ISSN 2458-8865 E-ISSN 2459-1505
www.fppc.com.tr
Family Practice and Palliative Care
https://doi.org/10.22391/fppc.391343

Original Article

Retrospective evaluation of patients hospitalized due to bronchial asthma during 1991-1995 at Dr. Sami Ulus Center for Pediatrics

1991-1995 yıllarında Dr. Sami Ulus Çocuk Sağlığı ve Hastalıkları Merkezi'ne yatan bronşial astımlı hastaların retrospektif değerlendirilmesi

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ABSTRACT

Introduction: Asthma is a heterogeneous disease characterized by chronic airway inflammation. Bronchial asthma is the most common chronic disease of childhood and is among the causes of frequent hospitalization in children. This study aims to describe the demographic and clinical characteristics of the patients hospitalized due to "bronchial asthma" within five years.

Methods: The hospital records of patients aged 0-15 years admitted with the diagnosis of bronchial asthma to the Dr. Sami Ulus Center for Pediatrics between 1991-1995 were examined. The sociodemographic characteristics, skin, and laboratory values of the patients and the medications they received were examined.

Results: Of the total 135 patients, 58.5% (n = 79) were males. The age distribution of the inpatients was mostly in the age group of 3-5 years (57.8%, n = 78). The mean annual hospitalization rate was 0.53%. Patients hospitalized for five days composed the largest group (39.3%, n = 53). Most of the hospitalized patients (74.1%; n = 100) were coming from urban settings. The most common pathologic condition on chest X-ray were increased aeration + infiltration (52%, n = 70). Sinusitis was accompanied to 78.5% of the hospitalizations. There was 50.4% (n = 68) leukocytosis in the hemograms. Most sensitive skin tests were mixed grass pollen and house dust. The primary medication used in prophylactic treatments was Ketotifen. Salbutamol was the most common medication used in the emergency department, theophylline and antibiotics for the bedside, and salbutamol syrup was the most prescribed medication for the discharged patients.

Conclusion: The greater proportion of male gender and 3-5 year-olds in the study group indicated that these risk factors were consistent with the previous literature. The similarity of annual admission rates within the years indicates that there is no change in asthma frequency in the population served over time. Even though the number of cases requiring antibiotics in bronchial asthma is high (similar to sinusitis), we believe that the use of antibiotics should be lowered.

Keywords: Child, asthma, epidemiology, antibiotics, atopy

ÖZ

Giriş: Astım, genellikle kronik hava yolu inflamasyonu ile karakterize heterojen bir hastalıktır. Bronşiyal astım çocukluk çağının en yaygın kronik hastalığıdır ve çocukların hastaneye sık yatış nedenleri arasındadır. Bu çalışma ile 5 yıllık bir süre içerisinde"Bronşiyal astım" tanısıyla hastaneye yatan hastaların demografik ve klinik özelliklerinin tanımlanarak değerlendirilmesi amaçlanmıştır.

Yöntem: Doktor Sami Ulus Çocuk Hastalıkları Merkezine, 1991-1995 yıllan arasında, Bronşiyal astım tanısıyla yatırılan 0-15 yaş arası hastaların kayıtları incelendi. Hastaların sosyodemografik özellikleri, deri ve laboratuvar değerleri ve aldıkları ilaç tedavileri incelendi.

Bulgular: Toplam 135 hastanın %58,5'i (n=79) erkekti. Hastaneye yatış yapılan hastalarda yaş dağılımı en çok %57,8 (n=78) ile 3-5 yaş grubuna aitti. Ortalama yıllık yatış oranı. %5,3 bulundu. Beş gün ve üzeri yatan hastalar en büyük grubu oluşturuyordu (%39,3; n=53). Yatan hastaların çoğu (%74,1; n=100) kentsel yerleşimliydi. Akciğer grafilerinde en sık görülen patolojik durum havalanma artışı + infiltrasyonun bir arada olduğu durumdu (%52; n=70). Sinüzit %78,5 oranda yatışlara eşlik ediyordu. Hemogramda %50,4 (n=68) lökositoz vardı. En çok duyarlı deri testleri, karma çayır polenleri ve ev tozuydu. Profilaktik tedavide öncelikle ketotifen kullanılıyordu. Acil serviste en fazla salbutamol, serviste teofilin ve antibiyotik; taburcu edilen hastalarda ise en fazla salbutamol şurup reçete edilmekteydi.

