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Review Article

Bacterial Etiology of Adult Community-Acquired Pneumonia in Pakistan: A Systematic Review and Meta-Analysis

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Abstract

Background: Accurate knowledge of the epidemiology of community-acquired pneumonia (CAP) is essential for guiding appropriate antimicrobial therapy. This systematic review and meta-analysis aimed to identify and quantify the prevalence of common bacterial pathogens responsible for CAP in adult patients in Pakistan to improve empirical treatment strategies.

Methods: We systematically searched EMBASE, PubMed, Web of Science, and Google Scholar for studies published in English between January 1, 2000, and December 1, 2024. Studies were included if they reported bacterial etiology of radiologically confirmed CAP in adult patients in Pakistan. Quality assessment was performed using standardized criteria, and a random-effects model was used for meta-analysis. Seven studies met the inclusion criteria, comprising 1,793 CAP patients from three major cities: Karachi (n=4 studies), Lahore (n=1), and Rawalpindi (n=1).

Results: Meta-analysis revealed Streptococcus pneumoniae as the predominant pathogen (14%, 95% CI: 8-20%), followed by Pseudomonas aeruginosa (12%, 95% CI: 3-21%), Haemophilus influenzae (9%, 95% CI: 2-16%), and Staphylococcus aureus (8%, 95% CI: 2-13%). Significant heterogeneity was observed across studies ($I^2 > 94\%$ for all pathogens), attributable to variations in patient demographics (mean age range: 44.8-63.6 years), diagnostic methods (primarily sputum and blood cultures), and clinical settings (5 inpatient and 2 outpatient studies).

Conclusion: While S. pneumoniae emerged as the leading pathogen in Pakistani adults with CAP, the high heterogeneity and limited geographic representation suggest the need for more comprehensive research. Future studies should: 1) include diverse geographic areas, particularly rural settings, 2) employ standardized diagnostic methods, and 3) investigate pathogen-specific impacts on disease severity and outcomes to enhance CAP management strategies in Pakistan.

Introduction

Community-acquired pneumonia (CAP) is an infection of the lung parenchyma that develops outside hospitals or other healthcare facilities [1]. It remains a significant global health challenge, contributing to substantial mortality and morbidity [2]. According to the Global Burden of Diseases, Injuries, and Risk Factors Study 2017, lower respiratory infections affected an estimated 471.8 million individuals and were responsible for 2.6 million deaths worldwide in that year [3]. There is a scarcity of recent data on the incidence of CAP in Pakistan. Geographical and seasonal differences in the frequency and types of organisms causing CAP have been reported [4]. In several studies, S. pneumoniae has been the most common causative agent. However, organisms like M. pneumoniae, C. pneumoniae, and L. pneumophila are being reported more often than expected [5].

In Asia, it is estimated that CAP causes around 1 million deaths among adults every year [6]. Many of these deaths occur in older adults [5]. However, adult CAP has not been studied

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adequately in Pakistan in recent years. There has been no systematic review of CAP etiology in Pakistan. For a successful outcome, selecting the right empirical antimicrobial medication is essential [7]. Based on the site of care (intensive versus non-intensive care unit) and pathogen-related risk factors, such as those for influenza viruses, Pseudomonas aeruginosa, and methicillin-resistant Staphylococcus aureus (MRSA), national and international CAP guidelines provide specific recommendations [8]. However, it remains uncertain whether these guidelines offer adequate antimicrobial coverage.

The eradication of CAP-related mortality and morbidity faces multiple challenges in Pakistan. The continuous emergence of new pathogen strains and changing resistance patterns complicate the maintenance of effective treatment protocols. Limited healthcare infrastructure and financial resources hamper the implementation of optimal diagnostic and treatment strategies [7]. Additionally, insufficient data on local pathogen prevalence and resistance patterns makes it difficult to develop evidence-based treatment guidelines specific to Pakistani populations. Socioeconomic factors, including poor living conditions and overcrowding, contribute to both the spread of respiratory pathogens and poor treatment outcomes [4]. Climate change and increasing air pollution levels add another layer of complexity to CAP management by potentially influencing the prevalence and severity of respiratory infections. These challenges underscore the critical importance of understanding local pathogen patterns and developing context-appropriate diagnostic and treatment strategies. While global guidelines provide a framework for CAP management, local epidemiological data is essential for developing targeted interventions that address Pakistan's specific healthcare needs and constraints.

