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ORIGINAL ARTICLE

Evaluation of Patients Presenting with Chronic Cough to the Pediatric Allergy Clinic According to Age Groups

Çocuk Alerji Polikliniğine Kronik Öksürük Nedeni ile Başvuran Hastaların Yaş Gruplarına Göre Değerlendirilmesi

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ABSTRACT

Background/Aims: Chronic cough is a prevalent issue in pediatric patients and is among the most common reasons for referral to pediatric allergists, significantly affecting quality of life and often necessitating specialized evaluation. This study aimed to analyze the clinical characteristics, etiologies, and management of chronic cough in children, providing insights into age-related prevalence.
Methods: Pediatric patients presenting with a chronic cough to our pediatric allergy clinic between 1st May 2023, and 31st May 2024 were included in this retrospective study. Patients previously diagnosed with allergic diseases or evaluated at other clinics were excluded. Medical records were reviewed for demographics, characteristics of cough, familial and environmental factors, and treatment regimes.
Results: Of 267 patients included, 54.7% were boys, and the median age was 6.99 [interquartile range (IQR) 4.47-11.54] years. Asthma (39%), protracted bacterial bronchitis (PBB) (25.8%), and upper airway cough syndrome (UACS) (22.1%) were the most common diagnoses. PBB was more prevalent in younger patients, whereas asthma was dominant in older age groups. Regardless of the cough etiology, antibiotic use was noted in 67.8% of patients before applying to the pediatric allergy outpatient clinic. Exposure to tobacco smoke was present in 40.1% of patients. The familial history of asthma was significantly more common in patients with asthma (p=0.03).
Conclusion: This study underscores the importance of distinguishing between chronic cough etiologies in children to prevent mismanagement and overuse of antibiotics. While asthma, PBB, and UACS were among the primary causes, many other potential diagnoses also warrant consideration. Comprehensive assessments are essential for accurate diagnosis, and a multi-disciplinary approach may enhance the outcomes of the management.

Keywords: Asthma, chronic cough, pediatric, protracted bacterial bronchitis.

ÖZ

Amaç: Kronik öksürük pediatrik hastalarda sık görülen bir sorundur ve pediatrik alerjistlere baş vurunun en sık nedenleri arasındadır. Çalışmamızda, çocuklarda kronik öksürüğün klinik özelliklerini, etiyolojilerini ve tedavi yönetimini analiz etmeyi ve yaşa göre prevalans farklılıklarına ilişkin bilgi sağlamayı amaçladık.
Gereç ve Yöntem: 1 Mayıs 2023-31 Mayıs 2024 tarihleri arasında kronik öksürük şikayetiyle pediatrik alerji polikliniğimize başvuran pediatrik hastalar retrospektif olarak taranarak çalışmaya dahil edildi. Önceden alerjik hastalık tanısı konulmuş veya başka bir çocuk alerji kliniğinde değerlendirilmiş olan hastalar çalışmaya dahil edilmedi. Tıbbi kayıtlardan hastaların demografik verileri, öksürük özellikleri, ailevi ve çevresel faktörler ile tedavileri değerlendirildi.
Bulgular: Çalışmaya 267 hasta dahil edildi. Hastaların %54,7'si erkek ve medyan yaşları 6,99 (çeyrekler arası aralık (ÇAA) 4.47-11.54) yıl idi. Hastalara en sık astım (%39), uzamış bakteriyel bronşit (UBB) (%25,8) ve üst solunum yolu öksürük sendromu (ÜSYÖS) (%22,1) tanıları koyuldu. UBB, daha çok küçük yaştaki hastalarda görülürken, astım ise daha büyük yaş gruplarında baskın tanı idi. Öksürük etiyolojisinden bağımsız olarak, hastaların %67,8'i çocuk alerji polikliniğine başvurmadan önce antibiyotik kullanmıştı. Hastaların %40,1'inde tütün dumanı maruziyeti tespit edildi. Ailede astım öyküsü, astım tanısı alan hastalarda diğer tanılara göre anlamlı derecede daha yüksek bulundu (p=0.03).
Sonuç: Çocuklarda kronik öksürük etiyolojisinin doğru bir şekilde belirlenmesi, yanlış tedavi ve gereksiz antibiyotik kullanımını önlemek için önemlidir. Astım, UBB ve ÜSYÖS çocuklarda kronik öksürüğün başlıca nedenleri olup göz önünde bulundurulması gereken birçok başka potansiyel tanı bulunmaktadır. Doğru teşhis için kapsamlı değerlendirme ve multidisipliner yaklaşım önemlidir.

