



Unawareness and undertreatment of asthma and allergic rhinitis in a general population[☆]

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Summary The aim of this study was to determine the extent of unawareness and undertreatment of asthma and allergic rhinitis in an adolescent and adult population in Copenhagen, Denmark.

Methods: Patients with asthma and rhinitis were recruited by a standardised asthma and rhinitis screening questionnaire. Out of a random sample of 10,877 subjects aged 14–44 years, 1149 subjects were treated or reported symptoms of asthma or rhinitis and agreed to participate. Those subjects were assessed on history, lung function tests, and skin prick tests. Disease severity and optimal treatment were decided according to the GINA and ARIA guidelines.

Results: A total of 726 participants suffered from asthma and/or allergic rhinitis. Concomitant upper and lower airways disease was found in 47%. Seventy-five per cent were allergic and 44% with a known allergy had been tested previously. Asthma was undiagnosed and untreated in 50% of all the asthmatics. According to the guideline recommendation, 76% of asthmatics were undertreated. Rhinitis was undiagnosed in 32% of patients and 83% with moderate to severe rhinitis were undertreated. Patient knowledge about self-care and education was low.

Conclusions: In this population a large proportion of patients were unaware of having asthma or rhinitis. The pharmaceutical treatment and management practice were inadequate. Our study emphasises the need for additional intervention.

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Abbreviations: ACAAI, American College of Allergy Asthma and Immunology; ARIA, Allergic Rhinitis and its Impact on Asthma; COPD, Chronic Obstructive Pulmonary Disease; ERS, European Respiratory Society; GINA, Global Initiative for Asthma

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Introduction

The incidence and prevalence of asthma and allergy are increasing concomitantly with improvements in the diagnosis, treatment, and understanding of the diseases.^{1–4} Identification of patients with asthma has the potential to lessen impairment in health and functional status and cut

down expenditure on health care.⁵⁻⁷ Allergy plays a role in the development of asthma and rhinitis, which are often chronic diseases. Patients with allergies may report poorer job or school performance and allergic rhinitis may interfere with sleep, intellectual functioning and recreational activities.^{8,9} Studies of randomly selected populations indicate that up to more than a third of patients with rhinitis and asthma are undiagnosed and suffer from symptoms of allergy and a decrease in the quality of life.^{8,10-14} This prompted a range of measures; guidelines, health promotion, patient education, and public information. Such initiatives should provide a unique environment for early diagnosis and optimal treatment. We, therefore, examined the current extent of unawareness and undertreatment of patients with asthma and allergic rhinitis after the above initiatives had been put into practice.

Material and methods

Screening population

In year 2000, a random population sample of 10,877 subjects aged 14-44 years (to minimise entry of patients with COPD) living in Copenhagen, Denmark, was taken from the civil registration list. All the subjects were sent a letter with an asthma and rhinitis screening questionnaire comprising 20 questions adapted from the ACAAI screening programme.¹⁵ Five thousand eight hundred forty-nine (response rate: 54%) subjects responded to the postal questionnaire. In the case of at least one affirmative response concerning respiratory tract symptoms or treatment, the subject was invited to take part in the present survey. The local ethical committee of Copenhagen, Denmark approved the study. All the participants were told about the study verbally and in writing and all patients, parents/guardians gave their informed consent.

Study population

Altogether, 1149 (10.6%) subjects reported respiratory symptoms or treatment and were examined.

Each of the subjects was given a physical examination and a disease-specific case history was taken by a respiratory specialist. Participants were asked not to use medication interfering with the tests described below. Of the 1149 responders, 726 patients (314 male, 412 female) met the current guideline criteria of asthma and/or allergic rhinitis ("doctor-diagnosed patients"). In the re-

maining 423 we could not confirm asthma or allergic rhinitis; i.e., the majority had asthma symptoms (e.g., cough), but no objective measurements of reversible airways, and were thus considered non-asthmatics; a small number with lower tract respiratory symptoms, such as shortness of breath or cough, but not asthma, suffered from sarcoidosis, chronic obstructive pulmonary disease, and cardiac illness.

