IMPACT OF AN ASTHMA CARE PROGRAMME ON PROCESS AND COST OUTCOME AMONGST CHILDREN WITH ASTHMA IN TWO MAJOR HOSPITALS IN MALAYSIA

by

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Thesis submitted in fulfillment of the requirements

for the degree of

Doctor of Philosophy

April 2012

ACKNOWLEDGEMENTS

In the name of ALLAH, the most Gracious, the most Merciful. Praise is to ALLAH for the *hidãyah* and assistance to complete this work.

I would like to thank my supervisor, Professor Dr Mohamed Izham Mohamed Ibrahim, who not only showed constant interest and enthusiasm but also for his comments, patience and the unwavering support – thank you for your time.

Special thanks to my co-supervisors, Dr Norzila Mohamed Zainudin and Dr Wan Jazilah Wan Ismail for their enthusiastic input and collaboration.

My gratitude goes to Dr Tahir Aris, Public Health Specialist (Methodologist and Biostatistician) for his time and invaluable advice on statistics. All my colleagues at the Institute for Health Systems Research - thank you for the encouragement and continual support.

I am grateful to all the staff in the Paediatric Wards and Record Offices of the Paediatric Institute Hospital Kuala Lumpur and Hospital Selayang for their assistance.

Finally to my parents and in-law for their constant *duã.*

DEDICATION

To my wife Samsinah Haji Hussain, son Muhammad Hafiz and daughter Sophia Nur Iman who are always by my side and a source of strength that made it possible for me to complete this thesis.

Sham, Hafiz and Iman, thank you for your stimulating companionships and constant *duã*.

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LIST OF ABBREVIATIONS

ACP	Asthma Care Programme
CPGs	Clinical Practice Guidelines
ED	Emergency Department
EMR	Electronic Medical Records
EPR	Expert Panel Report
FEV_1	Forced Expiratory Volume in 1 second
FVC	Forced volume capacity
GINA	Global Initiative for Asthma
HS	Hospital Selayang
ICS	Inhaled corticosteroids
ICU	Intensive Care Unit
IgE	Immunoglobulin E
LABA	Long acting β2-agonist
LM	Leukotriene modifiers
MCIS	Medical Care Information System
MOH	Ministry of Health
NAEPP	National Asthma Education and Prevention Program
NHLBI	National Heart Lung and Blood Institute
NHMS	National Health Morbidity Survey
OCS	Oral corticosteroids
PHDW	Paediatric High Dependency Ward
PIHKL	Paediatric Institute Hospital Kuala Lumpur
RM	Ringgit Malaysia
SABA	Short acting β2-agonist
THIS	Total Health Information System
USD	United States Dollar
WHO	World Health Organization

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LIST OF PUBLICATIONS AND COMMUNICATIONS

Ramli, Z. & Mohamed Izham, M.I. (2005). Economic impact of an asthma care programme on health care resource utilization amongst children with asthma. Internal presentation at the Discipline of Social and Administrative Pharmacy Postgraduate Work-in-Progress Meeting 2005.

Ramli, Z., Wan Jazilah, W.I., Samsinah, H. & Mohamed Izham, M.I. (2006). Asthma care before and after hospitalization: Potential role for pharmacists intervention. Poster presentation at the Malaysian Pharmaceutical Society, Pharmacy Scientific Conference 2006 (Kuala Lumpur).

Ramli, Z., Norzila, M.Z., Wan Jazilah, W.I., Samsinah, H. & Mohamed Izham, M.I. (2007). Impact of an Asthma Care Programme among inner-city children. Poster presentation at the World Asthma Meeting 2007 (Istanbul, Turkey).

Ramli, Z., Norzila, M.Z., Wan Jazilah, W.I., Samsinah, H. & Mohamed Izham, M.I. (2007). Impact of an Asthma Care Programme on health care utilisation amongst children with asthma. Poster presentation at the Malaysian Paediatric Association Congress 2007 (Kuala Terengganu).

IMPAK PROGRAM PENJAGAAN ASMA KE ATAS PROSES DAN HASILAN KOS DI KALANGAN KANAK-KANAK BERPENYAKIT ASMA DI DUA BUAH HOSPITAL UTAMA DALAM MALAYSIA

ABSTRAK

PENGENALAN: Penyakit asma dalam kanak-kanak merupakan salah satu daripada penyakit kronik yang umum. Akibat prevalensnya yang tinggi, penyakit asma menyebabkan beban ekonomi yang agak besar kepada sistem penjagaan kesihatan dan masyarakat. Pengurusan secara optima boleh mengawal gangguan ini dan pelbagai intervensi telah dilakukan berdasarkan saranan daripada beberapa garispanduan amalan klinikal (CPG). Meskipun terdapat garispanduan dan farmakoterapi yang berkesan, penjagaan seringkali gagal mencapai tahap amalan yang dianggap sebagai yang terbaik. Kajian ini bertujuan untuk menilai pengurusan semasa pesakit asma pediatrik berdasarkan adherens kepada garispanduan dan juga untuk menilai impak Program Penjagaan Asma (ACP) berstruktur terhadap penggunaan sumber dan kos rawatan.

