

Investigation on medication use and factors associated with levels of asthma control among asthmatic outpatients at University Medical Center Hochiminh City

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ABSTRACT

Asthma is a common chronic disease that affects millions of people of all ages. Despite the availability of evidence – based management guidelines focusing on asthma control, recent data showed that control of asthma was suboptimal worldwide. The assessment of asthma control and associated factors is thus very necessary in the management of asthma in both community and clinical settings. A descriptive cross-sectional study on 308 asthmatic outpatients aged 12 years old and over was conducted at University Medical Center Hochiminh City (HCMC). Asthma severity was classified by EPR-3 guideline. The level of asthma control was assessed by the Vietnamese version of ACT and factors associated with asthma control were evaluated by medical history, patients and disease characteristics. The mean age of study population was 45.47 ± 16.99 and 69.8% were female. The top three medications prescribed were inhaled corticosteroid (ICS), long – acting β_2 agonist, leukotriene receptor antagonist. The mean ACT score was 20.41 ± 3.96 ; 59.1% of the study population was found to be well-controlled ($ACT \geq 20$) and 40.9% was categorized as uncontrolled ($ACT < 20$). Education, asthma severity, step – up therapy, frequency of preventive medication use were found to be significantly associated with the level of asthma control. The high proportion of uncontrolled asthma suggested the need for strategies to enhance effectiveness of asthma control in University Medical Center HCMC in particular and in Vietnam in general. Further studies should be conducted on larger sample to determine the association between asthma control and comorbidities as well as ICS dosage.

1. INTRODUCTION

Asthma is serious global health problem and is the fourteenth most important disorder in terms of disability. The 2014 revised global estimate of asthma suggests that as many as 334 million people have asthma¹. The prevalence of asthma in the South East Asia region was 3.39%¹. In Vietnam, the prevalence of asthma among adults estimated in 2010 was 4%, much higher compared to the prevalence reported from

the previous study in 2007 (2%)². This dramatic increase reflected problems in asthma control in Vietnam that need to be investigated. Global initiative for asthma (GINA) was established in 1993 to provide information and scientific evidence in asthma management³. GINA reports have been updated annually since 2002, contributing tremendously in the improvement of asthma management in the community. The long-term goals of asthma management are to achieve good controls of symptoms, to maintain

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normal activities levels, to minimize future risk of exacerbations and medication side effects. Results from many studies showed that asthma control remained suboptimal all over the world^{4,5}. The assessment of asthma control and associated factors is thus very necessary in the management of asthma in both community and clinical settings.

There are several tools available to assess asthma control including Asthma Control Test (ACT). ACT is a commonly accepted and simple tool which was widely used to assess the level of asthma control. ACT Vietnamese version was validated and applied in many previous studies on Vietnamese asthmatic patients aged 12 years or older^{6,7}. However, the number of reports and studies about asthma control in Vietnam is still limited. The aim of this study is to investigate medication use and factors associated with the level of asthma control in asthmatic outpatients at University Medical Center HCMC.

2. MATERIALS AND METHOD

A descriptive cross-sectional study was conducted on 308 asthmatic out-patients aged 12 years old or over randomly selected at University Medical Center HCMC from February 2016 to May 2016.

Sample size was estimated using the following formula:

$$n = Z_{1-\alpha/2}^2 \times \frac{p \times (1-p)}{d^2}$$

d: desired margin of error, d chosen was 5%,
Z = 1.96

p: prior judgement of the correct value of the proportion of poorly controlled asthma in the study population

We chose $p = 0.184$ based on the proportion of poorly controlled asthma patients (18.4%) assessed by ACT score reported in the study of Mehuys E. et al¹².

Exclusion criteria included patients with other respiratory diseases, pregnant or lactating women and patients who refused to participate in the study.

Data were collected by interviewing patients with provided questionnaire and from medical history and examination results

(spirometry).

Asthma severity was classified by EPR-3 (Expert Panel Report – 3) guideline⁸. The level of asthma control was assessed by Vietnamese version of ACT downloaded from www.asthmacontroltest.com. The doses of inhaled corticosteroids (ICS) were converted to doses of fluticasone and classified into 3 groups based on GINA (Global Initiative for Asthma) guidelines: low dose (fluticasone dose 100 – 250 µg/day), medium dose (fluticasone dose > 250 - 500 µg/day) and high dose (fluticasone dose > 500 µg/day)⁹.

