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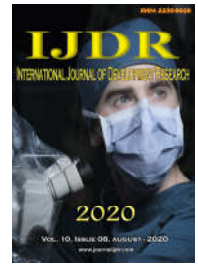
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PULMONARY AFFECTIONS ARISING FROM PREMATURE BIRTH: AN INTEGRATIVE REVIEW

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ABSTRACT

Introduction: Due to the increase in the number of premature births in recent years, there has been an increase in the occurrence of pathologies secondary to prematurity: a greater number of complications and disorders related to the development of systems, including the respiratory system. **Objective:** To identify, analyze, the most frequent respiratory disorders in children from premature births. **Methodology:** It is an integrative literature review, whose objective is to identify, analyze and synthesize results of studies in order to analyze and present, in an orderly manner, what is in the scientific publication about the relationship between pre-mature birth and the development of respiratory problems. **Results and Discussion:** Premature birth can cause several complications in the respiratory system, of which, impaired lung growth, development of less calibrated airways, and consequently, bronchiolitis, Transient Acute Respiratory Syndrome, Chronic Pulmonary Disease and Asthma stand out. **Conclusion:** It is suggested that, in addition to prematurity, variables related to the mother may be related to the development of problems in the child's respiratory system, making further studies on the subject necessary to better clarify the problem.

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INTRODUCTION

Responsible for causing approximately 40% of pediatric hospitalizations in Brazil, acute respiratory infections represent about 60% of the reasons for consultations with health services in several countries. Several factors can aggravate respiratory diseases and contribute to the increase in hospitalization rates. Among which are; low birth weight, malnutrition, lack of immunizations and social conditions (Mello, 2004). Due to the increase in the number of premature births in recent years, there has been an increase in the occurrence of pathologies

secondary to prematurity: a greater number of complications and disorders related to the development of systems, including the respiratory system (Morata-alba et al, 2019). The World Health Organization estimates despite several advances in prenatal care, that approximately 30 million babies are born prematurely, with low weight or become ill in the first weeks of life, per year in the world (WHO, 2018). The data obtained from the Born in Brazil survey, which consists of a national survey on childbirth and birth released in 2016, at the National School of Public Health (Ensp / Fiocruz), revealed that the Brazilian prematurity rate is around 11, 5% being almost

double that observed in Europe, with approximately 74% of cases, late preterm infants born between 34 to 36 gestational weeks (FIOCRUZ, 2016). Babies born extremely premature or with low birth weight have a tendency to present high rates of neonatal respiratory diseases, such as respiratory distress syndrome and bronchopulmonary dysplasia (Costeloe et al, 2012). Some studies suggest that these children are at increased risk for developing some type of chronic respiratory obstruction, in addition, premature birth associated with small size for gestational age increases the risk of developing childhood asthma (Van Der Gugten et al, 2011; Rasmussen et al, 2012; Hogg, 2004). Thus, this study aimed to identify, analyze, the most frequent respiratory disorders in children from premature births.

METHODOLOGY

It is an integrative literature review, whose objective is to identify, analyze and synthesize results of studies in order to analyze and present, in an orderly manner, what is in the scientific publication about the relationship between premature birth and the development of respiratory problems. This type of review aims to synthesize results obtained from research on a topic. It is called integrative, because it presents a wide amount of information about the subject/problem. In this way, it is possible to carry out an integrative review with different objectives, which can be focused on the definition of concepts, review of theories or analysis of study methods. (Ercole et al, 2014), which is the reason why we chose to choose this method (Marconi; Lakatos, 2018). It was decided to follow this sequence of procedures: 1-Definition of the guiding question; 2-Definition of the characteristics of the sample surveys; 3-Selection of the researches that comprised the review sample; 4-Analysis of the findings of the articles included in the review; 5-Interpretation of results and 6-Critical examination of the findings (Galvão; Pereira, 2015).

To guide this study, the guiding question was established: "How does preterm birth influence the appearance of conditions in the respiratory system in children?" The survey of articles was carried out from May to June 2020, through online access to the Virtual Health Library (VHL) website, where the investigation of articles is done in a wide way, using the database contained therein, namely: Latin American and Caribbean Literature in Health Sciences (LILACS), Digital Library Scientific Electronic Library Online (SciELO), and Medical Literature Analysis and Retrieval System Online (MEDLINE), among others, using the descriptors of the Descriptors in Health Sciences (DeCS) of the Virtual Health Library researched in the Portuguese language: "prematurity", "pneumopathies", and with the Boolean connective AND to associate them when crossing the keywords, it was also used, as inclusion criteria, articles published from 2010 to 2020. Initially, 195 references were found, filters for the main subject "pneumopathies + premature newborn + diseases of the premature" were used and only full texts were used. The number of 51 references reached. Subsequently, studies of the type "Economic evaluation in Health + Clinical practice guide" were excluded, thus resulting in 27 works that were read in full to compose the final sample to be analyzed. Of these, incomplete articles were excluded, which did not fit the type of study intended and were unavailable, totaling 15 articles as a sample to be analyzed, according to the flowchart in Figure 1.

