

REGULAR ARTICLE

Sex-specific trends in prevalence of childhood asthma over 30 years in Patras, Greece

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Keywords

Asthma, Childhood, Prevalence, Sex, Wheeze

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Received

30 December 2010; revised 17 February 2011;
accepted 1 March 2011.

DOI:10.1111/j.1651-2227.2011.02255.x

ABSTRACT

Aim: According to four surveys conducted during 1978–2003, the prevalence of childhood asthma and wheezing has risen in the city of Patras, Greece, albeit at a decelerating rate. We examined sex-specific wheeze and asthma prevalence in the same urban environment in 2008.

Methods: A cross-sectional parental questionnaire survey was performed in 2008 among third and fourth grade schoolchildren (8–9 year old), which was identical to previously conducted surveys in 1978 (n = 3003), 1991 (n = 2417), 1998 (n = 3076) and 2003 (n = 2725).

Results: The prevalence of current wheeze and asthma in 1978, 1991, 1998, 2003 and 2008 (n = 2688) was 1.5%, 4.6%, 6.0%, 6.9% and 6.9%, respectively (p for trend <0.001). Respective values for lifetime (ever had) wheeze and asthma in the 1991–2008 surveys were 8.0%, 9.6%, 12.4% and 12.6% (p for trend <0.001). The male:female ratio of current and lifetime wheeze and asthma increased during the 30-year surveillance period (p for trend <0.001). Irrespective of sex, diagnosed asthma declined among current wheezers by 17% (p < 0.001), but not among non-current ones (6.7%, p = 0.16) during 2003–2008.

Conclusions: Childhood wheeze and asthma have reached a plateau in an urban environment in Greece, while the male:female ratio increased. Asthma diagnosis declined among schoolage but not preschool wheezers during 2003–2008.

INTRODUCTION

The increase in the prevalence of childhood asthma in Western countries in the last three decades of the previous century raised concerns regarding the considerable burden of the disease on patients and society. Recent reports, however, suggest that the 'asthma epidemic' may have reached a plateau in high-prevalence countries (1–6), while phase III of the International Study of Asthma and Allergies in Children (ISAAC) revealed a decrease in current wheeze in the 12- to 14-year age group, particularly in English-speaking countries (7). Sex differences in wheeze and asthma incidence and prevalence have been well documented. During childhood, reported wheeze and asthma are more prevalent in boys than girls; however, the pattern changes in adolescence, at which time new onset wheeze is more frequent in girls than boys (1,2,8,9).

Using a validated standard parental questionnaire (10,11), previous surveys that were conducted in Patras, Greece, in 1978, 1991, 1998 and 2003 demonstrated a continuous increase in the prevalence of asthma among 8- to 10-year-old schoolchildren, albeit at a decelerating rate

(12). In 2008, using the same methodology, a repeat survey was conducted to investigate whether a plateau (or decrease) in asthma prevalence has been reached in the city of Patras. The prevalence data of the 30-year period were reanalysed with respect to sex and history of asthma symptoms.

Key notes

- After a continuous rise – albeit at a decelerating rate – monitored by 5 surveys, the prevalence of wheeze and asthma has reached a plateau in an urban environment in Greece over a period of 30 years.
- Contrary to other studies, the male:female ratio has consistently increased during this period.
- Asthma diagnosis has declined among schoolage wheezers but has remained stable among preschoolers during the period 2003–2008.

METHODS

The asthma parental questionnaire consisted of two questions on current (1978, 1991, 1998, 2003 and 2008 surveys) and two more questions on non-current asthma (four more recent surveys). The exact wording of the standard questionnaire and the definitions of current, non-current and lifetime wheeze/asthma have been presented previously (11,12). The parental questionnaire and the wheeze/asthma definitions used are included as a Appendix S1. In addition, patients with ≥ 2 episodes of diagnosed wheeze with or without a diagnosis of asthma within the last 2 years but not before were termed 'new onset wheeze/asthma', while patients with ≥ 2 episodes of diagnosed wheeze with or without a diagnosis of asthma that occurred both prior to and within the last 2 years were termed 'persistent wheeze/asthma'; the sum of 'new onset' and 'persistent' wheeze/asthma constitute 'current wheeze/asthma'. Patients with ≥ 2 episodes of diagnosed wheeze with or without a diagnosis of asthma prior to but not within the last 2 years were termed 'non-current wheeze/asthma'. Physician diagnosis of wheeze was a prerequisite for physician-diagnosed asthma. The ratios of current (total, new onset and persistent), non-current and lifetime physician-diagnosed asthma over the respective values of physician-diagnosed wheezing were calculated and compared as a means of assessing physician diagnosis of asthma in children with diagnosed wheeze.