KAEDAH: Kajian semula rekod-rekod perubatan secara retrospektif di 2 buah hospital utama untuk menilai tahap adherens kepada garispanduan. Sebelas indikator klinikal utama digunakan untuk mengukur adherens. Satu kajian kuasi-eksperimen, pre- pasca berserta kumpulan kawalan telah digunakan untuk menilai keberkesanan ACP. Pesakit-pesakit di bawah ACP telah menerima penjagaan seperti yang disyorkan oleh CPG merangkumi rawatan optima oleh doktor, pendidikan mengenai

asma semasa di hospital dan rancangan tindakan asma. Hasilan yang diukur adalah kadar kemasukkan semula ke hospital dan kehadiran ke jabatan kecemasan. Pengunaan sumber dan kos rawatan juga dinilai.

KEPUTUSAN: Pengurusan dan penjagaan penyakit asma pada keseluruhannya tidak mencapai tahap yang disyorkan dalam CPG. Kekurangan ditemui merentasi beberapa aktiviti-aktiviti klinikal yang penting. Dalam salah satu hospital, hanya 19.4% menerima pendidikan asma, 1.4% mempunyai rancangan tindakan asma, 27.8% mempunyai pengkelasan keterukan dan 6.9% telah didiscaj tanpa sebarang ubat asma. ACP telah mengurangkan peratusan kanak-kanak yang hadir semula ke jabatan kecemasan sebanyak 78% ($p < 0.001$) berbanding dengan kawalan. Walau bagaimanapun, tidak terdapat perbezaan yang signifikan dalam peratusan pesakit yang dimasukkan semula ke hospital dalam masa dua bulan berikutan dari kemasukan indeks walau pun terdapat penurunan sebanyak 50% didalam kumpulan intervensi. Kos purata penyakit asma bagi kumpulan ACP adalah dianggarkan pada RM 557.60 (IQR 301.10) berbanding RM 879.00 (IQR 307.70) bagi kumpulan kawalan. Peratusan yang paling tinggi adalah kos kemasukan ke hospital iaitu di antara 33.3% – 42.4% daripada jumlah kos langsung.

KESIMPULAN: Terdapat banyak peluang untuk memperbaiki penjagaan kanak-kanak berpenyakit asma. Perlaksanaan ACP telah dikaitkan dengan bertambahnya adherens kepada CPG, hasil kesihatan yang lebih baik dan kos rawatan yang lebih rendah. Usaha pada masa akan datang untuk memperbaiki pengurusan penyakit asma seharusnya disasarkan dalam membaiki komponen-komponen khusus penjagaan asma.

IMPACT OF AN ASTHMA CARE PROGRAMME ON PROCESS AND COST OUTCOME AMONGST CHILDREN WITH ASTHMA IN TWO MAJOR HOSPITALS IN MALAYSIA.

ABSTRACT

INTRODUCTION: Childhood asthma is one of the most common chronic diseases. Due to its high prevalence, asthma places a considerable economic burden on the health care system and society. Optimal management can help to control the disorder and various interventions have been put into place based on recommendations of clinical practice guidelines (CPGs). However despite the availability of these CPGs and effective pharmacotherapy, care often fall short of the accepted best practices. This study was aimed at assessing the current management of paediatric patients in terms of guideline adherence and to evaluate the impact of a structured Asthma Care Programme (ACP) on resource utilisation and cost associated with the management of asthma.

METHODS: A retrospective review of medical records at 2 major hospitals to assess the level of adherence to the guideline. Eleven key clinical indicators were used to measure adherence. A quasi-experimental, pre-post study with control group was used to evaluate the effectiveness of the ACP. Patients under the ACP received care as recommended by CPGs which include optimal care by physician, asthma education during hospitalisation and asthma action plan. The outcome measures were

the rate of re-hospitalisation and re-attendances to emergency department (ED). Resource utilisation and cost of care were also evaluated.