Anahtar kelimeler: Astım, kronik öksürük, pediatri, uzamış bakteriyel bronşit.

Introduction

Chronic cough is a prevalent issue in pediatric patients and is among the most common reasons for referral to pediatric allergists. Defined as a cough lasting more than four weeks, chronic cough can significantly impact the quality of life (QoL) of both affected children and their families, often leading to disrupted sleep, impaired daily activities, and missed school days (1-3). Unlike acute cough, which usually arises from viral respiratory infections and typically resolves within a few weeks, chronic cough in children can be associated with a range of underlying etiologies, from common conditions like asthma and allergic rhinitis to more complex diseases such as cystic fibrosis, protracted bacterial bronchitis (PBB), and bronchiectasis (4).

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Early and accurate diagnosis is crucial to prevent the progression of potential diseases such as asthma, bronchiectasis, or foreign body aspiration, thereby improving long-term health outcomes. Clinical guidelines recommend a systematic approach to the evaluation of chronic cough in children, involving detailed history-taking, physical examination, and appropriate diagnostic tests to identify the underlying etiology (1,5,6).

In our study, the clinical characteristics, accompanying symptoms, family history, environmental exposures, chronic cough etiology according to age groups, and treatments of the patients applying to pediatric allergy clinics with chronic cough were evaluated. By analyzing the prevalence of chronic cough in children concerning its various etiologies, this study aimed to improve the understanding and guide the evidence-based management approaches, ultimately improving patient outcomes and reducing the burden of chronic cough on the pediatric population and healthcare systems.

Methods

Pediatric patients evaluated for chronic cough in the pediatric allergy outpatient clinic of our department between 1st May 2023 and 31st May 2024 were included in the study. Patients who had previously been diagnosed with an allergic disease and those who had previously been evaluated in other allergy clinics due to their chronic cough were excluded. The institutional ethics committee approval was obtained before the initiation of the study (2024/38).

When evaluating patients presenting with chronic cough, the duration and nature of the cough (dry/wet), the presence of nocturnal awakenings, whether it worsens with exertion, such accompanying symptoms as nasal congestion, mouth breathing, and snoring, previous treatments for the cough, family history of atopy, and environmental exposures were questioned in detail in the medical history.

The demographic and clinical characteristics, diagnoses, and treatments of the patients were evaluated retrospectively from their medical records. Duration and nature of the cough, accompanying symptoms, familial history of atopy, environmental exposures, physical examination findings of the patients, and skin prick test (SPT) results, if any, were recorded.

Chronic cough was defined as the presence of a daily cough of more than four weeks (1). The approach and treatment of chronic cough were based on the CHEST Guideline and Expert Panel Report (1).

As stated in the European Respiratory Society guidelines, patients with chronic wet or productive cough, without specific cough markers, and those responding between 2-4 weeks of appropriate antibiotic treatment were diagnosed with PBB (7). The diagnosis of upper respiratory tract cough syndrome (UACS) was performed primarily in conditions affecting the upper respiratory tract, such as rhinitis (allergic or non-allergic), sinusitis (acute or chronic rhinosinusitis), and other nasal or pharyngeal inflammatory disorders (8). If the patient had a cough lasting longer than three weeks but not exceeding eight weeks following an acute upper respiratory tract infection, the diagnosis of post-infectious cough was considered (8).

The patients were divided into four groups according to their age: 0–2 years (infants and toddlers), 2–5 years (preschoolers), 5–12 years (school-age children), and over 12 years of age (adolescents).