Patient history

All participants filled in a questionnaire concerning their general health, respiratory and allergic symptoms (in the preceding 4 weeks or at any time in the past) and a questionnaire on their knowledge about self-care, their current medication, and smoking habits, referrals, and GP visits. Life time tobacco exposure was calculated as pack years (tobacco consumption [g/day]/20 × duration of smoking [years]). Height and weight were measured and the body mass index (BMI) was calculated as ((weight [kg])/(height [m]²)).

In patients with asthma, the severity of asthma (mild, mild persistent, moderate and severe) was classified according to the GINA guidelines.¹⁶ In addition, the severity of rhinitis was categorised in accordance with ARIA guidelines.¹⁷

Pulmonary function test and methacholine challenge test

Spirometry was done on a 7-L dry wedge spirometer (Vitalograph[®]) in accordance with the ERS recommendations¹⁸ and the percentage of predicted normal values was calculated. Airway responsiveness to inhaled methacholine was measured in accordance with the method of Yan et al.¹⁹ in all patients with a FEV₁ > 70%. The dose producing in a 20% fall in FEV₁ (PD₂₀) was calculated, and the dose-response slope (DRS) calculated as the decline in FEV₁ divided by the highest dose of methacholine given.^{20,21} A constant of 4 was added to all dose-response slopes to eliminate negative and zero values. Logarithmically transformed DRS values were used for analysis. Measurement of the FEV₁ was repeated 15 min after administration of 0.6 mg of salbutamol.

Skin prick test

A skin prick test was performed in duplicate with an ALK-Abello lancet with a 1-mm tip according to the EAACI recommendation.²² Patients were tested with 10 common inhalant allergens. A positive

result was defined as a weal response of at least 5 mm to one or more allergens. Patients with positive skin tests were considered atopic.

Diagnosis of asthma

Asthma was diagnosed on both a combination of respiratory symptoms (cough, chest tightness, dyspnoea, wheeze) and reversible airway signs, i.e. airway hyperresponsiveness (AHR) to inhaled methacholine $<4.0\ \mu\text{mol}$, or peakflow variability $>20\%$ over a period of 2 weeks (miniWright[®] Peak Flow meter), or at least a 500 ml increase in FEV₁ after bronchodilator challenge. Patients were considered asthmatics only, if one or several of the above symptoms were confirmed by one of the above tests. Subjects were asked, "Have you ever been told that you suffer from asthma?" Those, with no previous diagnosis, but with asthma-like symptoms within 12 months of (written self-reporting of symptoms) or 4 weeks before (physician-interviewed) the first visit were labelled undiagnosed symptomatic asthmatics. At the time of diagnosis, it was possible to assess from the severity of the disease and current medication whether patients were receiving optimal treatment, as suggested by the GINA guideline.¹⁶

Diagnosis of rhinitis

Allergic rhinitis was identified by symptoms of rhinitis when patients were exposed to aeroallergens and showed a positive allergen skin prick test. The questionnaire concerning severity of upper airway symptoms and definition of rhinitis

symptoms within the preceding 4 weeks (physician-interviewed) or at any time (written self-reports) were classified in accordance with ARIA guidelines.¹⁷ It was possible to assess from the disease severity and current medication whether patients were receiving optimal treatment, as suggested by the ARIA guidelines.

Analysis

The data were analysed with the statistical pack, SPSS for Windows. Frequencies were calculated for the entire group and differences were tested by χ^2 analysis. Furthermore, differences in mean (\pm SD) values between participants with and without respiratory symptoms were tested by parametric analysis (Student's *t*-test). A *P* value <0.05 was considered significant.

Results

Patients' characteristics

Of the 726 participants with a diagnosis of asthma or allergic rhinitis, 493 (68%) were diagnosed as having asthma with ($n = 338$) or without rhinitis ($n = 155$) and 571 (79%) rhinitis with or without asthma. One hundred and fifty-five (21%) had asthma only and 233 (32%) allergic rhinitis only, and 338 (47%) had both (Table 1). Of the asthma patients, 69% (338/493) also had rhinitis, and of those with rhinitis 59% (338/571) also suffered from asthma. Patients with asthma only and those with both asthma and rhinitis exhibited lower FEV₁,

Table 1 Patient characteristics (mean (SD)).

