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Coinfection with SARS-CoV-2 among patients with *Streptococcus pneumoniae* in Casablanca

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Abstract

Background During the COVID-19 pandemic caused by SARS-CoV-2, coinfections with *Streptococcus pneumoniae* have emerged as a significant public health concern. The impact of these coinfections on disease severity and mortality rates remains underexplored. This study aims to address this gap by analyzing the clinical outcomes of patients coinfecting with *S. pneumoniae* and SARS-CoV-2 at CHU Ibn Rochd in Casablanca, Morocco, between 2020 and 2022.

Methods A cohort of 120 hospitalized patients diagnosed with *S. pneumoniae* infection was studied retrospectively and prospectively. Clinical and demographic data, vaccination status, and infection characteristics were collected. Among these patients, 41 were identified as coinfecting with both pathogens. Statistical analyses, including multivariate logistic regression, were performed to assess associations between coinfection and clinical outcomes, such as ICU admission and mortality.

Results Compared to non-coinfecting patients, those coinfecting with SARS-CoV-2 had higher ICU admission (53.7% vs. 24.05%) and mortality (39.02% vs. 13.9%) rates. Multivariate analysis identified coinfection and increasing age as independent predictors of severe outcomes. The most frequent pneumococcal serotypes were 3, 19 A, 6 B, and 9 V, with 31.7% of cases involving non-vaccine types. Most coinfecting patients, especially those who died, were unvaccinated against pneumococcus or SARS-CoV-2.

Conclusions Coinfection with SARS-CoV-2 significantly increases the risk of severe outcomes in patients with *S. pneumoniae* infection. These findings highlight the importance of early detection and support the implementation of comprehensive vaccination strategies targeting high-risk populations.

Clinical trial number Not applicable.

Keywords Coinfections, SARS-CoV-2, *Streptococcus pneumoniae*, ICU admission, Mortality, Vaccination, Serotypes

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Introduction

The COVID-19 pandemic, triggered by the SARS-CoV-2 and first reported in December 2019, was declared a Public Health Emergency of International Concern by the World Health Organization (WHO) on March 11, 2020 [1]. In Morocco, the Ministry of Health reported the first confirmed case on March 2, 2020, marking the virus's official entry into the country [2]. This early detection prompted a rapid national response aimed at curtailing the epidemic's spread through containment measures and travel restrictions, which were crucial in managing the pandemic's initial health and economic impacts. The virus spreads mainly via respiratory droplets, affecting the upper respiratory tract with effects ranging from mild symptoms to severe conditions, especially in individuals over 60 years old or those with comorbidities [1].

Moreover, *Streptococcus pneumoniae*, also known as pneumococcus, continues to pose a significant challenge for public health, being a leading cause of severe respiratory infections, particularly among children [3]. It has frequently been identified as causing severe secondary infections, thereby increasing morbidity and mortality, especially in the context of viral pneumonia. Historically, it was the predominant coinfecting pathogen during influenza pandemics, contributing to a significant number of deaths during the early 20th-century H1N1 pandemic [4].

The concurrent presence of these pathogens underscores the necessity of understanding the implications of their coinfection. Recent studies highlight the complexity and potential for worsened clinical outcomes in at-risk populations due to coinfections by SARS-CoV-2 and pneumococcus [5, 6].

In response to these threats, vaccines have been globally deployed. For COVID-19, various vaccines, including those developed by Sinopharm, Sinovac, AstraZeneca, Johnson & Johnson, and Pfizer-BioNTech, have been introduced [7]. To combat *S. pneumoniae*, pneumococcal vaccines such as the 23-valent polysaccharide vaccine (PPV-23) and conjugate vaccines (PCV-7, PCV-10, and PCV-13) are available, providing protection against the most common pneumococcal serotypes [8].

Our study, conducted at the Ibn Rochd University Hospital in Casablanca, aims to provide insights into the distribution of *S. pneumoniae* among COVID-19 patients compared to those uninfected by the virus, and to explore the serotype distribution among coinfecting patients. By analyzing demographic characteristics and the association of coinfection with disease severity, we aim to provide valuable insights into the interactions between these pathogens and their clinical and epidemiological implications.

