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REVIEW

RISK FACTORS FOR PNEUMONIA IN SMALL CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF CASE CONTROL STUDIES

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Abstract

Introduction. Preventing new or recurrent episodes of acute respiratory tract infections in children under five years of age could improve antibiotic prescription practices and decrease unnecessary antibiotic use.
Objectives. This meta-analysis aimed at identifying the non-modifiable and modifiable risk factors for community-acquired pneumonia in small children.
Material and methods. Based on a comprehensive search of Cochrane and Medline databases, we included studies published between 2018 and 2022 that explored the cause and risk factors for community-acquired pneumonia in pediatric patients. The strength of this relationship was evaluated using odds ratios (ORs) with 95% confidence intervals (CIs).
Results. Overall, 11 studies involving 8255 participants were used for analysis after screening nearly 1831 abstracts. Indoor air pollution (OR=1.91; 95%CI: 1.58–2.30; Chi^2=171.22; I^2=96%), non- exclusive breastfeeding (OR=1.34; 95%CI: 1.11–1.60; Chi^2=49.10; I^2 = 90%), incomplete immunization (OR=1.74; 95%CI:

Résumé

Facteurs de risque de la pneumonie chez les petits enfants : une revue systématique et une méta-analyse des études cas-témoins

Introduction. La prévention des épisodes nouveaux ou récurrents d'infections aiguës des voies respiratoires chez les enfants de moins de cinq ans pourrait améliorer les pratiques de prescription d'antibiotiques et réduire l'utilisation inutile d'antibiotiques.
Objectifs. Cette méta-analyse vise à identifier les facteurs de risque non modifiables et modifiables de pneumonie communautaire chez les jeunes enfants.
Matériel et méthodes. Sur la base d'une recherche exhaustive dans les bases de données Cochrane et Medline, nous avons inclus des études publiées entre 2018 et 2022 qui ont exploré la cause et les facteurs de risque de pneumonie communautaire chez les patients pédiatriques. La force de cette relation a été évaluée à l'aide de rapports de cotes (OR) avec des intervalles de confiance (IC) à 95%.

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1.33–2.26; Chi²=72.91; I²= 95%) and prematurity (OR=2.56; 95%CI: 1.63–4.02; Chi²=0.07; I²=0%) were associated with community-acquired pneumonia in small children in a consistent manner across studies.
Conclusions. These results may allow clinicians and health policymakers to develop prompt assessment and correction of modifiable risk factors which could have profound effects on quality of life, primary care workload and pediatric morbidity caused by community-acquired pneumonia.

Keywords: pneumonia, pediatric population, risk factor.

List of abbreviations:
ARTI – acute respiratory tract infections
CAP – community-acquired pneumonia
CI – confidence interval
OR – Odds Ratio

Résultats. Dans l'ensemble, 11 études impliquant 8255 participants ont été utilisées pour l'analyse après avoir examiné près de 1 831 résumés. Pollution de l'air intérieur (OR=1,91; IC 95%: 1,58–2,30; Chi²= 171,22; I²=96%), allaitement non exclusif (OR=1.34; 95% CI: 1.11–1.60; Chi²=49.10; I²=90%), immunisation incomplète (OR=1.74; 95%CI: 1.33–2.26; Chi²=72.91; I²=95%), prématurité (OR=2.56; 95%CI: 1.63–4.02; Chi²=0.07; I²=0%) ont été identifiés comme étant associés à une pneumonie communautaire chez les jeunes enfants de manière cohérente dans toutes les études.
Conclusions. Ces résultats peuvent permettre aux cliniciens et aux décideurs de la santé de développer une évaluation et une correction rapides des facteurs de risque modifiables qui pourraient avoir des effets profonds sur la qualité de vie, la charge de travail des soins primaires et la morbidité pédiatrique causée par la pneumonie communautaire.

Mots-clés: pneumonie, population pédiatrique, facteur de risque.

