IgM) | 4 | 0 | 0 | (NOS, 7) 4 survived |
| Mansour et al. 2020[86], Lebanon | Retrospective cohort, single-center | 1 | 1 | 56 | Gender (not reported) AND 1 Arab | 1 | 0 | 0 | 1 Streptococcus pyogenes 1 Cysticerosis | Blood (culture) | 0 | 0 | 0 | (Modified NOS, high) 1 survived |

Table 1. Cont.
Table 1. Cont.

| Author, Year, Study Location | Study Design, Setting | Number of SARS-CoV-2 Patients | Coinfected Patients, n | Age (Months) | Male, n(%) AND Ethnicity, n (%) | Bacterial Coinfections, n | Fungal Coinfections, n | Respiratory Viral Co-infection, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for Co-Pathogen Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Triple Treatment Outcome) |
|-----------------------------|----------------------|-------------------------------|-----------------------|--------------|--------------------------------|---------------------------|---------------------------|-------------------------|-------------------|-----------------------------|------------------------|---------------------|-------------|---------------------------------------------------------|
| Marco et al. 2022 [75], Italy | Retrospective case report, single-center | 1 | 1 <1 | 0 (0) | 1 White (Caucasian) | 1 Multidrug-resistant Enterococcus ader | | | | | 1 Azithromycin; 1 Vancomycin; 1 Cotrimoxazole; 1 Gentamicin; 1 Meropenem; 1 Linezolid; 1 Amoxicillin; 1 Cefazolin; 1 Gentamicin | Blood (culture) | 1 1 1 | (Modified NOS, high) | 1 survived |
| Mulher et al. 2022 [11], India | Retrospective case report, single-center | 327 | 17 | Mean (SD), 137 (32) | 0.5 (10) | AND 17 Indian | 17 0 0 | 17 Mycobacterium tuberculosis | 17 Not reported | Blood culture (bacteria) | | 6 2 7 | (NOS, 7 | 3 survived 4 died |
| Mithal et al. 2020 [93], United States | Retrospective case series, single-center | 18 | 2 <5 | 1 (50) AND 2 Hispanic | | | | 2 RSV; 3 Mycoplasma genitalium; 3 Aspergillus fumigatus | 1 Antibiotics | RT-PCR for respiratory specimens (viruses) | 0 0 0 | (Modified NOS, high) | 2 survived |
| Mohamed et al. 2022 [95], Iran | Retrospective cohort, single-center | 45 | 4 | 1, 36, 72, and 120 | 2 (15) | AND 4 Persian | 0 0 4 | 4 Adenovirus | 0 | RT-PCR for respiratory specimens (viruses) | 0 0 0 | (NOS, 5 | 4 survived |
| Mo et al. 2021 [91], Pakistan | Retrospective cohort, single-center | 4226 | 4 | ≤ 180 (10-180) | 4 (10) | AND 4 Pakistani | 0 4 0 | 1 Coxsackievirus 1; 1 Coxsackievirus 2; 1 Coxsackievirus 3; 4 Antibiotics 4 Antibiotics | 4 Antibiotics; 4 Antifungals | Blood (culture) | | 1 1 1 | (NOS, 7 | 3 survived 1 dead |
| Morad et al. 2020 [91], France | Retrospective case report, single-center | 1 | 1 55 | 0 (0) | AND 1 White (Caucasian) | 0 0 1 | 1 EBV | 0 | RT-PCR for respiratory specimens (viruses) | 0 0 0 | (Modified NOS, high) | 1 survived |
| Mulule et al. 2021 [91], Botswana | Retrospective case report, single-center | 1 | 1 3 | 1 (33) | AND 1 Black | 1 0 0 | 1 Respiratory-sensible Mycobacterium tuberculosis | 1 Amikacin; 1 Gentamicin; 1 Isoniazid; 1 Pyrazinamide; 1 Ethambutol | PCR assay for gastric lavage (bacteria) | 1 1 1 | (Modified NOS, high) | 1 died |
| Ng et al. 2020 [91], United Kingdom | Retrospective case report, single-center | 8 | 3 | 12, 0, and 10 | 1 (33) | AND 3 White (Caucasian) | 0 0 5 | 2 Adenovirus 1 Other coronaviruses 2 (229E, NL63, and OC43) | 1 Amoxicillin; 1 Cotrimoxazole; 1 Gentamicin | RT-PCR for respiratory specimens (viruses) | 1 0 0 | (Modified NOS, high) | 3 survived |
| Nata-Moro et al. 2020 [93], Spain | Retrospective case report, single-center | 1 | 1 8 | 1 (33) | AND 1 White (Caucasian) | 1 0 0 | 1 Staphylococcus pneumoniae | 1 Azithromycin; 1 Imipenem; 1 Linezolid | Blood (culture) | 1 0 1 | (Modified NOS, high) | 1 survived |
| Nggay et al. 2020 [93], Denmark | Retrospective case series, multicenter | 2 | 2 24 and 132 | 1 (50) | AND 2 White (Caucasian) | 2 0 2 | 2 Parvovirus B19; 1 Enterovirus-producing Streplococcus aureus | 1 Enterovirus | 1 Meropenem; 1 Imipenem; 1 Amoxicillin | Blood PCR assay (viruses) | 1 1 1 | (Modified NOS, high) | 2 dead |
| Oba et al. 2020 [93], Brazil | Retrospective case report, single-center | 1 | 1 2 | 0 (0) | AND 1 Hispanic | 1 0 0 | 1 Clostridium difficile | 0 | Fecal PCR assay (bacteria) | 1 0 0 | (Modified NOS, high) | 1 survived |
| Ogihaya et al. 2020 [91], South Africa | Retrospective cohort, multicenter | 36 | 31 | Median (IQR), 16 (5–20) | 19 (61.3) | AND 31 Black | 0 0 53 | 25 Rhinovirus 19 RSV 8 Parainfluenza virus 3 | 33 Not reported | RT-PCR for respiratory specimens (viruses) | 2 31 Not reported 31 Not reported | (NOS, 7 | Treatment outcome (not reported) |
| Palme et al. 2020 [91], Argentina | Retrospective case series, multicenter | 4 | 4 | Range (60–192) | 4 Green (not reported) | AND 4 Hispanic | 4 0 0 | 4 Mycobacterium tuberculosis | 4 Isoniazid; 4 Clarithromycin; 4 Pneumococcal; 4 Ethambutol | Blood culture (bacteria) | 1 1 1 | (Modified NOS, high) | 3 survived 1 dead |
| Patek et al. 2020 [91], United States | Retrospective case report, single-center | 1 | 1 0.5 | 1 (33) | AND 1 White (Caucasian) | 1 0 0 | 1 MBSA | 1 Antibiotic; 1 Ampicillin | Wound (culture) | 1 0 1 | (Modified NOS, high) | 1 survived |
Table 1. Cont.