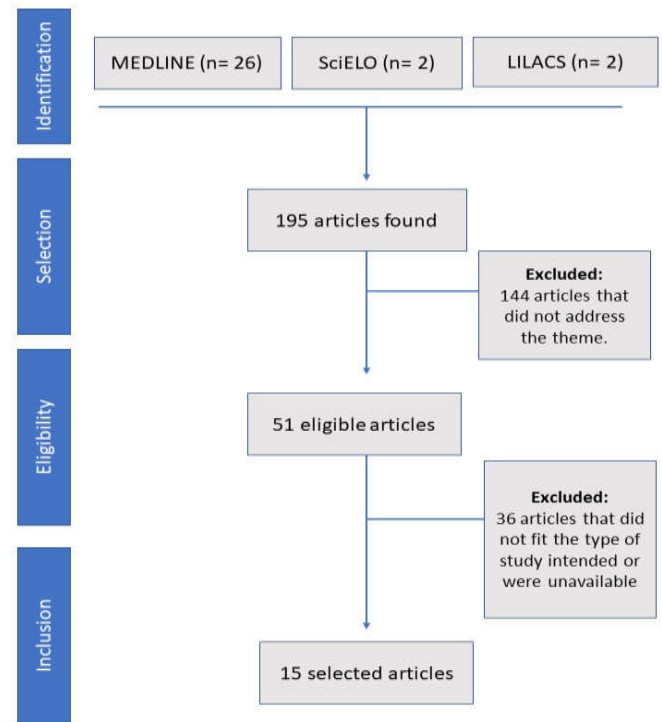


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Figure 1. Flowchart of the work selection process for review. Recife-PE, 2020

RESULTS AND DISCUSSION

Of the 15 studies selected for the sample, 5 (33.3%) were carried out in the United States of America (studies C, H, I, L and N), 2 (13.3%) in England (studies M and O), 2 (13.3%) in the Netherlands (studies B and G), 1 (6.6%) in Spain (study A), 1 (6.6%) in Canada (study D), 1 (6.6%) in Cuba (study E), 1 (6.6%) in Greece (study F), 1 (6.6%) in Brazil (study J) and 1 (6.6%) in Puerto Rico (study K). Regarding the journals in which the papers were published, 3 (20.0%) were published in the American Journal of Respiratory and Critical Care Medicine (studies C, I and O), 2 (13.3%) in the American Academy of Allergy, Asthma & Immunology (studies G and K), 2 (13.3%) in the European Respiratory Journal (F and L), and the others; European Journal of Pediatrics (study A), The Lancet Respiratory Medicine (study B), Cochrane Database of Systematic Reviews (study D), Revista Cubana de Pediatría (study E), Journal of Pediatrics (study H), Public Health Notebooks (study J), BMJ (study M), and Pediatrics (Study N), each corresponding to 6.6% of the sample. Concerning the study design, 6 (40%) were cohort studies (E, H, I, J, N and O), 4 (26.6%) were randomized clinical trials (studies A, B, C and F), 3 (20%) were reviews (studies D, G and L), 1 (6.6%) case-control study (study K) and 1 (6.6%) study using secondary data (study M). In relation to the original language of the study, 13 (86.6%) were published in English, 1 (6.6%) Spanish and 1 (6.6%) Portuguese from Brazil. The works were published in the period between 2010 and 2019. The information selected for the characterization of the studies were: study title, study type, year of publication and authorship as shown in Table 1. Premature babies, born before 32 weeks of gestation, have high rates of neonatal morbidity and mortality and, therefore, was the center of most research on outcomes after premature birth (Wood, 2000). On the other hand, data on long-term health outcomes for babies born between 32 and 36 weeks of gestation are scarce.

