

Pertussis in children: an integrative review

Coqueluche na infância: revisão integrativa da doença

Tos ferina en la infancia: revisión integrativa de la enfermedad

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ABSTRACT

Background and Objectives: Despite the efforts of the National Immunization Program, pertussis remains a serious health problem. Thus, this study described the evidence in the literature on pertussis during childhood, which elucidates the health-care practices necessary for prevention, promotion, and control of the disease. **Methods:** This is an integrative literature review conducted in the LILACS, MedLine, PubMed, SciELO, Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases, using the following descriptors: "Whooping Cough", "Epidemiology", and "Vaccination". The search was restricted to humanities, in English, Portuguese, or Spanish, without year delimitation. The search was completed on May 2020. **Results:** in total, 1,248 articles were selected, of which only nine articles were analyzed, mostly from North America, and 55% of the analyzed studies were about preventing pertussis. Regarding the authorship of the studies, epidemiologists participated in 67% of the publications. **Conclusion:** This study presents the necessary scientific evidence on pertussis during childhood is necessary for prevention, control, promotion, and epidemiological profile of this disease in this population. The results revealed a level of evidence of five, suggesting that the research in this area does not show strong evidence.

Keywords: *Pertussis. Epidemiology. Vaccination.*

RESUMO

Justificativa e Objetivos: Apesar dos esforços despendidos pelo Programa Nacional de Imunizações, a coqueluche é um agravo que ainda gera grandes preocupações para a saúde pública. Assim, o objetivo deste estudo foi descrever as evidências na literatura sobre coqueluche na infância que indicassem as práticas de assistência à saúde necessárias para sua prevenção, promoção e controle. **Método:** Revisão integrativa da literatura nas bases de dados LILACS, MedLine, PubMed, SciELO, Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL) utilizando os descritores *Whooping Cough, Epidemiology, Vaccination*. A revisão foi realizada em maio de 2020 e abrangeu a literatura disponível na íntegra, publicada em português, inglês ou espanhol, sem delimitação de ano. **Resultados:**

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Dentre os 1.248 artigos selecionados apenas nove foram analisados (a maioria norte-americana), dos quais 55% eram estudos realizados para prevenção de coqueluche. Quanto à autoria dos estudos, em 67% das publicações havia participação de um epidemiologista. **Conclusão:** Esta investigação mostra as evidências científicas sobre a coqueluche na infância, necessárias para prevenir, controlar, promover a assistência e definir o perfil epidemiológico desse agravo nessa população. Os resultados revelaram nível de evidência cinco, sugerindo que as pesquisas desenvolvidas na área não retratam fortes evidências.

Descritores: Coqueluche. Epidemiologia. Vacinação.

RESUMEN

Justificación y Objetivos: La tos ferina todavía es un grave problema de salud a pesar de los esfuerzos realizados por el Programa Nacional de Inmunización. El objetivo de este estudio fue identificar las evidencias científicas en la literatura sobre la tos ferina en la infancia que indican las prácticas de asistencia sanitaria necesarias a la prevención, promoción y control de la enfermedad. Métodos: Revisión integrativa de la literatura en las bases de datos LILACS, MedLine, PubMed, SciELO, Embase, Cumulative Index to Nursing and Allied Health Literature (CINAHL) utilizando las palabras clave: *Whooping Cough, Epidemiology, Vaccination*. Se llevó a cabo en mayo de 2020 la búsqueda de artículos publicados en portugués, inglés y español, disponibles en su totalidad y sin delimitación de año. **Resultados:** Se seleccionaron un total de 1.248 artículos, de los cuales solo se analizaron nueve, en su mayoría norteamericanos; el 55% de los estudios analizados fueron sobre la prevención de la tos ferina. Respecto de la autoría de los estudios, un epidemiólogo participó en el 67% de las publicaciones. **Conclusiones:** Esta investigación muestra evidencias científicas sobre la tos ferina en la infancia necesarias para la prevención, el control, la promoción de la asistencia y la definición del perfil epidemiológico de la enfermedad en esa población. Los resultados revelaron que el nivel de evidencia se remite a cinco, lo que sugiere que la investigación en el área no muestra evidencias **sólidas**.

Palabras clave: Tos ferina. Epidemiología. Vacunación.

