

Evaluation of the Risk Factors and Emergency Management Plan of Status Asthmatics in Children: A Simple Literature Review

Khaled Abdullaziz Alasous¹, Khalil Ibrahim Kariri², Sultan Mousa Bakri³, Sultan Masoud Almasoud⁴, Nawaf Fahad Alshuraym⁴, Abdulrahman Nabih Aljaber⁵, Wed Mohammed Alluhaibi⁶, Samia Zaben Almurshadi⁷, Zainab Ibrahim Albahouth⁷, Haidar Taher Aldulaim

1- Prince Sattam Bin Abdullaziz University, 2- Jazan University, 3- Prince Mohammed Ibn Nasser Hospital, 4- Imam Mohammed Ibn Saud Islamic University, 5- Qassim University, 6- Ibn Sina National College, 7- Riyadh Elm University

ABSTRACT

Background: Significant research papers were published to assess different risk factors associated with development of status asthmaticus (SA) in children and prevention. Understanding the different risk factors associated with SA development in children will help in the early prediction of the cases that might develop SA in future which may cause death in few cases.

Objectives: In this study, we aimed at evaluating the various risk factors, etiologies that stand behind of status asthmaticus development and Assessment of SA management in emergency department.

Methods: PubMed database were used for articles selection. All relevant articles related to our review were chosen to cover the following topics: Asthma, SA management, SA in children risk factors. We excluded other articles, which are not related our objectives. The data have been extracted according to specific form to be reviewed by the group members to assess the different risk factors, and management modalities of SA.

Conclusion: Delay in seeking medical help, poor compliance to the treatment, multiple previous admissions, frequent chest infections, and obesity are major risk factors of complicating asthma in children leading to life threatening attacks (SA). Preventing the risk factors is major task of the management and it is as important as the treatment of asthmatic attacks.

Keywords: Risk Factors, Emergency, Management Plan, Status Asthmatics, Children

INTRODUCTION

Asthma is a disease characterized by reversible airflow obstruction. Airway inflammation consisting with airway infiltration by eosinophils and activated T-lymphocytes is now recognized as central to the pathophysiology of asthma, in conjunction with smooth muscle bronchoconstriction and intraluminal mucus accumulation^{1,2}. The incidence and severity of asthma have increased in recent years, which escalate the number of the patients who will develop acute respiratory failure (ARF), also called status asthmaticus (SA)³. Status asthmaticus is considered a major cause of acute illness in children and one of the top indications for admission to a pediatric intensive care unit (ICU)^{4,5,6,7}.

Bronchial smooth muscle spasm, airway inflammation, and increased mucous production are the key components of acute asthma^{4,5,6}. This pathophysiology results in increased pulmonary resistance, small airway collapse, and dynamic hyperinflation. Unlike during normal breathing, in status asthmaticus a child's inspiratory muscle activity can persist through exhalation, significantly increasing respiratory muscle workload and fatigue^{4,5,6}. Additionally, because of heterogeneous areas of premature closure and obstruction, there can be significant ventilation-perfusion mismatching and hypoxemia.

As a result of the escalating number in the incidence of status asthmaticus during recent years, and the morbidity associated with it, the researchers

undertaken lots of investigations to explore etiologies behind it, and to assess the precautions that can be done to avoid the development of this condition. We therefore, reviewed the literatures cover this filed to assess the various etiologies, risk factors, management modalities, and prevention methods that could be achieved as well as providing a review paper that summarizes the recent advances in this research field.

MATERIALS AND METHODS

Sample

PubMed was chosen as the search database for the articles selection, because it is one of the major research databases within the suite of resources that have been developed by the National Center for Biotechnology Information (NCBI). The following topics were used: Asthma, SA management, SA in children risk factors. Restriction to the last 5 years, children under 18 years, and English language due to unavailable resources for translation were used. The chosen articles were screened by titles, and reviewing the abstracts yielded 4 articles which were enrolled. **Inclusion criteria:** the selected articles were those relevant to the topic of study which should include one of the following topics {asthma in children, SA risk factors in children, management of SA in children}. **Exclusion criteria:** all other articles which did not have one of these

topics as their primary end, or repeated studies, and reviews studies.

