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Exercise-induced bronchospasm related to different phenotypes of rhinitis without asthma in primary schoolchildren: the French Six Cities Study.

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ABSTRACT

Background: Exercise-induced bronchospasm (EIB) is frequent among asthmatic children.

However, opinions differ on the relation between EIB and rhinitis in the absence of asthma.

Objectives: We assessed the relationship between EIB and various phenotypes of rhinitis according to asthmatic status at the general population level in the Six Cities Study.

Methods: 7,781 schoolchildren with a mean age of 10 years underwent an EIB test and skin prick test to assess allergic sensitization. Their parents completed a standardized questionnaire. This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/cea.12310

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questionnaire recording asthma-like symptoms and past-year rhinoconjunctivitis, ever hay fever, and a score for allergic rhinitis (SFAR) ≥ 7 as a marker of 'past-year allergic rhinitis'. EIB was defined as a fall in peak expiratory flow rate $\geq 15\%$ after exercise.

Results: Of the 6,813 schoolchildren retained for analysis, 227 (3.33 %) experienced EIB after exercise. Odds ratios [95% confidence intervals] between EIB and allergic rhinitis phenotypes in the absence of asthma were 1.56 [0.92-2.63] for ever hay fever, 1.97 [1.16-3.35] for past-year rhinoconjunctivitis and 1.84 [1.16-2.91] for a SFAR ≥ 7 . Results were unchanged after adjustment for confounders. Multiple correspondence analysis showed that EIB, although related to asthma, constitutes a separate entity. EIB was not significantly related to familial history of asthma.

Conclusion: In our large population-based sample of children, different phenotypes of atopic rhinitis were associated with EIB, independently of asthma. EIB, although related to asthma, seems to constitute a separate entity.

Clinical relevance: In this large (6,813) sample of 10 years children drawn from the general population, exercise-induced bronchospasm is associated with rhinitis phenotypes in the absence of asthma. Furthermore, it constitutes an entity independent from asthma and is not related to a familial history of asthma. Thus, investigating these symptoms could be important in this disease, since a specific nasal treatment might improve EIB in these children.

INTRODUCTION

The term exercise-induced bronchospasm (EIB) is used to describe a transient narrowing of the airways that occurs after a standardized exercise test independently of asthma [1].

The prevalence of EIB in a population depends on the population surveyed, the method used to detect EIB (laboratory vs. exercise challenge), the intensity and duration of exercise, the humidity and temperature of the inspired air and the outcome measures to record airway obstruction [2]. In clinical studies performed on a limited number of patients, treadmill or bicycle exercise is used to determine EIB, which is usually defined as a 10% or greater exercise-induced decline in forced expiratory volume in 1s. In epidemiological studies, a challenge consisting of 6 minutes of continuous exercise at an intensity sufficient to raise the heart rate to 80% of the maximum predicted usually yields satisfactory data. In all these studies, a threshold of between 10 and 15% fall in peak expiratory flow rate (PEFR) is used, which is more specific, although less sensitive, in the assessment of EIB [3].

The prevalence of EIB in the general population of Western children varied between 4.7% [4] and 12 % [5], 25% in some fields of competitive athletics and up to 90% in known asthmatic patients [6, 7]. In clinical studies involving rhinitis patients, the prevalence of EIB varied substantially, and the association between EIB and rhinitis is still a matter of debate [8-10] being mostly attributed to asthma, to which rhinitis is strongly related.

The aim of this study was to determine the relationship of EIB with different phenotypes of rhinitis in the absence of asthma, using data from the French Six Cities Study conducted in a large population-based sample of primary schoolchildren residing in metropolitan France.

METHODS

Protocol and population

Between 1999 and 2000, 9,615 primary schoolchildren were randomly selected for the French Six Cities Study. Of these, 7,781 were included in the full survey protocol. Details of the survey are described elsewhere [11, 12]. Authorization to conduct the survey was sought and obtained from the French Data Protection Authority (CNIL) and the local ethics

committee. Children were given a letter at school informing them and their parents of the purposes and modalities of the survey and requesting written consent to take part.

Questionnaire and health outcome

Parents completed an enriched version of the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire. The following phenotypes were defined.

