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RESEARCH ARTICLE

Evaluation of Risk Factors, Etiology, Diagnosis, and Auxiliary Diagnostic Methods of Children With Recurrent Wheezing Between 1-24 Months

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ABSTRACT

Objective: Wheezing should be evaluated separately from recurrent lower respiratory tract infections in terms of both etiology and risk factors. Early initiation of etiologic studies and good identification of risk factors are important in terms of the prognosis of the disease.

Methods: In this study, children between the ages of 1-24 months who had at least three recurrent wheezing attacks or who had wheezing lasting more than 1 month were examined. Cases who received a specific diagnosis for recurrent wheezing or were followed up as one of the wheezing phenotypes were compared. Between 2010 and 2012, the files of children between 1 and 24 months who had at least three recurrent wheezing attacks or who had wheezing lasting more than 1 month were examined at the Istanbul Medeniyet University Göztepe Training and Research Hospital. A total of 970 files were scanned and 76 cases were included in the study. The cases were examined by file scan and families were called by phone for incomplete information. History, socioeconomic/demographic characteristics, physical examination findings, laboratory and imaging results, and etiological causes were retrospectively recorded.

Results: In 76 cases with repeated wheezing in this study; early transient wheezing was 16% (n=12), persistent atopic wheezing was 21% (n=16), non-atopic wheezing was 25 % (n=19), and specific diagnosed cases were 38% (n=29). When all cases were taken into consideration, an echocardiogram was performed in 79% of cases, thoracic CT in 26% of cases, videofluoroscopy in 5%, and esophagus-stomach-duodenum X-ray in 25% of cases, pHmeter in 34% and bronchoscopy in 8% of cases. In the group of 29 people who received a specific diagnosis with these diagnostic and imaging techniques; gastroesophageal reflux disease (GERD) 44% (n=13), aspiration pneumonia secondary to GERD 7% (n=2), GERD + oropharyngeal dysfunction 10% (n=3), bronchopulmonary dysplasia 10% (n=3), foreign body aspiration 7% (n=2), aspiration secondary to gastric volvulus 3% (n=1), bronchogenic cyst 3% (n=1), bronchiectasis 3% (n= 1), dilated cardiomyopathy was detected in 3% (n=1) and hypereosinophilic syndrome in 3% (n=1) patients. Cystic fibrosis was detected in one of the 64 patients who underwent sweat testing, and the diagnosis was confirmed by mutation analysis. When all the cases were examined, it was observed that winter is 45% (n=34) of the attack season at the time of admission due to wheezing. However, there was no statistical difference between the groups. When the first attack times of the cases presenting due to wheezing attack are examined; In 59% (n=49) it was detected between 1-6 months and there was no significant difference between the groups. Again, when all the cases were examined, 28% (n=21) girls and 72% (n=55) boys were detected, and there was no statistically significant difference between the groups. In all cases, the maternal age was 59.6% (n=45) and under 29 years of age, while 40.8% (n=31) cases were 30 years of age or older and there was no statistical difference between the groups. When the cases were evaluated in terms of growth retardation, it was statistically significantly higher in the group with a specific diagnosis ($p<0.01$). According to the presence of smokers in the family, the smoking rates of the cases in the wheezing phenotypes group were statistically significantly higher than the cases in the specific diagnosed group. When total IgE levels were examined in the group containing wheezing phenotypes, a significant elevation was detected in cases with persistent atopic wheezing ($p<0.01$). In addition, the eosinophil percentage of the early transient wheezing group was significantly lower than that of the persistent atopic and non-atopic wheezing diagnostic groups ($p<0.01$); There was no significant difference between the persistent atopic group and the non-atopic group.

Conclusions: In terms of recurrent wheezing attack cases, being in winter, case age between 1-6 months, maternal age being under 29 years of age, gender being male was found to be significantly higher. Wheezing phenotype group demographic characteristics of the presence of smokers at home was significantly higher, while in the group of cases with specific diagnosis, growth retardation on physical examination was significantly higher it was found to be significantly higher.

Keywords: Recurrent wheezing, sociodemographic characteristics, growth retardation

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INTRODUCTION

Wheezing is a common presentation for pediatricians. In 1/3 of asthmatic children diagnosed before the age of five, the first symptoms occur before the age of two. Recurrent episodes of wheezing affect the child's diet, quality of life, growth, and development. Early recognition of persistent wheezing and correction of the underlying risk factors are important not only because of the morbidity and mortality it causes but also because of its long-term sequelae in adulthood (1). Clinically, wheezing is a physical examination finding suggestive of lower respiratory tract disease, characterised by small and medium-sized bronchial obstruction with rhonchi as a result of increased bronchial secretion. Chronic or recurrent wheezing may be caused by different primary aetiologies in different age groups. In general, asthma and reactive airway disease are the most common causes of wheezing (2).

Of the phenotypes typified according to the characteristics of the wheeze;

a) Transient early wheezing; the development of the respiratory tract is adversely affected during intrauterine life and babies are born with lower respiratory function compared to healthy babies. The main causes are smoking during pregnancy, low maternal age, low birth weight, and prematurity. Atopy and eosinophilic inflammation are absent (3). As these children grow, the dimensions of their airways change, and viral infections no longer cause wheezing (4). However, pulmonary function tests (PFTs) cannot catch up with their counterparts at any time. Although the prognosis seems very good due to the cessation of wheezing attacks at an early age (<3 years), the possibility of developing chronic obstructive pulmonary disease in adulthood is very high, especially if they also smoke.

b) Non-atopic wheeze (wheeze caused by viral infection); it has been observed that attacks in this phenotype are associated with viral infections. It is thought that the control of airway tone is altered during viral infection, leading to airway obstruction (4). It has not yet been clarified whether this physiological abnormality is congenital or occurs after a lower respiratory tract infection such as Respiratory Syncytial Virus (RSV) infection. This abnormality also decreases with advancing age, and statistical significance disappears when children reach the age of 13 years (4).

c) Persistent atopic wheeze (allergy-related atopic asthma); 60% of these children develop aeroallergen sensitisation by the age of 6 years. This may occur before or after the age of 3 years. The main difference between the two is that those who develop atopy before the age of 3 years have the worst lung function between the ages of 6 and 11 years. Other epidemiological studies of patients with persistent asthma suggest that symptoms begin in the first years of life.

Wheeze related to viral infection usually decreases over time and disappears around the age of 6 years. However, it has also been reported that it may continue in the form of a wheeze due to viral infection at school age, or it may develop into a multi-triggered wheeze or disappear at much later ages (5).

Wheeze is most common in infancy. The prevalence of wheezing in this age group varies from 4% to 32% (6). The reason for this high prevalence is related to the pulmonary mechanics of the airways at this age. Asthma, allergies, bronchiolitis, infections, congenital anomalies, foreign body aspiration, cystic fibrosis, gastro-oesophageal reflux, and tuberculosis (TBC) cause wheezing (6). Recurrent wheezing is defined as more than three episodes of wheezing or episodes of wheezing lasting more than 1 month (7). A diagnostic dilemma arises particularly in infants presenting with recurrent wheezing in the first 2 years of life. This situation is a source of concern for both the family and the healthcare team.