All analyses were performed using the Statistical Package for Social Sciences Statistics for Windows, version 27.0 (SPSS, IBM Corp, Armonk, New York). Descriptive statistics were expressed as mean (SD) or median (range) for continuous variables and as case numbers (percentage) for nominal variables. The values were presented as medians (interquartile range [IQR]) for the data showing no normal distribution. The chi-square ($\chi 2$) test was used to compare nonparametric data; the Mann-Whitney U test was used in comparisons with non-normally distributed continuous data and the independent-samples t-test for normally distributed continuous data. A p-value of <0.05 was considered statistically significant.

Results

The study included a total of 267 patients, and 54.7% (n=146) of the patients were boys. The median age of the patients was 6.99 (IQR 4.47-11.54) years. When patients were evaluated according to age groups, 6.4% (n=17) were infants and toddlers, 23.2% (n=62) were pre-schoolers, 46.8% (n=125) were school-age children, and 23.6% (n=63) were adolescents.

The median duration of cough was eight (IQR 6-12) weeks. Of all patients, 47.6% (n=127) had a dry cough, and 52.4% (n=140) had a wet/productive cough.

Cough occurred mostly at night in 48.7% (n=130) of the patients, and 25.1% (n=67) had both daytime and

nocturnal cough. Nocturnal wake-ups occurred in 55.8% (n=149) of the patients, and exercise-induced cough was present in 70.4% (n=188) of the patients. Of all participants, 22.8% (n=61) had loud snoring, and 36% (n=96) had nasal congestion and mouth breathing. There was no significant difference between night waking-ups and exercise-induced cough among those with dry and wet cough (p=0.052, p=0.99, respectively). Snoring and nasal congestion were significantly higher in those with wet cough (p=0.041, p =0.014 respectively).

Regardless of the cough etiology, 67.8% (n=181) of the patients had received antibiotic treatment before applying to the pediatric allergy outpatient clinic, and 64.6% (n=117) received a single course of antibiotic treatment (69.2% with amoxicillin clavulanic acid, 18.8% with clarithromycin, 3.4% with azithromycin, and 8.5% with cephalosporins) while the remaining (n=64) were administered multiple courses. There was no significant difference in terms of antibiotic use between patients presenting with wet cough (72.9% (n=102)) and dry cough (62.2% (n=79)) before applying to the pediatric allergy clinic (p=0.063). In those with wet cough, the use of antibiotics more than once was observed more frequently (44.1%, n=45), compared with those with dry cough (24.1%, n=19 and p=0.005). Among those receiving a single course of antibiotic treatment, 42.7% (n=50) were treated for less than seven days, 45.3% (n=53) for seven-10 days, and 11.1% (n=13) for 11-14 days. Only one patient received treatment lasting more than 14 days.

Exposure to tobacco smoke was present in 40.1% (n=107) of the patients, and 30% (n=80) and 6.7% (n=18) were found to be exposed to pet dander and mold. There was no significant difference in terms of exposure to tobacco smoke, having a pet, and mold exposure among those with dry and wet cough (p=0.44, p=0.83, and p=0.21). The characteristics of patients with wet and dry cough are presented in Table 1.

Table 1. Characteristics of patients with wet and dry cough

	Dry Cough (n=127) (%)	Wet Cough (n=140) (%)	p-value
Age (years)	8.38 ± 4.4	7.62 ± 4.38	0.16
Duration of cough (weeks)	10.4 ± 6.3	11.5 ± 9.4	0.26
Nocturnal wake-ups	63 (49.6)	86 (61.4)	0.052
Exercise-induced cough	89 (70.6)	99 (70.7)	0.99
Nasal congestion	36 (28.3)	60 (42.9)	**0.014**
Snoring	22 (17.3)	39 (27.9)	**0.041**
Antibiotic use before allergy visit	79 (62.2)	102 (72.9)	0.063
Antibiotic use more than once	19 (24.1)	45 (44.1)	**0.005**
Exposure to smoking	54 (42.5)	53 (37.9)	0.44
Exposure to animal dander	39 (30.7)	41 (29.5)	0.83
Exposure to mold	6 (4.7)	12 (8.6)	0.21

Asthma (n=104) was the most common diagnosis in patients with chronic cough, followed by PBB (n=69) and upper airway cough syndrome (UACS) (n=59). Diagnoses of patients are summarized in Table 2. When the patients in the infant and toddler age groups were evaluated, the most common cause of chronic cough was PBB, whereas asthma was more frequently observed in older age groups. Concerning age groups, the etiology of chronic cough is shown in Table 3.