Allergic rhinitis

- Ever hay fever (EHF): “Has your child ever had hay fever?”.
- Past-year rhino-conjunctivitis (PYRC): “In the past 12 months, has your child had a problem with sneezing or a runny or a blocked nose, when he or she did not have a cold or “the flu”? and, “In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?”.
- Past-year allergic rhinitis as ascertained through a Score For Allergic Rhinitis value ≥ 7 (SFAR), questionnaire encompassing 8 features that has been validated as a diagnostic tool to ascertain allergic rhinitis in the absence of a medical diagnosis in the general population [13].

Asthma and asthma-like symptoms

- Wheezing ever (EW): “Has your child ever had wheezing or whistling in the chest at any time in the past?”.
- Current wheezing (CW): “Has your child had wheezing or whistling in the chest in the last 12 months?”

And in the case of wheezing in the past year:

- Wheeze attacks in the past year: “How many attacks of wheezing has your child had in the last 12 months?”, the possible responses being “None, 1 to 3, >3 ”.
- Sleep disturbance due to wheezing in the past year: “In the last 12 months, has your child been woken up by wheezing?”

- Shortness of breath at night in the past year: “Has your child ever been woken up by shortness of breath?”
- Respiratory distress at night as defined by sleep disturbance due to breathing difficulties at night: “Has your child ever been woken up by respiratory distress?”
- Wheezing associated with exercise in the past year: “In the last 12 months, has your child’s chest sounded wheezy during or after exercise?”.
- Dry cough at night in the past year: “In the last 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or a chest infection?”.
- Ever asthma (EA): “Has your child ever had asthma?”
- Asthma confirmed by a doctor: “Was your child’s asthma confirmed by a doctor?”
- Current asthma (CA) as defined on the basis of affirmative responses to the three questions: “Has your child had chest wheezing or whistling over the previous 12 months”, “Has your child ever had asthma?” (Ever asthma (EA) and “Was your child’s asthma confirmed by a doctor?”

The following potential confounders of the relationship between EIB and rhinitis phenotypes and asthma outcomes were also recorded: gender, parental allergy (“Had the parents ever suffered from at least one allergic disease: asthma, allergic rhinitis, eczema”), parental socio-economic status and education, child’s body mass index (through objective assessment during the medical visit), environmental tobacco exposure and humidity. Lastly, asthma medication use was recorded (inhaled corticosteroids, short-acting beta agonists or cromones). The season was defined on the basis of the day the survey was conducted.

EIB

EIB was assessed outdoors via a six-minute running test performed on school premises. Temperature and relative humidity (RH) were recorded. Children were excluded from the

test if they had baseline PEFR < 70% predicted, and if they had taken a bronchodilator within the preceding 48 hours. Inhaled corticosteroids were not discontinued. Three mini-Wright (Mini-Wright, Clement Clark international, UK) technically acceptable measurements of PEFR with a variability <10% from the maximum were taken, and the highest value was kept as baseline. Those included were asked to run at their own pace for one minute as a warm-up, then at a faster, constant pace for the next four minutes. During the sixth minute, they had to run as fast as they could. Heart rate (HR) was measured at the end of the run, after PEFR measurement. PEFR measurements were then taken 1, 5 and 10 minutes thereafter. A $\geq 15\%$ exercise-induced decline in PEFR was classified as EIB [14]. The survey team was unaware of questionnaire responses and SPT results.

Allergic sensitization

The allergens used were house dust mites, cat, dog, cockroach (indoors), mixed grass and tree pollens (outdoors) and *Alternaria* (both indoors and outdoors). Histamine and an uncoated lancet were used as positive and negative controls. Skin prick test (SPT) positivity was defined as a wheal at least 3 mm in diameter and larger than the negative control. Monosensitization was defined when only one SPT was positive, and polysensitization when ≥ 2 SPTs were positive.

Statistical analysis

Children were excluded from the statistical analyses if they made inadequate effort throughout the running test. We used χ^2 test to determine the significance of differences in categorical variables, and Wilcoxon-Mann-Whitney test for continuous variables. The relation between EIB and risk factors, including age, gender, body mass index, sensitization, season, and cities was analyzed by multiple logistic regression. Factors significantly related to EIB were considered as confounders of the relationship between EIB and asthma and rhinitis phenotypes. The relationship between EIB as a dependent variable and asthma and rhinitis phenotypes as independent variables was analyzed by the logistic regression model. Odds ratios (ORs) and related 95% confidence intervals were then computed. ORs between EIB

and rhinitis phenotypes were estimated in the entire population and after stratification according to asthmatic status (based on a positive response to EA). ORs adjusted for confounders were also computed to confirm the observed relationships. Lastly, multiple correspondence analysis (MCA) was used to establish relationships between asthma-like symptoms and EIB. $P < 0.05$ was considered as statistically significant. All analyses were performed using SAS ® version 9.

