

Review article

Impact of gender on asthma in childhood and adolescence: a GA²LEN review

A number of studies have shown gender differences in the prevalence of wheeze and asthma. The aim of this review was to examine published results on gender differences in childhood and adolescent asthma incidence and prevalence, define current concepts and to identify new research needs. A Medline search was performed with the search words (gender OR sex) AND (child OR childhood OR adolescence) AND (asthma). Articles that reported on absence or presence of gender differences in asthma were included and reviewed, and cross-references were checked. Boys are consistently reported to have more prevalent wheeze and asthma than girls. In adolescence, the pattern changes and onset of wheeze is more prevalent in females than males. Asthma, after childhood, is more severe in females than in males, and is underdiagnosed and undertreated in female adolescents. Possible explanations for this switch around puberty in the gender susceptibility to develop asthma include hormonal changes and gender-specific differences in environmental exposures. This aspect needs consideration of the doctors and allergists who diagnose and treat asthmatic individuals. In conclusion, sex hormones are likely to play an important role in the development and outcome of the allergic immune response and asthma in particular. By obtaining functional data from appropriate models, the exact underlying mechanisms can be unravelled. To examine the effect of gender-specific differences in environmental exposures and changes of asthma prevalence and severity in puberty, larger populations may need to be investigated.

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for the working group of GA²LEN WP
2.5 'Gender'**

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Until recently, there have been several reports on the proliferation of asthma and allergic diseases in western countries. The prevalence of asthma seems to have stabilized or even decreased in some countries in recent years, whereas it is still increasing in others, particularly in those with the lower rates of prevalence (1). Asthma prevalence is higher in boys than girls in childhood and then reverses in adolescence, with higher prevalence of asthma in adult women than men (2–10). It has been suggested that the stabilized or decreased prevalence of asthma or wheeze is mainly attributed to boys, but not girls, so that gender differences in the prevalence of asthma in childhood has reduced over time (11, 12).

The natural history of asthma, according to age and gender, has been well described. It has been suggested that an overall improvement in asthma during adolescence may result from diminished clinical and immunological responsiveness directly related to hormonal changes and that the effect of age on the prevalence of asthma in each sex may relate to differences in hormonal

status, possibly influencing airway size, inflammatory conditions, and smooth muscle and vascular functions (13, 14). However, few comprehensive studies are available and there are a number of plausible ways to go further to look into this. The aim of this review was to examine published results on gender differences in childhood and adolescent asthma incidence and prevalence, define current concepts and to identify new research needs. It is not an attempt to be a complete meta-analysis.

Methods

A Medline search was performed with the search words (gender OR sex) AND (child OR childhood OR adolescence) AND (asthma). About 105 original articles were identified and reviewed. Articles that reported on absence or presence of gender differences were included and placed in sections related to subject; gender differences in (i) prevalence of asthma, (ii) diagnosis of asthma, (iii) severity of asthma and (iv) environmental and genetic risk factors. In addition, cross-references were reviewed and an additional 56 articles were checked.

Some studies also include measures of lung function or allergen sensitization, but these outcomes are not primary in this review.

Results

Gender differences in asthma incidence and prevalence

A number of studies have shown gender differences in the prevalence of childhood wheeze and asthma. Boys are consistently being reported to have more prevalent wheeze and asthma than girls. Table 1 summarizes all the studies on gender differences in asthma prevalence. In most studies, approximately 2/3 of the subjects with asthma or wheezing are males and 1/3 are females, giving odds ratios (ORs) of 1.4–1.6 or above on comparing males to females (2–7, 9, 10, 15–17).

In adolescence, the pattern changes and adolescent-onset wheeze or asthma is more prevalent in females than males (18–23). In the Dunedin birth cohort, New Zealand, Mandhane et al. considered all study members, seen at least once between ages 7 and 26, for whom age at first wheezing (if wheezers) could be determined. By age 26, the cumulative percentage of subjects classified as wheezers was similar in boys and in girls. However, boys were more likely than girls to have developed wheeze by age 10 ($P = 0.002$), whereas girls were more likely than boys to develop wheeze between age 10 and 26 ($P < 0.001$) (10). In a school-based cross-sectional study, Venn et al. showed that the reversal in prevalence rates seems to occur at around age 12. After this age, the prevalence of wheeze decreased with age in boys, whereas there was a significant trend for an increase with age in girls (20). The female-to-male prevalence ratio for asthma has been reported to be approximately 35 : 65 in children, inverse (65 : 35) in adults and relatively similar (50 : 50) in adolescents (4, 24–26).