Chi square test was used to compare proportions, t-test or Mann Whitney test was used to compare means. Multiple logistic regression model was used to evaluate the association between asthma control and factors including age, sex, educational level, BMI, smoking, comorbidities, frequency of preventive medication use and FEV1.

All statistical analysis was performed using SPSS 22.0 software package.

3. RESULTS

3.1. Characteristics of the study population

The mean age of study population was 45.47 ± 16.99 , ranging from 12 to 85 years old. Female accounted for two-thirds of the study population. The mean BMI was 22.84 ± 3.20 kg/m². The most common comorbidity observed was allergic rhinitis (29.9%). The mean FEV1 was 85.49 ± 19.45 % (compared to predicted value). The majority of the study population experienced mild and moderate asthma (41.1% and 47.5%, respectively) (Table 1).

3.2. Medications indicated in asthma management

3.2.1. Types of medications indicated

Inhaled corticosteroids (ICS) and long-acting beta agonists (LABA) were the most commonly prescribed medications (96.4% and 82.8%, respectively). Leukotriene receptor antagonists (LTRA) were indicated in 65.6% of cases and montelukast was the only drug in this group. Proportions of medications indicated for the treatment of asthma in the study population were presented in Table 2.

Table 1. Baseline characteristic of the study population (N = 308)

	Variables	Frequency (N)	Percentage (%)
Age	12 - 16	15	4.9
	17 - 35	77	25.0
	36 - 60	156	50.6
	> 60	60	19.5
Sex	Male	93	30.2
	Female	215	69.8
Education	Primary school	59	19.2
	Secondary school	98	31.8
	High school	75	24.4
	College/university	76	24.7
Smoking	Yes	31	10.1
	No	208	67.5
	Passive smoking	69	22.4
Family history of asthma	Yes	88	28.6
	No	220	71.4
BMI	< 23 kg/m ²	166	53.9
	23 - < 25 kg/m ²	71	23.1
	≥ 25 kg/m ²	71	23.1
Comorbidity	Allergic rhinitis	92	29.9
	Sinusitis	43	14.0
	GERD	39	12.7
	Cardiovascular disease	39	12.7
	Anxiety	12	3.9
FEV1 (% of predicted value)	< 60%	24	9.1
	60 - <80%	78	29.4
	≥ 80%	163	61.5
Asthma severity	Mild	109	41.1
	Moderate	126	47.6
	Severe	30	11.3
Frequency of preventive medicine	Every day	195	63.3
	4 – 6 times/week	15	4.9
	1 – 3 times/week	10	3.2
	None	88	28.6
Asthma treatment	None	87	50.6
	Step-down therapy	63	36.6
	Step-up therapy	22	12.8

Table 2. The proportions of medications indicated for the treatment of asthma in the study population

Medications	Frequency	Percentage (%)
Inhaled corticosteroids (ICS)	297	96.4
Fluticasone	188	61.0
Budesonide	109	35.4
Long – acting β2 agonists (LABA)	255	82.8
Salmeterol	146	47.4
Formoterol	109	35.4
Leukotriene receptor antagonists (LTRA)	202	65.6
Short – acting β2 agonists (SABA)	92	29.9
Fenoterol	33	10.7
Salbutamol	59	19.2
Anticholinergics	41	13.3
Tiotropium	8	2.6
Ipratropium	33	10.7
Oral corticosteroid	34	11.0
Methylprednisolone	19	6.2
Prednisolone	15	4.8
Theophylline	8	2.6
Antibiotics	50	16.2

3.2.2. Combinations of medications

The most common combination was ICS + LABA + LTRA (50.2%), followed by ICS + LABA (22.6%). Tiotropium, a new long

– acting muscarinic antagonist (LAMA) was indicated in combinations with ICS, LABA (1.9%) and with ICS, LABA, LTRA (6.8%) (Figure 1).