RESULTS: The overall management and care of asthma fell short of the recommendations in the CPGs. Deficiencies were found across a range of key clinical activities. In one of the hospital, only 19.4% had asthma education, 1.4% has asthma action plan, 27.8% had severity classification and 6.9% was discharged without any asthma medication. The ACP reduces the proportion of children re-attending the ED by 78% ($p < 0.001$) in comparison to the controls. However, there was no significant difference in the proportion of patients who were re-admitted in the two months following the index admission although there was a 50% reduction in the intervention group. The median cost for asthma in the ACP group was estimated at RM 557.60 (IQR 301.10) compared to RM 879.00 (IQR 307.70) in the control group. The highest proportion was hospitalisation cost between 33.3% - 42.4% of the total direct costs.

CONCLUSION: There are opportunities to improve the care for children with asthma. Implementation of ACP was associated with an improvement in adherence to the CPG, better health outcomes and lower costs of treatment. Future efforts to improve asthma management should be targeted to improve the specific components of asthma care.

CHAPTER 1

INTRODUCTION

This research was conducted in an attempt to assess the current utilisation of health care resources in the management of asthma and to evaluate a new asthma intervention strategy to improve the quality of asthma care. The aim of this study is to propose strategies to improve the health outcome of children with asthma and subsequently reducing the cost for asthma management.

Chapter One gives an overview of the research problem and introduces the rationale and objectives of the study. The scope of asthma related to the paediatric population and the burden of asthma are discussed. The introduction served to lay the groundwork for an exploratory study which is to describe the resource utilisation and evidence of guideline adherence in the management of asthma. This is followed by a prospective quasi-experimental, pre test-post test design (with control group) with the intention of evaluating an intervention in the form of a structured Asthma Care Programme (ACP) in reducing the resource utilisation for patients with asthma.

1.1 Overview of the research problem

Asthma is one of the most common chronic diseases and has significant medical and socioeconomic impact on the society. The World Health Organization (WHO) estimates that 300 million people suffer from asthma worldwide and reported

that 255,000 died due to asthma in 2005. It is clearly a public health problem in all countries especially in low and middle income countries because over 80% of asthma death occurs in these countries (WHO, 2006). Childhood asthma is common and its prevalence is increasing in most countries of the world. The rising prevalence of asthma has been attributed to a number of factors including, change in diet and lifestyle, economic development, and increased exposure to allergens and pollutants (Weinmayr et al., 2007; Masoli et al., 2004; Ellwood et al., 2001; Stewart et al., 2001).

The International Study of Asthma and Allergy in Childhood (ISAAC) in their worldwide survey found the highest prevalence of asthma occurred in the United Kingdom (> 15%), New Zealand (15.1%), Australia (14.7%), the Republic of Ireland (14.6%), Canada (14.1%) and followed by the United States (10.9%) while the lowest were seen in several Eastern European countries such as Estonia (5.4%), Georgia (1.8%) and Greece (1.9%) (Masoli et al., 2004; ISAAC, 1998).

Within the Asia-Pacific region, the prevalence of asthma among children was found to be lower when compared to the developed countries. In comparison, the 12-month prevalence of wheezing was reported as 8.0% in the Asia-Pacific region and 16.7% in Western Europe (ISAAC, 1998; Kim et al., 1997). In the ISAAC study, the prevalence of asthma in countries within the Asia-Pacific region ranges from 1.1% in Indonesia to 6.5% in Thailand.

Asthma places a considerable economic burden on the health care systems and society. The economic impact due to asthma is substantial. In the United States

for example, asthma affects 16 million adults and 1.6 million children. These subsequently resulted in 2 million visits to the emergency department (ED), 70,000 hospitalisations and 5,000 deaths annually (MMWR, 2004). The direct medical cost for asthma amounted to USD 3.64 billion and the indirect economic losses was estimated at USD 2.6 billion (Weiss et al., 2000). In Europe, according to a survey by the European Respiratory Society, the total cost of asthma is estimated at € 17.7 billion (USD 21.7 billion) per annum. Cost for out-patient is € 3.8 billion (USD 4.6 billion) followed by anti-asthma drug which is € 3.6 billion (USD 4.4 billion). In-patients care cost is approximately € 0.5 billion (USD 0.6 billion) and the indirect cost in term of productivity losses is estimated at € 9.8 billion (USD 12.0 billion) (Braman, 2006).

In this region, the Asthma Insights and Reality in Asia Pacific (AIRIAP) study reported an annual per-patient direct costs ranging from USD 108.00 for Malaysia to USD 1,010.00 for Hong Kong. Urgent care costs accounted for 18% – 90% of total per-patient direct costs. The total per-patient direct costs were equivalent to 13% of per capita gross domestic product and up to 300% of per capita health care spending in some countries (Lai et al., 2006).

