

**A TEN – YEAR STUDY ON ACUTE SEVERE ASTHMA
PATIENTS IN THE INTENSIVE CARE UNIT
OF HOSPITAL UNIVERSITI SAINS MALAYSIA, KUBANG
KERIAN, KELANTAN**

By

DR RASHIDI BIN AHMAD

**Dissertation Submitted In
Partial Fulfilment Of The Requirement
For The Degree Of
Masters Of Medicine (Emergency Medicine)**

UNIVERSITI SAINS MALAYSIA

NOVEMBER 2001

ACKNOWLEDGEMENTS

BISMILLAHIRRAHMANNIRRAHIM. In the name of ALLAH, Most Benevolent and Most Merciful. ALHAMDULILLAH as he gave me the strength, courage and health to complete my dissertation.

I would like to take this opportunity to thank Prof Madya. Dr. Kamaruddin Jaalam, the Postgraduate Coordinator of Emergency Medicine and also my moderator, for his concern, encouragement and guidance in my work.

I should like to express my sincere gratitude also to him who never stop giving counselling and guidance which make this work possible. Many thanks to my lecturer. Dr. Wan Aasim Wan Adnan and my colleagues for their moral support, understanding and encouragement.

Last but not least, I would like to dedicate this work to my wife Norrohimah Sidek, my children Nurfithriyaani, Mohd Shahir, and Nur Humaira' for the many hours that I devoted, were obviously came from their time. Without their support, understanding, encouragement and love, this effort would surely have failed.

ABSTRAK

10 TAHUN KAJIAN PENYAKIT ASMA TERUK DI UNIT RAWATAN RAPI, HOSPITAL UNIVERSITI SAINS MALAYSIA, KUBANG KERIAN, KELANTAN

PENGENALAN

Serangan asma teruk dan tiba-tiba adalah senario biasa di Jabatan Kecemasan dan menjadi punca kemasukan ke hospital dan unit rawatan rapi. Kajian ini mendedahkan demografi pesakit tersebut dan juga sebab mengapa mendapat serangan yang teruk. Amat penting kita mengenal pasti pesakit yang cenderung mendapat asma teruk dan mengetahui faktor-faktornya agar dapat memberi rawatan optimum. Seterusnya mengurangkan kadar morbiditi dan mortaliti asma

OBJEKTIF

Menganalisa ciri demografi pesakit asma teruk yang mendapat rawatan di Unit Rawatan Rapi dan menganalisa faktor-faktor keterukan asma.

METODOLOGI

Ini adalah kajian 10 tahun iaitu dari tahun 1990 hingga 2000. Semua pesakit asma teruk yang memasuki Unit Rawatan Rapi HUSM adalah termasuk dalam kajian. Fokus kajian adalah ciri demografi, sejarah lelah, rawatan lelah, sejarah lelah dalam keluarga, sejarah penyakit lain, sejarah alahan, penyebab keterukan lelah, komplian, ventilasi or pemerhatian, komplikasi lelah dan lain-lain.

KEPUTUSAN

Terdapat 103 kes kajian. 60% adalah perempuan. Paling ramai yang menerima rawatan rapi dari kumpulan berumur 30 – 34 tahun. Purata umur ialah 33 tahun. 76% tidak merokok, 61% hadir sendiri mendapat rawatan, 77.3% mempunyai sejarah asma dalam keluarga, dan 60% adalah mereka yang dari kronik asma Faktor penyebab utama adalah jangkitan kuman respiratori atas (51.5%) 74.8% subjek kajian mempunyai sejarah kemasukan wad disebabkan asma dan 36.9% mempunyai sejarah kemasukan ke unit rawatan rapi. 73% adalah tidak komplian dan 79.8% pesakit didapati tidak betul teknik inhalasi. 35% mendapat komplikasi hypokalaemia. Komplikasi lain ialah pneumonia, abnormal rentak jantung dan sawan. Kebanyakan pesakit bertindakbalas dengan rawatan yang diberikan. Hanya satu kes kematian lelah di ICU, selebihnya adalah selamat.

