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PREVALENCE AND ETIOLOGY OF ASTHMA AND ITS ASSOCIATION WITH GASTRO -ESOPHAGEAL REFLEX DISEASE. A SYSTEMATIC REVIEW STUDY

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Abstract:

Background and aim: *to find out the prevalence, etiology and its association with Gastro-oesophageal reflux disease (GORD).because it has been linked to a number of extra esophageal symptoms and disorders, primarily in the respiratory tract. This systematic review aimed to provide an estimate of the strength and direction of the association between GORD and asthma, prevalence and risk factors*

Methods: *Studies that assessed the prevalence or incidence of GORD in individuals with asthma, or of asthma in individuals with GORD, or prevalence of asthma and risk factors of asthma were identified in Medline and EMBASE via a systematic search strategy.*

Results: *There are five striking patterns: first, asthma prevalence is increasing worldwide; second, asthma is generally more common in Western countries and less common in developing countries; third, asthma is more prevalent in English-speaking countries; fourth, asthma prevalence is increasing in developing countries as they become more Westernized or communities become urbanized; and fifth, the prevalence of other allergic disorders may also be increasing worldwide. Twenty-eight studies met the selection criteria. The sample size weighted average prevalence of GORD symptoms in asthma patients was 59.2%, whereas in controls it was 38.1%. The average prevalence of asthma in individuals with GORD was 4.6%, whereas in controls it was 3.9%. Pooling the odds ratios gave an overall ratio of 2.3 (95% CI 1.8–2.8) for those studies measuring the prevalence of asthma in GORD. One longitudinal study showed a significant association between a diagnosis of asthma and a subsequent diagnosis of GORD (relative risk 1.5; 95% CI 1.2–1.8),*

Conclusions*: This systematic review indicates that, asthma prevalence is increasing worldwide. There is a significant association between GORD and asthma, but a paucity of data on the direction of causality. Genetic predisposition is clearly evident, gene by-environment interaction probably explains much of the international variation in prevalence rates for allergy and asthma. Environmental factors such as infections and exposure to endotoxins may be protective or may act as risk factors, depending in part on the timing of exposure in infancy and childhood. But diet and nutrition, stress, use of antibiotics and mode of delivery may also affect the early development of allergy and asthma. Later in childhood, putative risk factors include exposure to allergens, family size and structure, and sex and gender.*

Key words: *asthma prevalence, etiology of asthma, chronic cough, asthma and its association with GORD.*

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INTRODUCTION:

Asthma is the chronic disorder of the airways that makes breathing difficult. It is well known that the prevalence of asthma has been reported to increase in many places around the world during the last decades. [1] An increased understanding of the causes of asthma is coming from the international comparisons of asthma prevalence, particularly those from the European Community Respiratory Health Survey of asthma prevalence in adults. There are five striking patterns: first, asthma prevalence is increasing worldwide; second, asthma is generally more common in Western countries and less common in developing countries; third, asthma is more prevalent in English-speaking countries; fourth, asthma prevalence is increasing in developing countries as they become more Westernized or communities become urbanized; and fifth, the prevalence of other allergic disorders may also be increasing worldwide.[2] The median prevalence for the ECRHS study was 20.7%, with a range in the Western countries of 8.5% (Pavia) to 32.0% (Dublin). However, the prevalence was 4.2% in Algiers and 4.1% in Bombay. [2]

Asthma comprises a range of heterogeneous phenotypes that differ in presentation, etiology and pathophysiology. The risk factors for each recognized phenotype of asthma include genetic, environmental and host factors. Although a family history of asthma is common, it is neither sufficient nor necessary for the development of asthma. [3] The substantial increases in the incidence of asthma over the past few decades and the geographic variation in both base prevalence rates and the magnitude of the increases support the thesis that environmental changes play a large role in the current asthma epidemic. [4]

gastro-oesophageal reflux disease (GORD) develops when the reflux of stomach contents into the oesophagus causes chronic troublesome symptoms or complications.[5] The most recognizable symptoms of GORD are heartburn and acid regurgitation, GORD is believed to lead to extra-oesophageal symptoms and complications, primarily in the respiratory tract. [6] An association between GORD and asthma has been accepted for many years, and has been the focus of numerous studies and reviews. [7,8] the aim of this systematic review is to provide a realistic estimate of the strength and direction of the association between GORD and asthma in adults. Despite the large number of publications examining the clinical and epidemiological nature of this association, ambiguity remains. For example, estimates of the prevalence of GORD in individuals with asthma vary from 30% to 90%. [9]