Asthma also creates an impact on the individuals, families and their quality of life. It affects the lifestyles and activities of those involved and their carer. Data from various organizations showed that there is significant morbidity and mortality among asthma patients (WHO, 2008; Williams et al., 2003). In children, asthma resulted in large proportion of school absenteeism, hospitalisation, emergency visits and time lost from work by the carers (Moorman et al., 2007; GINA, 2003). Children with

asthma are likely to miss a significant part of their education due to the disease. This can have an impact on the performance in school and future opportunities (Halterman et al., 2001).

Clinical practice guidelines (CPGs) based on current evidence were developed to help improve asthma care and reduce the economic and societal burden. Many advances in the science and treatment have been made in recent years. However, despite the availability of highly effective medications and CPG for asthma management, studies have shown that the treatment and care delivered to the patients often fall short of the accepted best practices (Mattke et al., 2007; Diette et al., 2001; Finkelstein et al., 2000; Zuckerman et al., 2000; Goodman et al., 1999). This was further supported by findings from large surveys in various regions such as the Asthma Insights and Reality in Europe (AIRE), the Asthma Insights and Reality in Asia-Pacific Study (AIRIAP) and Asthma in America. These reports showed that asthma is still under-diagnosed and under-treated (Lai et al., 2003; Rabe et al., 2000). This sub-optimal care reflects that the CPG is not effectively implemented and the goals of asthma care have not been met (FitzGerald et al., 2006; Rabe et al., 2004; Chapman et al., 2001). It remains a major challenge to ensure that children with asthma received the appropriate care. Sub-optimally controlled asthma not only puts patients at risk, but also has considerable social and economic implications.

Various strategies and approaches have been developed and implemented in a variety of settings to address these challenges (Bravata et al., 2007; Butz et al., 2005; Homer et al., 2005; Lozano et al., 2004). Poor physician adherence to the guidelines, patient’s non-compliance, inadequate education, incorrect inhaler technique and

failure to institute appropriate therapies were among the reasons cited for this gap in the management of asthma (Wisnivesky et al., 2008; Basheti et al., 2005; Sawyer & Fardy, 2003; Clark & Partridge, 2002; Farquhar et al., 2002; Haby et al., 2002; Cabana et al., 2001).

This gap in the management of asthma implies that patients are not receiving the optimal benefits from available therapy and health care systems. This sub-optimal care or gaps represents 'Achievable Benefits Not Achieved' (ABNA) by the health care systems and there are rooms for further improvement in the management of asthma (Birnbaum et al., 2006).

In the context of Malaysia, asthma prevalence among children was estimated at 4.5% in children (up to 14 years old) and 4.1% in adult (15 years and above). This estimates were reported in the Second National Health and Morbidity Survey (NHMS II) conducted in year 1996 (IPH, 1996). This figure rose to 7.1% in year 2006 as reported by the Third National Health and Morbidity Survey (NHMS III) (IPH, 2008). Other studies within smaller populations reported a higher figure ranging from 10.3% to 13.0% for children in urban populations (Norzila, 2000; Azizi, 1990).

Reports from the Health Informatics Centre, Ministry of Health Malaysia, showed that in the year 2006 almost 1.3 million patients visited the ED and more than 700,000 attended the outpatients department for diseases of the respiratory system (MOH, 2007). These represent the main principal causes of attendances at the ED and general outpatients department in the government hospitals. The morbidity

and expenditures for treating these can represent a substantial economic burden for society and health systems.

Limited studies on the economic costs of asthma care are available and the economic impact of asthma in Malaysia is not well documented. Reported costs on asthma care ranges from USD 15.00 to USD 112.00 per-person. In a study by Safiah et al. (1998), the hospitalisation cost for asthma was estimated at RM 395.11 (USD 112.00) per-patient and it accounted for 78.33% of the total cost. In another study conducted in a teaching hospital, Chan et al. (2002) reported a mean treatment cost of USD 22.97 and USD 15.56 for treating bronchial asthma in adult and children, respectively. Lai et al. (2003), in their AIRIAP study reported that utilisation of health care resources for asthma was high as 43.6% of patients were either hospitalized or attended ED or made an unscheduled visit for treatment within a year.

The gap in the management of asthma was also reported by local researches. Loh and Wong (2005), reported poor adherence to the CPGs by prescribers. Studies on knowledge and skills revealed that both children and parents have poor knowledge and are not being educated about asthma (Lee & Khoo, 2004; Loh et al., 2004; Bahari et al., 2003; Fadzil & Norzila, 2002). Parents of children with asthma were also reported as having poor skills in utilizing the inhalers and spacers (Aziz et al., 2006).