KESIMPULAN

Dari kajian ini terdapat beberapa faktor mengapa pesakit mendapat asma teruk. Antara faktor – faktor itu ialah pesakit pertengahan usia dan lanjut usia, serangan asma yang teruk secara mengejut, mereka yang tidak mengambil ubat secara teratur atau teknik penggunaan ubat penyedut yang tidak betul, dan sejarah kemasukan wad atau unit rawatan rapi. Serangan jangkitan saluran pernafasan dan radang paru-paru adalah penyebab utama serangan asma akut yang teruk. Komplikasi asma teruk adalah mimima. Kebanyakan pesakit kajian bertindakbalas dengan rawatan yang diberikan. Mereka hanya tinggal beberapa hari sahaja di ICU sebelum dipindahkan ke wad. Unit rawatan rapi adalah amat sesuai untuk pesakit asma yang teruk.

ABSTRACT

A TEN – YEAR STUDY ON ACUTE SEVERE ASTHMA PATIENTS IN THE INTENSIVE CARE UNIT (ICU) OF HOSPITAL UNIVERSITI SAINS MALAYSIA, KUBANG KERIAN, KELANTAN (HUSM)

INTRODUCTION

Acute exacerbation of severe asthma is a common presentation to the Emergency Department, hospital, and Intensive Care Unit admission. This study will review asthma patients that admitted into the intensive care unit of Hospital Universiti Sains Malaysia. By studying the demographic characteristics or patients' profile, and the precipitating factors, we can predict those asthmatics that will deteriorate or develop severe asthma symptoms. This is very important and essential to prevent the morbidity and mortality and to improve the outcome.

OBJECTIVE

The main objectives of this study are:

1. To analyze and identify the demographic characteristics of asthma patients that required admission into Intensive Care Unit.
2. To identify the common predisposing factors for severe asthma that required intensive care management

3. To identify the risk factors for severe asthma that admitted for mechanical ventilatory support.

METHODOLOGY

This is a 10-year observational study from 1999 to a 2000. All asthma cases that were admitted into Hospital University Science Malaysia Intensive Unit Care were included in the study. Variables on study were demographic characteristics, past medical history, allergic history, medications, and severity of illness, precipitating factors, compliance, complications, duration of stay, ventilation or observation and others.

RESULTS

There were 103 asthma cases in this study. Predominate by female patients (60.2%). Age group between 30 to 34 years old had a highest ICU admission. Mean age was 33 years old. 76% of the subjects were non-smoking asthma patients. 61.2% of the subjects were self-referred, 77.3% had a positive family history of asthma, and 58.1% had moderate severity of chronic asthma. Precipitating factors were upper respiratory tract infection (51.5%) and pneumonia (28.2%). 74.8% of subjects had previous history of hospital admission and 36.9% had previous history of ICU admission. 73% had a poor compliance to medication, and 79.8% had improper technique of using the inhaler. 35% of the subjects had

hypokalaemia and 16.5% had a hypoxic fit. Other complications were pneumonia, arrhythmias, and pneumothorax. 85% of subjects stayed less than 4 days in ICU. Majority of subjects responded to standard asthma therapy.

CONCLUSION

The great challenge in managing acute asthma patients in ED is to prevent the recurrence of asthma attack, to decide whether the required admission or not, and to prevent mortality. Our data showed middle and old asthma patients, sudden onset of severe asthma, severe chronic asthma, poor compliance, poor inhaler technique, history of hospital admission and ICU admission were important risk factors for the development of acute severe asthma. Upper respiratory infections and pneumonia were common precipitating factors of acute severe asthma. Regarding the risk for ventilation we noted it has a significant correlation or association with age, severity of chronic asthma, history of hospitalization, and ICU admission. Number of ventilated patients was high in middle age group, severe chronic asthma, those with a history of hospitalization and ICU admission, and also in those poor compliance patients and those who can't perform the technique of inhalation properly. Majority of the patients that admitted into ICU responded to standard therapy. The complications were minimal. These patients usually recover very fast and majorities of them stayed just for a few days in ICU.

TABLE OF CONTENTS

LIST OF TABLES	xii
LIST OF FIGURES	xiii
CHAPTER 1: INTRODUCTION	1
CHAPTER 2: LITERATURE REVIEW	5
2.1 Definition	5
2.2 Genetics and asthma	6
2.3 Airway hyperresponsiveness	6
2.4 Airflow limitation	7
2.5 Airway wall remodelling	9
1.6 Rapidity and severity of Exacerbation	10
2.7 Factors causing acute exacerbation of asthma	11
1.7 Risk factor for severe asthma	14
1.8 Key intervention to prevent arrest in managing acute exacerbation of asthma	17
1.9 Criteria for Admission to Intensive Care Unit	22

