APJAI
Asian Pacific Journal of
Allergy and Immunology

ORIGINAL ARTICLE

Characteristics and outcomes of treatment in status asthmaticus patients at emergency department

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Abstract

Introduction: The characteristics and treatment outcomes of status asthmaticus patients in emergency department (ED) have not been described previously especially in Thailand.

Objective: To describe the characteristics, treatment outcomes and factors associated with status asthmaticus in Thai patients presenting to a single center ED.

Methods: A prospective observational study was performed at Thammasat University hospital, Thailand. The data collected included demographics, asthma history and control, previous ED attendances and hospital admissions, presenting clinical, laboratory and radiographic features, treatments given, and outcomes. Multivariable regression was used to determine independent factors associated with status asthmaticus.

Results: Over one year (2015-16), 209 patients were recruited, aged 6 – 54 years (median 33 y), of whom 145 (69.3%) had status asthmaticus. The factors associated with status asthmaticus were: (i) age > 60 y, (ii) presence of a comorbidity, (iii) having uncontrolled asthma, (iv) hospitalizations or visits to the ED in the last year, and (v) using > 1 metered dose inhaler canister per month.

Status asthmaticus patients were significantly less likely to speak in sentences ($p = 0.001$) and more likely to have poor air entry and chest wall retraction ($p < 0.0001$), an abnormal chest X ray ($p = 0.011$), receive magnesium sulphate and be admitted into hospital ($p < 0.0001$). No patients died.

Conclusions: Status asthmaticus was common in this cohort of patients in our setting. Our findings are consistent with previous studies and underscore the need for better patient management.

Key words: Acute asthmatic attack, Asthma exacerbation, Emergency department, Status asthmaticus, Severe asthma

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Introduction

Asthma exacerbation is one of the most common respiratory illnesses seen in the Emergency Department (ED).[1] Globally, approximately 360 million people suffer from asthma and some 397,000 people die from asthma every year.[2] In Thailand, two studies conducted in Bangkok and Khon Kaen showed that the prevalence of wheezing in school-age children ranged from 10–13%,[3,4] and adult asthma was 4.6-9.4%.[5] Of these asthma patients, 36% had experienced an acute exacerbation, 35% had sought treatment in the ED, and 17% were hospitalized.[6]

Many asthma guidelines such as The Global Initiative for Asthma guidelines (GINA) and the Thai Asthma Guidelines recommend inhaled beta-agonist therapy, systemic steroids, and oxygen therapy as the initial treatment of acute asthma exacerbation, depending on its severity.[7] However, some patients do not response within an hour of inhaled bronchodilators and this defines them as having status asthmaticus[8,9] which needs more intensive treatment and observation and, in some cases, hospital admission.[10,11]

Status asthmaticus patients who need close observation at ED is the one of cause of ED overcrowding, including in our setting in Thailand. Studies evaluating the effects of ED crowding result in reduced quality of care, increased medical error, and increased mortality.[12-14] Therefore, having a better understanding of status asthmaticus and tis risk factors could reduce ED attendance and overcrowding.

Asthma exacerbation has been well descried in observational studies and its associated factors include a recent history of an antecedent acute exacerbation,[15] an ED visit or hospitalization in the previous year[16,17] uncontrolled asthma,[15,17-19] insufficient use of inhaled or oral corticosteroids,[19] and a history of a precipitating upper respiratory infection (URTI).[18,19]

There are few data on the outcomes of the initial management of acute asthma exacerbation in the ED in Thailand. Herein, we report the results of a study of asthma exacerbation in a Thai ED.

Methods

Study site and participants

This study was a prospective observational study conducted at the ED of Thammasat University Hospital (TUH), Thailand, from March 2015 to February 2016. All patients with a previous diagnosis of asthma in their medical record who presented with acute exacerbation were considered for inclusion. An exacerbations of asthma was defined by an episode of increased symptoms of shortness of breath, cough, wheezing or chest tightness and deteriorations in lung function from patient's usual status that require a change in treatment.[7] (2) All patients were enrolled into the study after being informed and having given their written consent. The exclusion criteria were out-of-hospital cardiac arrest due to asthmatic attack, and a diagnosis of COPD. According to the previous literatures, patients who do not respond within an hour of inhaled bronchodilators were defined as status asthmaticus. The study was approved by the committee on Human rights related to research involving human subjects, Faculty of Medicine, Thammasat University.

