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Research Article

Community-Acquired Pneumonia of Bacterial Origin in Paediatrics: Delphi Method about Symptoms, Aetiology, Diagnosis, and Treatment in Colombia

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A B S T R A C T

Introduction: Paediatric pneumonia causes 14% of deaths in children 0–5 years of age. In community-acquired pneumonia (CAP) of bacterial origin, only a third of children receive the antibiotics they need. The clinical management of bacterial CAP is complex and, in most cases, leads to the indiscriminate use of antibiotics.

Objective: To generate recommendations derived from a consensus of experts in paediatric infectious diseases to address CAP of bacterial origin in paediatrics.

Method: This research was carried out through a Delphi process with 16 paediatric infectious diseases specialists from Colombia and two specialists who reviewed the process, guaranteeing iterativity, anonymity of the answers, controlled feedback, and consolidation of the answers with statistical criteria.

Results: The recommendations agreed upon by the experts on the following topics of CAP are presented; signs and symptoms, aetiological agents, laboratory tests, radiological findings, criteria for hospitalisation and admission to the paediatric ICU, and antibiotic therapy.

Conclusion: This consensus document will help in the improvement of a few practices of physicians and paediatricians, who are the professionals who perform the initial approach to CAP, in order to unify some criteria that improve clinical outcomes.

Keywords: Community-Acquired Pneumonia, Bacterial Pneumonia, Paediatrics, Delphi

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Introduction

Community-Acquired Pneumonia (CAP) of bacterial origin is a process in the lung parenchyma, that occurs in patients without previous exposure to the hospital environment. World Health Organization (WHO) indicates that paediatric pneumonia causes 14% of deaths in children (0–5 years old), despite it is preventable with immunisation, adequate nutrition, and control of environmental risk factors. In bacterial CAP, only one-third of children receive appropriate antibiotic treatment.[1] Although hospitalisations for this cause have decreased with vaccination against *H. influenzae* and *S. pneumoniae*, based on the clinical practice of the experts consulted for this research, after the COVID-19 pandemic cases of complicated pneumonia have increased.

Differentiating viral or bacterial CAP based on clinical profile, laboratory findings, and radiological images is a complex process that leads to the indiscriminate use of antibiotics. This situation is a relevant public health problem in Colombia and is interrelated with malpractices in the use of antibiotics, which increases the frequency of bacterial resistance, morbidity, mortality, and health care costs.[2]

In this context, there are several international guidelines related to paediatric CAP. WHO describes the main causative agents (*Streptococcus pneumoniae, Haemophilus influenzae type b, respiratory syncytial virus*), forms of presentation (viral and bacterial), signs and symptoms (cough, respiratory distress, tachypnoea, chest indrawing, wheezing, loss of consciousness, hypothermia, seizures), risk factors (immunosuppression, comorbidities, environmental factors), treatment (amoxicillin), and prevention (vaccination, adequate nutrition, and reduction of indoor air pollution and overcrowding).[1] The British Thoracic Society published guidelines for CAP in children in 2002, updated in 2011, incorporating the evidence available only in English in the Cochrane Library, MEDLINE, and EMBASE, and highlighted that there was no agreed clinical opinion on the approach to this event.[3] The American Thoracic Society and Infectious Diseases Society of America have developed guidelines for CAP in adults.[4]

In relation to consensus documents of specialists in paediatric infectious diseases, the evidence is concentrated in Spain and Germany, without documents on CAP. This is confirmed after carrying out a systematic review in PubMed, OVID-MCare, Science-Direct, Scopus, Scielo, Cochrane, and Google Scholar, with the search "paediatr* infectious diseases or infectio*". For Colombia, there is a narrative review that highlights *Streptococcus pneumoniae, Haemophilus influenzae*, and *Staphylococcus aureus* as the most prevalent aetiological agents of CAP; and evaluation and management of the patient.[5] Since 2014, Colombia has had a Clinical Practice Guideline for pneumonia and bronchiolitis in children, whose application scenario includes low-complexity services in ambulatory care, and hospitalisation.[6]

The available guidelines have several limitations for their use in Colombia: i) they focus on evidence from Europe; ii) they are designed for adult patients; iii) they include general topics on aetiology, risk factors, clinical presentation, severity, and prevention without detailing specific recommendations; iv) they do not include the criteria or clinical experience of experts (paediatric infectious diseases specialists); v) they do not adjust to the clinical and epidemiological scenarios of the different regions of the country.