Table 1. Identification of the articles selected for analysis. Recife-PE, 2020

N	OBJETIVE	KIND OF STUDY	LANGUAGE	YEAR	AUTHORSHIP
A	Identify risk factors for bronchiolitis and asthma in premature and full-term babies, comparing the two groups up to the age of 8 years.	Randomized Clinical Trial	English	2019	Morata-Alba et al.
B	To analyze the prevention effect of Syncytial Respiratory Virus during childhood on asthma and lung function at 6 years of age.	Randomized Clinical Trial	English	2018	Scheltema et al.
C	Test the effect of Syncytial Respiratory Virus infection on the development of atopic asthma.	Randomized Clinical Trial	English	2017	Mochizuki et al.
D	To determine the effect of bronchodilators administered as prophylaxis or as treatment for Chronic Pulmonary Disease on mortality and other complications of premature babies at risk or identified as having CPD.	Review	English	2016	Ng et al.
E	To characterize late preterm infants admitted to the neonatology service of Hospital MaternoInfantil Dr. Ángel Arturo Aballi, from 2009 to 2013.	Cohort Study	Spanish	2016	Guzmán et al.
F	Examine lung function in school-age children who were born preterm.	Randomized Clinical Trial	English	2015	Yamine et al.
G	Examine lung function in school-age children who were born preterm.	Randomized Clinical Trial	English	2015	Den Dekker et al.
H	To study the relationship between maternal asthma and the development of bronchopulmonary dysplasia (BPD).	Cohort Study	English	2015	Gage et al.
I	To investigate whether the association between preterm birth and asthma varied according to the definition of asthma used.	Cohort Study	English	2015	He et al.
J	Assess the association between ventilatory support in the neonatal period and respiratory diseases up to six years of age.	Cohort Study	Portuguese	2015	Chiuchetta et al.
K	Examine whether asthma is associated with prematurity in Puerto Rican children.	Case-Control Study	English	2013	Rosas-Salazar et al.
L	To investigate whether the severity of maternal asthma, a history of exacerbation or use of oral corticosteroids during pregnancy are associated with risk of prematurity, low birth weight or small infants for gestational age (SGA).	Review	English	2012	Namazy et al.
M	Investigate the burden of a later disease associated with moderate/late preterm birth (32-36 weeks) and full-term birth (37-38 weeks).	Research with Secondary Data	English	2012	Boyle et al.
N	To assess the association of late preterm birth with asthma severity in young children.	Cohort Study	English	2012	Goyal et al.
O	To assess the degree of respiratory morbidity and impaired function at 11 years of age in children born with PE (that is, at least 25 full weeks of gestation).	Cohort Study	English	2010	Fawk et al.

Image caption: Mechan. (Mechanism); Ign. (Ignored).

Source: Own authorship.

Moderate (32 to 33 weeks) and late (34 to 36 weeks) premature babies account for 6-7% of all births and about 75% of premature births annually in the United Kingdom (Wood, 2000). Study A was a prospective study that evaluated individuals from birth to 8 years, comparing two groups; Group I: preterm infants (Gestational Age 32 weeks + 1 day to 35 weeks + 0 days, without comorbidities) and group II: full-term babies (gestational age \geq 37 weeks). About 66 (56.9%) of preterm infants and 43 (37.1%) of term infants developed bronchiolitis and recurrent wheezing was 52 (44.8%) in premature infants versus 36 (31.0%) in infants full-term. The authors identified that the main risk factors for asthma are: older siblings, allergic father, atopic dermatitis and treatment with antibiotics in the first 3 years of life, in addition to prematurity itself (Morata-alba et al, 2019). Study B verified the relationship between infection by the syncytial virus (RSV) in premature infants and the development of asthma in children up to six years of age, when carrying out a preventive intervention (Palivizumab) against RSV infection in the studied population. Thus, the authors concluded that RSV prevention was not successful in reducing the incidence of asthma or lung function at age 6 years. It was seen that the prevention of RSV reduced only the occurrence of wheezing reported by parents, making it uncommon at 6 years old, while the risk of diagnosed asthma did not decrease (Scheltema et al, 2018).

These data corroborate with study C, in which the authors performed a prophylactic intervention with the same medication in premature infants with gestational age between 33 and 35 weeks. The incidence of atopic asthma was not significantly different in the groups: 15.3% in the treated premature babies and 18.2% in the untreated ones. However, in the same way as the previous study, recurrent wheezing, diagnosed by the doctor, was observed in 15.3% in the treated group and 31.6% in the untreated group (Mochizuki et al, 2017). Study D reviewed Chronic Lung Disease (CLD), which is defined as oxygen dependence at 28 years of age with a chest compatible on radiography, characterizing it as a lung disorder that frequently occurs in premature infants (Ng et al, 2020). Study E carried out an observational cohort of newborns with gestational age between 34 and less than 37 weeks and full-term babies with gestational age between 37 and 41 weeks. Transient acute respiratory syndrome was observed, occurring in 6% of individuals in the first group, against 9% registered in the group of full-term babies. In addition to hyaline membrane disease, which affected 7.3% of premature babies and 0.04% of those born at term. There was also a record of persistent pulmonary hypertension in the newborn, occurring in 1.8% of preterm infants and 0.7% of those born at term (Guzman et al, 2016). In study F, the authors examined the airway function of 86 school children, born between 24 and 35 weeks of gestation and 49 children born at term, using