CHAPTER 5: DISCUSSION

5.1	Prevalence of acute severe asthma in ICU, HUSM	62
5.2	Influence of age, sex, ethnic, and locality in the prevalence of acute severe asthma	63
5.3	Smoking habit and the prevalence of acute asthma	66
5.4	Atopy and prevalence of acute severe asthma	67
5.5	Compliance and technique of inhaler influence the prevalence of acute severe asthma	68
5.6	History of hospitalization and ICU admission and the prevalence of acute severe asthma	69
5.7	Peak Flow Meter usage at home and home nebulizer	69
5.8	Precipitating factors	70
5.9	Onset of attack and the severity of asthma	71
5.10	Complications of severe asthma	72
5.11	Prevalence of acute asthma who required ventilation	73
5.12	Prevalence of patients who has respiratory arrest	74
5.13	Asthma management in ICU	75

CHAPTER 6: CONCLUSION

BIBLIOGRAPHY

APPENDIX

LIST OF TABLES

Table 1: The distribution of asthma patients ventilated and age group	31
Table 2: The distribution of patients ventilated and with respiratory arrest and gender of the patients	32
Table 3: The distribution of referral cases by Health Care Worker	34
Table 4: The distribution of patients ventilated and their smoking status	37
Table 5: The distribution of different types of atopy	38
Table 6: The distribution of patients ventilated and history of atopy	39
Table 7: The distribution of patients ventilated and family history of asthma	40
Table 8: The distribution of patients ventilated and with respiratory arrest and their severity of chronic asthma	44
Table 9: The distribution of patients medications	44
Table 10: The distribution of patients ventilated and the appropriateness of their medications according to chronic severity of asthma	47

Table 11: The distribution of precipitating factors for acute exacerbation of asthma	48
Table 12: Distribution of the subjects and their frequency of ICU admission	49
Table 13: The distribution of patients ventilated and those with respiratory arrest and history of ICU admission	50
Table 14: The distribution of a the subjects with a history of hospital admission	51
Table 15: The distribution of patients ventilated with poor compliance and poor inhaler technique	54
Table 16: The distribution of patients ventilated and the onset of severe asthma attack	57
Table 17: The distribution of complications during patients illnesses and ICU stays	58
Table 18: The distribution of subjects medication during the severe asthma attack	59
Table 19: The distribution of other type of medications used	59
Table 20: The distribution of subject's length of stay in ICU	60

LIST OF FIGURES

Figure 1: The distribution of number of asthma patient required ICUadmission from 1990 - 2000	28
Figure 2: The distribution of age group of asthma patients that required intensive care management	30
Figure 3: The distribution of asthma patients that admitted into ICU according to sex	33
Figure 4: The distribution region of asthma patients in the study	35
Figure 5: The distribution of smoking and non-smoking asthma patients.	37
Figure 6: The distribution of subjects with or without history of atopy	39
Figure 7: The distribution of subjects with a positive family history of	41
Figure 8: The distribution of severity of chronic asthma	43
Figure 9: The distribution of subjects who received either appropriate and inappropriate treatment for their chronic asthma	53

Figure 10: The distribution of patients compliance	53
Figure 11: The distribution of subjects technique of using inhaler	54
Figure 12: The distribution of onset of severe asthmatic attack	56

CHAPTER 1: INTRODUCTION

Asthma is derived from a Greek word, which means laborious breathing and panting. It is defined as a partial obstruction to airflow in the intra-thoracic airways that varies in severity over a short period of time, either spontaneously or as a result of treatment.

During the last two decades, the prevalence of asthma, asthma morbidity and mortality have increased by 33% in the last ten years. In the United States, the prevalence rate of asthma had increased from 3% in 1980 to 6% in 1994 (Thomas & Casale, 2000). Globally, The World Health Organization estimates that between 100 and 150 million people suffer from asthma. Deaths from this disease have also reached 180,000 annually (Dzulkifli, 2000). In our country, it is about 8-10% of our population or about 2 million Malaysian citizens are asthmatic in which 8% are an adult asthmatic and about 20% are childhood asthmatic (Loh Foon Fong, 1995). Asthma death in Malaysia was about 16.8 per million populations. This is double from developed countries, which are about 6 – 7 asthma deaths per million populations (Jeyaindran S, 1993)

In Hospital Universiti Sains Malaysia (HUSM), acute exacerbation of asthma is a common presentation to the Emergency Department (ED). There was an about 8 – 10 asthma cases per day. This comprised 0.1% of the ED attendances per day. Asthma is also a common disease that required hospitalization or Intensive Care Unit management. For example;

in 1999 there was 340 asthma patients admitted into the medical ward. Majority of them admitted via ED. They presented with a various degree of severity, from mild symptoms to life threatening condition. Those presented with a severe asthma will be managed either in the ward or in the intensive care unit. Basically the criteria for admission into the HUSM are based on clinical and failure of initial therapy in ED. We found out there was no criteria or protocol of asthma management, criteria for admission and how these patients were observed after therapy in HUSM.

