## **ORIGINAL ARTICLE**

# Asthma Exacerbation during the COVID-19 Pandemic

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## ARTICLE INFO

# ABSTRACT

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**Introduction:** Asthmatics, especially uncontrolled asthmatics, must be vigilant during the COVID-19 pandemic to avoid major respiratory complications. This study aimed to describe these characteristics in emergency unit patients with asthma and COVID-19 at Haji General Hospital, Surabaya, an East Java referral hospital.

**Methods:** The study gathered medical information on 160 asthma patients from March to December 2021. The collected data were related to socioeconomics, allergy history, family allergy history, and medications.

**Results:** 160 confirmed cases of asthma occurred during COVID-19 at Haji General Hospital, Surabaya. Most adult asthma sufferers were women (59.2%), high school graduates (31.25%), housewives (21.2%), had payment method with Social Health Insurance Administration Body (BPJS) insurance (73.8%), had a history of drug allergies (11.5%), had no family history of allergies (50.8%), and used albuterol control drugs (10.7%). Meanwhile, the majority of children with asthma were boys (53.3%), did not attend school or did not finish elementary school (33.3%), did not work (33.3%), had payment method with BPJS (73.3%), had a history of allergies to seafood and cow's milk respectively (10%), had no family history of allergies (40%), and used albuterol control drugs (16.7%).

**Conclusion:** The proportion of asthma in the emergency unit was dominated by women over 18 years old with a high school education. Most patients were housewives and used BPJS. Many of them had a history of allergies to medications (not asthma medication), and there was no family history of allergies. Commonly used medications were albuterol to control asthma.

# INTRODUCTION

Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is determined by a history of respiratory symptoms that can vary from person to person. Asthma symptoms include breathing difficulty, wheezing, coughing, tightness in the chest, and weakness. In a severe asthma attack, there may be speaking difficulty, blue lips, relievers not helping, feeling very depressed or tired from trying to breathe, and deep sucking movements in the throat or chest while trying to breathe.<sup>1,2</sup> Based on data from the World Health Organization (WHO), the number of people living with asthma worldwide has reached 300 million. There are around 250,000 deaths caused by asthma exacerbation each year, mostly from low-to-medium-income countries.<sup>3</sup> Asthma epidemiological studies, according to the Indonesian Ministry of Data and Information Center (2019), stated that the leading causes of asthma are unknown.<sup>4</sup> During the COVID-19 pandemic, the prevalence of asthma with COVID-19 worldwide was 6.9%. The incidence of asthma in the world continues to grow, with the proportion of adults (>18 years old) higher than

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The pathophysiology of asthma includes airway infiltration by inflammatory cells, including neutrophils, eosinophils, and lymphocytes, mast cell activation, and epithelial cell destruction. This inflammatory response causes the classic picture of airway swelling, increased mucus secretion, and bronchial muscle dysfunction, resulting in airflow limitation and asthma symptoms. Remodeling, a term used to describe ongoing structural changes in the airways, can occur and eventually lead to fibrosis, mucus hypersecretion, epithelial cell booth muscle hypertrophy, and angiogenesis.<sup>6</sup> There are various risk factors for atopic and non-atopic asthma. There are environmental risk factors revealed in genetic studies in adults and children, such as exposure to air pollution, cigarette smoke, atopy, stress, and obesity, all of which can increase the incidence of asthma in genetically susceptible individuals.<sup>6,7</sup>

An asthma diagnosis is an initial stage in providing interventions to asthma patients.<sup>2</sup> It is often more challenging to confirm the diagnosis of asthma once the patient has started controller medication, for it is necessary to understand the precipitating risk factors of asthma. Diagnosing asthma in a patient not on controller medication is based on identifying a characteristic pattern of respiratory symptoms and variable expiratory airflow limitation.<sup>7</sup> Intensive management of asthma patients includes controller and reliever therapy. This approach will reduce the incidence of asthma and slow its development.<sup>8</sup>

COVID-19 is the disease most often found in people with asthma. In a study by Sunjaya, *et al.* (2022), 8.08% of COVID-19 patients had comorbid asthma.<sup>9</sup> Due to the high incidence of COVID-19 patients who have comorbid asthma, which is the most common cause of death due to uncontrolled shortness of breath, this study aimed to investigate the determinants of asthma during the COVID-19 pandemic in the Emergency Unit, Haji General Hospital, Surabaya, from 16 March 2020 to 31 December 2021.