	Asthma only	Allergic rhinitis only	Asthma & rhinitis	All
No.	155	233	338	726
Gender (female)	67%	48%*	58%	57%
Age	27.56 (9.6)*	29.98 (8.8)	28.93 (9.1)	28.98 (9.2)
BMI	24.03 (4.4)	24.45 (5.1)	25.08 (5.3)	24.66 (5.1)
FEV ₁ absolute	3.44 (0.8)**	3.98 (0.8)	3.56 (0.8)	3.67 (0.8)
FEV ₁ % predicted	93.81 (16.8)**	98.80 (12.5)	93.2 (14.8)	95.5 (14.9)
FVC	4.24 (1.1)**	4.70 (1.0)	4.35 (1.0)	4.44 (1.0)
FVC % predicted	96.44 (13.0)	97.65 (12.7)	95.21 (14.3)	95.84 (14.3)
FEV ₁ /FVC ratio	81.99 (9.5)	85.1 (6.2)**	82.00 (8.3)	83.0 (8.1)
Atopy (i.e. pos. allergy skin test)	21%	100%	83%	75%
AHR logDRS	0.998 (0.4)	0.690 (0.1)**	1.002 (0.4)	0.898 (0.4)
Never smokers	20%	34%	34%	31%
Current smokers	49%	33%	36%	38%
Pack years	7.98 (7.7)	6.59 (7.9)	7.54 (8.8)	7.41 (8.3)

<0.05 , * $P < 0.01$, ** $P < 0.001$.

Airway hyperresponsiveness (AHR) (dose response slope (DRS))

compared with the rhinitis only patients ($P < 0.001$). Airway responsiveness was increased in asthmatics, who demonstrated a significantly higher logDRS than observed in patients with rhinitis only (0.998 or 1.002 versus 0.69, $P < 0.001$).

Altogether, 544 (75%) were sensitised to inhalant allergens. Out of the 155 asthmatics, 32 (21%) suffered from allergic asthma. Of the patients with both asthma and rhinitis, 279 (83%) were sensitised. The three most common sensitising allergens were grass (44%), birch (31%), and cat (30%). Only 56% of patients with allergic asthma had prior knowledge of allergic sensitisation.

Patients with undiagnosed asthma

At the time of enrolment the proportion of undiagnosed ("unaware") patients with asthma was 67%.

The frequency of "mild intermittent", "mild persistent", "moderate persistent", and "severe persistent" asthma was 26%, 20%, 25%, and 29%, respectively (Table 2). One hundred and eighty-six (38%) patients with moderate to severe persistent asthma (GINA 3–4) were unaware they had asthma and were also untreated (see below). The difference in unawareness between those with mild intermittent and mild persistent asthma and those with severe asthma reached statistical significance ($P < 0.05$).

Asthma treatment and disease severity

Most (62%) of the asthma patients were untreated (Table 3). Inhaled corticosteroids were the most commonly used drugs, but only 86 of 365 (24%) patients requiring inhaled corticosteroids (GINA 2–4) were using them. Patients with severe persistent asthma (GINA 4) received inhaled steroids more frequently than the patients with less disease severity (GINA 1–3).

The second most commonly used drug was β_2 -agonists and long acting β_2 -agonists were rarely used. Leukotriene modifiers were used by a few patients. Only 26% of GINA 3–4 patients were taking the recommended combination therapy (corticosteroid and β_2 -agonists). The ratio of inhaled corticosteroid use to short-acting bronchodilators was > 0.7 .

The total proportion of both undiagnosed and untreated asthma patients was 50% ($n = 245$).

Influence of rhinitis and atopy on asthma severity

We found no significant association between severity of asthma and the presence of rhinitis, although those with moderate to severe asthma had allergic rhinitis less often. The proportion of patients with allergic rhinitis, GINA (class 1 to 4) was 77%, 70%, 63%, and 65%, respectively ($P = 0.09$).

Table 2 Asthma awareness and disease severity.