The initial presentation of the severity of asthma is not the only factor that determines whether the patients required admission or not. They may be deteriorated later. It is clear that patients who present with severe dyspnea have severe bronchospasm; however, those without severe shortness of breath may also have severe obstruction. Therefore Emergency Department has an important role to identify those asthmatics whom susceptible to develop severe or life threatening asthma, so that prompt and aggressive asthma management can be started early. Subsequently patients will be referred for observation or early follow up. Recognition and appropriate management of severe acute asthma is essential, not only to prevent the morbidity and mortality but also to improve the outcome in the future.

Despite an increased understanding of the underlying pathophysiology and the improvement in the treatment of asthma, the morbidity and mortality are still high every year. Implicated reasons for this

enigma include genetic predisposition, physical environment, social environment, patient habits, the medical care that the patients receive, and the care that the patients deliver to themselves (Zorc & Joseph J. 2000). Other specific risk factors for severe asthmatic attacks are low economic status, previous history of hospitalization and mechanical ventilation, history of respiratory arrest, frequent emergency visit, non-compliance with therapy and sub-optimal therapy due to physician under-prescribing or patient underutilization of appropriate medications (Thomas & Casale, 2000). Furthermore, the clinical approach to treating patients with severe, life threatening exacerbations of asthma remains controversial (Spevetz AS et al, 1992). The purpose of this study was to explore these factors and their association with severe symptoms.

This study will review asthma patients that admitted into the intensive care unit of Hospital Universiti Sains Malaysia. By studying the demographic characteristics or patients' profile, and the precipitating factors, we can predict those asthmatics that will deteriorate or develop severe asthma symptoms. We also hope the findings of this study will help the medical officers or ED residents for a better management of asthma patients. Eventually, this can reduce the number of admissions into the emergency department, hospital, or Intensive Care Unit. It is not only can reduce the morbidity and mortality but ultimately it can improve patient's quality of life.

The main objectives of this study are:

1. To analyze and identify the demographic characteristics of asthma patients that required admission into Intensive Care Unit.
2. To identify the common predisposing factors for severe asthma that required intensive care management
3. To identify the risk factors for severe asthma that admitted for mechanical ventilatory support.

We hope this study will help the medical practitioners in making decision of which asthma patients required more attention and observation and also to decide whether to discharge the patient, to continue treatment, or to admit to the hospital.

CHAPTER 2 : LITERATURE REVIEW

2.1 Definition

Asthma is defined as a condition of airway hypersensitivity and reversible airway obstruction that results in intermittent symptoms of wheezing, dyspnea and cough. However, asthma is more than simple reversible airway obstructions.

Based on current knowledge, a working definition of asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play role in particular, mast cells, eosinophils, T-lymphocytes, macrophages, neutrophils, and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment. The inflammation also causes an associated increase in the existing bronchial hyper-responsiveness to a variety of stimuli (NHLBI/WHO Workshop report. 1995). The airway narrowing usually reversible but in some patients with chronic asthma the inflammation may lead to irreversible airways obstruction (Roche WR et al. 1989)

2.2 Genetics and asthma

The recent completion of the human genome project has increased the likelihood that the genetic contribution to development of asthma will be elucidated. At present, it does not appear that a single gene or single set of genes is likely to explain the pathogenesis of asthma. Current evidence suggests that the asthma phenotype involve the interaction of multiple sets of genes each contributing a small percentage to the phenotype. Characterisation of the genes contributing to the pathogenesis of asthma may identify subsets of asthma in which different combinations of "asthma" genes contribute to different asthma phenotypes (NHLBI/WHO Workshop report. 1995). Current study showed Interleukin (IL)-3 and granulocyte macrophage colony-stimulating factor (GM-CSF) may influence the inflammatory process in acute severe asthma through their regulatory role on eosinophil survival, differentiation and effector function (Lai CK et al. 1996).