The first step in recurrent wheezing should be a history, careful physical examination, and then a chest X-ray. In the history, both individual and family history of atopy (such as atopic dermatitis, allergic rhinitis, and asthma) should be taken very carefully. Regarding the tests to be performed, skin tests are usually negative in very babies. RAST tests are also false negative. Viral infections are the most common cause of reactive airway disease. Environmental factors such as smoking and air pollution can also increase wheezing.

Hand hygiene, vaccination, and the use of masks are the most important ways of preventing and treating susceptible infants. Allergen-induced asthma is rare in this age group. It has been shown that wheezing, which begins early in life, is a heterogeneous condition, and recurrent airflow obstruction may be associated with different underlying mechanisms and even different diseases (7).

Because of this heterogeneity, treatment difficulties and failures are greater in older patients with asthma. In addition, atypical wheeze further complicates this disease. Even if they present with a typical wheeze, doctors are concerned about the diagnosis. As mentioned above, wheezing should be evaluated separately from recurrent lower respiratory tract infections in terms of both etiology and risk factors. Early initiation of studies on the etiology and good identification of risk factors are important for the prognosis of the disease.

In this study, it was aimed to compare phenomenological, familial, environmental causes and laboratory-imaging techniques between wheeze phenotype groups (Transient early wheeze group, Non-atopic wheeze group, and Persistent atopic wheeze patient group ageing from1 month-24 months) and the group with a specific diagnosis (Ventricular septal defect, Cystic fibrosis, Gastroesophageal reflux, etc.) causing recurrent wheeze.

MATERIALS AND METHODS

This was a retrospective cross-sectional study. Between January 2010 and November 2012 (a period of 35 months), 76 cases (7.8%) with three or more wheezing episodes or wheezing for more than 1 month or recurrent wheezing between 1 and 24 months of age were selected from 970 patients who were hospitalised in our hospital

for wheezing. Socioeconomic and demographic characteristics, risk factors, etiology, diagnosis, and ancillary diagnostic methods were obtained and evaluated both from the registered files and by contacting the families by telephone **(Table 1).**

Table 1. 26 Questions recorded for information on the case history, sociodemographic characteristics, and physical examination findings

a) Analysis of history (anamnesis)

Age at the time of application…
Gender…
Birth weight, Birth method, Birth week…
What was the complaint during the admission?
a) Cough b) Wheeze c) Fever d) Foreign body aspiration
Is the wheezing attack season at the time of application?
Age at first wheezing attack…
Total number of wheezing attacks…
Did the mother use assisted pregnancy methods during the prenatal period?
Is there a family history of atopy or allergic disease?

b) Sociodemographic characteristics

Is there a bottle feeding method used?
How many people live in a family house?
How many siblings go to school or nursery?
What floor is the house on?
What is the house heated with?
Is there humidity in the house?
Are there pets at home?
Is there anyone smoking at home?
Is there anyone in your family with chronic lung disease or allergic disease?
Mother's education level? a) Pre-high school? b) High school and beyond?

c) Review of the Physical Examination

Are there any rales on the physical examination?
Is expiring length present on physical examination?
Is there intercostal retraction on the physical examination?
Is there tachypnoea on the physical examination?
Are there signs of upper respiratory tract infection on physical examination?
Is there any growth and developmental delay in the physical examination?

The inclusion criteria were as follows:

1. At least three episodes of wheezing or wheezing persisting for more than 1 month

2. Being between 1 and 24 months old

3. No known medical condition (neuromuscular disease, congenital heart disease, etc.) that could cause recurrent wheezing.

Patients diagnosed with laboratory and imaging tests and found to have an aetiological factor were included in the specific diagnostic group. Patients in whom no aetiological factor for wheezing was found were included in the wheezing phenotype group.

Because our study was a retrospective cross-sectional study, ethics committee approval was not required.

RESULTS

Of the 970 patients aged 1-24 months admitted to our hospital for wheezing, 76 (7.8%) had three or more episodes of wheezing or had a wheeze lasting more than 1 month and had recurrent wheeze. The first group consisted of n = 29 (38%) patients with a specific diagnosis. In the second group, early transient wheeze was 15.7% (n=12), persistent atopic wheeze was 21% (n=16) and non-atopic wheeze was 25% (n=19).

The mean number of wheeze episodes for all subjects was 3.66±0.92 per year. No statistically significant difference was found between the specific diagnosis group and the wheeze phenotype groups (p>0.05). When the seasons of the attack were examined for all subjects at the time of presentation for wheeze, 23.7% (n=18) were in spring, 11.8% (n=9) in summer, 19.7% (n=15) in autumn and 44.7% (n=34) in winter. When the age of the first attack of all cases was analysed, it was observed that 59.2% (n=49) were between 1-6 months, 19.7% (n=15) were between 7-12 months and 21.1% (n=16) were 13 months or more **(Table 2).**

Table 2. Evaluations Regarding Wheezing

		All Cases		Wheezing Phenotypes		Specific Diagnose		*p*
		Mean±SD		Mean ±SD		Mean ±SD		
Number of Wheezing Attacks		3,66±0,92		3,77±1,03		3,47±0,66		[a]***0,233***
		n	%	**n**	**%**	**n**	**%**	
Wheezing Attack Season	**Spring**	18	23,7	13	27,7	5	17,2	[c]***0,521***
	Summer	9	11,8	4	8,5	5	17,2	
	Autumn	15	19,7	10	21,3	5	17,2	
	Winter	34	44,7	20	42,6	14	48,3	
Age of the First Wheezing Attack	**0-6 Month**	45	59,2	26	55,3	19	65,5	[c]***0,675***
	7-12 Month	15	19,7	10	21,3	5	17,2	
	≥ 13 month	16	21,1	11	23,4	5	17,2	

When the seasons of the attack were examined for all subjects at the time of presentation for wheeze, 23.7% (n=18) were in spring, 11.8% (n=9) in summer, 19.7% (n=15) in autumn and 44.7% (n=34) in winter. In the wheezing phenotype group, 27.7% (n=13) were in spring, 8.5% (n=4) in summer, 21.3% (n=10) in autumn and 42.6% (n=20) in winter. In the specific diagnosis group, 17.2% (n=5) of the cases were in spring, 17.2% (n=5) in summer, 17.2% (n=5) in autumn and 48.3% (n=14) in winter. No statistically significant difference was found between the groups (p>0.05). These data are presented in **Table 2**.