METHODS:

Search strategy :

Studies published between 1960 and 2018 were searched in Medline and EMBASE using the following combinations of search terms: ‘asthma and reflux’ and ‘asthma and (reflux or GER or oesophagitis or hiatal hernia) and (risk or odds or incidence or prevalence)’, prevalence of asthama, risk factors of asthma and etiology of asthma.Articles that potentially assessed the prevalence or incidence of reflux symptoms, tells the prevalence of asthma, risk factors and etiology of asthma, abnormal oesophageal acid exposure, oesophagitis, hiatal hernia or Barrett’s oesophagus in adults with asthma, or the prevalence of asthma among adults with reflux symptoms or abnormal acid exposure were selected first based on the title, and then based on the abstract.

Study selection:

Studies conducted in a primary or secondary care setting were required to define asthma in accordance with American Thoracic Society (ATS) guidelines.[10] Patients were therefore required to have the following: a previous diagnosis of asthma with a history of discrete attacks of wheezing, coughing or dyspnea, and either an increase in the forced expiratory volume in one second (FEV1) of 20% from baseline after bronchodilator administration, or a decrease in FEV1 of 20% after methacholine Broncho provocation. F Studies describing the prevalence of reflux symptoms were required to give a description of the symptoms, including their severity and/or frequency. Studies that monitored oesophageal pH were excluded if the monitoring was performed for less than 24 hours. Or if the population source was not defined. Studies were excluded if they had a sample size of less than 50.

Analysis:

We determined overall prevalence estimates by pooling values from studies meeting the selection criteria and calculating average values weighted by sample size. For the studies reporting reflux symptoms, the average prevalence was calculated both with and without the studies reporting less frequent than weekly heartburn and/or acid regurgitation. Unadjusted odds ratios were pooled from studies that had included a comparison group to give overall estimates of the association between GORD and asthma. Heterogeneity was calculated using the I2 test.

RESULTS AND DISCUSSION:

Total 65 relevant studies were identified, 28 of these met our inclusion and exclusion criteria. The progression of studies through the search and

selection process is illustrated in fig 1,

Figure 1 Literature search strategy.

Asthma prevalence is increasing worldwide:

The first key pattern is that the prevalence of asthma is increasing worldwide.[11]Most studies that have determined the prevalence of asthma symptoms by using the same methodology in the same community at different times have reported that asthma prevalence has increased in recent decades and that the magnitude of the increase has in some cases been substantial (Table I).

TABLE I. Changes in prevalence of asthma or asthma symptoms in children and young adults

		Prevalence		
Country	**Period**	**1st Study (%)**	**2nd Study (%)**	**Reference**
Australia	1982-1992	5.6	10.5	Peat et al (1994)[21]
Canada	1980-1983	3.8	6.5	Infante-Rivard et al (1987)[22]
England	1956-1975	1.8	6.3	Morrison Smith (1976)[23]
	1966-1990	3.9	6.1	Whincup et al (1993)[24]
Finland	1961-1986	0.1	1.8	Haahtela et al (1990)[25]
France	1968-1982	3.3	5.4	Perdrizet et al (1987)[26]
Hong Kong	1989-1994	4.6	7.6	Lai et al (1997)[27]
Israel	1986-1990	7.9	9.6	Auerbach et al (1993)[28]
Japan	1982-1992	3.3	4.6	Nishima (1993)[29]
New Zealand	1969-1982	7.1	13.5	Mitchell (1983)[30]
	1975-1989	7.9	13.3	Shaw et al (1990)[31]
Norway	1981-1994	1.6	5.5	Nystad et al (1997)[32]
Papua New Guinea	1973-1984	0.0	0.6	Dowse et al (1985)[33]
Scotland	1964-1989	10.4	19.8	Ninan and Russell (1992)[34]
Singapore	1967-1994	4.0	20.0	Lee et al (1997)[35]
Sweden	1971-1981	1.9	2.8	Alberg (1989)[36]
Tahiti	1979-1984	11.5	14.3	Liard et al (1988)[37]
Taiwan	1974-1985	1.3	5.1	Hsieh and Shen (1988)[38]
United States	1971-1976	4.8	7.6	Gergen et al (1988)[39]
	1981-1988	3.1	4.3	Weitzman et al (1992)[40]
Vietnam	1961-1991	2.1	7.6	Nguyen (1995)*
Wales	1973-1988	4.2	9.1	Burr et al (1989)[41]

