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ORIGINAL RESEARCH

Prevalence and Characteristics of Self-Reported Adult Asthma in Cyprus: A Population-Based Observational Study

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Purpose: To estimate the prevalence of asthma in adults, by gender and age, in urban and rural areas of Cyprus.

Patients and Methods: This was a population-based, random-digit dialing, telephone nation-wide survey to recruit patients with asthma. Among 8996 random landline-telephone contacted from the five major urban and rural regions of Cyprus, 1914 were finally met the age criterion of ≥18 years old and 572 completed valid screening for prevalence estimation. The participants filled a short screening questionnaire in order for asthma cases to be recognized. Then, asthma cases filled the main ECRHS II questionnaire and were evaluated by a pulmonary physician. All underwent spirometry. Data on demographic characteristics, educational level, profession, smoking status, Body Mass Index (BMI), Total IgE and Eosinophil Cationic Protein levels were measured.

Results: The overall prevalence of bronchial asthma in adults in Cyprus was 5.57% (61.1% men and 38.9% women). Among the participants with self-reported bronchial asthma 36.1% were current smokers, while 12.3% were obese (BMI >30). A total value of IgE >115 IU and Eosinophil Cationic Protein (ECP) >20 IU was found in 40% of the participants with established bronchial asthma. Wheezing and chest tightness were the most frequently reported symptoms in asthma patients (36.1% and 34.5%, respectively), while 36.5% experienced at least one exacerbation during the last year. Interestingly, most of the patients were under-treated (14.2% were on maintenance asthma treatment, and 18% used solely reliever medication).

Conclusion: This was the first study estimating asthma prevalence in Cyprus. Asthma affects almost 6% of the adult population, with higher prevalence in urban areas and in men compared to women. Interestingly, one-third of the patients were uncontrolled and under-treated. This study revealed that in Cyprus there is space for improvement in the management of asthma.

Keywords: asthma, allergy, prevalence, Cyprus

Introduction

Asthma is a heterogeneous lung disease with different phenotypes, characterized by airway inflammation, reversible airflow limitation[1] and various respiratory symptoms. Asthma remains a major health problem world-wide affecting 1–18% of the population in different countries.[1] According to GINA and the European Community Respiratory Health Survey (ECHRS) and International Study of Asthma and Allergies in children (ISAAC) studies, it is expected that 400 million people of all ages will suffer from bronchial asthma by the year 2025.[1–5]

ISAAC the and ECRHS, two multicenter studies, have confirmed the variations of bronchial asthma worldwide in prevalence and manifestation. Prevalence of asthma ranged from 0.7% in Macau, 2% to 3.3% in Estonia, Germany, Spain, Austria and Algeria, 8% to 11.9% in the United Kingdom, New Zealand, and Australia, and 18.4% in Scotland.[2–5] Similarly, the prevalence of asthma-like symptoms varied across countries; wheeze ranged from 4.1% to 9.7% in India, Algeria and Italy, 19% in Greece, 23% to 32% in Sweden, Estonia, Denmark, USA, UK, Ireland and Australia.[6–11] An

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additional survey, designed by the World Health Organization (WHO) in 70 countries, the World Health Survey (WHS) estimated that the global prevalence of clinical/treated asthma in adults aged 18–45 was 4.5% (178.215 participants).[11]

A recent population-based, random-digit dialing, telephone nationwide survey in Greece revealed that the lifetime self-reported prevalence of asthma was 9.10%.[7] Up to now, limited data exist on asthma prevalence in Cyprus. The first study investigating the prevalence of asthma and allergies in children, using the ISAAC questionnaire, revealed an overall prevalence of 6.9%.[12] However, little data exist on adult asthma. In 2008, the National Statistical Service of Cyprus estimated that self-reported asthma prevalence was 5.1%.[13] However, this percentage is expected to be higher given the increase of asthma prevalence worldwide along with asthma diagnosis improvement.[14–17] The fact that the prevalence of asthma and allergic diseases, in Cyprus is on the rise was initially shown in the paediatric population by Kolokotroni et al nearly ten years ago.[18] Several risk factors for asthma development in Cyprus were acknowledged by these authors and others mainly pointing to environmental and lifestyle determinants.[19–21] Furthermore, a recent study on asthma economic burden in Cyprus estimated that the mean asthma patient cost was €579.64 with indirect costs accounting for 17.92% of the overall health expenses.[22] Thus, it is particularly important to estimate the prevalence of asthma in adults, as this is directly linked to the economic burden of the disease and could further guide the national policy of the Cyprus Healthcare System.