The identification of bacterial pathogens causing CAP has broader implications for both public health and antimicrobial stewardship. Accurate pathogen identification guides not only individual patient treatment but also shapes regional antibiotic prescribing patterns, helping to combat antimicrobial resistance [9,10]. In resource-limited settings like Pakistan, where antibiotic resistance rates are rising and diagnostic capabilities may be limited, understanding the local distribution of bacterial pathogens becomes crucial for developing cost-effective empiric treatment guidelines. This knowledge supports antimicrobial stewardship programs by enabling healthcare providers to select appropriate narrow-spectrum antibiotics when possible, thereby reducing unnecessary broad-spectrum antibiotic use and helping preserve these vital medicines for future generations.

The objective of this systematic review and meta-analysis is to consolidate and analyze the findings of studies investigating the etiology of CAP among adults in Pakistan, with a particular focus on bacterial pathogens. By synthesizing data from existing research, this review aims to provide a comprehensive understanding of the most prevalent causative organisms associated with CAP in the region. Furthermore, it evaluates the methodologies employed in these studies to identify potential limitations and gaps in the current research landscape, highlighting areas where further investigation is needed to improve diagnostic, therapeutic, and preventive strategies for CAP in Pakistan.

Methodology

This systematic review and meta-analysis were carried out using Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [11]. The protocol of this review is registered in the International Prospective Register of Systematic Reviews (PROSPERO).

Information sources

We identified relevant studies by searching online databases including the EMBASE, PubMed, and Web of Science from 1st Jan 2000 to 20th November 2024. We limited our search to those articles that were published in the English language and included human beings only. To find additional studies, we also searched for Google Scholar. Lastly, reference lists of included studies were manually screened to avoid missing out on any relevant studies.

Literature search

We developed a comprehensive and systematic literature search strategy to ensure the standardized identification and screening of studies reporting the prevalence or distribution of bacterial pathogens in adult patients with CAP in Pakistan. This approach aimed to capture all relevant studies addressing the bacterial etiology of CAP, regardless of their design or publication status. Keywords used to search for articles included "community-acquired pneumonia", "Pakistan", "etiology" and "pathogens". These key terms were used to combine search terms (OR, AND). Medical subject heading (MeSH) terms were also used to sensitize the search. A detailed description of the search strategy used is provided in the supplementary file (Table S1).

Study selection

Two authors independently reviewed all retrieved studies to determine their eligibility for inclusion. The review process was conducted in two phases. In the first phase, studies were excluded based on their titles and abstracts if they did not meet the inclusion criteria. In the second phase, the full texts of the remaining articles were manually screened for eligibility. Data extraction was subsequently performed for all studies that satisfied the inclusion criteria. Any disagreements between the authors during the study selection process were resolved through discussion and consensus. Articles were included in the meta-analysis if they met the following criteria: observational studies (retrospective or prospective cohort, cross-sectional or case-control), they involved patients with chest radiography-confirmed CAP, assessed the etiology of CAP, and were published in English. Exclusion criteria included case reports, case series, reviews, and editorials, as well as studies involving patients with conditions other than CAP.

Quality assessment, data collection procedures, and data analysis

Quality assessment of included studies was done using the New Castle Ottawa scale and the table presenting quality

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assessment findings is given in Table S2. We designed a structured data extraction sheet using an Excel spreadsheet to systematically extract relevant information from the included studies. The data collected included the author's name, year of publication, city, number of patients, and details of the microbial investigation. Extracted data were subsequently imported into STATA for analysis. This meta-analysis calculated the prevalence rate of each bacterial etiology causing CAP using a random-effects model with a 95% confidence interval (CI). Heterogeneity among the included studies was assessed using the I^2 statistic [12]. Heterogeneity levels were interpreted as follows: I^2 values between 25% and 49% indicated low heterogeneity, 50% to 74% signified moderate heterogeneity, and values of 75% or higher represented high heterogeneity [13]. All statistical analyses were performed using Stata version 17.0 (StataCorp LLC, College Station, TX, USA).

