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REVIEW ARTICLE

Aspergillus hypersensitivity and allergic bronchopulmonary aspergillosis in patients with bronchial asthma: systematic review and meta-analysis

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SUMMARY

BACKGROUND: The prevalence of *Aspergillus* hypersensitivity (AH) and allergic bronchopulmonary aspergillosis (ABPA) in bronchial asthma is reported differently in various studies.

OBJECTIVE: To determine the prevalence of AH and ABPA in asthma using a systematic review.

METHODS: We searched the MEDLINE and EMBASE databases for studies published from 1965 to 2008 and included studies that report the prevalence of AH/ABPA in asthma. We calculated the proportions with 95% confidence interval (CI) to assess the prevalence of AH/ABPA in the individual studies and pooled the results using a random effects model.

RESULTS: Our search yielded 21 eligible studies. The prevalence of AH in bronchial asthma was 28% (95%CI 24–34), and was higher with an intradermal test vs. a prick test (28.7% vs. 24.8%, $P = 0.002$), but did not vary with the type of antigen used (indigenous or commercial). The prevalence of ABPA in bronchial asthma and *Aspergillus*-hypersensitive bronchial asthma was respectively 12.9% (95%CI 7.9–18.9) and 40% (95%CI 27–53). There was a wide variation in the criteria used for the diagnosis of ABPA. There was significant statistical heterogeneity assessed by the I^2 test and Cochran Q statistic in all the outcomes.

CONCLUSIONS: There is a high prevalence of AH and ABPA in patients with bronchial asthma. Careful screening should therefore be performed in all patients with bronchial asthma. Intradermal tests are more sensitive than prick tests for the diagnosis of AH. Finally, there is a need to adopt a uniform methodology and criteria for the diagnosis of AH/ABPA.

KEY WORDS: ABPA; *Aspergillus* hypersensitivity; allergic bronchopulmonary aspergillosis; prevalence; meta-analysis

ALLERGIC bronchopulmonary aspergillosis (ABPA) is a complex hypersensitivity response to the presence of *Aspergillus fumigatus* in the bronchial mucosa.[1] The entity was first described by Hinson et al. in 1952 in the United Kingdom in a description of three cases of bronchopulmonary aspergillosis.[2] This was followed by reports of ABPA from Australia,[3] North America[4] and India.[5] The disease was initially considered to be rare in countries other than England,[6] until a number of series of articles was published in various countries.[7,8] The diagnosis of ABPA led to the reappraisal of *Aspergillus* hypersensitivity (AH), generally defined as the presence of immediate cutaneous reaction to an *Aspergillus* antigen.[9] ABPA can be conceptualised as an exaggerated form of AH, which is responsible for several of the features of this condition, and AH may be considered as the first step in the development of ABPA. However, it is believed that only a minority of patients with AH go on to develop the complete clinical picture for ABPA.[9]

Despite numerous case series being published on ABPA, the exact prevalence of AH and/or ABPA in patients with bronchial asthma remains speculative. The exact prevalence of AH is also difficult to ascertain due to the variability of the skin tests (intracutaneous vs. prick tests) and the diverse antigens (commercial vs. locally prepared) used for the performance of these skin tests. The criteria for the diagnosis of ABPA include bronchial asthma, immediate skin test reactivity to *A. fumigatus*, elevated total and *A. fumigatus*-specific serum immunoglobulin E (IgE), pulmonary opacities, central bronchiectasis, peripheral blood eosinophilia and positive serum precipitins (IgG) against the *Aspergillus* antigen. None of these are specific for ABPA, and there is still no consensus on the number of criteria needed for diagnosis or the optimum disease-specific cut-off values for the various serological tests used. Moreover, patients at different stages of ABPA may not fulfil all these criteria.[1] Furthermore, it is difficult to determine an exact population prevalence of

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AH/ABPA because the diagnosis of AH/ABPA is established by laboratory testing, which is difficult to perform in community-based surveys. The prevalence of ABPA seems to be on the rise, probably as a result of an increase in awareness among clinicians[10] and general practitioners.[11]

We have previously described the prevalence of AH and ABPA in a large data set of patients with bronchial asthma.[12] A study that systematically measures the prevalence of AH/ABPA in bronchial asthma will help clinicians understand the magnitude of the problem and will further strengthen screening practices for AH/ABPA in this group of patients. A meta-analysis is a procedure for summarising different studies, aggregating study results and relating them to the various study characteristics. The aim of this study was to generate a large database, thereby enhancing sample size and limiting geographic variations to determine the prevalence of AH/ABPA in patients with bronchial asthma using a meta-analytic procedure.