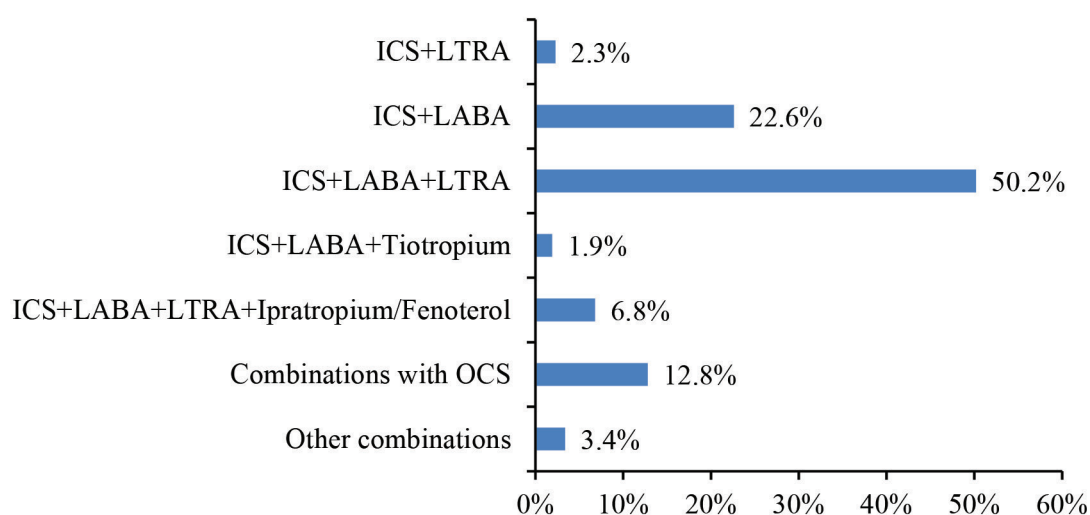


Figure 1. Combinations of medications indicated for the treatment of asthma in the study population (ICS: inhaled corticosteroids, LABA: long-acting beta agonists, LTRA: leukotriene receptor antagonists)

3.2.3. Combination of medications by severity of asthma

Mild asthma: the predominant combination was ICS/LABA/LTRA

Moderate asthma: the predominant combination was ICS/LABA/LTRA. Combination with OCS (oral corticosteroid) (11.7%) and ipratropium/fenoterol (0.8%) were more prevalent in moderate asthma than mild asthma.

Severe asthma: the predominant combinations were combinations with OCS (32.1%) and ipratropium/fenoterol (25.0%).

3.2.4. Dosage of corticosteroids

The total dose of oral corticosteroids (OCS) ranged from 60 to 560 mg for each course of treatment. The majority of the study population (76.5%) received lower dose of OCS than recommended (< 200 mg per treatment period), the remaining received total OCS dose from 200 to 600 mg per treatment period.

The average dose of ICS converting to fluticasone was 501.62 ± 355.45 ($\mu\text{g}/\text{day}$), ranging from 80 to 1000 $\mu\text{g}/\text{day}$. Among 297

outpatients indicated with ICS, 34.3% were indicated with low doses, 34.3% were indicated with medium doses and 31.3% were indicated with high doses of ICS (> 500 $\mu\text{g}/\text{day}$).

3.2.5. Frequency of preventive medication use

The frequency of preventive medication use was classified into 2 categories: frequent (≥ 4 times/week) and infrequent (≤ 3 times/week). Of 308 outpatients investigated, 68.2% were identified as “frequent” and 31.8% were identified as “infrequent” preventive medication users; 63.3% were indicated preventive medication daily and 28.6% received no preventive medication.

3.3. Treatment approach

Treatment approach was analysed based on the change in medications indicated between hospital visits. Data on medication history were available in only 172 out of 308 patients in the study population. The change in the choice of medications between hospital visits was presented in Table 3.

Table 3. The changes in the choice of medications between hospital visits

	Frequency	Percentage (%)
Unchanged	87	50.6
Step - down	63	36.6
Reduce ICS dose	47	27.3
Discontinue one or more medications	16	9.3
Step - up	22	12.8
Increase ICS dose	13	7.6
Add more medications	9	5.2

3.4. Levels of asthma control and associated factors

The mean ACT score was 20.41 ± 3.96 , well-controlled patients with ATC score ranging from 20 to 25 accounted for 59.1% and poorly-controlled patients with ACT score ranging from 5 to 15 accounted for 12.7% of the study population. The high proportion of uncontrolled asthma suggested the need for

strategies to enhance effectiveness of asthma control in UMC in particular and in Vietnam in general.