Introduction

Acute respiratory tract infections (ARTIs) are the most common cause for primary care consultations and hospitalizations in children. Worldwide, community-acquired pneumonia (CAP) is the most common acute respiratory disease, and it is associated with high morbidity among children aged less than 5 years[1]. Pediatric CAP is defined as signs and symptoms of an acute infection of the pulmonary parenchyma in a child who acquired the infection in the community, outside the hospital[2,3]. Annually, about 156 million new episodes of pneumonia occur worldwide; 13% of these episodes are severe enough to be life-threatening and require hospitalization[4]. Improved identification of determinants of CAP in children of small age might enable targeted interventions to prevent adverse outcomes. Preventing new or recurrent episodes of acute respiratory tract infections in children under five years old could reduce hospitalization rates, improve antibiotic prescription practices, and decrease unnecessary antibiotic use.

The objective of the study

This meta-analysis aimed at identifying the non-modifiable and modifiable risk factors for CAP in small children.

Material and methods

This meta-analysis was conducted between December 2021 – June 2022. Based on a comprehensive search of Cochrane and Medline databases, we included studies published between 2018 and 2022 that explored the cause and risk factors for CAP in pediatric patients.

The search included MeSH (Medical Subject Headings) terms and keywords, combinations thereof. Search strategies using different Boolean operators were used. Search terms were used independently and/or in combination using "OR" or "AND" or "NOT". Basic search terms and phrases were "under five", "children", "child", "infant", and "pneumonia", "lower respiratory infection", "causes", "risk factors", "determinants ", "associated factors", "predictors". Articles with original data that reported at least two of the following risk factors were included: economic status, nutritional status, outdoor pollution, indoor air pollution, child history of ARTI, prematurity, non-exclusive breast feeding, and vaccination status.

The inclusion criteria were articles written in English published in full in the period 2018-2022, age of the participants up to 5 years, observational case-control studies, the comparison groups: the group of cases – patients with CAP and the control group children without the diagnosis of CAP. Data were collected using a structured and pre-tested questionnaire.

Exclusion criteria included: cohort studies, inadequate age of participants, studies estimating risk factors for pneumonia severity or complications, mortality caused by it, incompletely presented studies (abstracts). According to the PRISMA guide, the steps of conducting the systematic review were followed (Figure 1): identification, screening, eligibility, and inclusion.