The aim of our study was to estimate the prevalence of bronchial asthma in adults by age and gender, in urban and rural areas of Cyprus. Data on demographic characteristics, educational level, profession, smoking status, asthma symptoms, total IgE levels and ECP values were collected to better recognize the main characteristics of the disease in the Greek-Cypriot population.

Patients and Methods

This two-stage report-based study covered a wide geographical range of Cyprus and a total population of more than 865,000 Greek-Cypriots, aged ≥18 years. The classification of the population by gender and region, urban and rural, was based on the geographical distribution of the population stated in the annual demographic report of the Statistical Service of Cyprus.[14] The study population was allocated to the five geographical regions of the Republic of Cyprus; Nicosia Larnaca, Paphos, Limassol and Ammochostos. The Nicosia region included a total population of 336,900 people; Limassol included 241,830; Larnaca 147,200; Paphos 91,940 and Ammochostos 47,900 people. The total number of inhabitants and number of subjects that completed the first screening per geographical region are shown in Figure 1 and Table 1.

Figure 2 illustrates the study consort diagram. Individuals were randomly selected using the telephone directory of Cyprus (comprises more than 90% of households-population). A random-digit telephone dialing was used, and more than

Figure 1 The study population was allocated to the five geographical regions of Cyprus; Nicosia Larnaca, Paphos, Limassol and Ammochostos. In the map of Cyprus total number of inhabitants and number of subjects that completed the first screening are shown per geographical region.

Table 1 The Table Shows the Total Number of Inhabitants and of Participants Completed the First Screening (in Brackets) in Urban and Rural Areas of the Five Geographical Regions of Cyprus

	Urban	Rural
	Number of inhabitants (number completed first screening)	
Paphos	64,894 (150)	27,100 (62)
Larnaka	86,700 (200)	60,500 (140)
Ammochostos	–	47,900 (111)
Limassol	184,100 (425)	57,730 (134)
Total number 865,824 (2000)	582,094 (1344)	283,730 (656)

8900 telephone calls were attempted to define the final participant number. A random-digit telephone dialing was used, and more than 8900 telephone calls were attempted. Our aim was to define the final participants' number. Phone calls were attempted between 28/9/2016 and 16/11/2016 and a total number of 1914 (21.3%) participants met the age criterion. All individuals completed an informed consent form and thereafter answered a screening questionnaire in Greek based on the ECRHS survey questionnaire (Appendix 1 and 2).[23]