The association between asthma control (well-controlled/uncontrolled) and other factors including age, sex, education, BMI, smoking, comorbidities, severity of asthma, FEV1, treatment approach and frequency of preventive medication use was analysed using logistic

regression model. Education (OR = 0.54, 95% CI 0.31 – 0.92), severity of asthma (OR = 26.67, 95% CI 5.82 – 122.19), step-up therapy (OR = 8.57, 95% CI 1.82 – 40.31) and

frequency of preventive medication use (OR = 0.07, 95% CI 0.01 – 0.90) were found to be significantly associated with asthma control (Table 4).

Table 4. Multiple logistic regression analysis on factors associated with asthma control

Factors	P	OR	95% CI
Age	0.33	0.64	0.26 – 1.56
Sex	0.77	0.82	0.22 – 3.09
Education	0.02	0.54	0.31 – 0.92
BMI	0.89	1.01	0.86 – 1.20
Smoking	0.48	0.64	0.19 – 2.20
Severity of asthma	< 0.001	26.67	5.82 – 122.19
Number of comorbidities	0.67	1.11	0.69 – 1.78
FEV1	0.37	5.55	0.13 – 238.93
Step-down therapy	0.53	0.67	0.19 – 2.35
Step-up therapy	0.01	8.57	1.82 – 40.32
Frequency of preventive medication use	0.04	0.07	0.01 – 0.90

Factors in bold: statistically significant

4. DISCUSSION

The most common medications indicated were ICS (96.4%), which was consistent with results from the studies of Hasegawa T. (86.1%)¹⁰ and Turktas H. (80.6%)¹¹. According to GINA and EPR-3, ICS is the most effective preventive medicine in the management of asthma. Only 2.6% of the study population was indicated with theophyllin, which was much lower than results from the studies of Mehuys E.¹² and Hasegawa T.¹⁰ (18.9% and 44.5%, respectively), possibly related to the side effects of this drug. The most common combination was ICS + LABA + LTRA (50.2%), followed by ICS + LABA (22.6%). This result proved the implementation of GINA guidelines in which the combination of ICS and LABA is recommended when patients fail to respond adequately to initial treatment.

The aim of asthma management is to optimize asthma control with the lowest effective dose. Results from the study of Holt S. showed that the dose-response curve of ICS increased significantly to 100-200 µg/day and peaked by 500 µg/day¹³. Data from the study of Powell H.

showed that no differences in efficacy were reported in plasma cortisol levels in doses up to 500 µg per day¹⁴. However, with increasing doses, the side effect rate progressively increases. In this study, 31.4% of the participants was prescribed with high doses of ICS (greater than 500 µg/day), which may lead to more adverse effects including hoarseness/dysphonia and oral candidiasis. Therefore, regular review of ICS dosage is very important to reach the lowest effective dose.

The mean ACT score observed was 20.41 ± 3.96, which was pretty close to the report from the studies conducted by Boonsawat W. (19.2 ± 4.4)¹⁵. Education, asthma severity, step-up therapy and frequency of preventive medication use were found to be significantly associated with asthma control. Patients with higher education level were less likely to have poorly - controlled asthma (p = 0.02; OR = 0.54; 95% CI 0.31-0.92). Schatz M.¹⁶ and Stanford R.H.¹⁷ also showed that poorly - controlled asthma was associated with low education level. Since poor adherence and incorrect inhaler techniques are common reasons of poorly - controlled asthma, clinicians

and pharmacists need to provide basic drug information and instruct inhaler technique for patients.