INTRODUCTION

Despite the efforts of the National Immunization Program (PNI), epidemiological surveillance and other international surveillance centers, it is estimated that between 20 and 50 million cases of pertussis occur every year, with approximately 200 to 400 thousand deaths, most being infants who have not been vaccinated or who had incomplete vaccination.¹

Data from the Department of Informatics of the Brazilian Unified Health System (Datusus) indicate that, from 2008 to 2014, 19,570 cases of pertussis were confirmed in the age group up to 4 years in Brazil, with 5,061 cases in the state of São Paulo.^{1,2} Confirmed cases from 2008 to 2014 increased progressively significantly, with more growth between 2011 and 2014, both in Brazil and in the state of São Paulo.² In 2015, 2,489 cases were confirmed in Brazil and out of those 439 cases in children of the same age group in the state of São Paulo, ² presenting a change in the growth curve.

Pertussis, a public health concern,² is defined as an acute infectious disease of the lower respiratory tract, of universal distribution, highly contagious and characterized by paroxysms of non-secreting cough. The etiological agent is the bacterium *Bordetella pertussis*, whose transmission occurs by direct contact, affecting people of any age group. In infants, complications and mortality may occur more frequently than in the general population.^{3,4}

The last hyperendemic cycle of whooping cough in the state of São Paulo began in 2011.⁵ The state of São Paulo improved the diagnosis of the disease at the

end of 2009, with the adoption of the polymerase chain reaction (RT-PCR) technique to optimize the laboratory confirmation of cases, in addition to the inference on the improvement of clinical suspicion.²

Susceptibility to whooping cough is general. Individuals become resistant if they eventually acquire the disease, which grants them a lasting but not permanent immunity.⁶ Basic immunization is carried out by means of the DPT vaccine (against Diphtheria – *Pertussis* –, whooping cough and tetanus). For the correct immunization, at least three doses of the vaccine are required: with two, four and six months of life, in addition to a booster dose at 5 years. However, it is already known that protection can decline between five and ten years (on average) after the last dose of the vaccine.⁶

One study analyzed three different vaccine strategies using a dynamic and age-dependent mathematical model, where booster doses were included to the currently used scheme. It concluded that the inclusion of a vaccine booster against pertussis at 12 years generates great benefits.⁷

A consensus named *The Global Pertussis Initiative* has shown that reinforcement in the preschool period is widely recommended in Central, Eastern and Middle Eastern Europe.⁸ In addition to discussion on the number of doses, the consensus also addressed vaccination in adolescents, which has been implemented in the Czech Republic and Hungary. Epidemiological data indicate that this vaccination could be beneficial in several other countries in Central and Eastern Europe.⁸

In the state of São Paulo, cases increased progressively between 2009 and 2014.² Data from The Information System of Notifiable Diseases (Sinan) showed that in 2009 123 cases were recorded. We noticed exponential growth in the number of cases until 2014 when 1,701 cases were recorded, which is an increase of 1,382.92% in 5 years. Of the total cases of pertussis in the state in 2014, 82.7% were children under 1 year. On the other hand, in 2015, there was an important reduction in the number of registrations compared to the previous year, with 439 confirmed cases, i.e. a reduction of 74.19%, which possibly demonstrates a phase of decline after the growth cycle observed in the previous five years.^{5,9}

Sinan data obtained from Datasus demonstrate that the municipalities of Botucatu and Marília have followed the growth curve of the state, quadrupling the number of cases registered between 2011 and 2014. In the municipality of Marília, of the forty confirmed cases in 2014, 80% were children under 1 year.¹⁰

Since November 2014, the Ministry of Health has been making the dTpa vaccine (acellular vaccine against diphtheria, tetanus and pertussis) available for pregnant women in the national calendar through the Unified Health System, with the aim of reducing the incidence and mortality caused by the disease among newborns. It is recommended to apply the dose between the 27th and 36th weeks of gestation, the effectiveness of which is estimated at 91%. However, the dose may be administered up to a maximum of twenty days before the likely date of delivery. The vaccine is also offered to health professionals working in maternity and Neonatal Intensive Care Unit (NICU) with booster doses every ten years.⁹

These data reinforce the need to expand vaccination coverage through revaccinations with dTpa (booster) for all. France was the Pioneer, followed by Australia, Germany, Italy, the United States and Canada, in carrying out the *Cocoon* strategy, whose objective is to protect newborns by immunizing their family members and caregivers. Vaccination would form a kind of protective "cocoon" around the child, which represents a benefit for the whole family.^{4,10} Since 2005 the Advisory Committee on Immunization Practices (Acip) recommends that this strategy be applied at least two weeks before contact with the baby.¹¹

A prospective multicenter study conducted from January 2009 to September 2011 in South Korea, in infants younger than 6 months, verified demographic and clinical data of these patients and performed diagnostic tests on household contacts, noting that in 85.7% of cases studied the probable source of infection were these contacts, especially the parents with 52.6%. The authors conclude that dTpa booster vaccination in those who care for and have contact with young infants is necessary in South Korea.¹²

Thus, considering the relevance of the practice of health care concerning pertussis during childhood, it is of utmost importance to conduct studies that seek to socialize the knowledge produced in the national and international literature on the subject. This justifies the interest

of this article in carrying out an integrative review of the literature to answer the following question: What is the characterization of publications about pertussis during childhood published in online journals of the health field?