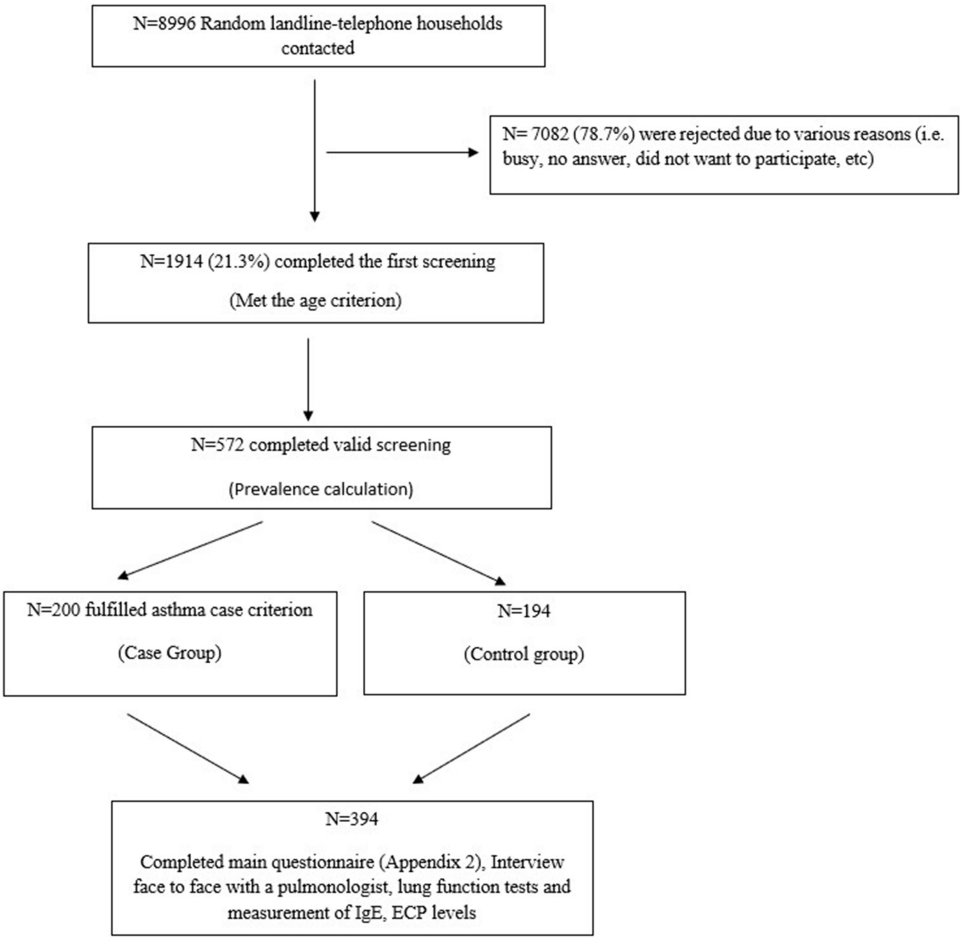

Figure 2 Study consort diagram.

Valid screening was completed in 572 participants. Since we had a representative sample size of the population at the first stage of the survey, we matched the potential asthma patients with a control that bears the same demographic characteristics in a second stage of analysis, given the original strata we used at stage 1. The inclusion criteria for the case group were any positive answer of the first seven questions of the screening questionnaire (Appendix 1). Individuals with negative answers to the above questions were allocated to the control group of the study. Each group was comprised of 200 and 194 individuals, respectively, so as gender, urban and rural regions of Cyprus, and geographical characteristics of the five regions to be represented.

For all eligible participants (N = 394) from both groups (case and control) an appointment was fixed with a respiratory physician at the Respiratory Department of Nicosia General Hospital, or regional hospitals (Limassol, Paphos and Larnaca Pulmonary Clinics) at each participating region of Cyprus. Exclusion criteria for the second phase of the study were only pregnancy and age ≤18 years old. During this visit, each participant signed an informed consent. All individuals answered a detailed main questionnaire of 47 questions in Greek (interview with pulmonologist face to face) based on the ECRHS II survey.[23] This included questions on demographics, occupational interests, asthma-like symptoms, comorbidities treated or untreated, allergy and smoking history.

Thereafter, each participant underwent lung function testing – spirometry before and after bronchodilation. All tests were performed with portable spirometers (Spirolab II), according to the American Thoracic Society (ATS) and European Respiratory Society (ERS) recommendations.[24] The spirometers were calibrated with a 3-Liter syringe (calibration limits of ±3%) daily. The individuals performed up to eight forced expiratory maneuvers until achieving three acceptable lung function tests with the best values of forced expiratory volume at the first second of expiration (FEV_1) and forced vital capacity (FVC).[24] The post bronchodilation lung function tests were performed 15 minutes after the inhalation of 400μg salbutamol (Inh Ventolin; Glaxo Smith Kline) via a spacer device. All the participants underwent blood analyses for the measurement of total IgE and Eosinophil Cationic Protein (ECP).

The prevalence of asthma among the eligible study population was defined according to the medical history of the participants, lung function tests (spirometry, pre and post bronchodilation) and GINA criteria,[1] measurement of total IgE and Eosinophil Cationic Protein levels.[25,26]

Statistical Analysis

For the statistical analysis of the data, all the answers were coded to proceed in statistical processing with the statistical program IBM SPSS Statistics v25. The statistical analysis of the survey data at the descriptive level included: tables of frequency distribution of the answers of the respondents when the variables were nominal and means (standard deviation) when the variables were continuous. In all cases of statistical tests, $\alpha = 0.05$ was used as the minimum level of statistical significance and the value was rounded to 3 decimal places.

