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PhD THESIS

**THE APPROACH
OF THE WHEEZING
IN
PEDIATRIC PRACTICE
OF
FAMILY DOCTOR**

ABSTRACT

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KEY WORDS

Wheezing, recurrent wheezing, bronchial asthma, tuberculosis in children.

STAGE OF KNOWLEDGE

INTRODUCTION

The literature data treats the wheezing problem disparately. Its approach sometimes as a symptom, other times as a sign, in important bibliographic resources, is pretty poor but its diagnostic significance is increasingly invoked. The wheezing has been nominated throughout time as a symptom in the asthmiform bronchitis, bronchiolitis, bronchial asthma or other rarer situations.

Present either as an isolated wheezing or accompanied by other signs and symptoms, placed either in an epidemiological context or in a context of family life conditions, or family history or the presence of specific risk factors, or of knowing the anamnesis data and especially, the context of correct identification of the meaning of the information received from the family, the wheezing can, sometimes, guide correctly the entire diagnostic approach and then the therapeutic one.

WHEEZING IN CHILDREN – GENERAL DATA

The books of medical semiology talk about the term "wheezing" as not being specific to paediatric pathology, to define "a characteristic whistling noise that is heard only from a distance and appears only in expiration" [Bruckner, 2002].

Important authors talk about the confusion of the definitions applicable to children under 6 years because many of those who will be diagnosed with asthma after preschool age have events of wheezing onset at preschool age [Stoicescu and Pleşca, 2009].

Referring to the age group under 6 years, the literature data used to issue recommendations based on evidence are very poor unfortunately. The working groups created to make recommendations took into account evidence of poor quality such as expert opinion or case reports. For this reason, the approach of wheezing in children under 6 years is in constant evolution; however, the recommendations may change from one guide to another [Brand et al, 2008]. The literature describes several wheezing phenotypes [Brand et al, 2008]

Depending on the temporal aspect, the episodic wheezing (viral) is described - the wheezing which occurs in association with episodes of viral infections suggested by the clinical appearance even with subtle signs and symptoms. The wheezing disappears when they stop. The other type is the wheezing with multiple triggers – the wheezing with discrete exacerbations even between infectious viral episodes.

Depending on duration, the transient wheezing is described – the symptoms begin before the age of 3, they can be identified even retrospectively and disappear until the age of 6. The other types are the persistent wheezing – the symptoms can be identified even retrospectively and persist over the age of 6 and the late-onset wheezing – the symptoms starting after the age of 3. These can be episodic or multiple triggers wheezing [Brand et al, 2008 Stoicescu and Pleşca, 2009].

The wheezing can be found in many illnesses in paediatric pathology. Common causes is: asthma, systemic allergic reactions, gastro-oesophageal reflux disease, respiratory infections, obstructive sleep apnea.

Rare causes can be: the aspiration of a foreign body, the bronchopulmonary dysplasia, congenital abnormalities such as laryngomalacia, cystic fibrosis and immunodeficiency syndromes, vocal cord dysfunction, benign or malignant tumor formations, produced by lymphadenopathy or of other cause [Stoicescu and Pleşca, 2009, Weiss, 2008].

Above there are the main conditions accepted as valid by specialized literature. In 2009, paediatricians reunited in Vienna for the Annual Congress of European Respiratory Society concluded that "the differential diagnosis of wheezing in children should also include a narrowing of the airways by a lymphadenopathy compression in tuberculosis" [Brand et al, 2011].

The introduction of respiratory tuberculosis among diseases that may occur with wheezing in children is not new. Various authors have talked about this possibility over the years, to bring into question the production mechanism in wheezing, as well [Daly et al 1952]. In addition to the compression mechanism, the bronchial perforation and endobronchial lesions are also cited, as other leading cause of wheezing [Lee et al., 2004].

From the epidemiological point of view, the data from the literature speaks about the fact that at least one third of children will develop an episode of wheezing in the first three years of life. This percentage reaches 50% up to 6 years old. The most common episodes for preschoolers are associated with respiratory infections and their recurrences [Brand et al, 2008]. It is estimated that the burden of diseases associated with wheezing in preschool children consumes about 0.15% of the total budget allocated to health in the UK [Stevens et al, 2003].