Results

Overall, 695 articles were obtained through online searching. Twenty-six studies were identified after title and abstract screening. Full-text of these 26 articles were obtained and a detailed assessment was done based on pre-defined inclusion and exclusion criteria. Of these 26 articles, 7 articles were included in the quantitative analysis (Figure 1).

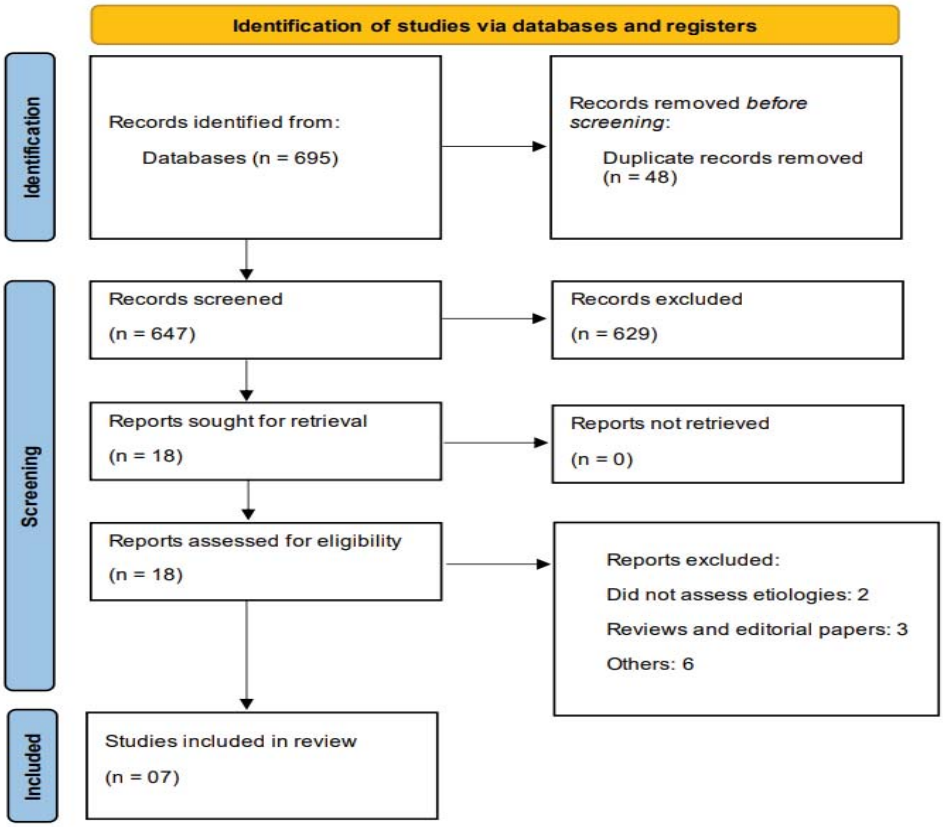
Study characteristics

Table 1 presents the characteristics of the included studies. Three studies were prospective, three were retrospective and 1 was a secondary analysis of the Global Initiative for MRSA Pneumonia (GLIMP). Most of the included studies reported similar exclusion criteria, typically involving immunosuppression, tuberculosis, lung cancer, pneumonia developing more than 48 hours after admission, or other terminal illnesses. Four of the seven included studies were conducted in Karachi, with one study each conducted in Lahore and Rawalpindi. Five studies focused on populations from inpatient departments, while two studies enrolled patients from outpatient departments. The mean age of the included studies ranged from 44.8 to 63.6. All studies used sputum and blood culture to identify pathogens responsible for CAP.