The parental questionnaire, similarly to the four previous surveys (11,12), was distributed during the months January and February 2008 to third and fourth grade schoolchildren (i.e. 8- to 9-year-old children, outliers aged 7 and 10) of 46 primary public schools in the city of Patras, Greece; 44 of these schools were also surveyed in 1998 and 2003. Patras is a coastal city and the regional capital of Western Greece. Its metropolitan area has about 220 000 inhabitants. The study population represented 88% of the target population (most recent national census, National Statistical Services 2001). The methodology used in the distribution and collection of the parental questionnaire and in the confirmation of responses (telephone communication with the respondents of positive answers and 350 randomly selected controls) was identical to that used in the three previous surveys (11); the response confirmation process resolved potential conflicts in the answers.

Formal approval was obtained from the University Hospital of Patras ethics committee and the Ministry of Education of Greece in association with the local Direction of Primary Education. The headmasters of the schools were approached, and the questionnaire was distributed accompanied by an informative statement on asthma. The researchers were assisted in the distribution and collection process by the teachers.

Statistical analysis

The prevalence was calculated as the ratio of cases to total number of children surveyed and was expressed in absolute and relative numbers. Prevalence ratios between surveys, corresponding 95% confidence intervals and prevalence

differences were calculated. The mean rate of change between surveys was calculated as change per year per measured prevalence in the previous survey (modified from Ronchetti et al.) (3). Prevalence rate ratios and prevalence rate ratios adjusted for sex were calculated using logistic regression analysis. Comparisons of the prevalence of asthma between boys and girls were performed using the z-test. An extension of the Mantel-Haenszel of the chi-square test for trend was used to evaluate tendency between time points. A p-value < 0.05 for two-sided hypotheses for between-group comparisons was considered as statistically significant. All calculations were performed with the SPSS 15 (SPSS Inc., Chicago, IL, USA) statistical software.

RESULTS

In 2008, 3173 questionnaires were distributed; 2688 (1304 boys) questionnaires were completed (overall response rate: 84.7%, range: 76.2–95.0%). Questionnaires with missing or inconsistent values (2.4%) were not included in the analysis. The overall sample included 12.6% non-Greek ethnic origin groups, i.e. 7.2% Albanian, 2.4% Serbian and essentially all the rest were from Eastern European countries. Telephone confirmation was achieved in 76.4% of positive responders; none of the negative controls that were contacted changed their answer.

Asthma/wheeze prevalence rates and trends and comparisons of consecutive prevalence rate ratios adjusted for sex of current (total, new onset and persistent), non-current and lifetime asthma as well as of sex ratios are presented in Table 1. The mean calculated increases in the prevalence per year per previous prevalence of current wheeze/asthma between surveys were 0.16 for 1978–1991, 0.04 for 1991–1998, 0.03 for 1998–2003 and 0.00 for 2003–2008.

The ratios of current (total, new onset and persistent), non-current and lifetime physician-diagnosed asthma over the respective values of physician-diagnosed wheeze, as well as the per cent changes over consecutive measurements in the surveys, are shown in Table 2. Sex-specific analysis of the above data revealed similar results (data not shown).

DISCUSSION

The 2008 follow-up survey of childhood asthma prevalence, which was the fifth in a period of 30 years, shows that current and lifetime prevalence of asthma has reached a plateau in Patras, Greece. During the 30-year period, there is a continuous increase in the male:female ratio among asthmatics, while a steep decline in the diagnosis of asthma among school-aged wheezers occurred during the 2003–2008 period.

Several studies from various parts of the world have reported increase in the prevalence of asthma from the 1960s through the late 1990s (12–16). However, according to a number of studies published in the last decade, this 'asthma epidemic' appears to have reached its peak and may even be declining in Western societies (1–7). The

Table 1 Prevalence in current (new onset and persistent), non-current and lifetime (ever had) physician-diagnosed wheeze/asthma in 1978, 1991, 1998, 2003 and 2008 in Patras, Greece