American authors talk about the fact that 25-30% of infants will develop an episode of wheezing. The percentage rises to 40% in children who turn 3 years old and 50% for those who have reached six years. [Weiss, 2008]

In a study conducted in Arizona, (Tucson Study) it was proved that only 51.5% of children aged 6 years did not show any episode of wheezing. 19.9% experienced at least one episode of lower respiratory tract affection, manifested with wheezing up to 3 years but have never experienced an episode of wheezing again by the age of 6 years. 15% did not show any episode of wheezing up to 3 years but had at least one episode by the age of 6 years and 13.7% had wheezing both before 3 years and after 3 years of age [Martinez et al, 1995].

WHEEZING IN CHILDREN. FUNDAMENTAL ELEMENTS OF DIAGNOSIS

For diagnosis, in a first stage it is necessary to evaluate the child from a clinical perspective. Depending on the way of the onset, sudden or insidious, associated signs and symptoms (fever, stridor, signs of acute respiratory failure such as beatings of nasal wings or retraction of intercostal muscles, changes in the nature of wheezing depending on the position, presence of cyanosis, suffocation, coughing with or without expectoration, the presence of subcrepitant, crepitant or sibilant rales, abnormal heart sounds, etc.) the clinician guides the immediate intervention to investigate the cause, usually after taking first aid measures where they are required.

Bronchial asthma. The diagnosis of asthma is very difficult especially in children under 5 years and the diagnostic criteria change each year.

Risk factors – they may play a role in favoring the occurrence of both asthma and crisis. We can list: infections – the respiratory syncytial virus is most commonly involved, bacteria are rarely involved, smoking - the risk of asthma in infants with smoking mothers is 4 times greater, diet – the protective role of breastfeeding is well known. But there are also some risk factors that are considered predisposing factors for developing asthma, in the category of food (tartrazine, peanuts), some drugs (aspirin, other nonsteroidal antiinflammatory drugs), physical exercise, air pollution and microclimate pollution, socio-economic status, a family history of atopy [GAMA, 2008].

The diagnosis of asthma in children is difficult. The main diagnostic criteria relate to the clinical aspect - paroxysmal wheezing dyspnea, atopic field - allergic rhinitis, atopic dermatitis, digestive food allergies, atopic manifestations in the family, functional criteria - reversible bronchial obstruction or therapeutic - effective response to short term treatment with bronchodilators and inhaled corticosteroids [GAMA, 2008].

Moreover, all the GINA guidelines and other papers approach this issue in the diagnosis of asthma in preschool children and asthma diagnosis in children over 5 years. The Romanian Guide for Asthma Management treats the asthma diagnosis for children aged more than five years the same as an adult bronchial asthma diagnosis. This is precisely due to the different possibilities to show the reversibility of bronchial obstruction which can be done only by therapeutic test in children under five years while for children over 5 years all technical means available for adults can be used. For this reason, for a long time it was preferred not to use the diagnosis of asthma in this age group [Bogdan et al, 2008].

Tuberculosis. In case of children with wheezing who come from a family where a case of tuberculosis evolves, it is necessary to exclude the diagnosis of tuberculosis. The suspicion is raised when there is epidemiological context and other clinical signs.

The following diagnostic algorithm is typically used: Epidemiological background / source, Suggestive clinical frame, IDR at PPD, Radiological frame, Laboratory exams (bacteriological diagnosis of TB) [Marica and Didilescu, 2011]

For a symptomatic child, the epidemiological criterion (the contact with a bacilifer case or chronic coughing) plays a very important role in diagnosing tuberculosis [Stoicescu and Crisan, 2006].

PERSONAL RESEARCH

MATERIAL AND METHODS

The initial group of study consisted of 1204 children born between 01.01.1997 - 30.06.2014 which have been registered in two medical offices in Sadova village between 2008-2015. From this initial group, using the presence of wheezing as criteria for case selection, two groups were set up in a first stage: **The main lot**, called "**Case lot**", which included children who presented at least one episode of wheezing in their lifetime and **The control lot** called "**Witness lot**" that included children who did not have any episode of wheezing in their lifetime.