When the ages of the first attack of all subjects were analysed, it was observed that 59.2% (n=49) were between 1-6 months, 19.7% (n=15) were between 7-12 months and 21.1% (n=16) were 13 months and older. In the wheeze phenotypes group,

55.3% (n=26) of the cases were between 1 and 6 months, 21.3% (n=10) between 7 and 12 months and 23.4% (n=11) at 13 months and above, while 65.5% (n=19) of the cases in the specific diagnosis group were between 1 and 6 months, 17.2% (n=5) between 7 and 12 months and 17.2% (n=5) at 13 months and above. No statistically significant difference was found between the groups (p>0.05). These data are shown in **Table 2.**

The mean age of all subjects was 11.71±6.05 months, the mean age of subjects in the wheeze phenotype group was 12.68±5.92 months and the mean age of subjects in the specific diagnosis group was 10.14±6.03 months. No statistically significant difference was found between the groups (p>0.05). These data are presented in **Table 3.**

The mean gestational age of all subjects was 37.61±3.23 weeks, the mean gestational age of subjects in the wheeze phenotype group was 37.30±3.07 weeks and the mean gestational age of subjects in the specific diagnosis group was 38.10±3.48 weeks. No statistically significant difference was found between the groups (p>0.05). These data are presented in **Table 3.**

The mean birth weight of all subjects was 2890.46±780.29 g, the mean birth weight of subjects in the wheezing phenotype group was 2858.83±770.51 g and the mean birth weight of subjects in the specific diagnosis group was 2941.72±806.93 g. No statistically significant difference was found between the groups (p>0.05). These data are presented in **Table 3.**

When analysing the mode of delivery of the cases, 57.9% (n=44) of all cases were C/S, 42.1% (n=32) were Normal Spontaneous Birth (NSB), 66% (n=31) of the cases in the wheezing phenotype group were C/S, 34% (n=16) were NSB and 44.8% (n=13) of the cases in the specific diagnosis group were C/S, 55.2% (n=16) were NSB. There was no statistically significant difference between the groups (p>0.05). These data are presented in **Table 3.**

In all cases, 27.6% (n=21) were female and 72.4% (n=55) were male. In the wheeze phenotype group, 29.8% (n=14) were female and 70.2% (n=33) were male, and in the specific diagnosis group, 24.1% (n=7) were female and 75.9% (n=22) were male. No statistically significant difference was found between the groups (p>0.05). These data are presented in **Table 3.**

While 22.4% (n=17) of all subjects were born at or before 37 weeks, 77.6% (n=55) were born after 37 weeks. In the wheeze phenotype group, while 27.7% (n=13) were born at or before 37 weeks and 72.3% (n=34) were born after 37 weeks, in the specific diagnosis group, 13.8% (n=4) were born at or before 37 weeks and 86.2% (n=25) were born after 37 weeks. There was no statistically significant difference between the groups (p>0.05). These data are presented in **Table 3.**

When the cases were analysed according to bottle use, it was found that all cases were 47.4% (n=36). While 53.2% (n=25) of the subjects in the wheeze phenotypes group had bottle use, 37.9% (n=11) of the subjects in the specific diagnosis group had bottle use. No statistically significant difference was found between the groups (p>0.05). These data are shown in **Table 4.**

When analysing the number of persons in the family, 56.6% (n=43) of the subjects had a family of 3-4 persons, 22.3% (n=17) had a family of 5 persons and 21.1% (n=16) had a family of 6 or more persons. No statistically significant difference was found between the wheeze phenotypes and the specific diagnosis group (p>0.05). These data are presented in **Table 4**.

When analysing the presence of a smoker in the family, smoking was observed in 53.9% (n=41) of the cases. Smoking was observed in 63.8% (n=30) of the families of subjects in the wheeze phenotype group and 37.9% (n=11) of the families of subjects in the specific diagnosis group. A statistically significant difference was found between the groups (p<0.05). Smoking rates were significantly higher in subjects in the wheezing phenotype group than in those in the specific diagnostic group. These data are presented in **Table 4.**

When analysed according to the heating types of the cases, it was observed that 51.3% (n=39) of the houses were heated with natural gas, 30.3% (n=23) with natural gas stoves, and 18.4% (n=14) with wood stoves. There was no statistically significant difference between the groups according to the heating methods (p>0.05). These data are shown in **Table 4.**

Table 3. Evaluation of Birth Anamnesis Features

		All Cases		Wheezing Phenotypes		Specific Diagnose		p
		Mean ±SD		Mean ±SD		Mean ±SD		
Age (month)		11,71±6,05		12,68±5,92		10,14±6,03		***[a]0,075***
Age of Gestation (week)		37,61±3,23		37,30±3,07		38,10±3,48		***[a]0,294***
Birth Weight (gr)		2890,46±780,29		2858,83±770,51		2941,72±806,93		***[a]0,656***
The type of birth	**C/S**	n=44	% 57,9	n=31	% 66	n= 13	% 44,8	
	NSD	n=32	% 42,1	n=16	% 34	n=16	% 55	
Gender	**Female**	n=21	% 27,6	n=14	% 29,8	n = 7	% 24,1	***[b]0,786***
	Male	n=55	%72	33	%70	n=22	%75,9	
Prematurity	**≤ 37 week**	n=17	%22,4	n=13	%27,7	n=4	%13,8	***[b]0,260***
	>37 week	n=59	%77	n=34	%72,3	n=25	%86	

NSD: normal spontaneous delivery, a Student-T-test, b Yates Continuity Correction

When a family history of lung disease (pulmonary tuberculosis) and allergic disease (family history of asthma) was analysed, 21.1% (n=16) of the families of all subjects had lung disease, whereas 78.9% (n=60) did not. No statistically significant difference was found between the groups according to the family history of lung disease (p>0.05). These data are shown in Table 4. However, the presence of asthma in the family history of 50% (n=8) of the subjects diagnosed with persistent atopic wheeze was found to be significantly higher in the wheeze phenotype group.

When analysing the presence of dampness in the houses of the cases, it was found that all cases had dampness. While 65.8% (n=50) had no dampness, 34.2% (n=26) had dampness. While no statistically significant difference was found between the groups according to the presence of dampness in the home (p>0.05), the high rate of dampness in the wheezing phenotype group was notable. These data are presented in **Table 4.**

When analysing the number of siblings attending school, it was found that in all cases 39.5% (n=30) had no siblings attending