Patients with severe asthma might have a higher risk of uncontrolled disease ($p < 0.001$; OR = 26.67; 95% CI 5.82 - 122.19). Seventy percent of patients with severe asthma were uncontrolled, this proportion was much higher compared to mild and moderate asthma (5.5% and 60.3%, respectively) (Figure 2). Our finding was consistent with results from previous studies. Miguel Diez J. demonstrated that the factor that most affected asthma control was asthma severity ($p < 0.0001$)¹⁸. Sullivan S.D. concluded that there was an association between poorly controlled asthma and severe

asthma-related events including course of oral steroids, emergency visit, hospitalization¹⁹. The definitions of “asthma control” and “asthma severity” could be confused in clinical settings and there was a common perception that well-controlled asthma corresponded to mild asthma. However, severe asthmatic patients can be well-controlled and reach symptomatic criteria of mild asthma with the exception of ICS dosage. On the contrary, mild asthmatic patients can still experience exacerbations when they have poor adherence to treatment. Therefore, it is important to distinguish between severe asthma and uncontrolled asthma because the latter one is more common and easier to improve²⁰.

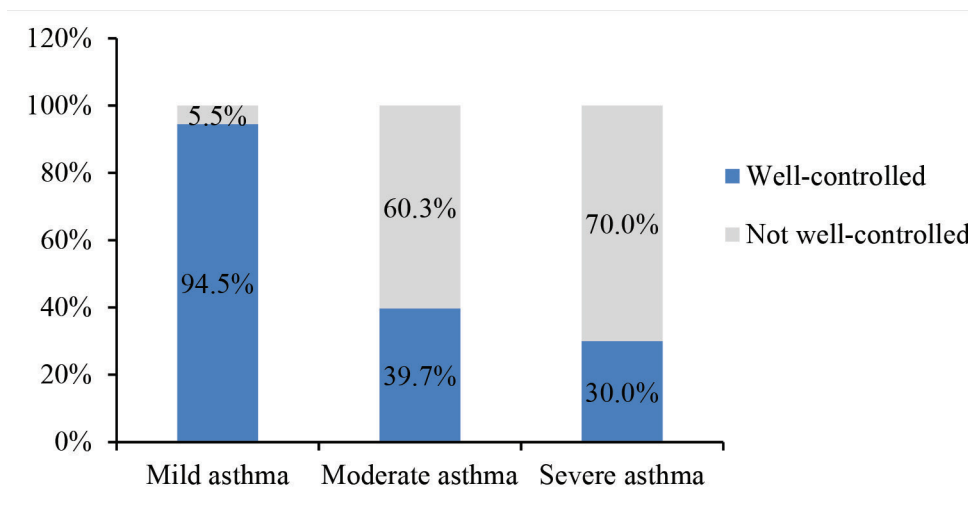


Figure 2. Distribution of the study population by asthma severity and asthma control

There was an association between asthma control and step-up therapy ($p = 0.01$; OR = 8.57; 95% CI 1.82 - 40.32). In the study population, 12.8% of the patients received step-up therapy, out of which 7.6% received increased ICS doses and 5.2% received more medications, mainly LABA. Increasing ICS doses has proved to be necessary in cases that respond poorly to current treatment or during exacerbations. However, the systematic review of Ducharme F. M. stated that in adolescents and adults with sub-optimal control on low dose ICS monotherapy, the combination of LABA and ICS is modestly more effective in

reducing the risk of exacerbations requiring oral corticosteroids than a higher dose of ICS²¹.

Data from our study showed that patients using more frequently preventive medicine were less likely to be uncontrolled ($p = 0.04$; OR = 0.07; 95%CI: 0.01-0.90). Similarly, Stanford R.H. showed that patients with poor adherence to controller medication were more likely to have uncontrolled disease¹⁷.

This study still has some limitations. Data were collected from direct interview and depended on patients’ recall of their diseases and medications. The sample size was small and data were collected from only one hospital,

which was not representative for overall Vietnam asthma population. Further studies should be conducted on larger sample to determine the association between asthma control and comorbidities as well as ICS dosage.

5. CONCLUSIONS

Upon analysis on 308 asthmatic out-patients aged 12 years old or over at University Medical Center HCMC, we identified types of medications indicated and factors associated with asthma control including education, severity of asthma, step-up therapy and frequency of medication use. These results provided data for establishing appropriate prevention and treatment guidelines for asthma at UMC as well as other Vietnamese hospitals, e.g. improving patients' knowledge of medication and strictly monitoring preventive medication usage.

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