MATERIAL AND METHODS

Search strategy

We first searched the literature for available systematic reviews that had evaluated the prevalence of AH/ABPA in patients with asthma. No systematic reviews were found. Our search strategy then aimed to identify studies that had described the prevalence of AH (defined for this review as the presence of an immediate-type cutaneous reaction to commercial or locally prepared extracts of *A. fumigatus* in the laboratory) and ABPA (no specific inclusion criteria was defined for inclusion in this review; however, we recorded the criteria used by different authors) in adults with bronchial asthma or the prevalence of ABPA in AH. We reviewed all published articles that reported the prevalence of AH/ABPA in patients with asthma, including both retrospective and prospective studies. We restricted the language of the publications reviewed to English. To identify studies for inclusion in the review, all the authors independently searched two computer databases, MEDLINE and EMBASE, for relevant studies published from 1965 to 2008 using the following free text terms: 'allergic bronchopulmonary aspergillosis' and 'ABPA'. The search was supplemented with several additional search strategies to identify relevant articles not found in electronic databases. We handsearched the indices of the *Journal of Allergy and Clinical Immunology* (1952–2008) and *Clinical Allergy* (1971–1988). We reviewed the reference lists of primary studies, reviews and editorials. We also reviewed our personal files. We excluded the following studies: 1) abstracts, editorials and case reports; 2) studies describing the prevalence of AH or ABPA in patients with cystic fibrosis; 3) studies describing the prevalence of AH or ABPA in children; and 4) studies in which the number of asthma patients screened (i.e., the denominator) was not reported.

Initial review of studies

The initial database created from the electronic searches was compiled and all duplicate citations were eliminated. Two reviewers (RA and ANA) screened these citations, without blinding, by title and abstract review to capture the relevant studies. Any disagreement was resolved by discussion between the authors. This database was then screened again to include only primary articles, and the full text of each citation was obtained and reviewed. Studies were eligible for inclusion if they reported the prevalence of AH/ABPA in patients with bronchial asthma.

Data abstraction

Data were recorded on a standard data extraction form. The following items were extracted: 1) publication details (title, authors and other citation details, including geographic area); 2) type of study (prospective or retrospective); 3) details of the criteria used for the diagnosis of ABPA; 4) type of skin test used (intradermal injection or skin prick test); 5) type of antigen used (commercial or locally prepared); 6) prevalence of AH and/or ABPA in patients with bronchial asthma where the numerator was the number of patients with AH or ABPA and the denominator was the number of patients with bronchial asthma; and 7) prevalence of ABPA in AH.

Determination of the pooled effect

The statistical software package (StatsDirect, version 2.6.7 for MS Windows; StatsDirect Ltd, Cheshire, UK) was used to perform the statistical analysis. We calculated the prevalence by calculating proportions with 95% confidence intervals (CIs) for each study and then

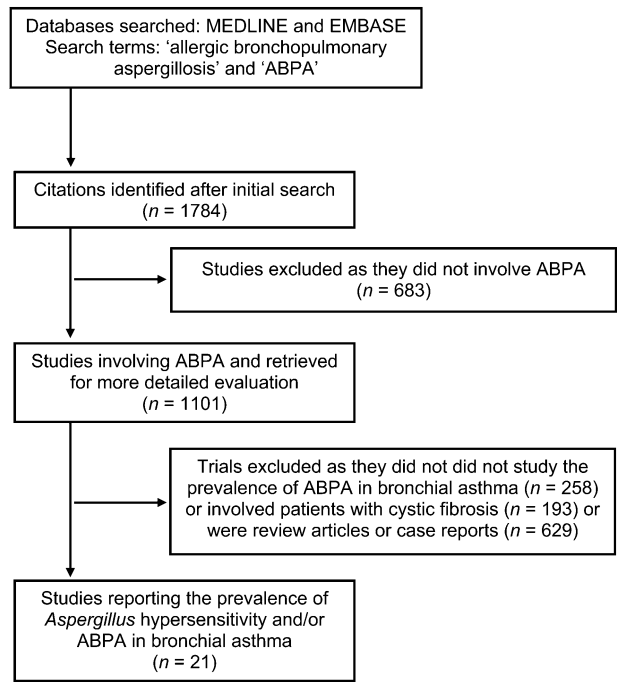

Figure 1 Citation selection process for the systematic review. ABPA = allergic bronchopulmonary aspergillosis.

pooled the data to derive a pooled proportion with 95%CI. For the purpose of proportion meta-analysis, the proportions were first turned into a quantity (the Freeman-Tukey variant of the arcsine square root transformed proportion) suitable for the usual fixed and random effects summaries.[13,14] The pooled proportion was calculated as the back-transform of the weighted mean of the transformed proportions, using DerSimonian weights for the random effects model[15] in the presence of significant heterogeneity.