the MBW nitrogen washing technique. The authors found that the Pulmonary Release Index (PRI), which reflects the homogeneity of global ventilation, did not differ between participants born at term and premature, no evidence of heterogeneity of ventilation dependent on diffusion at the acinar level was found, obtained by similar values of Sacin among studied groups, only 6% of premature births had elevated PRI. This data disagrees with a study that evaluated the global distribution of ventilation in schoolchildren born extremely premature, where the researchers reported that 58% of these children had a slightly elevated Pulmonary Release Clearance index (Lum et al, 2011). Such difference can be attributed to the inclusion of children born at less than 26 weeks of gestation in the study by Lum et al. However, Scond was elevated in more than half of premature births, which indicated a lack of homogeneous ventilation in the airway regions that depend on convection. More specific markers for heterogeneity of ventilation, such as Sacin and Scond, were not evaluated in the work of Lum and collaborators. In study G, the authors pointed out that early birth may be responsible for impaired lung function and childhood asthma. Spirometry measurement analyzes suggested that the Forced Expiratory Volume in the first second/Forced Vital Capacity (FEV1 / FVC) ratio greater than the Forced Expiratory Flow (FEF 75%) may explain 7% to 45% of the associations between initial growth characteristics and pulmonary function (Den Dekker et al, 2015).

Such results corroborate with other findings in the literature, from which it is possible to affirm that bad adaptations of development in intrauterine life or adverse exposures in early life, such as prematurity, can result in impaired lung growth, with less calibrated airways, decreased lung volume and, consequently, increased risk of bronchopulmonary dysplasia, asthma or chronic obstructive pulmonary disease (Canoy et al, 2007; Hancox et al, 2009; Barker et al, 1991). Previous studies suggest that asthmatic children already had their lung function reduced even in the first months of life and that this deficit progresses to childhood and adulthood (Bisgaard et al, 2012; Haland et al, 2006). In study H, Gage et al. (2015) observed, through a cohort study carried out in California, United States of America, that asthma not treated with corticosteroids during prenatal care may be related to the greater probability of premature births, regardless of whether the delivery is spontaneous or induced. Interestingly, premature babies born to untreated asthmatic mothers subsequently developed Bronchial Pulmonary Dysplasia (Gage et al, 2015). Two similar cohort studies, one conducted in Brazil (study J) and another in the United Kingdom (study M) did not show any influence on the development of asthma, or wheezing due to the mother not having been treated with corticosteroids in the prenatal period, however, it obtained similar results regarding the type of delivery variable (spontaneous or induced). In this study (study J), the main maternal variables associated with the development of respiratory problems in babies were; Low schooling, black skin color, being multiparous, under 20 years old, untreated urinary tract infection and being a smoker, similar to the maternal variables highlighted by the authors of the study O (Chiuchetta et al, 2015; Fawke et al, 2010). Through a review, the authors of study L identified that, although there are described cases in the literature of mothers who experienced exacerbations of asthma during pregnancy and had premature births, in general there was not a significant tendency to increase the incidence of preterm birth. term in asthmatics who experienced exacerbations during pregnancy

(Namazy et al, 2013; Boyle et al, 2012). Other studies, such as study I and M, also found the highest occurrence of asthma in children born prematurely, the prevalence of asthma varied in both age groups (7–43% in preterm infants; 2–25% in infants born full-term) even without the influence of other variables (HUAN HE; et al, 2015). In study K, Rosas-Salazar and collaborators obtained similar results from a Randomized Cohort, however, they add that the population of babies most affected is the male, which corroborates the findings of study J. In study O, Goyal and collaborators (2011) reported that 8.3% of a sample of 7925 children were diagnosed with asthma within 18 months of life.

CONCLUSION

Premature birth can cause several complications in the respiratory system, of which, impaired lung growth, development of less calibrated airways, and consequently, bronchiolitis, Transient Acute Respiratory Syndrome, Chronic Pulmonary Disease and Asthma stand out. Variables related to the gestation of asthmatic women who present or not exacerbations during pregnancy or who receive or not treatment with corticosteroids during this period, need to be deepened, since such events can contribute to premature birth and, later, the appearance of respiratory problems in the baby, and increasing the use of health services in the first years of life.

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