Table 2. Diagnoses of patients with chronic cough (n=267)

Diagnoses	n (%)
Asthma	104 (39)
PBB	69 (25.8)
UACS	59 (22.1)
Post-infectious cough	18 (6.7)
Reflux cough	4 (1.5)
Tic cough	3 (1.1)
Wheezy infant	3 (1.1)
Pneumonia	2 (0.7)
Congenital heart disease	1 (0.4)
Primary ciliary dyskinesia	1 (0.4)
Dysfunction of swallowing	1 (0.4)
Cystic fibrosis	1 (0.4)
Bronchiolitis obliterans	1(0.4)

PBB: Protracted bacterial bronchitis, UACS: Upper airway cough syndrome

Table 3. Etiology of chronic cough according to age groups

	Infants and Toddlers (n=17) (%)	Preschoolers (n=62) (%)	School-age children (n=125) (%)	Adolescents (n=63) (%)
Asthma	-	20 (32.3)	51 (40.8)	33 (52.4)
PBB*	11 (64.7)	13 (21)	38 (30.4)	7 (11.1)
UACS**	-	17 (27.4)	27 (21.6)	15 (23.8)
Post-infectious cough	2 (11.8)	7 (11.3)	4 (3.2)	5 (7.9)
Reflux cough	-	2 (3.2)	1 (0.8)	1 (1.6)
Tic cough	-	1 (1.6)	-	2 (3.2)
Pneumoniae	-	1 (1.6)	1 (0.8)	-
Congenital heart disease	-	-	1 (0.8)	-
Primary ciliary dyskinesia	-	1 (1.6)	-	-
Dysfunction of swallowing	-	-	1 (0.8)	-
Cystic fibrosis	1 (5.9)	-		-
Bronchiolitis obliterans	-	-	1 (0.8)	-
Wheezy infant	3 (17.6)	-		-

PBB: Protracted bacterial bronchitis, UACS: Upper airway cough syndrome

A previous history of chronic cough was found in 22.5% of the patients (n=60). Additionally, 83 patients (31.1%) had a history of bronchiolitis, and 122 patients (45.7%) had used salbutamol at least once in their lifetime. Even so, 28.8% (n=30) of the asthmatic patients had a previous history of chronic cough, and this rate was 18.4% (n=30) in patients with other diagnoses. While a history of previous bronchiolitis was present in 38.5% (n=40) of asthma patients and 26.4% (n=43) of patients with other diagnoses, 52.9% (n=55) of the patients with asthma and 41.1% (n=67) of the patients with other diagnoses had previous use of salbutamol. The history of chronic cough and the rate of previous bronchiolitis were significantly higher in patients diagnosed with asthma, (p=0.046 and p=0.038, respectively). However, no significant difference was found regarding the previous use of salbutamol (p=0.06).

Of the patients diagnosed with PBB, 39.1% (n=27) used no antibiotics during their chronic cough. Among those prescribed antibiotics (n=42), 64.3% (n=27) were found to receive a single course of antibiotic treatment, and the treatment duration was less than 14 days in all those patients.

When the patients were evaluated in terms of the characteristics of familial atopy, 20.2% (n=54) and 24.7% (n=66) were detected to have had a family history of asthma and allergic rhinitis, respectively. Asthma was also present in the mothers of 26 patients, in the fathers of 16 patients, and in the siblings of 12 patients. In those diagnosed with asthma, the familial history of asthma (26.9%, n=28) was significantly higher, compared to those with other diagnoses (16%, n=26 and p=0.03). However, there was no difference in the frequency of allergic rhinitis in the families of asthma patients (24%, n=25) and those with other diagnoses (25.2%, n=41 and p=0.84).

SPT was performed on 165 (61.8%) patients. At least one aeroallergen sensitization was detected in 48.5% (n=80) of the patients, and the findings of aeroallergen sensitization are shown in Figure 1. Eighty-four (51%) of the SPTs were performed on patients diagnosed with asthma, 30 (18.2%) on PBB patients, and 37 (22.4%) on UCAS patients. According to diagnoses, aeroallergen sensitization status was 54.8, 46.7, and 43.2% for asthma, PBB and UCAS, respectively. No significant difference was found between diagnoses in terms of aeroallergen sensitization (p=0.45).