In Colombia, there is no consensus document on recommendations to address bacterial CAP in paediatrics in relation to its symptoms, aetiology, diagnosis, and treatment consensuses arising from the need to standardise and increase the efficiency of a practice.[7] The Delphi method is the most rigorous and valid option for generating expert consensus documents due to its blind nature, a priori definition of the consensus mechanism (with statistical criteria and blind discussion), and other characteristics. The predictive capacity of this methodology is supported by the concept of a group of experts, under three basic postulates: i) in non-exact sciences or uncertain situations (without universal objective information), it is necessary to use expert judgment; ii) the judgment of a single expert is biased by focusing on the knowledge and experience of one person; iii) subjective group judgment generates better recommendations by combining a greater amount of information and experiences. It is used to obtain a more exhaustive and comprehensive understanding of a reality based on the sum of the perspectives and experiences of various experts.[8]

This method is determinant for agreement or standardisation of practices, to mitigate inappropriate practices (improve medical praxis) among non-specialists, on topics of interest on which conclusive research evidence is not available,[8] and in the absence of high-quality evidence to guide clinicians[9]. Added to this are the following specific considerations for this consensus document: i) when it is not pertinent to conduct a systematic review because the interests are diverse or broad in the topics of interest; ii) when time, effort, and financial resources are not available to carry out an exhaustive clinical practice guideline on each of the topics of interest in the consensus document, and it is important to have a quick guide; iii) when there are structural factors that prevent the application of external evidence, such as regional or contextual aspects that impact epidemiological outcomes, type of health care system or variations in access to diagnosis, treatment, and consultation with specialists, and iv) when the application of specialist criteria is limited in some areas of the territory.

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The objective of this work was to produce a consensus document of Colombian experts on the symptoms, aetiology, diagnosis, and treatment of bacterial CAP in paediatrics. This manuscript contributes to institutional initiatives of the Colombian Ministry of Health to respond to antimicrobial resistance and optimisation programmes of the use of antibiotics in hospital and outpatient settings.[2,10–12]

Method

Study design

Clinical guidelines through expert´s consensus using the conventional Delphi method based on facts or prioritising experience. The following attributes were guaranteed: i) iterativity, that is, each expert issues his concept on several occasions or rounds, so he can re-elaborate his opinion based on the answers and differences in criteria with other experts; ii) anonymity of the answers to avoid influences from the dominant members, inhibition of the youngest in the field, group thinking, or average positions, in addition to guaranteeing equity and diversity; iii) controlled feedback based on the discordant concepts; and iv) consolidation of the answers with statistical criteria.[8]

Selection of the Panel of Experts

The experts corresponded with paediatric infectious diseases specialists from Colombia who were invited to participate in this consensus (approximately 57); this sampling frame is made up of the faculties that offer this speciality and of groups formed by the initiative of these specialists. The invitation was sent by email and through WhatsApp groups. In addition, the invitation to participate in this consensus was extended to those attending the V meeting of paediatricians specialising in infectious diseases, organised by the Antioquia Foundation for Infectology (in Spanish FAI). The response for the three rounds of consultation was obtained from 16 experts and two specialists who reviewed the process, between January and December 2023.

Delphi Process

Preliminary Stage: Objectives, Identification of Items, and Location of Experts

In this phase, the context of the application and the objectives of the consensus document were defined, which focus on the orientation of the management of bacterial CAP in the outpatient setting and hospitalisation by general practitioners and paediatricians. This involved an extensive document to be exhaustive in addressing the symptoms, diagnostic aids, hospitalisation criteria, and antibiotic therapy. For this, a primary group of three paediatric infectious diseases specialists was formed, who selected the topics based on scientific literature and clinical experiences, and designed the instrument, to which appearance validity was carried out with the criteria of applicability (at the discretion of the coordinating team) and acceptability (consultation with six experts from different regions of Colombia) that endorsed the structure of the consultation instrument for the first round. This stage was completed with the invitation of a panel of experts to participate in this study, defining a minimum number of 15 specialists with whom it is possible to capture the greatest possible diversity of experiences on this topic in the main regions of the country.