Table 4. Evaluation of the Sociodemographic Characteristics

		All Cases	Wheezing Phenotypes	Specific Diagnose	*p*
		n (%)	n (%)	n (%)	
Baby Bottle Use	**No**	40 (%52,6)	22 (%46,8)	18 (%62,1)	[b]***0,290***
	Yes	36 (%47,4)	25 (%53,2)	11 (%37,9)	
Number of people in the family	**3-4 İndividual**	43 (%56,6)	29 (%61,7)	14 (%48,3)	[b]***0,363***
	5 İndividual	17 (%22,3)	8 (%17,0)	9 (%31,0)	[b]***0,254***
	≥ 6 İndividual	16 (%21,1)	10 (%21,3)	6 (%20,7)	[b]***1,000***
Presence of Smokers in the Family	**No**	35 (%46,1)	17 (%36,2)	18 (%62,1)	[b]***0,050****
	Yes	41 (%53,9)	30 (%63,8)	11 (%37,9)	
Warm-up method	**Natural gas**	39 (%51,3)	23 (%48,9)	16 (%55,2)	
	Natural Gas Stove	23 (%30,3)	13 (%27,7)	10 (%34,5)	[c]***0,355***
	Stove	14 (%18,4)	11 (%23,4)	3 (%10,3)	
Lung Disease in the Family-Allergic disease	**No**	60 (%78,9)	36 (%76,6)	24 (%82,8)	[b]***0,726***
	Yes	16 (%21,1)	11 (%23,4)	5 (%17,2)	
Presence of Moisture in the House	**No**	50 (%65,8)	27 (%57,4)	23 (%79,3)	[b]***0,089***
	Yes	26 (%34,2)	20 (%42,6)	6 (%20,7)	
Number of Siblings Going to School	**No**	30 (%39,5)	18 (%38,3)	12 (%41,4)	
	1 Brother	29 (%38,2)	18 (%38,3)	11 (%37,9)	[c]***0,950***
	≥2				
	Brothers	17 (%22,4)	11 (%23,4)	6 (%20,7)	

Table 5: Evaluation of Maternal Characteristics

		All Cases		Wheezing Phenotypes		Specific Diagnose		*p*
		n	%	n	%	n	%	
Mother Age	**< 20 years of age**	6	7,9	4	8,5	2	6,9	
	20-29 years of age	39	51,3	24	51,1	15	51,7	[c]***0,968***
	≥30 years of age	31	40,8	19	40,4	12	41,4	
Mother Age	**≤ 29 years of age**	45	59,2	28	59,6	17	58,6	
	> 29 years of age	31	40,8	19	40,4	12	41,4	[b]***1,000***
	Primary school	42	55,3	26	55,3	16	55,2	
Mother Education	**High School**	29	38,2	16	34	13	44,8	[c]***0,163***
	University	5	6,6	5	10,6	0	0	
Mother Education	**Under high school**	42	55,3	26	55,3	16	55,2	[b]***1,000***
	High School and Above	34	44,7	21	44,7	13	44,8	

[b]Yates Continuity Correction, [c]Pearson Chi-Square

school, 38.2% (n=29) had one sibling attending school and 22.4% (n=17) had two or more siblings.

No statistically significant difference was found between the groups according to the number of siblings attending school (p>0.05). These data are presented in **Table 4**.

The maternal age was less than 20 years in 7.9% (n=6), between 20 and 29 years in 51.3% (n=39), and 30 years or more in 40.8% (n=31) of all cases. In the wheeze phenotype group, 8.5% (n=4) had a maternal age less than 20 years, 51.1% (n=24) had a maternal age between 20 and 29 years, and 40.4% (n=19) had a maternal age of 30 years or more. In the specific diagnosis group, maternal age was less than 20 years in 6.9% (n=2), between 20 and 29 years in 51.7% (n=15), and 30 years or more in 41.4% (n=12). No statistically significant difference was found between the groups (p>0.05). These data are presented in **Table 5.**

No statistically significant difference was found between the maternal age of the wheeze phenotype group and the specific diagnosis group (p>0.05). These data are presented in **Table 5.**

The maternal education of 55.3% (n=42) of all subjects was primary school, 38.2% (n=29) high school, and 6.6% (n=5) university. In the wheeze phenotype group, 55.3% (n=26) had primary education, 34% (n=16) had high school education and 10.6% (n=5) had a university education. In the specific diagnosis group, 55.2% (n=16) had primary education and 44.8% (n=13) had high school education. No statistically significant difference was found between the groups (p>0.05). These data are presented in **Table 5.**

No statistically significant difference was found between the maternal education level of the wheeze phenotype group and the specific diagnosis group (p>0.05). These data are presented in **Table 5.**

Cough was observed in 50% (n=38) of all subjects. Cough was observed in 48.9% (n=23) of subjects in the wheeze phenotype group and 51.7% (n=15) of subjects in the specific diagnostic group. There was no statistically significant difference between the groups (p>0.05). Wheeze was observed in 64.5% (n=49) of all cases. Wheeze was observed in 59.6% (n=28) of subjects in the wheeze phenotype group and 72.4% (n=21) of subjects in the specific diagnostic group. There was no statistically significant difference between the groups (p>0.05).

Fever was observed in 36.8% (n=28) of all cases. In 38.3% (n=18) of the wheeze phenotype group and 38.3% (n=18) of the specific diagnostic group. Fever was observed in 34,5% (n=10). There was no statistically significant difference between the groups (p>0.05).

Atopy was observed in 15.8% (n=12) of all subjects. In 19.1% (n=9) of the wheeze phenotypes group, in 19.1% (n=9) of the subjects in the specific diagnostic group

Atopy was observed in 10.3% (n=3). No statistically significant difference was found between the groups (p>0.05). The lack of difference in terms of atopy may be because atopy requires at least 12-15 months of sensitisation and the high number of cases with early wheezing in the first 2 years of age group. There was no statistically significant difference between the

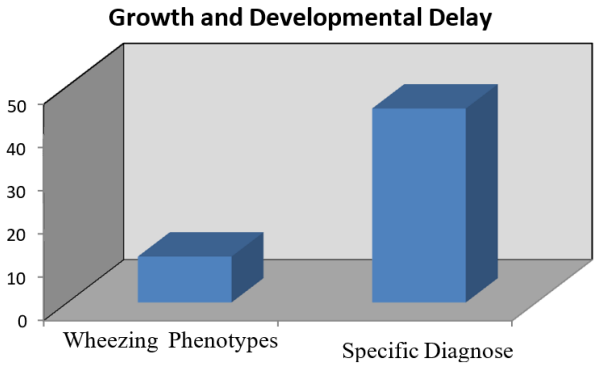

Figure 1: Distribution of Growth and Developmental Delay Rates.

Table 6. Evaluation of immunoglobulin Levels According to Groups

		All Cases		Wheezing Phenotypes		Specific Diagnose		[b]p
		n	%	n	%	n	%	
IgA	**Normal**	67	90,5	45	95,7	22	81,5	***0,108***
	Low	3	4,1	2	4,3	1	3,7	***1,000***
Total IgE	**Normal**	51	74,3	31	66	24	88,9	***0,050****
	Above	19	25,7	16	34	3	11,1	
IgM	**Normal**	64	86,5	43	91,5	21	77,8	***0,191***
	Low	2	2,7	1	2,1	1	3,7	***1,000***
	Above	8	10,8	3	6,4	5	18,5	***0,219***
IgG	**Normal**	65	87,8	39	83	26	96,3	***0,158***
	Low	6	8,1	6	12,8	0	0	***0,135***
	Above	3	4,1	2	4,3	1	3,7	***1,000***

[b]Yates Continuity Correction, p<0,05*

groups for the presence of rales, expiratory length, intercostal retraction, tachypnoea, and viral infection (p>0.05).