While the same increasing trend in the prevalence of asthma has been reported in boys and girls from the early 1980s to 1991 (25), a recent study reporting decreasing trends for current wheeze from 1989 to 2001 also reported this decrease particularly in boys (12), and other cross-sectional data suggest that the male-to-female ratio for the diagnosis of asthma is narrowing over time (11, 27).

The higher prevalence in girls after adolescence is related to higher incidence (21, 28). Besides assessing gender differences in asthma incidence, few studies have considered remission. Nicolai and co-workers investigated whether hormonal factors were related to the remission/persistence of asthma in a cohort of 155 asthmatics (7). At age 10, the male-to-female ratio of asthma was 61% : 39% and at 14 years of age, 35.5% of the subjects reported acute asthma symptoms during the previous 12 months, with similar gender ratio (boys 65.5%, girls 34.5%). There was no statistically significant relationship between reported signs of late puberty and loss of asthma or bronchial hyperresponsiveness (BHR), and at age 14, no association was found between asthma or BHR and level of andros-

tanediolglucuronide, in any sex. The same team also investigated the change in the gender ratio in asthma from childhood to adolescence in a case-control study of children recruited at age 10, and re-examined at age 14 and 20 (for cases), and at age 20 for controls (23). At age 20, 24.5% (21 males, eight females) of the cases still had asthma, with the gender ratio remaining male-dominated. In controls, at 20 years: 4.8% (48 of 1000) had current asthma, predominantly female: 6.4% (31 of 485) of control girls vs 3.3% (17 of 515) of boys ($P = 0.022$). Asthma at age 10 had no better prognosis in boys than in girls. This indicates that the change in gender predominance of asthma through the second decade of life is not caused by increased loss of established asthma in boys, but rather than the mechanism of changing gender ratio appears to be late incidence of asthma among girls.

Boys consistently show higher level of total immunoglobulin E (IgE) than girls (29, 30). Regarding sensitization and atopy, male gender is generally found to be a risk factor for any sensitization, whereas inconsistent results have been reported when sensitization to individual allergens is considered (3, 29, 31). In the study by Sears, the proportion of boys with current asthma was 1.6 times higher than in girls. However, the prevalence of any positive skin test was also greater in boys than in girls (50.1% vs 37.1%), and the gender differences for asthma became insignificant after adjustment for skin test responsiveness (3). While atopic sensitization appears to be a risk factor for asthma in both girls and boys in childhood, there are suggestions that the influence of atopy or parental atopy on the development of wheeze differs between males and females (16) and between childhood and adolescent-onset wheeze (10).

Gender differences in diagnosis of asthma

Several authors have investigated the relationship between wheeze and asthma diagnosis to test for potential gender differences. It has been argued (32) that male predominance in childhood asthma is attributed to boys having smaller airway diameters relative to lung volume (dysanapsis; 33) and more allergen sensitivities (3). Another possible explanation involves the 'Yentl syndrome', i.e. the undertreatment of women compared with men unless women develop severe manifestation of disease or a 'typical' disease presentation (34). In the Dunedin birth cohort, New Zealand, Sears et al. found no evidence for gender differences for recurrent wheeze not diagnosed as asthma (3). In adolescents, Yeatts et al. found that female gender was independently associated with undiagnosed frequent wheezing (OR: 1.45; 95% CI: 1.35–1.54) vs asymptomatic children in a cross-sectional survey involving more than 120 000 (12- to 18-year olds) in the USA (35). Interestingly, a similar pattern was observed for analyses comparing odds of undiagnosed frequent wheeze vs diagnosed asthmatics. In the cross-

Table 1. Gender differences in asthma incidence and prevalence in childhood and adolescence