Exploratory Stage: Consent and Consultation Rounds

An invitation was made to all paediatric infectious diseases specialists in the country to participate, from those who agreed to participate, consent was obtained, and consultation rounds began. Consensus was considered achieved when 75% or more (upper quartile) agreed on a response. Based on the contrary answers (those in which no consensus was reached), the consultation instrument was designed for the next round. In the second round, each expert was sent an instrument with the items (and their responses) that presented discrepancies during the first round, for them to reconsider their initial response or expand their arguments regarding the concepts that were different from theirs. With the responses from this round, the criterion of ≥ 75% was applied again to define consensus. In the third round, the arguments of the experts who did not agree with their colleagues were presented, and the contradictors were asked to reconsider their answers based on the new arguments or expand the support and argumentation of their previous answers.

Final Stage

For each response, the proportion of concordant responses in ≥ 75% of the specialists consulted to ensure consensus was calculated. All the agreed-upon recommendations were then grouped together in a document that was sent to all the experts to receive final feedback, prior to disclosure.

Results

For the clinical approach and diagnostic suspicion of bacterial CAP, all the experts agreed from the first round on the importance of fever and crackles. In the other criteria agreed upon in the first round, consensus was found in more than 80% of the participants. In the second round, consensus was achieved around the need to include bronchophony, the commitment of the General State of Health, and anorexia; it was also considered relevant to include the rejection of food, despite being non-specific (Table 1). During the second round, consensus was also achieved in relation to excluding paleness (100% agreement), hearing loss (81% agreement), and vomiting (100% agreement) due to their unspecific and low frequency.

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In relation to the compromise of the general state, its inclusion was considered, among other reasons, due to its frequency in the clinical description, despite its non-specificity and low frequency in mild pneumonia; however, it has a good positive predictive value for bacterial CAP when it occurs for two or more days. Bronchophonic crying was also included, despite its difficulty to identify in younger children. Anorexia and refusal to eat are non-specific but have significant frequency and usefulness in guiding possible hospitalisation or the severity of the clinical picture.

Table 2 describes the most frequent aetiological agents in the experience of the experts, with the percentage of agreement and the round in which it was achieved. In the second round, consensus was reached on the low relevance of *Mycoplasma pneumoniae* (75%), *Streptococcus pyogenes* (94%), *Chlamydophila pneumoniae* (88%), and *Staphylococcus aureus* (88%) in uncomplicated CAP, similar to those referred to for nontippable *Haemophilus influenzae* (81%), and *Streptococcus pyogenes* (75%) in complicated CAP.

In relation to inflammatory markers, radiological findings, and microbiological tests to support the diagnosis of CAP (complicated and uncomplicated), the diagnosis was easily achieved in the tests described in Table 3. In the second round, 94% of the experts considered that procalcitonin was not useful, 100% excluded micro-consolidations, 94% interstitial opacities, 94% lumbar puncture, 75% sputum evaluation, and from the first round, the exclusion of hyperinflation (88%), serology (81%), and urine tests (100%) had been defined. Among the reasons cited for excluding radiological diagnostic options, their greater relationship with viral aetiologies, chronicity, and sequelae was indicated; while the exclusion of laboratory tests was based on their poor cost-benefit relationship or not having some urine tests available on the market.

In the first round, the criteria for defining hospitalisation and admission to the paediatric ICU for bacterial CAP were agreed upon, but there was no significant discussion within the expert group (Table 4).

Table 5 shows the antibiotics recommended for empirical antibiotic treatment in cases of complicated and uncomplicated bacterial CAP, as well as the antibiotics which should be avoided and the situations in which starting the oral route would be recommended.