Given the above, this study aims to characterize the publications on pertussis during childhood that can elucidate the health care practices necessary to prevent this disease in this population, published in online journals in the health field.

METHODS

This is an integrative review of the literature pertinent to the scientific production about pertussis during childhood regarding the health care practices necessary to prevent this pathology in this population.

This research method is widely used in evidence-based practice, since it allows to gather and synthesize knowledge and incorporate the applicability of significant research results into practice.¹³

To develop this review, six steps were taken: definition of the problem and the guiding question, establishment of criteria for inclusion and exclusion of studies, search in the literature, categorization of the selected studies, analysis of the included studies, discussion and synthesis of the results.¹⁴

Then, we proceeded to the literature search, data collection, critical reading of the initial material, evaluation, content categorization and, subsequently, analysis and interpretation of the selected publications.

A search of the literature on the subject and a proposal for conducting this research has been carried out by means of searching online on the website of Capes, Pubmed, BVS, and on the databases Medline, Lilacs, BDNF, CidSaúde, Ibecs, SciELO, Embase, and CINAHL.

To select the sample, the following inclusion criteria were adopted: online articles available in full, published in Portuguese, English or Spanish, without limitation of period for bibliographic review, and that addressed pertussis during childhood with respect to care promotion, prevention, control and epidemiological profile of the disease, except theses and dissertations, reviews and duplicate publications and articles that did not address the topic.

The data were collected on April 20, 2017 (May 7 2020) via the following descriptors: (Coqueluche OR Tosse Comprida OR Tosse Convulsa OR Pertussis) AND (Epidemiologia) AND (Vacinação OR Imunização Ativa) AND (prevenção & controle OR controle OR prevenção OR medidas preventivas OR terapia preventiva OR profilaxia OR prevenção e controle), for the Portuguese search strategy. In English, we used the following descriptors: (*Whooping Cough* OR *Pertussis* OR *Pertussis* OR *Respiratory Bordetella pertussis Infection*) AND (*Epidemiology*) AND (*Vaccination* OR *Vaccinations* OR *Active Immunization* OR *Active Immunization*) AND (*Prevention and control* OR *preventive therapy* OR *prophylaxis* OR *preventive measures* OR *prevention OR control*), all recorded in Medical Subject Headings (MeSH) and Health Sciences Descriptors (Decs).

For data collection, an instrument validated in the USA was used,¹⁵ (a validated instrument¹⁵ for integrative reviews, including the following items: identification: article title, journal, authors, language and year of publication; methodological characteristics of the study: objectives and type of publication).¹⁵ To this data collection instrument we added the study context and the area of training of the authors to respond to the objectives proposed in this study. It should be noted that some questions were suppressed during its application. The analysis continued with the interpretation and synthesis of the results, comparing the data evidenced in each article.

The selected articles were ranked hierarchically as to their level of evidence. We opted for the categorization method of the agency for Healthcare Research and Quality (AHRQ) of the United States of America, which categorizes the quality of evidence in six levels,¹⁶ namely:

The flowchart of the crossed data and the result are presented in Figure 1 and followed the PRISMA recommendation.¹⁷

It is worth noting that this integrative review derives from a primary study "Vacina dTpa em gestantes na redução de infecção pelo microrganismo *Bordetella pertussis* na criança", which is a study integrated in the "umbrella" format of the PhD that originated this review, having received the approval of the Research Ethics Committee, with Opinion No. 2,485,887, dated February 5, 2018.

