

Factors Associated With Difficult Asthma In Outpatient Chest Clinics In Mukalla District, Yemen

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Abstract:

Background: Bronchial asthma is the commonest chronic respiratory disorder worldwide. Difficult asthma is characterized by difficulty to achieve disease control despite high-dose inhaled glucocorticoids plus long-acting β_2 -agonists (LABAs) or oral corticosteroids (OCSs). In difficult asthma some factors should be considered like occupational factors, indoor and outdoor exposure, non-adherence and non-compliance to therapy, allergic rhinitis and GERD. This study was conducted to analyze different factors associated with difficult asthma.

Methodology: A cross-sectional study was conducted in the period between December 2016 to February 2017. All patients with bronchial asthma attending the chest clinics in Mukalla during enrolled in the study. The data were collected by interview questionnaire. Analysis was done by using SPSS for Windows version 20. Descriptive statistics and Chi square analysis were used to show frequency distributions and association. The data was presented in tables and graphs.

Results: Two hundred and ten bronchial asthma patients were included in the study; 76 of them had difficult asthma, the majority were at age group (49-60 y.) with female predominance. Many factors affected their difficult asthma; half of them had indoor and outdoor exposure, more than half of them had occupational factors and allergic rhinitis. Only one third of patients were using inhaler technique correctly, and more than one third had financial difficulties as barrier to adherence, while less than one third believed that inhaled therapy well be a habit forming in their life. About comorbidities more than half of patients had GERD and anxiety with significant association, on the other hand less than one third had food allergy and obesity.

Conclusion: Difficult asthma is common in middle age. Many factors should be considered in diagnosing difficult asthma such as indoor and outdoor exposure, non-adherence and incorrect use of inhaler therapy. Most common comorbidities were allergic rhinitis followed by GERD, anxiety and obesity.

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العوامل المصاحبة للربو المستعصي في عيادات الصدر الخارجية بمديرية المكلا، اليمن

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الملخص:

المقدمة: يعتبر الربو أكثر اضطرابات الجهاز التنفسي شيوعاً في العالم، وبما أن الربو المستعصي يتميز بصعوبة السيطرة على أعراض الربو رغم تناول جرعة عالية من أدوية الربو. فإن عدم السيطرة على الربو بسبب سوء الرعاية الصحية، وعدم الالتزام بالعلاج، وإيضاً عدم اجادة استخدام البخاخ والمؤثرات البيئية لذا اجريت هذه الدراسة لغرض تحليل العوامل المصاحبة للربو المستعصي.

طريقة البحث: أجريت دراسة مقطعية عرضية خلال الفترة ما بين ديسمبر 2016 الى فبراير م 2017، كل مرضى الربو اللذين حضروا الى عيادات الصدر بالمكلا في الدراسة تمت دراستهم. وقد تم جمع البيانات من خلال مقابلة المرضى وتسجيل اجاباتهم في استبيان تم اعداده واختباره من قبل. بعدها تم التحليل الاحصائي باستخدام الحزمة الاحصائية لنظام الويندوز النسخة 20. وقد استخدم الاحصاء الوصفي، مربع كاي، لإظهار توزيع البيانات، والعلاقة بين المتغيرات. بعد ذلك تم توضيح النتائج بالجدول والرسومات البيانية

النتائج: أظهرت النتائج أن 210 من مرضى الربو الشعبي الذين تضمنتهم الدراسة، كان منهم 76 مصاباً بالربو المستعصي، وكانت الفئة العمرية الغالبة (60-49 سنة) معظمها من الإناث. وان نصف المرضى المصابين بالربو المستعصي لديهم عامل التأثير بالأمكان المغلقة والمفتوحة معا، وأكثر من نصف المرضى يعملون في أماكن تثير الربو ولديهم التهاب الأنف التحسسي. وان غالبية المرضى لا يلتزمون بالعلاج، ولثلاثهم لا يجيدون استخدام البخاخ. كما أظهرت النتائج أن أسباب عدم التزام المرضى بالعلاج: صعوبة مادية، واعتقاد المرضى أن استخدامهم للبخاخ سوف يعتبر عادة بحيث لا يستطيعون الاستغناء عنه. أما بالنسبة للعوامل المرضية المصاحبة للربو تبين لنا أن أكثر من نصف مرضى الربو المستعصي يعانون من ارتجاع المريء والقلق. وافتل من ثلث المرضى يعانون من السمنة وحساسية من بعض انواع الاكل