	Prevalence rate ratio adjusted for sex (95% CI)					
	1978	1991	1998	2003	2008	
Number surveyed	3003	2417	3076	2725	2688	
Male:Female	0.96:1	0.95:1	0.96:1	0.96:1	0.94:1	
Current diagnosed wheeze/asthma* [†]	45 (1.5)	112 (4.6)	184 (6.0)	189 (6.9)	185 (6.9)	
Male:Female [‡]	1.14:1 [§]	1.15:1 [§]	1.16:1 [¶]	1.22:1 [¶]	1.23:1 [¶]	
New onset	NA	51 (2.1)	53 (1.7)	30 (1.1)	44 (1.6)	
Male:Female		0.96:1	1.12:1**	0.88:1**	1.10:1	
Persistent* [†]	NA	61 (2.5)	131 (4.3)	159 (5.8)	141 (5.2)	
Male:Female		1.35:1 [¶]	1.18:1 [¶]	1.3:1 [¶]	1.27:1 [¶]	
Non-current diagnosed wheeze/asthma* [†]	NA	82 (3.4)	112 (3.6)	149 (5.5)	154 (5.7)	
Male:Female [‡]		1.1:1	1.43:1 [¶]	1.76:1 [¶]	1.8:1 [¶]	
Lifetime diagnosed wheeze/asthma* [†]	NA	194 (8.0)	296 (9.6)	338 (12.4)	339 (12.6)	
Male:Female [‡]		1.13:1 [¶]	1.26:1 [¶]	1.43:1 [¶]	1.46:1 [¶]	

Values are n (%) unless stated otherwise.

NA, not applicable; data on non-current asthma were not obtained in 1978.

*p for trend <0.001 for increase in asthma prevalence in overall population, boys and girls during the surveillance period.

†Mantel-Haenszel extension of the chi-square test for trend.

‡p for trend <0.001 for increase in male: female ratio during the surveillance period.

§p < 0.01 for between-gender comparisons.

¶p < 0.001 for between-gender comparisons.

**p < 0.05 for between-gender comparisons.

††p for trend <0.001 for increase in asthma prevalence in overall population and boys, and p for trend = 0.065 for increase in asthma prevalence in girls.

Table 2 Changes in current (new onset and persistent), non-current and lifetime (ever had) 'physician-diagnosed asthma' as proportion of 'physician-diagnosed wheeze'

Physician-diagnosed asthma	Proportion (%)					Absolute proportion change (p-value)					p for trend*
	1978	1991	1998	2003	2008	1991 vs. 1978	1998 vs. 1991	2003 vs. 1998	2008 vs. 2003		
Current	31/45 (68.9)	77/112 (68.8)	131/184 (71.2)	146/189 (77.2)	110/185 (59.5)	-0.1% (0.859)	+2.4% (0.759)	+6.0% (0.228)	-17.7% (<0.001)	0.997	
New onset	NA	26/51 (51.0)	29/53 (54.7)	15/30 (50.0)	12/44 (27.3)	NA	+3.7% (0.856)	-4.7% (0.855)	-22.7% (0.081)	0.019	
Persistent	NA	51/61 (83.6)	102/131 (77.9)	131/159 (82.4)	98/141 (69.5)	NA	-5.7% (0.471)	+4.5% (0.417)	-12.9% (0.013)	0.039	
Non-current	NA	45/82 (54.9)	85/112 (75.9)	129/149 (86.6)	123/154 (79.9)	NA	+21.0% (0.004)	+10.7% (0.039)	-6.7% (0.160)	<0.001	
Lifetime	NA	123/194 (63.4)	221/296 (74.7)	289/338 (85.5)	249/339 (73.5)	NA	+11.3% (0.010)	+10.8% (<0.001)	-12.0% (<0.001)	0.006	

Values are n (%) unless stated otherwise.

NA, not applicable, data on non-current asthma were not obtained in 1978.

*Mantel-Haenszel extension of the chi-square test for trend.

continuing increase in asthma prevalence among 12-year-old Welsh children reported by Burr et al. (17) in their 2003 follow-up in a series of three, 15 years apart, surveys may have missed a plateau in asthma prevalence in the late 1990s.