	GINA 1	GINA 2	GINA 3	GINA 4	Total
Diagnosed	43 (9%)	37 (8%)	36 (7%)	46 (9%)	162 (33%)
Undiagnosed	85 (17%)	60 (12%)	89 (18%)	97 (20%)	331 (67%)
Total	128 (26%)	97 (20%)	125 (25%)	143 (29%)	493 (100%)

Asthma severity and awareness in 493 patients with doctor-diagnosed asthma at the time of enrolment. Severity is classified according to GINA in four classes.

Table 3 Asthma severity and current treatment.

	GINA 1	GINA 2	GINA 3	GINA 4	Total
No treatment	88	61	79	75	303 (62%)
Short-acting β_2 -agonist (SABA)	18	19	14	23	74 (15%)
Long-acting β_2 -agonist (LABA)	1	1	3	4	9 (2%)
Inhaled steroids	11	5	14	23	53 (11%)
Inhaled steroid, SABA or LABA	10	11	15	18	54 (11%)
Total	128	97	125	143	493

Asthma severity and anti-asthmatic treatment in 493 patients with doctor-diagnosed asthma at the time of enrollment. Severity is classified according to GINA in 4 classes. One asthmatic received immunotherapy in addition to pharmacotherapy.

Patients' knowledge about asthma self-care and education

Patients with an asthma diagnosis (with or without rhinitis) before entering the study were asked about their knowledge of asthma and treatment principles. Almost half (48%) of the patients had been instructed by their primary care physician on how to use their asthma devices and 27% knew how to use peak flow meters (Table 4). Less was known about asthma triggering agents and how to avoid them, and little about adjustment of asthma medication. Only 1% had a written asthma management plan. Forty per cent had been referred to a specialist previously and 85% had seen their general practitioner within the last year.

Patients with undiagnosed rhinitis

Among the 571 patients with allergic rhinitis, 32% ($n = 182$) were undiagnosed ("unaware") (Table 5). Of the previously diagnosed patients, 251 (44%) were told they had a specific allergy to pets, pollen, dust, or moulds. Thus, allergy had not been diagnosed in 319 (56%) patients with allergic rhinitis. Unawareness was slightly lower in the

mildly affected than in the moderate to severe categories ($P < 0.01$).

Rhinitis treatment and disease severity

Table 6 shows the severity and treatment of rhinitis. In 388 "doctor-diagnosed" patients, 19% ($n = 72$) were untreated and the rest used antihistamines as needed or combined with intranasal corticosteroids (92%). In contrast, the majority (75%) of the undiagnosed patients were untreated ("untreated and undiagnosed", 138/183) and 18% took antihistamines or received other treatment. In general, antihistamine was the most commonly used medication. Intranasal corticosteroids were used only by 16% of patients with moderate to severe rhinitis. Immunotherapy treatment was rare (2%).

Undertreatment

According to recommendations for treatment in international guidelines, most of the patients (82%, $n = 592$) in this study would benefit from treatment. However, 49% ($n = 361$) with asthma and rhinitis were untreated, and only 72 untreated

Table 4 Patients' knowledge of asthma.

Have you been taught how to:	Yes %	N/A %
Use your asthma inhaler or device?	48	25
Use a peak flow meter?	27	41
Recognise asthma and rhinitis triggers and how to avoid them?	31	
Adjust your medication if you are exposed to asthma triggers?	19	
Adjust your medication when your asthma worsens or you have an attack?	22	
Do you have a written asthma management plan?	1	
GP visits within the past year?	85	
First visit to asthma specialist?	40	

Response of previously diagnosed asthma patients ($n = 162$) to questions about the asthma management provided by their primary physician before the study. Responses of patients who were not provided with a peak flow meter or were using inhalation devices are given under N/A (not applicable). Patients marked either Yes or N/A to the above questions.

Table 5 Rhinitis awareness and disease severity.

	Mild intermittent	Mild persistent	Moderate-severe intermittent	Moderate-severe persistent	Total
Diagnosed	134	43	84	128	389 (68%)
Undiagnosed	65	34	17	66	182 (32%)
Total	199 (35%)	77 (14%)	101 (18%)	194 (34%)	571

Severity of and awareness in 571 patients with physician-diagnosed rhinitis at the time of enrollment. Severity is classified according to ARIA in 4 classes.

Table 6 Rhinitis severity and current treatment.