1.2 Rationale of the study

Based on evidences which point to an increase in asthma prevalence, its economic impact and sub-optimal care, strategies aimed at reducing this burden should be further studied. This is particularly important in the context of the Malaysian health care system as there are limited published data available compared to evidences from other countries. Local studies on asthma among children focus mainly on specific components of care such as knowledge, skills, perceptions and prescribing patterns. While these studies are important in the management of asthma, other approaches aimed at enhancing the management of asthma need to be conducted as they are still lacking.

This study is aimed at contributing to fill up this gap in knowledge by utilizing a new asthma intervention strategy to improve the management of asthma where it was shown to be sub-optimal. In this way, an effective strategy to ensure that children with asthma received the appropriate care as recommended by the evidence-based guidelines could be determined.

1.3 Purpose of the study

The purpose of this study is to assess the current management of asthma amongst hospitalized children and to evaluate the impact of a structured Asthma Care Programme (ACP) on resource utilisation and cost associated with the management of asthma.

Process of care indicators were used to measure the degree of adherence to the interrelated components of effective asthma management as recommended by the CPG. The impact of a structured Asthma Care Programme (ACP) on the rate of readmissions to the hospital and re-attendances to the ED were evaluated.

The ACP consisted of a care programme that incorporates the components of asthma care. Patients under the ACP were managed according to their level of asthma severity, prescribed the appropriate therapy, provided with an education about asthma and a written asthma action plan during their hospitalisation period. The educational component mainly focuses on basic facts about asthma, the roles of medications, the skills in using inhalers or spacers and the practice of triggers avoidance. A pictorial asthma education chart was developed to aid understanding of patients and parents on asthma. A written asthma action plan was provided as a guide for them to follow when symptoms occured and how to take rescue action. Finally, the cost associated with the management of acute asthma in the ED and in-patients hospitalisation was estimated.

1.4 Specific objectives

The study consisted of two phases with the following specific objectives determined for each phases.

Phase 1 – Retrospective review of in-patients data

1.4.1 To evaluate the documentation of evidence in the medical records in relation to the requirements of the national guidelines on asthma management,

1.4.2 To describe the pattern of drug utilisation in the treatment of asthma across the different severity levels, and

1.4.3 To describe the utilisation of health care resources (hospitalisation and ED visits) among children with asthma.

Phase 2 - Prospective in-patients study

1.4.4 To determine the effectiveness of the structured Asthma Care Programme (ACP) in reducing the readmission and re-attendance rate, and

1.4.5 To estimate the cost of care for children attending the ED and hospitalized for asthma.

1.5 Contributions of study findings

The overall result from this study is expected to benefit the children with asthma and their carer as it was aimed to improve their health outcome and indirectly their quality of life. The intervention would also improve the awareness and ability of children to take charge of their own asthma management. This is expected to be achieved through the education on self-management and the use of written asthma action plan.

The intervention itself would enhance the understanding of the health care providers on interventions that improves the quality of asthma care. Hospitals or health centres can benefit from the ACP model as it can be incorporated into daily practice without much change to the existing delivery system. The strength of the ACP is the effective use of time as the education was provided while patients are in the hospital for treatment of asthma exacerbation.

CHAPTER 2

LITERATURE REVIEW

In this chapter, a review of the current literature provides the basis for this study. The first section describes asthma and factors influencing its development. The current trend in prevalence and burden of asthma is presented. This is followed by a review on the management of asthma, the use of evidence-based asthma guidelines, their barriers and issues. The final part of the literatures synthesized and discussed various strategies related to improving the care for asthma patients. This chapter reinforced the rationale of this study and explained how the study builds on from earlier work. Asthma situation in Malaysia is described and finally the conceptual framework, specific research questions and hypothesis are presented.

2.1 Asthma: Definition and Pathophysiology

Asthma is a chronic inflammatory disorder of the airways. Clinically, asthma is characterized by episodic exacerbation of symptoms such as coughs, wheezing, chest tightness and breathing difficulties. During an asthma attack, the airways become inflamed and swollen. The smooth muscles surrounding the airways contract, mucus forms and collects within the airways. The narrowing of the airways makes it difficult for the exchange of air in the lungs and this narrowing leads to the symptoms and physiological changes in asthma (Canonica, 2006). Several factors contribute to the development of airway narrowing and smooth muscle contraction. Mucus hypersecretion may lead to luminal occlusion (“mucusplugging”) and is a

product of increased mucus secretion and inflammatory exudates. Airway hyperresponsiveness is linked to both inflammation and repair of the airways and is partially reversible with therapy (Vignola et al., 2001). Asthma attacks can be exacerbated by triggers and the most common triggers are respiratory infections (Glezen et al., 2000). Other factors that can trigger an attack include allergen exposure, environmental pollution, environmental tobacco smoke (ETS), animal dander, dust mites, moulds, stress, exercise and changes in weather. Although treatment of symptoms can be effective, severe life-threatening attacks can still be fatal (McFadden, 2003).