Assessment of heterogeneity

The impact of heterogeneity on the pooled estimates of the individual outcomes of the meta-analysis was assessed using the Cochran Q statistic and I^2 test (measuring the extent of inconsistency among the results of the studies, interpreted as the approximate proportion of total variation in study estimates that is due to heterogeneity rather than sampling error).[16] An I^2 value of more than 40–50% indicates significant heterogeneity. As the Cochran Q test has a low

Table Studies describing the prevalence of *Aspergillus* hypersensitivity and/or ABPA in patients with bronchial asthma

Study (year), reference	Country	Type of study	Type of skin test	Type of antigen	Criteria used for diagnosis of ABPA	Prevalence of AH in asthma *n/N*	Prevalence of ABPA in asthma *n/N*	Prevalence of ABPA in AH *n/N*
Campbell et al. (1964)[18]	UK	Retrospective	Prick	Locally prepared	Major (A/R/T/E/P) Minor (C)	107/239	88/273	—
Longbottom et al. (1964)[19]	UK	Retrospective	Prick	Locally prepared	—	90/238	—	—
Agbayani et al. (1967)[20]	US	Prospective	Intradermal	Locally prepared	Major (A/R/T/E) Minor (C/B)	17/35	1/53	—
Henderson et al. (1968)[21]	UK	Prospective	Intradermal	Commercial (Bencard)	Major (A/R/T/E/P) Minor (C/B)	9/37	5/46	—
Hoehne et al. (1973)[22]	US	Prospective	Intradermal	Locally prepared	—	28/105	—	—
Hendrick et al. (1975)[23]	UK	Prospective	Prick	Commercial (Bencard)	—	86/656	—	—
Khan et al. (1976)[24]	India	Retrospective	Intradermal	Locally prepared	Major (A/R/T/E/P) Minor (C/SIII)	59/367	17/367	17/59
Louridas et al. (1976)[25]	UK	Prospective	Intradermal	Commercial (Bencard)	—	150/534	—	—
Schwartz et al. (1978)[26]	UK and US	Prospective	Prick	Commercial (Bencard)	—	49/193	—	—
Sobti et al. (1978)[27]	India	Prospective	Intradermal	Locally prepared	Major (A/R/T/E/P) Minor (C/SIII)	30/200	18/200	18/30
Malo et al. (1979)[28]	US	Prospective	Prick	Commercial (Bencard)	—	78/200	—	—
Benatar et al. (1980)[29]	South Africa	Retrospective	Prick	Commercial (Bencard)	—	110/500	—	—
Basich et al. (1981)[30]	US	Prospective	Intradermal	Locally prepared	Major (A/R/T/E/P/I/C)	18/42	12/42	12/18
Attapattu et al. (1991)[31]	Sri Lanka	Prospective	Intradermal	Commercial (Bencard)	Major (A/R/T/E/P) Minor (C)	58/134	8/134	8/58
Schwartz et al. (1991)[32]	US	Prospective	Intradermal	Commercial (Hollister-Stier)	Major (A/R/T/E/P/I/C/S)	—	—	38/100
Eaton et al. (2000)[33]	New Zealand	Prospective	Prick	Commercial (Hollister-Stier)	Major (A/R/T/E/P/I/C/S)	47/255	9/35	—
Kumar et al. (2000)[34]	India	Prospective	Intradermal	Locally prepared	Major (A/R/T/E/P/I/C/S) Minor (C/SIII/B)	47/200	32/200	32/47
Al-Mobeireek et al. (2001)[35]	Saudi Arabia	Prospective	Prick	Commercial (SoluPrick, ALK Laboratories)	—	12/53	—	—
Maurya et al. (2005)[36]	India	Prospective	Intradermal	Locally prepared	Major (A/R/T/E/P/I/C/S) Minor (C/SIII)	30/105	8/105	8/30
Agarwal et al. (2007)[37]	India	Prospective	Intradermal	Commercial (Hollister-Stier)	Major (A/R/T/E/P/I/C/S) Minor (SIII/B)	291/755	155/755	155/291
Prasad et al. (2008)[38]	India	Prospective	Intradermal	Not available	Major (A/R/T/E/P/I/C/S) Minor (C/SIII/B)	74/244	18/244	18/74

ABPA = allergic bronchopulmonary aspergillosis; A = asthma; R = radiological opacities; T = immediate positive skin test; E = eosinophilia; P = precipitins to *Aspergillus fumigatus*; I = IgE elevated; C = central bronchiectasis; S = specific IgG/IgE to *A. fumigatus*; C = sputum cultures of *A. fumigatus*; SIII = type III skin test positivity; B = brownish black mucus plugs.

sensitivity for detecting heterogeneity, a P value of <0.1 was considered to be significant for the presence of statistical heterogeneity.[17]

As this was a meta-analysis of published studies, institutional review board clearance was not required for the study.