Sonuç: Araştırma grubunda erkek cinsiyetin ve 3-5 yaş grubunun daha fazla olması, bunların önceki literatürle uyumlu risk faktörleri olduğunu göstermiştir. Yıllık yatış oranlarının yıllara göre benzer olması, hastanenin hizmet verdiği popülasyonda astım sıklığında zamanla bir değişiklik olmadığını göstermektedir. Bronşiyal astımda sinüzit gibi antibiyotik kullanımını gerektiren durumlar fazla olmakla birlikte, yine de antibiyotik kullanım oranını düşürülmesi gerektiğine inanıyoruz.

Anahtar Kelimeler: Çocuk, astım, epidemiyoloji, antibiyotik, atopi

Submission: Feb 07, 2018 **Acceptance**: Apr 9, 2018 **E-mail**: ya_guclu@hotmail.com

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Introduction

Asthma is a heterogeneous disease characterized by chronic airway inflammation. It is defined by a history of symptoms such as variable expiratory flow restriction, wheezing, shortness of breath, chest compressions and cough, which may change in frequency and extent over time [1]. Asthma is the most common chronic disease of childhood and is the leading cause of childhood morbidity due to chronic illnesses measured by loss of school days, emergency room visits, and hospital admission [2,3]. The distribution of the disease varies between 1% and 18% between countries and between regions within countries [2,4–6]. Asthma can occur at any age, but the highest incidence is at childhood. More than half of patients with bronchial asthma (B. asthma) are reported to have symptoms starting in childhood [7]. In a study conducted with children in Turkey, the cumulative prevalence of asthma was reported as 14.7% and the prevalence of asthma in the 12-month age group as 2.8% [8].

Asthma starts in males earlier than in females [9–11]. The majority of asthmatic children over three years of age have atopy, and atopy is one of the most important risk factors for asthma development [12]. Nevertheless, no intervention has been shown to prevent the development of asthma or alter its long-term natural course [1].

Some viral infections (respiratory syncytial virus and rhinovirus) are associated with recurrent wheezing in childhood. However, wheezing in this age group is highly heterogeneous, and wheezing per se in this age group does not necessarily indicate asthma. In addition, many young children may wheeze during viral infections. Therefore, it is difficult to evaluate respiratory tract infections and wheezing as an initial or recurrent clinical presentation of childhood asthma [10,13].

This study aimed to describe the demographic and clinical characteristics of patients with asthma in a 5-year period.

Methods

This study examined the records of patients aged 0-15 years who were admitted to the Dr. Sami Ulus Center for Pediatrics, between 1991 and 1995 with a diagnosis of B. asthma.

From the examined records of patients; age, gender, duration of hospitalization, the status of prophylactic treatment before admission, factors predisposing to admission, region and socioeconomic status of the patient, skin test results, emergency and in-patient treatment, outpatient management, history of atopy, and used medications were recorded.

Statistical analysis

Analyzes of the study were done with the SPSS for Windows v.5.01. The data are presented in numbers and percentages.

Results

Between 1991 and 1995, 135 children aged 0-15 years were hospitalized and treated due to B. asthma attack in the Dr. Sami Ulus Center for Pediatrics.

Table 1 summarizes the distribution of sex, age groups, number of hospitalized days, place of residence, and health insurance according to years of the children with asthma in the period between 1991-1995 at the Dr. Sami Ulus Center for Pediatrics. Patients aged 3-5 years (57.8%,n = 56) were more than the other age groups.Of the patients, 58.5% (n=79) were boys, while 41.5% (n=56) were girls. The number of days of hospitalization ranged from 1 day (5.9%, n=8)to 5 days (39.3%, n=53). Patients from urban settlements constituted 74.1% (n = 100). The majority of patients (40%) had green card health insurance.