Materials and methods

Study setting

This study was conducted at the Ibn Rochd University Hospital Center (CHU) in Casablanca, Morocco. This leading public tertiary care facility serves the Casablanca region. It receives cases of serious diseases such as meningitis and complicated diseases from other hospitals. Our study covers the period from January 1, 2020, to December 31, 2022, encompassing all patients diagnosed with *Streptococcus pneumoniae* infection during this timeframe.

Study design

This is a descriptive retrospective and prospective study focusing on hospitalized patients at CHU Ibn Rochd with pneumococcal infection and examining the impact of SARS-CoV-2 coinfection. Coinfection has been specifically studied since the emergence of COVID-19 in Morocco in March 2020. Patients of all ages with a confirmed *S. pneumoniae* infection were included.

Data collection

Data were collected from the hospital's clinical records and its computerized system, Kalisil®. *S. pneumoniae* infection was identified by isolating both invasive and non-invasive strains through initial culture, confirmed by RT-PCR testing. SARS-CoV-2 infection was confirmed through RT-PCR testing on respiratory samples. Demographic data, clinical features, vaccination status, and infection outcomes were extracted from medical records.

Identification and typing methods

All retained *S. pneumoniae* isolates were identified following standard bacteriology procedures, including α -hemolysis, optochin susceptibility, and bile solubility tests. The typing of *S. pneumoniae* serogroups was performed using the SSI Diagnostica Immulex™ Pneumotest Kit, which differentiates serotypes included in the 23-valent pneumococcal polysaccharide vaccine from non-vaccine types. Precise typing within identified serogroups by the Immulex™ kit was accomplished through a combination of the Quellung reaction and multiplex real-time polymerase chain reaction (RT-PCR), following guidelines from the Centers for Disease Control and Prevention (CDC) [9].

Statistical analysis

Statistical analysis was performed using GraphPad Prism 10® software. Categorical variables, including gender, clinical presentation, ICU admission, death, type of pneumococcal infection, as well as COVID-19 and pneumococcal vaccination statuses, were compared between groups using Chi-square tests or Fisher's exact test, as appropriate.

To assess the independent effect of SARS-CoV-2 coinfection on clinical outcomes, a multivariate logistic regression analysis was conducted. The dependent variable was severe outcome, defined as ICU admission or death. Covariates included age (as a continuous variable), SARS-CoV-2 PCR positivity, pneumococcal vaccination, and COVID-19 vaccination status.

Model performance was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC), and calibration was assessed using the Hosmer–Lemeshow goodness-of-fit test. Odds ratios (ORs) with 95% confidence intervals (CIs) were reported. A p -value < 0.05 was considered statistically significant.

Results

Sociodemographic data

In this study, we investigated the epidemiological and clinical characteristics of patients infected with *S. pneumoniae* and SARS-CoV-2 compared to those infected with *S. pneumoniae* only. A total of 41 patients were infected with both pathogens, while 79 patients were infected with *S. pneumoniae* alone. The analysis revealed no significant difference in gender distribution between the two groups ($p = 0.5623$). The age distribution among coinfecting individuals showed a statistically significant difference compared to those with *S. pneumoniae* infection alone ($p = 0.0082$), with a higher prevalence of coinfection observed in the 15–59 year age group, while infections solely by *S. pneumoniae* were predominant among patients aged 0 to 14 years.

Clinical presentation analysis demonstrated a higher prevalence of pneumonia in the coinfection group compared to the *S. pneumoniae* only group (43.9% vs. 31.6%), although the difference did not reach statistical significance ($p = 0.0731$). Furthermore, a significantly higher proportion of coinfecting patients required ICU admission (53.7% vs. 24.05%, $p = 0.0021$) and experienced mortality (39.02% vs. 13.9%, $p = 0.0027$) compared to those with *S. pneumoniae* only. Notably, there was no significant difference in the type of pneumococcal infection between the two groups ($p = 0.8476$). Additionally, a higher percentage of patients in the *S. pneumoniae* only group had received COVID-19 vaccination compared to the coinfection group (46.84% vs. 29.27%, $p = 0.0789$). Vaccination against *S. pneumoniae* in children under 15 years of age also revealed no significant difference between the two groups ($p = 0.7120$).