A statistically significant difference was found between the groups according to growth and developmental delay (p<0.01). The rate of growth and developmental delay observed in the specific diagnosis group was significantly higher than that observed in the wheeze phenotypes group. This is shown in **Figure 1.**

No statistically significant difference was found between the groups for WBC and CRP levels (p>0.05).

When the subjects were analysed according to IgA levels, no statistically significant difference was found between the normal and low levels groups (p>0.05). These data are presented in **Table 6.**

When analysed according to the total IgE measurement values of the subjects, the IgE elevation in the wheezing phenotype group was found to be statistically borderline significantly higher than in the subjects with specific diagnosis (p<0.05). These data are presented in **Table 6.**

When analysed according to the IgM measurement values of the cases; no statistically significant difference was found between the groups according to the normal, low, and high measurement values (p>0.05). These data are shown in **Table 6**.

When the subjects were analysed according to IgG levels, no statistically significant difference was found between the groups according to normal, low, and high levels (p>0.05). These data are presented in **Table 6.**

When total IgE was analysed according to the case status, the mean values were 206.00±134.21 U/ml for persistent atopic wheeze, 16.61±16.754 U/ml for non-atopic wheeze and 17.18±16.256 U/ml for early transient wheeze. A statistically significant difference was found between the diagnostic groups (p<0.01). The persistent atopic diagnostic group was statistically significantly higher than the other diagnostic groups. These data are shown in **Figure 2.**

When the eosinophil percentage of the patients was analysed according to the presentation status, it was 3.59±2.10%

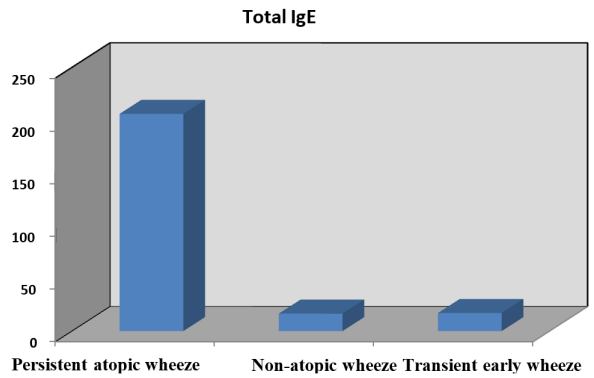

Figure 2: Total IgE distribution of the wheezing phenotype groups.

for persistent atopic diagnosis, 2.56±1.44% for non-atopic diagnosis, and 0.73±0.51% for early transient wheeze diagnosis. A statistically significant difference was found between the diagnostic groups (p<0.01). The eosinophil percentage in the group diagnosed with early transient wheeze was significantly lower than that in the groups diagnosed with persistent atopic and non-atopic wheeze (p<0.01); no significant difference was found between the persistent atopic group and the non-atopic group (p>0.05).

When the chest radiograph parameters of the cases were analysed, 2.7% (n=2) of all cases had a difference in aeration, 29.3% (n=22) had excess aeration, 25.3% (n=19) had infiltration, 16% (n=12) had perihilar infiltration and 26.7% (n=20) were normal, whereas 36.2% (n=17) of the wheeze phenotype group had excess aeration, 19. 1% (n=9) had infiltration, 10.6% (n=5) had perihilar infiltration and 34% (n=16) were normal, whereas in the specific diagnosis group, 7.1% (n=2) had ventilation difference, 17.9% (n=5) had infiltration, 14.3% (n=4) had perihilar infiltration and 25% (n=7) were normal. No statistically significant difference was found between the groups according to chest radiograph parameters (p>0.05). These data are shown in **Table 7.**

When analysing the chest CT results, a statistically significant difference was found between the rates of subjects with normal chest CT results according to the groups (p<0.05). Normal chest CT results were statistically significantly higher in the wheeze phenotype group than in the specific diagnostic group. No statistically significant difference was found between the distributions according to the chest CT results (p>0.05). These data are presented in **Table 7.**

A statistically significant difference was found between the distribution of esophagus-stomach-duodenal (ESD) radiographs according to groups (p<0.05). The detection rate of gastro-oesophageal reflux in ESD was significantly higher in patients with specific diagnoses. These data are shown in **Table 7**.

There was a statistically significant difference between the pH metre distributions according to the groups (p<0.05). The rate of gastro-esophageal reflux detection in the pH metre was found to be significantly higher in cases with specific diagnoses. These data are shown in Table 7.

Videofluoroscopy was used in the diagnosis of 5 cases in the specific diagnosis group, and oropharyngeal aspiration was detected in 4 cases. These data are shown in **Table 7**.

There was no statistically significant difference between the echocardiography (ECHO) distributions according to the groups (p>0.05). However, it is noteworthy that all 4 cases with abnormalities in ECHO were in the specific diagnostic group. Secundum ASD (n=2), Bicuspid aorta (n=1), and Dilated cardiomyopathy (n=1) were detected in the patients with pathological ECHO results. These data are shown in **Table 7.**

Alpha-1 antitrypsin results also did not show any statistically significant difference between groups (p>0.05) Cow's milk

Table 7. Evaluation of Chest X-ray, Thorax CT, ESD graph, ECHO, Sweat Test, pHmeter Results

	All Cases		Wheezing Phenotype	Specific Diagnose	*b*
	n	%	n (%)	n (%)	
Chest X-Ray					
Difference in aeration	2	2,7	0 (%0)	2 (%7,1)	***0,264***
Increased aeration	22	29,3	17 (%36,2)	5 (%17,9)	***0,155***
Infiltration	19	25,3	9 (%19,1)	10 (%35,7)	***0,186***
Perihilar infiltration	12	16,0	5 (%10,6)	4 (%14,3)	***0,918***
Normal	20	26,7	16 (%34,0)	7 (%25,0)	*0,574*
Thorax CT					
Normal	12	61,3	8 (%72,7)	4 (%20,0)	***0,012****
Mosaic Pattern	2	6,5	0 (%0,0)	2 (%10,0)	***0,749***
Mass	1	3,2	0 (%0,0)	1 (%5,0)	***1,000***
Interstitial infiltration	2	6,5	0(%0,0)	2 (%10,0)	***0,749***
Ground Glass Image	7	22,6	1 (%9,1)	6 (%30,0)	***0,377***
Bronchiectasis	1	3,2	0 (%0,0)	1 (%5,0)	***1,000***
Atelectasis	5	16,1	3 (%27,3)	2 (%10,0)	***0,459***
Consolidation	4	12,9	2 (%18,2)	2 (%10,0)	***0,928***
ESD graph					
Normal	10	52,6	7 (%100,0)	3 (%25,0)	***0,007****
Reflux	9	47,4	0 (%0,0)	9 (%75,0)	
ECO					
Normal	58	95,1	38 (%100,0)	20 (%87,0)	***0,094***
Abnormal	3	4,9	0 (%0,0)	3 (%13,0)	
Sweat test					
< 40	53	82,8	33 (%82,5)	20 (%83,3)	***1,000***
40–60	10	15,6	7 (%17,5)	3 (%12,5)	***0,859***
> 60	1	1,6	0 (%0,0)	1 (%4,2)	***0,795***
Phmetre					
Normal	19	73,1	17 (%100,0)	2 (%22,2)	***0,001****
Reflux	7	26,9	0 (%0,0)	7 (%77,8)	

[b]Yates Continuity Correction, p<0,05*, p<0,001**

protein IgE results did not show any statistically significant difference between groups (p>0.05). However, cow's milk protein-specific IgE levels were found to be significantly high in 2 cases in the wheezing phenotype group.

