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KLEBSIELLA PNEUMONIAE COINFECTION IN PEDIATRIC PATIENTS WITH COVID-19: A REVIEW

COINFECÇÃO POR KLEBSIELLA PNEUMONIAE EM PACIENTES PEDIÁTRICOS COM COVID-19: UMA REVISÃO

COINFECCIÓN POR KLEBSIELLA PNEUMONIAE EN PACIENTES PEDIÁTRICOS CON COVID-19: UNA REVISIÓN

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ABSTRACT

COVID-19 in pediatric patients, although often less severe than in adults, can be complicated by bacterial co-infections, particularly by Klebsiella pneumoniae (KP), an opportunistic pathogen associated with high rates of antimicrobial resistance and adverse clinical outcomes. This article systematically reviews the literature on KP co-infection in children with COVID-19, highlighting its prevalence, risk factors, clinical impact, and management strategies. An integrative literature review was performed, covering articles published between 2020 and 2025 in PubMed, Scopus, Web of Science, and ScienceDirect databases. Observational, retrospective, and prospective studies were included, focusing on pediatric patients diagnosed with COVID-19 and KP co-infection. Thematic analysis identified patterns of prevalence and clinical severity. This study reinforces that, although COVID-19 in children often presents a mild to moderate course, KP co-infection represents an aggravating factor, and highlights the lack of robust pediatric studies addressing KP co-infection in pediatric patients with COVID-19.

Keywords: Antimicrobial Resistance. COVID-19. Healthcare-Associated Infections (Hais). Klebsiella Pneumoniae. SARS Cov-2.

RESUMO

A COVID-19 em pacientes pediátricos, embora frequentemente menos grave do que em adultos, pode ser complicada por coinfecções bacterianas, particularmente por Klebsiella

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pneumoniae (KP), um patógeno oportunista associado a altas taxas de resistência antimicrobiana e desfechos clínicos adversos. Este artigo revisa sistematicamente a literatura sobre coinfecção por KP em crianças com COVID-19, destacando sua prevalência, fatores de risco, impacto clínico e estratégias de manejo. Foi realizada uma revisão integrativa da literatura, abrangendo artigos publicados entre 2020 e 2025 nas bases de dados PubMed, Scopus, Web of Science e ScienceDirect. Foram incluídos estudos observacionais, retrospectivos e prospectivos, com foco em pacientes pediátricos diagnosticados com COVID-19 e coinfecção por KP. A análise temática identificou padrões de prevalência e gravidade clínica. Este estudo reforça que, embora a COVID-19 em crianças frequentemente apresente um curso leve a moderado, a coinfecção por KP representa um fator agravante e destaca a falta de estudos pediátricos robustos abordando a coinfecção por KP em pacientes pediátricos com COVID-19.

Palavras-chave: Resistência Antimicrobiana. COVID-19. Infecções Relacionadas à Assistência à Saúde (HIS). Klebsiella Pneumoniae. SARS-CoV-2.

RESUMEN
La COVID-19 en pacientes pediátricos, aunque a menudo menos grave que en adultos, puede complicarse con coinfecciones bacterianas, en particular por Klebsiella pneumoniae (KP), un patógeno oportunista asociado con altas tasas de resistencia a los antimicrobianos y resultados clínicos adversos. Este artículo revisa sistemáticamente la literatura sobre la coinfección por KP en niños con COVID-19, destacando su prevalencia, factores de riesgo, impacto clínico y estrategias de manejo. Se realizó una revisión bibliográfica integradora que abarcó artículos publicados entre 2020 y 2025 en las bases de datos PubMed, Scopus, Web of Science y ScienceDirect. Se incluyeron estudios observacionales, retrospectivos y prospectivos, centrados en pacientes pediátricos diagnosticados con COVID-19 y coinfección por KP. El análisis temático identificó patrones de prevalencia y gravedad clínica. Este estudio refuerza que, si bien la COVID-19 en niños suele presentar una evolución leve a moderada, la coinfección por KP representa un factor agravante y destaca la falta de estudios pediátricos sólidos que aborden la coinfección por KP en pacientes pediátricos con COVID-19.

Palabras clave: Resistencia a los Antimicrobianos. COVID-19. Infecciones Asociadas a la Atención Médica (IAAS). Klebsiella Pneumoniae. SARS-Cov-2.