Analysis

No software was used to analyze the data. The data was extracted based on specific form that contain (Title of the study, name of the author, Objective, Summary, Results, and Outcomes), these data were reviewed by the group members to assess the risk factors contributing in complicating asthma attacks, and the modalities of managing and preventing their occurrence. Double revision of

each member's outcomes was applied to ensure the validity and minimize the mistakes.

RESULTS

We enrolled 4 studies according to our inclusion, and exclusion criteria described above. 2 of them were retrospective cohort studies, and 2 were case-control studies. All of studies aimed at evaluating the various risk factors that stand behind status asthmaticus development. The studies characteristics are shown in Table 1.

Table 1

Study (Year)	Study Design	Country	Objective	Duration of Study	Outcome	Ref.
<i>S. Sheikh et al.</i>	Retrospective Cohort study	USA	Improve our understanding of the epidemiology, clinical course, and outcomes of children with asthma who present with status asthmaticus	8 Years	Factors associated with severe life-threatening asthma exacerbations include failure to diagnose asthma, inadequate therapy of prior asthma, poor compliance with therapy, delay in seeking help, and history of previous asthma admissions	8
<i>Aragona et al.</i>	retrospective cohort study	USA	Determining the effect of obesity on outcomes among urban children hospitalized with status asthmaticus	2 Years	Obesity appears to be associated with increased risk of ED visits in urban children admitted with asthma	9
<i>Belessis et al.</i>	Case- Control Study	Australia	Evaluation the potential risk factors for an admission to the ICU in children with asthma	1 Year	increased Emergency Department utilization in the previous year, atopy, asthma duration, and low oxygen saturation were significant predisposing factors for an ICU admission in hospitalized children	10
<i>Roberts et al.</i>	Case- Control Study	UK	Evaluation whether persistent food allergy and degree of atopy are risk factors for life-threatening asthma.	5 Years	Frequent previous admissions and clinical food allergy are independent risk factors for life-threatening asthma.	11

Sheikh *et al.*⁸ retrospectively evaluated the medical records of all patients between ages of 5-20 years admitted at Nationwide Children's Hospital, Columbus, OH, with status asthmaticus between 2000 and 2007 to assess the epidemiology, clinical course, and outcomes. They found that the factors associated with severe life-threatening asthma exacerbations include failure to diagnose asthma, inadequate therapy of prior asthma, poor compliance with therapy, delay in seeking help, and history of previous asthma admissions.

Aragona *et al.*⁹ retrospectively enrolled a total of 333 children between ages of 2-18 years according to specific criteria to determine the effect of obesity on outcomes among urban children hospitalized with status asthmaticus. They found that overweight/obese status was associated with subsequent emergency department visits especially in preschool-age children (<5years) were 2.3 times more likely to have a subsequent emergency department visit than lean peer. The association between overweight status and increased emergency department visits may be explained by increased airway obstruction at higher body mass index percentiles. Also, this conclusion can be explained by chronic inflammation and oxidative stress in obesity which induce a link between asthma and obesity. Obesity is associated with several comorbidities, such as gastro esophageal reflux, and obstructive sleep apnea, which can worsen asthma. Also, unintentionally the authors found during reviewing the medical records that asthma severity was higher in children with gestational age <32 week. **Aragona *et al.***⁹ finalized that interventions to decrease obesity can improve asthma outcome.