The sweat test results also did not show any statistically significant difference between groups (p>0.05). These data are shown in **Table 7.**

PPD was performed on all cases and PPD positivity was detected in one case, and there was no statistically significant difference between the groups (p>0.05).

DISCUSSION

Wheezing is a multifactorial symptom with different causes for each age group and is common in children. Atopy, genetic causes such as family history, frequent viral infections, and environmental causes such as exposure to cigarette smoke are risk factors for chronic wheezing. Despite many studies, it is not yet clear why the same environmental factors do not cause the same symptoms even in siblings. At least 30% of children experience a wheezing attack before the age of 3 and 50% before the age of 6. In persistent wheezing, loss of lung function begins after the first year, becomes apparent at the age of 6, and continues until adulthood (8). Twenty-five percent of children under one year of age and 13% of children aged 1 to 2 years develop respiratory tract infections, and half of these cases involve wheezing (9). There is strong epidemiological evidence that approximately two-thirds of wheezing episodes during the early school years are due to viral infection (9). Viruses, primarily Respiratory Syncytial Virus (RSV) and less frequently Adenovirus and Parainfluenza viruses, generally

cause wheezing attacks in the first 3 years of life. Our research has determined that wheezing attacks are more intense in the winter months. Since these viruses are more common in the winter months, it is likely that the cause of wheezing is mostly viral infection or triggered by viral infection.

The most important factors in the evaluation of a wheezy child are the age of onset of wheezing, whether it is recurrent or chronic, the presence of symptoms such as fever, developmental delay, chest deformity, clubbing, familial allergy history, and whether there is a response to bronchodilator treatment (10). Thus, etiology should be investigated within the framework of a specific algorithm. A careful history and physical examination can detect diseases such as foreign body aspiration, cystic fibrosis, gastroesophageal reflux disease, viral pneumonia, or pulmonary tuberculosis (11). Anatomical defects, congenital heart disease, laryngo-tracheo-malacia, and diaphragmatic hernia should be investigated for early medical and surgical treatment.

When the time of the first wheezing attacks of children with wheezing is considered, it is seen that it is mostly in the 0-6 months period. The fact that the largest patient group in our study was 1-6 month-old babies (59.2%) can be explained by anatomical reasons and the inadequate development of the immune system. Inal et al. (10) also determined the first attack age as 0-6 months period in their study. Our results are parallel to the results of this study. In addition to the local effects of viral infection in the small respiratory tract, many anatomical factors contribute to the narrowing of the respiratory tract in infants. The narrowness of the peripheral respiratory tracts in children causes them to become easily obstructed. In infants, many mucous glands are secreted in the respiratory tract, and the respiratory tract mucosa is looser. Thus, submucosal edema occurs more easily. However, the foramina of Kohn are fewer in number and less developed in the infant lung. Therefore, collateral ventilation is not as effective as in adults. Excessive ventilation and atelectasis develop more easily. In our study, atelectasis was detected in 16.1% (n=5) of the cases in which thoracic CT was performed, 2 of the cases were 5 months old, 1 case was 3 months old, 1 case was 4 months old, and 1 case was 9 months old. The risk of wheezing attacks increases in premature babies and babies with a birth weight of less than 2,500 grammes. In a study conducted in our country, wheezy children were investigated in terms of birth weight, and no significant difference was found between wheezy children and healthy children (12). Sherriff et al. tried to determine the risk factors in wheezy children and determined only low birth weight (<2,500 grammes) as a definite risk factor (13).

In our study, no significant difference was found in the specific diagnosis group and the wheezing phenotype group with birth weight and premature birth. The results of studies investigating gender as a risk factor contain differences. While wheezing was determined as a definite risk factor for the male gender in one study (13), no connection was found between the male gender and wheezing in another study (14). In our study, wheezing was found to be significantly higher in males in both groups, but no statistical difference was found between the groups.

It is thought that the risk factors that determine the tendency to wheeze and asthma may be effective at an early age and perhaps even in the intrauterine environment. These factors include fetal nutrition (15), gestational age (16), exposure to cigarette smoke (17), environmental air pollution (3), postnatal nutrition, breastfeeding, family size, maternal age, socioeconomic status, and exposure to allergens (18-20). Exposure to passive smoking is a risk factor for infants, especially if the mother smokes. In one study, the relationship between prenatal and postnatal familial smoking and wheezy infants was examined in two different populations. As a result of this study, a significant relationship was found between both maternal smoking during pregnancy and exposure to passive smoking and wheezy infants, and it was suggested that the dose-dependent effects of prenatal and postnatal exposure of infants to tobacco smoke may be important (21). Family smoking, especially maternal smoking, increases the risk of wheezing symptoms and lower respiratory tract diseases (22). Another study has shown that wheezy children are more exposed to passive smoking than healthy children (23). In 496 cases with recurrent wheezing attacks who were followed up to 14 months of age, maternal smoking, especially in the first 2-3 months, was found to be a risk factor (24).

In this study, because the number of mothers who smoked during pregnancy was low (only the wheezing phenotype group (n=2)), no comparison was made. When the rates of smoking in the family were examined, the wheezing phenotype group was found to be significantly higher than the specific diagnostic group.

While breastfeeding is thought to reduce wheezing attacks in children, there is still no evidence-level data on its protective effect against persistent asthma. Due to ethical concerns, the number of studies on the subject is almost non-existent. In addition, the World Health Organisation also recommends that all children with and without a risk of allergy be breastfed for the first 6 months to prevent malnutrition, which is still common worldwide. A study in China has shown that formula feeding contributes to respiratory illness requiring hospitalisation in the first 18 months (18). It was observed that the risk of wheezing was higher in children living in houses heated with wood (25). In our study, no significant difference was found between formula feeding and home heating devices in both groups.

