นิพนธ์ต้นฉบับ ▪ Original Article

ปัจจัยกระตุ้น และปัจจัยเสี่ยงต่อการนอนโรงพยาบาลของผู้ป่วยโรคหืดกำเริบเฉียบพลัน: การศึกษาจากฐานข้อมูลการลงทะเบียนในโรงพยาบาลระดับตติยภูมิในภาคตะวันออกเฉียงเหนือของประเทศไทย

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Triggers and Risks Factor for Admission in Patients with Asthma Exacerbation: A Study from an Emergency Room Registration Database in a Tertiary Hospital in Northeastern Thailand

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หลักการและวัตถุประสงค์: โรคหืดกำเริบเฉียบพลันเป็นหนึ่งในสาเหตุสำคัญของการมาตรวจรักษาที่ห้องฉุกเฉิน หากทราบปัจจัยเสี่ยงต่อการนอนโรงพยาบาลของผู้ป่วย จะทำให้รักษาผู้ป่วยได้อย่างทันท่วงที และช่วยในการตัดสินใจรับรักษาเป็นผู้ป่วยในได้เร็วขึ้น นอกจากนี้หากทราบปัจจัยกระตุ้นของโรคหืดกำเริบเฉียบพลันก็จะทำให้ป้องกันการหืดกำเริบได้ดีขึ้น การศึกษานี้จึงมีวัตถุประสงค์ค้นหาปัจจัยเสี่ยงต่อการนอนโรงพยาบาล และปัจจัยกระตุ้นของการเกิดโรคหืดกำเริบเฉียบพลัน

วิธีการศึกษา: การศึกษานี้เป็นการศึกษาย้อนหลังเชิงพรรณนาจากฐานข้อมูลการลงทะเบียนผู้ป่วยโรคหืดกำเริบเฉียบพลันที่มารับการรักษาที่แผนกฉุกเฉิน โรงพยาบาลศรีนครินทร์ มหาวิทยาลัยขอนแก่น จังหวัดขอนแก่น โดยศึกษาในผู้ป่วยที่มีอายุตั้งแต่ 12 ปีขึ้นในช่วงเดือนพฤศจิกายน 2559 -ธันวาคม 2560 ข้อมูลที่ศึกษาประกอบด้วยข้อมูลทางประชากร ปัจจัยกระตุ้น ประวัติโรคหืด ลักษณะทางคลินิกแรกรับ และการรักษาที่แผนกฉุกเฉิน โดยเปรียบเทียบความแตกต่างของผู้ป่วยที่ต้องนอนโรงพยาบาลกับผู้ป่วยที่ไม่ต้องนอนโรงพยาบาลเพื่อหาปัจจัยเสี่ยงต่อการนอนโรงพยาบาลของผู้ป่วยโรคหืดกำเริบเฉียบพลัน

ผลการศึกษา: ผู้ป่วย 73 ราย ได้รับเข้าในการศึกษา ผู้ป่วยหกราย (ร้อยละ 8.21) ต้องได้รับการรักษาเป็นผู้ป่วยใน โดยปัจจัยเสี่ยงของการนอนในโรงพยาบาล ได้แก่ มีโรคประจำตัวเกี่ยวกับหัวใจและหลอดเลือด หรือทางเดินหายใจ (OR 6.38, 95%CI 1.07-38.1, p = 0.044) ต้องใช้ออกซิเจนในการรักษา (OR

Background and objective: Asthma exacerbation is one of the common causes of emergency room visits. Recognizing risk factors for admission could lead to early management and a rapid decision for admission. Identifying the triggers of asthma exacerbation could help to establish effective preventive strategies. This study aimed to identify risk factors for hospital admission and triggers of asthma exacerbation.

Methods: A descriptive, retrospective study was conducted using data from the asthma exacerbation registration database of Emergency department, Srinagarind hospital, Khon Kaen university, Thailand. Children and adults aged ≥ 12 years with asthma exacerbation, who visited our emergency room from November 2016- December 2017, were registered in the database. The registration data consisted of demographic data, triggers of asthma exacerbation, asthma history, clinical presentation at initial assessment, and management at an emergency room. The data of admitted and non-admitted patients were compared and analyzed to identify risk factors for admission.