Author, reference of publication, study centre	Study method, date collected, setting	Total (% participation) N male (M)/N female (F)	Age (years)	Results (comments)	M : F ratio
Gender differences in incidence					
Anderson (19), Department of Public Health Sciences, St George's Hospital Medical School, London, UK	British national cohort of children born during 1 week in 1958, followed up to age 23	3583 M/3642 F	0-7 8-11 12-16 17-23	Percentage/year with new asthma or wheeze Age 0-7 8-11 12-16 17-23	F 2.3 1.0 0.58 0.94 M : F ratio 1.23 1.31 1.47 0.59
Chen (21), Department of Epidemiology and Community Medicine, University of Ottawa, Ontario, Canada	Longitudinal data from first and second cycles of the National Population Health Survey 1994-1996	12 636, without asthma at baseline 5747 M/6889 F	≥ 12	2-year cumulative incidence of asthma in the age group of 12-24 years M (n = 1134) F (n = 1134) 2.8 (1.7-3.9) 5.3 (3.6-7.0) % (95% CI)	
Larsson (50), Department of Pulmonary Medicine, Östersund Hospital, Östersund, Sweden	Questionnaires sent in 1990 and 1993 in individuals born in 1974	2579 (71%) in both surveys, 2308 no asthma 1990 1188 M/1120 F	16-19	Percentage/year with new symptoms of: Shortness of breath Wheeze Asthma ever Doctor-diagnosed asthma Current asthma drugs	F (%) 3.3 1.9 1.5 1.4 1.8 P-value <0.005 0.17 <0.02 <0.02 <0.005
Gender differences in prevalence in cross-sectional population-based survey					
Chen (51), Department of Epidemiology and Community Medicine, University of Ottawa, Ontario, Canada	Cross-sectional National Population Health Survey	17 605	≥ 12	Percentage doctor-diagnosed asthma At age 12-24 years >25 years	F (%) 11.2 4.9-6.4
Devenny (11), Department of Medical Paediatrics, Royal Aberdeen Children's Hospital, Aberdeen, UK	Four cross-sectional surveys 1964, 1989, 1994, 1999	3537 (84%)	9-12	Male-to-female ratio for the diagnosis of asthma In 1964 In 1989 In 1994 In 1999	2.2 : 1 1.9 : 1 1.4 : 1 1.1 : 1
Henriksen (22), Department of Lung Medicine, University Hospital of Trondheim, Norway	Cross-sectional study (Phase I)	Phase I 8571 (Phase II, see Table 2)	13-19	Phase I Current wheeze (%) Doctor-diagnosed asthma (%) Cumulative prevalence of asthma and wheeze	F (%) 30 10.5 P-value <0.01 ns
Luyt (15), Department of Child Health, University of Leicester, UK	Cross-sectional study 1990	1422 (86.2%) 51.1% boys/48.9% girls	1-5	Asthma diagnosis Wheeze Percentage with current wheeze	F (%) 9.2 13.5 P-value 0.03 0.03
Mommers (12), Care and Public Health Research Institute, University of Maastricht, the Netherlands	Four cross-sectional surveys 1989, 1993, 1997, 2001	1102 (96%) M 51%/F 49%	8-9	1989 1993 1997 2001 P-value for decreasing trend over time	F (%) 11.1 11.9 10.7 8.6 0.144

Table 1. (Continued)