Belessis *et al.*¹⁰, tried to assess the potential risk factors for an admission to the ICU in children with asthma, by assessing personal characteristics, background asthma management, prior medical history and comorbid conditions, parental asthma knowledge, environmental risk factors, and health-service utilization. A total of 141 child enrolled according to specific criteria (71 Cases ICU, 70 Controls general medical ward). They found that majority of children in ICU were under 5 years of age and there was a male preponderance. Children who were admitted to the ICU were more likely to have frequent episodic or persistent asthma, multiple prior hospital admissions for asthma, an admission in the last year, and multiple presentations to the emergency department in the previous year. They were also more likely to have had asthma for a longer time. Mothers of children admitted to the ICU were less likely to have completed tertiary education. The study assessed the relation between recent chest infection and ICU admission, and it was found that the presence of a

recent infection did not distinguish between children admitted to the ICU and controls, nor did the presence of multiple infections in the same child. Also, **Belessis *et al.***¹⁰ found that large proportion of both cases and controls were atopic, although cases were more likely to be allergic to three or more allergens. Similarly, cases were more likely to have higher levels of IgE, and increasing number of admissions in the autumn.

Belessis *et al.*¹⁰ finalized that respiratory specialist care of children who had moderate to severe asthma and at least three ED visits and one hospitalization resulted in improved clinical outcomes, reduced health service utilization, and fewer healthcare costs.

Roberts *et al.*¹¹ tried to address whether persistent food allergy and degree of atopy are risk factors for life-threatening asthma. A total of 19 Cases, and 38 controls were enrolled between the ages of 1-16 years according to specific criteria. They found that, compared to controls, cases had the following risk factors: food allergy, multiple allergic diagnoses, early onset of asthma, and frequent admissions. After regression analysis, only frequent admission with asthma and food allergy were independently associated with life threatening asthma. Half the cases had food allergy compared to only 10% of controls. Food allergy was observed in the first few years of life and is potentially a useful marker that would allow increased supervision of this group of high risk children with asthma to reduce subsequent asthma morbidity and mortality.

DISCUSSION

Status asthmaticus is a major cause of acute illness in children and one of the top indications for admission to a pediatric intensive care unit (PICU). It is a life-threatening condition characterized by progressive respiratory failure due to asthma or air entrapment in the lungs that is unresponsive to standard therapeutic measures. Mortality is rare after a child arrives at medical attention, but morbidity can be high with some children requiring days or weeks of hospitalization and recovery¹².

The pathophysiology of acute asthma can be defined by three components which are bronchial smooth muscle spasm, airway inflammation, and increased mucus production. These three problems will lead to increased pulmonary resistance, small airway collapse, and dynamic hyperinflation. Therefore, among these circumstances, the respiratory muscles will be extremely fatigued because they try to overwhelm the airway obstruction and release the entrapment of the air. The result of this will be significant ventilation-perfusion mismatching and therefore severe hypoxemia. This asthma exacerbation process

mostly start because of a trigger like smoke, dust mites or other allergens. Unlike the normal population, asthma patients' lungs respond to the triggering with hypersensitivity reaction to which is mostly IgE mediated immune response. This reaction is the cause of the three components of status asthmaticus. So, in our study we reviewed 4 studies that assessed the risk factors of status asthmaticus in children and why it happens in some more often than the others¹².

By looking at the included studies, we found that the main factor behind the complications of status asthmaticus is failure of the treatment. It is failure of the prior prescribed therapy in controlling the condition or stopping the attacks⁸⁻⁹⁻¹⁰⁻¹¹. This was mentioned clearly by S. Sheikh et al.⁽⁸⁾. In the same study, inadequate therapy was not the only factor⁸. They also pointed at the poor of compliance and adherence to the treatment. It is suggested that this issue was related to the education of the mothers because as it is mentioned by **Belessis et al.**¹⁰ that mothers of children admitted to the ICU were less likely to have completed their tertiary education¹⁰. **Sheikh et al.**⁸ showed that the parents did not take all the blame. They found that the delay of intervention is because ER doctors sometimes do not reach to the correct diagnosis and use the correct management⁸.

Aragona et al.⁹ focused on the obesity and its role in asthma as a significant risk factor especially in preschool children⁹. The results showed that obese children visit ED because of asthma more often than the control group, which were lean patients and they also, have higher percentage of ICU admissions resulting from asthma. This finding was explained by increased airway obstruction at the higher BMI percentiles. This was suggested to be the explanation behind the association between obesity and other comorbidities such as, Obstructive Sleep Apnea (OSA) and Gastroesophageal Reflux disease (GERD). The abundance of oxidants in obese patients may be the reason of the exaggeration of every inflammation, leading to the presence of chronic inflammation in the lungs affecting their normal function and structure resulting in poor response to the usual therapy or to the prior treatment in cases of status asthmaticus. Therefore, the intervention in this group of patients should be toward losing weight and decrease obesity to reduce the severity and improve the asthma outcome⁹.