Asthma is more prevalent in Western countries:

The second pattern is that asthma prevalence is generally higher in Western countries than in developing countries. T by the ECRHS findings in which the rates for "wheezing in the last year" are considered. The median prevalence for the ECRHS study was 20.7%, with a range in the Western countries of 8.5% (Pavia) to 32.0% (Dublin). However, the prevalence was 4.2% in Algiers and 4.1% in Bombay.

The highest asthma prevalence rates are in English-speaking countries:

These patterns are consistent with the preliminary ISAAC study findings, in which the highest prevalence rates were observed in centers from the British Isles, Australia, New Zealand, and the Republic of Ireland.

Table 2

Language	**English**	**Spanish**	**Chinese**
Country	New Zealand	Spain	China
(No. of centers)	(6)	(5)	(5)
Written questionnaire (wheeze, any)	30.2	9.7	4.2
Video questionnaire (wheeze at rest)	18.4	7.4	2.0

Asthma prevalence is increasing in developing countries as they become more westernized or become urbanized:
Hsieh and Tsai [12] examined the prevalence of allergic disorders in schoolchildren 7 to 15 years of age in Taipei, Taiwan, and found that the prevalence of childhood asthma increased from 1.3% to 5.8%.the prevalence of asthma among Xhosa children living in a Cape Town township was more than 20 times greater than those from a rural area in the Transkei.

The prevalence of other allergic disorders is also increasing worldwide:
The fifth pattern is that the prevalence of other allergic disorders such as allergic rhinitis, atopic eczema and urticaria are also increasing worldwide. [13]

Etiology of and risk factors for asthma:
Genetics:
Family and twin studies have indicated that genetics plays an important role in the development of asthma and allergy,[14] Genome-wide linkage studies and case–control studies have identified 18 genomic regions and more than 100 genes linked with asthma and allergy in total 11 different populations.

Diet and nutrition:
Several studies have demonstrated that higher intake of fish or fish oil during pregnancy is associated with lower risk of atopic disease (specifically eczema and atopic wheeze) up to age 6 years. Similarly, higher prenatal vitamin E and zinc levels have been associated with lower risk of development of wheeze up to age 5 years.3

Mode of delivery:
Infants born with emergency c section have more prone to develop atopy[15] although no such association occurred with elective cesarean section.

Lung function:
Decreased airway calibre in infancy has been reported as a risk factor for transient wheezing, perhaps related to prenatal and postnatal exposure to environmental tobacco smoke. [16]

Family structure:
This may be exemplified in the real world by large family size, whereby later-born children in large families would be expected to be at lower risk of asthma than first-born children, because of exposure to their older siblings' infections

Socio-economic status:
Children of parents with lower socio-economic status have greater morbidity from asthma. [17]

Antibiotics and infections:
The use of antibiotics has been associated with early wheezing and asthma in several studies [18]. Respiratory infections in early childhood are associated with early wheezing, [19] but it is unclear whether infection alone has a role in the development of persistent asthma

Sex and gender:
Sex have effects on the development of asthma in a time-dependent manners. Until age 13–14 years, there greater the incidence and prevalence of asthma ratio in boys than among . Studies through puberty have shown a greater incidence of asthma among adolescent and young adult females and a greater proportion of males with remission of asthma. Up to the age 12, boys have more severe asthmatic attacks than girls, with higher rates of admission to hospital. In contrast, adult females have more severe asthma than males, with more hospital admissions. [4]