Author, reference of publication, study centre	Study method, date collected, setting	Total (% participation) N male (M)/N female (F)	Age (years)	Results (comments)	M (%)	F (%)
Osman (27), Department of Child Health, University of Aberdeen, Aberdeen, UK	Four cross-sectional surveys 1989, 1994, 1999, 2004	1920 (57%) M 49%/F 51%	8–9	Percentage with ever asthma	M (%)	F (%)
				1989	13.0	7.5
				1994	22.8	16.2
				1999	26.0	22.6
				2004	26.2	25.6
				χ^2 trend over time 24.0 ($P < 0.0001$)		
Schatz (26), Department of Allergy, Kaiser-Permanente Medical Care, San Diego, CA, USA	Cross-sectional; asthmatic patients identified 1999–2000	60 694		Male-to-female prevalence ratio for asthma		
			2–13	Age (years)	Ratio	
			14–22	2–13r	65 : 35	
			23–64	14–22r	50 : 50	
				23–64r	35 : 65	
Sennhauser (4), Department of Pulmonology, Ostschweiz, Kinderspital, Switzerland	Cross-sectional survey in St Gallen canton, Switzerland	4338 M 50.9%/F 49.1%		Any symptoms* in last 12 months		
			7	Age (years)	M (%)	F (%)
			12	7	22.1	18.2
			15	12	16.9	17.1
				15	11.3	18.2
Venn (20), Division of Respiratory Medicine, City Hospital Nottingham, UK	Cross-sectional; questionnaire survey in schools	27 826 (80%) M 51%/F 49%	11–16	Percentage wheeze last 12 months		
				Age (years)	M (%)	F (%)
			11	11	19.0	17.2
			12	12	18.5	20.4
			13	13	17.1	20.9
			14	14	17.0	22.4
			15	15	14.5	23.0
			16	16	14.5	22.0
				Percentage wheeze last 12 months		
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				>12 wheezing attacks	1.4	0.8
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				Cough	10.8	9.1
SIDRIA (Italian Studies on Respiratory Disorders in Childhood and the Environment) (5)	Cross-sectional northern and central Italy	18 737 M 9674/F 9062	6–7	Wheeze last 12 months	9.2	6.1
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Author, reference of publication, study centre	Study method, date collected, setting	Total (% participation) N male (M)/N female (F)	Age (years)	Results (comments)
Sears (3), Department of Medicine, McMaster University, Ontario, Canada	Prospective birth cohort established 1972–1973 Dunedin, New Zealand	662 subjects M 52%/F 48%	13	Male-to-female prevalence ratio for: M : F ratio Current asthma 1.6 : 1 Ever-diagnosed asthma 1.4 : 1 Recurrent wheeze ns Positive skin test 1.4 : 1
Gender differences in population databases and twin registers				
Lichtenstein, (6) Institute of Medical Epidemiology, Karolinska Institutet, Stockholm, Sweden	Cross-sectional study twin register	1339 twin pairs (90%)	7–9	M/F OR for asthma OR = 2.19 (95% CI: 1.40–3.45) $P < 0.001$
Sentiliselvan (25), Department of Community Health and Epi. Centre for Agricultural Medicine, University of Saskatchewan, Saskatoon, Canada	Medical Claim Insurance Branch (MCIB) database 1981–1990		0–64	Male-to-female OR for the likelihood of first visit to doctors for asthma Age (years) 0–4 1.74 1.70–1.78 95% CI P -value 5–14 1.55 1.52–1.58 <0.001 15–34 0.98 0.97–1.00 <0.04 35–64 0.87 0.86–0.89 <0.001
Gender differences in case-control surveys				
Nicolai (23), Dr von Haunersches Kinderspital, Universitäts Kinderklinik Munich, Germany	Case-control based on asthma at 10 years with follow-up at 20 years of age	274 cases, 1000 controls M 60%/F 40%	10 20	See text Percentage with asthma at age 20 among controls at baseline study M (%) 3.3 F (%) 6.4 P -value <0.022

*Exercise-induced, allergen-induced, morning tightness and chronic night cough.

sectional analysis (Phase I) of the health survey of north-Trondelag, involving 8571 adolescents aged 13–19, current wheeze was more frequently reported by girls but no difference was observed for the prevalence of a doctor-diagnosed asthma (22). Among subjects with current wheeze, the likelihood of a doctor-diagnosed asthma was reduced in girls compared to boys (OR: 0.82, 95% CI: 0.68–0.98). In the case-control analysis (Phase II), more girls than boys with current wheeze had BHR (62% vs 50%, $P < 0.02$), whereas more boys than girls reported doctor-diagnosed asthma (44% vs 32%, $P < 0.02$). In Swiss children, Sennhauser also reported a reversal in the prevalence of symptoms from a higher prevalence in boys at age 7 to a higher prevalence in girls at age 15, whereas the percentage of subjects reporting a diagnostic label of ‘asthma’ was twice as high in boys than in girls, irrespective of the age (4).

Wright et al. recently showed that girls with symptoms were less likely than boys to see a doctor and to be labelled as having asthma (36). This is consistent with the results from the SIDRIA study, which showed that there was a higher percentage of subjects diagnosed with asthma in boys who reported wheeze at any time in life, when compared to girls with wheeze (33% vs 23%, $P < 0.05$), whereas there was no gender difference in the prevalence of asthma diagnosis in non wheezers (5).