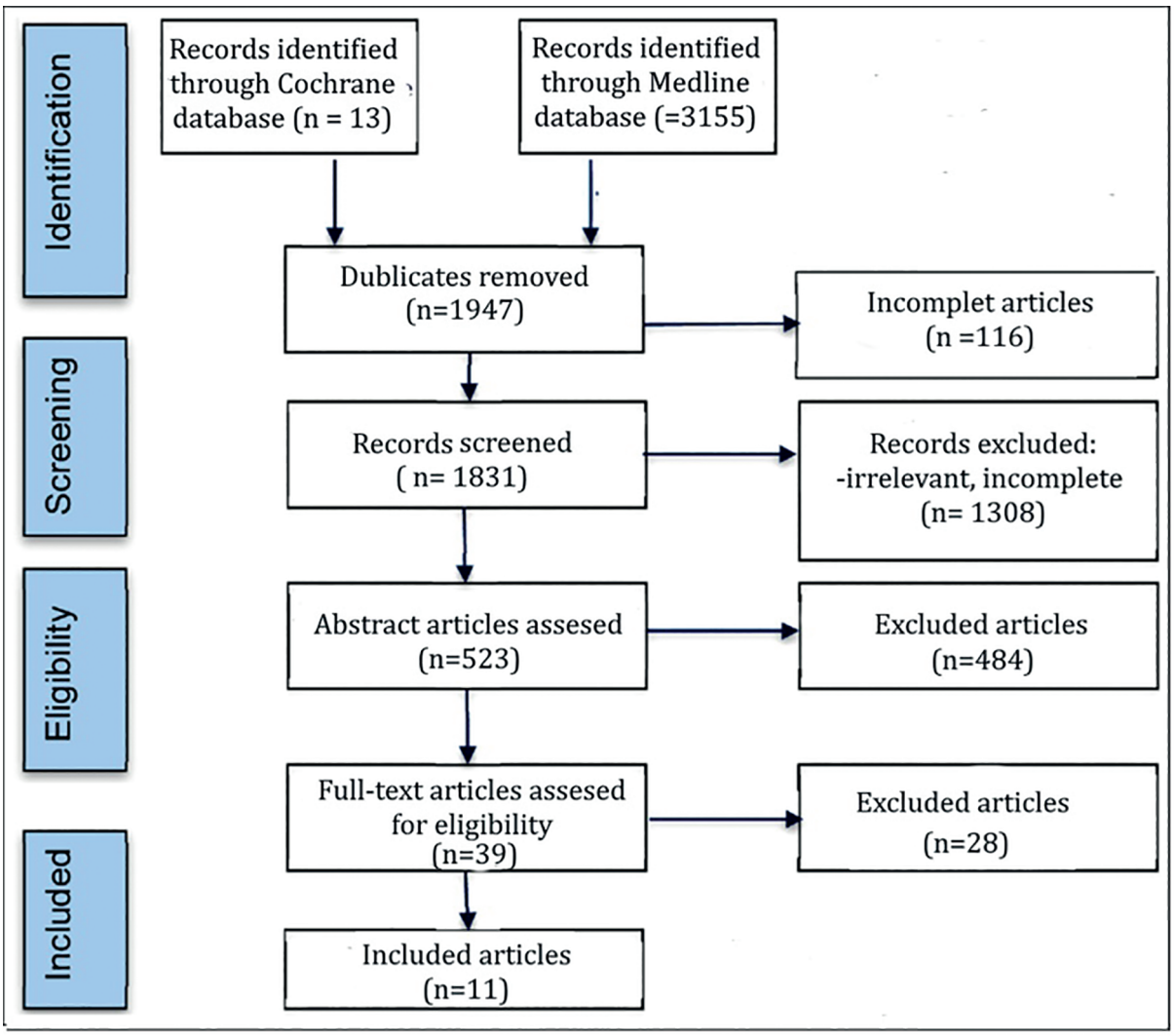

Figure 1. PRISMA flowchart for inclusion and exclusion of studies

The Cochrane RevMan 5.4.1 software was used for statistical data processing. The strength of relationship between risk factors and pneumonia was evaluated using odds ratios (ORs) with 95% confidence intervals (CIs). The forest plot diagram was used to visualize heterogeneity among the studies, publication bias was assessed using funnel plots.

Results

We identified 3155 articles in the Medline database and 13 in the Cochrane database, removed duplicates and excluded irrelevant studies after reviewing the title and abstract. Two researchers then independently assessed the eligibility of each study (n=39) for inclusion. A third reviewer was consulted when consensus could not be reached. After applying the exclusion criteria, 11 studies[5-14] investigating risk factors for CAP in young children and involving 8255 participants were used for further statistical analysis. The majority of included studies were from developing and least developed countries.

Table 1 summarizes the characteristics of the 11 included studies in the systematic review and meta-analysis. The ninth study reveals unpublished data (Revenco, 2022): this is a case-control study in two main pediatric hospitals in Chisinau, Republic of Moldova – the Mother and Child Institute and the Municipal Children's Clinical Hospital no.1 Data collection started in December 2020 and is currently underway.

Overall, 11 studies involving 8255 participants were used for analysis after screening nearly 1831 abstracts. Of the eight risk factors examined in 11 articles, only four risk factors presented statistically significant evidence in at least two studies. Indoor air pollution, non- exclusive breastfeeding, incomplete immunization, prematurity, were identified associated with CAP pneumonia in small children in a consistent manner across studies.