Table 2 shows hospitalization rates of asthmatic children for every 1000 hospitalized patients. Accordingly, the average annual asthma incidence per year between 1991 and 1995 was calculated as 5.3.

The proportion of those with atopy in their family was 35.5%. Thirty-nine of the patients with atopy in the family had B. asthma, five had allergic rhinitis, and seven had eczema.

Table 3 shows the evaluation of the laboratory results of the asthmatic patients. Pulmonary functions were normal in 52.0% (n = 14), while pathologic in the remaining patients. The most common pathologic condition was a combination of increased aeration + infiltration (52%, n = 70). Water's X-ray was found to be abnormal (significant aeration loss and/or mucosal thickening) in 78.5% of cases (n = 44). Sweat test, PPD, and electrolytes were within normal limits. 50.4% (n = 68) of the hemograms demonstrated leukocytosis with peripheral smears showing left shift in 44.0% (n = 59) and eosinophilia in 3.5% (n = 5). Eosinophilia was present in 67% (n = 14) of the nasal smears examined. High IgE was observed in 27.0% (n = 27) of the patients.

Table 1. Distribution of sex, age groups, number of hospitalized days, place of residence and health-care providers according to years (n = 135) in asthmatic children hospitalized between 1991-1995 at the Dr. Sami Ulus Center for Pediatrics.

	1991		1992		1993		1994		1995		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Sex												
Male	12	57.1	21	58.3	17	65.4	15	50.0	14	63.6	79	58.5
Female	9	42.9	15	41.7	9	34.6	15	50.0	8	36.4	56	41.5
Age groups												
0-2	3	14.3	12	33.3	6	23.1	10	33.3	8	36.4	39	28.9
3-5	15	71.4	20	55.6	18	69.2	15	50.0	10	45.5	78	57.8
6-15	3	14.3	4	11.1	2	7.7	5	16.7	4	18.1	18	13.3
Days hospitalized												
1	1	4.8	5	13.9	1	3.8	0	0.0	1	4.5	8	5.9
2	6	28.6	5	13.9	4	15.4	0	0.0	1	4.5	16	11.9
3	6	28.6	12	33.3	10	38.5	5	16.7	5	22.8	38	28.1
4	4	19.0	6	16.7	3	11.5	6	20.0	1	4.5	20	14.8
5 and more	4	19.0	8	22.2	8	30.8	19	63.3	14	63.7	53	39.3
Settlement												
Urban	14	66.7	25	69.4	20	76.9	24	80.0	17	77.3	100	74.1
Rural	7	33.3	11	30.6	6	23.1	6	20.0	5	22.7	35	25.9
Health coverage												
Self	11	52.4	6	16.7	8	30.8	14	46.7	7	31.8	46	34.1
Insured	6	28.6	10	27.7	7	26.9	7	23.3	5	22.7	35	25.9
Green card	4	19.0	20	55.6	11	42.3	9	30.0	10	45.5	54	40.0

Values represent column percentages.

Table 2. Admission rates of children aged between 0 and 15 years at the Dr.Sami Ulus Center for Pediatrics

Years	Number of total admissions	Number of asthma cases	Ratio (/thousand)
1991	4687	21	4.5
1992	5274	36	6.8
1993	5049	26	5.1
1994	5110	30	5.9
1995	5229	22	4.1
Total	25347	135	5.3

Table 3. Evaluation of laboratory results of asthmatic patients hospitalized between the years 1991-1995 at the Dr. Sami Ulus Center for Pediatrics.

			n	%
Chest X-ray	Increased aeration + infiltration		70	52.0
	Only increased aeration		50	37.0
	Atelectasis		1	0.7
	Normal		14	10.3
Water's graph	Abnormal		44	78.5
	Normal		12	21.5
Electrolytes	Abnormal		0	0.0
	Normal		135	100.0
Hemogram	Leucocyte	Normal	67	49.6
		Abnormal(Leukocytosis)	68	50.4
	Hemoglobin	Normal	123	91.0
		Düşük	12	9.0
	Peripheral smear	Normal	65	48.0
		Left shift	59	44.0
		Eosinophilia	5	3.5
		Lymphocytosis	6	4.5
Nasal smear	Eosinophil (+)		14	67.0
	Eosinophil (-)		7	33.0
Sweat test	Abnormal		0	0.0
	Normal		36	100.0
PPD	Abnormal		0	0.0
	Normal		58	100.0
IgE	Normal		46	73.0
	High		17	27.0