#### METHODS

This retrospective study was conducted at the Emergency Unit, Haji General Hospital, Surabaya. The study utilized secondary data from medical records of patients who visited the hospital during the COVID-19 pandemic from 16 March 2020 to 31 December 2021, following specific inclusion criteria. These criteria included being diagnosed with asthma based on the Indonesian Society of Respirology (PDPI) Guidelines and receiving standard therapy for asthma based on the PDPI Guidelines for at least one year.<sup>10</sup> The inclusion criteria for asthma patients included asthma attacks and

exacerbations (ICD-10 code J45), which were determined through medical history, physical examination, and chest X-ray.

Out of 160 asthma patients who visited the hospital from March to December 2021, all patients fulfilled the requirements and underwent a comprehensive examination. This examination included gathering demographic characteristics (sex, education, occupation, payment methods), comorbidities (such as COVID-19), allergy history, family allergy history, and medication history.

A Chi-Square test using the Statistical Package for the Social Sciences (SPSS) program was employed to analyze the association between asthma and their respective comorbidities, family allergy history, and medication history. This study diagnosed asthma from medical history, physical examination, and lung function tests. Asthma by age is categorized as child asthma for patients under 18 years old and adult asthma for patients under 18 years old and above. Adult asthma patients (over 18 years old) have the right to give informed consent to medical procedures, including the diagnosis and treatment of asthma. This study provided adult patients with informed consent to participate in the study. For asthma patients (under 18 years old), parents or legal guardians were responsible for giving informed consent.

This study obtained ethical clearance from the Health Research Ethics Committee Haji General Hospital, Surabaya, with the number 073/14/KOM/ETIK/2022.

## RESULTS

There were 4,015 COVID-19 patients admitted to the hospital from March to December 2021. 160 (0.04%) of the total COVID-19 patients were diagnosed with asthma exacerbation in the emergency unit. The majority, 130 patients (81.3%), were adult asthma, and 30 (18.7%) were child asthma.

Table 1 shows that most child asthma cases were 16 males (53.3%), 10 patients (33.3%) were not enrolled in school yet or not finished elementary school, 10 patients (33.3%) were not working, with payment methods of 22 patients (73.3%) by Social Health Insurance Administration Body (BPJS). Meanwhile, most adult asthma cases were 77 females (59.2%), 50 patients (31.25%) were high school graduates, 34 patients (21.2%) were housewives, followed by 33 patients (20.6%) were private employees, with payment methods of 96 patients (73.8%) by BPJS.

The difference in education and occupation between child and adult asthma was significant.

					Asthma	'n
betwee	n ch	ild an	d adult asth	ma		
Table	1.	The	difference	in	socioeconomic	determinants

	Ast	р-	
Variables	Child	Adult	value
	n=30(%)	n=130(%)	
Sex			0.210
Males	16(53.3%)	53(40.8%)	
Females	14(46.7%)	77(59.2%)	
Education			
No education/not finished	10(33.3%)	3(1.9%)	0.000*
Elementary school			
Middle school	3(10.0%)	3(1.9%)	
High school	1(3.3%)	50(31.2%)	
College or equivalent	2(6.6%)	9(5.6%)	
Bachelor	0(0.0%)	12(7.5%)	
No data	14(46.7%)	53(33.1%)	
Occupation			
Not working	10(33.3%)	16(10.0%)	0.000*
School	6(20.0%)	0(0.0%)	
Housewives	0(0.0%)	34(21.2%)	
Civil servants/police/soldiers	0(0.0%)	1(0.6%)	
Private employees	1(3.3%)	33(20.6%)	
Self-employed	0(0.0%)	1(0.6%)	
Laborer/driver/HH asistant	0(0.0%)	1(0.6%)	
Others	1 (3.3%)	4 (2.5%)	
No data	12(40.0%)	40(25.0%)	
Payment methods			
BPJS	22(73.3%)	96(73.8%)	1.000
Cash	8(26.7%)	34(26.2%)	
Total	30(100.0%)	130(100.0%	)

Table 2 shows the highest allergy history in children, 3 patients (10.0%) of seafood and cow's milk, respectively. Meanwhile, the highest allergy history in adults was an allergy to some medicine (not asthma drugs) of 15 patients (11.5%), and dust/smoke/hair of 5 patients (3.1%). The family differences in allergy history between child and adult asthma were significant.