Recent understanding of asthma pathogenesis has resulted in the disease being redefined from an episodic airways disease to a chronic inflammatory disorder. The Global Initiative for Asthma (GINA) defined asthma as: '*Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation causes an associated increase in airway hyper responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment'* (GINA, 2003).

This definition describes the basic problem with asthma, which is the obstruction to the flow of air due to the narrowing of airways. Based on the definition of asthma as an inflammatory disorder, the approach of the current asthma management is not only to treat the symptoms but also to suppress the underlying inflammatory disorder. This understanding brought about changes in the approach

and management of asthma. Therapy to suppress inflammation must be used and early intervention with antiinflammatory therapy may modify the disease process. Inhaled corticosteroids (ICSs) are considered the most potent and effective long-term control medications for asthma. As such the use of corticosteroids has become the mainstay in the treatment of asthma (Gupta et al., 2004) and ICSs have now become the first-line treatment. Evidences have shown the value of steroids as the foundation of asthma therapy (Barnes, 2006; Rowe et al., 2000).

2.2 Asthma: Risk Factors

The probability of an individual developing asthma may increase or decrease depending on risk factors. There are a number of factors that influence a person's risk of developing asthma. The risks factors can be classified as host factors i.e. factors within individual such as genetic predisposition, atopy, airway hyper-responsiveness, gender and race/ethnicity. Another factor, which is modifiable, is the environmental factor such as allergens, respiratory infections, tobacco smoke, diet and air pollution (indoor and outdoor).

2.2.1 Host factors

Asthma is hereditary and children of asthma subjects are susceptible to phenotype associated with asthma. Multiple genes may be involved in different ethnic groups and genes associated with serum immunoglobulin E (IgE) level has been associated with an increased risk of asthma (Graves et al., 2000; Buchard et al., 1999; Holgate, 1999; Holloway et al., 1999). Progress in identifying the genes was

made when the ADAM-33 gene, a locus on the short arm of chromosome 20 was identified and linked to asthma and bronchial hyper-responsiveness (Holgate et al., 2004; van Eerdewegh et al., 2002).

Atopy is strongly associated with asthma and over 80% of people with asthma have evidence of allergic sensitization (Rhodes et al., 2001). The presence of parental history of atopy or other allergic disorders (such as eczema, rhinitis) are risk factors for persistent asthma in the first six years of life (Martinez et al., 1995). In the early childhood, the prevalence of asthma was found to be greater in boys than in girls (de Marco et al., 2000). The increase risk in male was associated with higher IgE and increased airway tone (Gissler et al., 1999; Sears et al., 1993). At puberty more females developed asthma than males resulting in the higher prevalence of female in adult asthma (de Marco et al., 2000). The reason for this gender related difference however, remains unclear. Studies have found some differences in prevalence of asthma between races or ethnicity. Research from United States showed that the prevalence of asthma among black children is twice when compared to white (McDaniel et al., 2006; Litonjua, 1999; Schwartz et al., 1990). In the UK, people of South Asians origins are three times as likely to be admitted to hospital for asthma compared to white Europeans (Netuveli et al., 2005). Results from these studies suggest that racial disparities in asthma may continue to pose risks for black children. Genetic factor may contribute to this condition along with their life style, allergen exposure and socio-economic factors (Pearce et al., 2000a).

2.2.2 Environmental factors

Exposure to indoor allergens (house mites, animal dander, cockroaches, moulds and yeast) and outdoor allergen (pollens) was associated with increased risk for asthma exacerbations (Sporik et al., 1990; Platts-Mills et al., 2000; Sporik & Platts-Mills, 2001). However, there is ongoing controversy between allergen exposure and the development of the disease. Direct evidence linking allergen exposure as a major primary cause of asthma was relatively weak as many other factors can contribute to wheezing (Lau et al., 2000; Pearce et al., 2000b). As such there is no simple relationship between allergen exposure and asthma. The role of allergens in the development of asthma is yet to be fully resolved, but it remains important.

Respiratory infections can cause asthma exacerbations in children. The most common virus is respiratory syncytial virus (RSV) which causes wheezing. Infants with RSV bronchiolitis were associated with development of asthma later in their childhood years (Sigurs et al., 2000). RSV is not the only virus associated with wheezing as other severe respiratory viral infections have been shown to increase the risk of wheezing (Gern, 2000). Although there are evidences to associate viral infections and development of asthma, a study by IIIi et al. (2001) found that repeated viral infections (other than lower respiratory tract infections) provide a protective effect of upper respiratory infections and the risks of developing atopy and asthma.