RESULTS

Our initial database search retrieved a total of 1784 citations (Figure 1). Of these, 683 studies were excluded as they did not involve ABPA. A final 21 studies that met our inclusion criteria and that reported prevalence data on AH and/or ABPA were included in the final analysis.[18–38] The studies were published worldwide; 17 were prospective and four were retrospective (Table). Twenty studies (5092 asthma patients) described the prevalence of AH in patients with asthma,[18–31,33–38] 12 (2454 asthma patients) reported the prevalence of ABPA in asthma[18,20,21,24,27,30,31,33,34,36–38] and nine (650 *Aspergillus*-hypersensitive asthma patients) evaluated the prevalence of ABPA in patients with AH.[24,27,30–32,34,36–38] Most of the studies reported the prevalence of AH and ABPA in a group of chronic asthma patients; the remaining two studies[20,30] reported the prevalence of AH/ABPA in a group of chronic glucocorticoid-dependent asthma patients. Neither the prevalence of AH nor that of ABPA could be shown to be consistently increasing or decreasing over the last half a century (Figure 2).

Prevalence of AH in bronchial asthma

In eight studies the skin test was performed by the prick method; in the remainder the intradermal technique was used. Nine studies used a locally prepared *Aspergillus* antigen for cutaneous testing, whereas the others used a commercially prepared antigen (Table). The prevalence of AH in bronchial asthma varied from 15% to 48%, with the pooled prevalence being 28% (95%CI 24–34) by the random effects model (Figure 3); the difference between industrialised vs. developing countries was not statistically significant (659/2534, 26.0% vs. 711/2558, 27.8%). Significant clinical heterogeneity was reflected in the different antigens used for skin testing and the variable clinical criteria used for the diagnosis of ABPA (Table). There was also significant statistical heterogeneity (I^2 93.2, 95%CI 91.3–94.5, Cochran Q statistic 279.2, $P <$ 0.0001). The prevalence of AH was higher if an intradermal test (791/2758, 28.7%, 95%CI 27–30.4) was used compared to a prick test (579/2334, 24.8%, 95%CI 23.1–26.6); this difference was statistically significant ($P = 0.002$). Although the prevalence was slightly higher when a locally prepared antigen (426/1531, 27.8%, 95%CI 25.6–30.1) was used for skin testing compared to a commercially available antigen (870/3317, 26.2%, 95%CI 24.8–27.8), the difference was not statistically significant ($P = 0.24$).

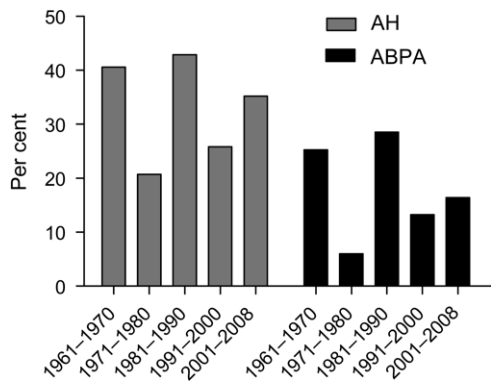

Figure 2 Prevalence of AH and ABPA over the last 50 years. There is no consistent increase or decrease in prevalence of AH or ABPA. AH = *Aspergillus* hypersensitivity; ABPA = allergic bronchopulmonary aspergillosis.

Prevalence of ABPA in bronchial asthma

The prevalence of ABPA in bronchial asthma ranged from 2% to 32%, with a pooled prevalence of 12.9% (95%CI 7.9–18.9) by the random effects model (Figure 4). The prevalence of ABPA reported from industrialised countries (115/449, 25.6%) was higher than in developing countries (255/2005, 12.7%); the difference was statistically significant ($P = 0.0001$). There was wide variation in the criteria used for the diagnosis of ABPA, as shown in the Table. There was significant clinical (Table) and statistical heterogeneity, with an I^2 value of 93.4% (95%CI 90.8–95) and Cochran Q statistic of 166.2 ($P < 0.0001$).

The prevalence of ABPA in *Aspergillus*-hypersensitive bronchial asthma varied from 6% to 68%, with a pooled prevalence of 40% (95%CI 27–53; Figure 5). There was statistical heterogeneity with both the I^2 test (89.7, 95%CI 83–93) and the Cochran Q statistic (77.9, $P < 0.0001$).

DISCUSSION

The results of this meta-analysis suggest a prevalence of AH and ABPA of approximately 28% and 13%, respectively, in patients with bronchial asthma. The prevalence of AH did not differ when stratifying the results based on reports from industrialised or developing countries; however, the prevalence of ABPA was significantly higher in reports from the developing world. One reason is that the number of patients reported from industrialised countries was far lower (almost one fifth) compared to the developing world. However, as there were no reports from many developing countries, such as Africa, and no further reports from other European or American industrialised countries, this poses some limitations on the interpretation of the results. The prevalence of ABPA in *Aspergillus*-hypersensitive bronchial asthma is very high, around 40% in this meta-analysis. Although the presence of clinical and statistical heterogeneity limits the confidence in the estimates of prevalence,