The materials were obtained from two different data sources: (a) the records of primary care for the patients in the study and (b) the evaluation form of the living conditions from the social inquiry completed by the Local Council Sadova.

The inclusion criteria for the Case Group were: patients of paediatric age born between 01.01.1997 - 30.06.2014, subscribed to two GP surgeries in Sadova village and their records in the range 2008-2015; patients who were submitted to consultation with a manifestation of wheezing in the range 2008-2015; patients who had at least one episode of wheezing in their antecedents. As inclusion criteria for the Witness Group, we used patients of paediatric age registered in the two offices who did not show any episode of wheezing.

The criteria of exclusion were related to patients who have fulfilled at least one of the following criteria: patients consulted in the cabinet with or without wheezing who are not registered in the two offices; patients of paediatric age registered at a

certain moment, but born outside the selected range; patients who were initially recorded in the offices during the research but were transferred to other offices making it impossible to be followed.

This study type was "**Case - Control**" and had two components: **The retrospective** component that included patients of paediatric age who suffered at least one episode of wheezing until 2008 and **The prospective** component that included patients of paediatric age who experienced at least once a wheezing episode in the two offices between 2008-2015.

The data from the study group were selected and organized into two sets of parameters. They were stored into the computer as "Database" files.

The two sets of parameters analyzed were the following: epidemiological parameters (ethnicity, family status at birth, the mother's educational level, the family's social level, exposure of the pregnant woman to risk factors such as active smoking or passive smoking, exposure of the infant to risk factors focusing on tobacco smoke, the child's diet during the first 6 months of life, clinical parameters, maternal age at birth, sex of the patient, patient's age, excess weight, age at the time of confirmation of the diagnosis, specific family history, number of respiratory episodes in the last 6 months before confirmation of the diagnosis by physicians from other medical specialties, comorbidities relevant to the diagnosis, symptoms associated with wheezing onset) and specific parameters (duration of wheezing, the temporal aspect of wheezing).

THE STUDY OF THE GENERAL CLINICAL CONTEXT

The distribution of cases with wheezing in groups according to diagnosis is the following: asthma 69 cases (9.76% case group - total 5.73%), TB with wheezing onset 3 cases (0.4% -0.24%) , 59 cases of systemic allergic reactions (7.9% - 4.9%), obstructive sleep apnea 6 cases (0.8% - 0.49%), respiratory infections with wheezing 604 cases (81, 07% - 50 16%), GERD 4 cases (0.53% - 0.3%).

The prevalence of asthma in the study groups is 5.73%. According to statistics we see that the percentage is lower than 8%, considered as being the maximum figure by some authors. Actually, expert literature estimates a prevalence between 1 and 8%, the range being quite wide [GAMA, 2008]. 61.8% of children in the research experienced at least one episode of wheezing.

All of the children are registered on the lists of two family physicians in Sadova; 95% of them coming from this village. This aspect offers several features to the group, that customizes it as rural population, predominantly agricultural area, increased number of population who benefit from the minimum guaranteed income; low educational level, homogeneous exposure to the same environmental factors and cultural influences, the absence of air pollution among possible risk factors, increased accessibility to the pneumologist physician, epidemiological context for tuberculosis, constant health services through Sadova Permanence Center, the professional conduct of two doctors involved in the research is relatively similar.

With reference to the age groups used in specialized literature as classical age limits for defining the periods of childhood, I have found that the period in which wheezing is mainly manifested regardless of the cause is the age group 1-3 years, that is the toddler age (antepreschooler) (358 cases) and most children diagnosed with asthma are found before 3 years of age (72.4%).

With reference to the age groups used in literature as threshold values for evaluating wheezing, I have found that it manifested itself as first symptom before the

age of 3, in nearly half of the children who developed wheezing during their childhood. Considering all the studied patients, the results are that up to 3 years of age, 30.31% developed wheezing. By the age of 6 years, 51.4% had at least one episode of wheezing and up to 18 years 61.86 % developed wheezing.