Breastfeeding practices and immunization status of children

Six from 11 studies found a significant association between non-exclusive breast-feeding and CAP among

Table 1. Characteristics of included studies[5-14].

Author	Year	Country	Study design	Age range months	Sample size
Bazie	2020	Northeast Ethiopia	Case-control	2–59	444
Chanie	2021	Amhara Region, Ethiopia	Case-control	2–59	888
Demissie	2021	Ethiopia	Case-control	2–59	414
Fadl	2020	Egipt	Case-control	1–59	660
Gothankar	2018	India	Case-control	0-59	3671
Lema	2019	Oromia Region, Ethiopia	Case-control	2–59	344
Ngogho	2019	Tanzania	Case-control	2–59	449
Nirmolia	2018	Dibrugarh town ,India	Case-control	12–59	624
Revenco	2022	Republic of Moldova	Case-control	2–59	150
Seramo	2022	Ethiopia	Case-control	2–59	435
Sutriana	2021	Indonesia	Case-control	10–59	176

children less than 5 years-old (OR=1.34; 95%CI: 1.11–1.60; Chi^2=49.10; I^2=90%). The qualitative visual analysis of the studies' results suggests between-study variability. Also, we can observe a difference in the risk factor effect magnitude among studies. The CI for each study's non-exclusive breast-feeding effect (horizontal lines) overlap one another, but the upper and lower limits of the CI do not consistently line up on a vertical axis, indicating differences in estimation of the population risk factors effect among studies. These qualitative results suggest that there is heterogeneity. The quantitative test of heterogeneity – Chi^2 was significant 49.10, the I^2 value was 90%. These quantitative results suggest study heterogeneity (Figure 2).

Five studies found a significant association between an incomplete vaccination in children and pneumonia (OR=1.62; 95%CI: 1.23–2.14). Regarding publication bias, a funnel plot showed an asymmetrical distribution. The quantitative test of heterogeneity – Chi^2 was significant 72.91, the I^2 value was 95%, which also showed heterogeneity (Figure 3).

Indoor air pollution

This meta-analysis also documented a significant association between indoor air pollution and pneumonia, according to seven studies (OR=1.91; 95% CI: 1.58–2.30). The forest plot showed a significant degree of heterogeneity. Quantitative tests of heterogeneity: Chi^2=171.22; I^2 = 96% (Figure 4).

Prematurity

There were 2 studies mentioning the significant association (OR = 2.56; 95% CI: 1.63–4.02) between prematurity and CAP in small children. A qualitative visual analysis of the studies' results suggests little between-study variability. These qualitative results suggest that there is little heterogeneity. The chi-square test for heterogeneity was nonsignificant. The I^2 value was zero. These quantitative results suggest that there was little between-study variability. Regarding publication bias, a funnel plot showed a symmetrical distribution (Figure 5).