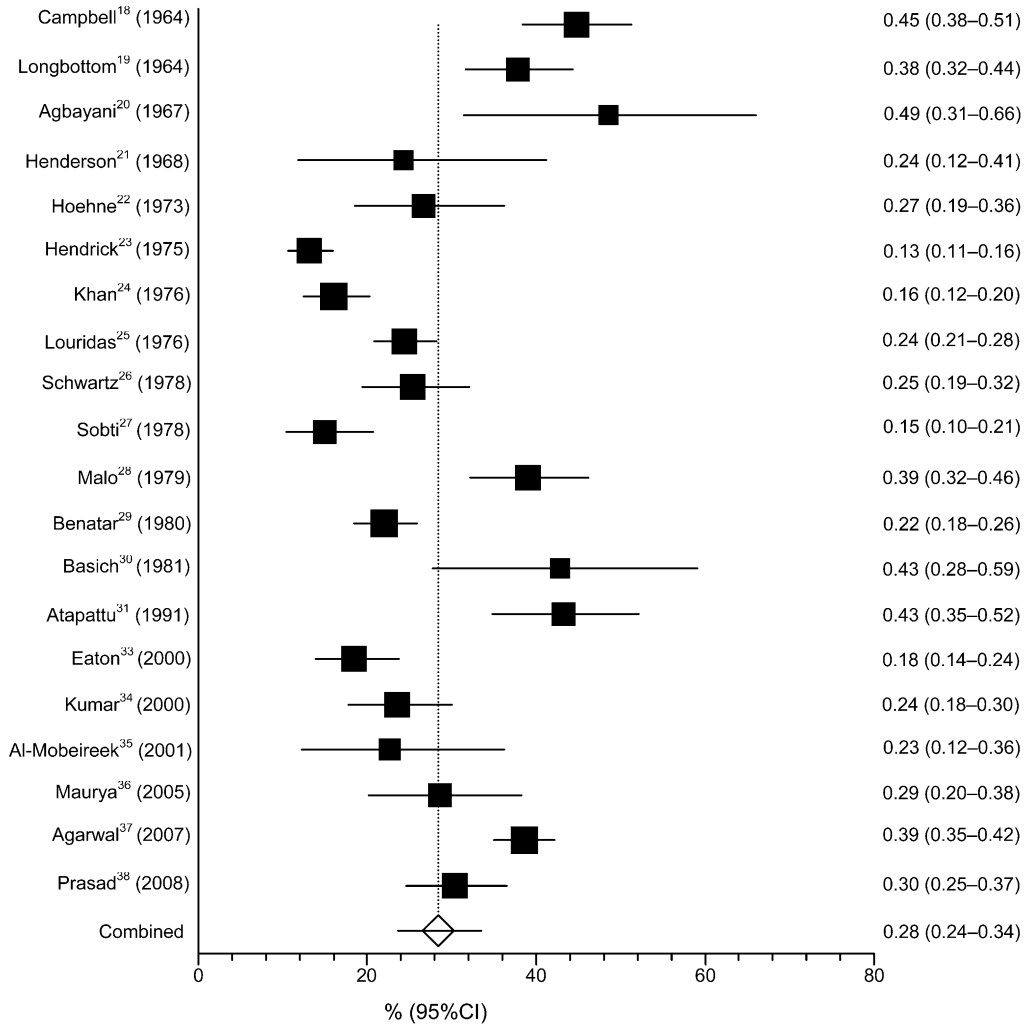

Figure 3 Prevalence of AH in patients with bronchial asthma (random effects model). The prevalence of AH in the individual studies is represented by a square (percentage) through which runs a horizontal line (95%CI). The diamond at the bottom represents the pooled prevalence from the studies (28.4%, 95%CI 23.6–33.9). CI = confidence interval; AH = *Aspergillus* hypersensitivity.

this was partially compensated for by adopting the DerSimonian and Laird's random effects model for pooling the individual studies.[16] Since its original description in England in 1952, ABPA has been diagnosed with greater frequency and certainty. However, the true population prevalence of AH/ABPA is still not clear, as most studies on ABPA are hospital-based and represent institutions/groups with a special interest in ABPA, which is likely to overestimate the prevalence. On the other hand, ABPA is also underdiagnosed, in part due to a lack of routine skin testing in most asthma clinics.[39] Variations in diagnostic criteria among centres may also be an equally important source of diagnostic uncertainty.