Table 1.Signs and Symptoms for the Initial Approach to Bacterial CAP

Signs and Symptoms	% (n) [a]
Consensus in the first round	
Fever	100 (16)
Tachypnoea	94 (15)
Respiratory grunt	81 (13)
Nasal flaring	88 (14)
Chest pain	81 (13)
Dullness on chest percussion	81 (13)
Bronchophony	88 (14)
Pectoriloquy	81 (13)
Tubaric sounds	88 (14)
Crepitus - rales	100 (16)
Cough	94 (15)
Retractions (subcostal, supraclavicular, intercostal)	94 (15)
Abdominal pain	81 (13)
Consensus in the second round	
Constitutional symptoms	100 (16)
Bronchophonic crying	94 (15)
Anorexia	75 (12)
Consensus in the third round	
Rejection of food	88 (14)

[a]Experts that agree with the criteria

Table 2.Main Aetiologies of Interest to Guide Initial Treatment

Aetiologies	% (n) [a]
Uncomplicated bacterial CAP	
Consensus in the first round	
Streptococcus pneumoniae	100 (16)
Haemophilus influenzae nontippable	81 (13)
Consensus in the second round	
Haemophilus influenzae type b	100 (16)
Consensus in the third round	
Moraxella catarrhalis	88 (14)
Complicated bacterial CAP	
Consensus in the first round	
Streptococcus pneumoniae	100 (16)
Staphylococcus aureus	100 (16)
Consensus in the second round	
Haemophilus influenzae type b	94 (15)

[a]Experts that agree with the criteria

Table 3.Useful Diagnostic Aids in CAP

Diagnostic Aids	% (n) [a]
Inflammatory marker	
Leukocytosis	81 (13)
Neutrophilia	88 (14)
CRP (C-reactive protein)	94 (15)

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Radiological finding	
Lobar consolidation	100 (16)
Segmental consolidation	94 (15)
Multilobar consolidation	94 (15)
Pleural effusion	94 (15)
Lung abscess	94 (15)
Pneumatoceles [b]	81 (13)
Body fluid or tissue	
Blood	94 (15)
Bronchoalveolar lavages [b]	88 (14)
Tracheal aspirate in a ventilated patient [b]	94 (15)
Pleural fluid [b]	100 (16)
Laboratory test	
Gram stain	88 (14)
Pleural fluid examination	88 (14)
Pleural fluid culture	88 (14)
Multiplex PCR	94 (15)
Molecular diagnosis	81 (13)

[a]Experts that agree with the criteria
[b]Consensus in the second round

Table 4.Criteria for Hospitalisation and Admission to the Paediatric ICU

Criteria (Consensus in the First Round)	% (n) [a]
Hospitalisation	
Oxygen saturation on room air (1% below the lower limit) according to height above sea level	94 (15)
Age < 3 months	100 (16)
Ill-appearing	100 (16)
Social factors	100 (16)
Geographic factors	94 (15)
Comorbidities: congenital or acquired	94 (15)
Significant lung dysfunction	100 (16)
Pulmonary complications	100 (16)
Vomiting and dehydration that make oral treatment difficult	100 (16)
Lack of response to empirical antibiotic treatment 48h after initiation	94 (15)
Paediatric ICU	
Respiratory distress with PaO_2/FiO_2 < 250	94 (15)
Need for mechanical ventilation	100 (16)
Severe haemodynamic instability	100 (16)
Acute renal failure	94 (15)
Disseminated intravascular coagulation	100 (16)
Meningitis	88 (14)
Coma or Glasgow < 8	100 (16)
Shock or systemic inflammatory response syndrome	100 (16)
Use of vasopressors	100 (16)