Clinical management and data collection

Data were collected on a standard case record form (CRF) which included demographic data, comorbidities, current and previous treatment for asthma. The asthma control status was defined and graded by the GINA assessment guidelines, which consist of 4 questions: in the past 4 weeks, has patient had (1) Daytime asthma symptoms more than twice/week? (2) Any night waking due to asthma? (3) Reliever needed for symptoms more than twice/week? (4) Any activity limitation due to asthma? If none of these: well-controlled, 1-2: partly-controlled, and 3-4: uncontrolled.[7] The vital signs, clinical presentation and initial laboratory investigations of all patients were recorded. In addition, peak expiratory flow rate (PEFR) which was measured by peak flow meter was applied to patients who are able to use the device.

All treatments were given followed a standard TUH protocol and depended on the severity of asthma: mental status, pulse rate, respiratory rate, accessory muscle use, oxygen saturation, as judged by responsible emergency medicine residents. After 1 hour of treatment, all patients were reviewed and those who did not respond were defined as having status asthmatics.[8,9]

Sample size and data analysis

The sample size was based on previous retrospective study at TUH that showed that the 24% of acute asthma exacerbation patients remained in the ED > 4 hours.[1] We used the precision method. Estimating a status asthmaticus rate of 25%, a precision of 7.5, we would need to recruit at least 129 patients.

Data were analyzed using descriptive statistics (proportion, mean, standard deviation, median, range). Proportional data were compared using Chi-squared or the Fisher exact test, as appropriate. Continuous variables between groups were analyzed using Wilcoxon Rank sum (skewed data) or unpaired student t (normally distributed data) tests.

We used a generalized linear model to determine risk factors associated with status asthmaticus, entering independent variables with a univariate association of $p < 0.1$. Data were analyzed by STATA software version 14 (Stata Corporation, Texas, USA). A p-value of < 0.05 was considered to be statistically significant in multivariable analysis.

Results

A total of 209 patients with asthma exacerbation were included in this study. Of which the median age was 29 years, range 7 to 50, and females slightly outnumbered males. According the previously mentioned criteria, 145 (69.3%) patients were classified with status asthmaticus. Baseline characteristic of patients with acute asthma exacerbation and status asthmaticus are shown in the **Table 1**. As shown, patients with status asthmaticus had more severe asthma symptoms before ED visit, more hospitalization and ED visit, and more patients needing MDI reliever > 1 canister per month than those with non- status asthmaticus.

Comparing the status asthmaticus group to the non- status asthmaticus group by univariate analysis, the following parameters were significantly greater in the status asthmaticus group: (i) age < 6 and > 60 y, (ii) comorbid illnesses, (iii) having partly or uncontrolled asthma, (iv) hospitalizations and visits to the ED in the last year, (v) using > 1 metered dose inhaler (MDI) canister per month, (vi) history of a recent URTI, but (vii) were significantly less likely to be using asthma controller (e.g. inhaled β agonist/steroid).

There were overlapping clinical features between the two groups, notably a history of fever, median respiratory rate, and mean pulse rates and oxygen saturations but the latter two were significantly higher and lower, respectively, in the status asthmaticus group (**Table 2**). Other significantly different clinical features were the inability to complete full sentences, chest wall retraction, poor air entry on auscultation, having a chest X ray (CXR) performed and having an abnormal CXR.

The non- status asthmaticus group had significantly lower: (i) number of nebulizer treatments, (ii) time to receiving steroids, and (iii) time spent in the ED. None needed magnesium sulphate and none was admitted to hospital.

The multivariable analysis (**Table 3**) demonstrated fewer significant associations with status asthmaticus and were age > 60y, the presence of a comorbid illness, uncontrolled asthma, an ED visit within the previous year, and using > 1 MDI/month. The only protective factor for status asthmaticus was being on an asthma controlling treatment.

Table 1. Baseline characteristics of acute asthma exacerbation presented at emergency department.