Etiology results

Table 2 presents the pooled analysis of the etiological agents causing community-acquired pneumonia (CAP) in Pakistan, while Table 3 compares these findings with a review of CAP studies conducted in Asian countries.

Streptococcus pneumoniae emerged as the most frequently identified pathogen, with an overall prevalence of 14%. The prevalence of S. pneumoniae varied significantly across studies, ranging from 6% in the study by Carugati et al. (2020) to 28.5% reported by Perveen et al. (2017). In three of the seven included studies, S. pneumoniae was identified as the leading cause of CAP. A high degree of heterogeneity was observed across the studies.



Study Characteristics

Figure 1: PRISMA flowchart of study selection.

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Table 1: Characteristics of included studies.

Author name, Year	City	Duration of Study	Study Design	Study Setting	Sample Size	Most Prevalent Pathogen	Mean Age (Years)
Carugati et al., 2020 [14]	NS	March to June 2015	Retrospective	In patient	101	S.aureus	NS
Iqbal et al., 2018 [15]	Karachi	January 2011 to December 2016	Retrospective	Inpatient	509	S.aureus	63.6
Irfan et al., 2009 [16]	Karachi	January 2002 to August 2003	Retrospective	Inpatient	329	S.pneumoniae	62
Khawaja et al., 2013 [17]	Karachi	March 2002 till December 2008	Retrospective	Inpatient	189	S.aureus	60
Perveen et al., 2017 [18]	Rawalpindi	April 2016 to April 2017	Prospective	Outpatient	341	S.pneumoniae	NS
Rahman et al., 2013 [19]	Lahore	NS	Prospective	Inpatient	200	S.pneumoniae	44.8
Zubairi et al., 2012 [20]	Karachi	February 2007 to March 2008	Prospective	Out patient	124	H.influenzae	56.5

NS: Not specified.

Table 2: Pooled analysis of bacterial pathogens causing CAP.

Organism	Pooled Rate (%)	95% CI	I-Square (%)
Staphylococcus aureus	8	2 to 13	96.28
Streptococcus pneumoniae	14	8 to 20	94.05
Haemophilus influenzae	9	2 to 16	97.76
Pseudomonas aeruginosa	12	3 to 21	96.18v
Klebsiella pneumonia	7	3 to 14	97.07

CI: Confidence interval.

Table 3: Comparison of current study findings with meta-analysis including Asian studies.

Organism	Pakistani Studies (n= 7) Pooled rate (%)	Asian Studies (n= 38) Pooled rate (%)
Streptococcus pneumoniae	14%	13.30%
Haemophilus influenzae	9%	6.90%
Staphylococcus aureus	8%	4.00%

Pseudomonas aeruginosa was identified as the second most common pathogen in the pooled analysis, with an overall prevalence of 12%. Among the included studies, the highest prevalence (21.7%) was reported by Perveen et al. (2017). However, in this study, P. aeruginosa ranked as the third most common pathogen after Haemophilus influenzae and S. pneumoniae. Significant heterogeneity was also noted for P. aeruginosa prevalence among the studies.

The pooled prevalence of Haemophilus influenzae was 9%, making it the third most common pathogen. In most studies, the prevalence of H. influenzae was below 5%, except for the study by Perveen et al., which reported a notably higher rate of 37%, exceeding that of S. pneumoniae and P. aeruginosa. This variability contributed to substantial heterogeneity in the study findings.

Staphylococcus aureus accounted for 8% of cases in the pooled analysis, ranking as the fourth most common pathogen. The prevalence of S. aureus varied widely across individual studies, ranging from 0.8% to 19.8%. Only one study identified S. aureus as the most frequent pathogen causing CAP in its population. High heterogeneity was again evident in the reported rates.