The prevalence of AH varied from 15% to 48%, and was significantly higher when an intradermal test was used for diagnosis compared to a prick test, although the type of antigen (locally prepared vs. commercial) had no effect. Skin testing for determining AH is usually performed by introducing a small quantity of *Aspergillus* antigen into the epidermis by the prick method or by intradermal injection. After the allergen has been introduced, it diffuses through the skin, where it binds to IgE antibodies (with specificity for the allergy) that are affixed to mast cells. When an allergen cross-links two or more mast cell-bound IgE antibodies, it leads to histamine release, with a resultant positive skin test. The outcome of a skin test is affected by the storage conditions of the aqueous allergen solutions, the complexity of the allergen extracts, the relative concentrations of the allergens in the extract (affecting the potency as well as the overall allergen concentration) and the technical expertise in performing the test (e.g., differences in needle pressure and/or interpretation of the test).[40] Skin tests are also sensitive to inhibition by drugs such as antihistamines, which can block the allergic response and give a false-negative result. In addition, extracts of some

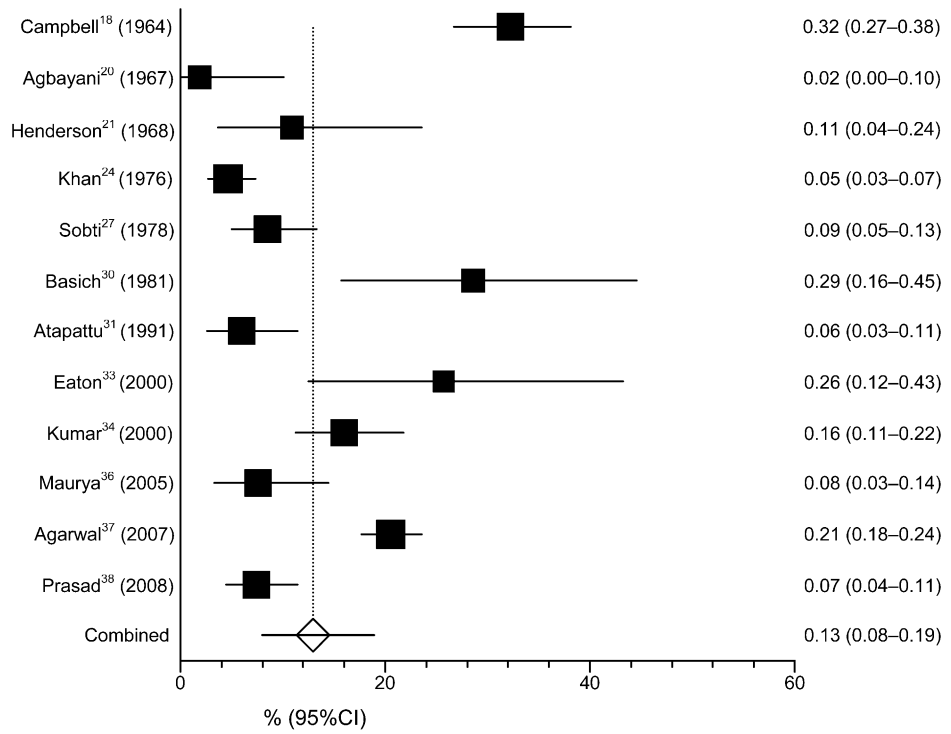

Figure 4 Prevalence of allergic bronchopulmonary aspergillosis (12.9%, 95%CI 7.9–18.9) in patients with bronchial asthma (random effects model). Prevalence of AH in the individual studies is represented by a square (percentage) through which runs a horizontal line (95%CI). The diamond at the bottom represents the pooled prevalence from the studies. CI = confidence interval.

allergens may contain irritants or chemicals that mimic an allergic response and produce a false-positive result. Standardisation of allergen extracts has always been difficult due to the complexity of the raw materials involved; however, use of well-defined pharmaceutical preparations is not without its problems.[40]

Although theoretically both the intracutaneous and prick tests should perform in a similar manner, it has