Characteristic	Number (%)		p-value
	Status asthmaticus (n = 145)	Non-status asthmaticus (n = 64)	
Female gender	86 (59.3)	37 (57.8)	0.839
Age, year†	33 (6, 54)	30 (17, 43)	0.386
Age group, year			0.004
< 6	35 (24.1)	10 (15.6)	
6 to 15	14 (9.7)	4 (6.3)	
16 to 60	69 (47.6)	47 (73.4)	
> 60	27 (18.6)	3 (4.7)	
Comorbid conditions‡	33 (22.8)	3 (4.7)	< 0.0001
Family history of asthma	46 (31.7)	12 (18.8)	0.054
History of allergy	57 (39.3)	18 (28.1)	0.120
Allergic rhinitis	49 (33.8)	15 (23.4)	
Food	5 (3.4)	3 (4.7)	
Drug	1 (0.7)	0	
Other	2 (1.4)	0	
Using asthma controller	64 (44.1)	41 (64.1)	0.008
Asthma symptom control before ED visit			< 0.0001
Well controlled	15 (10.3)	40 (62.5)	
Partly controlled	99 (68.3)	21 (32.8)	
Uncontrolled	31 (21.4)	3 (4.7)	
Hospitalization for asthma in past year	45 (31.0)	2 (3.1)	< 0.0001
ED visit for asthma in past year	138 (95.2)	25 (39.1)	< 0.0001
Intubation for asthma in the past	6 (4.1)	0	0.099
Recent use of oral corticosteroid	10 (6.9)	1 (1.6)	0.111
MDI reliever > 1 canister/month	44 (30.3)	2 (3.1)	< 0.0001
Pre-hospital nebulization	110 (90.2)	44 (83.0)	0.181
Precipitating with respiratory infection	132 (91.0)	36 (56.3)	< 0.0001
ED shift			0.441
Day	49 (33.8)	27 (42.2)	
Afternoon	52 (35.9)	22 (34.4)	
Night	44 (30.3)	15 (23.4)	

† median(interquartile ranges), ED emergency department, MDI meter dose inhaler
‡ Comorbid conditions included: hypertension, diabetes mellitus, and dyslipidemia

Table 2. Clinical presentation, treatment and outcomes of treatment of acute asthma exacerbation patients.

Clinical presentation and outcomes	Asthma acute exacerbation n (%)		p-value
	Status asthmaticus (n = 145)	Non-status asthmaticus (n = 64)	
Fever	127 (87.6)	59 (92.2)	0.959
Heart rate, beat/min†	119.2 (25.9)	107.5 (22.7)	0.002
Respiratory rate/min‡	29.9 (24-32)	28.4 (23-28)	0.461
Initial O_2 saturation, %†	94.6 (4.7)	96.8 (2.6)	0.001
Initial predicted PEF, %†	46.9 (12.3)	57.2 (24.7)	0.359
Agitation	4 (2.8)	0	0.180
Talk			0.001
Sentence	112 (77.2)	63 (98.4)	
Phrase	32 (22.1)	1 (1.6)	
Word	1 (0.7)	0	
Retraction	110 (75.9)	16 (25.0)	< 0.0001
Wheezing			< 0.0001
Expiratory wheezing	7 (4.8)	23 (35.9)	
Inspiratory/expiratory wheezing	102 (70.3)	37 (57.8)	
Poor air entry	36 (24.8)	4 (6.3)	
Cyanosis	2 (1.4)	0	0.345
Time to start bronchodilator, minute‡	8.7 (7.31-10.0)	11.2 (7.00-15.47)	0.146
Bronchodilator nebulization in ED, No.†	8.7 (7.5-9.9)	1.9 (1.0-3.0)	< 0.0001
Steroid treatment at ED	107 (73.8)	45 (70.3)	0.603
Time to steroid, minute‡	80.5 (20.0-100.0)	39.5 (18.0-54.0)	0.005
Magnesium sulphate treatment at ED	55 (37.9)	0	< 0.0001
Time to magnesium sulphate, minute‡	140.5 (70.0-160.0)	0	n/a
Non-invasive ventilation	3 (2.1)	0	< 0.0001
Neutrophil count, %‡	8.2 (4.8-10.8)	7.4 (4.2-9.8)	0.282
Basophil count, % ‡	0.8 (0.3-0.8)	0.5 (0.3-0.6)	0.209
Eosinophil count, % ‡	4.8 (1.3-7.5)	5.4 (1.4-7.4)	0.515
Chest radiography done	142 (97.9)	40 (62.5)	< 0.0001
Abnormal Infiltration at chest radiography	21.0 (14.8)	0	0.011
ED LOS, minute‡	658.6 (240.0- 780.0)	150.3 (115.0-180.0)	< 0.0001
Admit	55 (37.9)	0	< 0.0001
Refer to another hospital	18 (12.4)	0	< 0.0001
In-hospital mortality	0	0	n/a
Revisit in 48 hours	1 (0.7)	3 (3.1)	0.172
Revisit in 1 week	4 (2.76)	1 (1.6)	0.602

† mean(SD), ‡ median (interquartile ranges), °C degrees Celsius, PEF peak expiratory flow, No. number, n/a not available, ED emergency department, LOS length of hospital stay

Table 3. Factors associated with status asthmaticus in Thai patients presenting to the Emergency Department.