RESULTS

General characteristics of the entire population-based sample

Of the 7,781 children recruited in 108 schools, 6,813 with a mean age ($\pm$ SD) of 10.4 ($\pm$ 0.7) years and a sex ratio (men/women) of 0.99 performed the running test. There was no significant difference in age, sex, social class and asthma medications between children who took the test and those who did not.

Of those taking part, 19.6, 7.8, 9.8, 4.4 and 7.35 % declared EW, CW, EA, CA and doctor's diagnosis of asthma, respectively. Past year wheezing, associated with exercise and dry cough at night were reported by 3.3% and 16.3% of children, respectively. 1.14% of the children were taking corticosteroids, 0.79% short-acting beta agonists, and 0.31% cromones. 11.7, 13.1 and 15.1% of children reported PYRC, EHF and a SFAR ≥ 7 respectively. Mean overall SFAR score (standard deviation) was 4.75 (4.73). During the survey period, RH and temperature ranged between 45-60% and 12-22 °C, respectively.

Prevalence of EIB

Mean HR on cessation of exercise was 146 beats/min. A fall in PEFR $\geq 15\%$ after exercise was found in 227 (3.33 %) children. In winter, the prevalence of EIB was significantly higher than in other seasons (table 1). No other significant relationships were observed.

Relationship between EIB and asthma phenotypes

The prevalence of different phenotypes and asthma-like symptoms is given in table 2. EIB was significantly related to asthma and asthma-like symptoms: ORs were 5.81 (4.24-7.90), 5.73 (4.23-7.76), 5.65 (4.01-7.88) for EA, CA, and doctor-diagnosed asthma, respectively. The prevalence of EIB rose significantly with asthma severity according to the type of symptoms. Results were unchanged when age, geographical zone and season were taken into account as potential confounders. EIB was significantly related to asthma medication in the case of short-acting beta agonists (OR=2.5; 95% CI: 1.13-4.47) but not in that of inhaled corticosteroids (OR=1.57; 95% CI: 0.81-3.03).

MCA showed that, although EIB is related to asthma and asthma-like symptoms, it constitutes a separate entity (Fig. 1). However, it indicated a high specificity of EIB in asthma ascertainment, since the absence of EIB (EIB – in the graph) was close to the absence of asthma-like symptoms (SYM – in the graph). In addition, EIB was not significantly related to familial history of asthma, not even among asthmatics ($\chi^2 = 1.76$; p -value = 0.185 in the total population, $\chi^2 = 0.58$; p -value = 0.445 in non-asthmatics and $\chi^2 = 1.88$; p -value = 0.170 in asthmatics).

Relation between EIB and rhinitis phenotypes

Rhinitis phenotypes significantly ($p < 0.0001$) increased the risk of EIB, with the greatest OR value being observed for PYRC, followed by SFAR and EHF (Table 3). The prevalence of EIB in children with EHF, PYRC or SFAR ≥ 7 but without asthma was also significantly greater (3.22, 3.80 and 3.81% respectively). As expected, when asthmatics were excluded, the observed ORs between EIB and rhinitis phenotypes were smaller than those observed in the entire population: 1.56 (0.92-2.63), 1.97 (1.16-3.35) and 1.84 (1.16-2.91) for EHF, PYRC and SFAR ≥ 7 , respectively (Table 4). Results were unchanged when age, cities and season were taken into account as confounders.

Relation between EIB and atopic sensitization

To better understand the interrelationships between EIB, rhinitis and asthma, we investigated the associations between EIB and allergic sensitization. Allergic sensitization to at least one allergen significantly ($p=0.0001$) increased the risk of EIB in asthmatics and in non-asthmatics [OR=4.48 (2.53-8.15) vs. 3.13 (2.04-4.7), respectively]. Allergic sensitization to indoor allergens was more closely related to EIB than allergic sensitization to outdoor allergens: OR=2.56 (1.86-3.52) vs. 4.27 (3.24-5.63) (Table 5). Polysensitization was associated with a greater risk of EIB than monosensitization [OR=4.97 (3.76 -6.56)].