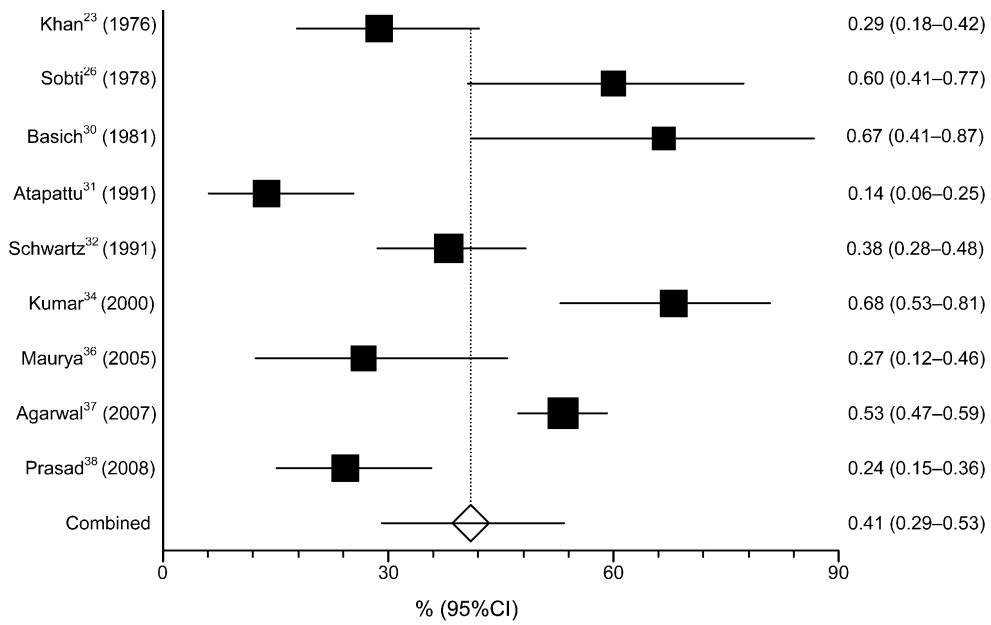

Figure 5 Prevalence of allergic bronchopulmonary aspergillosis (41%, 95%CI 29–53) in patients with *Aspergillus* hypersensitive bronchial asthma (random effects model). Prevalence of AH in the individual studies is represented by a square (percentage) through which runs a horizontal line (95%CI). The diamond at the bottom represents the pooled prevalence from the studies. CI = confidence interval.

been found that intradermal tests are generally more sensitive than prick tests.[40] The higher prevalence of AH with intradermal testing compared to the prick test has also been described previously in patients with ABPA,[28] and this meta-analysis reinforces this finding. If technically feasible, a prick test should therefore be performed for *Aspergillus* skin testing, and if negative it should be confirmed by an intradermal test.

The significance of AH, besides being a possible forerunner of ABPA, remains unclear. In the recently published European Community Respiratory Health Survey, the frequency of sensitisation to *Alternaria* or *Cladosporium*, or both, was a powerful risk factor for severe asthma in adults.[41] Previous studies have shown that exposure to environmental fungi increases the frequency of hospital admissions,[42] the risk of death from asthma[43] and the frequency of acute attacks of asthma requiring admission to an intensive care unit.[44] However, none of these studies specifically evaluated AH with the severity of asthma. In a study published in 1979, AH in bronchial asthma was related to the severity of airways obstruction.[28] In another study from India, although the duration of asthma was longer and the age at onset of asthma was significantly earlier in patients with AH, the lung function tests did not vary significantly.[36] More studies are required to understand the impact of AH in patients with bronchial asthma without ABPA. In this study, the prevalence of ABPA in patients with AH varied from 27% to 53%. This is an important observation, and suggests that all patients with AH should be evaluated for the diagnosis of ABPA, which should be carefully excluded.

The population prevalence of ABPA in patients with bronchial asthma is not currently known. Two unpublished questionnaire-based surveys[45] and one published study[46] did attempt to address this issue. In the study from Ireland (which included a catchment area population of around half a million), 14 patients with allergic bronchopulmonary mycosis were identified from a total of 1390 new referrals, estimating a period prevalence of just above 1%.[46] In a questionnaire-based survey carried out in 2.4 million people in Orange County, California, 143 cases of ABPA were under the care of pulmonary and allergy specialists.[45] In 1991, the ABPA Committee of the American Academy of Allergy, Asthma and Immunology conducted another survey among members of the academy to ascertain the number of ABPA cases under their treatment. Of the 33% respondents, it was observed that 703 patients with ABPA were under current care, and that other general physicians shared 49% of these. If the same case rate is assumed amongst the non-respondents, this figure might increase to two thousand. Both of the above surveys carried out in the United States projected the maximum number of ABPA patients in 1991 to be around 11 000 (in a total population of 260 million), representing 1% of the estimated 12 million asthma patients in the US.[45] However, neither survey was peer-reviewed and they represent a crude estimate of the prevalence of ABPA.

Is the prevalence of ABPA in bronchial asthma as high as 12%, as suggested in this study? Probably not, but the prevalence of ABPA in bronchial asthma patients who visit specialised chest clinics or are in a particular geographic area is likely to be high. Although most reviews on ABPA report a prevalence of ABPA in bronchial asthma of approximately 1–2%, this inference is not based on any definite evidence, as discussed above.

An important limitation of the results of this meta-analysis is the presence of clinical heterogeneity. In this systematic review, various studies have adopted different methodologies (including the use of various antigens for skin testing) and criteria for the definition of ABPA. This is inevitable, as the understanding, diagnosis and management of this entity have been evolving over the last six decades, and the criteria used in the older studies were those that were prevalent during that era. Thus, based on our study results, asthma clinics should adopt a policy for screening all patients with asthma for ABPA with an *Aspergillus* skin test (and probably IgE levels). Further work-up for ABPA is warranted only if screening tests are positive. The aim of early diagnosis and treatment of ABPA is to prevent bronchiectasis, which is not only a sign of irreversible lung destruction but also a poor marker of prognosis in patients with ABPA, because patients with ABPA who have bronchiectasis are prone to recurrent relapses and failure to achieve complete remission.[37]