	Mild intermittent	Mild persistent	Moderate–severe intermittent	Moderate–severe persistent	Total
No treatment	125	50	53	111	339 (59%)
Antihistamine	55	21	37	43	156 (27%)
Antihistamine & nasal steroids	16	5	9	28	58 (10%)
Nasal steroids	1	1	1	8	11 (2%)
Immunotherapy	0	0	0	3	3 (1%)
Other treatment	2	0	1	1	4 (1%)
Total	199	77	101	194	571

Severity and treatment of rhinitis in 571 patients with physician-diagnosed rhinitis at the time of enrollment. Severity is classified according to ARIA in 4 classes. Eleven patients received immunotherapy, 8 in combination with pharmacotherapy (not shown in the table).

patients were classified as having very mild disease, which did not require daily treatment.

Sixty-eight patients with GINA 1 severity were undertreated, i.e. no treatment was prescribed. Patients with GINA 2–4 severity should be treated with an anti-inflammatory agent. Thus, of the patients with asthma, 76% ($n = 276$) were undertreated (i.e. untreated or treated only with β_2 -agonists). Long-acting β_2 -agonists are recommended for patients with GINA 3 and 4. Only 22 (4.5%) of all the asthmatics, were treated accordingly.

Of the rhinitis patients, 339 (59%) were untreated and 244 (83%) with moderate to severe rhinitis were undertreated (untreated or treated only with antihistamines). Only 12 (2%) patients were receiving allergen immunotherapy. Eleven suffered from allergic rhinitis and one from mild allergic asthma and rhinitis. After careful assessment of each participant, we found that 12 (2%) with allergic asthma, 219 (31%) with moderate–severe rhinitis and 146 (21%) with both asthma and rhinitis met the current indications for immunotherapy. On re-evaluating the asthma and rhinitis treatment and diagnosis in all 726 participants at entry, 50% ($n = 361$) subjects were found to be untreated and 71% ($n = 513$) undiagnosed.

Discussion

The objectives of the present study were to evaluate the unawareness and undertreatment of asthma or rhinitis among a general asthma and

rhinitis patient population, and not to assess the frequency of respiratory diseases. One way to approach the general population with non-acute illness is by mail. In this way we were able to perform a screening of a large general population for relevant respiratory symptoms.

The prevalence of physician-diagnosed asthma and rhinitis in Northern Europe is increasing and is about 5–10% and 10–20%, respectively.^{1–3,23,24} Although, ours is not a true epidemiological study, we found a frequency of 4.5% doctor-diagnosed asthma and 5.2% doctor-diagnosed rhinitis patients. This is lower than that reported previously in questionnaire-based studies with self-reported symptoms. Furthermore, we included only those with a positive skin prick test, defined by a 5 mm weal, which is a higher threshold value compared to epidemiological studies that generally define all reactions above 3 mm as significant for atopy.^{2,3} Thus, these frequencies based on a doctor-diagnosis rather than patient's self-reported symptoms, and lower skin test threshold values probably reflect a true approximation of the current disease burden.

The present study shows that about 50% of patients with asthma or rhinitis are undiagnosed and undertreated. This agrees with recent studies, which report that less than half of those who were classified as having doctor-diagnosed asthma had been diagnosed as asthmatics by a physician previously.^{10,25–27} In comparison to earlier studies that report lower frequencies (3–11%) of undiagnosed asthma this study includes symptoms as described in the GINA guidelines (including cough as the sole symptom of asthma) and lung function tests with methacholine challenges in

the asthma diagnosis. This may increase the number of subjects suspected of asthma and thus lead to a higher frequency of undiagnosed asthmatics, as compared to previous studies.²⁸ However, it is important to note that we verified symptoms of airway hyper-responsiveness by lung function tests as well.

On the other hand, some caution should be observed when interpreting these data. The response rate was low and the data may not reflect the true population in an epidemiological sense. Then, to be considered is the patients' motivation to call the clinic for an appointment. This may cause a selection bias with more symptomatic undiagnosed and untreated patients at the clinic. This may cause overestimation of the frequencies and disease severities. Thirdly, the earlier diagnosis was made on the patients' own reports and understanding of the information given by their doctors. Because of poor recall, lack of patient information/education and understanding of the diseases may have resulted in underreporting by the patients. However, in their study, van den Boom and co-workers²⁹ found only 13% cases of diagnostic misclassification.