Table 3 compares the overall rates of pathogens causing CAP in this review with those from a broader review of Asian studies [21], highlighting notable differences in the ranking of the most common bacteria. In our review, the top three pathogens were Streptococcus pneumoniae (14%), Haemophilus influenzae (9%), and Staphylococcus aureus (8%). Similarly, Streptococcus pneumoniae was identified as the most common pathogen in the Asian studies (13.3%). However, Mycoplasma pneumoniae, which ranked as the second most common pathogen in the Asian review, was not reported in any of the studies included in our review. On the other hand, Haemophilus influenzae was also identified in the Asian review, with a prevalence of 6.9%, consistent with its prominence in our findings. These differences may reflect variations in diagnostic practices, regional pathogen distributions, or study methodologies.

Discussion

This review synthesizes findings from published studies on the etiology of community-acquired pneumonia (CAP) in Pakistan, highlighting several important patterns. A pooled analysis of seven studies identified Streptococcus pneumoniae as the most frequently detected pathogen, with an overall prevalence of 14%, followed by Pseudomonas aeruginosa and Haemophilus influenzae. In comparison, a separate review of studies from Asian countries also reported a higher proportion of patients with S. pneumoniae as the predominant pathogen [21]. However, that review did not include studies from Pakistan. Additionally, another review encompassing 23 studies from European countries similarly reported S. pneumoniae as the most common causative organism [22]. One key difference between our study and previous reviews involving Asian studies is that our analysis included only seven studies, five of which focused on in-patient settings, while the Asian review contained more than 40 studies and added both inpatient and outpatient settings.

Three out of four studies included in this review identified *S. pneumoniae* as a common causative agent, with the mean age of patients ranging from 44.8 to 62 years. Similarly, studies reporting *S. aureus* as a common pathogen indicated a mean patient age ranging from 60 to 63.6 years. A previous study found that an age of 60 years or older was not associated with any specific microbial etiology [23]. However, it reported that comorbidities could significantly influence the causative pathogens. While it is important to assess how the organisms causing CAP vary across age subgroups and comorbidities, the

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limited number of studies included in this review precluded subgroup analyses or meta-regression. Future research is needed to address these gaps, particularly in Pakistan, to guide optimal empirical treatment for CAP.

Some pathogens cause more severe CAP compared to others. For example, S. pneumonia remains the most significant and common bacterial agent in CAP associated with increased mortality and severity as found in past studies. For example, Nascimento-Carvalho et al reported that the incidence of S. pneumonia increased from 13.2% in non-severe cases to 35.3% in very severe instances, indicating that it is more common in severe and very severe CAP patients [24]. The kidneys, heart, and lungs are among the organs that S. pneumoniae might acutely harm. In developed nations, the case fatality rate can reach 30% when the bacterium enters the central nervous system, but in low-income nations, it can approach 50% [25]. Although previous studies conducted reported how severity and mortality vary across different bacterial pathogens, none of the included studies assessed this.

The meta-analysis revealed Klebsiella pneumoniae as having a relatively lower prevalence rate of 7% (95% CI: 3% to 14%) compared to other major pathogens. This lower prevalence is noteworthy given that K. pneumoniae is often considered a significant pathogen in Asian populations. The predominantly urban hospital setting of most included studies might not reflect the complete epidemiological picture, as K. pneumoniae infections may have different distribution patterns in rural or community settings. Additionally, the high heterogeneity observed (I^2 = 97.07%) suggests considerable variation in detection rates across studies, which could be attributed to differences in patient populations, local antibiotic prescribing practices, or regional environmental factors. It's also possible that prior antibiotic use, which was not consistently reported across studies, may have affected the detection rates of this organism [24].

Differences in diagnostic practices can significantly contribute to the variability in pathogen identification [26]. Variations in sampling techniques, laboratory capacities, and diagnostic tools, such as the use of culture-based methods versus molecular assays, may influence detection rates. Furthermore, inconsistencies in clinical criteria for suspecting specific pathogens and variations in antimicrobial use before sampling can affect diagnostic yield [27,28]. These disparities underscore the need for standardized diagnostic protocols to ensure more consistent and accurate pathogen identification across studies.