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1 INTRODUCTION

Klebsiella pneumoniae (KP) is a Gram-negative bacterium associated with hospital-acquired and community-acquired infections, such as pneumonia and sepsis, especially in pediatric and immunosuppressed patients. In regions such as sub-Saharan Africa and South Asia, this microorganism has a significant impact on infant mortality and is frequently identified as one of the agents responsible for deaths in children under five years of age [1]. Furthermore, in intensive care units (ICUs), the spread of carbapenem-resistant KP has become a critical challenge, due to the scarcity of effective therapies and the risk of local epidemics. The emergence of multidrug-resistant strains further worsens patient prognosis, increasing mortality rates and burdening healthcare systems with additional costs. [2].

Age significantly influences the immune response of children exposed to KP, with several factors such as the maturity of the immune system, underlying health conditions, and specific immune cell functions playing crucial roles. The immune response in children is not uniform and varies with age, affecting the susceptibility and outcomes of KP infections [3, 4].

Co-infections involving bacterial and viral pathogens represent an important factor in morbidity and mortality on a global scale [5]. Evidence from previous outbreaks, such as those caused by the influenza virus, shows that approximately one-third of cases develop secondary bacterial infections, with a higher prevalence among critically ill patients admitted to ICUs [6].

COVID-19 is a disease of zoonotic origin, where its infectious agent is SARS-CoV-2, possibly originating from wild animals. However, the virus has developed the ability to affect other species, including the ability to infect humans, through a process called spillover. Currently, the vast majority of diseases that infect humans (about 75%) originate from zoonoses, and this occurs due to human proximity to the animal environment and, consequently, due to the increased rate of exposure to infectious agents that surround it, increasing the risk of spillover [7, 8].

SARS-CoV-2 enters host cells primarily through the angiotensin-converting enzyme 2 (ACE2) receptor, which is abundantly expressed in the respiratory tract and other tissues such as the gastrointestinal tract and nervous system [9–11].

Scientific evidence shows that COVID-19, like other viral infections, is often associated with bacterial and fungal complications. Observational study conducted by Morovati and collaborators [12] identified a rate of 33.5% of co-infections in individuals with a confirmed diagnosis of the disease. The specialized literature indicates that between 25%

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and 42% of hospitalized patients develop secondary infections, with a higher incidence in severe cases, and this factor is significantly correlated with unfavorable clinical outcomes [13–15].

Co-infection of KP with SARS-CoV-2 may negatively impact the course of the disease, as it may contribute to poor patient prognosis, especially in the case of high-risk populations, such as the elderly [16]. Hospitalized patients with COVID-19 are highly susceptible to secondary infections, with KP being identified as the second most prevalent bacterial agent in respiratory co-infections in this context, preceded only by Streptococcus pneumoniae [17].

This study aimed to map and analyze the data available in the scientific literature on KP co-infections in children with COVID-19, a topic that has been little explored compared to studies in adults. The aim was to identify and systematize the existing evidence on the occurrence and outcomes of this specific co-infection in the pediatric population, considering the relative scarcity of research dedicated to this age group. The investigation focused on understanding which aspects of the problem have already been described for children and which knowledge gaps persist.

2 METHODOLOGY

This is a qualitative study with an exploratory approach and bibliographic method, carried out based on the analysis of scientific articles published in recognized databases. The objective was to identify and analyze the impacts of Klebsiella pneumoniae coinfection in patients diagnosed with COVID-19.

2.1 SEARCH TYPE

This is a qualitative exploratory study, based on a bibliographic survey, aiming at the systematization and critical interpretation of the scientific knowledge available on the subject. Bibliographic research allows the gathering, categorizing and analysis of previously published information, favoring the understanding of patterns, relationships and gaps in the field investigated.

2.2 SEARCH STRATEGY

Systematic searches were conducted in the PubMed, Scopus, Web of Science and ScienceDirect databases. A combination of controlled and uncontrolled descriptors in English was used, with the use of Boolean operators ("AND", "OR") to construct the search

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strategies. The main terms used were: "Klebsiella pneumoniae", "COVID-19", "coinfection", "bacterial infection", "pediatric" and "clinical outcomes".

2.3 INCLUSION AND EXCLUSION CRITERIA

Articles published between January 2020 and May 2025 were included. Written in English. Available in full text. Original studies (cohort, case-control, observational studies) and literature reviews. Conference abstracts, letters to the editor, editorials and isolated case reports, duplicate articles, studies that did not explicitly address co-infection between Klebsiella pneumoniae and COVID-19 in pediatric patients were excluded..