[a]Experts that agree with the criteria

Table 4.Recommendations Related to Starting Empirical Treatment

Treatment	% (n) [a]
Uncomplicated bacterial CAP	
Amoxicillin	100 (16)
Crystalline penicillin G	81 (13)
Ampicillin	94 (15)
Treatment days: 5	94 (15)
Avoid using	
Clarithromycin	81 (13)
Oxacillin	94 (15)
Vancomycin	94 (15)
First-generation cephalosporins	94 (15)
Second-generation cephalosporins	81 (13)
Ceftaroline	94 (15)
Third-generation cephalosporins [b]	100 (16)
Complicated bacterial CAP	
Vancomycin	88 (14)
Third generation cephalosporins	94 (15)
Ceftaroline [b]	88 (14)
Treatment weeks: 2 to 4	94 (15)
Avoid using	
Amoxicillin [b]	100 (16)
Crystalline penicillin G [b]	100 (16)
Ampicillin [b]	100 (16)
Ampicillin-sulbactam [b]	75 (12)
Azithromycin [b]	100 (16)
First-generation cephalosporins [b]	94 (15)
Second-generation cephalosporins [b]	94 (15)
Criteria for transferring an antibiotic to the oral route	
Afebrile for 24 h	94 (15)
Optimal oxygen saturation according to sea level	81 (13)
Oral tolerance	100 (16)
Normal respiratory rate according to age	81 (13)
Caregiver adherence to oral administration	100 (16)
24 h after removal of the chest tube and without clinical deterioration [b]	100 (16)

[a]Experts that agree with the criteria
[b]Consensus in the second round

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Discussion

Several international and national initiatives aimed at an adequate diagnosis and treatment of bacterial CAP to decrease antibiotic resistance, improve child survival, reduce infant mortality, and reduce preventable mortality from pneumonia, as key issues of the 2030 agenda on sustainable development goals.[1,2,10–12] In line with the achievement of these goals, this manuscript gathers the consensus of a group of experts in paediatric infectious diseases from Colombia about signs and symptoms suggestive of bacterial CAP, aetiologies of clinical interest to guide initial treatment, types of diagnostic aids to be used, criteria for hospitalisation and admission to the paediatric ICU, and recommendations on starting empirical treatment, which is of great interest given the small number of specialists in this field in the country.

In Colombia, there are several structural barriers to the care of this and other paediatric diseases. For example, the density of health care workers is low at 80.8 per 10,000 inhabitants, medical and nursing personnel at 39.6 per 10,000 inhabitants; the number of paediatricians in the country is 4,149, of whom less than 100 have training in infectious diseases; the demand for health care has increased in a greater proportion than the supply of services, including news about closures or cuts in medical services with the subsequent reduction of beds, and there is little availability of paediatric services, which is why oversaturation of paediatric emergencies is common.[13–15]

In addition, paediatric care is limited, with few follow-ups (especially in the population of the subsidised regime). Some trends have indicated that Colombia has about 85,000 hospital beds, with about 12% for paediatric care. Therefore, it is urgent to decrease the number of emergency consultations and hospitalisations through training for doctors and the generation of consensus documents for physicians who perform paediatric triage or care of children in the first level of care in order to improve the resolution capacity at clinics of low and medium complexity.[14,15]

In some updates on CAP (but focused on adults), recommendations similar to those of the current consensus have been reported, which become more relevant when considering the following facts: CAP is a challenge for health given its high morbidity and mortality risk; it constitutes one of the main infections that requires a high use of antibiotics; the evidence shows a high frequency of antibiotic-resistant causative agents; and economic studies show the high economic burden that it implies for health systems.[16,17] For this reason, it is crucial to have these types of recommendations, that optimise initial management, reduce hospitalisations or hospital stays, and reduce resistance to antibiotics, complications, and healthcare cost overruns, which agrees with the *American Thoracic Society and Infectious Diseases Society of America*.[18]

Despite advances in vaccines, diagnostic tests, and antibiotics, CAP continues to present a challenge for clinical management given the following conditions: after an episode of CAP, the risk of death remains for a long time due to the inflammation it generates and its high coexistence with other comorbidities; pneumococcal vaccines affect circulating serotypes; studies of new antibiotics exclude seriously ill patients; and most focused on multi-drug resistant pathogens unrelated to CAP, which restricts their general use.[19]