The first three skin tests in patients with bronchial asthma withthe highest positivity were tree pollen mixture (58%, n = 11), house dust mix (56%, n = 18), and animal hair(53%, n = 17) (Table 4).

Table 4. Assessment of skin tests seen in asthmatic children between 1991-1995 at the Dr. Sami Ulus Center forPediatrics

	Negative		Positive		
Skin tests	**n**	**%**	**n**	**%**	**Total**
Wool	7	53.8	6	46.2	13
Grass	18	47.4	20	52.6	38
Wood	8	42.1	11	57.9	19
House dust	14	43.8	18	56.2	32
Mushroom	7	50.0	7	50.0	14
Milk	22	50.0	22	50.0	44
Dermatophagoides	13	54.2	11	45.8	24
Animal hair	8	47.1	9	52.9	17
Other	21	53.8	18	46.2	39

Table 5 shows the treatment of asthmatic children with various conditions. 29.3% (n = 40) of the asthmatic patients received prophylactic treatment before hospitalization. Distribution of the prophylactic medications were as follows: 29 ketotifen, 6 Na-chromoglycate, 4 steroid inhalers and 1 immunotherapy. The most common medications applied in the emergency department were salbutamol (puff or nebulizer) (52%; n = 71) and adrenaline (36%; n = 49). Inpatients received most commonly theophylline (cofilin) syrup (92.6%; n = 125), antibiotics (85.0%, n = 115), aminophylline (66.6%; n = 90), and salbutamol (61.5%, n = 83) in the form of nebulizer or inhaler. The patients were discharged from the hospital most commonly on salbutamol syrup (85%, n = 115), theophylline syrup (74%; n = 100), and sodium cromoglycate (4.4%; n=6).

Table 5. Medications of the asthmatic patients in different settings (n=135)

Type of medication		n	%
Prophylactic	**Received**	40	29.3
	Ketotifen	29	
	Na-Cromoglycate	6	
	Steroid (inhaler)	4	
	Immunotherapy	1	
	Did not receive	95	70.7
Emergency ward	Adrenaline	49	36.0
	Steroid (IVP,2 mg/kg)	34	29.0
	Salbutamol	71	52.0
	Aminophylline(IVP)	15	11.0
Inpatient wards	Aminophylline (Infusion)	90	66.6
	Steroid (IVP)	45	33.0
	Steroid (oral)	17	12.6
	Salbutamol (nebulizer, puff, or inhaler)	83	61.5
	Salbutamol (syrup)	25	18.5
	Theophylline (cofilin) syrup	125	92.6
	Antibiotics	115	85.0
Discharge	Steroid tabletsor inhaler	14	10.4
	Ketotifen syrup	37	27.0
	Salbutamol syrup	115	85.0
	Theophyllinesyrup (cofilin)	100	74.0
	Na-Cromoglycate	6	4.4
	Antibiotics	97	72.0

IVP: Intravenous perfusion.

Children with asthma included in this study were invited for control in the allergy policlinics within 7-10 days after being discharged from the hospital. Of the patients, 67% (n = 90) came to the control and had their follow-up.

Discussion

In this study, the health records of children who were hospitalized were investigated in a period of five years, and descriptive statistics of the patients' socio-demographic, laboratory and medication records were analyzed to support the hypothesis about the etiology of the disease and/or to contribute to new hypotheses.