Results

A total of 8996 individuals were contacted by phone. Of those, 7082 subjects (78.7%) did not answer the phone at all or did not give their consent to participate in the survey. A total of 1914 individuals (21.3%) participated in the first stage of the study (Figure 2). Most of the participants were men (62.4%). The mean age of the study population was 48.5 years old and the mean body mass index (BMI) was 27.1. Among the participants, 55.4% lived in urban areas whereas 44.6% lived in rural areas. Regarding the educational status of the participants 9.4% had completed primary school, 29.8% high school and 51% had a University degree. Regarding occupation, 8.2% were unemployed, 36.7% were employed in the private sector, 17.6% were government employees, and 17.1% were pensioners. One-third (33%) of the study population were current smokers (pack-years 29±11, mean±SD), and one-fifth (21%) were ex-smokers (pack-years 32±15, mean±SD). One out of four (24.8%) reported any type of allergies (asthma, rhinitis, dermatitis, eczema, conjunctivitis) while 327 (17.1%) reported an asthma diagnosis by a physician (Figure 3).

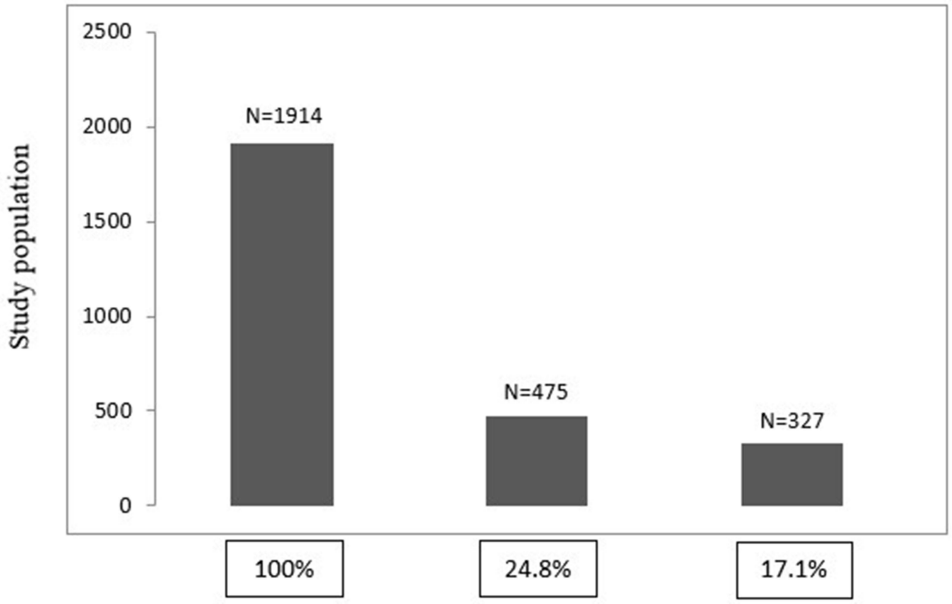

Figure 3 Self-reported history of allergy and asthma in those completed the first screening (N = 1914). One out of four (24.8%) reported any type of allergies (asthma, rhinitis, dermatitis, eczema, conjunctivitis) while 17.1% had asthma confirmation by a physician.

Respiratory Symptoms and Characteristics of the Subjects with Self-Reported Asthma (First Stage of the Survey)

Bronchial asthma prevalence was higher in men (61%) than in women (39%), and in the age group of 41–59 years (41.7%) as compared to age groups ≤40 years old (27.8%) and ≥60 years old (30.6%). Among the participants with self-reported asthma 36.1% were current smokers. Forty percent of them had IgE levels higher than 115 IU, and Eosinophil Cationic Protein (ECP) higher than 20 IU. For the participants in whom asthma was not evident, these percentages were 26.3% and 21.3%, respectively.

Self-reported respiratory symptoms in those completed the first screening (N = 1914) and those with asthma confirmed by a physician (N = 327) are shown in Figure 4. Wheezing and chest tightness were the most frequently reported symptoms in asthma patients (36.1% and 34.5%, respectively), with early morning dyspnea occurring in 25.3% and night awakenings due to respiratory symptoms occurring in 13.7%. Self-reported symptoms were statistically significantly more evident in asthma patients compared to these reported in the population of the first screening (Figure 4). Of note, although 86.5% of participants with self-reported asthma had a diagnosis by a physician, only 14.2% were on maintenance asthma treatment, and 18% used solely reliever medication. Among asthma patients, 36.5% experienced at least one exacerbation during the last year (Figure 5). Furthermore, it is interesting that the diagnosis and follow-up of asthma was made by a respiratory physician in half of the cases, while the rest were assessed by physicians of internal medicine (32.1%), general practitioners (9%), allergists (5.5%), or physicians of some other specialty (3.5%) (Figure 6).