Occupational asthma:
Asthma related to workplace exposures has been documented in many occupational settings. Commonly associated occupations and exposures include car painting (isocyanates), hairdressing (various chemicals), domestic and commercial cleaning (cleaning solutions), health care professions (latex) and baking (flour dust), among many others. [4]

Asthma in individuals with GORD:
We identified a total of 15 studies that evaluated the presence of asthma in adults with GORD. Eleven studies met our inclusion criteria (table 3) and four studies were excluded out Of the included studies, nine were cross-sectional and two were cohort studies. Seven studies were general population surveys, three took their data from large administrative databases and one was based in secondary care. Nine studies reported the prevalence of asthma in individuals with GORD, giving an average prevalence of 4.6%. The average prevalence in controls was 3.9%, reported in seven of the studies. When only those studies that reported the prevalence of at least weekly heartburn and/or acid regurgitation were included (n = 4), the average prevalence increased to 12.3%, largely because of the exclusion of a very large database study (n = 101 366), which

reported the lowest prevalence of asthma in GORD (4.3%).Overall, seven cross-sectional studies included a control group. Pooling the unadjusted odds ratios using a random effects model gave an overall odds ratio of 2.27 (95% CI 1.814–2.834; fig 5). The calculated I2 was 85%.

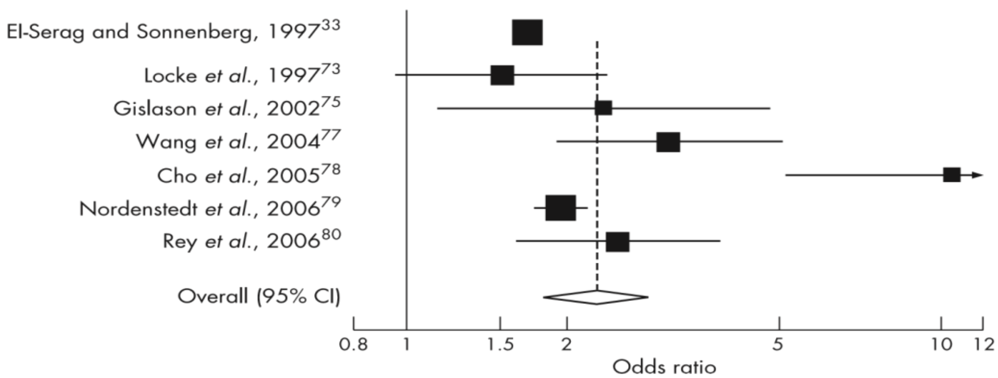

Figure 5 A forest plot of odds ratios obtained from seven cross-sectional studies that examined the prevalence of asthma among patients with GORD. The point estimate and 95% CI for the pooled odds ratio (represented by the diamond) is 2.26 (1.813–2.834).

Table 7 Included studies reporting the prevalence or incidence of asthma in individuals with symptoms of gastro-oesophageal reflux disease or evidence of oesophagitis