In this study, the percentage of male gender of asthmatic patients was higher than that of females. In a study conducted in the Portland area from 1966 to 1987, 0 to 4 age group was the most common age among 0 to 14-year-old children with asthma. Males constituted 70% of the 0-4-year-old patients, while the proportion of males among the 5-14-year-old decreased to 62%, and finally equalized with the girls during adolescence [14]. Again in a hospital-based study in 2012, the male gender ratio among asthmatic children aged 7-14 years was reported as 67%[15]. Childhood asthma is more common among boys. This is because the respiratory tract in men is narrower and has higher tonus, which can easily cause

difficulties in the airflow due to various effects. Since the difference in diameter equalizes between sexes after age 10, so does the prevalence of the disease [3]. Our results are consistent with these studies.

In our study, the five-year average hospitalization rate of children with asthma was found at 5.3%. This rate increased from 7.1% in 1969 to 13.5% in 1982 in New Zealand. Between 1974 and 1983 in Canada, there was a two-fold increase[16,17]. In the study conducted by Burt Gerstman and colleagues, the rate of childhood asthma among children aged 5-14 years increased from 2.3% in 1980 to 4.5% in 1984 but decreased during the following years. While the prevalence was 2.2% in 1980 among the 10-14 years aged, this ratio increased to 3.2% in 1984 and became 3% in 1986 [18]. In a study conducted in Boston in 1992, the hospitalization rate for asthmatic children was reported as 4.2% [19].
While significant increases in asthma hospitalization have been reported in many countries, there was no such increase during our study period. Most of the asthmatic patients hospitalized in our hospital were generally severely ill, and they were residing in the low socioeconomic areas of the city. Having received not many light cases may be due to the availability and easy access to the many private clinics in the area, who were dealing mainly with light cases. As a matter of fact, a similar reduction in hospitalization has been reported in a study in Finland as a result of private outpatient clinics, especially providing nebulizer treatment[20].

More than half of the patients in this study were between the ages of 3-5 years. We find it noteworthy to think about the reasons of this change over the years. The risk group for each year is age 3-5. Several studies have reported that B. asthma symptoms start in the majority of patients before age five[21]. The rate of hospitalization among asthmatic children in the community is particularly high in the 0-5 age group [16,22]. Our findings are consistent with other studies in this area.

Asthmatic children who were admitted to our hospital for more than five days constitute the largest group with 39.3%. A study of asthmatic children in the Portland area between 1966 and 1987 showed that hospital stay was as follows: 1 day 82%, 2-3 days 7.4%, five days 6%, and more than six days 5% [14]. Since most of the inpatients were not well-trained and educated, the length of the hospitalization can be regarded as an opportunity to provide both the necessary training and do the necessary examinations. When compared, the duration of hospitalization of our patients is longer than others reported in the literature.

More than two-thirds of patients with bronchial asthma were located in urban areas. There are differences in asthma prevalence between urban and rural areas according to different studies [23–25]. Breastfeeding is longer in the rural area; in this way, the risk of developing a cow's milk allergy is reduced. In urban life, environmental pollution, warming, and fuels of motor vehicles, and house dust mites allergens increase the risk of asthma [3]. In America, asthma rates are higher in urban areas. This is attributed to the large black population living in urban settings. There is also an increase in admissions because the health care system cannot provide the necessary care and education [18].

In other studies, asthma prevalence was found to be low in children who were raised in high-income families and high among children of families earning below the poverty line. Weitzmann et al. reported that asthma rates were higher in poor and black children who were primarily dependent on social and economic support [22,26]. The majority of the cases coming from urban and suburban settlements are consistent with the above-mentioned general findings.

About half of the patients with asthma who were hospitalized were green card owners. Thus, we can claim that most of the patients included in this study constitute patients from the low-income community. As mentioned in many studies, asthma prevalence and hospitalization rates are higher in the low-income segments [18,22,26].

Many patients had a family history of atopy. An important clue in the diagnosis of B. asthma is the presence of other allergy-related diseases such as asthma, allergic eyes, hay fever, or eczema in the family. Many authors have reported familial atopy as more than 50%. There is no doubt about genetic susceptibility. However, predisposition does not always lead to the disease;different grades of severity and different clinical pictures may appear in the genealogy [3,27,28].