Asthma Prevalence

The overall prevalence of bronchial asthma in adults estimated as 5.57% and was defined according to the medical history of the participants (screening and main questionnaires), lung function tests (spirometry pre and post bronchodilation, GINA criteria).[1,17,18]

Anthropometric characteristics and descriptive statistics of the study population (394 subjects) are shown in Table 2. The spirometric measurements, and measurements of total IgE, and ECP in the matched case-control groups (n = 394) are shown in Table 3.

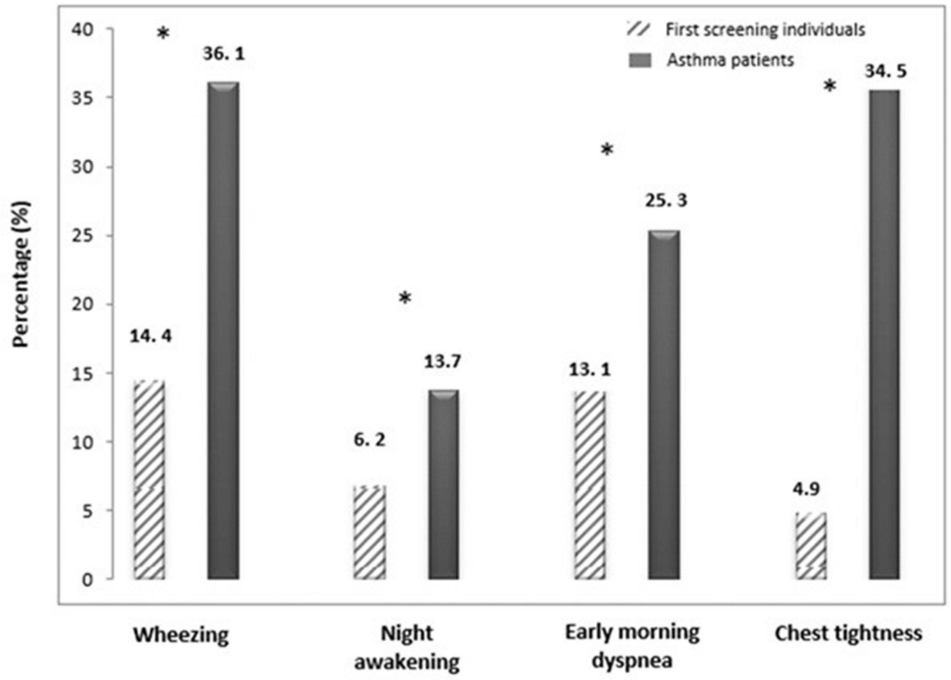

Figure 4 Self-reported respiratory symptoms in those completed the first screening (N = 1914) and those with self-reported asthma (N = 327). *Indicates statistical significant difference, $p < 0.05$.