Among coinfecting patients, the distribution of outcomes varied across age groups. Specifically, 70% of individuals aged 60 and above, as well as 62.5% of children under 15 years old, experienced fatal outcomes. In contrast, 27.78% of adults aged between 15 and 60 succumbed to the infection. Our data analysis, conducted using the Chi-square test, revealed significant

associations between age groups and various outcome categories (deceased, complicated cases, and recoveries) among individuals coinfecting with COVID-19 and pneumococcus. The distribution of outcomes across different age groups is illustrated in Fig. A2 in Appendix A, indicating a statistically significant correlation ($p = 0.0440$). Furthermore, detailed epidemiological and clinical characteristics are summarized in Table 1.

Predictors of severe clinical outcomes

A multivariate logistic regression was performed to identify independent predictors of severe clinical outcomes (ICU admission or death). As shown in Table 2, SARS-CoV-2 coinfection was independently associated with a significantly increased risk of severe outcomes (OR = 2.861; 95% CI: 1.215–6.888). Age was also a significant predictor (OR = 1.028; 95% CI: 1.004–1.055).

Vaccination against *S. pneumoniae* (OR = 2.267; 95% CI: 0.7587–7.095) and COVID-19 (OR = 0.4855; 95% CI: 0.1912–1.188) were not statistically significant, as their confidence intervals included 1. The model demonstrated acceptable discriminative power (AUC = 0.71; 95% CI: 0.62–0.81; $p < 0.0001$), with good calibration (Hosmer–Lemeshow test $p = 0.29$) and an overall correct classification rate of 67.5%.

Coinfection with SARS-CoV-2 in hospitalized patients with *S. pneumoniae*

The observed data from 2020 to 2022 reveal variations in COVID-19 and *Streptococcus pneumoniae* coinfections across age groups, with a notable peak in 2021, particularly in adults aged 15–60 years. A subsequent decline in all age categories was recorded in 2022. The Chi-square test results yielded a p -value of 0.8846, indicating no statistically significant difference in the annual distribution of coinfections (Fig. 1).

Treatment and evolution of coinfecting patients

Regarding treatment, all patients were administered third-generation cephalosporin (Ceftriaxone), either as monotherapy or in combination with aminoglycosides. In this study, individuals infected with the COVID-19 virus received symptomatic treatment, including the administration of Vitamin C, Vitamin D, and Paracetamol. Additionally, for adults identified as vulnerable due to one or more risk factors for complications, a specific curative treatment was recommended, which involved the use of Nirmatrelvir/Ritonavir or Molnupiravir.

The post-hospitalization outcomes of the 41 patients showed favorable outcomes in 12 cases, while complications necessitating transfer to the Intensive Care Unit occurred in 22 cases. Seventeen coinfecting patients died, with 10 of them being in the ICU before passing away. Notably, 29.41% (5/17) were children under 15 years old,

Table 1 Characteristics of patients with Pneumococcal infection associated with SARS-CoV-2 coinfection compared to patients with Pneumococcal infection alone, Casablanca, 2020–2022

Epidemiological and Clinical Characteristics	Patients infected with <i>S. pneumoniae</i> and SARS-CoV-2, no. (%), <i>n</i> = 41	Patients infected with <i>S. pneumoniae</i> only, no. (%), <i>n</i> = 79	<i>P</i> -value
Gender	25 (60.98)	43 (54.43)	0.5623
Male	16 (39.02)	36 (45.57)	
Female			
Age Group	8 (19.51)	38 (48.10)	0.0082
0–14 years	25 (60.98)	35 (41.77)	
15–59 years	8 (19.51)	6 (10.13)	
≥ 60 years			
Clinical presentation	1 (2.4%)	16 (20.3%)	0.0731
Various non-invasive Infections	4 (9.8%)	5 (6.3%)	
Ocular Infections	18 (43.9%)	25 (31.6%)	
Pneumonia	10 (24.4%)	17 (21.5%)	
Meningitis	8 (19.5%)	12 (15.2%)	
Bacteremia	0 (0%)	4 (5.1%)	
Osteomyelitis/ Septic Arthritis			
ICU admission	22 (53.7%)	19 (24.05%)	0.0021
Yes	19 (46.3%)	60 (75.95%)	
No			
Died	16 (39.02%)	11 (13.9%)	0.0027
Yes	25 (60.98%)	68 (86.1%)	
No			
Pneumococcal Infection Type	18 (43.9)	33 (41.77)	0.8476
Invasive Infection	23 (56.1)	46 (58.23)	
Non-invasive Infection			
Covid-19 Vaccination	12 (29.27)	37 (46.84%)	0.0789
Vaccinated	29 (70.73)	42 (53.16%)	
Not Vaccinated			
Pneumococcal Vaccination (< 15 years)	<i>N</i> = 8	<i>N</i> = 38	0.7120
Vaccinated with PCV-10	5 (62.5)	17 (47.37)	
Vaccinated with PCV-13	1 (12.5)	1 (13.16)	
Not Vaccinated	2 (25)	24 (39.47)	