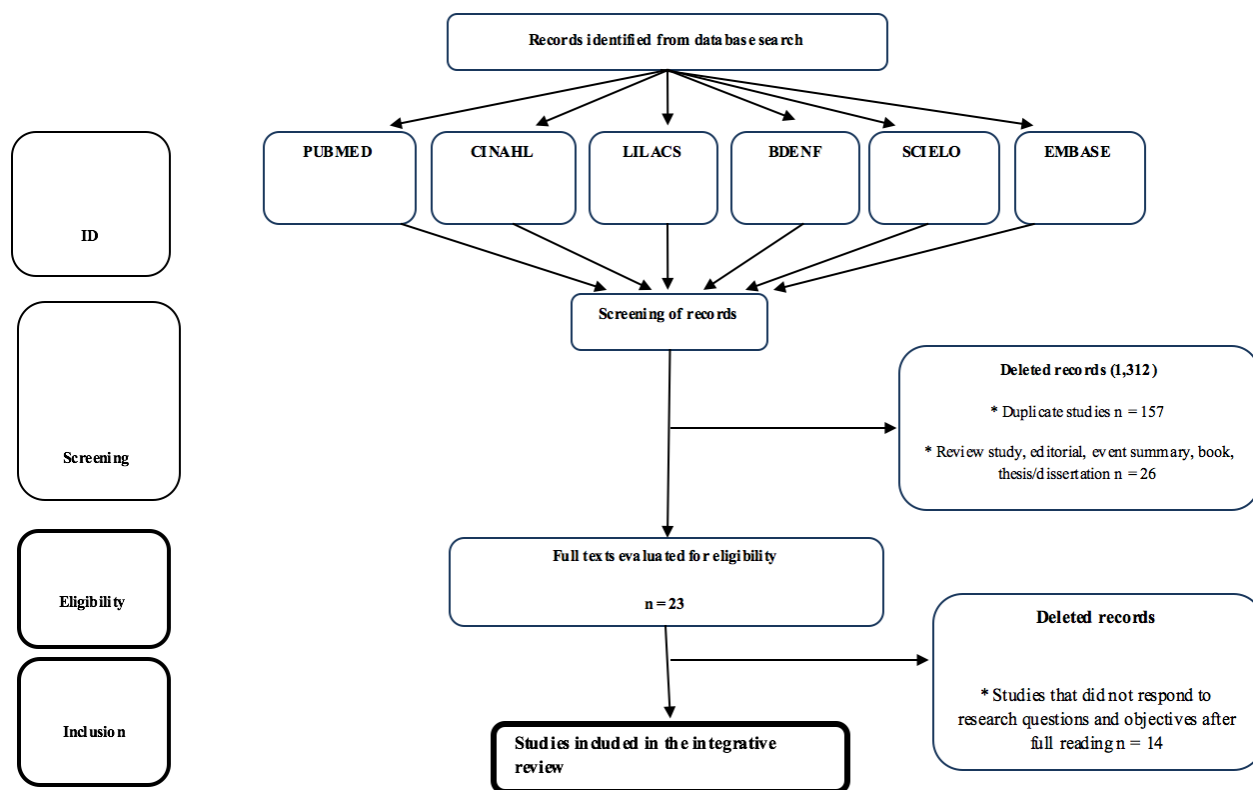
Table 1. Classification of studies.

Variables	Description
Level 1	Meta-analysis of multiple controlled studies.
Level 2	Individual study with experimental design.
Level 3	A study with a quasi-experimental design, such as a non-randomized study with a single pre-and post-test group, time series or case-control.
Level 4	Study with non-experimental design, such as descriptive correlational and qualitative research or case studies.
Level 5	Case report or data obtained systematically, of verifiable quality, or containing program evaluation data.
Level 6	Opinion of respected authorities based on clinical competence or the opinion of expert committees, including interpretations of information not based on research.

Source: Prepared by the authors.

RESULTS

1,335 articles on pertussis during childhood were identified, of which 23 were chosen for full reading and nine were selected for analysis to obtain the necessary evidence



Source: Prepared by the authors.

Figure 1. Flowchart of crossed data and search results.

to prevent this disease in this population for safe care.

In 2015 there was a linear growth in the number of articles published, with five publications (55%). Five studies were descriptive, qualitative and classified with evidence level 4 (55%). Of the nine articles, three were published in the USA

and the others in Australia, Argentina, Spain, Israel and South Korea. Regarding the authors, it is noteworthy that in 67% of the publications the epidemiologist participated. Several studies have more than one contribution to patient safety in child care, focusing on preventing whooping cough (Table 2).

Table 2. SProfile of publications about whooping cough during childhood.