The gender distribution was analyzed in the batches and groups studied. In our study, the data is not statistically significant.

Comparing the gender distribution I have found that male patients are progressively more affected in the case group. The most affected patients were the ones who experienced wheezing within asthma manifestations.

There are studies that highlight ethnic differences as a result of the environment, lifestyles and economic characteristics [von Mutius, Hartert, 2013]. Our group shows the feature of origin from the same rural environment but with cultural and especially behavioural influences.

The distribution by ethnicity of patients included in the study group shows a predominant distribution of the majority ethnic group, the ratio being close to 2/1.

I have found that in the group of children with respiratory infections, those born from the ethnic majority seem to have a higher risk of developing isolated wheezing in childhood compared to Roma children therefore Roma ethnicity can be considered a protective factor because the difference is statistically significant - OR = 0.7478; (95% CI 0.5809 - 0.9627); $p = 0.0241$ (<0.05).

The data obtained show that there is no predisposition regarding asthma based on ethnic considerations but if a Roma child has wheezing, it is less likely to be only an isolated wheezing.

Analyzing the incidence according to the environment, we note that the distribution is approximately equal comparing the case group vs the control group, with a slight shift in the share increase in the urban area for the wheezing group and it can not be considered a risk factor because the difference is not statistically significant.

Analyzing the mother's age at childbirth, we observed that for children born from mothers aged over 30 years at birth, the parameter could be considered a protective factor for the occurrence of wheezing in children but it is not statistically significant.

The youngest age of a mother whose child has developed wheezing is 13 years and the oldest age of a mother whose child has developed wheezing is 42 years, both extremes recruited from the group of patients diagnosed with respiratory infections. The average age of occurrence of wheezing is comparable and very similar in the 3 groups.

The statistical analysis shows that the academic education level of the mother can be considered a risk factor for the occurrence of wheezing that is statistically significant - OR = 1.9467; (95% CI 1.0043 - 3.7732); $p = 0.0449$ (<0.05). For the group with asthma, the parameter can be considered a risk factor because it is highly statistically significant - OR = 6.313559; (95% CI 2.6134 - 15.2525); Z score = 4,095; $\chi^2 = 21.1952$; $p = 0.000004$ (<0.01). In the case of asthma even the high school level can be considered a risk factor for asthma that is statistically significant - OR = 2.034954; (95% CI 1.0365 - 3.9954); Z score = 2.064; $\chi^2 = 4.4054$; $p = 0.035824$ (<0.05). But if we consider that mothers with academic education have also a high school education level, the results of the statistical analysis show that the parameter that takes into account all mothers who graduate high school, can be considered a risk factor for asthma which is highly statistically significant - OR = 3.3898; (95% CI 1.9164 - 5.996); $p = 0.000012$ (<0.01).

During my research I issued several work hypotheses to justify this association:

- The hypothesis of the association with another risk factor, significant or insignificant for this population;
- The hypothesis of the easier access to medical services, the result being thus represented by an over-diagnosis;
- The hypothesis of some behavioural influences during pregnancy and growth.

The socioeconomic level is one of the risk factors for the development of atopy (GINA, 2015) in the sense that a low socioeconomic level is a risk factor. A good socio-economic level can be a risk factor for developing wheezing - OR = 1.5496; (95% CI 1.1064 - 2.1704); $p = 0.0108$ (<0.05), asthma - OR = 2.93; (95% CI 1.6275 - 5.3012); $p = 0.000213$ (<0.01) and for isolated wheezing - OR = 1.43; (95% CI 1.0171 - 2.0294); $p = 0.0397$ (<0.05)

The share analysis of the two extremes reveals that both the low level and especially the good socioeconomic level is more frequent in the group of children who developed asthma. However, a statistical significance presents, surprisingly, the good socioeconomic level but not in the sense that it should be a protective factor but on the contrary.

We can cite the "hygiene hypothesis" to support these data, which suggests that keeping as poor hygiene as possible leads to a reduced risk of developing allergic diseases, asthma included [GAMA 2008].