| Author, Year, Study Location | Study Design, Setting | Number of SARS-CoV2 Patients | Co-Pathogens, n | Male, n (%) AND Ethnicity, n | Bacterial Co-isolates, n | Fungal Co-isolates, n | Respiratory Viral Coinfection, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for Co-Pathogens Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Risk of Bias Treatment Outcome) |
|-----------------------------|-----------------------|-----------------------------|-----------------|----------------------------|-------------------------|------------------------|--------------------------|-----------------|------------------------|--------------------------------|----------------|-------------------|--------|-----------------------------|
| Peng et al. 2020 [91], China | Retrospective cohort, single-center | 75 | 42 | Mean ± SD; 72.2 ± 57.4 | Gender (not reported) AND 42/74 | 31/0 | 8 | 28 Mucorales | 1 Moraxella catarrhalis | 1 Staphylococcus aureus | 1 Streptococcus pneumoniae | 3.5% | 1 influenza A virus | 2 Acinetobacter | 1 Cytophaga | 1 RSV | Ret-PCR for respiratory specimens (virus) | Serum antibody test (IgM) for Mucorales | 0/0/1 | 2022 (NOS, 7) 42 survived |
| Payey et al. 2021 [99], Switzerland | Retrospective cohort, single-center | 51 | 7 | Median (IQR); 30.4 (24.4–43.4) | Gender (not reported) AND 7/White (Caucasian) | 0/0 | 9 | 4 Rhinovirus | 2 Other co-isolates | 1 influenza A virus | 2 Adenovirus | 1 Influenza | 1 Methicillin-resistant | 1 RSV | 7 Not reported | Ret-PCR for respiratory specimens (virus) | Serum antibody test (IgM) | 0/4/0 | 2022 (NOS, 7) 42 survived |
| Pabari et al. 2020 [100], Italy | Retrospective case series, single-center | 9 | 4 | 36, 120, 120, and 120 | Gender (not reported) AND 4/White (Caucasian) | 15/0 | 0 | 4 Mucorales | 1 Moraxella catarrhalis | 2 Adenovirus | 4 White (Caucasian) | 1 Streptococcus | 1 Methicillin-resistant | 1 Clostridium | 1 RSV | 7 Not reported | Ret-PCR for respiratory specimens (virus) | Serum antibody test (IgM) | 0/4/0 | 2022 (NOS, 7) 42 survived |
| Pokorska-Swierczak et al. 2021 [101], Poland | Prospective cohort, single-center | 15/1 | 1 | Not reported | Gender (not reported) AND 1/White (Caucasian) | 0/0 | 1 | 1 influenza A virus | 6 RSV | 2 Influenza | 2 Influenza | 22/0 | 1 Not reported | Ret-PCR for respiratory specimens (virus) | Serum antibody test (IgM) | 0/4/0 | 2022 (NOS, 7) 42 survived |
| Pucarelli-Labruno et al. 2022 [102], Brazil | Retrospective case series, single-center | 105/9 | 1 | Median, 45 | Gender (not reported) AND 9/Hispanic | 0/0 | 10 | 1 coronavirus | 2 Influenza | 2 Influenza | 22/0 | 9 Not reported | Ret-PCR for respiratory specimens (virus) | Serum antibody test (IgM) | 0/4/0 | 2022 (NOS, 7) 42 survived |
| Rastogi et al. 2021 [103], India | Retrospective case series, single-center | 19 | 1 | 108 | Gender (not reported) AND 1/Indian | 1/0 | 0 | 1 Mycobacterium tuberculosis | 1 Influenza | 1 Influenza | 22/0 | 1 PCR assay of bronchoalveolar lavage | 0/0 | 0 | 2022 (NOS, 7) 42 survived |
| Ratnami et al. 2021 [104], India | Retrospective cohort, single-center | 1 | 1 | 96 | Gender (not reported) AND 1/Indian | 1/0 | 1 | 1 Dengue virus | 0 | IgM antibody test (dengue) | 0/0 | 0 | 2022 (NOS, 7) 42 survived |
| Raychaudhuri et al. 2020 [105], India | Prospective cohort, single-center | 102/43 | Median (IQR); 54 (4.8–90) | 23 (53.4) AND | 43/Indian | 26/0 | 12 | 2 MSSA | 1 Staphylococcus aureus | 1 Escherichia coli | 1 Pseudomonas aeruginosa | 1 Rhinovirus | 1 Mycobacterium avium complex | 36 Antibiotics | 27/15 | 14 | 2022 (NOS, 7) 42 survived |
| Rehail et al. 2022 [21], Portugal | Retrospective case report, single-center | 1 | 1 | 168 | Gender (not reported) AND 1/Arab | 1/0 | 0 | 1 Neisseria meningitidis | 1 Neisseria meningitidis | 1 Neisseria meningitidis | 1 Neisseria meningitidis | 1 Neisseria meningitidis | 1 Neisseria meningitidis | 38 Antibiotics | 1/1 | 1 | 2022 (NOS, 7) 42 survived |
| Sidd et al. 2022 [106], Saudi Arabia | Retrospective cohort, single-center | 1 | 1 | 10 | Gender (not reported) AND 1/Arab | 1/0 | 0 | 1 Escherichia coli | 1 Escherichia coli | 1 Escherichia coli | 1 Escherichia coli | 1 Escherichia coli | 1 Escherichia coli | 5 Antibiotics | 1/1 | 1 | 2022 (NOS, 7) 42 survived |
| Sanchez Solano and Grisham 2021 [107], United States | Retrospective cohort, single-center | 1 | 1 | 192 | Gender (not reported) AND 1/White (Caucasian) | 1/0 | 0 | 1 MSSA | 1 Staphylococcus aureus | 1 Staphylococcus aureus | 1 Staphylococcus aureus | 1 Staphylococcus aureus | 1 Staphylococcus aureus | 38 Antibiotics | 1/1 | 1 | 2022 (NOS, 7) 42 survived |
| Santoro et al. 2021 [108], Indonesia | Retrospective cohort, single-center | 90 | 1 | Not reported | Gender (not reported) AND 1/Arab | 0/0 | 1 | 1 Dengue virus | 1 Neisseria meningitidis | 1 Neisseria meningitidis | 1 Neisseria meningitidis | 1 Neisseria meningitidis | 1 Neisseria meningitidis | 38 Antibiotics | 1/1 | 1 | 2022 (NOS, 7) 42 survived |
| Schioler et al. 2020 [109], Multi-country | Retrospective cohort, single-center | 413 | 54 | 415.4 (4.6–129.2) | Gender (not reported) AND Ethnicity (not reported) | 24/0 | 32 | 24 Bacterial | 33 Viral | 3 Azithromycin | 3 Azithromycin | 3 Azithromycin | 3 Azithromycin | 38 Antibiotics | 10/4 | 4 | 2022 (NOS, 7) 42 survived |
| Author, Year, Study Location | Study Design, Setting | Number of SARS-CoV2 Patients Cohort, n | Confirmed Patients, n | Age (Months) a | Male, n (%) AND Ethnicity, n b | Bacterial Co-infections, n | Fungal Co-infections, n | Respiratory Viral Co-infection, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for Co-pathogens Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Final Treatment Outcome) |
|------------------------------|----------------------|----------------------------------------|----------------------|----------------|-------------------------|-----------------------------|-------------------------|-----------------------------|----------------|-------------------------|---------------------------------|------------------|-----------------|--------|--------------------------------------|
| Sae et al. 2020 [112], Malaysia | Retrospective case report, multicenter | 4 | 1 | 46 | 0 (2) AND 1 Asian | 0 | 0 | 1 | 1 Influenza A virus | 1 Piperacillin/tazobactam | RT-PCR for respiratory specimens (virus) | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
| Serrano et al. 2021 [113], Spain | Retrospective case report, single-center | 1 | 1 | 96 | 1 (3) AND 1 White (Caucasian) | 1 | 0 | 0 | 0 | 1 Mycoplasma pneumoniae | 1 Not reported | IgM and IgG antibody tests (RV pneumonia) | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
| Shabrawishi et al. 2021 [115], Saudi Arabia | Retrospective case series, single-center | 7 | 1 | 165 | 0 (3) AND 1 Arab | 1 | 0 | 0 | 0 | 1 Mycobacterium tuberculosis | 1 Ceftriaxone 1 Azithromycin 1 Ketoconazole 1 Rifampicin 1 Pyrazinamide 1 Ethionamide | Blood culture (bacteria) | 0 | 0 | 0 | (Modified NOS, high) 1 survived |
| Shi et al. 2021 [114], China | Retrospective case report, single-center | 1 | 1 | 3 | 1 (3) AND 1 Asian | 0 | 0 | 1 | 1 RV | 1 Cefotaxime | RT-PCR for respiratory specimens (virus) c | 1 | 0 | 1 | (Modified NOS, high) 1 survived |
| Sibao et al. 2021 [111], United States | Retrospective cohort, single-center | 1 | 1 | 36 | 1 (3) AND 1 White (Caucasian) | 1 | 0 | 0 | 0 | 1 Staphylococcus epidermidis | 1 Vancomycin 1 Chloramphenicol 1 Piperaclillin/ tazobactam | Blood culture | 1 | 1 | 0 | (Modified NOS, high) 1 survived |
| Sik et al. 2020 [116], Turkey | Retrospective cohort, single-center | 14 | 1 | 3 | 1 (3) AND 1 White (Caucasian) | 0 | 0 | 1 | 1 RV | 1 Antibiotics | IgM antibody test (virus) | 0 | 0 | 1 | (NOS, 7) 1 survived |
| Semarang et al. 2020 [117], Indonesia | Retrospective case report, single-center | 1 | 1 | 72 | 1 (3) AND 1 Asian | 0 | 0 | 1 | 1 Dengue virus | 1 Antibiotics | IgM antibody test (virus) c | 1 | 1 | 1 | (Modified NOS, high) 1 died |
| Sun et al. 2020 [118], China | Retrospective cohort, single-center | 36 | 23 | Mean (range), 6-43 (2-72) Gender (not reported) AND 23 Asian | 25 Not reported | 23 Not reported | 23 Not reported | 1 Unspecified number of Co-infections, HBV and Mycoplasma pneumoniae | 15 Co-infections 15 Antibiotics | RT-PCR for respiratory specimens (virus) c | 1 | 1 | 1 | (NOS, 7) 22 survived 1 died |
| Sun et al. 2020 [119], China | Retrospective case report, multicenter | 8 | 1 | 96 | 1 (3) AND 1 Asian | 0 | 0 | 1 | 1 Influenza A virus | 1 Antibiotics | RT-PCR for respiratory specimens (virus) c | 1 | 1 | 1 | (Modified NOS, high) 1 Retained in ICU |
| Tadonki et al. 2020 [120], Cameroon | Retrospective cohort, single-center | 49 | 1 | 3 | 1 (3) AND 1 Black | 1 | 0 | 0 | 0 | 1 Mycobacterium tuberculosis | 1 Antibiotics 1 Ethionamide 1 Pyrazinamide 1 Ethionamide | Blood culture (bacteria) | 0 | 0 | 0 | (NOS, 7) 1 survived |
| Tagari et al. 2020 [121], India | Retrospective cohort, single-center | 41 | 2 | Median (IQR), 36 (10-72) Gender (not reported) AND 0 (2) Ethnicity (Not reported) | 0 | 0 | 2 | 2 RV | 2 Not reported | RT-PCR for respiratory specimens (virus) c | 0 | 0 | 0 | (NOS, 7) 2 survived |
| Tan et al. 2020 [110], China | Retrospective case report, single-center | 10 | 3 | 24, 305, and 111 | 1 (3) AND 3 Asian | 4 | 0 | 0 | 0 | 3 Mycoplasma pneumoniae | 1 Mycoplasma pneumoniae | 1 Antibiotics | Serum antibody test (IgM) | 3 Not reported | 3 Not reported | 3 Not reported | (Modified NOS, high) 1 untreated (not reported) |
| Taveard et al. 2020 [122], Thailand | Retrospective case report, single-center | 1 | 1 | 67 | 1 (3) AND 1 Asian | 2 | 1 | 4 | 1 Influenza virus-4 | 1 Antibiotics | Alveolar fluid culture | RT-PCR for respiratory specimens (virus) | 1 | 1 | 1 | (Modified NOS, high) 1 died |
| Thalassia et al. 2021 [123], France | Retrospective cohort, single-center | 1 | 1 | 1.5 | 1 (3) AND 1 Indian | 1 | 0 | 0 | 0 | 1 Citrobacter lwoei | 1 Ceftriaxone | 1 Doxycycline | 1 Gentamicin | 0 (0) | 0 | 0 | (Modified NOS, high) 1 survived |
| Tripathi et al. 2020 [124], India | Retrospective case report, single-center | 1 | 1 | 169 | 0 (2) AND 1 White (Caucasian) | 0 | 0 | 1 | 1 RV | 1 Ceftriaxone 1 Azithromycin | Dengue NS1 antigen IgM antibody test (virus) | 1 | 0 | 1 | (NOS, 7) 1 survived |
| Trifone et al. 2020 [125], Bulgaria | Retrospective cohort, multicenter | 242 | 16 | All patients were <50 (< 50) AND 36 (n = 1) Gender (not reported) AND 16 White (Caucasian) | 16 Not reported | 16 Not reported | 2 | 2 Influenza A virus | 16 Not reported | RT-PCR for respiratory specimens (virus) c | 1 | 0 | 0 | (NOS, 7) 16 survived |

a Age reported in months. 

b Ethnicities reported: White (Caucasian), Arab, Black, Indian, Asian, Indian, White (Caucasian). 

The table contains data on the assessment of study risk of bias for the final treatment outcome, which is categorized as 1 (high), 2 (moderate), or 3 (low).
Table 1. Cont.

| Author, Year, Study Location | Study Design, Setting | Number of SARS-CoV2 Patients Co-Pathogens, n | Contacted Patients, n | Age (Months) a | Male, n (%) AND Ethnicity, n b | Bacterial Co-infections, n | Fungal Co-infections, n | Respiratory Viral Coinfections, n | Antimicrobials Used, n | Laboratory Techniques for Co-Pathogen Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Tool) | Treatment Outcome |
|-----------------------------|------------------------|---------------------------------------------|-----------------------|----------------|---------------------------------|--------------------------|--------------------------|-------------------------------|------------------|---------------------------------------------|------------------|--------------------------|---------|-------------------------------|------------------|
| Vazquez et al. 2020 [115], Argentina | Retrospective, case reports, single-center | 1 | 1 | 204 | 1 (93) AND 1 Hispanic | 1 | 1 | 0 | 0 | 1 Mycobacterium tuberculosis 1 Isospora belli | PCR assay (bacteria) | 0 | 0 | 0 | (Modified NOS, moderate) | Survived |
| Vazquez et al. 2021 [121], Brazil | Prospective, cohort, multicenter | 92 | 31 | Median (IQR), 64.5 (24–122.4) | Gender (not reported) AND 31 Hispanic | 0 | 0 | 0 | 30 | 29 Respira 1 Enterovirus 5 Azithromycin | RT-PCR for respiratory specimens (virus) c | 4 | 0 | 0 | (NOS, 7) | Survived |
| Vélez et al. 2020 [131], The Netherlands | Retrospective case report, single-center | 1 | 1 | 0.05 | 0.05 AND 1 White (Caucasian) | 1 | 0 | 0 | 0 | 1 Staphylococcus aureus 1 Flucloxacin | RT-PCR for respiratory specimens (virus) c | 1 | 1 | 1 | (Modified NOS, high) | Survived |
| Vidal et al. 2020 [137], Multi-country | Retrospective cohort, multicenter | 29 | 12 | Median, 36 | Gender (not reported) AND 12 White (Caucasian) | 0 | 0 | 12 | 12 Adenovirus 12 Not reported | RT-PCR for respiratory specimens (virus) c | 2 | 12 Not reported | 12 ARDS | (NOS, 7) | Treatment outcome (not reported) |
| Vu et al. 2021 [116], United States | Retrospective case report, single-center | 1 | 1 | 46 | 1 (93) AND 1 White (Caucasian) | 1 | 0 | 0 | 1 Streptococcus pneumoniae 1 Calfimococcal 1 Amoxicillin | Pleural fluid (culture) | 1 | 1 | 1 | (Modified NOS, high) | Survived |
| Wang et al. 2020 [111], United States | Retrospective cohort, multicenter | 713 | 113 | Age group ≥12: 37 (52.4%) patients (total coinfection) Age group 12<60: 40 (56.5%) patients (total coinfection) | Gender (not reported) AND Ethnicity (not reported) | 113 Not reported | 113 Not reported | 113 | 113 RSV | 113 Not reported | RT-PCR for respiratory specimens (virus) c | 113 Not reported | 113 Not reported | 113 Not reported | (NOS, 6) | Treatment outcome (not reported) |
| Ward et al. 2020 [110], Germany | Retrospective case report, single-center | 1 | 1 | 4 | Gender (not reported) AND 1 White (Caucasian) | 0 | 0 | 0 | 1 | 1 Influenza A virus | RT-PCR for respiratory specimens (virus) c | 0 | 0 | 0 | (Modified NOS, high) | Survived |
| Wu et al. 2020 [111], China | Retrospective cohort, multicenter | 19 | 34 | Median, 72 (1.2–109.9) | Gender (not reported) AND 19 Asian | 16 | 10 | 8 | 15 | 16 Mycoplasma pneumonia 1 RSV | RT-PCR for respiratory specimens (virus) c | 16 | 15 | 1 | (NOS, 7) | Survived |
| Xia et al. 2020 [103], China | Retrospective case series, single-center | 20 | 8 | Median, 24 | Gender (not reported) AND 8 Asian | 4 | 0 | 5 | 15 | 3 Mycoplasma pneumoniae 1 RSV | RT-PCR for respiratory specimens (virus) c | 0 | 0 | 0 | (Modified NOS, high) | Survived |
| Yakovleva et al. 2022 [115], Russia | Retrospective cohort, single-center | 267 | 32 | Median (IQR), 32 (6.4–64) (total coinfection) | Gender (not reported) AND 32 White (Caucasian) | 16 | 0 | 34 | 11 Respira 4 Other enteroviruses (ECHO 1, ECHO 43) 4 Influenza A virus 4 Parainfluenza virus 4 Mycoplasma pneumoniae 1 RSV | RT-PCR for respiratory specimens (virus) c | 32 Not reported | 32 Not reported | 32 Not reported | (NOS, 7) | Treatment outcome (not reported) |
| Zeng et al. 2020 [114], China | Retrospective cohort, single-center | 3 | 1 | Median, 7.75 | 1 (93) AND 1 Asian | 1 | 0 | 0 | 1 Enterovirus 1 Antibiotics | Bled (culture) | 1 | 1 | 1 | (NOS, 7) | Survived |
| Zhang et al. 2020 [115], China | Retrospective case series, multicenter | 34 | 16 | Median (IQR), 33 (10-94.2) | Gender (not reported) AND 16 Asian | 9 | 0 | 15 | 9 Mycoplasma pneumoniae 4 Influenza A virus 2 RSV | RT-PCR for respiratory specimens (virus) c | 9 Not reported | 11 Antibiotics 9 Azithromycin | 1 RSV | (NOS, 7) | Treatment outcome (not reported) |
| Zhang et al. 2021 [116], United States | Retrospective case series, multicenter | 16 | 2 | Mean ± SE, 204 ± 61.5 | Gender (not reported) AND Ethnicity (not reported) | 0 | 0 | 4 | 1 Rhinovirus 1 Adenovirus 1 Influenza A virus | RT-PCR for respiratory specimens (virus) c | 2 Not reported | 2 Not reported | 2 Not reported | (Modified NOS, high) | Treatment outcome (not reported) |
Table 1. Cont.