Since the infiltrative appearance of bronchial asthma may be related to small atelectatic areas due to mucus plugs, it is more appropriate not to start antibiotics in the absence of leukocytosis, leftshift, and sinusitis. The use of antibiotics in our study patients was usually limited to such patients. Besides, chest X-ray routines may not be required in each attack if there is no obvious pathology in patients with prior follow-up and available chest X-ray. The second important issue is the high prevalence of abnormal sinus findings. Compatible with the literature, sinusitis adversely affects asthma [29]. IgE and nasal smears are not discriminant but merely supportive indicators.

Allergens that mostlydisturb allergic asthmatics are house dust mites. These are small creaturesresembling cockroaches or heater bugs, which are not seeable by the naked eye. Approximately 60% of allergic asthmatics in Turkey are sensitive to insects. The most common types of these creatures are Dermatophagoides pteronyssinus (Dpt) and Dermatophagoides farinea (Df). The most common type in Turkey is Dpt [3].

In the study of Arslan et al. [30], house dust (31.7%), mixed grass (2.2%), wood (4.8%) and cat hair (2.4%) constitute the most common allergens in the skin tests. Blok et al.'s study, on the other hand, demonstrated sensitivities to house dust (43%), grass (21%), wood (16%), cat hair (20%), and weeds (4%). In a study conducted in Yedikule Chest Diseases Hospital, skin tests were found to be positive in 23.8% of the cases, and they claimed that dermatofhagoides were the most common antigens among B. asthmatic patients in Turkey. Mites, grass, mold, and woodwere the most common antigens in a study of skin tests done in the USA. Supported by most studies, it is concluded that screening for house dust and mixed grass pollen can be sufficient, which complies with our work.

One-third of the patients were receiving prophylactic treatment, and the vast majorities were using ketotifen. In addition, the majority of our study population was between the ages of 3 and 5 years. There were difficulties in the supply of nebulizer and inhalermedications due to the disadvantaged socioeconomic status of the patients. Additionally, the soothing effects of ketotifen in allergic rhinitis, urticaria, and food allergy, as well as the ease of oral use have been the reasons for this preference. In children at an appropriate age, who may be more cooperative, cromolyn and steroids may be used more frequently with a spacer device.

The most common treatments in the emergency department were salbutamol (puff, nebulizer), adrenaline, intravenous perfusion (IVP) steroid at a dose of 2 mg/kg, and IVPaminophylline. The severity of asthma should be categorized at the emergency ward as mild, moderate, or severe and the peak flow value should be recorded. The treatment should be tailored accordingly[31]. In moderately severe asthmatics suffering from acute exacerbations, steroidsusually achieve control of the symptoms, improvement in lung functions, and a reduction in bronchial hyperresponsiveness. Oralprednisolone initiated in the emergency department reduces the hospitalization rate. Oral administration is as effective as the intravenous route. However, there is no increased benefit at doses above 2 mg/kg [32]. It has been noted that the use of aminophylline in addition to steroids and beta agonists (inhaler) does not provide additional benefit [33].

The frequency of antibiotic use increases parallel to the frequency of sinusitis. However, considering the other available data, it is observed that there is an excess in the use of antibiotics.

Of the patients, 67% came to their control visits. In the United States, 76% of the 348 patients followed closely in a university hospital came to their follow-ups and 19% of them were followed up more frequently[27]. Standardized history-taking, spirometer measurements, histamine provocation test, and skin tests are used during the follow-up and diagnosis [27,34]. In our study, 1/3rdof the patients did not come for follow up. Patients under regular follow-up are less likely to have sudden attacks, also giving the medical team an opportunity for patient and family education.

Conclusion

Consistent with the previous literature, male sex, and 3-5-year-old age group were observed as likely risk factors. Doctors should consider this finding when serving their patients. The similarity of annual admission rates during the studied years indicates that there is no change in asthma frequency in the population over time. For a chronic disease such as asthma, the high number of hospitalizations isimportant concerning the compliance with treatment as well as increased health expenses. However, effort should be given to reduce the number of hospitalization days. To avoid the use of high and unnecessary antibiotics, treatments must be implemented according to the rules of rational antibiotic use. Training and awareness programs for doctors, patients and pharmacists should be conducted in this regard. Patients should be avoided from known allergens, for which patient and family educations are invaluable.