Why are patients undiagnosed?

It has been suggested that asthmatics with mild disease are often not recognised as asthmatics by their doctor. This does not seem to apply in the present study, as the proportion of undiagnosed asthmatics was higher in the severe disease categories. It is generally accepted that most asthma care should be provided at the primary care level, but patients who may benefit from consultation with a specialist should be identified and referred accordingly. The high number of patients with undiagnosed moderate to severe persistent asthma in this study may suggest that this recommendation is not being effectively managed. This was confirmed by our finding that 60% of the patients had not seen a specialist previously. However, 85% of the patients had seen their doctor within 1 yr, which indicates that this was not because of reluctance to seek medical help. Considering that rhinitis and asthma are associated disorders and 59% of our rhinitis patients suffered from asthma they should have been checked for asthma. In fact, the above suggests that increased awareness among physicians would provide an excellent opportunity for the early detection of airflow obstruction and rhinitis.

Why do patients accept symptoms?

A large number of patients are symptomatic and accept this. Several studies show that patients' perceptions of their overall asthma control do not match the severity of the symptoms they report. We did not assess their self-perception of the severity, but the study indicates that awareness and knowledge were low and may be one reason for accepting the symptoms. Although, 60% of the patients with known asthma had seen an asthma specialist before entering the study the data indicate that those patients were not adequately trained about their asthma and treatment. Moreover, current smoking was high (49%) among asthmatics and perhaps the asthma symptoms were simply overlooked or neglected and thus accepted by the patients.

Why are patients undertreated?

Almost 40% of patients with moderate to severe asthma were not receiving anti-inflammatory treatment. These patients are at risk of acute exacerbation. Our results of corticosteroid usage rates agree with recent studies reporting suboptimal use of inhaled corticosteroids in patients with mild to severe persistent asthma. Another important finding in our study was that use of long-term β_2 -agonists was strikingly low and bronchodilator therapy for quick relief was inappropriately high in relation to the use of inhaled corticosteroids and the severity of the asthma symptoms. This conforms with recent European studies showing an inappropriate ratio of inhaled corticosteroids to short-acting bronchodilators.³⁰⁻³³ Although more than half of our patients had been instructed in the handling of their asthma devices a high number of patients were self-taught. Moreover, the data demonstrated inadequate monitoring of lung function by peak flow. In addition, written management plans were virtually non-existent. This implies that perhaps the asthma management guidelines are not being adequately put in practice by physicians and patients.

The management of allergic rhinitis includes avoidance of allergens, medication, and immunotherapy. Patients with moderate-severe symptoms should be treated with intranasal corticosteroids and immunotherapy should be considered. Patients with allergic rhinitis and seasonal asthma are likely candidates for immunotherapy. Considering that optimal management of rhinitis may partly improve coexisting asthma, it

is disappointing to note that 38% with both asthma and rhinitis were untreated. Furthermore, 21% received treatment for rhinitis but not for asthma.

Immunotherapy may prevent occurrence of asthma in patients with moderate to severe rhinitis.³⁴ The very low number of patients on immunotherapy thus indicates that very little attention has been paid to this type of treatment.

An initial definition of the patients' allergic status will affect therapeutic decisions. Less than half of the patients with a known allergy had previously been diagnosed as such. This increases the likelihood of non-compliance on the part of the patient who does not understand the rationale behind the treatment, follow-up, and appropriate alterations in the therapeutic plan. This may also explain why the majority of our patients did not have a better understanding of how to recognise and avoid external/internal precipitants with the potential to induce or aggravate symptoms.

In conclusion, the study was undertaken to assess the current status of diagnosis and treatments for asthma and allergic rhinitis after the promotion and publication of GINA and ARIA guidelines. This study indicates that despite increased knowledge, publication of guidelines, improved drug treatment, increased awareness, and education of primary care physicians the diagnosis and treatment of patients with asthma and rhinitis are insufficient. Thus, further measures must be considered. Possibly patient education must be improved and public awareness should be increased. Further efforts must be made to improve management of asthma and rhinitis in general practice.

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