الخلاصة: الربو المستعصي أكثر شيوعاً في متوسط العمر، وهناك عدة عوامل ينبغي أخذها بعين الاعتبار عند تشخيص الربو المستعصي يأتي في مقدمتها التهاب الأنف التحسسي وبيئة العمل ثم يتبعها ارتجاع المريء، القلق، المؤثرات بالأمكان المغلقة والمفتوحة معا وعدم الالتزام بالعلاج أو استخدامه بالطريقة الصحيحة.

Introduction:

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.⁽¹⁾

The annual mortality rate per 100,000 people from asthma in Yemen has decreased by 50.0% since 1990, an average of 2.2% a year to 2010. and smoking and occupational allergen factors response to 17.5% of the total deaths caused by asthma in Yemen during 2013.⁽²⁾

Asthma And Allergy Research Group Of The National Heart And Lung Institute (London) : define difficult asthma as symptomatic asthma despite high dose inhaled corticosteroid therapy (>1000ug/day of beclomethasone dipropionate or equivalent) and long acting B2-agonist or theophylline treatment or patients treated with long- term (>3months)oral corticosteroids for asthma.⁽³⁾

Difficult asthma definition developed started in 1999 when a European Respiratory Society (ERS) Task Force defined difficult asthma as “asthma remaining uncontrolled despite of the high dose inhaled glucocorticosteroids with or without systemic glucocorticosteroids”⁽⁴⁾.

A year later 2000, the American Thoracic Society (ATS) definition of severe refractory asthma was very similar, and included six criteria that specified asthma control⁽⁵⁾.

In 2010, the World Health Organization (WHO) added responsiveness of treatment to definition of difficult asthma for asthma control. WHO distinguished three subtypes of severe asthma: severe untreated asthma, difficult to control severe asthma, and severe refractory asthma⁽⁶⁾. In 2011, the Innovative Medicines Initiative introduced the term “problematic” asthma to cover all patients with “poorly controlled” asthma; factors that can make asthma difficult to control. These include non-adherence to treatment, inadequate inhalation technique, continuous exposure to environmental triggers and comorbidities⁽⁷⁾. Difficult asthma has been diagnosed by the American Thoracic Society (ATS) guidelines as: when one or both major criteria and two minor criteria, is described as follows.

The major criteria: is one when patients achieve control on level of mild-moderate persistent asthma,

these are:

1. Treatment with continuous or near continuous (>50% of year) oral corticosteroids
2. Requirement for treatment with high-dose inhaled corticosteroids.

The minor criteria these are:

1. Requirement for daily treatment with a controller medication in addition to inhaled corticosteroids, long-acting β -agonist, theophylline or leukotriene antagonist.
2. In Asthma symptoms requiring short- acting β -agonist use on a daily or near daily basis.
3. Persistent airway obstruction (FEV1, 80% predicted; diurnal peak expiratory flow (PEF) variability. 20%).
4. One or more urgent care visits for asthma per year.
5. Three or more oral steroid “bursts” per year.
6. Prompt deterioration with <25% reduction in oral or inhaled corticosteroid dose.
7. Near fatal asthma event in the past.⁽⁵⁾

A study conducted in Egypt found that 43% of cases of difficult asthma were due to concomitant conditions, Gastroesophageal Reflux Disease (GERD) was the most common of them (41%) followed by non-compliance(28%), allergic rhinitis(24%) and nasal polyposis(7%)⁽⁸⁾. **Sontag and coworkers** recorded a figure of (45%) of GERD association of difficult asthma⁽⁹⁾ and some other authors reported (80%) association between asthma and GERD using 24-h pH monitoring studies⁽¹⁰⁾⁽¹¹⁾. On the other hand, **Garcia et al** referred to non-compliance among asthmatic population up to be (55%)⁽¹²⁾. **Bousquet and coworkers** described (20-70%) association between allergic rhinitis and asthma⁽¹³⁾. In UK a study has suggested that after detailed systematic evaluation, about 50% of patients have a concomitant disease make their asthma difficult to control⁽¹⁴⁾.