In the study by Venn, the authors acknowledged that a tendency for girls to over-report asthma symptoms and boys to deny them may have overestimated the size of the sex difference observed after the age of 12 years (20). However, they argued that such a bias cannot explain the results fully as the effect persisted when parental responses was used, or when the analysis was restricted to current wheezers with a doctor-diagnosed asthma, both of which measures may be less affected by sex.

Gender differences in asthma severity

Gender differences in asthma severity can be assessed through prevalence of hospitalization and use of medication. The higher prevalence of childhood wheeze and asthma in boys is reflected in hospital admissions being more frequent in males than in females, with the gender gap reversed in adolescence (37, 38). Likewise, the cumulative incidence of asthma hospitalizations has been shown to be substantially higher for young boys than girls, and reversed for adults. The incidence ratio for females vs males for asthma hospitalization is seen to increase in adolescence and adults (5, 23, 28), irrespective of whether the patient data comes from maternal reports or medical records (39) (Table 2).

Concurrently, among children presenting to an Emergency Department (ED), there does not seem to be any difference in admission rates for boys or girls, and no sex differences for relapse or ongoing exacerbation (40). This suggests that asthma is not inherently more severe in boys with asthma compared to girls, and that the increased

rate of hospitalizations in young boys is due to differences in prevalence, not severity. In another study, where 20 277 (23.3%) subjects with first diagnosis of asthma were readmitted to hospital for asthma, the incidence rate of rehospitalization showed little sex difference between age 1 and 9, but was markedly higher in females than in males aged 10–19 (41).

Others have shown that asthma severity and medication appeared to be significantly greater in males (2–13 years), whereas females aged 14–22 years had more outpatient and ED visits and used more oral steroids than males (26).

In the Aberdeen study, a trend for decreasing prevalence of wheeze (with P -value for trend: 0.001 in boys, 0.144 in girls) between 1989 and 2001 suggests that healthcare utilization has increased in the meantime, in both boys and girls. The proportion of wheezy children using medication increased during those years in boys (43% vs 65%; $P = 0.003$), but not significantly so in girls (34% vs 46%, $P = 0.1$) (11).

Commonly observed differences between sexes in the impact of asthma on lung function may reflect differences in the duration and age of onset of asthma in males and females. In a cohort of 2277 fourth- and seventh-graders followed up twice during a 4-year period, males >6 years since diagnosis had significant deficits compared with <3 years since diagnosis, similarly to females though fewer subjects (42). In an Italian longitudinal study of school children on two occasions, BHR was shown to decline from childhood to adolescence, paralleling the increase in lung function during this period, with a less pronounced decline in females (43). Other studies in 7- to 11-year-old children have not found any substantial sex difference in lung function between the sexes (17, 44).

Gender differences in environmental and genetic factors

In addition to the gender differences in atopic sensitization and asthma described above, there is obviously a genetic difference between males and females, and there are many ongoing studies to determine the role of genetics in males and females. A few studies have reported differences in susceptibility to environmental factors between males and females. Male children with parents who smoked, had increased BHR (OR = 4.3, $P = 0.009$) compared to children whose parents did not smoke in an Italian study based on 172 subjects (45). A greater susceptibility of females to environmental pollutants has been proposed to explain the stronger association reported between exposure to gas for cooking and respiratory symptoms in girls than in boys (46), the increased vulnerability of women to the effects of ozone (47), and also the stronger effect of smoking observed on lung function in girls (48). In adolescence and adults, incidence of asthma has been reported to be associated with smoking status (49–51) and household pets (21) in females but not in males. In a prospective birth cohort established during 1972–1973, in Dunedin, New Zealand

Table 2. Gender differences in asthma diagnosis, medication and severity (hospitalization) in childhood and adolescence