| Author, Year, Study Location | Study Design, Setting | Number of SARS-CoV-2 Patients Tested for Co-Pathogens, n | Coinfected Patients, n | Age (Months) a | Male, n (%) AND Ethnicity, n b | Bacterial Coinfection, n | Fungal Coinfection, n | Respiratory Viral Coinfection, n | Total Organisms, n | Antimicrobials Used, n | Laboratory Techniques for Co-Pathogen Detection | Admitted to ICU, n | Mechanical Ventilation, n | ARDS, n | Assessment of Study Risk of Bias (Tool Used, Finding) and Treatment Outcome |
|-------------------------------|-----------------------|-----------------------------------------------------------|------------------------|----------------|--------------------------------|-------------------------|-------------------------|-------------------------------|-------------------|------------------------|-----------------------------------------------|----------------|--------------------------|---------|---------------------------------------------------------------|
| Zheng et al. 2020 [137], China | Retrospective cohort, multicenter | 25 | 3 | Median (IQR), 36 (24–108) | 2 (66.7) AND 3 Asian | 4 | 0 | 2 | 3 | Mycoplasma pneumoniae 2 Influenza B virus 1 Enterobacter aerogenes | 5 Meropenem 1 Linezolid | RT-PCR for respiratory specimens (viruses) c | 1 | 1 | 1 | (NOS, 7) 3 survived |
| Zheng et al. 2020 [138], China | Retrospective cohort, single-center | 4 | 1 | 180 | 1 (25) AND 1 Asian | 0 | 0 | 1 | 1 | Influenza B virus | 1 Antibiotics | RT-PCR for respiratory specimens (viruses) c | 0 | 0 | 0 | (NOS, 7) 1 survived |
| Zhu et al. 2020 [139], China | Retrospective cohort, single-center | 257 | 11 | <180 | Gender (not reported) AND 11 Asian | 20 | 2 | 3 | 11 | Not reported | RT-PCR for respiratory specimens (viruses) c | 0 | 0 | 0 | (NOS, 7) 11 survived |
| Zou et al. 2020 [140], China | Retrospective case report, single-center | 2 | 2 | 28 and 156 | 1 (50) AND 2 Asian | 0 | 0 | 2 | 2 | Influenza A virus | 1 Cefticlor | Serum antibody tests (IgM and IgG) | 0 | 0 | 0 | (Modified NOS, high) 2 survived |

Abbreviations: ARDS, acute respiratory distress syndrome; CONS, coagulase-negative Staphylococcus species; CMV, Cytomegalovirus; COVID-19, coronavirus disease 2019; CSF, cerebrospinal fluid; EBV, Epstein–Barr virus; ICU, intensive care unit; IgG, immunoglobulin G; IgM, immunoglobulin M; IQR, interquartile range; MRSA, Methicillin-resistant Staphylococcus aureus; MSSA, Methicillin-susceptible Staphylococcus aureus; NOS, Newcastle–Ottawa scale; RT-PCR, real-time reverse transcription–polymerase chain reaction; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation. a Data are presented as median (25th–75th percentiles), or mean ± SD. b Patients of black ethnicity include African-American, Black African, African, and Afro-Caribbean patients. c PCR assay for multiple respiratory viruses (including influenza virus types A and B, respiratory syncytial virus type A/B, human metapneumovirus, parainfluenza virus types 1–4, other coronaviruses (229E, NL63, and OC43), metapneumovirus, rhinovirus, enterovirus, adenovirus, parechovirus, and Isavirus).
3.2. Demographic, Clinical Characteristics, and Treatment Outcomes of Children with COVID-19 and Bacterial, Fungal, and/or Respiratory Viral Coinfection

The included studies comprised a total of 17,588 children with confirmed SARS-CoV-2 infection who were tested for co-pathogens, as detailed in Table 1. Among these 17,588 COVID-19 patients, bacterial, fungal, and/or respiratory viral coinfections were reported (n = 1633, 9.3%). The median patient age ranged from 1.4 months to 144 months across studies. There was an increased male predominance in pediatric COVID-19 patients diagnosed with bacterial, fungal, and/or viral coinfections in most of the studies (male gender: n = 204, 59.1% compared to female gender: n = 141, 40.9%) [6,7,9,13,20,21,36,38,39,41,42,44,47,48,50,52,56,59,60,62,63,65,69,71,75–77,79,84,87,91,93,97,99–101,111,114,115,121,126–128,130,133]. Asian (n = 205, 24.8%) [8,9,22,23,37,45,54,65,66,80–83,98,108,110,113,116,117,120,131,132,134,135,137–140], Indian (n = 71, 8.6%) [11,31,51,63,72,74,103–105,122], and Black (n = 51, 6.2%) [6,9,15,19,46,55,60,63,95,118] ethnicities.

COVID-19 children coinfected with bacteria, fungi, and/or respiratory viruses were reported to have received antibiotics in 77 studies [5,8,9,12–16,19–23,36,38–40,42,45,46,50–52,55,56,59,60,63–70,72,74–77,80,86–88,90,100,103–107,109,110,112–114,116–118,120–122,124–126,128,131,134–138,140]. The most prescribed antibiotics were azithromycin (n = 109) [9,15,36,39,64,65,70,76,80,87,93,98,100,109,112,116,122,125,131,135], 1st/2nd/3rd generation of cephalosporins (n = 66) [12,13,42,45,60,65,67,77,87,98,100,113,116,121,128], ceftriaxone (n = 29) [12,14,21,38,39,51,52,60,67,68,72,74,86,100,107,112,122,128], isoniazid (n = 13) [19,51,55,59,74,96,103,112,118,124], pyrazinamide (n = 13) [19,51,55,59,74,96,103,112,118,124], rifampicin (n = 13) [19,51,55,59,74,96,103,112,118,124], ethionamide (n = 12) [51,55,59,74,96,103,112,118,124], meropenem (n = 11) [16,20,21,40,50,74,75,80,87,93,137], vancomycin (n = 11) [13,16,21,60,72,74,87,107,114,128], amoxicillin/clavulanic acid (n = 9) [9,45,59,60,76,121], amoxicillin (n = 8) [14,15,20,40,67,77,92,128], clindamycin (n = 8) [13,20,38,60,67,93,100,107,114], ampicillin/sulbactam (n = 7) [39,60,100], and gentamycin (n = 6) [9,19,42,87,92,121]. There were children who were admitted to the intensive care unit (n = 214, 18.6%) [4–9,11–13,15,16,18–23,35,36,39,42,46,51,53,56,58,61,63,64,66,67,72,74,80,81,83–85,87,90,92–97,105,107,109,113,114,116,117,122,123,125–128,131,133,134,137], intubated and placed on mechanical ventilation (n = 98, 9.2%) [4–9,11–13,15–23,35,36,39,42,46,51,56,58,61,67,72,74,80,81,83,87,90,96,105,107,109,114,116,117,126,128,134,137], and suffered acute respiratory distress syndrome (n = 100, 12.5%) [4,6–9,11–13,16–23,39,42,45,48,51,55,56,58,61,66,67,72,74,80,81,83,84,87,90,93,96–98,105,107,109,113,115–117,122,126,128,131,134,137].

Clinical treatment outcomes for the COVID-19 children who were coinfected with bacteria, fungi, and/or respiratory viruses and died was documented in 43 (4.4%) cases [4–23,90,96,105,116], while 931 (95.6%) of the COVID-19 cases recovered [4–11,31,33–36,38,40,42,43,45–48,50–52,54–57,59,60,62–70,72,74–77,80,81,84–97,100–107,110–116,118,119,121–126,128,130–132,134,135,137–140], and final treatment outcome was reported in one patient who remained in the intensive care unit (n = 1, %) [117].

3.3. Meta-Analysis of Bacterial, Fungal, and Respiratory Viral Coinfections in Children with SARS-CoV-2

The overall pooled proportions of COVID-19 children who had laboratory-confirmed bacterial, fungal, and respiratory viral coinfections were 4.73% (95% CI 3.86 to 5.60, n = 445, 34 studies, I² 85%, p < 0.01), 0.98% (95% CI 0.13 to 1.83, n = 17, six studies, I² 49%, p < 0.08), and 5.41% (95% CI 4.48 to 6.34, n = 441, 32 studies, I² 87%, p < 0.01), respectively; (Figures 3–5).
Figure 3. Pooled estimate for the prevalence of bacterial coinfections in children with COVID-19 stratified by the ICU admission (ICU and non-ICU compared to ICU only). [4–9,12,13,20,23,32,36,39,57,58,63,64,66,69,77,80,81,84,85,88,98,105,109,131–133,135,137,139].
In bacterial coinfected COVID-19 children, subgroup analysis showed some difference in the rates between all patients (patients in the ICU and non-ICU group or ICU only group); the ICU and non-ICU group showed a prevalence of 4.91% (95% CI 3.97 to 5.84, \(n = 431\), 28 studies, \(I^2 = 87\%\), \(p < 0.01\)), while the ICU only group showed a prevalence of 3.02% (95% CI 1.70 to 4.34, \(n = 14\), six studies, \(I^2 = 0\%\), \(p = 0.90\)), respectively; Figure 3.

In fungal coinfected COVID-19 children, subgroup analysis showed almost a threefold increase in the rates between all patients (patients in the ICU and non-ICU group or ICU only group); the ICU only group showed a prevalence of 1.72% (95% CI 0.45 to 2.99, \(n = 11\), three studies, \(I^2 = 0\%\), \(p = 0.63\)), while the ICU and non-ICU group showed a prevalence of 0.62% (95% CI 0.00 to 1.55, \(n = 6\), three studies, \(I^2 = 54\%\), \(p = 0.11\)), respectively; Figure 4.