I found no percentage differences between the case group and the control group regarding the family status at childbirth . The legal status of the family cannot be considered a risk factor.

The infant exposure to passive smoking both during pregnancy and infancy is one of the auxiliary risk factors [Bogdan et al, 2008].

The prenatal maternal exposure to tobacco smoke is associated with disorders in the lung development of the fetus [GAMA, 2008]. I found that exposing the pregnant woman to both active and passive smoking is not a statistically significant risk factor for the wheezing group and isolated wheezing but for the group of children with asthma it is a highly statistically significant risk factor - OR = 2.7; (95% CI 1.5985 - 4.5714); $p = 0.000138$ (<0.01).

When conducting consultations at home, many times I found the existence of smoke or just tobacco smell. During the study, we tried to evaluate the impact of infant exposure to tobacco smoke.

The correlation of the two parameters (exposure of pregnant women to smoking and exposing the infant to tobacco smoke in infancy) shows that in the group of children with asthma, from 69 cases, 42 children were exposed to passive smoking in the first year of life and all of them plus two others were exposed to passive or active smoking of the pregnant woman in prenatal stage. Therefore, we will not consider this risk factor.

One of protective factors for the development of atopy is the exclusive natural diet in the first 6 months of life. The World Health Organization states that the protective effect of exclusive nutrition is highlighted in infants who are fed exclusively during the first 3 months of life [WHO, 2014].

Our data confirm the literature data but they are not statistically significant due to the small number of children who are artificially fed in the first year of life both in the control group (23- 8.7%) and in the case group (6-5%).

We found an equal distribution in the share of wheezing and isolated wheezing cases compared to the control group, examining children who have a positive family history and it cannot be considered a risk factor, because the result was not statistically significant. But they have a higher risk of developing asthma OR 4.14; (95% CI 2.1954 - 7.8337); $p = 0.000003$ (<0.01).

Regarding asthma, our data are correlated with literature data establishing an easily identifiable risk by during the anamnesis.

During the research I have identified comorbidities that specialized literature cites as associated with atopy in general and with asthma in particular. These were the following: rhinitis, allergic conjunctivitis, atopic dermatitis, urticaria.

The statistical analysis reveals the fact that the association with other atopic diseases can be considered a risk factor for the wheezing manifestation which is highly statistically significant - OR = 2.2415; (95% CI 1.7339 - 2.8976); $p = 0.000..1$ (<0.01), for asthma - OR = 10.89474; (95% CI 5.9198 - 20.0507); $p = 0.00000..1$ (<0.01) and for the manifestation of isolated wheezing - OR = 2.76; (95% CI 2.1431 - 3.575); $p = 0.0001$ (<0.01).

Overweight is a risk factor assumed by literature. In our study the data is not statistically significant.

The lack of statistical significance is possible because of the small number of overweight children compared to the entire researched group or control group. Only 15.25% of the children in the control group show weight excess.

THE STUDY OF THE GROUP OF PATIENTS WITH ASTHMA

For the group of patients with bronchial asthma a separate analysis of some clinic and specific epidemiological parameters was required and, especially, an analysis of the correlations between various parameters that may be significant for the medical practice.

Assessing the number of respiratory episodes before confirming the diagnosis of asthma, we found that 21.74% of the children had 3 suggestive respiratory episodes prior to the confirmation of the diagnosis, 31.88% between 4-6 episodes and 46.38% more than 6 episodes. As we have no reference parameter for the control group, it can not be measured statistically.

Analyzing the symptoms associated with the wheezing onset, we found that the clinical picture was dominated by the triad: fever, cough, dyspnoea. Only 17 cases representing 24.7% had only dry cough associated to the wheezing, 1 case (1.44%) only presented dyspnoea and wheezing, 6 cases (8.7%) associated wheezing, coughing, dyspnoea and 45 cases (65 , 21%) associated coughing, dyspnoea, and fever to wheezing. The cough was associated to wheezing in 98.55% of cases, dyspnoea in 75.36% and fever in 65.21% .