Table 2 Multivariate logistic regression analysis of risk factors associated with severe clinical outcomes (ICU admission or death)

Risk factor	OR	95% CI
Age (per year increase)	1.028	1.004–1.055
Coinfection with SARS-CoV-2	2.861	1.215–6.888
Vaccination against <i>S. pneumoniae</i>	2.267	0.7587–7.095
Vaccination against COVID-19	0.4855	0.1912–1.188

29.41% (5/17) were adults between 15 and 60 years old, and 41.18% (7/17) were patients aged over 60 years.

It is noteworthy that only four of the reported deaths had received the recommended three doses of the PCV-10 vaccine, all of whom were pediatric cases.

Distribution of *S. pneumoniae* serotypes isolated in patients with *S. pneumoniae* / SARS-CoV-2 coinfection

In our cohort of coinfecting patients, we investigated the correlation between clinical outcomes and pneumococcal serotypes. Among the 41 patients studied, the most prevalent serotypes were serotype 3 (21.95%, 9/41), serotype 19 A (19.51%, 8/41), followed by serotype 6 B (9.76%,

4/41), and 9 V (7.32%, 3/41). Additionally, serotype 23 F was observed in 4.88% (2/41) of the cases, whereas serotypes 4 and 18 C were present in 2.44% (1/41) each. Notably, the occurrence of patients infected with serotypes not covered by PCV-10 and PCV-13 vaccines was highest in our cohort, encompassing SNV, serotypes 11/11 A, and serotype 8, constituting 31.71% (13/41) of patients. Serotypes 19 A and 3 exhibited the highest mortality rates in our series, accounting for 14.63% (6/41) and 12.20% (5/41) of cases, respectively.

The results revealed that the *p*-value for the chi-square test was 0.2443, indicating the absence of a significant relationship between bacterial serotypes and clinical outcomes of patients. Further details are provided in Fig. 2.

Vaccination status and clinical outcomes in coinfecting patients

The vaccination status of coinfecting patients indicates that 58.54% (24 out of 41) had not received either pneumococcal vaccines or the COVID-19 vaccine. This subgroup displayed the highest mortality rates, with 12