However, in the respiratory viral coinfected COVID-19 children, subgroup analysis showed a slight difference in the rates between all patients (patients in the ICU and non-ICU group or ICU only group); the ICU and non-ICU group showed a prevalence of 5.31% (95% CI 4.31 to 6.30, \(n = 418\), 28 studies, \(I^2 = 88\%\), \(p < 0.01\)), while the ICU only group showed a prevalence of 6.61% (95% CI 5.06 to 8.17, \(n = 23\), four studies, \(I^2 = 0\%\), \(p = 0.90\)), respectively; Figure 5.

Funnel plots for possible publication bias for the pooled effect size to determine the prevalence of bacterial, fungal, and/or fungal coinfections in children with COVID-19 appeared asymmetrical on visual inspection, and Egger’s tests confirmed asymmetry with \(p\)-values < 0.05; Figures 6–8.
Figure 5. Pooled estimate for the prevalence of respiratory viral coinfections in children with COVID-19 stratified by the ICU admission (ICU and non-ICU compared to ICU only). [4–7,9,12,20,23,32,36,39,57,58,63,64,66,69,77,80,81,84,88,98,105,109,131–133,135,137,139].
3.4. Bacterial, Fungal, and Respiratory Viral Co-Pathogens in COVID-19 Children

Specific bacterial co-pathogens were reported in 71/130 (54.6%) studies, which is about 31.8% of the reported coinfections. The most common bacteria were *Mycoplasma pneumoniae* (*n* = 120), *Streptococcus pneumoniae* (*n* = 65), *Mycobacterium tuberculosis* (*n* = 31), *Staphylococcus aureus* (*n* = 12), *Escherichia coli* (*n* = 11), *Haemophilus influenza* (*n* = 10), *Chlamydia pneumoniae* (*n* = 9), and *Pseudomonas aeruginosa* (*n* = 9) (Table 2).
### Table 2. Proportion of all identified bacterial co-pathogens in children with COVID-19 (N = 520).

| Bacterial Pathogen Type                  | Identified Number (%) |
|-----------------------------------------|-----------------------|
| Unspecified bacteria                    | 181 (34.8)            |
| *Mycoplasma pneumoniae*                 | 120 (23.1)            |
| *Streptococcus pneumoniae*              | 65 (12.5)             |
| *Mycobacterium tuberculosis*            | 31 (6)                |
| *Staphylococcus aureus*                 | 12 (2.3)              |
| *Escherichia coli*                      | 11 (2.1)              |
| *Haemophilus influenza*                 | 10 (1.9)              |
| *Chlamydia pneumoniae*                  | 9 (1.7)               |
| *Pseudomonas aeruginosa*                | 9 (1.7)               |
| MSSA                                     | 8 (1.5)               |
| *Moraxella catarrhalis*                 | 7 (1.3)               |
| *Scrub typhus*                          | 7 (1.3)               |
| MRSA                                     | 6 (1.1)               |
| *Salmonella typhi*                      | 5 (1)                 |
| Group A *Streptococcus*                 | 4 (0.8)               |
| *Klebsiella pneumoniae*                 | 4 (0.8)               |
| CONS                                     | 3 (0.6)               |
| *Acinetobacter baumannii*               | 2 (0.4)               |
| *Bordetella pertussis*                  | 2 (0.4)               |
| *Klebsiella oxytoca*                    | 2 (0.4)               |
| *Klebsiella pneumoniae*                 | 2 (0.4)               |
| *Neisseria meningitidis*                | 2 (0.4)               |
| *Prevotella species*                    | 2 (0.4)               |
| *Streptococcus constellatus*            | 2 (0.4)               |
| *Streptococcus agalactiae*              | 1 (0.2)               |
| *Streptococcus intermedius*             | 1 (0.2)               |
| *Streptococcus mitis*                   | 1 (0.2)               |
| *Citrobacter koseri*                    | 1 (0.2)               |
| *Clostridium difficile*                 | 1 (0.2)               |
| *Enterobacter*                          | 1 (0.2)               |
| *Enterobacter aerogenes*                | 1 (0.2)               |
| *Enterobacter cloacae*                  | 1 (0.2)               |
| *Enterobacter asburiae*                 | 1 (0.2)               |
| *Escherichia hermannii*                 | 1 (0.2)               |
| Gram-negative bacilli                   | 1 (0.2)               |
| *Mycobacterium bovis*                   | 1 (0.2)               |
| *Salmonella enteritis*                  | 1 (0.2)               |
| *Staphylococcus epidermidis*            | 1 (0.2)               |

Abbreviations: CONS, coagulase-negative *Staphylococcus* species; COVID-19, coronavirus disease 2019; MRSA, Methicillin-resistant *Staphylococcus aureus*; MSSA, Methicillin-susceptible *Staphylococcus aureus*. 
Fungal co-pathogens were reported in 8/130 (6.1%) studies, which is equal to only 1.4% of the reported coinfections. The most common fungal organisms were *Aspergillus* species (n = 3), fungal bezoars (n = 2), *Candida albicans* (n = 1), *Candida auris* (n = 1), *Candida glabrata* (n = 1), *Candida rugosa* (n = 1), and *Candida tropicalis* (n = 1) (Table 3).

**Table 3.** Proportion of all identified fungal co-pathogens in children with COVID-19 (N = 23).

| Fungal Pathogen Type   | Identified Number (%) |
|------------------------|-----------------------|
| Unspecified fungi      | 13 (56.5)             |
| *Aspergillus* species  | 3 (13)                |
| Fungal bezoars         | 2 (8.7)               |
| *Candida albicans*     | 1 (4.3)               |
| *Candida auris*        | 1 (4.3)               |
| *Candida glabrata*     | 1 (4.3)               |
| *Candida rugosa*       | 1 (4.3)               |
| *Candida tropicalis*   | 1 (4.3)               |

Respiratory viral co-pathogens were reported in 88/130 (67.7%) studies, representing about 66.8% of the reported coinfections. The most common respiratory viruses were RSV (n = 342), Rhinovirus (n = 209), *Influenza A* virus (n = 80), *Adenovirus* (n = 60), *Parainfluenza* virus (types 1–4) (n = 29), *Influenza B* virus (n = 28), *Metapneumovirus* (n = 27), EBV (n = 14), *Cytomegalovirus* (n = 12), *Dengue* virus (n = 12), *Coronaviruses* (HKU-1/OC 43) (n = 11), and *Bocavirus* (n = 10) (Table 4).

**Figure 8.** Funnel plot to evaluate publication bias for the pooled effect size to estimate the prevalence of respiratory viral coinfections in children with COVID-19 based on ICU admission.
Table 4. Proportion of all identified respiratory viral co-pathogens in children with COVID-19 (N = 1090).

| Viral Pathogen Type                          | Identified Number (%) |
|----------------------------------------------|-----------------------|
| RSV                                          | 342 (31.4)            |
| Rhinovirus                                    | 209 (19.2)            |
| Unspecified viruses                           | 198 (18.2)            |
| Influenza A virus                             | 80 (7.3)              |
| Adenovirus                                    | 60 (5.5)              |
| Parainfluenza virus (types 1–4)               | 29 (2.7)              |
| Influenza B virus                             | 28 (2.6)              |
| Metapneumovirus                               | 27 (2.5)              |
| Rotavirus, adenovirus, and norovirus          | 25 (2.3)              |
| EBV                                          | 14 (1.3)              |
| Cytomegalovirus                               | 12 (1.1)              |
| Dengue virus                                  | 12 (1.1)              |
| Coronavirus (HKU-1/OC 43)                     | 11 (1)                |
| Bocavirus                                     | 10 (0.9)              |
| Coronavirus (229E, NL63, and OC43)            | 6 (0.5)               |
| Enterovirus                                   | 5 (0.4)               |
| Herpes simplex virus                          | 5 (0.4)               |
| Coronavirus NL63                              | 5 (0.4)               |
| Varicella zoster virus                        | 4 (0.4)               |
| Rotavirus                                     | 2 (0.2)               |
| Human Herpesvirus 6                           | 1 (0.1)               |
| Norovirus                                     | 1 (0.1)               |
| Parechovirus                                  | 1 (0.1)               |
| Pareovirus B19                                | 1 (0.1)               |
| Hepatitis A virus                             | 1 (0.1)               |
| Herpes virus 4                                | 1 (0.1)               |

Abbreviations: EBV, Epstein–Barr virus; RSV, respiratory syncytial virus.

4. Discussion

This systematic review and meta-analysis included 17,588 laboratory-confirmed COVID-19 children from 130 observational studies to estimate the prevalence of coinfections with bacteria, fungi, and/or respiratory viruses. Children with SARS-CoV-2 infection had the following prevalence of pathogen coinfections: bacterial (4.7%, 95% CI 3.8–5.6), fungal (0.9%, 95% CI 0.1–1.8), and respiratory viral (5.4%, 95% CI 4.4–6.3). COVID-19 children had higher fungal and respiratory viral coinfections in ICU units (1.7%, 95% CI 0.4–2.9 and 6.6%, 95% CI 5–8.1, respectively) than mixed ICU and non-ICU patients. However, bacterial coinfection was lower in children infected with SARS-CoV-2 in ICU group (3%, 95% CI 1.7–4.3). Children with COVID-19 seem to have a distinctly lower susceptibility to bacterial, fungal, and/or respiratory viral coinfections than adults. Our study documents that 4.7% (bacteria), 0.9% (fungal), and 5.4% (viral) of the pediatric COVID-19 population harbor microbiologically confirmed coinfections, which is much lower than the recent systematic review and meta-analysis, including 72 studies, conducted from 1 December 2019 to 31 March 2021, portraying coinfection rates of 15.9% (bacterial), 3.7% (fungal), and 6.6% (viral) in the adult COVID-19 population [141]. Lower rates of bacterial, fungal,
and/or respiratory viral coinfection in children with SARS-CoV-2 infection compared to the adult COVID-19 population may have different explanations. Immunologically, children seem to have an immature receptor system, immune-system-specific regulatory mechanisms, and possible cross-protection from other common bacterial, fungal, and viral infections occurring in children [142,143]. A growing body of evidence suggests that children’s immune systems can neutralize SARS-CoV-2 because their T cells are relatively naïve and mostly untrained, and thus might have a greater capacity to respond to new viruses and eliminate SARS-CoV-2 before it replicates in large numbers [144–146]. Children are also the main reservoir for seasonal coronaviruses, and some researchers have suggested that antibodies for these coronaviruses might confer some protection against SARS-CoV-2 [143,146]. Moreover, children are more protected at the cellular level, as the expression of angiotensin-converting enzyme 2, which is the receptor that SARS-CoV-2 uses for host entry, is less frequently expressed in the epithelial cells of the nasal passages and lungs of younger children [147]. Otherwise, differences can be explained by the numerous different study designs to a large extent, as well as selection bias, consideration of respiratory and extra-respiratory pathogens, microbiological investigations employed, use of culture and non-culture methods, time of specimen collection, exclusion/inclusion of contaminants, climate, temporal variations in microbial epidemiology and the study population itself.