The highest asthma among children and adults had no family allergy history. The difference in family allergy history between child and adult asthma was insignificant.

Table 3 shows the highest of asthma control drugs in children, namely albuterol oral of 5 patients (16.7%), whereas in adults, namely albuterol oral of 14 patients (10.7%), and fenoterol inhalation of 9 patients (6.9%), respectively. The difference in control drugs between child and adult asthma was significant.

 Table 2. The difference in allergy history between child and adult asthma

	Ast	n voluo	
Variables	Child	Adult	p-value
	n (%)	n (%)	
Allergy history			0.000*
No allergy	15 (50.0%)	89 (68.5%)	
Cold temperature	1 (3.3%)	2 (1.5%)	
Seafood	3 (10.0%)	1 (0.7%)	
Chocolate	1 (3.3%)	0 (0.0%)	
Medicine*	0 (0.0%)	15 (11.5%)	
Catfish	1 (3.3%)	0 (0.0%)	
Dust/smoke/hair	0 (0.0%)	5 (3.1%)	
Cow milk	3 (10.0%)	0 (0.0%)	
Fried food	0 (0.0%)	1 (0.7%))	
Coconut cream	0 (0.0%)	1 (0.7%))	
Egg	1 (3.3%)	0 (0.0%)	
No data	5 (16.7%)	16 (12.3%)	
Family allergy history			
Yes	1 ( 3.3%)	3 (2.3%)	0.561
No	12 (40.0%)	66 (50.8%)	
No data	17 (56.7%)	61 (4.,9%)	
Fotal	30 (100.0%)	130 (100.0%)	

\*: Allergy to some medication, not asthma drug

 Table 3. The difference in control drugs between child and adult asthma

	Ast			
Control drugs	Child	Adult	p-value	
	n (%)	n (%)		
			0.031*	
None	6 (19.8%)	28 (21.5%)		
Albuterol oral	5 (16.5%)	14 (10.7%)		
Dexamethasone oral	1 (3.3%)	0 (0.0%)		
Fenoterol inhalation	0 (0.0%)	9 (6.9%)		
Budesonide inhalation	1 (3.3%)	0 (0.0%)		
Drug combination*	3 (10.9%)	9 (7.8%)		
No data	14 (46.2%)	69 (53.1%)		

 Total
 30 (100.0%)
 130 (100.0%)

 \*Drug combination: (1) Fenoterol inhalation with albuterol oral and codeine oral, (2) Fenoterol inhalation with levofloxacin oral and acetylcysteine oral, (3) Albuterol oral with chlorpheniramine maleate oral and tiotropium bromide inhalation, (4) Albuterol oral with acetylcysteine oral and codeine oral, (5) Albuterol oral and albuterol inhalation, (6) Fenoterol inhalation and albuterol oral, (7) Albuterol oral and ephedrine HCl oral, (8) Albuterol oral with acetylcysteine oral and fenoterol inhalation, (10) Budesonide with formoterol, (11)

 Pseudoephedrine HCl with triprolidine HCl, (11) (Ipratropium bromide with albuterol), (12) Ephedrine HCl, (12) (Ephedrine oral

#### DISCUSSION

The determinants of education, occupation, the history of allergies, and the use of preventive medicine

control asthma was significantly different between child and adult asthma. The determinants of sex, payment methods, and family allergy history were not significantly different between child and adult asthma.