Reference	Country	Study design	Patient recruitment	Sampling frame	Definition of GORD	Definition of asthma	Method of data collection	Prevalence or incidence of asthma in individuals with GORD (%)	Prevalence or incidence of asthma in controls	OR/RR (95% CI) Unadjusted	OR/RR (95% CI) Adjusted
El-Serag and Sonnenberg 1997[33]	USA	Cross-sectional	All patients in Veterans Affairs system	Administrative database	Physician-diagnosed oesophagitis or stricture	Physician diagnosis	Database review	4314/101 366 (4.3%)	2602/101 366 (2.6%)*	OR 1.5 (1.4 to 1.6)	–
Locke et al 1997[73]	USA	Cross-sectional	Random	General population	Heartburn and/or acid regurgitation at least weekly	Self-reported	Questionnaire	35†/303 (11.6%)	51†/642 (7.9%)‡	OR 1.5 (1.0 to 2.4)†	OR 1.0 (0.6 to 1.3)§
Ruhl et al 2001[74]	USA	Cohort	Random	General population administrative database	Physician-diagnosed oesophagitis or hiatal hernia	Physician diagnosis	Database review	Incidence 2.6 cases per 1000 py (10/537)	Incidence 1.0 per 1000 py‖ (67/6391)	–	RR 2.1 (1.1 to 4.2)#
Gislason et al 2002[75]	Iceland, Belgium, Sweden	Cross-sectional	Random	General population	Nocturnal heartburn or belching at least weekly	Self-reported physician diagnosis	Questionnaire	9†/101 (8.9%)	84/2096 (4.0%)**	OR 2.3 (1.1 to 4.8)†	OR 2.2 (1.0 to 4.7)††
Jaspersen et al 2003[76]	Germany, Austria, Switzerland	Cross-sectional	Not reported	Patients referred for endoscopy	Erosive oesophagitis on endoscopy	Self-reported (recurrent wheezing)	Questionnaire	169/3245 (5.2%)	–	–	–
Khoshbaten 2003[37]	Iran	Cross-sectional	Random	General population	Heartburn at least 3 times in the last 2 weeks	Self-reported (asthma or wheezing)	Physician interview	4/70 (5.7%)	–	–	–
Wang et al 2004[77]	China	Cross-sectional	Random	General population	Symptom severity and frequency score of at least 3	Self-reported physician diagnosis	Questionnaire	28/430 (6.5%)	46/2102 (2.2%)‡	OR 3.1 (1.9 to 5.0)†	–
Ruigomez et al 2005[30]	UK	Cohort study with nested case-control analysis	Random	General population administrative database	Physician diagnosis	Physician diagnosis	Database review	Incidence 6.0 cases per 1000 py (4.9–7.3) (103/5653)	Incidence 3.8 cases per 1000 py (3.1–4.6)‡‡ (99/8105)	–	RR 1.2 (0.9 to 1.6)§§
Cho et al 2005[78]	Korea	Cross-sectional	Random	General population	Heartburn and/or acid regurgitation at least weekly	Self-reported	Questionnaire	13†/50 (26.0%)	39†/1205 (3.2%)‡	OR 10.5 (5.2 to 21.3)†	OR 2.6 (1.4 to 4.8)‖‖
Nordenstedt et al 2006[79]	Norway	Cross-sectional	Random	General population	Severe heartburn and/or acid regurgitation	Self-reported	Questionnaire	420/3153 (13.3%)	2940/40210 (7.3%)‡	OR 1.9 (1.7 to 2.2)†	OR 1.6 (1.4 to 1.9)##
Rey et al 2006[80]	Spain	Cross-sectional	Random	General population	Heartburn and/or acid regurgitation at least weekly	Self-reported	Questionnaire	30†/245 (12.2%)	91†/1709 (5.3%)‡	OR 2.5 (1.6 to 3.8)†	OR 1.0 (0.7 to 1.5)***

CI, Confidence interval; GORD, gastro-oesophageal reflux disease; OR, odds ratio; py, person-years; RR, relative risk.
*Controls were patients without a diagnosis of oesophagitis or oesophageal stricture.
†Calculated based on values given in publication.
‡Controls were individuals from the general population who had no symptoms of GORD.
§Adjusted for age, sex, psychosomatic symptom score and each of the remaining atypical symptoms.
‖Controls were individuals from the general population without hiatal hernia, oesophagitis, asthma, chronic bronchitis, emphysema or chronic cough at baseline.
#Adjusted for age, sex, marital status, education, body mass index, physical activity, smoking and diabetes.
**Controls were individuals from the general population without nocturnal symptoms of GORD.
††Adjusted for possible confounders.
‡‡Controls were age and sex-matched primary care patients without a diagnosis of asthma or GORD at baseline.
§§Adjusted for age, sex, smoking, previous morbidity and healthcare utilisation.
‖‖Adjusted for age, sex and remaining atypical symptoms.
##Adjusted for age, sex, body mass index, smoking and use of asthma medication.
***Adjusted for age, sex, coffee consumption, alcohol consumption, smoking, psychosomatic symptom score and all other atypical symptoms.