Three previous systematic reviews and meta-analyses reported on bacterial, fungal, and respiratory viral coinfections; however, these studies included mixed populations of adults and children, included a smaller number of studies (with most data for adults and very few pediatric patients), and sensitivity analysis to study the proportion of coinfection in COVID-19 children was not conducted [148–150]. To the best of our knowledge, this is the first and largest systematic review and meta-analysis to report exclusively on bacterial, fungal, and respiratory viral coinfection in children with COVID-19, and we pooled evidence from 130 studies, including at least Mycoplasma pneumoniae, Streptococcus pneumoniae, Mycobacterium tuberculosis, Staphylococcus aureus, RSV, rhinovirus, influenza A or B virus, adenovirus, parainfluenza virus, and metapneumovirus due to their virulence and prevalence, in an attempt to avoid measurement bias. Of the 98.6% who had additional respiratory viruses or bacteria detected, we found that the most common identified virus and bacterium in children with COVID-19 were RSV ($n = 342, 31.4\%$) and Mycoplasma pneumonia ($n = 120, 23.1\%$), in line with findings in two previous systematic reviews and meta-analyses, which reported that RSV and Mycoplasma pneumonia were the most commonly isolated co-pathogens in the adult population with SARS-CoV-2 infection [148,150]. RSV and Mycoplasma pneumonia cause acute respiratory tract illness in people of all ages, and all children are infected with RSV by 2 years of age [151], while approximately one-half of patients infected with Mycoplasma pneumonia are <6 years old (school-age years) [152]. RSV is the most common cause of lower respiratory tract infection in children <1 year of age [153], and bronchiolitis (up to 80% of which is caused by RSV) is a leading cause of hospital admission [154] and an important cause of death in infants and young children [155]. Mycoplasma pneumonia is the second most common cause of respiratory tract infections, and upper and lower respiratory tracts may be affected [156]. This pathogen causes a wide spectrum of illness, ranging from asymptomatic to severe community-acquired pneumonia or extrapulmonary manifestations necessitating ICU admission [157,158]. Several countries have reported that there has been a suppression of RSV and Mycoplasma pneumonia circulation, and their typical seasonality, since early 2020 due to the preventive infection control measures and non-pharmaceutical interventions against SARS-CoV-2 [159–164]. However, RSV and Mycoplasma pneumonia activity rebounded in early–mid 2021 at a fast pace, as public health restrictions and social distancing regulations were relaxed; higher hospitalization rates were reported, and most of the hospitalized children required ICU admission [165–167]. Although two recent studies demonstrated no association between SARS-CoV-2 and RSV coinfection and clinical severity (need or use of supplemental oxygen, ICU admission, mechanical ventilation, and mortality), the evidence was only based on
three small studies [167,168]. In contrast, evidence of clinical severity regarding cases coinfected with SARS-CoV-2 and *Mycoplasma pneumonia* is well-established, and several studies reported such coinfection as being associated with an increase in inpatient mortality, length of hospital stay, and need for mechanical ventilation [69,100,169,170]. In children, both RSV and *Mycoplasma pneumonia* are similar to SARS-CoV-2; as potential triggers for a cytokine storm, leading to the development of Multisystem Inflammatory Syndrome in Children (MIS-C), they appear to play a role in the pathogenesis, and may contribute to the subsequent clinical severity of COVID-19. The cytokines tumor necrosis factor-alpha, interleukin-8, interleukin-6, and interleukin-1 beta were detected in the airway secretions of children infected with RSV and *Mycoplasma pneumonia*, which may act as a double whammy of respiratory pathogens and correlate with severe pathogenesis [171–174]. As coinfection with either the highly contagious RSV or *Mycoplasma pneumonia* and SARS-CoV-2 can modify the disease course and contribute to severity, and can cause serious compilations in children, especially those with high-risk comorbidities, healthcare workers need to consider RSV or *Mycoplasma pneumonia* and SARS-CoV-2 coinfection in the differential diagnosis of acute febrile illness in the endemic areas.

It is noteworthy that in the studies where the laboratory techniques for co-pathogen detection were described, a high number of bacterial and viral coinfections in children infected with SARS-CoV-2 included in our review were diagnosed serologically through the detection of immunoglobulins M and/or G. One of the easiest, most convenient, and fastest point-of-care testing to diagnose COVID-19 and other bacterial, fungal, and/or respiratory co-pathogens is by rapid serology tests; however, serology testing has been associated with many false-positive antibody test results for COVID-19 and mixed pathogens [111,175,176]. Therefore, application of serologic laboratory techniques for co-pathogen detection across all studies was likely to reveal an even higher overall coinfection proportion and high rates of anti-infective use for admitted children with SARS-CoV-2 infection to treat documented or presumed bacterial, fungal, and/or respiratory viral coinfections [177–179]. In line with previous studies, we identified high anti-infective use in pediatric patients with COVID-19 [177,180,181]. As the prevalence of bacterial, fungal, or respiratory viral coinfections in children with COVID-19 is not high, and anti-infectives likely provide minimal benefit as an empirical treatment, clinicians should prescribe anti-infectives wisely, and only in cases with an objective diagnosis of coinfection, as injudicious use of anti-infectives is associated with unintended consequences, such as adverse events, toxicity, resistance, *Clostridioides difficile* infections, risk of emergence and transmission of multidrug-resistant organisms, morbidity, and death [182–187]. Undoubtedly, coinfection in children with COVID-19 is likely to be an important modifier in the development of these abovementioned unintended consequences; however, the degree to which co-pathogens interact with SARS-CoV-2 remains uncertain in many cases, and even where we know that interactions are occurring, the mechanisms are often poorly defined [188,189].

The combined pooled prevalence for fungal coinfections reported in our review in COVID-19 children is very low (0.98%). In general, very low numbers of fungal species, out of thousands of fungi, are pathogenic [190], and fungal infections in children, other than those caused by *Candida* species, are uncommon [191]. This can be explained by the strong natural immunity towards fungi in healthy children, and almost every invasive fungal infection that occurs in children is opportunistic [192]. In line with previous studies, all children infected with SARS-CoV-2 who were coinfected with fungi had recognized risk factors for fungaemia, such as use of central lines, malignancy, renal failure, mechanical ventilation, immunosuppression, neutropenia, solid organ transplant recipients, and use of broad-spectrum parenteral antibiotics and corticosteroids [193,194]. Fungal infections in children can be curbed by early diagnosis and timely treatment with the optimal prescription of antifungals based on culture and susceptibility tests, along with adopting appropriate hygienic and sanitization measures [195,196].
Limitations of the Study

We acknowledge that our study is not without some limitations. First, while all of the evidence discussed was based on many cohorts and case series, and some case reports, many of these were small and performed in single centers, and not necessarily generalizable to children infected with SARS-CoV-2 who had bacterial, fungal, or respiratory viral coinfections. Second, almost all studies included in this review were retrospective in design, except seven prospective studies, which could have introduced potential reporting bias due to reliance on obtaining illness histories regarding the identified pediatric cases with COVID-19 and coinfection from household members or contacts and clinical case records. Third, to assess factors associated with the clinical severity in children infected with SARS-CoV-2 who have coinfections, a larger cohort of patients is needed. Last, the study was not registered in Prospero, an international prospective register of systematic reviews, as this might have added extra work and the merit was mostly limited to the avoidance of duplication.

5. Conclusions

Children with COVID-19 seem to have distinctly lower rates of bacterial, fungal, and/or respiratory viral coinfections than adults. RSV and Mycoplasma pneumoniae were the most common identified virus and bacterium in children infected with SARS-CoV-2. Knowledge of bacterial, fungal, and/or respiratory viral coinfections has potential diagnostic and treatment implications in COVID-19 children.

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Abbreviations

ARDS, acute respiratory distress syndrome; CMV, Cytomegalovirus; CONS, coagulase-negative Staphylococcus species; COVID-19, coronavirus disease 2019; CSF, cerebrospinal fluid; EBV, Epstein–Barr virus; ICU, intensive care unit; IgG, immunoglobulin G; IgM, immunoglobulin M; MRSA, Methicillin-resistant Staphylococcus aureus; MSSA, Methicillin-susceptible Staphylococcus aureus; NOS, Newcastle–Ottawa scale; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RSV, respiratory syncytial virus; RT-PCR, real-time reverse transcription–polymerase
chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

References

1. Rubenstein, S.; Grew, E.; Clouser, K.; Kwok, A.; Veerapandiyathan, A.; Korntz, J.; Pecor, K.; Ming, X. COVID-19 in Pediatric Inpatients: A Multi-Center Observational Study of Factors Associated with Negative Short-Term Outcomes. Children 2021, 8, 951. [CrossRef] [PubMed]

2. Fainardi, V.; Meoli, A.; Chiari, J.; Motta, M.; Skenderaj, K.; Grandinetti, R.; Bergomi, A.; Antodaro, F.; Zona, S.; Esposito, S. Long COVID in Children and Adolescents. Life 2022, 12, 285. [CrossRef] [PubMed]

3. Jugulete, G.; Pacurar, D.; Pavelescu, M.L.; Safta, M.; Gheorghe, E.; Borcos, B.; Pavelescu, C.; Oros, M.; Merisescu, M. Clinical and Evolutionary Features of SARS-CoV-2 Infection (COVID-19) in Children, a Romanian Perspective. Children 2022, 9, 1282. [CrossRef] [PubMed]

4. Anderson, E.M.; Diorio, C.; Goodwin, E.C.; McNerney, K.O.; Weirick, M.E.; Gouma, S.; Bolton, M.J.; Arevalo, C.P.; Chase, J.; Hicks, P. Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) antibody responses in children with multisystem inflammatory syndrome in children (MIS-C) and mild and severe coronavirus disease 2019 (COVID-19). J. Pediatr. Infect. Dis. Soc. 2021, 10, 669–673. [CrossRef] [PubMed]

5. Choudhary, R.; Webber, B.J.; Womack, L.S.; Dupont, H.K.; Chiu, S.K.; Wang, V.; Gerdes, M.E.; Hsu, S.; Shi, D.S.; Duls, T.M. Factors Associated with Severe Illness in Patients Aged <21 Years Hospitalized for COVID-19. Hosp. Pediatr. 2022, 12, 760–783. [CrossRef] [PubMed]

6. Diorio, C.; Henrickson, S.E.; Vella, L.A.; McNerney, K.O.; Chase, J.; Burudipakdee, C.; Lee, J.H.; Jasen, C.; Balamuth, F.; Barrett, D.M. Multisystem inflammatory syndrome in children and COVID-19 are distinct presentations of SARS-CoV-2. J. Clin. Investig. 2020, 130, 5967–5975. [CrossRef]

7. Garazzino, S.; Lo Vecchio, A.; Piantoni, L.; Calò Carducci, F.I.; Marchetti, F.; Meini, A.; Castagnola, E.; Vergine, G.; Donà, D.; Bosis, S.; et al. Epidemiology, Clinical Features and Prognostic Factors of Pediatric SARS-CoV-2 Infection: Results from an Italian Multicenter Study. Front. Pediatr. 2021, 9, 649358. [CrossRef]

8. He, B.; Wang, J.; Wang, Y.; Zhao, J.; Huang, J.; Tian, Y.; Yang, C.; Zhang, H.; Zhang, M.; Gu, L. The metabolic changes and immune profiles in patients with COVID-19. Front. Immunol. 2020, 11, 2075. [CrossRef]

9. Kanthimathinathan, H.K.; Buckley, H.; Lanning, C.; Davis, P.; Ramnarayan, P.; Feltbower, R.; Draper, E.S. Characteristics of severe acute respiratory syndrome coronavirus-2 infection and comparison with influenza in children admitted to UK PICUs. Crit. Care Explor. 2021, 3, e0362. [CrossRef]

10. Le Glass, E.; Hoang, V.T.; Boschi, C.; Ninove, L.; Zandotti, C.; Boutin, A.; Bremond, V.; Dubourg, G.; Ranque, S.; Lagier, J.-C. Incidence and outcome of coinfections with SARS-CoV-2 and rhinovirus. Viruses 2021, 13, 2528. [CrossRef]

11. Mathur, S.B.; Saxena, R.; Pallavi, P.; Jain, R.; Mishra, D.; Jamb, U. Effect of Concomitant Tuberculosis Infection on COVID-19 Disease in Children: A Matched, Retrospective Cohort Study. J. Trop. Pediatr. 2022, 68, fmac056. [CrossRef] [PubMed]

12. Aragón-Nogales, R.; Zurita-Cruz, J.; Vázquez-Rosas, G.; Arias-Flores, R.; Gómez-González, C.; Montaño-Luna, V.; Sámano-Aviña, M.; Pacheco-Rosas, D.; Flores-Ruíz, E.; Villasis-Keever, M. Clinical presentation of pediatric patients with symptomatic SARS-Cov-2 infection during the first months of the COVID-19 pandemic in a single center in Mexico City. Front. Pediatr. 2022, 10, 912784. [CrossRef] [PubMed]

13. Brothers, E.M.; Lidsky, S.; Simmons, J.; Nakagawa, T. A Child With COVID-19, Type 1 Diabetes, and Candida glabrata: A Case Report and Literature Review. Clin. Pediatr. 2021, 60, 554–558. [CrossRef] [PubMed]