DISCUSSION

Our population-based data showed that various phenotypes of rhinitis were significantly associated in primary schoolchildren with EIB in the absence of asthma. MCA showed that EIB, although related to asthma, constituted a separate entity. In addition, EIB in this population was not significantly related to familial history of asthma.

Several studies, including prospective population studies, have indicated that both allergic and non-allergic rhinitis are risk factors for the development of asthma [15-18]. However, opinions differ on the relation between rhinitis and EIB, and whether it is independent of asthma has yet to be investigated. A relation between rhinitis and EIB has been found in epidemiological studies but is not always reported in clinical studies [8, 9, 19-22]. On the basis of bronchial hyper-responsiveness (BHR) to pharmacological agents, non-asthmatic children with allergic rhinitis were more likely to have BHR than those without [23]. In addition, Italian outpatients with perennial allergic rhinitis due to continuous exposure to allergens, which is often related to asthma, had a heightened risk of BHR compared to subjects with seasonal rhinitis [24, 25]. However, asthma was not directly taken into account in these two Italian studies. In a nested case-control study of schoolchildren [22], past history

of “rhinitis” was associated with EIB, but the authors expressed reservations about how accurately or reliably this question could be answered. In the Six Cities Study, we found that various rhinitis phenotypes were related to EIB independently of asthma.

In our study, MCA showed that EIB, although related to asthma, constituted a separate entity. This was also shown, albeit indirectly, by the lack of association between EIB and parental history of asthma. Familial history of asthma may be the strongest predisposing risk factor for asthma occurrence in children. Clinical studies have found that first-degree relatives of asthmatic patients, including subjects without asthma symptoms, have higher rates of BIE [26-28]. However, our study provided no evidence of this.

The currently accepted explanation for the pathogenesis of EIB is the osmotic hypothesis, according to which the airway becomes dry causing the release of mediators during effort. Alteration of nasal function due to blockage of the nose, as in rhinitis, favors mouth breathing. This may lead to increased exposure of the lower airways to dry air and induce an increase in BHR [29]. Chronic nasal inflammation may also be associated with bronchial inflammation, as nasal challenge in adults increases lower airway inflammation [30].

The prevalence of EIB in our survey (3.3%) is in the low range compared to that of previous studies (table 6). This low prevalence may be explained, first, by recent, substantial changes in treatment, with the use of inhaled bronchial [31] and nasal corticosteroids [32], which decrease the occurrence of EIB [4] and may protect asthmatic children from non-specific BHR; and, second, by the exclusion of children who were unable to attain 70% of the PEFR predicted, and who had used bronchodilators or other antiasthma drugs in the 48 h preceding the test. Thirdly, seasonal variability in the pattern of response may occur, as observed in Ghana [33] (4.2% in the dry season versus 1.3% in the wet season in urban rich children). As shown in table 1, the prevalence of EIB was highest in winter, when the air was dry and cold. For the rest of the year, prevalence was higher in spring, than in summer or

autumn, probably because of exposure to outdoor airborne pollens. More than half of the exercise-induced tests were performed in spring, when the air was humid and not cold. Lastly, it is possible that maximal effort was not attained by all the children during the test. However, the similarity of EIB prevalence among cities suggests that the degree of exercise was similar and thus that the data were comparable.

In our general population sample, the prevalence of EIB was, respectively, 11.8, 11.3 and 11.8% in children suffering from CA, asthma diagnosed by a doctor and EA, which is lower than that classically reported in asthmatic patients. In a worldwide study of >10.000 asthmatic patients, currently taking medications or having had asthma symptoms within the last year, EIB was observed in a third to a half [34]. In children having intermittent asthma, the prevalence of EIB was 27% [35].

In our study population, sensitization to outdoor and indoor allergens, and polysensitization rather than monosensitization significantly increased the risk of EIB in our population. Previous findings showed that atopy is a significant risk for EIB in the general population of sensitized schoolchildren, even if they have no other indications of asthma [36-38]. In a general population of soldiers, the OR of having EIB was greater in subjects with higher levels for perennial allergens, but remained significant in those with high levels for seasonal allergens [20]. In a Spanish general population study, the strongest associations between EIB and atopy were found in subjects with sensitization to timothy-grass, mites and olive [39]. EIB increased significantly during the pollen season in subjects with asthma who were allergic to pollen, but not in subjects who were allergic to pollen but non-asthmatic [40].