Overall, epidemiologic studies suggest that health-care access and use, smoking status, poor adherence to doctor's advice, critical errors in inhaler use, oral corticosteroid use, and lack of regular specialist care are significant factors associated with poor asthma control⁽⁷⁾.

To our knowledge there are no published studies in Hadhramout about factors associated with difficult asthma. Our study was conducted to analyze different factors that was mention in Global Initiative for Asthma (GINA) and could lead to difficult asthma.

Methods:

The present study was an analytical cross-sectional study. The study targeted all bronchial asthma patients attending outpatient chest clinics in Mukalla city in the period from 1st December 2016 to 28th of February 2017.

This study includes bronchial asthma patients attending outpatient chest clinics who met the following criteria:

- At age 12 years and above.
- Duration of bronchial asthma at least 6 months.

A total of three private outpatient chest clinics were included in our study. All patients with bronchial asthma who met the inclusion criteria during the period 1st December 2016 to 28th of February 2017 were taken for the study, these patients were selected using convenient sampling. The data was collected by the researcher using a questionnaire on face to face in an interview which include

frequency of difficult asthma according to the American Thoracic Society guidelines were one or both major criteria and two minor criteria. The data was collected also include socio-demographic characteristics, adherent and barrier to therapy, inhaler technique use, comorbidity and exposure to allergen which include:

1. Smoking exposure (current smoking and passive smoking).
2. Environmental exposure (indoor, outdoor and both).
3. Drugs induced asthma (aspirin, NSAIDS and beta blocker).
4. Work exposure (work exacerbation asthma include painter, builder, hair dresser, worker at floor factory...etc).
5. Exposure to atopic condition this include: allergic rhinitis, allergic conjunctivitis and allergic dermatitis.

Weight and height of patients were taken in to consideration after the face to face interview patients.

The information obtained from the questionnaires were coded, checked and processed with the (SPSS) version 20. Descriptive statistics were calculated and association between variables was assessed using Pearson's Chi square test with p-value <0.05 as the significance level.

Methods:

Two hundred and ten patients with bronchial asthma

were enrolled in the study. They were divided in two groups: difficult asthma (76 patients) and variable degree of response (134 patients). The associated factors were investigated on difficult asthma patients only -age ranged from 12 to 80 year old- with the mean age of $M \pm SD$ (36 ± 17.8). More than one third of patients had difficult asthma (36.2%), while (63.8%) had asthma with variable degree of response.

Regarding age (27.7%) of the difficult asthma patients were in the range of 49-60 y as shown in figure (1), with female predominance (57.9%) figure 2.

Table 1 shows that half of patients with difficult asthma (50%) had indoor and outdoor exposure, one third (39.5%) of difficult asthma patients have indoor exposure, and the remaining (10.5%) have outdoor exposure, there is no significant association (0.4). and 20 patients (26.3%) have had previous smoke exposure, while drug induced asthma is not common difficult asthma patients (5.3%).

More than half (56.6%) of difficult asthma patients were influenced with their work exacerbation asthma, with no significant association.

Regarding to atopic condition 26.3% of difficult asthma patients have allergic dermatitis with significant association p-value (0.03) and (43.4%) of difficult asthma have allergic conjunctivitis without significant association, while more than half of difficult asthma have allergic rhinitis (56.6%).

Table 2: show that (36.8%) of difficult asthma are not adherent to therapy and (27.7%) of difficult asthma patients do not use the device properly, while the most frequent comorbidity factors of difficult asthma patients are allergic rhinitis (56.6%) followed by GERD, anxiety with same percentage (55.3%) with significant association p-value (0.01). This is followed by obesity (22.4%) and food allergy (18.4%) without significant association.

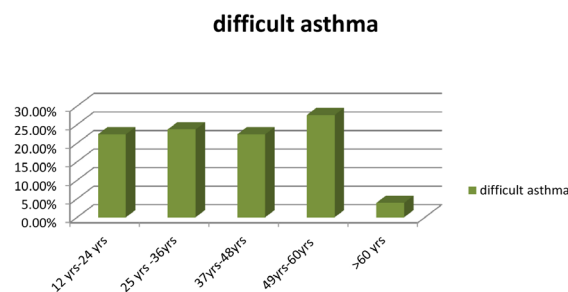


Fig. 1: Distribution of difficult asthma patients according to age.