Results: Seventy-three patients were included. Six patients (8.21%) were admitted. Risks for admission

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1.2,95%CI 1.04-1.34, p = 0.01) และอัตราการหายใจแรกรับมากกว่าหรือเท่ากับ 28 ครั้งต่อนาที (OR 2.44, 95%CI 1.94-3.6, p =0.005) ปัจจัยกระตุ้นโรคหืดกำเริบเฉียบพลันที่พบบ่อยที่สุด คือ การติดเชื้อทางเดินหายใจส่วนต้น (ร้อยละ 38.81%) และการใช้ยาไม่สม่ำเสมอ (ร้อยละ 16.42%) ตามลำดับ

สรุป: ปัจจัยเสี่ยงต่อการนอนโรงพยาบาลของผู้ป่วยโรคหืดกำเริบเฉียบพลัน ได้แก่ มีโรคประจำตัวเกี่ยวกับหัวใจและหลอดเลือดหรือทางเดินหายใจ ต้องใช้ออกซิเจนในการรักษา และอัตราการหายใจแรกรับมากกว่าหรือเท่ากับ 28 ครั้งต่อนาที ปัจจัยกระตุ้นโรคหืดกำเริบเฉียบพลันที่พบบ่อยที่สุด คือ การติดเชื้อทางเดินหายใจส่วนต้น และใช้ยาไม่สม่ำเสมอ

คำสำคัญ: โรคหืดกำเริบเฉียบพลัน, ปัจจัยเสี่ยงต่อการนอนโรงพยาบาล, ปัจจัยกระตุ้นโรคหืดกำเริบเฉียบพลัน

were presence of underlying cardiovascular or respiratory diseases (OR 6.38, 95%CI 1.07-38.1, p = 0.044), requiring oxygen therapy (OR 1.2,95%CI 1.04-1.34, p = 0.01), and initial respiratory rate ≥ 28 breaths/minute (OR 2.44, 95%CI 1.94- 3.6, p =0.005). The most common and the second most common triggers of asthma exacerbation were upper respiratory tract infection (38.81%) and poor adherence (16.42%), respectively

Conclusion: Risk factors for admission in patients with asthma exacerbation were presence of underlying cardiovascular or respiratory diseases, requiring oxygen therapy and initial respiratory rate > 28 breaths/minute. Upper respiratory tract infection and poor adherence were the two most common triggers of asthma exacerbation

Keyword: asthma exacerbation, risk factors for admission, triggers of asthma exacerbation

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Introduction

Asthma exacerbation is one of the common causes of emergency room visits[1,2]. A significant number of asthmatic patients needs hospital admission[3,4], causing personal and public health burdens[5]. Hospitalization also increases risk of fatal and near-fatal asthma and is a risk factor for fixed airflow limitation[6].

Several clinical scoring systems with varied validity have been developed for assessing the severity of asthma exacerbation[7,8]. However, there is no consensus on which scoring system should be used. Furthermore, in an emergency situation and overcrowded emergency room setting, it is difficult for physicians to memorize and calculate severity scores, let alone remember the cut-off points. In addition, identifying the triggers of asthma exacerbation could help to establish effective preventive strategies. Therefore, we conducted a study to identify specific and feasible clinical markers, and risk factors for hospital admission, for routine use in a real-life emergency setting, assisting physicians to make rapid decisions when admission may be needed. Triggers of asthma exacerbation were also assessed.

Methods

We conducted a descriptive, retrospective study using data from the asthma exacerbation registration database of Srinagarind hospital, Khon Kaen university, Thailand. Srinagarind hospital is a tertiary referral center in northeast Thailand. Patients with asthma exacerbation aged ≥ 12 years, who visited our emergency room from November 2016- December 2017, were registered in the database. Asthma exacerbation was diagnosed by typical features of shortness of breath, wheezing or chest tightness , which then the diagnosis was confirmed by emergency medicine specialists. Patients presenting with wheezing or dyspnea whose diagnoses were uncertain or not confirmed by an emergency medicine specialist were excluded.

The registration data consisted of the following details (1) demographic data: age, gender, and underlying diseases; (2) triggers of asthma exacerbations; (3) asthma history: duration of asthma, prior treatment, previous emergency room visits, and history of intubation; (4) clinical presentation at initial assessment: respiratory rate, pulse rate, room air oxygen saturation, peak expiratory flow (PEF), visible cyanosis, alteration of consciousness, and use of accessory muscles, and overall severity of asthma exacerbation, as categorized by GINA the guideline[9] ; and (5) management of

asthma exacerbation at emergency room. Patients who did not show any improvement or deteriorated after one hour of treatment were admitted.