Literature cites among the symptoms that constitute a warning the particular aspect in which wheezing is manifested, coughing, difficulties in breathing, limitation in activities and nocturnal predominance to which the frequency criterion was added. [GINA, 2015].

In our research we considered the fever as well because for children less than 5 years, suggestive asthma symptoms start especially in infectious context [GINA, 2015]. Moreover, the fever was encountered in our group especially at this age group, 40 out of 45 cases with fever, (88.8%) met the symptom before the age of 6 years. Only 5 children (11.2%) older than 6 years who experienced the fever onset have been diagnosed with asthma.

Nothing in our research leads to data which could guide us to asthma only focused on the symptoms, as early as possible. We can suspect or not that a child with wheezing has a debut of asthma according to these symptoms and the association with other elements that sustain the diagnosis.

In our approach we tried to classify wheezing in phenotypes using the current recommendations. Thus, classifications in the wheezing phenotype according to duration is a difficult step that is not recommended in current practice but which has value in research and can be used to analyze population cohorts. However, a classification according to the temporal aspect of wheezing may have clinical importance. [Brand et al, 2008].

The distribution of cases diagnosed with asthma according to the duration of wheezing shows that more than half of patients (53.62%) were enrolled in the "transitory" phenotype, 39,13% in the "late-onset" phenotype and 7.24% in the "persistent" phenotype.

The classification of the asthma phenotype according to the temporal aspect of wheezing in children diagnosed with asthma reveals that more than a half (59.03%) were enrolled in the phenotype "wheezing with multiple triggers." A number of 28 (40,57%) patients could be included in the "episodic (viral)" phenotype, presenting as a characteristic the occurrence of exacerbations in the context of viral infections and mainly during cold seasons.

THE STUDY OF THE GROUP OF PATIENTS WITH PULMONARY TUBERCULOSIS

During the research I met a number of 4 patients diagnosed with ganglionic pulmonary tuberculosis, associated or not with pleuresy. In the study we included 3 children in the group of patients with tuberculosis and one in the control group, considering that he showed no wheezing.

At the beginning of the chapter the clinical characteristics of the four cases included in the study are described. One clinical case belongs to the asthma group and presents wheezing in infancy associated with close contact with the father suffering from tuberculosis, positive, in the first 3 months of age and three cases of pulmonary tuberculosis associated with wheezing.

The analysis reveals that three out of the four patients with tuberculosis had wheezing as a manifestation in the clinical picture and 3 cases were women.

The distribution by sex of TB patients included in the study group shows predominance of female gender, all 3 TB cases with wheezing were in the age group 1-3 years. Also, 2 out of 3 patients come from Roma population, all 3 children came from disorganized, non-legally constituted families, with a primary level of educational for the mother (2 cases) or at most secondary (1 case), with low socioeconomic level (3 cases). All 3 children with tuberculosis and wheezing had close contact with sick family members. The manner of onset for tuberculosis in terms of wheezing - associated symptoms did not present a specific pattern. The dry cough was the common element together with wheezing.

The baby spends more time with the parents or other family members, thus creating the conditions for a persistent contact with bacilifer sources. These data correlate with the higher provenance of rural children who have been diagnosed, the characteristics of rural housing with a smaller air volume than those in urban areas favoring the development of the disease. [Bulucea 2006]

Tuberculosis in children is well known to indicate the presence of a source of infection among contacts in the family and also at school [Bulucea et al, 2006]. As a result, in an area with a high TB incidence, the family doctor must provide special attention to children who develop suggestive symptoms, including the wheezing which may be induced by tuberculosis.

The cases presented have evolved during the periods of maximum incidence in Sadova. Case no.1, in 2009 (the incidence of TB in Sadova = 223.5‰000), case no.2 in 2007 (incidence of TB in Sadova = 236.3‰000), case no. 3 in 2006 (incidence of TB in Sadova = 247‰000). Also, the case with tuberculosis in children without wheezing was notified in 2008.

Note that 2006, 2007, 2008, 2009 are the years in which the number of new cases in the researched area had reached the highest value in the last 10 years. These came from families where there was a source case in intimate contact, in 2 of the above situations, patients presenting low compliance to treatment.