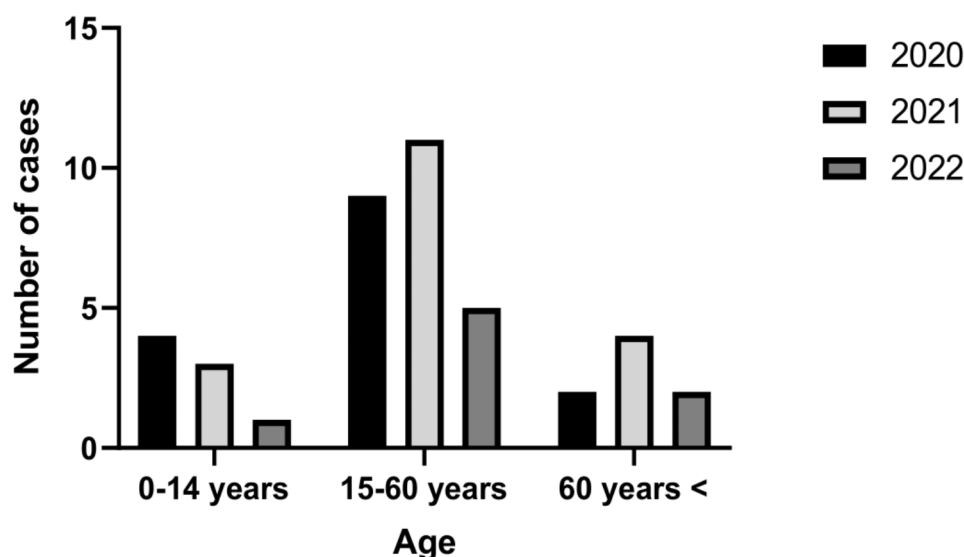


Fig. 1 Distribution of COVID-19 cases coinfecting with *S. pneumoniae* by age group during the study period

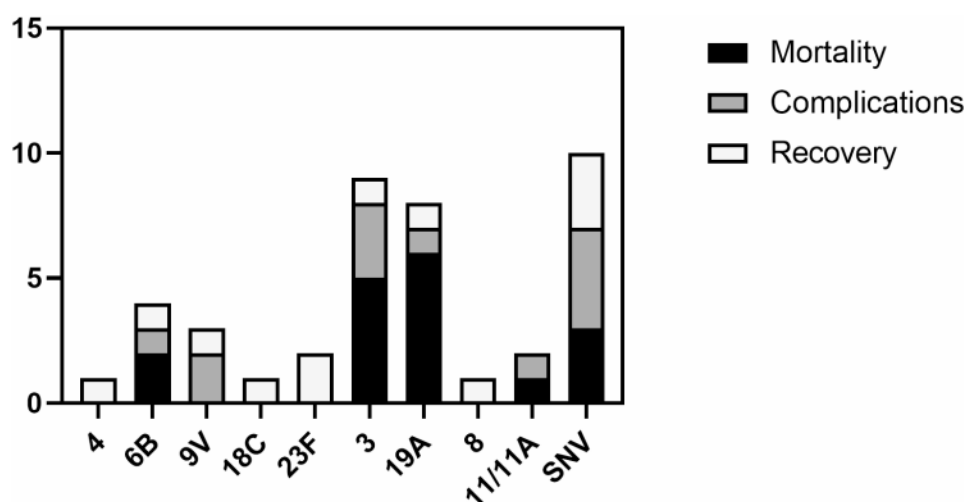


Fig. 2 Distribution of clinical outcomes by Pneumococcal Serotype in COVID-19 coinfecting patients

unvaccinated patients among the 17 reported deaths, accounting for 70.58%. Significantly, in the cohort of individuals vaccinated against SARS-CoV-2, the majority consisted of adults, with 10 individuals, and one elderly person over the age of 60, alongside a notable exception of a single pediatric case a child aged 13 years.

Regarding the administered PCV vaccine types for children, five children received PCV-10, one child had PCV-13 documented in their vaccination history, and two were unvaccinated. Among the five children who received PCV-10, four developed pneumococcal disease associated with PCV-13/non-PCV-10 serotypes, and one with non-vaccine serotypes. The only child vaccinated with PCV-13 had an infection with a non-vaccine serotype. The two unvaccinated children had infections caused

by PCV-13 serotypes. Additional details and a graphical representation are available in Appendix A, Fig. 1a.

Discussion

To our knowledge, this is the first study conducted in Morocco and Africa to investigate the coinfection between SARS-CoV-2 and *Streptococcus pneumoniae*. The incidence rate of bacterial coinfection in COVID-19 patients remains uncertain. Previous research has predominantly focused on coinfections in patients primarily diagnosed with COVID-19. However, studies specifically addressing coinfection between SARS-CoV-2 and *S. pneumoniae* are scarce, highlighting significant variations in incidence rates depending on the geographical area, pandemic phase, and diagnostic methods employed [4]. Pneumococcal pneumonia typically presents as unilateral

opacity on chest radiographs, but it can also manifest as a bilateral interstitial pattern. This bilateral pattern is radiographically similar to pneumonia caused by SARS-CoV-2, presenting a diagnostic challenge amidst the current pandemic [10].