2.4 DATA COLLECTION

Initially, articles were identified according to the search criteria and screened by titles and abstracts. Then, the full texts of the selected articles were read in full to confirm eligibility.

2.5 DATA ANALYSIS

The data extracted from the selected articles were analyzed using thematic analysis, as proposed by Braun and Clarke [18]. This qualitative technique allows us to identify, organize and describe patterns of emerging themes from the data.

The analysis aimed to summarize the main clinical and epidemiological impacts attributed to Klebsiella pneumoniae coinfection in pediatric patients with COVID-19, considering outcomes such as mortality rates, length of hospital stay, infectious complications and use of antimicrobials.

2.6 ETHICAL CONSIDERATIONS

As this is a study based on secondary data in the public domain, without direct involvement of human beings, this study was exempted from the need for approval by a Research Ethics Committee, in accordance with Resolution No. 510/2016 of the National Health Council.

3 RESULTS AND DISCUSSION

According to the established search strategies, 10 publications were identified in the PubMed database, of which 4 met the inclusion criteria. In the Scopus database, 36 articles were found, of which 3 were selected after applying the criteria. In the Web of Science, only

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1 article was located, but it did not meet the inclusion criteria. In the ScienceDirect database, no articles relevant to the objectives of the study were found. To support the discussion, the bibliographic search resulted in 8 scientific articles that met the inclusion criteria, as shown in Table 1.

Table 1

Results of the research of scientific articles to support the discussion

Author/year	Country	Title	Type of Study	Objective	Main Results
Zhu *et al.*, (2020)	*China*	*Co-infection with respiratory pathogens among COVID-2019 cases*	retrospective study	To explore the prevalence of respiratory co-infections in patients with COVID-19	Lower co-infection rates in children vs. adults, suggesting lower frequency/severity.
Singh *et al.*, (2021)	*EUA*	*SARS-CoV-2 respiratory co-infections: Incidence of viral and bacterial co-pathogens*	observational study	Analyze incidence of viral/bacterial copathogens in COVID-19+	*K. pneumoniae* among identified bacterial pathogens; lower rates in COVID-19+.
Raychaudhuri *et al.*, (2021)	*Índia*	*COVID-19 and Co-infection in Children: The Indian Perspectives*	prospective observational study	Assess the spectrum of co-infections in children with COVID-19	15.03% with co-infections; *K. pneumoniae* among the main pathogens, associated with greater severity.
Ciptaningtyas *et al.*, (2022)	*Indonésia*	*Bacterial colonization of the upper airways of children positive and negative for SARS-CoV-2 during the COVID-19 pandemic*	cross-sectional exploratory study	Comparing bacterial colonization in children with COVID-19+ vs. COVID-19−	Significant differences in colonization patterns, with impact on respiratory microbiota.
Xu *et al.*, (2024)	*China*	*Analysis of the potentially pathogenic bacteria of lower respiratory tract infections in*	retrospective study	Impact of the pandemic on pediatric bacterial infections	Reduction of *K. pneumoniae* during the pandemic; effect of sanitary measures

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		children per-, during and post-COVID-19: a retrospective study			
Yakovlev *et al.,* (2024)	*Russia*	*Prevalence and Clinical Impact of Viral and Bacterial Coinfections in Hospitalized Children and Adolescents Aged under 18 Years with COVID-19 during the Omicron Wave in Russia*	retrospective study	Characterize coinfections in the Omicron wave in hospitalized children	Approximately one-third of COVID-19 cases in the study were associated with co-infections, with *K. pneumoniae* among the identified bacterial pathogens.
Qing Li *et al.,* (2024)	*china*	*Pediatric respiratory pathogen dynamics in Southern Sichuan, China: a retrospective analysis of gender, age, and seasonal trends*	retrospective study and cohort study	Respiratory pathogen trends in children post-COVID-19	*K. pneumoniae in 4.9% of severe cases, associated with worse outcomes.*
Yue *et al.,* (2025)	*China*	*Changes in children respiratory infections pre and post COVID-19 pandemic*	retrospective study	Assess changes in post-pandemic respiratory infections	Increase in *K. pneumoniae* after relaxation of health measures.

Resistant KP has attracted increasing attention worldwide in recent years. During the COVID-19 pandemic, a significant increase in serious nosocomial bacterial infections caused by KP has been observed in several countries, although most available studies have focused on adult populations.[15, 16, 19–21]. However, data on co-infection between KP and SARS-CoV-2 in pediatric patients remain scarce despite the increasing importance of understanding the impact of these associated infections in the pediatric population.