In term of triggers of asthma exacerbation, poor adherence was defined by more than 1 week of withholding the prescribed asthma-controller medicine, and inadequate treatment was defined by more than 1 week of lower than prescribed dose of the asthma-controller medicine and/or bronchodilators. These were assessed by history taking, prescription data and medical record. Data between the patients who were admitted (admitted group) and the patients who were discharged from the emergency room (non-admitted group) were compared and analyzed. The study was approved by Khon Kaen University Ethics Committee for Human Research.

Statistical analysis

Data were analyzed using non-parametric descriptive statistics (percentage, median, standard deviation, median, interquartile range; IQR), as the data were mainly non-normally distributed. Proportional data were compared using Chi-squared or the Fisher exact test, as appropriate. Continuous variables between groups were analyzed using Mann–Whitney U test. Odds ratio (OR) and 95% confidence interval (CI) were used to determine admission risk factors. All data analyses were performed by SPSS version 19. P-value < 0.05 was considered significant.

Results

One hundred and one patients presented with wheezing during the studied period. A total of 73 patients met the criteria and were included in this study. Thirty-seven of them (50.68%) were male. The median age was 43 years (IQR 48-59) Eighteen patients were children aged 12-18 years. Six of the 73 patients (8.21%) were admitted into the hospital's non-Intensive Care Unit wards. Sixty-seven patients were discharged (Table 1).

Forty-seven patients (64.38%) had underlying diseases. A significantly higher proportion of patients in the admitted group had cardiovascular or respiratory diseases than those in the non-admitted group: 66.67 vs 23.88 % (p-value = 0.044), respectively. These diseases were associated with a greater risk for admission (OR 6.38, 95%CI 1.07-38.1). The diseases included hypertension, coronary artery disease, and pulmonary tuberculosis. Only one of allergic disease other than asthma was found, allergic rhinitis, and was not significantly different between the two groups.

Regarding the patients' asthma history, the median duration of asthma was 5 years (IQR 2-10). Fifty-nine patients (80.82%) had received prior asthma treatment. Fifty patients (68.49%) had previous emergency room visits, 4 of whom had not received asthma treatment. Of the other 46 patients, 9 patients did not use any relievers and 13 patients did not use any controllers. Eight of the 73 patients (10.96%) had been intubated in the past, and one of them did not use any controllers. The asthma history was not significantly different between the admitted and non-admitted groups.

In terms of clinical presentation, the median initial respiratory rate of the admitted group was significantly higher than that of the non-admitted group: 34 (IQR 31-39) vs 24 breaths/minute (IQR 24-38), respectively (p =0.01, Table 1). Initial respiratory rate ≥ 28 breaths/minute was associated with admission (OR 2.44, 95%CI 1.94- 3.6, p =0.005).

Oxygen therapy was provided in patients who upon or subsequent to arrival did not meet target oxygenation according to the GINA guideline[9]. A significantly higher proportionate of the patients in the admitted group required oxygen therapy relative to the non-admitted group: 100 vs 45 % (p-value = 0.01), respectively. The odds ratio for oxygen therapy and admission was 1.2 (95%CI 1.04-1.34).

Upper respiratory tract infection and poor adherence were the most common (38.81%) and the second most common (16.42%) triggers of asthma exacerbation, respectively (Figure 1). The triggers of asthma exacerbation were not significantly different between the admitted and non-admitted groups.

Subgroup analysis in children did not found any statistical significance differences.

Discussion

Asthma exacerbation is a common and challenging problem, especially in overcrowded emergency rooms in Thailand, a developing country with limited medical resources[10]. Patients with asthma exacerbation need a quick assessment, prompt treatment, and a rapid decision regarding admission. We conducted a retrospective study using data from the asthma exacerbation registration database to identify specific, feasible clinical markers and risk factors for admission among patients with asthma exacerbation. We also assessed triggers of asthma