Conflict of interest: None
Financial disclosure: None

References

1. Global Initiative For Asthma (GINA). Global Strategy For Asthma Management and Prevention. Glob Initiat Asthma 2017:http://ginasthma.org/2017-gina-report-global-strat. doi: https://doi.org/10.1183/09031936.00138707
2. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: Executive summary of the GINA Dissemination Committee Report. Allergy Eur J Allergy Clin Immunol 2004;59:469–78. doi: https://doi.org/10.1111/j.1398-9995.2004.00526.x
3. Barış IY. Epidemiyoloji. In: Barış IY, editor. Bronchial asthsı. 1st ed. Ankara: Türkiye akciğer hastalıkarı vakfı yayınları; 1991, p. 1–7.
4. Sağlık Bakanlığı Temel Sağlık Hizmetleri Genel Müdürlüğü. Chronic airway disease (Asthma-COPD) prevention program, action plan, Turkey (2009-2013). Ankara: Kuban Matbaacılık; 2009.
5. Hamzaçebi H, Ünsal M, Kayhan S, Bilgin S, Ercan S. Prevalence of asthma and respiratory symptoms by age, gender and smoking behaviour in Samsun, North Anatolia Turkey 2006;54:322–9.
6. Akcay A, Tamay Z, Dağdeviren E, Zencir M, Ones U, Güler N. Denizli 'deki 6-7 yaş okul çocuklarında allerjik hastalıklarının prevalansları. The prevalences of allergic diseases symptoms among 6-7 yr-old school children in Denizli. Ege Tıp Derg 2007;46:145–50.
7. Simpson CR, Sheikh A. Trends in the epidemiology of asthma in England: A national study of 333,294 patients. J R Soc Med 2010;103:98–106. doi: https://doi.org/10.1258/jrsm.2009.090348
8. Türktaş H, Türktaş İ. Bronchial asthma in children. 1st ed. Ankara: Bozkır matbaacılık; 1998.
9. Bisgaard H, Szefler S. Prevalence of asthma-like symptoms in young children. Pediatr Pulmonol 2007;42:723–8. doi: https://doi.org/10.1002/ppul.20644
10. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and Wheezing in the First Six Years of Life. N Engl J Med 1995;332:133–8. doi: https://doi.org/10.1056/NEJM199501193320301
11. Kuehni CE, Strippoli MPF, Low N, Brooke AM, Silverman M. Wheeze and asthma prevalence and related health-service use in white and south Asian pre-schoolchildren in the United Kingdom. Clin Exp Allergy 2007;37:1738–46. doi: https://doi.org/10.1111/j.1365-2222.2007.02784.x
12. Sly PD, Boner AL, Björksten B, et al. Early identification of atopy in the prediction of persistent asthma in children. Lancet 2008;372:1100–6. doi: https://doi.org/10.1016/S0140-6736(08)61451-8