14. Chacón-Cruz, E.; Lopatynsky, E.Z.; Machado-Contreras, J.R.; Gatica-Herrera, R.; Zazueta, O.E. Fatal Pediatric Meningococcal Invasive Disease Caused by Neisseria meningitidis Serogroup C and Co-Infected With SARS-CoV-2: Report of a Case in Tijuana, Mexico. Cureus 2022, 14, e22100. [CrossRef]

15. Freij, B.J.; Gebara, B.M.; Tariq, R.; Wang, A.-M.; Gibson, J.; El-Wiher, N.; Krasan, G.; Patek, P.M.; Levasseur, K.A.; Amin, M. Fatal central nervous system co-infection with SARS-CoV-2 and tuberculosis in a healthy child. BMC Pediatr. 2020, 20, 429. [CrossRef]

16. Hamzavi, S.S.; Ghohami, M.A.; Dashti, A.S. A Case of COVID 19 and Staphylococcus Coinfection. Arch. Iran. Med. 2020, 23, 568–569. [CrossRef]

17. Hashemi, S.A.; Safamanesh, S.; Ghasemzadeh-moghaddam, H.; Ghafoori, M.; Azimian, A. High prevalence of SARS-CoV-2 and influenza A virus (H1N1) coinfection in dead patients in Northeastern Iran. J. Med. Virol. 2021, 93, 1008–1012. [CrossRef]

18. Hashemi, S.A.; Safamanesh, S.; Ghasemzadeh-Moghaddam, H.; Ghafoori, M.; Mohajerzadeh-Heydari, M.; Namdar-Ahmadabad, H.; Azimian, A. Report of death in children with SARS-CoV-2 and human metapneumovirus (hMPV) coinfection: Is hMPV the trigger? J. Med. Virol. 2021, 93, 579. [CrossRef]

19. Mulale, U.K.; Kashamba, T.; Strysko, J.; Kyokunda, L.T. Fatal SARS-CoV-2 and Mycobacterium tuberculosis coinfection in an infant: Insights from Botswana. BMJ Case Rep. CP. 2021, 14, e239701. [CrossRef]

20. Nygaard, U.; Petersen, A.; Larsen, A.R.; Rytter, M.J.H.; Hartling, U.; Kirkby, N.; Hansen, R.N.; Nielsen, A.B.; Lundstrøm, K.; Holm, M. Fatal SARS-CoV-2-Associated Panton-Valentine Leukocidin-producing Staphylococcal Bacteremia: A Nationwide Multicenter Cohort Study. Pediatr. Infect. Dis. J. 2022, 41, e142–e145. [CrossRef]

21. Rebelo, A.; Dias, D.I.; Sousa, E.; Alves, J.F.; Pinto, M.; Pereira, M.; Menezes, F. Fatal meningococcaemia in a SARS-CoV-2-positive adolescent. J. Paediatr. Child Health 2022, 58, 354. [CrossRef] [PubMed]
46. Ciucu, C.; Fabi, M.; Di Luca, D.; Niro, F.; Ghizzi, C.; Donati, A.; Balducci, A.; Rocca, A.; Zarbo, C.; Gargiulo, G.D. Myocarditis and coronary aneurysms in a child with acute respiratory syndrome coronavirus 2. *ESC Heart Fail.* 2021, 8, 761–765. [CrossRef]

47. Danis, K.; Epaulard, O.; Bénét, T.; Gaymard, A.; Campoy, S.; Botelho-Nevers, E.; Bouscambert-Duchamp, M.; Spaccaferrà, G.; Ader, F.; Mailles, A. Cluster of coronavirus disease 2019 (COVID-19) in the French Alps, February 2020. *Clin. Infect. Dis.* 2020, 71, 825–832. [CrossRef]

48. Danley, K.; Kent, P. 4-month-old boy coinfected with COVID-19 and adenovirus. *BMJ Case Rep.* 2020, 13, e236264. [CrossRef]

49. DeBiasi, R.L.; Song, X.; Delaney, M.; Bell, M.; Smith, K.; Pershad, J.; Anususinha, E.; Hahn, A.; Hamdy, R.; Harik, N. Severe coronavirus disease-2019 in children and young adults in the Washington, DC, metropolitan region. *J. Pediatr.* 2020, 223, 199–203.e1. [CrossRef]

50. Demirkan, H.; Yavuz, S. COVID-19 complicated with acute renal failure due to mycotic bezoars in two children. *Arch. Esp. Urol.* 2021, 74, 712–715.

51. Dhanawade, S.S.; Kurade, A.V. Tuberculous Meningitis and COVID-19 Coinfection: A Diagnostic Challenge. *Pediatr. Infect. Dis. 2021*, 3, 79–80. [CrossRef]

52. Di Nora, A.; Pizzo, F.; Costanzo, G.; Ruggieri, M.; Falsaperla, R. Human herpes 6 encephalitis in co-infection with Covid-19. *Acta Neurol. Belg.* 2022, 2, 1–2. [CrossRef] [PubMed]

53. Dikkranian, L.; Barry, S.; Ala, A.; Chiotos, K.; Gist, K.; Bhalala, U.; Danesh, V.; Heavner, S.; Gharpure, V.; Bjornstad, E.C. SARS-CoV-2 With Concurrent Respiratory Viral Infection as a Risk Factor for a Higher Level of Care in Hospitalized Pediatric Patients. *Pediatr. Emerg. Care 2022*, 38, 472–476. [CrossRef] [PubMed]

54. Dong, X.; Cao, Y.; Liu, P.; Xiong, G.; Yang, Z.; Wang, M.; Li, Y.; Yu, X.-j. Coinfection of SARS-CoV-2 and multiple respiratory pathogens in children. *Pediatr. Transplant.* 2022, 26, 200060. [CrossRef] [PubMed]

55. Essajee, F.; Solomons, R.; Goussard, P.; Van Toorn, R. Child with tuberculosis meningitis and COVID-19 coinfection complicated by extensive cerebral sinus venous thrombosis. *BMJ Case Rep.* 2020, 13, e238597. [CrossRef] [PubMed]

56. Ferdous, A.; Hassain, M.M.; Afrin, M.; Shirin, M. Dengue With Co-infection and Multiple Organ Dysfunction in a Child. *Cureus 2021*, 13, e20763. [CrossRef] [PubMed]

57. Frost, H.M.; Sebastian, T.; Keith, A.; Kurtz, M.; Dominguez, S.R.; Parker, S.K.; Jenkins, T.C. COVID-19 and Acute Otitis Media in Children: A Case Series. *J. Prim. Care Community Health 2022*, 13, 2351. [CrossRef]

58. Garazzino, S.; Montagnani, C.; Donà, D.; Meini, A.; Felici, E.; Vergine, G.; Bernardi, S.; Giaccher, R.; Vecchio, A.L.; Marchisio, P. Multicentre Italian study of SARS-CoV-2 infection in children and adolescents, preliminary data as of 10 April 2020. *Eurosurveillance 2020*, 25, 200060. [CrossRef]

59. Goussard, P.; Solomons, R.S.; Andronikou, S.; Mfingwana, L.; Verhagen, L.M.; Rabie, H. COVID-19 in a child with tuberculous airway compression. *Pediatr. Pulmonol.* 2020, 55, 2201–2203. [CrossRef]

60. Guy, K.; Lelegren, M.; Shomaker, K.; Han, J.; Lam, K. Management of complicated acute sinusitis in the setting of concurrent COVID-19. *Am. J. Otolarngol.* 2022, 1–2. [CrossRef] [PubMed]

61. Halabi, K.C.; Wang, H.; Leber, A.L.; Sánchez, P.; Ramilo, O.; Mejias, A. Respiratory Syncytial Virus and SARS-CoV-2 Coinfections in Children. *Pediatr. Pulmonol.* 2022. [CrossRef]

62. Hare, D.; Gonzalez, G.; Dean, J.; McDonnell, K.; Carr, M.J.; De Gascon, C.F. Genomic epidemiological analysis of SARS-CoV-2 household transmission. *Access Microbiol.* 2021, 3, 000252. [CrossRef]

63. Hassoun, A.; Daham, N.; Kelly, C. A case series of SARS-CoV-2 RT-PCR-Positive hospitalized infants 60 Days of age or younger from 2 New York city pediatric emergency departments. *Clin. Pediatr. 2021*, 60, 247–251. [CrossRef] [PubMed]

64. Hertzberg, E.; Lim, C.A.; Eiting, E.; Yung, S.; Nunez, J.; Calderon, Y.; Barnett, B. Respiratory Viral Co-infection with Novel Coronavirus in Children: A Case Series. *Res. Sq. 2020*. [CrossRef]

65. Jarmolinski, T.; Matkowska-Kocjan, A.; Rosa, M.; Olejnik, I.; Gorczyńska, E.; Kalwak, K.; Ussowicz, M. SARS-CoV-2 viral clearance during bone marrow aplasia after allogeneic hematopoietic stem cell transplantation—A case report. *Pediatr. Transplant.* 2021, 25, e13875. [CrossRef] [PubMed]

66. Jiang, S.; Liu, P.; Xiong, G.; Yang, Z.; Wang, M.; Li, Y.; Yu, X.-j. Coinfection of SARS-CoV-2 and multiple respiratory pathogens in children. *Clin. Chem. Lab. Med.* 2020, 58, 1160–1161. [CrossRef] [PubMed]

67. Jose, P.-M.M.; Paola, Z.-S.; Eduardo, D.-G.; Arturo, S.-M.M.O.; Fernando, B.-G. A case of coinfection of a pediatric patient with acute SARS-COV-2 with MIS-C and severe DENV-2 in Mexico: A case report. *BMC Infect. Dis.* 2021, 21, 1072. [CrossRef] [PubMed]

68. Kakuya, F.; Okubo, H.; Fujiyasu, H.; Wakabayashi, I.; Syouji, M.; Kinebuchi, T. The first pediatric patients with coronavirus disease 2019 (COVID-19) in Japan; The risk of co-infection with other respiratory viruses. *Jpn. J. Infect. Dis.* 2020, 181, 377–380. [CrossRef]

69. Karaaslan, A.; Çetin, C.; Akin, Y.; Tekol, S.D.; Sobü, E.; Demirhan, R. Coinfection in SARS-CoV-2 infected children patients. *J. Infect. Dev. Cities.* 2021, 15, 761–765. [CrossRef]

70. Karimi, A.; Tabatabaei, S.R.; Khalili, M.; Sadr, S.; Alibeik, M.; Omidmalayeri, S.; Fahimzad, S.A.; Ghaniee, R.M.; Armin, S. COVID-19 and chickenpox as a viral co-infection in a 12-year-old patient, a case report. *Arch. Pediatr. Infect. Dis.* 2020, 8, e105591. [CrossRef]

71. Katz, J.; Yue, S.; Xue, W. Herpes simplex and herpes zoster viruses in COVID-19 patients. *Ir J. Med Sci.* 2021, 191, 1093–1097. [CrossRef]
72. Kazi, M.A.; Ghosh, S.; Roychowdhury, S.; Giri, P.P.; Sarkar, M. A Case Study of Dual Infection of Dengue and COVID-19: Presenting as Multigorgan Dysfunction in an Infant. J. Trop. Pediatr. 2020, 67, fmaa080. [CrossRef] [PubMed]

73. Keshavarz Valian, N.; Pourakbari, B.; Asma Ashari, K.; Hosseinpour Sadeghi, R.; Mahmoudi, S. Evaluation of human coronavirus OC43 and SARS-COV-2 in children with respiratory tract infection during the COVID-19 pandemic. J. Med. Virol. 2022, 94, 1450–1456. [CrossRef] [PubMed]

74. Khataniar, H.; Sunil, D.; Lalitha, A. A case report on disseminated tuberculosis in the setting of coronavirus disease 2019: Cause or consequence? Emerg. Crit. Care Med. 2022, 2, 175–178. [CrossRef]

75. Lambrou, M.; Antari, V.; Totikidis, G.; Papadimitriou, E.; Roilides, E.; Papakonstantinou, E. Coinfections and pulmonary embolism in a patient with onset of Leukemia concomitantly with COVID19 Case report. J. Clin. Case Rep. Med. Imag. Health Sci. 2022, 1. Available online: https://jmedcasereportsimages.org/articles/JCRMHS-1004.pdf (accessed on 14 October 2022).