	Type of study and level of evidence	Country	Specialization of the 1st author	Type of health care strategy	Epidemiological profile	Recommendations/conclusion
Skoff et al. ¹⁸ 2015	Case study N 4	United States	Epidemiologist	Prevention	1,306 cases of whooping cough in children under 1 year. Period: from January 2006 to December 2013.	Recommendations for vaccination during pregnancy should directly increase the protection of infants, regardless of the main source of infection.
Terry et al. ¹⁹ 2015	Comparative study N 4	Australia	Epidemiologist	Control	Children aged 5-11 years are the main sources of whooping cough in the environment.	Higher risk of domestic transmission among younger groups is attributed to higher susceptibility, more sensitive cases for diagnosis, low immunity.
Tiwari, Baughman and Clark ²⁰ 2015	Retrospective study N 4	United States	Epidemiologist	Prevention	The majority of deaths occurred in infants who could not initiate routine childhood vaccination at 2 months with combined diphtheria and tetanus toxoids and whole cell pertussis (wP) or acellular pertussis (aP) or vaccine with whole cell diphtheria, tetanus and pertussis (DTwP) or diphtheria-tetanus-acellular pertussis (DTaP); or who received three doses of DTwP/DTaP until 6 months.	The first dose of pertussis vaccine and antibiotic treatment protect against death, hospitalization and pneumonia.
Fernández, Armadans, Campins and Martí ²¹ 2015	Cost study N 5	Spain	Nurse	Prevention	40% of the subjects affected were infants under one year.	The high risk of whooping cough in infants requires direct action with short-term protective measures. The authors indicate that vaccination would be more appropriate for the approach than for the cocoon strategy.
Zamir, Dahan and Shoob ²² 2015	Control case N 3	Israel	Epidemiologist	Prevention and control	Incidence in Israel increased predominantly in children under one year and in children aged 5 to 14 years.	Babies at risk need special attention from professionals involved in vaccinations. Parents should be informed that pertussis vaccines protect against hospitalizations and clinical symptoms of whooping cough in their babies. The timeliness of the first dose of pertussis vaccine is especially important given the early age of infections.
Bertilone, Wallace and Selvey La ²³ 2014	Case study N 4	Australia	Epidemiologist	Prevention	Notification rates were higher in the 5-9 year age group, followed by the 0-4 year group and the 10-14 year age group.	Recent evidence suggests that prenatal vaccination would significantly reduce the risk of whooping cough in children under 3 months.
Pesco et al. ²⁴ 2013	Retrospective study N 4	Argentina	Physical-chemical researcher	Prevention	In 2012, 8,670 suspected cases of whooping cough were reported to the National Surveillance System (Sivila). Of these, 6,911 were children under 1 year.	Vaccination of pregnant women is a remarkable strategy, considering only the effect mediated by the transmission of antibodies. Immunization of 50% of mothers reduces by 43% the number of severe cases in less than 2 months.
Kwon et al. ²⁵ 2012	Observational study N 4	South Korea	Pediatrician	Promotion, prevention and control	Out of a total of 65 clinically suspected cases, 21 infants (32.3%) were enrolled in this study to be the confirmed cases of B. pertussis infection. The age range was 22 to 198 days, with an average age of 2.5 months.	Family members have been identified as a source of pertussis infection and should be encouraged to receive booster immunization with dTpa to minimize transmission to this vulnerable group of infants. The national dissemination of pertussis is also urgent to better understand its disease transmission patterns in order to recognize and prevent its outbreak earlier and to evaluate the vaccination policy. The universal recommendation for 11 to 12 year pertussis booster vaccination is expected to decrease pertussis transmission in households in South Korea. Surveillance of the whooping cough outbreak should be continuous to control this disease.
Bigard et al. ²⁶ 2005	Control case N 4 N 3	United States	Epidemiologist	Prevention: assessing the effectiveness of the vaccine	Children from 6 to 59 months.	Any combination of three or more doses of DTP/dTpa vaccine for children aged 6 to 59 months protects against whooping cough.

Legend: N = level of evidence.

DISCUSSION

The production of knowledge about whooping cough during childhood pointed out a considerable number of publications on the subject. However, with respect to childhood and health care for preventing this pathology, in the aspects of promotion, prevention, control and epidemiological profile, there is a small number of publications available, representing 0.7% (9) of the 1,335 articles selected.