Clinical variable	Univariable analysis		Multivariable analysis	
	RR (95%CI)	p-value	RR (95%CI)	p-value
Age group, year (16 – 60 reference)				
Less than 6	1.31 (1.05-1.62)	0.015	1.26 (0.97-1.63)	0.088
6 to 15	1.31 (0.98-1.75)	0.069	1.10 (0.87-1.41)	0.422
More than 60	1.51 (1.25-1.83)	< 0.0001	1.22 (1.01-1.46)	0.036
Family history of asthma	1.21 (1.01-1.44)	0.033	1.01 (0.85-1.19)	0.908
Comorbid conditions	1.42 (1.22-1.64)	< 0.0001	1.19 (1.01-1.41)	0.046
Controller used	0.78 (0.65-0.94)	0.009	0.75 (0.63-0.88)	0.001
Asthma symptoms control before ED visit (Well controlled reference)				
Partly controlled	3.03 (1.95-4.69)	< 0.0001	1.21 (0.85-1.72)	0.280
Uncontrolled	3.34 (2.14-5.21)	< 0.0001	1.57 (1.07-2.30)	0.021
Hospitalization for asthma in past year	1.55 (1.35-1.78)	< 0.0001	0.94 (0.80-1.10)	0.428
ED visit for asthma in past year	5.56 (2.80-11.04)	< 0.0001	2.32 (1.24-4.37)	0.009
Using > 1 MDI canister/month	1.54 (1.35-1.77)	< 0.0001	1.21 (1.01-1.45)	0.033
Time to come to ED > 24 hours	1.33 (1.12-1.57)	0.001	1.01 (0.88-1.15)	0.922
Tachycardia > 100 beats/min	1.24 (0.99-1.54)	0.056	0.87 (0.73-1.03)	0.111
Initial O_2 saturation > 90 %	0.69 (0.60-0.79)	< 0.0001	1.03 (0.86-1.24)	0.752
Talking in words and phrases	1.52 (1.34- 1.72)	< 0.0001	1.06 (0.89-1.25)	0.491
Retraction	2.07 (1.60-2.69)	< 0.0001	1.28 (1.01-1.61)	0.038
Wheezing (Expiratory wheezing reference)				
Inspiratory/expiratory wheezing	3.14 (1.63-6.06)	0.001	1.21 (0.66-2.25)	0.538
Poor air entry	3.86 (1.99-7.44)	< 0.0001	1.29 (0.69-2.42)	0.410
Precipitating URTI	2.48 (1.57-3.91)	< 0.0001	1.46 (0.99-2.14)	0.054
Time to steroid more than 1 hour	1.30 (1.12-1.52)	0.001	1.09 (0.95-1.24)	0.235

RR risk ratio, CI confidence interval, ED emergency department, LOS length of hospital stay, MDI meter dose inhaler, URTI upper respiratory tract infection

Discussion

Acute asthma exacerbation is common and challenging problem for ED visit in a patient with asthma. Status asthmaticus, which is a severe form of asthma exacerbation, usually leads to the development several complications, and prolong hospital stay. However, data on status asthmaticus were limited, and most studies were conducted in children, and in the intensive care setting. The present study reports the characteristics and outcomes of patients with asthma exacerbation and status asthmaticus in an ED in Thailand, a middle income Asian country. In this study, we have shown that more than two thirds of patients with asthma exacerbation at ED had status asthmaticus. However, in a previous article, the incidence of status asthmaticus at the ED was reported to be 20-30%.[20] This difference could be explained by the heterogeneity in patients' characteristics among studies.