A comprehensive study conducted in the Luzhou region (Southern Sichuan, China) analyzed 12,546 children, where pre-COVID-19 and during COVID-19 periods were investigated, reported a pathogen detection rate of 52.8%, indicating that more than half of the cases presented identifiable respiratory pathogens. Viral infections accounted for 32%, while bacterial infections accounted for 29.8% of cases, with Staphylococcus aureus (S. aureus) being the most prevalent (7.3%) [22].

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The study observed an increase in KP detection rates, particularly in severe cases of respiratory tract infections (RTI). It was notably present in 4.9% of the severe group, indicating its association with more severe health outcomes in children. The study reported that as the severity of infection increased, the detection rates of bacterial pathogens, including KP, also increased. This correlation emphasizes the importance of monitoring this pathogen in clinical settings, especially in severe cases. KP was part of a broader discussion on co-infections, which have been identified as a significant risk factor for the development of pneumonia in children. The study highlighted that co-infections can exacerbate the severity of respiratory infections, with KP being a notable bacterial contributor. The study highlights the need for targeted diagnostic and treatment strategies to effectively manage infections caused by this bacterium in children. [22].

An Indian study conducted during the pandemic (Raychaudhuri et al. 2021) revealed that 15.03% of children with confirmed COVID-19 had co-infections, with 20.6% of these cases progressing to moderate to severe disease. This highlights the significant burden of severe disease among children with COVID-19. The predominant pathogens included methicillin-resistant S. aureus (MRSA) and methicillin-sensitive S. aureus (MSSA). KP has been identified as one of the major Gram-negative bacteria responsible for co-infections in children with COVID-19. The findings regarding KP in children mirror the trends observed in adult studies, where this bacterium also plays a significant role in sepsis, particularly with prolonged ICU stays. In adults, KP and Escherichia coli were found to increase in prevalence with longer ICU stays. The presence of KP in co-infected pediatric patients is associated with increased morbidity. Children with co-infections, including those caused by KP, required more intensive medical interventions, such as mechanical ventilation and longer stays in the Pediatric Intensive Care Unit (PICU). [23].

A study in Russia that evaluated 574 pediatric patients during the pandemic reported that one-third of COVID-19 cases in the study were associated with co-infections. The study highlighted those bacterial co-infections, including those caused by KP, were associated with a higher incidence of pneumonia compared with SARS-CoV-2 monoinfection. This suggests that KP, together with other bacterial pathogens, may significantly contribute to the severity of disease in children with COVID-19. [24]. This indicates a notable occurrence of simultaneous infections among pediatric patients during the Omicron wave in Russia.

The study by Xu et al., [25], conducted in Suzhou, Southeast China, analyzed 85,659 (ages 28 days to 16 years) diagnosed with lower respiratory tract infections (LRTI), it was

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observed that the overall positive rate for bacterial pathogens decreased from 39.7% in the pre-COVID-19 period to 38.3% during COVID-19, and then to 30.4% in the post-COVID-19 period. A decline in KP detection rates was observed during and after the pandemic compared to the pre-COVID-19 period. The decrease was attributed to public health interventions (social distancing, mask use, enhanced hygiene). Seasonal epidemiological trends, including those of KP, have not yet returned to pre-pandemic levels, indicating persistent changes in pathogen circulation. The data support the positive impact of containment strategies in reducing bacterial infections. The failure to normalize bacterial circulation patterns post-pandemic suggests a need for continued surveillance [25].

Another Chinese study in Shandong, located between the north and south of the country, revealed distinct patterns in KP circulation in respiratory specimens from children in three critical epidemiological periods: it reported that before the COVID-19 pandemic, KP had a stable positivity rate of 5.17% among respiratory tract specimens collected from January 2018 to December 2019. This indicates a consistent presence of KP in respiratory infections during this period. During the COVID-19 pandemic (January 2020 to December 2022), the KP positivity rate decreased significantly to 1.35%. This decline suggests that non-pharmaceutical interventions implemented during the pandemic effectively reduced KP circulation among children. After the lifting of COVID-19 restrictions in January 2023, the KP positivity rate increased to 8.52%. This resurgence can be attributed to the phenomenon of “immunity debt”, where the relaxation of restrictions has led to a sudden increase in infections due to reduced population immunity. [26]

The study revealed a significant increase in the prevalence of co-infecting bacteria, particularly KP, in the post-pandemic period, suggesting an important change in the epidemiology of pediatric respiratory infections. This indicates a change in the dynamics of respiratory infections, where KP may now be more frequently involved in co-infections with other pathogens. KP is particularly relevant in younger populations, with the highest susceptibility observed in children aged 3 years and older. This age group is critical for monitoring respiratory infections caused by KP and other pathogens [26].