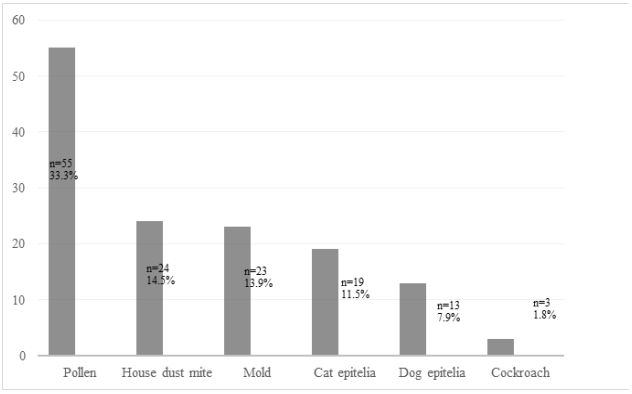

Figure 1. Aeroallergen sensitization of the patients

Physical examination findings of the patients are summarized in Table 4. The diagnosis of adenoid hypertrophy was carried out by ear nose and throat (ENT) specialists.

Table 4. Findings of physical examination of the patients

	n (%)
Oropharynx	
Tonsillar hyperemia/hypertrophy Postnasal drip	16 (6) 40 (15)
Ears	
Acute otitis media Serous otitis	8 (3) 3 (11.2)
Respiratory system	
Crackles Rhonchus Crackles and rhonchus	5 (1.9) 7 (2.6) 4 (1.5)
Cardiovascular system	
Cardiac murmur Situs in *versus* totalis	4 (1.5) 1 (0.4)
Pectus carinatum/excavatum Absence of pectoralis major	5 (1.9) 1 (0.4)
Adenoid hypertrophy	23 (8.6)

All patients with PBB were treated with antibiotics. The treatment of inhaled corticosteroids (ICSs) was initiated in 97.1% (n=101) of the patients with asthma. In other patients with asthma (n=3), treatment was started with montelukast. In addition to ICSs, 26 asthma patients also required antibiotics, 14 received antihistamines along with nasal steroids, four were treated with antihistamines and montelukast, and one patient was prescribed a proton pump inhibitor. In the treatment of UACS patients, antibiotics (n=23), antihistamines (n=42), nasal corticosteroids (n=32), and montelukast (n=19) were used in combinations. Two patients with confirmed pertussis infection were treated with macrolides; however, the other patients with post-infectious cough were followed up without treatment.

Discussion

The presented study provides a comprehensive analysis of pediatric patients presenting with chronic cough, highlighting the diverse etiologies, associated factors, and treatment approaches. In our study, the predominant diagnoses included asthma, PBB, and UACS.

In our study, asthma was identified as the leading cause of chronic cough among pediatric patients, accounting for 39% of the cases. Studies conducted in our country on chronic cough in children have also shown that asthma is the leading cause and responsible for 25 to 44% of chronic cough in pediatric patients (9-13). On the other hand, studies conducted by Marchant et al. and Chang et al. have identified PBB as the leading cause of chronic cough (14, 15). These discrepancies may be attributed to differences in study populations, diagnostic criteria, and regional variations in disease prevalence. Nonetheless, all studies emphasize the importance of considering multiple potential causes when evaluating chronic cough in pediatric patients.

In a large cohort study, Martinez et al. showed that recurrent wheezing in the first six years of life increased the risk of developing asthma later in childhood (16). Similarly, there was a significant association between the history of bronchiolitis and asthma in our study. In patients diagnosed with asthma, the familial history of asthma was significantly higher, compared to those with other diagnoses, which was an expected finding aligning with existing literature linking genetic predisposition to the development of asthma. Numerous studies have established that parental asthma significantly increases the likelihood of the condition in offspring.

PBB is a significant and often underrecognized cause of chronic wet cough in children responding typically to antibiotic treatment (17, 18). Although children with PBB are typically young, there have also been reports of children diagnosed with PBB at older ages (7, 19). PBB was also the second most common diagnosis in our study. Consistent with the literature, it was particularly prevalent in younger age groups while it was observed across all age groups.