76. Le Roux, P.; Millardet, E.; Duquenoy, A.; Labbé, F.; Vandendriessche, A. Pleuropneumonia resulting from varicella and COVID-19 co-infection in a 10-month-old infant. Arch. Pédiatrie 2020, 27, 509–510. [CrossRef]

77. Leclercq, C.; Toutain, F.; Baleydier, F.; L’Huillier, A.G.; Wagner, N.; Lironi, C.; Calza, A.-M.; Ansari, M.; Blanchard-Roher, G. Pediatric acute B-cell lymphoblastic leukemia developing following recent SARS-CoV-2 infection. J. Pediatr. Hematol. Oncol. 2021, 43, e1177–e1180. [CrossRef]

78. Lee, B.R.; Harrison, C.J.; Myers, A.L.; Jackson, M.A.; Selvarangan, R. Differences in pediatric SARS-CoV-2 symptomology and Co-infection rates among COVID-19 Pandemic waves. J. Clin. Virol. 2022, 154, 105220. [CrossRef]

79. Leuzinger, K.; Roloff, T.; Gosert, R.; Sogaard, K.; Naegle, K.; Rentsch, K.; Bingisser, R.; Nickel, C.H.; Pargger, H.; Bassetti, S. Epidemiology of severe acute respiratory syndrome coronavirus 2 emergence amidst community-acquired respiratory viruses. J. Infect. Dis. 2020, 222, 1270–1279. [CrossRef]

80. Li, H.; Chen, K.; Liu, M.; Xu, H.; Xu, Q. The profile of peripheral blood lymphocyte subsets and serum cytokines in children with 2019 novel coronavirus pneumonia. J. Infect. 2020, 81, 115–120. [CrossRef]

81. Li, Y.; Wang, H.; Wang, F.; Lu, X.; Du, H.; Xu, J.; Han, F.; Zhang, L.; Zhang, M. Co-infections of SARS-CoV-2 with multiple common respiratory pathogens in infected children: A retrospective study. Medicine 2021, 100, e24315. [CrossRef]

82. Lin, D.; Liu, L.; Zhang, M.; Hu, Y.; Yang, Q.; Guo, J.; Guo, Y.; Dai, Y.; Xu, Y.; Cai, Y. Co-infections of SARS-CoV-2 with multiple common respiratory pathogens in infected patients. Sci. China Life Sci. 2020, 63, 606–609. [CrossRef] [PubMed]

83. Ma, Y.-L.; Xia, S.-Y.; Wang, M.; Zhang, S.-M.; Wen-Hui, D.; Chen, Q. Clinical features of children with SARS-CoV-2 infection: An analysis of 115 cases. Chin. J. Contemp. Pediatr. 2020, 22, 290–293.

84. Mania, A.; Pokorska-Spiewak, M.; Figlerowicz, M.; Mazur-Melewska, K.; Faltin, K.; Talarek, E.; Zawadka, K.; Dobrzeniecka, A.; Ciechanowski, P. Pneumonia, gastrointestinal symptoms, comorbidities, and coinfections as factors related to a lengthier hospital stay in children with COVID-19—Analysis of a paediatric part of Polish register SARSTer. Infect. Dis. 2022, 54, 196–204. [CrossRef] [PubMed]

85. Mannheim, J.; Gretsch, S.; Layden, J.E.; Fricchione, M.J. Characteristics of hospitalized pediatric coronavirus disease 2019 cases in Chicago, Illinois, March–April 2020. J. Pediatr. Infect. Dis. Soc. 2020, 9, 519–522. [CrossRef]

86. Mansour, A.; Atoui, R.; Mohsen, R.; Fares, Y.; Fares, J. First Case of an Infant with COVID-19 in the Middle East. J. Med. Virol. 2020, 92, e7520. [CrossRef]

87. Marest, C.; Capretti, M.G.; Aceti, A.; Vocale, C.; Carfagni, F.; Serra, C.; Campoli, C.; Lazzarotto, T.; Corvaglia, L. Severe neonatal COVID-19: Challenges in management and therapeutic approach. J. Med. Virol. 2022, 94, 1701–1706. [CrossRef]

88. Mithal, L.B.; Machut, K.Z.; Muller, W.J.; Kociolek, L.K. SARS-CoV-2 infection in infants less than 90 days old. J. Pediatr. Infect. Dis. Soc. 2020, 9, e140–e142. [CrossRef] [PubMed]

89. Mohammadi, M.; Bid-Hendi, S.; Baghershiroodi, M.; Chehrazi, M.; Yahyapour, Y.; GouranOurimi, A.; Sadeghi, F. Detection of Human Adenovirus among Iranian Pediatric Hospitalized Patients Suspected to COVID-19 Epidemiology and Comparison of Clinical Features. Res. Sq. 2022. [CrossRef]

90. Moin, S.; Farooqi, J.; Rattani, S.; Nasir, N.; Zaka, S.; Jabeen, K.C. Auris and non-C. auris candidemia in hospitalized adult and pediatric COVID-19 patients; single center data from Pakistan. Med. Mycol. 2021, 59, 1238–1242. [CrossRef]

91. Morand, A.; Roquelaure, B.; Colson, P.; Amранne, S.; Bosdure, E.; Raoult, D.; Lagier, J.-C.; Fabre, A. Child with liver transplant recover from COVID-19 infection. A case report. Arch. Pédiatrie 2020, 27, 275–276. [CrossRef]

92. Ng, K.F.; Bandi, S.; Bird, P.W.; Tang, J.W.-T. COVID-19 in neonates and infants: Progression and recovery. Pediatr. Infect. Dis. J. 2020, 39, e140–e142. [CrossRef] [PubMed]

93. Nieto-Moro, M.; Ecclesia, F.G.; Tomé-Masa, I.; Caro-Patón, G.D.L.; Leoz-Gordillo, I.; Cabrero-Hernández, M.; García-Salido, A. SARS-CoV-2 and Streptococcus pneumoniae coinfection as a cause of severe pneumonia in an infant. Pediatr. Pulmonol. 2020, 55, 2198–2200. [CrossRef] [PubMed]

94. Oba, J.; Silva, C.A.; Toma, R.K.; Carvalho WBd Delgado, A.F. COVID-19 and coinfection with Clostridioides (Clostridium) difficile in an infant with gastrointestinal manifestation. Einstein 2020, 18. [CrossRef] [PubMed]

95. Ogbunbayo, A.E.; Mogotsi, M.T.; Sondlaine, H.; Nkwadipo, K.R.; Sabiu, S.; Nyaga, M.M. Pathogen Profile of Children Hospitalised with Severe Acute Respiratory Infections during COVID-19 Pandemic in the Free State Province, South Africa. Int. J. Environ. Res. Public Health 2022, 19, 10418. [CrossRef]

96. Palermo, D.; Levi, A.; Casco, N.; González, N.; González, C.; Pizarro, M.; Poropat, A.; Tullas, M.; Jajati, M. COVID-19 y tuberculosis en 5 hospitales de la Ciudad de Buenos Aires. Rev. Am. Med. Respir. 2020, 251–254.
122. Tiwari, L.; Shekhar, S.; Bansal, A.; Kumar, P. COVID-19 with dengue shock syndrome in a child: Coinfection or cross-reactivity? BMJ Case Rep. CP. 2020, 13, e239315. [CrossRef]

123. Trifonova, I.; Christova, I.; Madzharova, I.; Angelova, S.; Voleva, S.; Yordanova, R.; Tchervenkiarova, T.; Krumova, S.; Korsun, N. Clinical significance and role of coinfections with respiratory pathogens among individuals with confirmed severe acute respiratory syndrome coronavirus-2 infection. Front. Public Health 2022, 2855. [CrossRef] [PubMed]

124. Vanezetti, C.P.; Salvo, C.P.; Kuschner, P.; Brusca, S.; Solveyra, F.; Vilela, A. Coinfección tuberculosis y COVID-19. Medicina 2020, 80, 100–103. [PubMed]

125. Varela, F.H.; Sartor, I.T.S.; Polese-Bonatto, M.; Azevedo, T.R.; Kern, L.B.; Fazolo, T.; de David, C.N.; Zavaglia, G.O.; Fernandes, I.R.; Krauser, J.R.M. Rhinovirus as the main co-circulating virus during the COVID-19 pandemic in children. J. Pediatr. 2022, 98, 579–586. [CrossRef] [PubMed]

126. Verheijen, A.C.; Janssen, E.E.; van der Putten, M.E.; van Horck, M.W.; van Well, G.T.; Van Loo, I.H.; Hütten, M.C.; Van Mechelen, K. Management of severe neonatal respiratory distress due to vertical transmission of severe acute respiratory syndrome coronavirus 2: A case report. J. Med. Case Rep. 2022, 16, 140. [CrossRef] [PubMed]

127. Vidal, A.R.; Vaughan, A.; Innocentii, F.; Colombe, S.; Nerlander, L.; Rachwal, N.; Ciancio, B.C.; Mougkou, A.; Carvalho, C.; Delgado, E. Hepatitis of unknown aetiology in children—epidemiological overview of cases reported in Europe, 1 January to 16 June 2022. Eurosurveillance 2022, 27, 2200483.

128. Vu, K.C.; Heresi, G.P.; Chang, M.L. SARS-CoV-2 and Streptococcus pneumoniae Coinfection in a Previously Healthy Child. Case Rep. Pediatr. 2021, 2021, 890794. [CrossRef]

129. Wang, Q.; Gerdes, M.E.; Shi, D.S.; Choudhary, R.; Dulsik, T.M.; Hsu, S.; Idubor, O.I.; Wendel, A.M.; Agathis, N.T. Characteristics and clinical outcomes of children and adolescents aged <18 years hospitalized with COVID-19—Six hospitals, United States, July–August 2021. Morb. Mortal. Wkly. Rep. 2021, 70, 1766.

130. Wehl, G.; Laible, M.; Rauchenzauner, M. Co-infection of SARS-CoV-2 and influenza A in a pediatric patient in Germany. Klin. Pädiatrie 2020, 232, 217–218. [CrossRef]

131. Wu, Q.; Xing, Y.; Shi, L.; Li, W.; Gao, Y.; Pan, S.; Wang, Y.; Wang, W.; Xing, Q. Coinfection and other clinical characteristics of COVID-19 in children. Pediatrics 2020, 146, e20200961. [CrossRef]

132. Xia, W.; Shao, J.; Guo, Y.; Peng, X.; Li, Z.; Hu, D. Clinical and CT features in pediatric patients with COVID-19 infection: Different points from adults. Pediatr. Pulmonol. 2020, 55, 1169–1174. [CrossRef]

133. Yakovlev, A.S.; Belyatdinolov, I.K.; Mazankova, L.N.; Samitova, E.R.; Osmanov, I.M.; Gavelya, N.V.; Volok, V.P.; Kolpakova, E.S.; Shishova, A.A.; Dracheva, N.A. SARS-CoV-2 infection in children in Moscow in 2020: Clinical features and impact on circulation of other respiratory viruses: SARS-CoV-2 infection in children in Moscow in 2020. Int. J. Infect. Dis. 2022, 116, 331–338. [CrossRef] [PubMed]

134. Zeng, L.; Xia, S.; Yuan, W.; Yan, K.; Xiao, F.; Shao, J.; Zhou, W. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. JAMA Pediatr. 2020, 174, 722–725. [CrossRef] [PubMed]

135. Zhang, C.; Gu, J.; Chen, Q.; Deng, N.; Li, J.; Huang, L.; Zhou, X. Clinical and epidemiological characteristics of pediatric SARS-CoV-2 infections in China: A multicenter case series. PLoS Med. 2020, 17, e1003130. [CrossRef]

136. Zhang, D.D.; Acree, M.E.; Ridgway, J.P.; Shah, N.; Hazra, A.; Ravichandran, U.; Kumar, M. Characterizing coinfection in children with COVID-19: A dual center retrospective analysis. Infect. Control. Hosp. Epidemiol. 2021, 42, 1160–1162. [CrossRef] [PubMed]