This study showed that the highest number of children with asthma were males, while adult asthma occurred in females but was insignificant. Likewise, Litanto, et al. (2021) showed that childhood asthma was high in boys.<sup>11</sup> Wardhani, et al. (2020) showed that women were significantly associated with a high incidence of asthma in adults.<sup>12</sup> Asthma is more common in males under 13 years old (65% prevalence), and the incidence rate is greater (65% prevalence) in adult women than in men. This is caused by a conflict between the ovarian hormones and testosterone when inflammation occurs in the airways of asthmatics. When women with asthma use hormonal contraception during pregnancy and menopause, as sex hormones change and increase, asthma increases dramatically.<sup>13</sup> According to Naeem, et al. (2019), one of the factors that influence asthma cases was obesity and body mass index (BMI).14 In adults, obese women are more likely to experience asthma than men. In children with a high BMI, as found in male patients, a high BMI will increase the risk of asthma in boys compared to girls.<sup>14</sup> On the other hand, Khaidir, et al. (2019) showed that gender did not affect the degree of bronchial asthma.<sup>15</sup>

Indonesia Basic Health Research 2018 showed higher asthma prevalence among non-educated or college-to-university graduates. This study found that children with asthma mainly were not enrolled in school or had not finished elementary school, and adults with asthma had high school education.<sup>3</sup>

Zeng, *et al.* (2018) showed that the risk of asthma incidence was approximately doubled in subjects with a primary or secondary educational level compared to subjects with a university educational level.<sup>16</sup> Lower educational level was a risk factor for adult asthma. One of the most critical aspects of treatment is educating the individual with asthma. If adequately educated, individuals could recognize symptoms earlier and respond to changes with a predetermined action plan.<sup>16</sup>

Housewives face significant exposures that trigger allergy and asthma symptoms. Meanwhile, Tiotiu, *et al.* (2020) found that adults with asthma with full-time occupations who were younger and more often had non-manual occupations, experienced fewer asthma symptoms, used fewer asthma medications, and smoked less than subjects with occupation disabilities.<sup>17</sup> Moreover, Mungan, *et al.* (2019) showed that asthma patients had significant exposures to occupations that worsened their symptoms.<sup>18</sup> Hence, asthmatics and clinicians need to be educated about the prevalence and

risks of exposure in the workplace (as well as at home) to minimize asthma triggers and exacerbations.<sup>18</sup>

Stolbrink, *et al.* (2022) showed no difference in adherence between patients, indicating that prescription costs did not impact adherence to maintenance therapy for asthma or chronic obstructive pulmonary disease (COPD).<sup>19</sup> According to Chen, *et al.* (2020), COPD costs were strongly correlated with disease severity, hospitalization was the primary contributor to medical costs, and non-adherence to maintenance treatment negatively correlated with resource utilization and health care costs.<sup>20</sup> Similarly, in this study, most asthma patient payments among children were by cash. Meanwhile, among adult asthma patients, the most popular payment method was by BPJS.

In this study, the most allergy history of asthma patients among adults was of medicine. It was similar to the study by Hyrkäs, et al. (2022) which stated that adult asthmatics with poor asthma control were likelier to experience cold weather-related symptoms.<sup>21</sup> Meanwhile, seafood and cow's milk were the biggest allergens for asthma patients among children in this study. Safri (2018) discovered that more than 170 foods could cause allergies.<sup>22</sup> The most common causes of food allergies in children are cow's milk, eggs, seafood, and peanuts. According to van Neerven, et al. (2019), cow's milk allergy in children will primarily result in excessive allergies and immunological tolerance to cow's milk before the age of three to four years.<sup>23</sup> Some data suggests that allergies may play a key role in children with severe asthma, according to Arasi, et al. (2019).<sup>24</sup> Many children with severe asthma also have an allergic disease. Food, mold, pollen, and pet allergies have all been correlated to the onset of asthma and severe asthma exacerbations.<sup>24</sup>