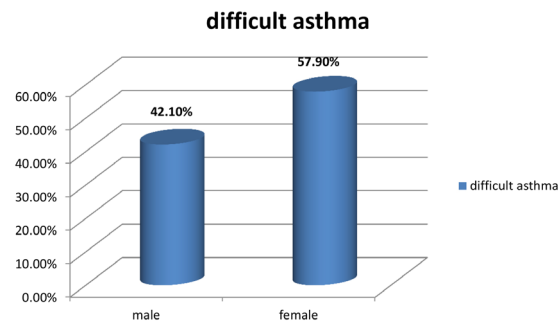


Fig. 2: Distribution of difficult asthma patients according to sex.

Table 1: Relation between difficult asthma patients and Exposure to allergen factors:

Exposure to allergen factors		N =76		Chi square	P .value
Environmental exposure	Indoor	30	39.5	1.6	0.44
	Outdoor	8	10.5		
	Indoor and outdoor	38	50		
Smoking exposure	Smoker	20	26.3	1.3	0.16
	Non smoker	56	73.7		
Drugs induced asthma	Yes	4	5.3	1.6	0.46
	NO	72	94.7		
WORK	WORK exacerbation asthma	43	56.6	6.7	0.07
	WORK not exacerbation asthma	33	43.4		
Atopic condition	Allergic rhinitis	yes	43	0.6	0.25
		No	33		
	Allergic conjunctivitis	yes	33	2.3	0.08
		No	43		
	Atopic dermatitis	yes	20	4	0.03
		No	56		

Table 2: relation between difficult asthma patients, drug use and comorbidities factors

		N	%	Chi-square	P value
Adherence	Adherence	48	63.2	0.4	0.29
	Non adherence	28	36.8		
Inhaler technique	Correct use of Inhaler	25	34.1	0.4	0.79
	In Correct use of Inhaler	22	27.7		
Comorbidity	rhinitis	43	56.6	0.6	0.25
	Sinusitis	23	30.3	0.2	0.35
	GERD	42	55.3	5.8	0.01
	Anxiety	42	55.3	11.5	0.01
	Food allergy	14	18.6	0.93	0.22
	Obesity	17	22.4	2.7	0.07
	Obstructive sleep apnea	2	2.6	0.98	0.45

Discussion:

The global prevalence of asthma is estimated to be 300 million and is expected to grow by >100 million by 2025⁽¹⁵⁾. Patients with difficult-to-treat asthma comprise a small proportion (5%-10%) of all patients with asthma, yet they are responsible for a disproportionate degree of asthma morbidity and costs.⁽¹⁶⁾

The findings of current study estimated that the percentage of difficult asthma was more than one third (36.2%) of respondents, which was in consistent with the percentage of 34% reported in a Brazilian study⁽¹⁷⁾. Female predominance was noticed in difficult asthma patient which was consistent with studies conducted in many studies^(8,18-21)

The socio-demographic factors (27.6%) of difficult asthma patients were age group (49 - 60 y). This was inconsistent compared with studies conducted in Saudi Arabia where the result reported was at age group (25-36 yrs.) (36.5%)⁽¹⁸⁾, on the other hand the gender reported in the current study was (57.9%) were females. This was nearly similar to studies in Saudi Arabia and Netherlands female predominance (62.2%)⁽¹⁸⁾, 60%⁽²²⁾ respectively. In this study findings mean age of asthmatic patients was $M \pm SD$ (36 \pm 17.8), this is which lower than study in US revealed that (44.4 year) was mean age.

In this study work related factors leading to difficult asthma represent (56.6%), in contrast with a study in UK showed (36%)⁽¹⁴⁾ of difficult asthma patients had work exacerbation factors, this result may be explained by the preventive measures usually used in the work field in developed countries. In the other hand, most people in our study had low education level and most of them work as farmers, builders, painters and hair dressers.