Children with school-age siblings and infants in nurseries are at a high risk of experiencing attacks (25). However, in terms of the development of atopic diseases, many studies in Western countries have shown an inverse relationship between the number of siblings and atopic diseases, and it has been suggested that increasing the number of siblings has a protective effect by increasing the risk of infection. However, while some studies have identified the presence of a sibling as a risk factor, others have not been able to identify a relationship between wheezing and the presence of a sibling. Thus, contrary

to previous publications, new studies have found early viral respiratory tract infections to be protective against asthma, and a clear consensus has not yet been reached on this issue (26). In our study, no significant difference was found in terms of viral infection in both groups. Strachan and colleagues determined that humidity in bedrooms is an important risk factor for wheezing (27). In our study, no statistically significant difference was found between the groups according to the presence of humidity in the house, but the high humidity rate in the wheezing phenotype group was remarkable. Humidity can of course lead to mould formation in the house over time, which can lead to mould allergy in the future. However, considering the average age of the group we examined (<2 years), it seems a bit early for this. For this, it is necessary to be approximately 12-15 months older.

Tachypnea, retraction, and prolonged expiration are common findings on physical examination; cyanosis and nasal flaring may also be seen depending on the severity of the disease (28). The expiratory length was found to be 97%, rales 64%, tachypnea 27%, and intercostal retraction 23%, and no significant difference was found between the groups. Growth and developmental delay were found to be significantly higher in the specific diagnosis group than in the wheezing phenotype group. This is an expected result and should be considered natural.

There are many studies investigating the role of immunoglobulin levels in wheezy infants, especially considering the susceptibility to respiratory tract infections and immune deficiency. While some studies could not find any relationship between immunoglobulin levels and wheezing (29), Öner et al. found low IgG3 and/or IgG4 levels and high IgE levels in their study and concluded that immunoglobulins may play a role in the pathogenesis of childhood wheezing (30).

Independent of allergen-specific reactivity, studies in children and adults have reported a close relationship between total serum IgE levels and the prevalence of asthma. A prospective population study showed that children who were sensitised early and had persistent wheezing had high IgE levels throughout childhood. Consequently, it may be useful to know in which children IgE is effective in determining disease risk. When laboratory findings were evaluated in our study, it was observed that both total IgE and total eosinophil percentage were significantly higher in the persistent atopic cases of the wheezing phenotype group compared with the cases of other wheezing phenotype groups. In addition, a partial IgA decrease was detected in 3 cases, a total IgE increase was detected in 19 cases, an IgM decrease was detected in 2 cases, and an IgG decrease was detected in 6 cases. It was observed that immunoglobulin levels increased in the follow-up of cases with hypogammaglobulinemia. These are likely to be either physiological or transient hypogammaglobulinemias, at which time the infection has either been prolonged or relapsed.

In a wheezy child, increased ventilation in both lungs (more than seven ribs ventilation, ribs becoming parallel, diaphragm flattening, reduction in the mediastinum and heart area, increase in the retrosternal space on the lateral radiograph), peribronchial infiltrates and atelectasis can be seen radiologically. Patchy density increase can also develop due to atelectasis and secondary bacterial infection (28). In all our cases, it was observed that 2.7% (n=2) had a difference in ventilation, 29.3% (n=22) had excess ventilation, 25.3% (n=19) had infiltration, 16% (n=12) had perihilar infiltration, and 26.7% (n=20) were normal. No statistically significant difference was found between the groups in terms of chest X-ray findings ($p>0.05$). When thoracic CT results were examined, normal (%61), ground-glass appearance (%22.6), atelectasis (%16.1), consolidation (%12.9), mosaic pattern (%6.5), interstitial infiltration (%6.5), bronchiectasis (%3.2), and mass (%3.2) were detected in all cases. The normality of the thorax CT results of the cases in the wheezing phenotype group was statistically significantly higher than the cases in the specific diagnostic group. No statistically significant difference was found between the distributions according to the thorax CT results ($p>0.05$). The advanced examinations (PPD, sweat test, pH metre) of the patient with bronchiectasis were found to be normal. A case with a mass was taken to surgery, and the mass was found to be a bronchogenic cyst because of pathological examination. Gastroesophageal reflux disease (GERD) causes recurrent cough, wheezing, and aspiration pneumonia, especially in the first years of life, and therefore constitutes an important problem in the differential diagnosis of wheezy infants. Wheezing after feeding, frequent vomiting, prominent nocturnal symptoms, and worsening with bronchodilator treatment should be particularly alert for GERD. The most reliable method for diagnosing GERD is to record the pH changes in the lower esophagus with a pH metre for 24 h (31). In one study, 40 patients with respiratory symptoms were investigated for GERD, and GERD was detected in 35% of the patients (32). It was observed that there was a significant improvement in the respiratory symptoms of the patients who were diagnosed with GERD and started on anti-reflux treatment. In another study, reflux scintigraphy was performed on 43 of 110 children with wheezing attacks, and GERD was found to be positive in 24 patients (12). In our study, 25% (n=19) of the cases underwent Esophagus Stomach Duodenum (ESD) graphs and GERD was detected in 11% (n=10). pH metre was used in 34% (n=26) of the cases and GERD was detected in 9% (n=7). In total, GERD was detected in 10 cases with ESD and 7 cases with pH metre. In 2 of the cases, GERD was detected with orotracheal aspiration, 2 with aspiration pneumonia, 1 with gastric volvulus, and 1 with hypogammaglobulinemia. Tuberculosis continues to be a major problem all over the world, especially in developing countries and is included in the etiology of patients presenting with wheezing (33). In one study, a patient who was hospitalised with a preliminary diagnosis of a foreign body due to short-term wheezing and chest X-ray findings was reported to have tuberculous lymphadenitis after histopathological and microbiological examination of a mass that caused extraluminal compression of the airways as a result of bronchoscopy (34). In our study, the PPD test was found to be positive in 1 case, but the case had

no history of contact, chest X-ray was normal, thorax CT was normal, the Quantiferon test was negative, ARB (Acid-Resistant Bacillus) was negative in fasting gastric juice and no growth was detected in mycobacteria culture. The most common food allergy in infancy is cow's milk allergy. In developed countries, the incidence in infants under 2 years of age is around 2%. Almost half of them are IgE-dependent, and the other half are not. It occurs not only with direct cow's milk but also with the ready-made formula. The allergic reaction starts within the first 4 weeks after starting the ready-made formula. The vast majority recover before the age of 3 (35). In our study, a cow's milk IgE test was performed in 90% (n=68) cases and cow's milk-specific IgE was detected as positive in two cases in the wheezing phenotype group. The formula they were using was stopped and the amino acid-based formula was started. Wheezing due to cardiovascular anomalies occurs in the first weeks of life. It is heard both inspiratory and expiratory during cardiac auscultation. Wheezing due to the right main bronchus, abnormal left pulmonary artery compression, and double aortic arch may occur with difficulty swallowing (2). However, cardiac causes leading to heart failure may cause recurrent wheezing. In our study, ECHO was performed in 86% (n=65) of the patients and dilated cardiomyopathy was detected in 1 case, bicuspid aortic valve in 1 case, and secundum ASD in 2 cases.