Ours is the only study in a Greek population and one of the few available worldwide that has surveyed asthma prevalence at several time points over an extended time period using standardized methodology. The ISAAC Phase I, which was conducted in 1994–1995 in one Greek centre in Athens, showed a prevalence rate of self-reported wheeze in the last 12 months of 3.7% among 13- to 14-year-old children and a rate (parental report) of 7.6% among 6- to 7-year-olds (18); the ISAAC Phase II, which was conducted in 10-year-old children in 2001–2002 in two centres, Athens and Thessaloniki, showed prevalence rates (parental report) of wheeze in the last 12 months of 5.6% and 8.4%, respectively (19). In the present report, which expands our previously published data of four previous cross-sectional surveys (1978, 1991, 1998 and 2003) to 2008, we found that the prevalence of current wheeze/asthma among 8- to 9-year-old schoolchildren in Patras, Greece, did not change in the last two surveys (6.9% in 2003 and 2008). This plateau in prevalence has occurred at a much lower rate in our population as compared to other reports (1–5,7); this is, at least partly, because of the much more 'restrictive' phrasing of our questions on wheezing, i.e. 'physician-diagnosed wheezing', and the prompting of parents to respond with a negative answer if in doubt. Others have confirmed that conceptual understanding of the term 'wheeze' differs between parents and physicians (20). Parents reporting physician-diagnosed asthma – with very few exceptions – also reported physician-diagnosed wheezing in all five surveys; therefore, it appears that the diagnosis of childhood asthma is reserved for children with wheeze by Greek physicians caring for children. Furthermore, our questionnaire did not address cough; it has been shown that the presence of persistent or recurrent cough without wheeze is rarely associated with asthma in children (21). The issues regarding the use of standardized written questionnaires to measure prevalence (22), the effects of diagnostic transfer (23,24) as well as the inclusion of non-Greek ethnic origin children in the analysis have been discussed previously (12). In addition, to make our results more comparable to those of other studies, we expressed the yearly increase in the prevalence of current asthma as percentage of the prevalence of the previous survey. Thus, although the prevalence of wheeze was much higher in Aberdeen (1,2), the between-survey mean yearly increase per previous prevalence in current wheeze/asthma in Patras after 1991 was comparable to that calculated from the Aberdeen data during the periods 1989–1994, 1994–1999 and 1999–2004 (0.05, 0.02 and -0.02, respectively).

Male over female predominance among current (total), non-current and lifetime wheezers/asthmatics was observed in all five surveys, and there was an increasing secular trend in the male:female ratio throughout the 30 years of surveillance. However, although there was an increasing secular trend of current and lifetime wheeze/asthma in both

sexes, there was no trend for increase among female non-current wheezers/asthmatics. Persistence of male predominance over time is in accordance with some reports (25), but other studies support a diverging increase in favour of girls (2,26). The age of children surveyed is important when determining sex differences in asthma as the incidence pattern reverses from male predominant to female predominant during adolescence (8,9). Sex-specific expression of genetic polymorphisms, hormonal changes and their effects on lung growth and immunity in relation to age, as well as sex-specific environmental exposures and social/behavioural changes, have been implicated in the explanation of these patterns (27). Our childhood population consisted of 8- to 9-year-olds, while the Aberdeen children were 9–11 years (1,2,14,15) and the Munster older ISAAC group were 13–14 years (26). Therefore, our surveys consisted essentially of prepubertal children while children from the two other groups were more likely to have entered puberty. Surprisingly, girls also predominated in the younger (6–7 years) Munster group (26). During the 20th century, a secular trend for earlier onset of sexual maturation has been universally reported, particularly for girls. During the last 30 years, pubertal onset decreased in Greek girls from 10.6 to 10.0 years but remained essentially unchanged in boys (28,29). Thus, our results could only minimally be influenced by pubertal onset, while their pattern contradicts that of pubertal maturation.

The pronounced increase in the diagnosis of non-current asthma among non-current (6- to 7-year-old) wheezers from 54.9% in 1991 to 86.6% in 2003 has stabilized at 79.9% in 2008, thus suggesting that diagnostic transfer has ceased in this age group; this stabilization may be a good starting point for a decrease in overdiagnosis and therefore overtreatment of asthma in young wheezers. Conversely, the 17.7% drop in the ratio of 'physician-diagnosed asthma': 'physician-diagnosed wheeze' among current wheezers in the 8- to 9-year-old group during 2003–2008 may reflect underdiagnosis and therefore undertreatment of true asthma.

In a 30-year surveillance period, the prevalence of physician-diagnosed wheeze – monitored by five identical cross-sectional parental questionnaire surveys – reached a plateau during 2003–2008 in Patras, Greece. This plateau occurred at a lower prevalence rate than in other Western countries, probably due to the particular choice and phrasing of the questions used. Contrary to other reports, male predominance of wheeze and asthma increased throughout the surveillance period. In the last two surveys, physician diagnosis of wheeze as asthma remained stable in preschool wheezers but decreased among schoolage children, possibly indicating underdiagnosis of asthma in the later group.

ACKNOWLEDGEMENTS

The authors express their gratitude to the children and the teachers of the schools for participating in the study and to all their colleagues that were involved in conducting the surveys through the 30 years.

CONFLICTS OF INTEREST

No conflicts of interest to disclose

FUNDING

No financial support.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Study questionnaire and definitions.

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