2.3 Airway Hyperresponsiveness

An important component of asthma underlying the instability of the airways is the presence of an exaggerated bronchoconstrictor response to a wide variety of exogenous and endogenous stimuli. Several mechanisms have been proposed to explain this airway hyperresponsiveness. They may be classified as causing airflow limitation directly by

stimulating airway smooth muscle (e.g., methacholine and histamine) or indirectly by releasing pharmacologically active substances from mediator-secreting cells, such as mast cells (exercise hyper- and hypo-osmolar stimuli) or nonmyelinated sensory neurons (sulfur dioxide, bradykinin) or a combination of both mechanisms.

The clinical consequences of airway hyperresponsiveness are reflected in an increased variation in airway caliber both within and between days. Nocturnal and/or early morning symptoms with a diurnal variation in peak expiratory flow (PEF) (which correlates well with FEV1) of 20 percent or more are highly characteristic of asthma. An increase of 15 percent or more in FEV1 or PEF 10 to 20 minutes after inhalation of a short-acting beta2-agonist is accepted as diagnostic (NHLBI/WHO Workshop report, 1995).

2.4 Airflow Limitation

The recurrent episodes of airflow limitation in asthma have four forms. Each relates to the airway inflammatory response

1. Acute bronchoconstriction.

The mechanism of acute airflow limitation varies according to the stimulus. Allergen-induced acute bronchoconstriction results from the IgE-

dependent release of mediators, including histamine, prostaglandins, and leukotrienes from airway mast cells that contract the smooth muscle.

2. Airflow Limitation in Asthma

Acute airflow limitation may also occur because airways in asthma are hyperresponsive to a wide variety of stimuli consequent to the underlying inflammation. Many stimuli can cause acute bronchoconstriction, such as inhalation of allergens, exercise, cold air, fumes, and chemicals, and strong emotional expressions like crying and laughing. Their mechanisms for causing bronchoconstriction use differing combinations of direct contraction of smooth muscle, mediator release from cytokine "primed" inflammatory cells, and stimulation of local and central neural reflexes. The acute bronchoconstriction form of airflow limitation is rapidly reversed with an inhaled bronchodilator agent, such as short-acting beta2-agonist

3. Swelling of the airway wall.

Airflow limitation also results from edematous swelling of the airway wall with or without smooth muscle contraction, or bronchoconstriction. Bronchodilators may relieve some of this component of airflow limitation, but it is more effectively reversed with anti-inflammatory drugs, especially corticosteroids. The increase in microvascular

permeability and leakage leads to the mucosal thickening and swelling of the airway outside the smooth muscle. This causes swelling of the airway wall and loss of elastic recoil pressure. Both phenomena contribute to airway hyperresponsiveness in asthma

4. Chronic mucus plug formation.

This more intractable airflow limitation, which has been little studied, usually takes 6 weeks or longer to resolve following the introduction of corticosteroid treatment. It is dominated by increased mucus secretion that, with exuded serum proteins and cell debris comprises the mucus plugs characteristically occluding the more peripheral airways in severe asthma (NHLBI/WHO Workshop report. 1995).

2.5 Airway wall remodeling.

Airflow limitation sometimes fails to reverse with corticosteroid treatment. The cellular and molecular basis of this "steroid resistance" may be at the steroid receptor transduction level or may be associated with structural changes to the airway matrix accompanying longstanding and severe airway inflammation.

From a clinical standpoint, airway inflammation is the most likely variable factor to account for varying severity of asthma and is therefore the element most responsive to controlling medications such as

sodium cromoglycate, nedocromil, and corticosteroids. However, even in the absence of symptoms and overt airflow limitation, asthma continues to exist in the form of mild airway inflammation and airway hyper-responsiveness. Death resulting from asthma is most usually characterized by extensive infiltration of the airways with eosinophils, mast cells and mononuclear cells with extensive involvement of large as well as small airways. Between these extremes lies the common exacerbation of asthma in which mucosal swelling, excess secretions, and increased airway responsiveness are features of the inflammatory response. (NHLBI/WHO Workshop report. 1995).

2.6 Rapidity and Severity of Exacerbation

Asthma symptoms may vary in a variety of ways (e.g., age of patient, contributing mechanisms, response to medications). Patients may experience clinically significant decreases in pulmonary function over a period of minutes, hours, or days. When these alterations occur abruptly, patients will almost always note this change and alter their medication schedule or seek medical help as soon as possible. In contrast, when these alterations occur over a period of days or weeks, the patient's perception of his or her lung function is often quite different in comparison to objective measurements of lung function. These individuals will underestimate their functional impairment and may not seek appropriate

help or treatment early. These individuals have been termed poor perceivers (NHLBI/WHO Workshop report. 1995).