The role of diet, particularly breast-feeding and development of asthma has been studied and results showed that infants fed on formulas have a higher incidence of wheezing compared to those fed on breast milk (Friedman & Zeiger, 2005). Increased use of processed foods and decreased intakes of n-3 polyunsaturated fatty acid (PUFA) (oily fish) have been suggested as a factor contributing to the increase in asthma and atopic disease in some population (Deveraux & Seaton, 2005). Omega-3 PUFA has been shown to have anti-inflammatory effects *in vitro* and studies to link it with lower prevalence of asthma have been conducted (Nagakura et al., 2000; Weiland et al., 1999). However, a Cochrane review reported that there is little evidence that the intake of fish oil will improve asthma control (Thien et al., 2002).

Exposure to environmental tobacco smoke (ETS) or passive smoking has been associated with risk of lower respiratory tract infection in children (Gilliland et al., 2000; Ferrence & Ashley, 2000). Maternal smoking during pregnancy and among family member was found to increase the risk of developing asthma and wheeze in children (Ehrlich et al., 1996). The chemical and carcinogenic constituents of tobacco have profound effects on children's health as they may disrupt normal biological development (Hogg et al., 2004). Exposure to tobacco smoke is an important factor which can affects sensitization, development and aggravation of asthma. Apart for ETS, outdoor pollutants from industrial particulate and indoor pollutants which include cooking gases, wood fires and materials from building and furnishing materials have been linked to asthma (Koenig, 1999). However, the role of pollutants in asthma development was said to be inconclusive (Jones, 2000).

2.3 Asthma: Burden

2.3.1 Prevalence, morbidity and mortality

Worldwide, asthma affects people of all ages and it was estimated that more than 300 million people from all ethnic backgrounds suffer from asthma. Global prevalence of asthma ranges from 1% - 18% of the population in different countries (Cerveri et al., 1999; ISAAC, 1998). Its prevalence has been increasing in some countries but at the same time has stabilized or decline in others (Asher et al., 2006; Yan et al., 2005; Garcia-Marcos et al., 2004). It is estimated that there may be an additional 100 million people with asthma by 2025 as the proportion of the world's population living in urban areas are likely to increase (Law et al., 2005; Rosado-Pinto & Morais-Almedia, 2004). However, there are insufficient data to explain the variations of prevalence between the various populations (Bateman et al., 2008).

Asthma can have a major influence on the quality of life of the patients, their family and society. Asthma has a substantial impact on the daily functioning and emotional well being of a person (Ford et al., 2003). In children, asthma is a major cause of school absenteeism, interrupted sleep and limited physical activities (Lai et al., 2003; Lenney, 1997). In the United States, children aged 5 - 17 were reported to miss 10.5 million school days in year 2008 (Akinbami et al., 2011). Asthma also affects the family's daily activities as parents or carers may need to take time off from work to care for their children. The World Health Organization (WHO) uses the term Disability Adjusted Life Years (DALYs) as a measure for the years of 'healthy'

life loss as a measurement of the gap between the current health status and an ideal situation where everyone lives into old age free of disease and disability. DALYs combine information about morbidity and mortality in terms of healthy years lost. WHO has estimated that 15 million DALYs are lost annually due to asthma, representing 1% of the total global disease burden (WHO, 2006).

The impact of asthma and treatment on individuals can be expressed by health related quality of life (HRQoL), which is broadly defined as an indication of the functional impairments (physical, emotional and social) of an individual. Research has highlighted that functional impairments are troublesome in children with asthma (Juniper et al., 1996; Osman & Silverman, 1996). Children can be troubled as they feel isolated and left out by their peers, which can cause them to feel frustrated, irritable and angry (Juniper, 2001). The importance of incorporating an assessment on HRQoL is now recognised by physicians in managing patients with asthma and there are evidences to show a correlation between how patients feel and the clinical measures (Juniper et al., 1993; Townsend et al., 1991). In order to obtain a complete picture of the patient's health status, HRQoL need to be measured together with the clinical asthma measures such as peak flow rate, FEV_1 and asthma control. Various instruments are available such as, the Paediatric Asthma Quality of Life Questionnaire (PAQLQ) (Juniper et al., 1996) and the Paediatric Asthma Health Outcome Measure (PAHOM) (Chiou et al., 2005) that can be used to measure HRQoL. These measurements are necessary as they provide a more comprehensive understanding of the impact of asthma on the children's quality of life.