Specifically, in children (0–5 years old), CAP is the leading cause of death; Being one of the main diagnoses of infectious diseases in children entails a high use of antibiotics and hospitalisations. For this reason, it is necessary that each country have different tools to face this challenge in order to make optimal use of antibiotics, reduce complications, hospitalisations, and deaths; reduce hospital stay times; improve clinical outcomes; increase survival; increase quality of life, and aligns with 2030 agenda.[20]

This consensus joins previous systematic reviews that have concluded the importance of periodically updating clinical recommendations on the management of this disease due to the constant clinical-epidemiological changes in paediatric CAP. For example, in a synthesis of evidence applied in other countries, the following findings have been highlighted: i) hypoxemia and higher breathing work as the main signs of CAP; ii) wheezing is a good predictor of viral infection; iii) chest X-ray without abnormalities and procalcitonin < 0.25 ng/dL have a high negative predictive value (92% and 93%, respectively); iv) criteria for hospitalisation such as difficulty swallowing, severe vomiting, seizures, chest retractions, cyanosis, lethargy, nasal flaring, rales, and oxygen saturation < 90%; v) severity predictors as pleural effusions and multilobar infiltrates; vi) oral amoxicillin is the main outpatient treatment, in hospitalised patients are ampicillin, aqueous penicillin G, or intravenously amoxicillin.[21]

The latter coincides with other reviews that conclude that in children under five years of age, the first treatment is high-dose amoxicillin, or clindamycin, azithromycin, clarithromycin, and levofloxacin for patients with type 1 hypersensitivity to penicillin, while in non-type 1 hypersensitivity cephalosporins could be used. This is supported in a context where the main bacterial aetiologies have been *Streptococcus pneumoniae, Haemophilus influenzae, Streptococcus pyogenes, Staphylococcus aureus,* and *Moraxella catarrhalis*.[22] For example, in Colombia, a study of 525 children and adolescents with CAP showed that 29% had severe pneumonia, 61% mixed aetiology, 28% pyogenic bacteria, 21% atypical bacteria, and the main causal agents were *Mycoplasma pneumoniae* and *Streptococcus pneumoniae*.[23]

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Other reviews specify that the proper use of antimicrobials is based on aetiology, vaccination policies, and local profiles of antibiotic resistance. Therefore, it is crucial to have this type of consensus document while progress is made in local epidemiological studies. Despite this caveat, some international publications present the following recommendations for children: use expectant management in uncomplicated pneumonia due to the risk of viral infection; in severe CAP use oral amoxicillin for five days with doses depending on local profile resistance; macrolide-based regimen does not have higher quality evidence. In hospitalisation, narrow-spectrum intravenous beta-lactams are as effective as broad-spectrum cephalosporins; in severe CAP broad-spectrum therapy is proper; and in empyema, rapid switching from IV to oral is similar to prolonged IV therapy.[24]

A meta-analysis on antibiotic use for paediatric CAP reports that the optimal dosing of amoxicillin, and the choice of amoxicillin or broader-spectrum antibiotics are unclear. More research should be conducted on the clinical efficacy of antibiotics for pneumococcal, staphylococcal, and mycoplasma infections, and the impact of first-line drugs on clinical outcomes and resistance reduction.[25] Other systematic reviews of hospital settings only found four clinical trials that compared various antibiotic regimens for paediatric CAP in 84 subjects, concluding that their effects are not clear, their level of evidence is of low quality, and the current evidence is insufficient to ensure the superiority of any antibiotic regimen,[26] which makes the type of evidence generated by the Delphi even more relevant.

Conclusion

This consensus is a valuable resource in the Colombian setting, where multiple barriers persist for optimal care of bacterial CAP in paediatrics, and worldwide, where the evidence systematised in different reviews reiterates the insufficiency and low quality of the available data, highlighting the need to have specific tools for each location. In this sense, this consensus document is aimed at improving some practices among general practitioners and paediatricians, who are the professionals who provide CAP care, in the following topics: signs and symptoms, aetiological agents, laboratory tests, radiological findings, criteria for hospitalisation and admission to the paediatric ICU, and antibiotic therapy.

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