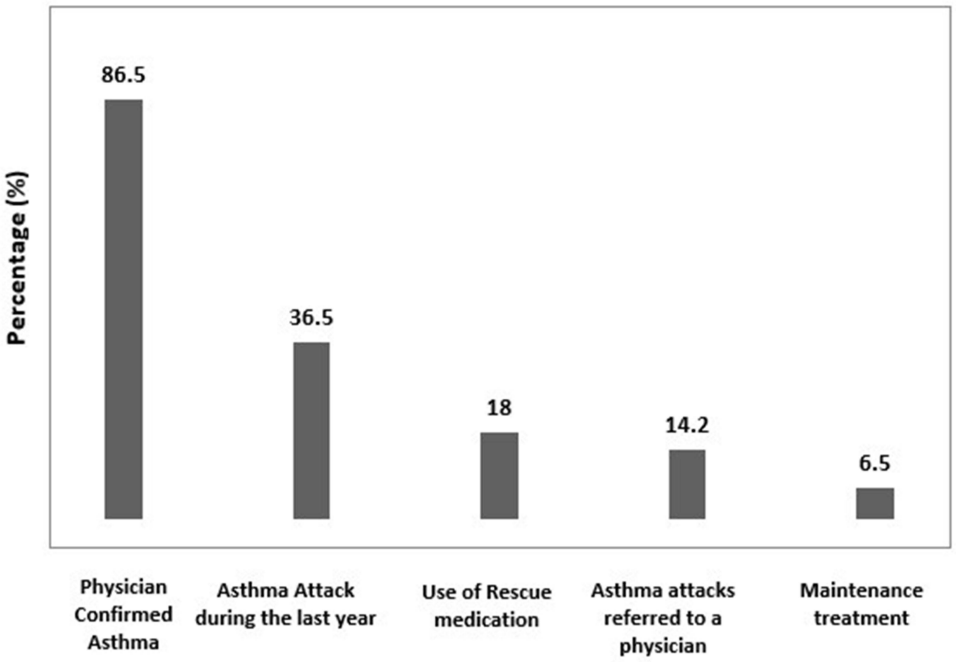

Figure 5 Management of asthma in patients with self-reported asthma (N = 327).

From the analysis of the matched groups (asthma and control, 394 subjects) in the second phase of the survey asthma was found more often in men than in women (63.2 versus 36.8%), in accordance to the observation from the first screening. Asthma patients had a higher percentage of unemployment compared to the control group (Table 2). Furthermore, asthma patients had significantly lower FEV_1/FVC, and higher reversibility compared to the control

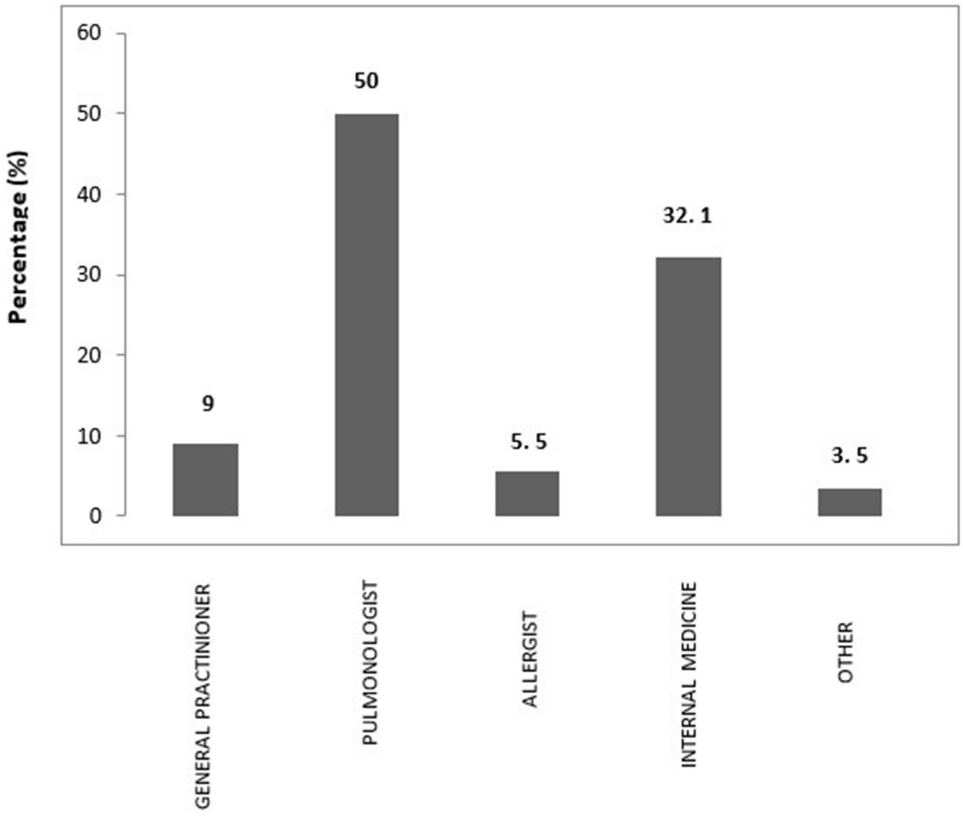

Figure 6 Physicians handling asthma in Cyprus.

group. No significant difference was found in IgE levels between the groups. ECP >20 IU was statistically significantly higher in the control group (Table 3).