Singh et al., [27] in the USA, reported 33% of SARS-CoV-2 positive patients in the study had a concomitant bacterial infection in the first wave of the pandemic, with KP being the most prevalent bacterial co-infections in both SARS-CoV-2 positive and negative patients, accounting for 2.14% of pathogens in SARS-CoV-2 co-infection.

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The Indonesian study conducted by Ciptaningtyas et al. [28] investigated upper respiratory tract bacterial colonization in asymptomatic children during the COVID-19 pandemic, revealing that KP accounted for 1.8% of the isolated bacteria. In a previous investigation, the same authors reported that KP was the most frequently identified bacterial agent in lower respiratory tract infections in children under five years of age in Indonesia, with a prevalence of 7% [29]. The authors highlight that, during the period of reduced mobility and school closures due to the pandemic, the lower exposure of children to community settings may have contributed to the decrease in KP transmission.

In Jiangsu Province, eastern China, during the pandemic period, ZHU et al,. [17] reported a co-infection rate of 92.8% in the pediatric population. This indicates that a significant majority of pediatric patients had co-infections with one or more respiratory pathogens along with SARS-CoV-2, presenting with mild to moderate symptoms, with the majority of asymptomatic cases in this age group being female (68.2%). In the broader context of co-infections, the study indicated that 11 pathogens were found in the pediatric group, KP being one of them. However, specific numerical data regarding the exact number of cases involving KP in this age group were not detailed. [17].

The observed variability in SARS-CoV-2 detection rates across regions can be attributed to several factors, including differences in testing policies, implementation of public health measures, and diagnostic capacity between locations. [30]. Although SARS-CoV-2 infection is generally milder in pediatric patients when compared to adults over 60 years of age [31], Bacterial co-infection in this population represents a significant challenge, particularly due to the peculiar immunological characteristics of children [3, 4].

Children's developing immune systems respond differently to infections, making them more susceptible to secondary bacterial complications [4]. In this context, KP emerges as a relevant pediatric public health problem, with studies demonstrating its considerable impact in this population. Available data, although still limited, reveal that KP infection in pediatric patients is associated with more severe clinical outcomes, including increased need for mechanical ventilation and prolonged pediatric ICU stays. Studies such as that of Li et al. [22] in China demonstrated that the bacteria was present in 4.9% of severe cases, with a particular impact on children aged 3 and over [26]. These findings highlight the importance of greater attention to this pathogen, especially considering the growing challenge of antimicrobial resistance and the need for specific therapeutic protocols for the pediatric population.

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Despite the initial perception of COVID-19 as less severe in children, co-infection with KP represents a relevant clinical concern that warrants further investigation and the implementation of specific surveillance systems for this population. Existing data, although still scarce, point to the need to develop clinical guidelines that consider the physiological and immunological particularities of children, as well as regional resistance patterns, to better address this significant pediatric public health problem.

4 FINAL CONSIDERATIONS

The results of this review indicate that KP co-infection in pediatric patients with COVID-19 can negatively impact clinical prognosis, contributing to worsening of the disease, increased length of hospital stay, and increased demand for intensive therapeutic support. Although there is increasing data on bacterial co-infections in adults, studies specifically focused on the pediatric population are still scarce. Given the immunological particularities of children, whose immune systems are still developing and respond differently to infectious agents, it is essential to conduct research that investigates not only the prevalence and clinical outcomes of co-infection, but also the immunological mechanisms involved in this pathogen-host interaction.

In addition, the identification of multidrug-resistant strains of KP in hospital settings highlights the importance of microbiological surveillance, rational use of antibiotics, and strengthening infection control policies in pediatric units. The advancement of knowledge about the inflammatory response in co-infected children can provide valuable support for the development of more precise and effective therapeutic strategies.

Therefore, this review reinforces the need for clinical, immunological and epidemiological investigations aimed at the child population, to support medical interventions and public policies that contribute to the containment of bacterial resistance and to the improvement of outcomes in children affected by severe viral respiratory infections.

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