In our cohort of 120 patients, common features included early screening, diagnosis, and treatment of COVID-19 and pneumococcal coinfection, along with patient clinical record monitoring until successful discharge and recovery or otherwise. Among 120 patients with pneumococcal infection, 41 (34%) were also infected with SARS-CoV-2, a proportion higher than that reported by Newell et al., who found a 20% coinfection rate between invasive pneumococcal diseases (IPD) and COVID-19 [11]. A study in China by Zhu et al. discovered that *Streptococcus pneumoniae* accounted for 60% of coinfection cases in COVID-19 patients [12]. Similarly, Im et al. confirmed *S. pneumoniae* as the most common bacterial coinfection in COVID-19 patients [1].

Our analysis revealed that gender did not play a significant role in coinfection vulnerability, aligning with studies from the United States and China [11, 12]. We also found no significant differences in the distribution of invasive and non-invasive infections between coinfecting and non-coinfecting patients, consistent with a Spanish study [13]. This study suggested viral coinfection could directly damage the lower respiratory tract and facilitate pneumococcal invasion.

Age analysis indicated a statistically significant difference in coinfection vulnerability, with higher prevalence among individuals aged 15 to 59, consistent with findings by Zhu et al. and supported by reports of increased susceptibility among teenagers and young adults to SARS-CoV-2 [12, 14]. A study involving 6 million cases demonstrated a higher probability of COVID-19 infection in this age group, likely attributable to the relaxation of social distancing measures, which contributed to increased infection rates between 2020 and 2022 [15].

Our study noted eight cases of coinfection in children, differing from findings by Amin-Chowdhury et al. in England, where no coinfections were detected in children [6]. However, this aligns with previous studies, like those by Launes et al., highlighting a high coinfection rate of 62% with other respiratory viruses in children with pneumococcus. These findings emphasize the importance of considering these interactions to optimize treatment for pediatric pneumococcal infections [13].

Recent research, including ours, establishes a link between bacterial coinfections and an increased risk of death in COVID-19 patients. We observed significantly higher rates of intensive care admission and mortality among patients coinfecting with SARS-CoV-2 and pneumococcus compared to those infected only with *S. pneumoniae*, with intensive care unit admission rates (53.7%

vs. 22.8%) and mortality rates (41.5% vs. 13.9%). These results support findings indicating that disease severity is associated with an increased risk of coinfection and that bacterial coinfection can significantly increase mortality risk [5, 16, 17]. A study in the UK also showed a high fatality rate among coinfecting patients, highlighting a potentially dangerous interaction between pathogens [6]. Moreover, the presence of coinfection can delay appropriate treatment, thereby increasing mortality risk [5, 18].

In addition to univariate comparisons, we performed a multivariate logistic regression analysis to identify independent predictors of severe outcomes, defined as ICU admission or death. This model revealed that patients coinfecting with SARS-CoV-2 and *Streptococcus pneumoniae* were approximately 2.86 times more likely to experience severe outcomes compared to those infected with *S. pneumoniae* alone (OR=2.861; 95% CI: 1.215–6.888). This finding highlights the exacerbating role of viral-bacterial coinfections, which may increase disease burden through synergistic mechanisms of pathogenesis, immune evasion, or treatment delays [19].

Age was also an independent risk factor, with each additional year associated with a 2.8% increase in the odds of severe outcome (OR=1.028; 95% CI: 1.004–1.055), supporting existing evidence on the heightened vulnerability of older individuals to infectious diseases [20].

Pneumococcal vaccination was not significantly associated with reduced risk (OR=2.267; 95% CI: 0.7587–7.095). This may reflect the predominant impact of SARS-CoV-2 on outcomes, potentially masking any protective effect of pneumococcal immunization in this context.

Conversely, COVID-19 vaccination was associated with a non-significant trend toward protection (OR=0.4855; 95% CI: 0.1912 to 1.188), suggesting a potential beneficial effect in reducing severe outcomes among coinfecting patients. Although this finding did not reach statistical significance, likely due to limitations in sample size, it aligns with previous studies demonstrating that COVID-19 vaccination reduces disease severity, intensive care unit admissions, and mortality [21].