It is important that Romania is a country that constantly occupied first place in the European Union regarding tuberculosis [Bobarnac 2013].

Special attention will be distributed to children who first come from countries where BCG vaccination is optional, targeting only the groups at risk. BCG vaccination is a method of prevention for tuberculosis.

FINAL COMMENTS ON THE RESULTS

In my approach I focused on classifying and measuring the risk factors that can be attributed to the paediatric case with wheezing, setting the significance of some of them within the group of children diagnosed with asthma and highlighting the situation of the child with tuberculosis, a rare but extremely important situation.

Analyzing the impact of these risk factors on the whole wheezing group, we notice that only one of these correlates highly significantly from a statistical point of view, namely the association with other atopic comorbidities, and one significantly - the socio-economic level. I have identified the risk factors that are significantly correlated from a statistical point of view with bronchial asthma: Relevant comorbidities for the diagnosis, The mother's educational level - higher education, Specific family history, The family's social level – good, Exposure of the pregnant woman to active or passive smoking, Exposure of the infant to tobacco smoke

Analyzing the impact of these risk factors on the isolated wheezing group, we notice that only one of these correlates highly significantly from a statistical point of view, namely the association with other atopic comorbidities and two other statistically significant factors – the social level of the family - good and ethnicity.

As **prospects for future research** I have identified the following aspects:

- Evaluation in the future, through prospective cohort studies, the influence of these risk factors considered significant
- • To prove the hypothesis issued in this thesis about the factors that determine the risk in children born from mothers with higher education and those who come from families with good socio-economic level regarding the late contact with allergens.
- • The research will continue, to identify and then evaluate the interventions proposed in the case of parents with higher education and good socioeconomic level so that children born in such families should be less likely to develop atopy;
- • Studies in the local community on factors which prevent the adherence to bronchodilator treatment
- • Identification of the most suitable solutions for monitoring the proper administration of bronchodilator treatment;
- • The appropriate implementation and measurement of the most suitable tool for monitoring children with asthma;
- • Development of guidelines for wheezing management in children.

CONCLUSIONS

- For a child with wheezing, the presence in the personal history of relevant comorbidities for bronchial asthma (allergic rhinitis, allergic conjunctivitis, atopic dermatitis, urticaria) represents one of the most relevant guiding indicators and the one with the highest degree of probability;
- The presence of atopic diseases in the family history is a highly significant risk factor for the manifestation of wheezing in general, particularly in the group of children with a diagnosis of asthma;
- The provenance of the child from a family with low socio-economic level subjectively stated as "good" by the family is a risk factor for developing asthma;
- The academic and post-secondary levels in the mother's education correlates highly significantly with the risk of asthma and the high school education level correlates statistically significantly in a population where the vast majority of mothers are at most lower secondary education graduates;
- The prenatal exposure of the child to tobacco smoke is a highly significant risk factor for asthma that also has the ability to be modifiable;
- In the study groups a repeating behavior of parents regarding the infant's exposure to tobacco smoke was highlighted;
- No difference between the manifestation of asthma in Roma population compared to the ethnic majority was determined;
- The presence of wheezing associated to a respiratory infection is more frequent in Romanian ethnicity rather than in the Roma ethnic group;
- In a locality or region with a high incidence of tuberculosis, for a child who manifests wheezing, in close contact with a patient with tuberculosis it is very important to exclude the bacillary cause first. The younger the child is, the more important this aspect becomes ;
- For children born in EU countries who have not been vaccinated BCG, it is important to be recovered as soon as possible to prevent severe forms of tuberculosis such as miliary and tubercular meningitis;
- In the case of a child with wheezing, the provenance from an area with good socio-economic level and advanced studies of the mother pleads for asthma, while the origin of a child in families with low socio-economic level, non-legal families and suggestive epidemiological context obliges the GP to exclude tuberculosis;
- In the study group I have found differences compared to specialized literature due to the peculiarities of the group. For a family physician, especially in rural areas, it is important to know the characteristics of the population group looked after, to make the best diagnostic decision..

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