137. Zheng, F.; Liao, C.; Fan, Q.-h.; Chen, H.-b.; Zhao, X.-g.; Xie, Z.-g.; Li, X.-l.; Chen, C.-x.; Lu, X.-x.; Liu, Z.-s. Clinical characteristics of children with coronavirus disease 2019 in Hubei, China. Curr. Med. Sci. 2020, 40, 275–280. [CrossRef]

138. Zheng, X.; Wang, H.; Su, Z.; Li, W.; Yang, D.; Deng, F.; Chen, J. Co-infection of SARS-CoV-2 and influenza virus in early stage of the COVID-19 epidemic in Wuhan, China. J. Infect. 2020, 81, e128–e129. [CrossRef]

139. Zhu, X.; Ge, Y.; Wu, T.; Zhao, K.; Chen, Y.; Wu, B.; Zhu, F.; Zhu, B.; Cui, L. Co-infection with respiratory pathogens among COVID-19 cases. Virus Res. 2020, 285, 108805. [CrossRef] [PubMed]

140. Zou, B.; Ma, D.; Li, Y.; Qiu, L.; Chen, Y.; Hao, Y.; Luo, X.; Shu, S. Are they just two children COVID-19 cases confused with flu? Front. Pediatr. 2020, 8, 341. [CrossRef]

141. Alhumaidi, S.; Al Mutair, A.; Al Alawi, Z.; Alshawi, A.M.; Alomran, S.A.; Almuhanna, M.S.; Almuslim, A.A.; Bu Shafia, A.H.; Alotaibi, A.M.; Ahmed, G.Y. Coinfections with bacteria, fungi, and respiratory viruses in patients with SARS-CoV-2: A systematic review and meta-analysis. Pathogens 2021, 10, 809. [CrossRef]

142. Lyu, J.; Miao, T.; Dong, J.; Cao, R.; Li, Y.; Chen, Q. Reflection on lower rates of COVID-19 in children: Does childhood immunizations offer unexpected protection? Med. Hypotheses 2020, 143, 109842. [CrossRef]

143. Sinaei, R.; Pezeshki, S.; Parvaresh, S.; Sinaei, R. Why COVID-19 is less frequent and severe in children: A narrative review. World J. Pediatr. 2021, 17, 10–20. [CrossRef] [PubMed]

144. Loske, J.; Röhmel, J.; Lukassen, S.; Stricker, S.; Magalhães, V.G.; Liebig, J.; Chua, R.L.; Thürmann, L.; Messingschläger, M.; Seegebarth, A. Pre-activated antiviral innate immunity in the upper airways controls early SARS-CoV-2 infection in children. Nat. Biotechnol. 2020, 40, 319–324. [CrossRef] [PubMed]

145. Weisberg, S.P.; Connors, T.J.; Zhu, Y.; Baldwin, M.R.; Lin, W.-H.; Wontakal, S.; Szabo, P.A.; Wells, S.B.; Dogra, P.; Gray, J. Distinct antibody responses to SARS-CoV-2 in children and adults during the COVID-19 clinical spectrum. Nat. Immunol. 2021, 22, 25–31. [CrossRef]

146. Nogrady, B. How kids’ immune systems can evade COVID. Nature 2020, 588, 382–383. [CrossRef] [PubMed]
170. Li, Y. The role of respiratory co-infection with influenza or respiratory syncytial virus in the clinical severity of COVID-19 patients: A systematic review and meta-analysis. *Authora Prepr. 2022*, 12, 05040. [CrossRef]

171. Li, A.; Zhou, X.; Lu, W.; Zhou, Y.; Liu, Q. COVID-19 in two infants in China. *Immun. Inflamm. Dis. 2020*, 8, 380–383. [CrossRef]

172. Rangroo, R.; Young, M.; Davis, A.; Pack, S.; Thakore, S.; Schepcow, A.; Oyesanmi, O. The Severity of the Co-infection of Mycoplasma pneumoniae in COVID-19 Patients. *Cureus 2022*, 14, e24563. [CrossRef]

173. Zhang, Y.; Mei, S.; Zhou, Y.; Huang, M.; Dong, G.; Chen, Z. Cytokines as the good predictors of refractory Mycoplasma pneumoniae pneumonia in school-aged children. *Sci. Rep. 2016*, 6, 37037. [CrossRef] [PubMed]

174. Yang, J.; Hooper, W.C.; Phillips, D.J.; Talkington, D.F. Cytokines in Mycoplasma pneumoniae infections. *Cytokine Growth Factor Rev. 2004*, 15, 157–168. [CrossRef] [PubMed]

175. McNamara, P.; Flanagan, B.; Selby, A.; Hart, C.; Smyth, R. Pro-and anti-inflammatory responses in respiratory syncytial virus bronchiolitis. *Eur. Respir. J. 2004*, 23, 106–112. [CrossRef] [PubMed]

176. Pinto, R.A.; Arredondo, S.M.; Bono, M.R.; Gagiero, A.A.; Diaz, P.V. T helper 1/T helper 2 cytokine imbalance in respiratory syncytial virus infection is associated with increased endogenous plasma cortisol. *Pediatrics 2006*, 117, e878–e886. [CrossRef]

177. Yan, G.; Lee, C.K.; Lam, L.T.; Yan, C.; Chua, Y.X.; Lim, A.Y.; Phang, K.F.; Kew, G.S.; Teng, H.; Ngai, C.H. Covert COVID-19 and false-positive dengue serology in Singapore. *Lancet Infect. Dis. 2020*, 20, 536. [CrossRef]

178. Liu, V.; Leaungwutiwong, P.; Thippornchai, N.; Thawornkuno, C.; Chatchen, S.; Chancharoenthana, W.; Tandhavanant, S.; Muangnoicharoen, S.; Piyaphanee, W.; Chantratita, N. False Positivity of Anti-SARS-CoV-2 Antibodies in Patients with Acute Tropical Diseases in Thailand. *Trop. Med. Infect. Dis. 2022*, 7, 132. [CrossRef]

179. Grau, S.; Hernández, S.; Echeverria-Esnal, D.; Almendral, A.; Ferrer, R.; Limón, E.; Horcajada, J.P.; (Vincat-Proa), O.B.O.T.C.I.C.A.S.P. Antimicrobial Consumption among 66 Acute Care Hospitals in Catalonia: Impact of the COVID-19 Pandemic. *Antibiotics 2021*, 10, 943. [CrossRef]

180. Lai, C.-C.; Wang, C.-Y.; Hsueh, P.-R. Co-infections among patients with COVID-19: The need for combination therapy with non-anti-SARS-CoV-2 agents? *J. Microbiol. Immunol. Infect. 2020*, 53, 505–512. [CrossRef]

181. Mazumder, P.; Kalamdhad, A.; Chaminda, G.T.; Kumar, M. Coalescence of co-infection and antimicrobial resistance with SARS-CoV-2 infection: The blues of post-COVID-19 world. *Case Stud. Chem. Environ. Eng. 2021*, 3, 100093. [CrossRef]

182. Silva, A.R.O.d.S.; Salgado, D.R.; Nagem, L.P.; Castanheira, D.; Emmerick, I.C.M.; Lima, E.D.C. Increased use of antibiotics in the intensive care unit during coronavirus disease (COVID-19) pandemic in a brazilian hospital. *Front. Pharmacol. 2021*, 12, 778386. [CrossRef]

183. Mah-E-Muneer, S.; Hassan, M.Z.; Biswas, M.A.A.J.; Rahman, F.; Akhtar, Z.; Das, P.; Islam, M.A.; Chowdhury, F. Use of antimicrobials among suspected COVID-19 patients at selected hospitals, Bangladesh: Findings from the first wave of COVID-19 pandemic. *Antibiotics 2021*, 10, 738. [CrossRef] [PubMed]

184. Ahmad, N.; Khan, M.; Saleem, W.; Karobari, M.I.; Mohamed, R.N.; Heboyan, A.; Rabaan, A.A.; Mutair, A.A.; Alhumaid, S.; Alsaadiq, S.A. Evaluation of bi-lateral co-infections and antibiotic resistance rates among COVID-19 patients. *Antibiotics 2022*, 11, 276. [CrossRef] [PubMed]

185. Thoma, R.; Seneghini, M.; Seiffert, S.N.; Vuichard Gysin, D.; Scanferla, G.; Haller, S.; Flury, D.; Boggian, K.; Kleger, G.-R.; Filipovic, M. The challenge of preventing and containing outbreaks of multidrug-resistant organisms and Candida auris during the coronavirus disease 2019 pandemic: Report of a carbapenem-resistant Acinetobacter baumannii outbreak and a systematic review of the literature. *Antimicrob. Resist. Infect. Control. 2022*, 11, 12. [PubMed]

186. Luo, Y.; Grinspan, L.T.; Wu, Y.; Adams-Sommer, V.; Willey, D.K.; Patel, G.; Grinspan, A.M. Hospital-onset Clostridioides difficile in COVID-19 Patients. *Cureus 2022*, 14, 120496. [CrossRef]

187. Temperoni, C.; Caiazzo, L.; Barchiesi, F. High prevalence of antibiotic resistance among opportunistic pathogens isolated from patients with COVID-19 under mechanical ventilation: Results of a single-center study. *Antibiotics 2021*, 10, 1080. [CrossRef]

188. Martinez-Guerra, B.A.; Gonzalez-Lara, M.F.; de-Leon-Cividanes, N.A.; Tamez-Torres, K.M.; Roman-Montes, C.M.; Rajme-Lopez, S.; Villalobos-Zapata, G.I.; Lopez-Garcia, N.I.; Martinez-Gamboa, A.; Sifuentes-Osornio, J. Antimicrobial resistance patterns and antibiotic use during hospital conversion in the COVID-19 pandemic. *Antibiotics 2021*, 10, 182. [CrossRef]

189. Chen, Z.; Guo, J.; Jiang, Y.; Shao, Y. High concentration and high dose of disinfectants and antibiotics used during the COVID-19 pandemic threaten human health. *Environ. Sci. Eur. 2021*, 33, 11. [CrossRef]

190. Bassetti, M.; Kollef, M.H.; Timsit, J.-F. Bacterial and fungal superinfections in critically ill patients with COVID-19. *Intensive Care Med. 2020*, 46, 2071–2074. [CrossRef]

191. Hoque, M.N.; Akter, S.; Mishu, I.D.; Islam, M.R.; Rahman, M.S.; Akhter, M.; Islam, I.; Hasan, M.M.; Rahman, M.M.; Sultana, M. Microbial co-infections in COVID-19: Associated microbiota and underlying mechanisms of pathogenesis. *Microbiol. Pathog. 2021*, 156, 104941. [CrossRef]

192. Pana, Z.D.; Vikelouda, K.; Rolilides, E. Rare fungal infections in children: An updated review of the literature. *Curr. Fungal Infect. Rep. 2014*, 8, 21–36. [CrossRef]

193. Noni, M.; Stathi, A.; Velegraki, A.; Malamati, M.; Kalampaliki, A.; Zachariadou, L.; Michos, A. Rare invasive yeast infections in greek neonates and children, a retrospective 12-year study. *J. Fungi 2020*, 6, 194. [CrossRef] [PubMed]

194. Jain, A.; Jain, S.; Rawat, S. Emerging fungal infections among children: A review on its clinical manifestations, diagnosis, and prevention. *J. Pharm. Bioallied Sci. 2010*, 2, 314. [CrossRef] [PubMed]
195. Zaoutis, T.E.; Prasad, P.A.; Localio, A.R.; Coffin, S.E.; Bell, L.M.; Walsh, T.J.; Gross, R. Risk factors and predictors for candidemia in pediatric intensive care unit patients: Implications for prevention. *Clin. Infect. Dis.* 2010, 51, e38–e45. [CrossRef] [PubMed]

196. Santolaya, M.E.; Alvarado, T.; Queiroz-Telles, F.; Colombo, A.L.; Zurita, J.; Tiraboschi, I.N.; Cortes, J.A.; Thompson, L.; Guzman, M.; Sifuentes, J. Active surveillance of candidemia in children from Latin America: A key requirement for improving disease outcome. *Pediatr. Infect. Dis. J.* 2014, 33, e40–e44. [CrossRef] [PubMed]