Table 1 Patient characteristics and outcomes

Characteristics	All patients (n = 73) n (%)	Admitted group (n= 6) n (%)	Non- admitted group (n = 67) n (%)	p-value
Demographic data				
Age (year, IQR)	43 (48-59)	69.5 (12.75-76.5)	47 (20-60)	0.150
Male gender$	37 (50.68)	3 (50)	34 (50.7)	1.000
Underlying diseases				
Any underlying diseases	47 (64.38)	6 (100)	26 (38.81)	0.005*
Allergic diseases	3 (4.1)	0 (0)	3 (4.48)	1.000
Cardiovascular or respiratory diseases†	20 (27.4)	4 (66.67)	16 (23.88)	0.044*
Asthma history				
Duration of asthma (year, IQR)	5 (2-10)	6 (0.97-22.5)	5 (2-10)	0.847
Receiving prior asthma treatment	59 (80.82)	6 (100)	53 (79.1)	0.588
Using reliever before arrival	49 (67.12)	4 (66.66)	45 (67.16)	1.000
Using controller	40 (54.79)	3 (50)	37 (55.22)	1.000
- Inhaled corticosteroid (ICS)	39 (53.42)	3 (50)	36 (53.73)	-
- Leukotriene receptor antagonist	1 (1.37)	0 (0)	1 (1.49)	-
- Theophylline	2 (2.74)	0 (0)	2 (2.99)	-
Previous emergency room visit	50 (68.49)	6 (100)	44 (65.67)	0.168
Ever intubated	8 (10.96)	0 (0)	8 (11.94)	0.573
Clinical presentation				
Respiratory rate (breath/minute, IQR)	26 (24-28)	34 (31-39)	24 (24-28)	0.010*
Pulse rate (beat/minute, IQR)	100 (85-110)	107 (103-114)	98 (84-110)	0.150
Oxygen saturation (%, IQR)	96 (93-98)	93 (88-98)	96 (94-98)	0.465
PEF‡ (liter/minute, IQR)	150 (100-200)	125, (70-265)	150, (100-200)	0.730
Accessory muscle uses	22 (30.14)	2 (33.33)	20 (29.85)	1.000
Alteration of consciousness	0 (0)	0 (0)	0 (0)	-
Visible cyanosis	0 (0)	0 (0)	0 (0)	-
Severity of asthma exacerbation#				
Mild to moderate	20 (27.4)	1 (16.67)	19 (28.36)	1.000
Severe	53 (72.6)	5 (83.33)	48 (71.64)	-
Management at emergency room				
Oxygen therapy	36 (49.32)	6 (100)	30 (44.78)	0.011*
Nebulized B2-agonist (doses, IQR)	2 (1-3)	2 (1-2.25)	2 (1-3)	0.756
Systemic corticosteroids	47 (64.38)	5 (83.33)	45 (67.16)	1.000
Systemic B2-agonist	13 (17.81)	3 (50)	10 (14.92)	0.065

IQR, inter quartile range; PEF, peak expiratory flow, $ Percentage of the patients in the same groups

† Cardiovascular or respiratory diseases included: hypertension, coronary artery disease, and pulmonary tuberculosis

‡ Obtained from 47 patients, # Categorized by GINA the guideline, *p-value < 0.05 was considered statistically significant.