Author, reference of publication, study centre	Study method, date collected, setting	Total sample (% participation) N male (M)/N female (F)	Age (years)	Results (comments)
Berhane (42), Department of Preventive Medicine, University of Southern California, Los Angeles, CA, USA	Prospective study, of two cohorts established in fourth and seventh grades Follow-ups at least twice in 4 years	2277 (62%) M 52%/F 48%	8–12, 12–15	Asthma duration and medication at last follow-up visit In 4-graders M (<i>n</i> = 134) F (<i>n</i> = 95) Short duration: 0 med 17.9 23.2 Short duration: + med 30.6 34.7 Long duration: 0 med 17.2 15.8 Long duration: + med 34.3 26.3 Cumulative incidence of asthma hospitalization (cases /1000) Age (years) M F 0 45.1 21.2 1–4 30.4 17.2 5–9 10.0 6.6 10–14 5.3 4.5 15–19 3.0 6.4 In 7-graders M (<i>n</i> = 64) F (<i>n</i> = 62) 10.9 6.5 10.9 38.7 23.4 14.5 54.8 40.3 M : F ratio 2.14 1.77 1.51 1.18 0.47
Chen (28), Department of Epidemiology and Community Medicine, University of Ottawa, Ontario, Canada	Longitudinal data from first 3 years of the National Population Health Survey 1994–1997	9 486 173 hospital records for a 3-year period (1994–1997)		
Chen (41), Department of Epidemiology and Community Medicine, University of Ottawa, Ontario, Canada	Cross-sectional National Population Health Survey 1994–1997	86 863; 20 277 (23.3%) readmitted for asthma during a 3-year period	20	Incidence rate of hospital readmission (IR/year) Age at first admission (years) M F <1 30.6 26.3 1–4 18.9 18.5 5–9 12.9 13.7 10–14 12.5 18.7 15–19 11.9 16.1 M : F ratio 1.16 1.02 0.94 0.67 0.74
Debley (38), Division of Pulmonary Medicine, University of Washington, WA, USA	Population-based retrospective birth cohort 1980–1985, hospitalization 1987–2001	407 428 M 49%/F 51%	2–18	Asthma hospitalization rate M F Peak Age (years) 4 17 Rate 12.7/10 000 9.4/10 000 (11.1–14.3) (7.8–11) Trough Age (years) 18 2 Rate 4.1/10 000 5.2/10 000 (2.8–5.4) (4.2–6.2) Male-to-female ratio reversed at 13–14 years
Henriksen (22), Department of Lung Medicine, University Hospital of Trondheim, Norway	Cross-sectional study (Phase I, see Table 1) Case-control (Phase II)	Phase II 401 cases, 213 controls	13–19	Phase II More females than males had current wheeze. Gender differences in subjects with current wheeze: M (%) F (%) BHR (%) 50 62 Doctor-diagnosed asthma (%) 32.0 44.0 <i>P</i>-value 0.02 0.02

Table 2. (Continued)

Author, reference of publication, study centre	Study method, date collected, setting	Total sample (% participation) N male (M)/N female (F)	Age (years)	Results (comments)
Mommers (12), Care and Public Health Research Inst, University of Maastricht, the Netherlands	Four cross-sectional surveys 1989, 1993, 1997, 2001	1102 (96%) M 51%/F 49%	8–9	Percentage of wheezy children who used medication last month 1989 M (%) 42.9 F (%) 34.0 1993 54.0 55.7 1997 57.3 50.6 2001 64.8 45.7 P-value for increasing trend 0.003 over time Hospitalization for asthma
Schatz (40), Department of Allergy, Kaiser-Permanente Medical Care, San Diego, CA, USA	Prospective cohort study in children presented to ED with acute asthma	1602 M 61%/F 39%	2–13	Admission rate M (%) 20 F (%) 22 Relapse 8 11 Exacerbation 9 11 Ratio of hospital admission for asthma Age (years) M (%) F (%) 0–5 66 34 6–10 63 37 11–20 49 51 21–30 32 68 M : F ratio 1.94 1.70 0.96 0.47
Skobeloff (24), Department of Emergency Medicine, Medical College of Pennsylvania, Philadelphia, PA, USA	Hospital admission registers 1986–1989 five counties of SE Pennsylvania, USA	33 269	0–30	
Yeatts (35), Department of Epidemiology, University of North Carolina, NC, USA	Cross-sectional; questionnaire survey in schools, 1999–2000	122 829	12–18	Risk of having frequent wheezing undiagnosed as asthma: OR for 'undiagnosed wheeze' vs diagnosed asthma M 1.0 F 1.56 (95% CI: 1.47–1.69) OR for "undiagnosed wheeze" vs asymptomatic children M 1.0 F OR 1.45 (95% CI 1.35–1.54)
Wright (36), Arizona Respiratory Center, Arizona Health Sciences Center, Tucson, AZ, USA	Prospective study; Tucson Respiratory Children's Study 1980–1984	1089 (87.4%) M 49.2%/F 50.8%	2–18	Among subjects with symptoms of wheeze: Visit to doctor M (%) 83.4 F (%) 74.1 Diagnosed with asthma 53.8 43.3 P-value <0.001 <0.009
SIDRIA (Italian Studies on Respiratory Disorders in Childhood and the Environment) (5)	Cross-sectional northern and central Italy	18 737 M 9674/F 9062	6–7	Hospital admission for asthma M (%) 3.4 F (%) 1.7 P-value < 0.001

