

## Characteristics of Asthma Patients Admitted to the Intensive Care Unit of a Tertiary University Hospital in Madrid, Spain: A 5-Year Experience

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Current asthma guidelines succinctly cover the management of near-fatal asthma (NFA), also known as life-threatening asthma and critical asthma syndrome [1]. NFA encompasses a subset of asthma patients who are at an increased risk of death owing to their condition [2-5].

During exacerbations of NFA, patients are admitted to the intensive care unit (ICU) and receive targeted asthma treatment alongside necessary respiratory support. While most patients can be stabilized with noninvasive respiratory support, invasive mechanical ventilation may be required in very severe cases. Approximately 2%-4% of all patients hospitalized for acute asthma develop respiratory failure necessitating invasive mechanical ventilation [6-11].

The mortality rate of these patients has decreased substantially in recent years, owing mainly to

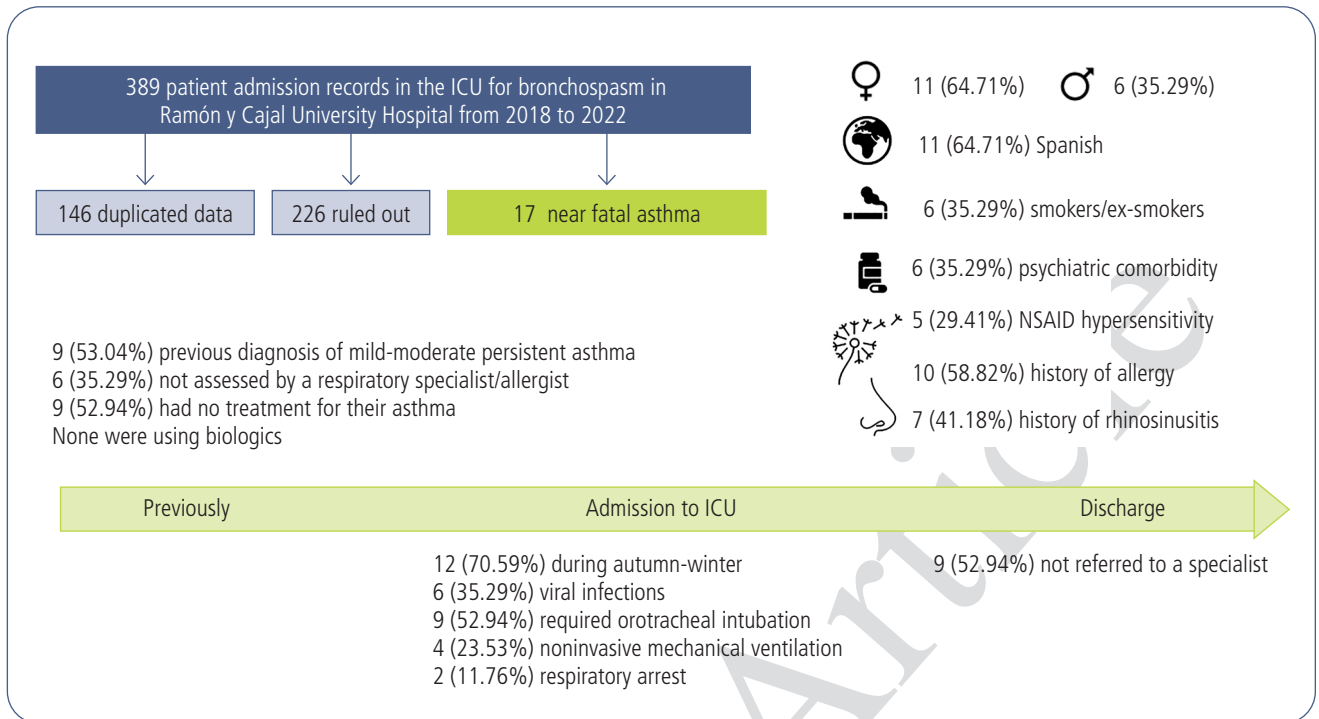
significant advances in pharmacological treatment and management [9-10].

We describe a cohort of severe asthma patients who were admitted to the ICU at a tertiary university hospital in Madrid, Spain. Cohorts of this type have received little attention in the literature; therefore, our data constitute a novel contribution to current knowledge. The data we report will enhance our understanding of the clinical profile of such patients and enable us to determine preventive and cost-effective strategies for management.

This retrospective study reports information gathered from pseudonymized (encoded) data following the latest data protection legislation. Data on patients admitted to the ICU at Ramón y Cajal University Hospital in Madrid, Spain from 2018 to 2022 were retrospectively retrieved from the electronic health records database by statisticians. The data were then reviewed by both an intensive care unit specialist and a clinical allergist. The study was approved by the Ethics Committee of Ramón y Cajal University Hospital. We aimed to describe this unique and small group of patients with potentially fatal asthma through a prospective follow-up 5 years after discharge from the ICU. The information retrieved could serve to modify current protocols, streamline referral of patients to severe asthma units, and improve management of NFA and severe asthma.