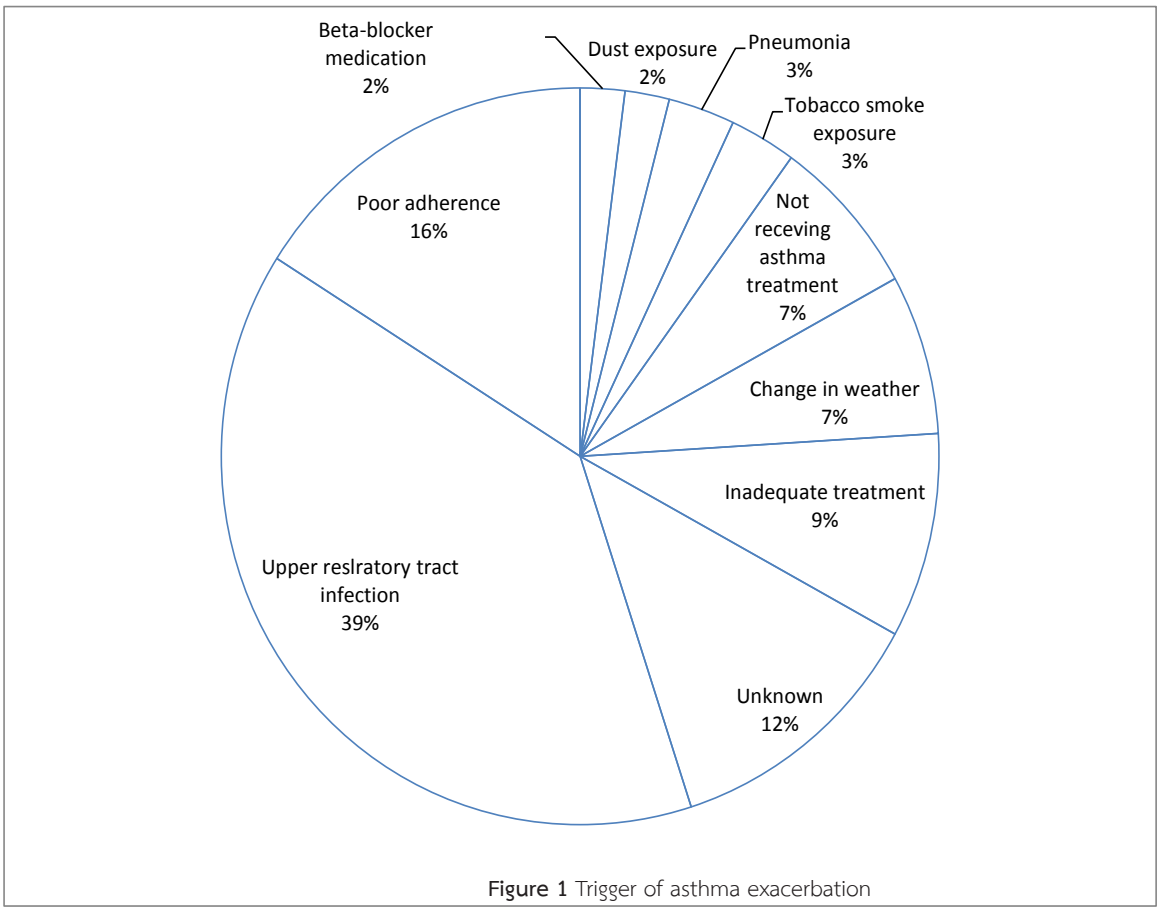

Figure 1 Trigger of asthma exacerbation

exacerbation, which can help to establish an effective prevention plan.

The overall severity of asthma exacerbation according to the GINA guideline was not significantly different between the admitted and non-admitted groups. However, we found that a specific clinical marker for admission was initial respiratory rate. Patients in the admitted group had a significantly higher initial respiratory rate than patients in the non-admitted group, with a cutoff point of 28 breaths/minute. Respiratory rate is frequently included as a parameter of asthma exacerbation severity scores[8,11]. Nevertheless, few studies have demonstrated a specific respiratory rate that increases risk for admission. A prospective, observational study conducted in Canada[12] found that a respiratory rate of greater than 22 breaths/min was associated with admission. However, a large proportion of asthma patients in Thailand overestimate their asthma control and have inappropriate concepts about asthma treatment[4]. This leads to delayed recognition and increased severity of asthma exacerbation and their severity of asthma exacerbation increased. Hence, a respiratory rate that is not significantly different from a normal range[13], may be less feasible in this context.

Previous study has shown that low oxygen saturation is a predictor of hospital admission[12] and that admission rate increases with decreased oxygen saturation[14]. In our study, oxygen saturation, as measured on arrival at the emergency room was not significantly different between the admitted and non-admitted patients. However, oxygen therapy was provided in patients who upon or subsequent to arrival did not meet target oxygenation according to the GINA guideline[9]. We found that the patients who required oxygen therapy at any time were more likely to be admitted. This result is similar to a finding in a study by Pola-Bibian et al.[15], which showed that admitted patients require more treatment, including oxygen therapy, indicating a higher severity of exacerbation relative to patients who are discharged. Therefore, asthmatic patients who require oxygen therapy upon arrival to the emergency room or at any point thereafter should be considered for admission.

In contrast to the previous study [16], the PEF between the admitted and non-admitted group was not significantly different. One possible explanation is that the majority of our patients had severe asthma exacerbation at the initial presentation, and only 64.38 percent of the patients were able to perform PEF upon

arrival at the emergency room. Therefore, pre-treatment PEF has a limited evaluation capacity in patients who initially present with severe clinical manifestations.