($n = 613$ subjects, age 9–26 years), more than one in four children had wheezing that persisted from childhood to adulthood or that relapsed after remission (9). The factors predicting persistence or relapse were sensitization to house dust mites, BHR, female sex (OR 1.71; $P = 0.03$), smoking, and an early age at onset. In the 6- to 7-year-old subjects from the SIDRIA, the prevalence of wheeze or dry cough with pollens, or with house dust was higher in boys than in girls (5.7% vs 3.6%; $P < 0.001$) and (6.5% vs 4.9%; $P < 0.001$), respectively, whereas no difference was observed for the prevalence of symptoms with pets (1.4% vs 1.3%; 5).

A raised body mass index (BMI) was associated with asthma and atopy in females but not males in a study involving 7605 subjects aged 12 years or more who participated in the Canadian National Population Health Survey in 1994–1995 (51). In the longitudinal prospective cohort from Dunedin New Zealand, population-attributable fraction calculations estimate that 28% (95% CI: 7–45) of asthma developing in women after age 9 is due to overweight (52). In females, becoming overweight or obese between 6 and 11 years of age increased the risk of developing new asthma symptoms and increased BHR during the early adolescent period in the Tucson birth cohort (53), and BMI has been suggested to be a significant predictor of atopy, allergic symptoms and BHR in teenage girls (54).

Discussion

This review reports on considerable gender differences in asthma and allergic diseases in childhood and adolescence. It suggests that gender is an important determinant for asthma and allergies. The impact of gender varies considerably from childhood into adolescence and adulthood. In childhood, boys are consistently found to be at increased risk of asthma, which has been explained by differential growth of lung/airway size, and immunological differences (13, 14). There does not seem to be any major difference in the severity of symptoms in asthmatic males when compared to asthmatic females in childhood.

This suggests that boys do not have more frequently diagnosed asthma because of more severity of asthma. The higher prevalence of wheeze in boys is reflected in a higher prevalence of diagnosed asthma. In contrast, in early adolescence, girls are more likely to have wheeze not diagnosed as asthma, when compared to adolescent male wheezers. This difference in diagnosis is seen mainly in prevalence data from cross-sectional studies generally showing a higher risk of wheeze in girls that is not necessarily reflected by a higher prevalence of diagnosed asthma. However, prospective studies do support the hypothesis of a higher incidence of asthma and wheeze in girls after puberty. The rate of hospitalization for asthma follows the same pattern as the incidence data, with a reversal towards a higher risk in girls after puberty. Altogether these results argue in favour of a switch around puberty in the gender susceptibility to develop asthma. Possible explanations for these gender differences include hormonal changes during puberty, but also gender-specific differences in environmental exposures. Taken together, asthma after childhood is more severe in females than in males, and is underdiagnosed and undertreated in female adolescents. This aspect needs the consideration of doctors and allergists who diagnose and treat asthmatic individuals.

In conclusion, sex hormones are likely to play an important role in the development and outcome of the allergic immune response and asthma in particular, as outlined by many epidemiological studies. By obtaining functional data from appropriate models, the exact underlying mechanisms can be unravelled. To examine the effect of gender-specific differences in environmental exposures and changes of asthma prevalence and severity in puberty, larger populations may need to be investigated.

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