Discussion

This is the first, two-stage population-based study, on asthma prevalence in Cyprus. The strength of this endeavor was the two stages design, comprised initially with a phone interview (first stage) followed by a face-to-face consultation by

Table 2 Anthropometric Characteristics of the Study Population

		Asthma Patients		Control Group		p
		n	%	n	%	
Gender	**Male**	132	63.2	115	61.5	0.733
	Female	68	36.8	79	38.5	
Age	**≤40 years old**	58	27.4	84	37.4	0.104
	41–59 years old	102	49.1	74	42.9	
	≥60 years old	40	23.6	36	19.8	
Body mass index (BMI)	**<20, Under**	9	4.3	8	5	0.065
	20–25, Normal	57	27.1	58	33.7	
	25–30, Over	87	42.9	84	46.4	
	>30, Obesity	47	25.7	38	14.9	

(*Continued*)

Table 2 (Continued).

		Asthma Patients		Control Group		p
		n	%	n	%	
Living regions	**Urban**	107	51.4	108	60	0.088
	Rural	93	48.6	72	40	
Geographical regions	**Nicosia**	94	45.3	79	38.5	0.724
	Limassol	46	22.6	52	26.9	
	Larnaca	30	16	31	17	
	Paphos	16	8.5	16	8.8	
	Ammochostos	14	7.5	16	8.8	
Educational level	**Primary school**	24	11.3	13	7.2	0.003
	Elementary school	19	9.0	19	10.6	0.102
	High school	77	36.3	40	22.2	
	University	9	43.4	108	60	
Profession	**Unemployed**	25	11.8	7	3.9	0.01
	Students	0	0	0	0	0.253
	Private employed	81	38.2	63	35	
	Civil servants	36	17.0	33	18.3	
	Self-employment	29	13.7	44	24.4	
	Pensioners	35	16.5	32	17.8	
	Other	6	2.8	1	0.6	

Table 3 The Spirometric Measurements and Measurements of Total IgE, and ECP in the Study Population (394 Subjects)

		Asthma Patients N=200 (%)	Control Group N=194 (%)	p
FEV_1 (±SD)		96.6±17	99.6±15	0.070
FEV_1/FVC (±SD)		83±7	85±6	0.022
Reversibility (±SD)		4±8	1±4	0.026
ECP (IU)	<20	82	71	0.009
	>20	18	29	0.008
Total IgE (IU)	<115	69	76	0.099
	>115	31	24	0.088

Abbreviations: FEV_1, Forced expiratory volume in 1 second; FVC, Forced vital capacity; ECP, Eosinophilic Cationic Protein; IgE, Immunoglobulin E.

a respiratory physician, spirometry evaluation and blood test analyses (second stage). It is also the first national study that covered a wide geographical area of Cyprus and a total population of more than 865,000 Greek-Cypriots.

The overall prevalence of adult bronchial asthma in Cyprus was estimated to be 5.57%. Although there are no official data for the prevalence of adult asthma in Cyprus, a self-reported percentage was estimated at 5.1% by the National Statistical Service in 2008.[27] The prevalence of adult asthma in Cyprus is estimated to be much lower than the reported in children. In 2008, the ISAAC questionnaire estimated an overall asthma prevalence in Cypriot children aged 7–8 years of 17.4%.[18] Few years later, Middleton et al[19] reported the prevalence of active asthma in 15–17-year-old Greek Cypriot teenagers ranging between 5% and 7.4% depending on the exposure to power plants. Although rising, the prevalence of adult asthma in Greek-Cypriots is much lower than the lifetime self-reported prevalence of asthma in Greece (9.10%)[7,28] or other countries in the Mediterranean region.[30,31]

Our study revealed higher asthma prevalence in men compared to women in contrast to data coming from Greece and surveys in other countries.[7,32,33] Although this study was not designed to investigate the causes of asthma, the difference between males and females could be attributed to social variables, and variances in indoor and outdoor environmental exposure (occupation, smoking, etc.) between sexes in this island. Interestingly, asthma was more frequent in the age range of 41–59 years. It is evident from this survey that with almost 70% of asthmatic patients belonging to the productive period of human life span (<60 years old) the economic burden of asthma may be substantial. Zannetos et al[22] retrospectively estimated the economic burden of asthma in Cyprus based on a probabilistic prevalence-based cost of illness model that included direct and indirect costs. The total cost of asthma per patient was estimated at €579.64 (95% CI: €376.90–€813.68), with the highest costs referring to asthma medication accounting for 35.88% of the overall cost of the disease and 43.70% of the direct costs.[22]