Chang et al. demonstrated the importance of early antibiotic intervention in resolving symptoms of PBB and improving outcomes (20). In another study, it was emphasized that when PBB is left untreated, more severe conditions, such as bronchiectasis may occur (21). In our study, it was noteworthy that although about 70% of the patients with a chronic cough had received antibiotic treatment, a significant part of the patients with persistent bacterial bronchiolitis had either not prescribed antibiotic treatment or received it for a short time.

The use of evidence-based antibiotic protocols has proven to be beneficial not only in resolving acute symptoms but also in enhancing the overall QoL for affected children and reducing healthcare utilization. Given the potential for serious complications, early recognition and treatment of PBB remain crucial, underscoring the need for healthcare providers to distinguish the condition from other causes of chronic cough and ensure that children receive the appropriate course and duration of antibiotics (18,22).

UACS, previously known as postnasal drip syndrome, is characterized by a cough resulting from nasal or sinus pathology leading to upper airway irritation. In children, UACS is a significant cause of chronic cough and is often associated with allergic, non-allergic rhinitis, sinusitis, or adenoid hypertrophy (23,24). In our study, UACS was found to be the third most common cause of chronic cough in all children and the second most common cause in preschoolers and adolescents. Management typically involves treating the underlying nasal or sinus condition, which may include the use of antihistamines, nasal corticosteroids, or antibiotics, depending on the etiology (23).

In our study, PBB was identified as the primary cause of chronic cough in younger age groups, while asthma was more common in older age groups. Similarly, the literature reports that PBB is predominantly observed in younger children, whereas asthma is more frequently diagnosed in older ages (4,9,14). These findings highlight the importance of considering age-specific etiological differences during the diagnostic and treatment process.

Environmental factors, particularly exposure to tobacco smoke, are well-known contributors to respiratory symptoms in children (25,26). Our study found that 40.1% of the patients were exposed to tobacco smoke; however, there was no significant difference in terms of exposure to tobacco smoke among those with dry and wet coughs. Such a feature aligns with the existing literature demonstrating the detrimental effects of passive smoking on respiratory health and the exacerbation of chronic cough (27) . The association between environmental irritants

and respiratory symptoms, even in the absence of significant differences between cough types, highlights the need for public health initiatives aiming at reducing children's exposure to tobacco smoke and other pollutants

A detailed evaluation of children presenting with chronic cough is crucial, as it ensures that less common but potentially serious conditions are not overlooked. While asthma, PBB, and UACS are frequent causes of chronic cough, numerous other potential diagnoses require consideration. These include gastroesophageal reflux disease, primary ciliary dyskinesia, congenital airway abnormalities, and even conditions such as aspiration syndromes or immunodeficiency disorders (1). Missing these diagnoses can lead to significant morbidity, prolonged symptoms, and delayed treatment, potentially resulting in long-term damage to the respiratory system (5). Therefore, a comprehensive assessment including a thorough history, physical examination, and appropriate diagnostic testing is essential to identify or rule out these conditions. This approach not only guides the targeted therapy but also helps prevent unnecessary treatments, such as the overuse of antibiotics or corticosteroids. Recognizing and treating the full spectrum of possible causes for chronic cough can markedly improve a patient's outcomes and overall QoL (1,5).

A multi-disciplinary approach, involving collaboration between the specialists of pediatric allergy, pulmonology, ENT, and gastroenterology, appears advantageous for chronic cough management, especially in cases with overlapping etiologies (3). This strategy allows for comprehensive assessment and can reduce the need for unnecessary antibiotic treatments, which is a common issue in chronic cough management. Integrating findings from a multi-disciplinary framework can improve diagnostic accuracy, support early intervention, and potentially reduce healthcare costs associated with repeated consultations and inappropriate treatments (3).

In conclusion, chronic cough in children is a complex condition with diverse etiologies that vary significantly according to age group and require a detailed history and systematic approach to ensure effective diagnosis and management. Environmental assessments are also important to improve outcomes for pediatric patients with chronic cough.

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