In our status asthmaticus cohort, the adherence to controller medications was unexpectedly low. This low adherence rate could be a result of patients' factors, for example low socioeconomic status, insufficient understanding of asthma management, misconceptions about asthma, and lack of agreement with treatment prescribed. Moreover, previous report has shown than the providers' factors, for example insufficient knowledge of current recommendations, resistance to changing practice, lack of time and resources also play an important role in the adherence to treatment.[21]

The vital signs at presentation do not only indicate the severity and urgency of patients' condition, but also reflect the chance of developing status asthmaticus.[22,23] Our study showed that some initial vital signs (e.g. pulse rate and oxygen saturation) were associated with the development of status asthmaticus,

even though, these associations were not significant in multivariable analysis. Therefore, vital signs should be promptly assessed and regularly monitored in all patients with acute asthma exacerbation.

In our study, pre-treatment PEFR was assessed at presentation in only 5% of the patients. Hence, 17% of our patients received PEFR measurement at 1 hour after treatment. The PEFR measurement is challenging in the ED, especially when patients are first seen because they may not have sufficient energy to perform the test. Clearly, more needs to be done to encourage physicians to conduct all of the GINA recommendations so that asthma management can be improved.[7]

In the current study, a quarter of patients did not receive steroids as a treatment for asthma exacerbation. In those received steroids, the median time to steroid administration was 80.5 minutes. However, GINA guidelines recommend steroid administration within one hour of arriving in the ED because this is associated with reduced hospitalization rates and length of hospital stay, and increased pulmonary function.[24-26] Magnesium sulphate ($MgSO_4$), an adjunctive therapy, is recommended for patients who do not improve clinically within one hour after receiving first-line treatment.[7,26] In our study, approximately 40% of the status asthmaticus group received $MgSO_4$ at a median time of 2h 20 minutes. None of the non-status asthmaticus group needed $MgSO_4$. The percentage of using intravenous $MgSO_4$ in asthma exacerbation at ED varies among countries such as 7.7% in Australia and New Zealand,[27] 2.5% in North America,[28] and 93% in UK.[29]

40% of our status asthmaticus patients needed hospital admission. This number is lower than what has been reported by Peter et al.[9] In that study, the admission rate was over 80%, however that was an ICU-based study. In TUH, there is limited access to beds in the general ward and ICU; therefore, patients must be treated over several hours, median of 11 h, in the ED, and this accounts for our relatively low admission rate. Delayed transfer from the ED has been shown to increase all-cause inpatient mortality, length of stay and costs for admitted patients.[14] Nevertheless, no patients died in our series and a small proportion of patients returned to the ED following an ED discharge at 48 h (< 1%) and one week (< 3%).

The significant factors independently associated with status asthmaticus were advanced age (> 60 y), the presence of comorbidities (e.g. hypertension, diabetes mellitus, dyslipidemia), and features of poor asthma control (uncontrolled asthma by history, ED visit in the past year, using > 1 MDI canister/month). Patients who adhered to their treatment and used their inhalers were protected from status asthmaticus. Our findings agree with previous studies done in pediatric status asthmaticus patients by Chiang et al.[18] and Carroll et al.[11] They found that poor disease control and an URIT were factors associated with hospital admission.

Even though, there were several limitations in the present study. Firstly, this was a single-center study, hence the results might not be generally applied to all patients with asthma exacerbation. Secondly, the data was collected only at the ED. Therefore, the clinical information after ED disposition was not included. Our prospective cohort study was the first report of status asthmaticus in ED of Thailand and provided useful information for improving the asthma management.

To date, there was limited data on the impact of asthma treatment on the economy in Thailand. A previous study in Thailand reported the cost of asthma treatment was approximate $200 per admission per case.[30] However, it was notified that this figure was actually lower than the real expense.[30] Therefore, the treatment strategy aiming at the prevention of acute exacerbation should be generally emphasized.

Our study provided several important issues for improving the asthma management in Thailand. More patients' education should be implemented, including more thorough training on MDI techniques, and emphasizing the need to regularly use inhalers, which have been proven to prevent asthma exacerbations. Hence, they reduce asthma symptoms, improve lung function and quality of life, and reduce asthma-associated mortality.[31-33]

Conclusions

The current prospective study in acute asthma exacerbation patients has reconfirmed the factors associated with status asthmaticus. Hence, more research is needed to understand cultural and patient centered factors in our setting in order to optimize asthma management using a holistic approach.

Acknowledgements

All authors have no conflict of interest. This study was financial supported by Faculty of Medicine, Thammasat University's research fund. KA designed the study, data collection, performed the statistical analysis, interpretation the results, wrote the manuscript. JL, WS, and ID contributed to data collection. All authors read and approved the final manuscripts.

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