Differences in asthma prevalence were found in the various geographical regions of Cyprus, with higher asthma prevalence reported in urban areas, such as Nicosia, as compared to Ammochostos which is a mainly rural region. These observations are in accordance with the findings of the Greek studies,[6,7,28,34] but also with the reports from other areas in the Mediterranean region and other countries assessing the self-reported prevalence of asthma in adult population.[11,29–31] In Greece, although in 2012 the first nation-wide, cross-sectional, community-based survey of asthma and asthma-like symptoms using a questionnaire based on the ECRHS revealed higher asthma prevalence in Athens (10.9%) with no significant difference between rural and urban areas (8.5% and 7.8%, respectively),[34] in 2018 the prevalence was found higher in urban areas.[7] The variability in the prevalence of asthma may be attributed to the great variability of known risk factors of asthma across countries, like smoking prevalence, indoor and outdoor air pollution, obesity index and diet. Likewise, our study revealed that 36.1% of the participants with established bronchial asthma were current smokers, whereas the overall occurrence of smoking habit in the study population was 33%. The high prevalence of smoking remains a major barrier to combating the global burden of asthma.

The higher prevalence of asthma in urban areas is associated with a continuing rise in the prevalence of allergic diseases.[35,36] In our survey, one out of four (24.8%) of the participants that completed the first screening reported seasonal allergy symptoms such as rhinitis, sneezing, conjunctivitis, etc, while increased levels of IgE (>115 IU) and of Eosinophil Cationic Protein (>20IU) were found in 40% of the asthmatic participants. These findings indicate an increased percentage of atopy in asthmatic and non-asthmatic population in Cyprus.[17–19] The parallel rise in asthma and allergy prevalence in Cyprus was earlier documented in the study of Kolokotroni et al.[18] This study investigated temporal changes in the prevalence of asthma and allergies in children of 7–8 years old in the two main urban districts of the Republic of Cyprus (Nicosia and Limassol) based on two cross-sectional surveys eight years apart (200 and 2008). During these eight years, allergic rhinitis and eczema were doubled while wheezing increased by 25%.

An interesting finding of this study, was that more than 35% of asthma patients had uncontrolled asthma, as wheezing, chest tightness, night symptoms/awakenings, and asthma attacks. This finding is in line with other reports from Greece[6,7,28,34] and other European countries.[37–40] Interestingly, although 86.5% of asthma patients were diagnosed by a physician, a low percentage of patients were on maintenance treatment or referred to a physician for an asthma attack. Half of the patients were followed-up by a chest physician, while the rest were referring to other specialties, such as internists, allergists and general practitioners. It is acknowledged that gaps in patient education by the physicians affect the quality of care provided resulting in patient's dissatisfaction and critical errors in the use of medication and in the

management of asthma. In a cross-sectional multi-centered observational study conducted in Nicosia and Ammochostos state hospitals in North Cyprus patients claimed that they were not well informed and were not satisfied with the information they received from the physicians regarding potential difficulties with their asthma management and side effects.[41] This has also been demonstrated in several other studies[42,43] underlying the extent of the problem.

At this point, we should acknowledge the limitations that telephone surveys and self-reported questionnaires may pose. Several reports acknowledge that they may lead to non-representative results for several reasons, namely households without telephone services are automatically excluded, the response rate seems to be lower comparing to the "face to face" surveys and the information provided could be misleading.[19]

Conclusions

This study indicated that asthma affects almost 6% of the adult population in Cyprus. It also revealed higher asthma prevalence in urban areas and in men compared to women. Interestingly, although 86.5% of asthma patients were diagnosed by a physician a low percentage of patients were on maintenance treatment. Half of the patients were followed-up by a chest physician, while the rest were referring to other specialties. It is acknowledged that gaps in patient education by the physicians affect the quality of care provided resulting in critical errors in asthma management.

Abbreviations

GINA, Global Initiative for Asthma; ISAAC, International Study of Asthma and Allergies in children; ECRHS, European Community Respiratory Health Survey; WHS, World Health Survey; ATS, American Thoracic Society; ERS, European Respiratory Society; FEV1, Forced Expiratory Volume at the first second of expiration; FVC, Forced Vital Capacity; IgE, Immunoglobulin IgE; ECP, Eosinophil Cationic Protein.

Data Sharing Statement

The data presented in this study are available in this article.

Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of Sotiria Thoracic Diseases General Hospital, Athens, Greece (protocol number 24510, date of approval 5/12/2017).

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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