2.7 Factors causing acute exacerbation of asthma

1. Allergens.

Allergen exposure is a common precipitant of asthmatic symptoms in both children and adults. Allergic asthma involves first, the process of sensitization (IgE antibody formation in a genetically predisposed individual) and second, subsequent exposure with the generation of the allergic response in the lower airway. The demonstration that allergen exposure can produce inflammation in the lower airway has markedly influenced the treatment of asthma..

The formation of antigen-specific IgE antibody to aeroallergens does not usually occur until 2 to 3 years of life. It begins to increase in prevalence during later childhood and adolescence, and peaks in the second decade of life. Once established in genetically predisposed individuals, however, IgE-mediated reactions are a major contributor to both chronic airway inflammation and acute asthmatic symptoms. Long-term, low-level exposure to indoor allergens, and dust mite and cat proteins in particular, may play a major role in asthma pathogenesis and

contribute to chronic and recurrent symptoms (Duff AL & Platts-Mills TAE. 1992).

The ideal treatment of allergen-induced asthma involves strict avoidance of the allergen. If this is not possible, premedication prior to allergen exposure is advisable. Administration of cromolyn sodium, nedocromil sodium, or a beta-agonist (eg, albuterol) 5 to 10 minutes prior to exposure significantly attenuates the immediate response; of these agents, only cromolyn and nedocromil have been shown to block the late response as well (Cockcroft DW & Murdock KY. 1987).

2. Virus Infections.

Viral respiratory infections are major causes of wheezing in-patients of all ages. For infants, respiratory syncytial virus infections frequently lead to wheezing. The increased risk in boys appears to relate to a tendency for smaller lung capacity in these children. As these infants grow older, the majorities have fewer episodes of wheezing, and the eventual development of asthma is infrequent. The diminished frequency of wheezing with respiratory infections with increasing age relates to the development of immunity to the infecting virus and growth in lung function. (NHLBI/WHO Workshop report. 1995).

Similarly, in-patients with established asthma; viral respiratory infections are major causes of a wheezing exacerbation. Recent evidence by Johnston (Johnston SL et al. 1995) and Nicholson (Nicholson KG et al.

1996) has shown viruses as the cause of wheezing in nearly 80% of asthma exacerbations, with rhinovirus the predominant virus detected. It is noteworthy that the susceptibility to wheezing with rhinovirus is seen in asthmatic patients of all ages. If the attacks of asthma or wheezing illnesses related to viral infections occurred in both adults and infants, it can be severe and lead to hospitalization.

Although the mechanisms by which viral respiratory infections lead to increased asthma frequency of attack have not been fully established, several important possibilities exist, including enhancement of underlying allergic inflammation. There is an evidence that rhinovirus infections promote the development of the late allergic reaction, enhance eosinophil recruitment to the airway following antigen exposure, and cause eosinophilic infiltration of the airway. There is also evidence from in vitro experiments that respiratory viruses can stimulate the generation of proinflammatory cytokines including IL-1beta, tumor necrosis factor alpha, and IL-11. These observations suggest that respiratory viruses enhance existing allergic inflammation by promoting the production of inflammatory mediators and up-regulating existing airway inflammation (NHLBI/WHO Workshop report. 1995).

3. Air Pollution

A number of researchers believed that air pollution causing the increment of asthma prevalence in general. Jonathan M. Samet

from Baltimore, Maryland that air pollution could exacerbate asthma. Some intriguing information about diesel exhaust particles and other particulate matter, and the development of allergy and asthma, suggest there may be some interactions that are worthy of further investigation (Samet JM. 2000).

4. Impact of Environmental Tobacco Smoke Exposure

There has been particular interest in recent years in the health effects of environmental tobacco smoke, including the potential impact of this problem on higher asthma prevalence rates. Mannino reported that the greatest risk factor for asthma related to environmental tobacco smoke occurs with postnatal or pre- and postnatal exposure. Postnatal exposure was associated not only with an increased risk for the development of asthma but also with increased respiratory symptoms, increased wheezing, decreased lung function, and increased asthma severity (Mannino DM. 2000).

2.8 Risk factors severe asthma

Episodes of fatal and near fatal asthma, although not high in number considering the prevalence of the condition, remain all too common and are increasing. Ongoing studies try to describe the reasons

for this trend and improved understanding of the clinical circumstances underlying and leading to fatal or near fatal episodes of asthma. The hope is that recognizing risk factors for severe asthma and designing appropriate interventions will lead to fewer asthma morbidity and mortality in the future.