Our study has certain limitations. Free running is accepted as the form of exercise which most reliably provokes bronchoconstriction in susceptible individuals, whereas treadmill running is considered to be more useful in determining bronchial response to exercise, since the intensity and the environmental conditions in which it is performed can be thoroughly controlled. However, if environmental conditions (temperature and humidity),

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exercise intensity, and airway status are controlled at the time of the test, treadmill and free running can be used indifferently as asthma-inducing exercises [41]. When two standard deviations below the mean value (10% fall in FEV1, 12,5% fall in PEF) are used for FEV1, sensitivity is 53.3% in treadmill running and 56.7% in free running with a specificity of 100% in both tests [41]. For peak expiratory flow, sensitivity is 43.3% in treadmill running and 26.7 % in free running with specificities of 93.3% and 96.7%, respectively". Information obtained by questionnaire is susceptible to false memory, particularly for symptoms at any time in the past. The ISAAC questionnaire has nevertheless shown its overall reliability in the case of 12-month symptoms. The cross-sectional design of our study has the inherent limitation of not establishing clear causal relationships but longitudinal studies have shown a relationship between rhinitis and subsequent onset of asthma in the general population. Lastly, our study involved only urban schoolchildren, and our findings may not be applicable to other populations with different types and levels of physical activity.

The strengths of our study are the large population-based sample and the use of objective tools. The use of the SFAR constitutes an added value.

CONCLUSION

The main findings to emerge from our study of a sample of children drawn from the general population are that EIB was associated with rhinitis phenotypes in the absence of asthma and that it constituted an entity independent from asthma and was not significantly related to familial history of asthma. Taken together, these results support the one-airway hypothesis. Further studies are needed to confirm and elucidate our findings.

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Conflict of interest None

Table 1. The prevalence of EIB was higher in winter than in spring and autumn

Season (ref: winter)	EIB (+) N (%)	EIB (-) N (%)	OR (95% CI)
Winter	77 (4.36)	1691 (95.64)	
Spring	109 (3.11)	3395 (96.89)	0.70 (0.52-0.95)
Summer	6 (2.01)	292 (97.99)	0.45 (0.19-1.04)
Autumn	35 (2.82)	1208 (97.18)	0.64 (0.42-0.95)

Table 2. The prevalence of different phenotypes of asthma and asthma-like symptoms

Asthma phenotypes	Prevalence (%)
Ever wheeze	19.6
Current wheeze	7,8
Ever asthma	9.8
Current asthma	4.4
Doctor's diagnosis of asthma	7,35

Table 3: Relationship between exercise-induced bronchospasm (EIB) and different phenotypes of rhinitis in the French Six Cities Study.

	EIB (+)	EIB (-)	p-value	OR
	N (%)	N (%)	(chi2)	(CI 95%)
EHF				
No	135 (2.66)	4941 (97.34)		
Yes	49 (6.41)	715 (93.59)	<0,0001	2.51 (1.79-3.51)
PYRC				
No	118 (2.54)	4564 (97.46)		
Yes	45 (7.21)	579 (92.79)	<0,0001	2.99 (2.10-4.25)
SFAR ≥7				
No	134 (2.56)	5108 (97.44)		
Yes	63 (6.98)	839 (93.02)	<0,0001	2.62 (1.94-3.53)

- EIB (+) = Exercise-induced bronchospasm positive, EIB (-) = exercise-induced bronchospasm negative. EHF: ever hay fever; PYRC: past-year rhinoconjunctivitis, SFAR ≥7: past year allergic rhinitis. OR: Odds Ratio. CI: confidence interval 95%

Table 4: Relationship between exercise-induced bronchospasm (EIB) and isolated (without asthma) phenotypes of rhinitis in the French Six Cities Study.

	EIB (+)	EIB (-)	p-value	OR
	N (%)	N (%)		(95% CI)
EHF				
Without EHF and EA	98 (2.09)	4595 (97.91)	<0,0001	
With EHF, without EA	17 (3.22)	511 (96.78)		1.56 (0.92-2.63)
Without EHF, with EA	35 (10,48)	299 (89,52)		5.49 (3.67-8,21)
With EHF and EA	31 (13,96)	191 (86,04)		7.61 (4.6-11.69)
PYRC				
Without PYRC and EA	87 (1.97)	4338 (98.03)	< 0,0001	
With PYRC without EA	17 (3.80)	430 (96.20)		1.97 (1.16-3.35)
Without PYRC, with EA	27 (10,04)	242 (89,96)		5.56 (3.55-8,73)
With PYRC and EA	30 (15,79)	160 (84,21)		9.35 (6.00-14.58)
SFAR ≥7				
SFAR < 7 without EA	104 (2.11)	4828 (97.89)	< 0,0001	
SFAR ≥ 7 without EA	23 (3.81)	581(96.19)		1.84 (1.16-2.91)
SFAR < 7 with EA	31 (9,97)	280 (90,03)		5,14 (3.38-7.81)
SFAR ≥ 7 with EA	40 (13,89)	248 (86,11)		7.49 (5.09-11.02)