In this study, child and adult asthma mostly had no family history of allergy. Meanwhile, Saito, et al. (2022) showed a history of allergies and bronchial asthma in one or both parents was significantly related to allergies in children.<sup>25</sup> Thus, according to Yu, et al. (2021), asthma is genetically predetermined.<sup>26</sup> However, if shared environmental factors are controlled, the family background can provide helpful information for susceptibility genes. Asthmatic parents have been linked to an increased risk of asthma in their children.<sup>5</sup> The Centers for Disease Control and Prevention (CDC) report stated that an individual who has a parent with asthma is three to six times more likely to acquire asthma than someone without asthma.<sup>5</sup> In addition, Mahrunnisa, et al. (2021) showed a family history of allergic disease was a risk factor for developing allergic manifestations, both single and multi-mobility allergic diseases.27

This study showed that albuterol (salbutamol) was the most commonly used drug to prevent asthma in children and adults. Thus, according to Marques, et al. (2022), using drugs to control or prevent asthma primarily uses first selective short-acting beta-agonists (SABA), one of which is albuterol (salbutamol).<sup>28</sup> Albuterol (salbutamol) could be taken orally, through intravenous fluids (IV), intramuscular injections (I.M.), subcutaneous injections, or inhaled. SABA has been used as a standard asthma treatment, including monotherapy in patients with mild asthma symptoms. As a reliever, a combined inhaled corticosteroid-fastacting beta-agonist is a better option.<sup>29</sup> This drug is consistent with this study and other studies. The inhaled corticosteroid long-acting beta-agonists (ICS-LABA) are the most commonly prescribed combination of drugs to treat asthma.<sup>30</sup> According to Xu, et al. (2021), the R.R. = 1.77 [0.63, 4.98] showed that the salbutamol group had a 77% higher risk of experiencing side effects compared to the ipratropium bromide + salbutamol group.<sup>31</sup> In addition, the R.R. = 0.79 [0.66, 0.95] indicated that the ipratropium bromide + salbutamol group had about a 21% lower hospitalization risk than the salbutamol group.

## LIMITATION OF THE STUDY

The study on the profile of asthma exacerbation patients admitted to the Emergency Unit, Haji General Hospital, Surabaya, during the COVID-19 pandemic has several limitations. Firstly, the data collection process relied solely on variables such as allergy history, family allergy history, medication, and socioeconomic data. The data did not include important factors such as active or passive smoking status, which could have provided valuable insights into potential exacerbating factors for asthma. This limitation restricts a comprehensive understanding of the patients' complete profile and may limit the accuracy of the findings. Future studies should consider incorporating more comprehensive variables to gather a more holistic understanding of asthma patients during the COVID-19 pandemic.

## CONCLUSION

In conclusion, this study examined the profile of asthma exacerbation patients admitted to the Emergency Unit, Haji General Hospital, Surabaya, during the COVID-19 pandemic. Most cases were adult asthma, while a smaller portion was child asthma. Female adults and male children were more prevalent among the asthma exacerbation patients, although the difference was not statistically significant. Education level played a significant role, with high school education being the most common among adult asthma patients. In contrast, many child asthma exacerbation patients were either not enrolled in school or had not finished elementary education. Occupational differences were observed, with housewives and not working being the most represented among adults and children.

Allergy history varied between adult and child asthma exacerbation patients, with medicine allergies being more prevalent among adults and seafood and cow's milk allergies among children. Albuterol was the most commonly used preventive medicine for adult and child asthma patients. This study highlighted the importance of education in asthma exacerbation management and the need to address occupational exposures that can worsen asthma symptoms. Additionally, differences in payment methods were observed, with child asthma exacerbation patients predominantly using cash for payments and adult asthma exacerbation patients relying on BPJS.

Overall, this study provided insights into the profile of asthma exacerbation patients admitted to the Emergency Unit, Haji General Hospital, Surabaya, during the COVID-19 pandemic. These findings can contribute to a better understanding the demographics, educational needs, occupational risks, and treatment preferences of asthma patients in the region. Further research and interventions can be designed to improve asthma management and patient outcomes based on these insights.

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#### **Conflict of Interest**

The authors declared there is no conflict of interest.

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#### **Authors' Contributions**

Conceptualized the idea for the manuscript, designed the methodology, performed the literature review, developed research protocol, data collection, data screening, validated and supervised the manuscript: NIS, BR. Formal analysis and visualization of the results: NIS, ASA, SCSA, VAKW. Reviewed and edited the

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