There are multiple risk factors for fatal and near fatal asthma, including genetic predisposition, physical environment, social environment, patient habits, the medical care patients receive, and the care patients deliver to themselves. Specific risk factors that have been identified include a slightly higher death rate for females, low economic status, previous hospitalization, emergency department visits, respiratory arrest, or life threatening disease. Others studies have suggested additional risk factors, including psychosocial problems and noncompliance with therapy; sub optimal therapy either due to physician under prescribing or patient under utilization of appropriate medications; substance abuse; and in some cases, environmental exposure (Hannaway & Paul J. 2000). Recognition and appropriate intervention can modify some of these risks factors.

Investigators have become interested in whether there is relationship between patient perceptions of symptoms and dyspnea and life threatening asthma. In a study by Schwartzin RM , some patients feel dyspnea with forced expiratory volume in 1-second (FEV1) values of 90%, whereas others are not dyspneic even when their FEV1 values are 60%

(Schwartzstein RM. 2000). A 1993 study in the British Medical Journal, for example, found that 60% of subjects did not recognize the severity of their air flow obstruction measured by peak flow meter (Kendrick AH & Higgs CM. 1993)

Not all the dyspnea is the same; different perceptions may be based on different physiologic parameters. Some patients who complain of air hunger may have poor gas exchange and hypoxia. Others who complain of having a hard time breathing or requiring an increased effort may have an increase in restrictive loads. Patients who complain of not being able to have or take deep breath may have hyperinflation. Those subjects complaining primarily of chest tightness might have a component of afferent nerve stimulation in the respiratory tree. Schwartzstein noted chest tightness might be a better early warning sign of potentially fatal event than other symptoms (Schwartzstein RM. 2000). Therefore, it is vital for the doctors to recognize all of these types of symptoms and perform the appropriate diagnostic tests to help recognize and manage these patients. Thus, patients also need to be advised that monitoring their lung function is important because even with some symptomatic improvement, they may still be at risk for a fatal event.

Another factor that has been associated with fatal asthma is a delay in patients seeking care. What is not known is whether poor perception of symptoms directly relates to such delays. It was noted that

patients with near-fatal and fatal attacks of asthma often wait 24 hours or more before seeking a treatment (Harver A. 2000).

2.9 Key interventions to Prevent Arrest in managing acute exacerbation of severe asthma

Severe exacerbation of asthma can lead to several forms of sudden death. One classification scheme categorizes asthma on the basis of the onset of symptoms. Signs of rapid-onset asthma develop in <2.5 hours, signs and symptoms of slow-onset asthma develop over several days (Wasserflan J et al. 1990).

Cardiac arrest in-patients with severe asthma has been linked to:

1. Severe bronchospasm and mucous plugging leading to asphyxia (Robin ED & Lewiston N. 1989). This condition causes the vast majority of asthma-related deaths.
2. Cardiac arrhythmias due to hypoxia, which is the common cause of asthma-related arrhythmia. In addition, arrhythmias are caused by use of β -adrenergic agonists. (In rare instances these arrhythmias may be due to prolongation of the QT interval resulting from β -adrenergic agonists (Robin Ed & mc Cauley R. 1992) or toxicity caused by medications such as theophylline.)
3. Auto-PEEP (positive end-expiratory pressure) occurs in some patients who are intubated and mechanically ventilated. Patients fail

to expire as much air as they took in; gradual buildup of pressure occurs and reduces blood flow and blood pressure. Auto-PEEP is secondary to air trapping and "breath stacking" (breathed air entering and being unable to escape).

4. Tension pneumothorax (often bilateral)

Most asthma-related deaths occur outside the hospital. The number of patients with severe attacks of asthma who present to the Emergency Department at night is 10 times greater than the number presenting during the day (Brenner BE et al. 1999).

The major clinical action is to treat the severe asthmatic crisis aggressively, before deterioration to full arrest. The specific agents and the treatment sequence will vary according to local practice. Emergency treatment and ICU management will include some combination of the agents and interventions discussed below.