Rhinitis is very common in asthma, and associated with worsening of asthma control, and increased emergency room visits⁽²³⁾. In the present study, more than half (56.6%) of difficult asthma cases had allergic rhinitis, which is similar to study in Saudi Arabia (54.1%)⁽¹⁸⁾ and china (57.5%)⁽²⁴⁾, and higher than study in Egypt at Assiut (24%)⁽⁸⁾ and Netherlands (26.5%)⁽²²⁾, this could be due to weather and environmental factors. This study showed a significant association between difficult asthma and allergic rhinitis.

In the current study indoor and outdoor exposure is another common factor in difficult asthma (50%). This result was lower than study in London which reported (92.7%) of difficult asthma patients had indoor and outdoor allergen exposure⁽¹⁴⁾. The result of current study was higher than study in Belfast where (30.5%) of difficult asthma patients were related to

indoor and outdoor exposure⁽¹⁴⁾. Smoking contributes to the development of difficult asthma; asthmatic smokers are more symptomatic and have more severe and frequent exacerbations and emergency care need; have a reduced response to corticosteroids; and a more rapid decline in pulmonary functions⁽²⁵⁾. The effect of smoking exposure in the study was (26.3%) which almost consistent with study in UK (32%)⁽¹⁴⁾. In this study found that more than one third (36.8%) of difficult asthma patients were non adherent to medication which is near to that reported in Egypt (28%)⁽⁸⁾ and London (32%)⁽¹⁴⁾. The result of current study could be due to an improper use of medication, which may affect improvement in their condition hence the patients stops using the treatment but different from studies in UAE (59%)⁽²⁶⁾ and China (77.3%)⁽²⁴⁾.

In this study (14.5%) of difficult asthma patients had financial reasons stand against getting their proper medications, this was similar to England study showed that (13%)⁽⁷⁾ and lower than study reported in Egypt which showed that (76.8%)⁽²⁷⁾. In this study (27.6%) of difficult asthma patients had a belief that once they start using inhalers, it would be a habit in their life. This result was lower than study in UAE (59%) of patients⁽²⁶⁾ and Saudi Arabia (37%)⁽²⁸⁾. This result might be due to lack of knowledge about importance of inhaler use in treatment of asthma. Our finding in this study revealed (27.7%) of difficult asthma patients were incorrectly use their inhalers, although during the data collection, we observe the clinicians describing the technique of inhalers use to patients. These results were nearly similar to those obtained in Netherlands (20.3%)⁽²⁹⁾, in contrast with Brazilian study reported a percentage of (55.8%)⁽³⁰⁾.

Gastroesophageal reflux disease had been identified as an important factor contributing to the severity of asthma. And generally high prevalence of GERD were reported in patients with difficult asthma^(8-11,31,32), this study revealed that more than half of difficult asthma patients had GERD (55.3%) which was similar to Malaysian study (56.7%)⁽³¹⁾ and Tunisian (57.9%)⁽³²⁾, but less similar than Egyptian (41%)⁽⁸⁾ and Netherlands (26%)⁽²²⁾. This may be related to the preference of spicy food in countries with higher percentage. The current study revealed a significant association between GERD and difficult asthma similarly to Tunisian and Malaysian.

Anxiety was found to be an important factor in difficult asthma. Current study showed that (55.3%) of difficult asthma patients had anxiety, which was similar to study in Poland (52.4%)⁽³³⁾ of difficult asthma had anxiety. A significant association was detected in our study in contrast to the Poland study which

showed no significance.

This study found that (22.4%) of difficult asthma patients were obese, which less than study in America (33%)(34), UK(48.3%)(14) and New England (29.9%)(7) of difficult asthma patients had obesity. Food allergy was found in (18.4%) of difficult asthma patients in our study, which was higher than study in Netherlands reported a result of (9.4%)(29). No significant association between food allergy and difficult asthma was detected in the study, while in Netherlands one was significant association. Obstructive sleep apnea was uncommon cause of difficult asthma in this study (2.6%), this result was lower than that obtained from a study in Tunis (26%)(32). No significant association was detected in the study similarly to the Tunisian study.

Conclusion:

The frequency of difficult asthma in Mukalla was high. The most common factors associated with difficult asthma were allergic rhinitis, occupation related factors, GERD, anxiety, indoor and outdoor exposure, and non-adherence.

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