Three of the four studies found that history of previous asthma admissions is frequently associated with higher possibility of developing status asthmaticus and it was detailed in **Belessis et al.**¹⁰ conducted a case control study about the factors leading the asthmatic children to be admitted. It showed that recent chest infection is a major risk

factor beside the mentioned earlier, previous admissions. The chest infection can be a trigger to the asthma attack. So, the parents should be alert and cautious when their asthmatic child or any of his or her siblings develop any infection. History of previous admissions could mean that his condition is poorly controlled either due to inadequate therapy or to the noncompliance to the treatment¹⁰.

Despite our improved understanding of the pathophysiology of asthma, the availability of effective anti-inflammatory therapy, and also, the new guidelines that get updated every now and then, Asthma is still very common chronic childhood disease and can have significant morbidity and may result in life-threatening exacerbations requiring intensive care. Therefore, the key of management that we could extract from the included studies is prevention, either prevention of the exposure to the triggers that are known to be irritant to this patient's lungs or by treating the condition with the adequate therapy as prescribed and as needed. In addition, the complications can be prevented before they occur by seeking the medical help as early as possible because the delay of intervention can lead to disastrous complications that could be irreversible sometimes.

Frequent admissions can also mean that the body react to the triggers in some asthmatic patients with severe abnormal hypersensitive responses more than the others leading to undesirable damages and cannot be prevented by the usual first line therapy⁸. Thus, this group of patients needs special attention and extreme care in order to prevent any future attack because it can be irreversible at time leading to the end organ perfusion, which is the life threatening level. Regarding this point and in order to avoid any delay, all the parents should be of good awareness about their children condition. These information are important to be known by the family, regardless their educational level¹⁰. These information are preferred to be taken in multiple detailed learning sessions and help the family to understand Asthma, and its management, and learn how to react if the attacks occur. It will not be just helpful regarding making the parents more compliant to the treatment, it also will be helpful when ER doctors take the history from the parents because one of the factors associated with life threatening attacks was found to be underestimating the severity of it. In addition, it is important for the patient's management plan to be reviewed and adjusted as needed on regular basis by a pulmonology specialist in order to optimize the results. Similarly, another group of asthma patients as well should be seen by chest physician and taken good care of regarding their asthma. Whom is the children who experienced multiple previous food allergy. As in Roberts et al. article, food allergy is

strongly associated with life threatening attacks of asthma. This relation might be because of their extreme resistant hypersensitivity that can affect multiple organs¹¹.

Treatment in Emergency:

We will start mentioning briefly the steps of treatment of status asthmaticus starting with the general measures. First, any child in status asthmaticus requires cardiorespiratory monitoring. A comfortable and supportive environment should be provided, ideally with a parent or family member present. While hypoxemia and anxiety will lead to agitation and restlessness, sedatives are contraindicated in the non-intubated asthmatic patient¹³. Secondly, the immediate medicinal treatment is supposed to be initially started with Salbutamol 5 mg (or terbutaline 10 mg) nebulized with O₂, Hydrocortisone 100 mg IV or prednisolone 40–50 mg PO or both if the patient were very ill and in severe distress, and we should start O₂ if his saturations was <92%¹⁴. Our aim of his saturation is supposed to be from 94% to 98%. If life-threatening features still present, we should give Salbutamol nebulizers every 15 minutes, or 10 mg continuously per hour¹⁴. Adding ipratropium 0.5 mg into nebulizers should be considered. Giving single dose of Magnesium Sulfate (MgSO₄) 1.2–2 g IV over 20 min should be considered as well. If the condition persisted, we should refer to ICU for consideration of ventilatory support and intensification of medical therapy, e.g. Aminophylline, or IV Salbutamol. However, if the patient condition improved within 15–30 minutes, nebulized Salbutamol every 4 hours would be enough for short term maintenance and Prednisolone 40–50mg PO OD for 5–7 days¹⁴.