The publications are concentrated in international journals: 77.7% were indexed to PubMed, but at a level of evidence 4. The *Pediatric* journal stood out, with three productions (30.0%). A study corroborates our result by showing that pertussis is still a public health challenge and indicates that more studies should be carried out considering the reemergence of the disease caused by the possibility of genetic changes of *Bordetella pertussis* strains.²⁶

In 2015 there was linear growth in the number of articles published: five publications. This result corroborates previous studies regarding the reemergence of the disease, highlighting that since 2000 the notifications of the disease have been increasing (especially in 2012 to 2014), as evidenced in developed countries, which suggests several associated causes, new diagnostic methods that made it possible to identify the disease, reduction of vaccine effectiveness with absence of booster doses after five years, and improvement of the surveillance system. That is, causes that may have collaborated to increase the reporting of cases. In Brazil, despite the increase in the number of cases, there are no studies indexed in journals discussing this situation.²⁷

In the analysis of the articles, two thematic categories were established: prevention was used for categorization in studies that presented the practices of health care and caring against pertussis in the prevention of the disease; the topic promotion and control presented publications that integrated the actions of promotion and control of the disease. The publications that presented the epidemiology of the disease were categorized with the topic epidemiological profile, addressing the age group with the highest incidence.

In the prevention category some articles reported the importance of the vaccination schedule for children with the first dose and booster during their 11 to 12 years, as well as the cocoon strategy (vaccination of all family members) and prenatal vaccination as protective measures against whooping cough.^{12,18-24}

Other studies corroborate these data by presenting the prevention strategies: the complete vaccination schedule during childhood, with three doses and two boosters, avoiding delays; vaccination at the 20th week of gestation as a protective factor of the baby, from birth until receiving its first dose of vaccine; the cocoon strategy to prevent the transmission of the disease by family members living in the house where the baby will live. These studies also consider the possibility of booster doses at 10 to 12 years, since at this stage the protection of the vaccine no longer exists in the child. In addition,

they point out the need to extend the vaccine to health professionals who have contact with children under one year. Therefore, these measures were considered protective and have shown good results in preventing whooping cough during childhood.^{8,28-33}

The promotion and control category presented antibiotic treatment in reducing mortality, hospitalizations and complications, the urgent need to disclose information to parents and the entire community about the patterns of transmission of the disease for early prevention, identifying the vaccine as the main strategy, highlighted the risk of home transmission among the group with low immunity and therefore more susceptible, and surveillance continues to control outbreaks.^{18,21,24}

Studies have shown that the antibiotic helps to control the disease, particularly avoiding the spread of the micro-organism in the household, and blocking via chemoprophylaxis is necessary for the control between the communicating participants, and they emphasize the importance of strategies to extend the control of pertussis with a booster vaccination at the possibility of replacing the dT vaccine (diphtheria and tetanus) for dTpa (diphtheria, tetanus and pertussis), which are measures related to epidemiological surveillance, as well as information about the mechanisms of transmission and early symptoms detection of the disease.^{8,26,28,34-36}

In the epidemiological profile category, 88.88% of the articles presented a higher incidence of illness and deaths via pertussis in children under one year, followed by children aged 5 to 14 years who presented as main sources of pertussis the environment in which they were reported.¹⁸⁻²⁵ These results corroborate studies that show the age group of children under 1 year as the most vulnerable to pertussis, as well as their higher risk of mortality, based on the assumption that their vaccination schedule is incomplete.^{9,12,30,37}

Other studies state that the vaccine does not protect permanently and that after five to ten years the protection no longer exists, making adolescents vulnerable to pertussis.^{7,28}

Thus, it can be stated that the publications indicate actions of promotion, prevention and control, and describe the epidemiological profile of pertussis, collaborating to implement strategies for controlling this condition.

CONCLUSION

This study presented the scientific evidence on pertussis during childhood necessary for prevention, control, promotion of care and defining the epidemiological profile of the disease in this population.

Available studies have shown that prenatal vaccination of family members can significantly reduce the risk of pertussis in children under three months, and indicate the need for a booster dose at 11 or 12 years.

However, the available evidence on pertussis during childhood regarding the promotion of care, prevention, control and epidemiological profile revealed an evidence level of five, suggesting that the research developed in

the field does not portray strong evidence.

However, the need to expand research on the topic is stressed, and we propose to implement strategies to control pertussis once the disease is reemerging.

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AUTHORS' CONTRIBUTIONS

Caroline Suemi Ogusuku conducted the strategies, data calculation, initial selection and formatting of the database.

Gabriela Correa Carvalho and Rafaela Aparecida Prata contributed to data analysis and selection of articles to be included.

Paula Fernandes Chadi and Ione Corrêa contributed, respectively, with co-orientation and guidance in the study as well as planning and design of the article, review and final approval.

All authors have approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.