13. Caudri D, Wijga A, A. Schipper CM, et al. Predicting the long-term prognosis of children with symptoms suggestive of asthma at preschool age. J Allergy Clin Immunol 2009;124. doi: https://doi.org/10.1016/j.jaci.2009.06.045
14. Vollmer WM, Osborne ML, Buist AS. Temporal trends in hospital-based episodes of asthma care in a health maintenance organization. Am Rev Respir Dis 1993;147:347–53. doi: https://doi.org/10.1164/ajrccm/147.2.347
15. Yakari S. Assessment of asthma risk factors in children with food allergy. Hacettepe Üniversitesi Tıp Fakültesi, 2012.
16. Friday GA, Fireman P. Morbidity and mortality of asthma. Pediatr Clin North Am 1988;35:1149–62. doi: https://doi.org/10.1016/S0031-3955(16)36554-3
17. Parks DP, Ahrens RC, Humphries CT, Weinberger MM. Chronic cough in childhood: approach to diagnosis and treatment. J Pediatr 1989;115:856–62.
18. Gerstman BB, Bosco LA, Tomita DK. Trends in the prevalence of asthma hospitalization in the 5- to 14-year-old Michigan Medicaid population, 1980 to 1986. J Allergy Clin Immunol 1993;91:838–43. doi: https://doi.org/10.1016/0091-6749(93)90340-L
19. Gottlieb DJ, Beiser AS, O'Connor GT. Poverty, race, and medication use are correlates of asthma hospitalization rates: A small area analysis in Boston. Chest 1995;108:28–35. doi: https://doi.org/10.1378/chest.108.1.28
20. National institutes of Health. Global Strategy for Asthma Management and Prevention. 1995.
21. Mutlu B, Balcı S. Asthma risk factors, clinical features, and prevention in children. TAF Prev Med Bull 2010;9:79–96.
22. Arshad SH, Matthews S, Gant C, Hide DW. Effect of allergen avoidance on development of allergic disorders in infancy. Lancet 1992;339:1493–7. doi: https://doi.org/10.1016/0140-6736(92)91260-F
23. Valet RS, Gebretsadik T, Carroll KN, et al. High asthma prevalence and increased morbidity among rural children in a Medicaid cohort. Ann Allergy, Asthma Immunol 2011;106:467–73. doi: https://doi.org/10.1016/j.anai.2011.02.013
24. Lawson JA, Janssen I, Bruner MW, Madani K, Pickett W. Urban-rural differences in asthma prevalence among young people in Canada: The roles of health behaviors and obesity. Ann Allergy, Asthma Immunol 2011;107:220–8. doi: https://doi.org/10.1016/j.anai.2011.06.014
25. Pesek RD, Vargas PA, Halterman JS, Jones SM, McCracken A, Perry TT. A comparison of asthma prevalence and morbidity between rural and urban schoolchildren in Arkansas. Ann Allergy, Asthma Immunol 2010;104:125–31. doi: https://doi.org/10.1016/j.anai.2009.11.038
26. Taylor WR, Newacheck PW. Impact of childhood asthma on health. Pediatrics 1992;90:657–62.
27. Roorda RJ, Gerritsen J, Vanaalderen WMC, et al. Risk-Factors for the Persistence of Respiratory Symptoms in Childhood Asthma. Am Rev Respir Dis 1993;148:1490–5. doi: https://doi.org/10.1164/ajrccm/148.6_Pt_1.1490
28. Reed CE. The natural history of asthma. J Allergy Clin Immunol 2006;118:543–8. doi: https://doi.org/10.1016/j.jaci.2006.06.020
29. Rachelefsky GS, Katz RM, Siegfel SC. Chronic sinus disease with associated reactive airway disease in children. Pediatrics 1984;73:526–9.
30. Arslan Z, Teziç T, Laleli Y, Yurdakul A, Evliyaoğlu O. The value of diagnostic methods in airway allergy. Turkiye Klin J Pediatr 1993;2(3):132-135.
31. Seber O. Pulmonary function tests in asthma. In: Barış İY, editor. Bronş astması., Ankara: Türkiye akciğer hastalıkarı vakfı yayınları; 1991, p. 117–41.
32. Scarfone RJ, Fuchs SM, Nager AL, Shane SA. Controlled trial of oral prednisone in the emergency department treatment of children with acute asthma. Pediatrics 1993;92:513–8.
33. Strauss RE, Wertheim DL, Bonagura VR, Valacer DJ. Aminophylline therapy does not improve outcome and increases adverse effects in children hospitalized with acute asthmatic exacerbations. Pediatrics 1994;93:205–10.
34. Roorda RJ, Gerritsen J, van Aalderen WM, et al. Follow-up of asthma from childhood to adulthood: influence of potential childhood risk factors on the outcome of pulmonary function and bronchial responsiveness in adulthood. J Allergy Clin Immunol 1994;93:575–84. Doi: https://dx.doi.org/10.1016/S0091-6749(94)70069-9