EIB (+) = Exercise-induced bronchospasm positive, EIB (-) = exercise- induced bronchospasm negative, EHF: ever hay fever; PYRC=past-year rhinoconjunctivitis; SFAR≥7: past year allergic rhinitis, EA: Ever asthma, OR: Odds Ratio (CI: confidence interval 95%),

Table 5: Exercise-induced bronchospasm (EIB) and allergic sensitization in the French Six Cities Study.

	EIB (+)	EIB (-)	p-value	OR
	N (%)	N (%)	(chi2)	(CI 95%)
Allergic sensitization				
At least one allergen				
Monosensitization	110 (2.06)	5233 (97.94)		
Polysensitization	102 (9.45)	977 (90.55)	< 0,0001	4.97 (3.76 -6.56)
SPT+ to outdoor allergens				
No	158 (2.80)	4976 (97.97)		
Yes	54 (6.87)	1234 (91.88)	<0,0001	2.56 (1.86-3.52)
SPT+ to indoor allergens				
No	103 (2.03)	5478 (97.20)		
Yes	109 (8.12)	732 (93.13)	<0,0001	4.27 (3.24-5.63)

Table 6: Prevalence of EIB in different countries

<i>Author</i>	<i>Country</i>	<i>n</i>	<i>Region or group</i>	<i>Age</i>	<i>PEFR fall</i>	<i>FEV₁ fall</i>	<i>Prev</i>	<i>Season</i>
Burr(1974) ⁽⁴²⁾	UK	817	U	12	15%	ND	6.7	Unk
Burr(1989) ⁽⁴³⁾	UK	960	U	12	15%	ND	7.7	Unk
Barry (1991) ⁽⁵⁾	N-Zealand	873	U	12	15%	ND	12.1	Unk
Burr (2006) ⁽⁴⁾	UK	1019	U	12	15%	ND	4.7	Unk
Bardagi(1999) ⁽²²⁾	Spain	2114	U	9-14	15%	ND	6.6	Dec-March
Priftnaji (2001) ⁽⁴⁴⁾	UK	1000	U	10	15%	ND	5.4	Unk
Priftnaji (2001) ⁽⁴⁴⁾	Albania	1000	U	10	15%	ND	0.7	Unk
Anthracapoulos (2012) ⁽⁴⁵⁾	Greece	607	U	12	ND	> 13	10.4	Jan-March
Ng'ang'a (1998) ⁽⁴⁶⁾	Kenya	573 479	U R	8-12 8-12	ND	> 10	22.9 13.2	Unk
Addo-Yobo (1997) ⁽⁴⁷⁾	Ghana	425 142	UR UP	9-12	12.5%	ND	4.2 2.2	Dry
Addo-Yobo (2002) ⁽³³⁾	Ghana	624 607	UR UR	9-16	12.5%	ND	4.2 1.3	Dry Wet
Addo-Yobo (2007) ⁽³⁸⁾	Ghana	599 220	UR UP	9-16	12.5%	ND	8.33	Dry
Van Niekerk (1979) ⁽⁴⁸⁾	S-Africa	671 694	R U	6 -9	15%	ND	0.14 3.17	Unk
Keeley (1991) ⁽⁴⁹⁾	Zimb	726 642	UR UP	7- 9	15%	ND	5,8 3,1	Unk

U: Urban; R: Rural; UP: Urban Poor; UR: Urban Rich; PEFR: Peak Expiratory Flow Rate; Prev: Prevalence; Unk: unknown

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Fig 1: Exercise-induced bronchospasm and asthma-like symptoms (multiple correspondance analysis)

- N: No
- Y: Yes
- Cough: dry cough at night in the past year
- SOB: shortness of breath at night ever
- Resp.distress: respiratory distress ever.
- E.I.Wheezing: wheezing associated with exercise in the past year

Asthma.attacks: ever asthma attacks.