These findings underscore the need for vigilant clinical monitoring of patients coinfecting with SARS-CoV-2 and *S. pneumoniae*, particularly among older adults and immunocompromised individuals. They reinforce the critical role of COVID-19 vaccination in reducing severe outcomes in these high-risk groups, and support public health efforts to maintain high vaccination coverage.

Our research emphasizes age as a determining factor in coinfection outcomes, increasing mortality rates among the youngest (under 15 years) and oldest (60 years and older), with death rates of 29.41% and 41.18% respectively. Children, while generally less affected by

COVID-19, face an increased risk of severe complications when coinfecting with pneumococcus [22]. Older individuals are also more likely to experience severe complications, as shown by a study of patients with severe COVID-19 pneumonia admitted to intensive care, with an average age of 61 years [23]. This is supported by research indicating that, despite COVID-19's minimal impact on children, often asymptomatic or presenting mild symptoms, coinfection with pneumococcus significantly increases their risk [24].

Our findings indicate no significant correlation between specific *Streptococcus pneumoniae* serotypes and clinical outcomes in the studied patients (p -value = 0.2443). Previous studies have also shown varied results, reflecting the complexity of host-pathogen interactions. Weinberger et al. observed that, despite certain serotypes being associated with different mortality risks, host-specific factors had a major impact on clinical outcomes [25].

Our study reveals that, among 41 patients, the most common pneumococcal serotypes were 3, 19 A, 6 B, and 9 V. Furthermore, 31.71% of patients were infected with serotypes not included in the PCV-10 and PCV-13 vaccines, representing a significant portion of the cohort. These observations are partially corroborated by studies in Japan, showing a high prevalence of serotypes covered by the 23-valent pneumococcal polysaccharide vaccine (PPV-23), including serotype 3, and in Germany, where serotype 3 was predominant in adult community-acquired pneumonia [26, 27]. Moreover, the increase in serotypes not covered by the PCV-10 and PCV-13 vaccines has been highlighted in several studies [28].

Since January 2023, Morocco has reintroduced PCV-13 into its National Vaccination Program, aiming to protect children against pneumococcal infection and reduce the prevalence of these infections. However, monitoring the effect of this vaccination on the Moroccan population is crucial, as the experience of other countries has shown that the introduction of PCV vaccines can lead to an increase in serotypes not covered by these vaccines [28]. Additionally, the effectiveness of PCV-13 against certain serotypes, particularly 3 and 19 A whose prevalence has increased in several European countries, has raised questions, revealing a potentially variable vaccine efficacy against these serotypes [29].

It is also worth noting that PCV-20, initially approved for adults, has recently been authorized for use in children aged 6 weeks to 17 years in the United States. Its broader serotype coverage offers enhanced protection against *Streptococcus pneumoniae*, which could help reduce the burden of pneumococcal infections and the impact of bacterial and viral coinfections. This aspect is particularly relevant to the objectives of our study [30].

Our data reveal that pneumococcal serotypes 19 A and 3 have the highest mortality rates, respectively 14.63% and 12.20%. These findings are consistent with other studies highlighting the increased risk of severe complications and mortality associated with certain serotypes targeted by the PPSV-23 and PCV-13 vaccines, such as 3, 6 B, 19 A, and 11 A [31]. This underscores the importance of studying the specific virulence of these serotypes within our Moroccan population.

In our study, 58.54% of patients were not vaccinated against either pneumococcus or COVID-19, and presented the highest rates of mortality and complications. Despite the absence of a significant correlation due to the small number of vaccinated patients, our observations suggest an important role for vaccination in reducing mortality and complications in high-risk coinfecting patients. Previous research has indicated that pneumococcal vaccination, especially with PCV-13, can provide preventive benefits against infections, including those associated with COVID-19 [1]. Moreover, Thindwa et al. demonstrated that the PPV-23 vaccine could prevent 33–40% of pneumococcal diseases in the elderly, thereby contributing to the reduction of morbidity and mortality associated with pneumococcal coinfections during the COVID-19 pandemic [3]. Our results highlight the importance of vaccination in reducing mortality, complications, and severe infections in coinfecting patients, supporting recommendations for vaccination against *S. pneumoniae* with PCV-13 and PPV-23 vaccines to minimize the risk of coinfections, which may further reduce the risk of severe infections, including COVID-19, in children and the elderly [1].