Strengths and Limitations

During articles selection, we doubled-reviewing the studies, and their results to assure that we enroll the studies related to our aim, and to avoid any error in the results. . We acknowledge the limitations we had in this study. We tried to include articles that fit with our outcome criteria for inclusion into our review. Certainly, a bigger sample size would provide more significant results.

For future perspective:

In *Belessis et al.*¹⁰ paper, admitted cases were more likely to have three or more siblings and to be admitted in the autumn. We advise to conduct a research regarding this issue and see if more sibling means more sources of chest infections and triggers.

*Aragona et al.*⁹ found that asthma severity was higher in children with gestational age <32 weeks. This finding needs further case control and cohort studies to assess the relation between gestational

age and occurrence of asthma, and evaluate the procedures that can be done in order to provide a better management plan for preterm infants.

Weight reduction was suggested to be a factor in improving the outcome. So, we recommend conducting a study on a group of asthmatic obese preschool children and investigate the effect of weight reduction and decreasing the obesity in improving the prognosis of asthma and status asthmaticus.

CONCLUSION

Prevention is the pearl of management of asthma. Knowing the risk factors is important for us and for the parents in order to prevent them from triggering the asthma attack or exaggerating the condition. We found that poor compliance to the treatment, multiple previous admissions, frequent chest infections, and obesity are major contributors to complicating asthma leading to life threatening attacks.

REFERENCES

1. **Bousquet J, Chanez J, Lacoste B et al. (1990):** Eosinophilic inflammation in asthma. *N. Engl. J. Med.*, 323:1033–1039.
2. **Smith D, Deshazo R (1993):** Bronchoalveolar lavage in asthma: an update and perspective. *Am. Rev. Respir. Dis.*,148:523–532
3. **Corbridge T, Hall J (1995):** The assessment and management of adults with status asthmaticus. *Am J Respir Crit Care Med.*, 151:1296-1316
4. **Werner H (2001):** Status asthmaticus in children. *Chest*,119: 1913–1929
5. **Chippes B, Murphy K (2005):** Assessment and treatment of acute asthma in children. *J Pediatr.*,147: 288–294
6. **Mannix R, Bachur R (2007):** Status asthmaticus in children. *Curr Opin Pediatr.*, 19: 281–287
7. **Kercsmar C (2000):** Acute inpatient care of status asthmaticus. *Respir Care Clin N Am.*, 6: 155–170
8. **Sheikh S, Khan N, Nancy A et al. (2013):** Demographics, Clinical Course, and Outcomes of Children with Status Asthmaticus Treated in a Pediatric Intensive Care Unit: 8-Year Review. *Journal of Asthma*, 50(4): 364-69.
9. **Aragona E, El-Magbri E, Wang J et al. (2016):** Impact of Obesity on Clinical Outcomes in Urban Children Hospitalized for Status Asthmaticus. *Hospital Pediatrics*, 6(4): 211-18.
10. **Belessis Y, Dixon S, Thomsen A et al. (2004):** Risk Factors for an Intensive Care Unit Admission in Children with Asthma. *Pediatric Pulmonology*, 37(3): 201-09.
11. **Roberts G, Patel N, Levi-Schaffer F et al. (2003):** Food Allergy as a Risk Factor for Life-threatening Asthma in Childhood: A Case-controlled Study. *Journal of Allergy and Clinical Immunology*, 112(1): 168-74.
12. **Christopher C, Kathleen A (2013):** Pediatric Status Asthmaticus. *Critical Care Clinics*, 29(2): 153-66.
13. **Werner H (2001):** Status Asthmaticus in Children. *Chest*, 119(6):1913-929.
14. **Longmore M, Ian W, Andrew B et al. (2014):** Oxford Handbook of Clinical Medicine 9th Edition. Oxford Medicine Online. doi:10.1093/med/9780199609628.001.0001.