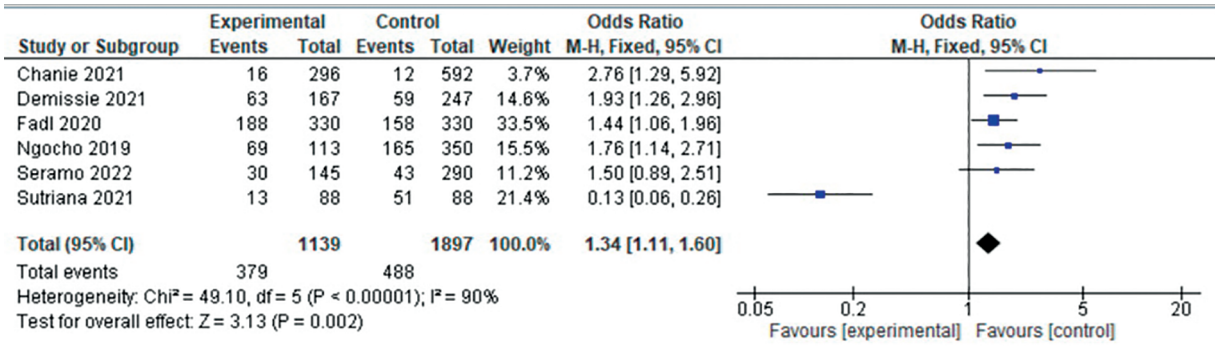

Figure 2. Non-exclusive breastfeeding as risk factor for CAP in small children

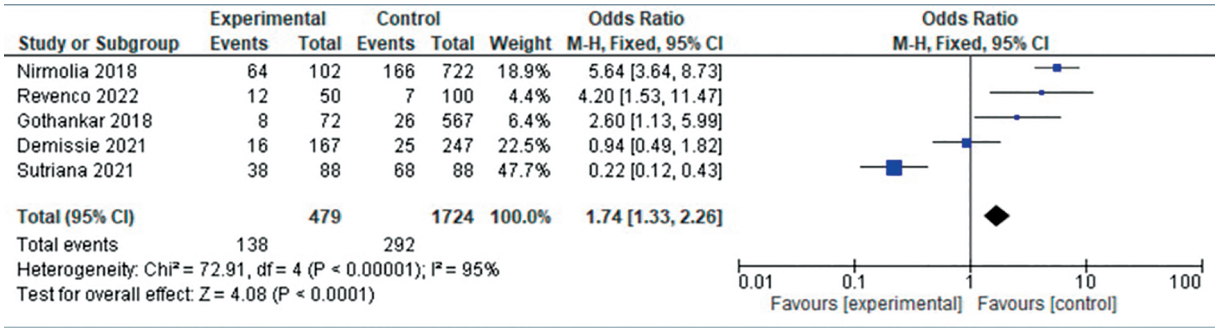

Figure 3. Incomplete immunization as a risk factor for CAP in small children.