During this period, we evaluated 389 patients with a history of potential NFA exacerbation (Figure). After filtering by the exact cause of the exacerbation and ruling out duplicates, 17 patients were finally included as NFA cases (11 women [64.71%], all 17 with a low educational level). Eleven were natives of Spain, 3 patients were smokers, and 3 were ex-smokers. Six of the 17 patients had a psychiatric comorbid condition (35.29%). Notably, 6 patients had not been assessed by a respiratory specialist or allergist prior to admission to the ICU (35.29%), and 9 had not been referred to a respiratory specialist after discharge (52.94%). Nine patients had a previous diagnosis of mild-to-moderate persistent asthma (53.04%). Five patients were pet owners (29.41%): 4 owned dogs and 1 owned a cat. Of particular interest, 6 patients had a history of allergy to animal dander, with 5 allergic to dog dander and 1 to cat dander.

Various comorbidities were recorded. Five patients had a potential diagnosis of hypersensitivity to nonsteroidal anti-inflammatory drugs (29.41%), and 10 had a history of allergy (58.82%). Seven patients had 1 or more positive skin prick test results prior to ICU admission (41.18%). Furthermore, 7 patients had a history of rhinosinusitis (41.18%), although only 2 had been diagnosed with nasal polyps. In terms of treatment, 9 patients were not receiving any treatment for their asthma (52.94%). Among those taking at least 1 medication, 10 were taking short-acting  $\beta$ -agonists (58.82%) and 5 were taking oral corticosteroids (29.41%). Interestingly, none of the 17 patients admitted to the ICU were taking biologics.



**Figure.** Characteristics of asthma patients admitted to the intensive care unit of a tertiary university hospital in Madrid, Spain: A 5-year experience. ICU indicates intensive care unit; NSAID, nonsteroidal anti-inflammatory drug.

Nine patients required orotracheal intubation (52.94%), and 4 required noninvasive mechanical ventilation (23.53%). Two patients experienced respiratory arrest (11.76%); one of them died immediately and the other died some time after. An apparent seasonal pattern was observed, with 7 patients admitted during September-October and 5 patients admitted during January-February. Two patients experienced a fatal asthma exacerbation (11.76%). The known etiologies for the exacerbations in 6 patients included influenza, parainfluenza, rhinovirus, and SARS-CoV-2 infection. Despite being admitted to the ICU for NFA, 2 patients experienced 1 severe asthma exacerbation, 2 patients experienced at least 2 severe exacerbations, and 3 patients experienced 3 severe exacerbations. A prospective follow-up was carried out 5 years after discharge from the ICU. Three patients were readmitted to the ICU owing to an NFA exacerbation (17.65%).

Serrano-Pariente et al [11] reported that 225 000 people worldwide died of asthma in 2005, with the number projected to increase to 428 000 deaths annually by 2030 [12]. Although a formal and widely accepted definition of NFA is lacking, the criteria used for the identification of these types of exacerbations typically include multiple aspects [11-12] (Table 1, Supplementary material).

Patient factors implicated in asthma-related deaths include nonattendance at office visits, major psychiatric illness, refusal to take corticosteroids, poor adherence to prescription medication, fear of asthma, sleep apnea, and refusal to remove an animal from the home [5].

Importantly, while episodes of NFA (and asthma-related deaths) are more common in patients with severe asthma,

patients with mild and moderate asthma can also experience NFA [13]. The EAGLE project (Estudio del Asma Grave en Latinoamérica y España), a case-control study in which 2593 clinical records of asthma patients with an exacerbation episode requiring hospitalization were analyzed, showed that up to 4.9% of patients with mild-to-moderate asthma required admission to the ICU and that 2.1% required intubation and mechanical ventilation. Overall, 1.3% experienced cardiopulmonary arrest, and 0.4% died during admission [14].

A recent retrospective review of all admissions because of asthma exacerbation in a single hospital recorded 400 NFA episodes between 2000 and 2010, with a mortality rate of 3.1% [15].

Moreover, some characteristics of patients with asthma may be risk factors for NFA (Table 2 Supplementary material).

Different profiles of patients with NFA based on demographic characteristics, triggers of asthma attacks, pathogenesis, comorbidities, and clinical presentation of exacerbations have been described elsewhere (Tables 3 and 4, Supplementary material).

Asthma-related mortality is currently low in high-income countries, and the causes of exacerbations vary with age and season, as we observed in our sample.

More than a third of cases of NFA in our series were not assessed by a respiratory specialist or allergist before admission to the ICU, and, strikingly, over 50% were not referred to a respiratory specialist after discharge. The information retrieved could serve to modify current protocols, streamline referral of patients to severe asthma units, and improve management of NFA and severe asthma. Various comorbidities may interact

and could be of the utmost importance for prognosis. We are conducting a prospective assessment of this cohort of patients to explore whether any of the comorbid conditions serve as prognostic markers.

NFA is a preventable trait of severe asthma, considering that, as previously published, over 50% of the patients in our series had a prior diagnosis of mild-to-moderate persistent asthma.

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#### Conflicts of Interest

The authors declare that they have no conflicts of interest.

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