CONCLUSION:

Many cross-sectional studies have confirmed raised in the incidence and prevalence of asthma over the past 2 to 3 decades, but much remains unknown as to the fundamental immunologic, genetic and environmental mechanisms underlying the development of this condition and its increased expression, especially in the developed world. Nonetheless, some risk factors have now been clearly and consistently identified. For instance, avoidance of maternal smoking in pregnancy and in the early postpartum period can be strongly encouraged, as can avoidance of known occupational sensitizers. In contrast, previous advice to avoid animals and to breastfeed as long as possible to reduce the risks of asthma has been challenged by more recent studies. It is likely that detailed studies of gene-by-environment interactions and of epigenetics will eventually untangle the inconsistencies among the many putative exposures and outcomes. This systematic review indicates that there is a significant association between GORD and asthma, but a paucity of data on the direction of causality

REFERENCE:

1. Yangzong Y, Shi Z, Nafstad P, Håheim LL, Luobu O, Bjertness E. The prevalence of childhood asthma in China: a systematic review. BMC public health. 2012 Dec;12(1):860.
2. Beasley R, Crane J, Lai CK, Pearce N. Prevalence and etiology of asthma. Journal of allergy and clinical immunology. 2000 Feb 1;105(2):S466-72.
3. Beasley R, Crane J, Lai CK, Pearce N. Prevalence and etiology of asthma. Journal of allergy and clinical immunology. 2000 Feb 1;105(2):S466-72.
4. Subbarao P, Mandhane PJ, Sears MR. Asthma: epidemiology, etiology and risk factors. Cmaj. 2009 Oct 27;181(9):E181-90.
5. Vakil N, Veldhuyzen van Zanten S, Kahrilas P, et al. The Montreal definition and classification of gastro-esophageal reflux disease (GERD)—a global evidencebased consensus. Am J Gastroenterol 2006;101:1900–20.
6. Hungin AP, Raghunath A, Wiklund I. Beyond heartburn: a review of the spectrum of reflux-induced disease. Fam Pract 2005;22:591–603.
7. Field SK. Gastroesophageal reflux and asthma: are they related? J Asthma 1999;36:631–44.
8. Sontag SJ. Gastroesophageal reflux disease and asthma. J Clin Gastroenterol 2000;(Suppl 3):S9–30.
9. Field SK. A critical review of the studies of the effects of simulated or real gastroesophageal reflux on pulmonary function in asthmatic adults. Chest 1999;115:848–56
10. Cropp GJA, Bernstein IL, Boushey HA. Guidelines for bronchial inhalation challenges with pharmacologic and antigenic agents. Am Thorac Soc Bull 1980;6:11–19.
11. Anderson HR, Butland BK, Strachan DP. Trends in prevalence and severity of childhood asthma. BMJ 1994;308:1600-4.
12. Hsieh HH, Tsai YT. Increasing prevalence of childhood allergic disease in Taipei, Taiwan, and the outcome. In: Miyamoto T, Okuda M, editors. Progress in allergology and clinical immunology. Vol 2. International Congress of Allergology and Clinical Immunology, Kyoto, Japan, October 1991. Gottingen, Germany: Hogrefe & Huber Publishers; 1992. p. 223-5
13. 7. Williams HC. Is the prevalence of atopic dermatitis increasing? Clin Exp Dermatol 1992;17:385-91.
14. Willemsen G, van Beijsterveldt TCEM, van Baal CGCM, et al. Heritability of selfreported asthma and allergy: a study in adult Dutch twins, siblings and parents. Twin Res Hum Genet 2008;11:132-4
15. . Annesi-Maesano I, Moreau D, Strachan D. In utero and perinatal complications preceding asthma. Allergy 2001;56:491-7.
16. Martinez FD, Wright AL, Taussig LM, et al. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. N Engl J Med 1995;332:133-8
17. Strachan DP, Anderson HR, Limb ES, et al. A national survey of asthma prevalence, severity, and treatment in Great Britain. Arch Dis Child 1994;70:174-8.
18. . Alm B, Erdes L, Mollborg P, et al. Neonatal antibiotic treatment is a risk factor for early wheezing. Pediatrics 2008;121:697-702.
19. Friedlander SL, Jackson DJ, Gangnon RE, et al. Viral infections, cytokine dysregulation and the origins of childhood asthma and allergic diseases. Pediatr Infect Dis J 2005;24(Suppl):S170-6. 110. Becker A, Watson W, F