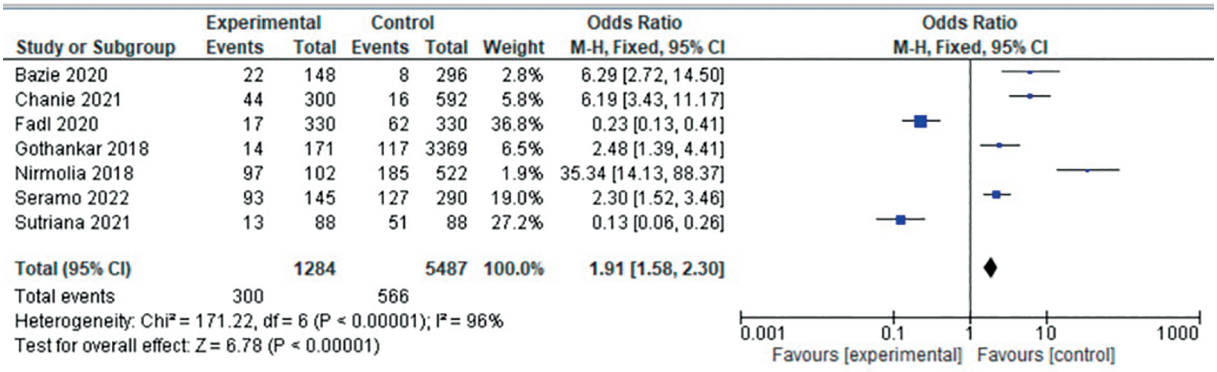

Figure 4. Indoor air pollution as a risk factor for CAP in small children

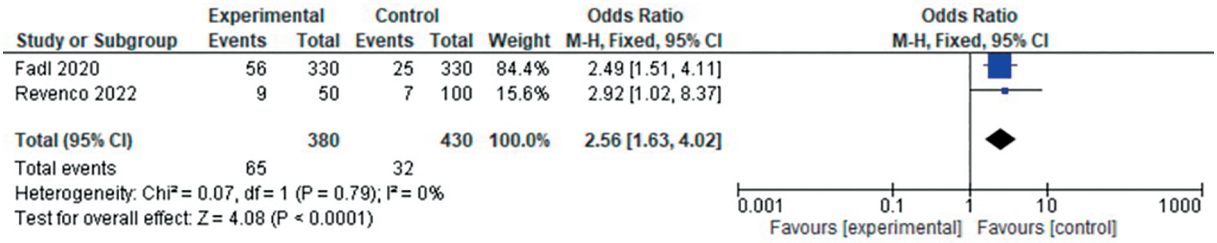

Figure 5. Prematurity as a risk factor for CAP in small children.

Discussion

CAP in young children remains an important public health burden, and knowledge of the risk factors that contribute to its development would allow to develop effective public health measures. According to this meta-analysis, the exposure to indoor air pollution increases the risk of pneumonia in children under five years old. The link between exposure to household air pollution and pneumonia in young children was supported by several studies[15,16]. The reason behind this association might be the effect of indoor pollutants on ciliary oscillations and structure, as well as mucous flow[17]. According to data published by Collaborators G.B.D.L.R.I., the countries that implemented measures to decrease exposure to household air pollution reduced pneumonia mortality by around 8%, and increased exposure to ambient air pollution increased mortality by around 4%[18].

Over the time, an increasing number of studies has investigated the role of breastfeeding as a protective factor. The effect of non-exclusive breastfeeding on childhood pneumonia in children below the age of 5 years was strongly demonstrated in this study. Thereby, these findings were accordant with different studies conducted across many countries[19,20]. Evidence from this study revealed that pneumonia can be prevented by immunization. This result was in line with the latest studies conducted in India[21] and Ethiopia[22]. Thus, the undertaking of measures to actively and continuously promote vaccination policies to ensure vaccination coverage above 95%, with the aim of reducing the morbidity and mortality of children through vaccine-preventable respiratory diseases, must remain one of the main priorities of the medical system in our country.

Higher odds of pneumonia were observed in children under 5 years-old, born prematurely[21,22]. The underlying reason could be the effects of premature birth, such as less transplacental antibody transfer, anaemia, suboptimal breastfeeding, delayed/missing vaccinations, and the resultant of childhood growth failure. A decrease in growth failure indices, such as stunting and wasting, can offer a significant decrease in pneumonia mortality[18,23]. Not all eleven studies investigated these risk factors, thereby only two studies revealed consistent data with previous evidence.

To help our national policymakers to develop public health measures to reduce CAP burden in young children, we continue to advocate for health interventions at the primary care level, such as parental education relating the importance of avoiding children's exposure to various indoor air pollutants, including cigarette smoke, promoting exclusive breastfeeding in the first 6 months of life and the importance of vaccination according to the National Immunization Program. Parallel strategies to improve access to health care services and living conditions, to closely monitor the respiratory function in children born prematurely are of equal importance.

Conclusions

The results of this meta-analysis may allow clinicians and health policymakers to develop prompt assessment and correction of modifiable risk factors which could have profound effects on quality of life, primary care workload and pediatric morbidity caused by CAP.

This systematic review and meta-analysis have some strength: it was focused on a pediatric population only and it was based on the most recent studies published within the last five years. Nevertheless, a general limitation of meta-analyses of observational studies is that the result may be a precise, but biased estimate because of inherent biases and confounding in the original studies and high heterogeneity might be present. There may be also publication bias because not all grey literature was included.

Author Contributions:

N.R, O.G, A-M.B. and D.B were responsible for the methodology, conceptualization and software, A. H-B, D.S and O.C; A-M.B. analyzed the data; supervising, N.R; N.R and A-M.B. wrote the manuscript. All authors have read and agreed to the published version of the manuscript.

Compliance with Ethics Requirements:

„The authors declare no conflict of interest regarding this article"

„The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. "

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