To summarise, we have systematically measured the prevalence of AH/ABPA in bronchial asthma. The current work goes some of the way in addressing this issue, although, as with all systematic reviews, the quality of the information that is yielded depends on the quality of the individual trials that are being analysed. The results of this study show that the prevalence of AH/ABPA in the asthma clinic is sufficiently high to justify the use of a protocol for routine screening for AH/ABPA in patients with asthma. We have also shown that intradermal tests perform better than skin prick tests for AH screening. The limitations of this study include the wide variation of the individual studies regarding the diagnostic methods and the criteria used for the diagnosis of ABPA. There was also a wide range in the reported prevalence of AH and ABPA in the different studies, also reflected by the presence of significant statistical heterogeneity in all the outcomes of this meta-analysis. Although we did use a random effects model to pool the individual studies, this only partially solves the problem. Future studies should try to adopt a uniform methodology for the performance of the various tests used in the diagnosis of ABPA, including the use of a standardised antigen and technique for the performance of *Aspergillus* skin testing. There is also a need to adopt uniform methodology and diagnostic criteria for the diagnosis of ABPA.

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RÉSUMÉ

CONTEXTE : La prévalence de l'hypersensibilité à *Aspergillus* (AH) et de l'aspergillose bronchopulmonaire allergique (APBA) dans le cadre de l'asthme bronchique fait l'objet de données différentes dans diverses études.
OBJECTIF : Déterminer la prévalence de l'AH et de l'APBA dans l'asthme en réalisant une revue systématique.
MÉTHODES : Nous avons recherché les données de MEDLINE et de EMBASE au sujet des études publiées entre 1965 et 2008 et avons inclus celles qui ont signalé la prévalence de l'AH/ABPA dans l'asthme. Nous avons calculé les fréquences avec un intervalle de confiance à 95% (IC) pour évaluer la prévalence de l'AH/ABPA dans chaque étude individuelle et nous avons regroupé les résultats en utilisant un modèle d'effets aléatoires.
RÉSULTATS : Notre recherche a rassemblé 21 études éligibles. La prévalence de AH dans l'asthme bronchique est de 28% (IC95% 24–34) et est plus élevée lors de l'utilisation du test intradermique qu'après un test de ponction cutanée (28,7% vs. 24,8% ; $P = 0{,}002$), mais elle ne varie pas selon le type d'antigène utilisé (fabrication locale ou commerciale). La prévalence de l'ABPA dans l'asthme bronchique et celle de l'asthme bronchique avec hypersensibilité à *Aspergillus* a été respectivement de 12,9% (IC95% 7,9–18,9) et 40% (IC95% 27–53). On a observé de larges variations dans les critères utilisés pour le diagnostic de l'ABPA. On a noté une hétérogénéité statistique significative évaluée par le test I^2 et par la statistique Cochrane Q sur tous les résultats.
CONCLUSIONS : Chez les patients atteints d'asthme bronchique, la prévalence d'AH et d'ABPA est élevée. Dès lors, un dépistage soigneux doit être pratiqué chez tous les patients atteints d'asthme bronchique. Les tests intradermiques sont plus sensibles que les prick tests pour le diagnostic de l'AH. Finalement, il est nécessaire d'adopter une méthodologie et des critères uniformes pour le diagnostic de l'AH/ABPA.

RESUMEN

MARCO DE REFERENCIA : La prevalencia de hipersensibilidad a *Aspergillus* (AH) y de aspergilosis broncopulmonar alérgica (ABPA) en casos de asma bronquial difiere en los diferentes estudios.
OBJETIVO : Determinar la prevalencia de AH y ABPA mediante una evaluación sistemática.
MÉTODOS : Se investigaron las bases de datos MEDLINE y EMBASE en busca de estudios publicados entre 1965 y 2008 y se incluyeron los que referían la prevalencia de AH y de ABPA en el asma. Con el objeto de evaluar estas prevalencias en cada estudio, se calcularon las proporciones con un intervalo de confianza (IC) del 95% y se obtuvieron resultados acumulados mediante un modelo de efectos aleatorios.
RESULTADOS : Se encontraron 21 estudios idóneos. La prevalencia de AH en casos de asma fue de 28% (IC95% 24–34) y fue más alta con la prueba intradérmica que con la prueba por punción (28,7% comparado con 24,8% ; $P = 0{,}002$), pero no varió con el tipo de antígeno utilizado (natural o comercial). La prevalencia de ABPA en el asma fue del 12,9% (IC95% 7, 9–18,9) y la de asma con AH 40% (IC95% 27–53). Se observó una amplia variación en los criterios diagnósticos de la ABPA. La heterogeneidad estadística, evaluada mediante las pruebas I^2 y Cochran Q, fue significativa para todas las variables analizadas.
CONCLUSIONES : Existe una alta prevalencia de AH y de ABPA en los pacientes con asma bronquial. En consecuencia, se debería realizar una detección sistemática cuidadosa en todos los pacientes con asma. En el diagnóstico de AH son más sensibles las pruebas intradérmicas que las pruebas por punción. Por último, es preciso adoptar un método y criterios uniformes en el diagnóstico de AH y de ABPA.