Study limitations

The present meta-analysis has certain limitations. Firstly, only seven studies were included, which may limit the generalizability of findings. To robustly identify common microbial agents causing CAP, a larger number of studies are necessary. Secondly, the small number of studies hindered subgroup analyses or meta-regressions to explore variations in microbial etiology based on age, comorbidities, or other demographic factors. None of the included studies evaluated the association between specific pathogens and CAP severity or mortality, a critical gap for understanding clinical outcomes and guiding management strategies. Additionally, out of the seven studies, four were conducted in Karachi, with none performed in rural regions of Pakistan. This geographical limitation restricts insights into the pathogen distribution across diverse regions where climate, resource availability, and treatment practices may influence etiology. Furthermore, the small number of studies raises concerns about potential publication bias, as studies with significant findings are more likely to be published. This bias may skew the representation of pathogens and their clinical relevance. Future research should incorporate systematic efforts to minimize publication bias, such as including unpublished or gray literature. To address the gap in pathogen-specific severity data, prospective multicenter studies with standardized protocols are needed to assess severity and mortality outcomes associated with specific pathogens. Expanding research to rural areas and underrepresented regions of Pakistan is also critical for a more comprehensive understanding of CAP etiology nationwide.

Research implications

Currently, the data related to microbial etiologies, the severity of CAP concerning microbial etiology, antimicrobial resistances, and susceptibilities is lacking in Pakistan contexts. CAP in Pakistan is under-studied due to limited healthcare infrastructure, insufficient disease surveillance, and constrained research funding. Additionally, a lack of national registries, regional healthcare disparities, and competing priorities, such as infectious diseases like tuberculosis, further hinder research efforts. This contrasts with neighboring countries that prioritize CAP surveillance and research.

Addressing these gaps could improve empirical antibiotic selection, reduce mortality, and enhance CAP management strategies tailored to the Pakistani healthcare context. Randomized comparisons of different empirical treatment procedures are another method of direct treatment. In Pakistan, comparatively few trials have assessed treatment plans for adult CAP to date. By reducing the requirement for non-standard diagnostics—apart from perhaps a sputum sample for tuberculosis—such trials could be carried out even in areas where etiology investigations are difficult. Given that Pakistan is one of the most highly populated countries in the world, these trials may produce trustworthy data to support the empirical management of CAP in that region.

Practice Implications

The findings from this systematic review have several important implications for the development of future national treatment guidelines in Pakistan. The predominance of Streptococcus pneumoniae (14%) as the leading pathogen, followed by Pseudomonas aeruginosa (12%) and Haemophilus influenzae (9%), suggests that empirical antibiotic regimens should provide adequate coverage for these organisms. However, the notable presence of Pseudomonas aeruginosa, which is not typically covered by standard CAP regimens in many international guidelines, may warrant special consideration

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in the Pakistani context. This finding could influence recommendations for initial empiric therapy, particularly in patients with specific risk factors or in regions where this pathogen is more prevalent. Additionally, the significant heterogeneity in pathogen distribution across different regions and healthcare settings indicates that guidelines may need to incorporate location-specific recommendations.

Conclusion

In conclusion, the appropriate selection of empirical treatment and diagnostic tests for CAP relies on a thorough understanding of the common pathogens identified in etiology studies and therapeutic trials. However, the available etiology data from Pakistan is limited, and developing guidelines based on studies conducted outside the region may be inappropriate due to differences in patient characteristics and treatment practices. This review identified *S. pneumoniae* as the most common pathogen, but these findings are based on a limited number of studies. Future research is essential to better understand the etiology of CAP in both adult and pediatric populations in Pakistan.

Author contributions

Rahil Khowaja: Study design, study searching, study selection, quality, assessment, data analysis, manuscript drafting; Fazila Karimi: Study design, study searching, study selection, manuscript drafting. The final version of the meta-analysis was reviewed by both authors.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Use of AI

We have used AI in this paper to improve readability and correct grammar and language errors.

(Supplementary Tables S1, S2)

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