Furthermore, our study revealed a peak in pneumococcal-SARS-CoV-2 coinfections in 2021, decreasing in 2022, attributable to successive COVID-19 waves and the impact of vaccination campaigns. Variants like Delta increased coinfections in 2021, while vaccination reduced virus transmission and coinfections in 2022 [32, 33]. Current data show that vaccination against SARS-CoV-2 is extremely effective in reducing infection, case severity, and pandemic-related mortality [34]. Studies confirm this efficacy, with a notable reduction in infection among vaccinated individuals compared to the unvaccinated [35]. Research in Los Angeles indicates significantly lower infection and hospitalization rates among fully vaccinated individuals, especially after booster doses, compared to the unvaccinated, highlighting the importance of complete vaccinations and boosters against variants like Omicron [36].

This study has several limitations that should be acknowledged. The observed reduction in *Streptococcus pneumoniae* infections during the lockdown period may not reflect long-term trends. Measures such as social distancing, mask-wearing, and school closures significantly

curtailed transmission. Consequently, the conclusions drawn during this specific period may not be fully applicable to non-lockdown contexts.

Additionally, resource limitations during the pandemic, combined with national and local recommendations, prioritized COVID-19 diagnostics over pneumococcal testing. As a result, the study focused on testing patients with confirmed pneumococcal infections for SARS-CoV-2 rather than systematically testing all COVID-19 patients for coinfections. This pragmatic approach, driven by logistical and financial constraints, likely underestimated the prevalence of coinfections and limits the broader applicability of the results.

Furthermore, the relatively small sample size, particularly among coinfecting patients, may constrain the generalizability of the findings.

The inclusion of patients of all age groups, from children to the elderly, represents another limitation. The small number of cases in each age subgroup, especially among coinfecting children, did not permit age-stratified analyses. To address this, age was incorporated as a continuous variable in the multivariate regression model to ensure proper adjustment while preserving statistical robustness.

In addition, patients in this study presented with a variety of pneumococcal disease manifestations, including invasive, non-invasive, and less frequent forms such as ocular infections. This clinical heterogeneity may influence the interpretation of the findings and limit their applicability to more uniform clinical populations.

Data were also collected from a single hospital, which may not fully represent the diversity of patient profiles nationally or regionally. Together, these limitations highlight the importance of larger, multicenter studies to validate and expand these findings in varied epidemiological contexts.

Conclusions

Our research highlights a concerning issue regarding coinfections with SARS-CoV-2 and *Streptococcus pneumoniae*, demonstrating their critical role in exacerbating clinical case severity and increasing mortality rates. It underscores the vital importance of vaccination against these pathogens and emphasizes the need for continued vigilant monitoring of pneumococcus, especially following the introduction of the 13-valent conjugate vaccine (PCV-13). Age has proven to be a critical susceptibility factor, showcasing increased risks for certain age groups, particularly children and the elderly, underscoring the need for focused attention on these populations in prevention and vaccination programs.

This study highlights the need for a reevaluation and adjustment of current vaccination policies to enhance protection against coinfections. Continued

epidemiological surveillance of pneumococcus and its serotypes is essential, requiring constant adaptation of our strategies to the changing epidemiological landscape. By adopting such an approach, we can significantly improve public health management and responses to coinfections, thereby strengthening our ability to protect vulnerable groups and minimize the overall impact of these conditions.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-025-10953-z>.

Supplementary Material 1

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Author contributions

Conceptualization: MK, AEK, KK, and AAB conceived and designed the study. Data collection: KK, ID, NN, and MSA conducted the case surveillance and collected clinical data. Laboratory work: MK, AEK, and KK conducted the laboratory assays. Data analysis: MK and AEK analyzed the data. Manuscript preparation: MK, AEK, and KK drafted the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and approved by the Ethical Committee of Hospital University of Marrakech, Morocco (approval number: N°033/2020). Informed consent was obtained from all participants and, for minors under 18 years of age, from their parents or legal guardians. The consent process ensured that participants were fully informed about the nature of the study and the storage of samples for a specified period prior to testing.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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