Hypereosinophilic syndrome, a rare cause of wheezing in children, is sometimes revealed by detecting eosinophilia during routine examinations. The diagnosis is made after excluding other conditions known to cause chronic eosinophilia (36). The patient in the specific diagnosis group diagnosed with hypereosinophilic syndrome had a history of hyperemic (macular) rash that started at the age of 6 months and then recurrent wheezing attacks. The eosinophil level was 13.2% (2.400/mm3) and the serum IgE level was 460 IU/ml at presentation. The diagnosis was made after excluding other causes of hypereosinophilia (intestinal parasitosis, hematological malignancy, hyper IgE syndrome, Churg-Strauss syndrome). It was thought that the asthma that developed in this patient could be related to the eosinophilic involvement of the airways. Flexible bronchoscopy is recommended to visualise the respiratory tract in cases presenting with recurrent wheezing when history, clinical, and laboratory findings do not lead to a possible diagnosis to elucidate the etiology or in cases with late or unresponsive response to treatment. Flexible bronchoscopy and BAL (bronchoalveolar lavage), which is a critical step in evaluating congenital anomalies of the larynx or bronchi, could be performed in 5 cases. Tracheomalacia with aspiration pneumonia was detected in 1 case, aspiration pneumonia in 1 case, foreign body aspiration in 2 cases, and the findings were normal in 1 case. In the virtual bronchoscopy experience from the literature, foreign body aspiration (FBA), sunflower, and fruit seeds were detected in some cases. While one of our cases had a history of FBA, no history of FBA was detected in the other. A sunflower seed was detected as a foreign body in one case and a fruit seed in one case.

In every case with recurrent wheezing attacks and where allergic/atopic asthma is not considered, other causes should be considered. Anatomical defects, congenital heart disease, laryngo-tracheomalacia, and diaphragmatic hernia should be investigated for early medical and surgical treatment. A careful history and physical examination can detect diseases such as FBA, cystic fibrosis, GERD, viral pneumonia, or pulmonary tuberculosis (11). Many studies have identified cystic fibrosis as the etiology of wheezy children and have shown that wheezing develops more frequently due to airway hyperreactivity (37). In addition, although the most common cause of wheezing is bronchial asthma when it occurs in the neonatal period and does not respond to bronchodilator treatment, a hereditary disease such as cystic fibrosis or a congenital anomaly should be considered first (38). In the study conducted by Çevik D et al., the sweat test results were found to be >60 mmol/L in 19 out of 69 patients (29%) (12). In our study, a sweat test was performed in 64 (84%) of the cases, and the sweat Cl was found to be <40 mEq/L in 52 (82.8%), 40–60 mEq/L in 7 (10%), and >60 mEq/L in 1 (1.6%). In the case with sweat test results >60 mmol/L, the sweat test result was found to be over 60 mmol/l again and the Delta F508 mutation was detected in the mutation analysis, and cystic fibrosis was diagnosed.

Children born because of in vitro fertilisation (IVF) are more likely to require neonatal intensive care because of the higher frequency of prematurity due to multiple pregnancies (39). It has been reported that respiratory distress syndrome develops more frequently, hospitalisation is longer, and perinatal death frequency increases in children born because of IVF compared with the control group. It has been shown that there is a statistically significant increase in the frequency of hospital admissions up to the age of 4 years, and this increase is particularly evident in the infant period (40). In addition, it has been thought that the drugs used for IVF (GnRH, purified FSH) may increase the frequency of allergic diseases and asthma in children born with IVF by affecting epigenetic modification and gene expression in the DNA structure of the fetus, but sufficient evidence has not been found (40). In our study, there was a history of IVF in 2 cases in the wheezing phenotype group. A case was born at 30 weeks of gestation weighing 1,300 grammes, and the other was born at 36 weeks of gestation weighing 2,900 grammes. Because IVF was not applied to a sufficient number of cases, no significant difference was found between the two groups.

Bronchopulmonary dysplasia (BPD) is a chronic lung disease in which oxygen dependence and/or the need for assisted ventilation continue in newborn babies due to reasons originating from the lungs. In a study conducted in China on the etiology of wheezy children, BPD was found to be 4.4% (41). In our study, this rate was determined as 0.5% (n=3). In Switzerland, preterm cases in the first year of their life with (n=78) and without (n=48) BPD were examined. Cough was detected in 80% of these cases, and wheezing was detected in 44%. Frequent contact with other children was evaluated as the major risk factor for wheezing (42). In our study, BPD was detected in 3 cases and they were under 1 year old. While cough and wheezing were present together in 2 cases, 1 case had only wheezing. In one case, the number of siblings

attending the nursery was 1, and in two cases, the number of siblings attending school was 2.

CONCLUSION

Wheezing is a common symptom in children. Although it is often caused by bronchiolitis, it can be difficult to distinguish it from infant asthma. Therefore, less common but not uncommon causes of wheezing, such as GERD, FBA, cystic fibrosis, and immune deficiency, should also be investigated. Early identification of the persistent atopic wheezing group, especially accompanied by atopy, is important in terms of controlling attacks before irreversible changes occur in the bronchi. Therefore, the first step of detailed examinations is the history and physical examination. To make this differential diagnosis and determine the treatment and prognosis, risk factors and etiology must be revealed. In this study, cases with specific diagnoses (such as bronchopulmonary dysplasia, GERD, and cystic fibrosis) and those with the wheezing phenotype group were examined in our cases between 1-24 months of age. It was found that the male gender was a significant risk factor in both groups, that the first attacks were significantly more frequent between 1 and 6 months in all cases, and that the attack season was significantly more in the winter months. While no significant difference was found in the history comparison, growth and developmental delay in the physical examination were found to be significantly higher in the specific diagnostic group. Among the sociodemographic characteristics, the presence of a smoker at home was found to be significantly higher for wheezing in the wheezing phenotype group. Higher total IgE levels were found in persistent atopic wheezing cases in the wheezing phenotype group compared with cases diagnosed with other wheezing phenotypes. In terms of serum eosinophil percentage, it was found to be significantly higher in cases diagnosed with persistent atopic wheezing and non-atopic wheezing compared with cases diagnosed with early transient wheezing. The results of this study suggest that we should be careful not to have a smoker at home to reduce the development of asthma or its severity in cases in the wheezing phenotype group and that diseases such as GERD, FBA, and cystic fibrosis, in addition to atopy and allergic asthma, may cause persistent wheezing in infants with wheezing.

Ethics Committee Approval: Since this was a retrospective study on patients treated in 2010 and 2012, ethics committee approval was not obtained.

Informed Consent: Since this was a retrospective study, consent was not obtained.

Peer Review: Externally peer-reviewed.

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