Our study demonstrated that cardiovascular and respiratory comorbidities which were hypertension, coronary artery disease, and pulmonary tuberculosis increase risk of hospital admission. Patients with these underlying diseases may have delayed recognition and response to worsening asthma due to the tendency to attributing exacerbation symptoms to aging or underlying diseases[17]. In addition, cardiovascular diseases significantly deteriorate the clinical course of asthma[18] and vice versa[19]. Similar to previous research[20], hypertension, the most common cardiovascular disease in our patients, correlated with increased admission rates. A possible explanation for hypertension having an impact on asthma lies in the medications frequently used to treat the condition, especially B1-adrenergic blockers, one of triggers of asthma exacerbation found in our study, can worsen asthma[21]. Furthermore, use of systemic corticosteroids is linked to hypertension[22]. Physicians should be aware of the risks and benefits of prescribing beta-blocker medications to asthmatic patients, and such medication should be initiated only under close medical supervision. Patients with underlying cardiovascular or respiratory diseases should be guided in early recognition of asthma exacerbation, and a holistic approach to treatment and intensive management at the emergency room should be provided.

Interestingly, 5.47 % of the patients in our study, had pulmonary tuberculosis, a higher prevalence than at the national level[23]. Previous studies have found that a subset of patients developed tuberculosis subsequent to being diagnosed with asthma and vice versa[24]. Patients with tuberculosis can develop bronchial asthma due to bronchopulmonary damage, by which allergens may gain access and cause inflammation. In addition, use of inhaled corticosteroids, the main controller of asthma, increases the risk of tuberculosis[25]. Therefore, patients with asthma whose symptoms have not been controlled should be evaluated for pulmonary tuberculosis and vice versa.

A history of intubation or previous emergency care visits increases the risk of asthma related-death[6]. Surprisingly, a significant number of patients with these risk factors in our study who had these histories did not use controller and/or reliever medications. Hence, the importance of regularly using controller medication and guided asthma self-management education should be emphasized.

Systemic corticosteroids enhance the resolution of exacerbation and should be prescribed in all but the mildest of exacerbations[26]. Surprisingly, one patient who required admission did not receive systemic corticosteroid at the emergency room. Undoubtedly, this indicates that more needs to be done to encourage physicians to improve asthma exacerbation management and guideline implementation.

The most common trigger of asthma exacerbation in our study was upper respiratory tract infection, which is similar to previous finding[27]. Viral respiratory tract infections lead to lower airway inflammation and altered pulmonary physiology[28]. Therefore, asthmatic patients should initiate short-term step up during viral infections. The second most common trigger was poor adherence. Poor adherence has been found to be widespread among patients with asthma[29] and is also a key modifiable risk of asthma exacerbation[30]. Adherence should be emphasized and regularly assessed. Established adherence interventions and strategies should be applied including self-management education, patient adherence monitoring and feedback, and taking advantage of information technology tools to remind and support patient regarding adherence[31].

Potential limitations of this study of this study include the following. Firstly, the number of patients was limited. We included only patients whose diagnosis of asthma exacerbation were confirmed by emergency medicine specialists. Patients presented with wheezing whose diagnosis was uncertain were excluded, as they may have a different clinical entity from asthma[32]. Although the majority of patients visiting emergency room with asthma exacerbation were young children. We included only children aged ≥ 12 years in order to limit variation due to difference normal range of vital signs. Secondly, some of the clinical presentations were not included in this study, such as inspiratory-expiratory ratio and asthma history, including previous asthma control and duration of asthma exacerbation. However, patients may have poor insight of their symptoms and deliver incorrect history[7]. Thirdly, only clinical presentations at initial assessment were analyzed. Considering that clinical status after commencement of treatment have also been found to be important predictors for admission[33], these data should be collected to

improve our registration database and future analyses. Lastly, investigations which were found to be risk factors for admission in other studies, such as allergen sensitization[34], blood eosinophil count[15], and immunoglobulin E level[35], were not included. However, such investigations were not feasible in our setting due to limited medical resources and the fact that blood works are not routinely done in typical cases of asthma exacerbation.

In conclusion, our study identified practical and specific risk factors that can aid in making admission decision. These risk factors were initial respiratory rate ≥ 28 breaths/minute, requiring oxygen therapy upon or subsequent to arrival, and presence of underlying cardiovascular or respiratory diseases. Patients with these risk factors need early recognition and attentive treatment. URI and poor adherence were common triggers of asthma exacerbation. A significant number of patients did not receive adequate treatment despite having previous emergency room visits or even history of intubation.

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