1. Oxygen

Use a concentration of inspired oxygen to achieve a PaO₂ of > 91 mm Hg. High-flow oxygen by mask is sometimes necessary. In patients with an asthmatic crisis, the following signs indicate that the need for rapid tracheal intubation is imminent:

1. Findings of obtundation
2. Profuse diaphoresis

3. Intravenous Corticosteroids

By 2000 it became a common practice in accident and emergency departments to begin corticosteroid therapy early (in the first 30 minutes) for patients with life-threatening asthma. Corticosteroids should be started early, but oxygen and β -agonists always have priority as the initial agents. Clinicians typically use 125 mg of methylprednisolone (or equivalent hydrocortisone 200 mg IV) as a starting dose in cases of severe asthma (Rowe BH. 1992). Doses can range as low as 40 mg to as high as 250 mg IV or its equivalent.

4. Nebulized Anticholinergics

Use ipratropium, an inhaled anticholinergic agent, as a moist nebulizing agent in combination with albuterol at a dose of 0.5 mg (Karpel JP et al 1996). Unlike β_2 -agonists, which have an immediate onset of action, nebulized anticholinergic agents have a delayed onset of approximately 20 minutes.

5. Intravenous aminophylline

Aminophylline, now used as secondary therapy after β_2 -agonists and corticosteroids, can enhance the effects of those agents. As a bronchodilator aminophylline is approximately one third as potent as β_2 -agonists. Clinicians use aminophylline much more frequently in children than in adults. Addition of this agent to high doses of β_2 -agonists is

thought to increase side effects more than it increases bronchodilation.

This is most evident in patients already taking theophyllines. The risk-benefit ratio may be different in patients not taking theophyllines

(Littenberg B. 1988)

6. Intravenous Magnesium Sulfate

A number of authors have reported success with magnesium sulfate in patients refractory to inhaled adrenergic agents and corticosteroids.

Although not consistently effective, magnesium is widely available and can be administered with few side effects at a dose of 2 to 3 g (Schiermeyer RP & Finkelstein JA. 1994)

7. Parenteral or Subcutaneous or Intramuscular Epinephrine or Terbutaline

Subcutaneous administration of epinephrine or terbutaline may prevent the need for artificial ventilation in cases of life-threatening asthma, especially in patients who do not respond to inhaled β_2 -agonists. For convenience and easy recall a non-weight-based dose of 0.3 mg usually is given to adults. This dose of epinephrine (0.3 mg) can be repeated twice at 20-minute intervals to a total of 3 injections.

The dose of terbutaline is 0.25 mg SC every 30 minutes; up to 3 doses may be given. At this time there is no good evidence of advantages for IV β -agonists over inhaled bronchodilators (Gibbs NA et al. 2000).

8. Ketamine

Ketamine is a parenteral dissociative anesthetic that has been found to be a useful bronchodilator. Most experts think that ketamine is the anesthetic agent of choice for intubation of severe asthmatics. Ketamine potentiates catecholamines and directly induces relaxation of smooth muscle. It also increases bronchial secretions and can cause emergent reactions. The initial dose of ketamine is 0.1 to 0.2 mg/kg followed by an infusion of 0.5 mg/kg per hour (Hemmingsen C et al. 1994)

2.10 Criteria for Admission to Intensive Care Unit

Intensive care, generally in an intensive care unit with consultation of an asthma specialist or a critical care specialist experienced in treating asthma, is indicated if the patient has any of the following:

- A lack of response to initial therapy in the emergency department and/or rapidly worsening asthma
- Presence of confusion, drowsiness, other signs of impending respiratory arrest (diaphoresis with recumbency, staring facies, bradypnea), or loss of consciousness
- Impending respiratory arrest: hypoxemia despite supplemental oxygen (PO_2 less than 60 mm Hg and/or PCO_2 greater than 45 mm Hg).

- Intubation may be needed if there is continued deterioration in clinical features despite optimal therapy, if the patient is exhausted, and/or if the PCO₂ is increasing.

(Working Party of the Malaysian Thoracic Society. 1996)

CHAPTER 3 : METHODOLOGY

3.1 Type of study

This study was a cross-sectional observation study from 1990 to 2000. A detailed analysis of all medical reports of patients with acute asthma admitted to multidisciplinary Intensive Care Unit of Hospital University Science Malaysia were included in the study.

3.2 Inclusion criteria

All asthma patients that required intensive care admission were included in this study. Life threatening asthma in this study was defined as severe attacks of asthma poorly responsive to adrenergic agents, and associated with signs and symptoms of impending respiratory failure, any history of drowsiness as a result of asthma, loss of consciousness, respiratory arrest, mechanical ventilation, or admission to the ICU for asthma treatment (The British guidelines on asthma management 1995 review and position statement, 1997)