Asthma deaths are rare in the developed countries, WHO estimated the annual worldwide death from asthma at 255,000 annually (WHO, 2006). However, mortality rate does not appear to be correlated with prevalence of asthma. Recent trends have shown a progressive reduction in mortality rates of 0.23 per 100,000 in 2004 and 2005 (Wijesinghe et al., 2009). One of the possible reasons for this decline is the widespread use of ICS which have been demonstrated to reduce the risks of death (Suissa et al., 2000). The risk factors for asthma death depends on the following; disease severity, medical care factor both before and during attack, health behaviour (such as non-compliance to medication, poor inhaler technique and reduce contact with primary care services) and adverse psychosocial factor (Sturdy et al., 2002; Lanes et al., 2002).

2.3.2 Social and economic burden

Asthma places a considerable financial burden on the health care system and society. The burden could be seen from the following aspect: (i) an increased risk for early death; (ii) its impact on the quality of life of the children and that of their family or carers and; (iii) increased utilisation of health care resources and costs associated with the disease.

Studies on the economic costs of asthma in developed countries have revealed that the economic cost of asthma is substantial, for both direct cost (such as hospitalisation and medication) and indirect cost (such as time lost from work and premature death) (Braman, 2006; Cisternas et al., 2003; Weiss et al., 2000). Hospitalisation and emergency care account for the largest proportion of the cost of

asthma care (Smith et al., 1997). This cost account for more than 60% of asthma related health care cost and a significant portion of these expenditures for asthma occur in the ED (Stanford et al., 1999). Asthma is the leading cause of hospitalisations among children and accounts for a large portion of the direct cost (CDC, 2000; Gergen & Weiss, 1990). Children with asthma have almost three times the health care expenditures for asthma and more than twice as many ED visits compared to children without asthma (Lozano et al., 1999).

In total, per-person annual cost of asthma in the USA averaged USD 4,912.00 with direct and indirect cost accounting for USD 3,180.00 (65%) and USD 1,732.00 (35%), respectively (Cisternas et al., 2003). The largest components within direct costs were medications USD 1,605.00 (50%), hospital admissions USD 463.00 (15%) and non-emergency ambulatory visits USD 342.00 (11%). Collectively, for children and adults with asthma, the annual projected estimates for asthma was USD 12.7 billion for direct and indirect costs (Weiss & Sullivan, 2001). In Netherlands the annual estimated health care cost per asthmatic patient was USD 293.00 (1993 dollars) and majority of the costs were attributed to medication use and in-patients hospitalisation (Rutten van Molken & Feenstra, 2001). Kiivet et al. (2001) reported an annual treatment cost in Estonia amounting to € 118.00 and the biggest contributors to the overall costs were medications (63%) and hospitalisations (27%). In Switzerland it was reported that direct medical expenditure contributed to 65% of the total estimated cost of asthma (Szucs et al., 1999).

Comparing the costs of illness (COI) from six studies in conducted in Australia, Sweden, United Kingdom and United States, the authors showed an annual

burden per person affected by asthma ranges from USD 326.00 to USD 1,315.00 (inflated to 1991 US dollars). Out of this amount, approximately 40-50% of the costs were attributed to direct medical cost (Weiss & Sullivan, 2001). As seen from these studies, there were large variations in the cost of asthma among countries and it is difficult to make direct comparison. This is due to differences in the health care system, definition of cost and sources for unit cost. However, the direct medical expenditures are apparent for each country studied and were consistently found to be high. Hospitalisation and unscheduled emergency care were also notably high.

The burden of asthma remains significantly high and it is an ongoing challenge to focus on minimizing the impact of asthma. Intervention efforts aimed at reducing the burden especially in children remain important. Therefore measures taken or aimed at reducing the hospitalisation and emergency visits will have a significant impact on the overall cost of the disease.

2.4 Asthma: Management

2.4.1 Diagnosis and assessment of severity

Establishing an accurate diagnosis is essential in the management of asthma. The diagnosis of asthma is based on symptoms, patient's medical history, physical examination and supportive diagnostic test. A correct diagnosis of asthma is essential as other conditions such as bronchiectasis, obstructive lung disease, endobroncial lesions, foreign bodies, extra or intrathoracic narrowing of the trachea, pneumonia and pulmonary emboli can be confused with asthma (Bush, 2007; Levy et al., 2006).

Symptoms such as wheeze, chest tightness, shortness of breath and cough are suggestive of asthma. More so if these symptoms are recurrent, worsen at night or early morning and triggered by exercise, irritants or viral infections. However, the signs and symptoms may vary from patients to patients and over period of time (Taylor et al., 2008).

Information about patient's history should include current symptoms, pattern of symptoms, precipitating factors, present treatment, previous hospital admission, typical exacerbations, family history of atopy, response to prior treatment and prolonged upper respiratory tract infection (URTI) symptoms. Signs of chronic illness includes, hyper-expansion of the thorax, wheezing during normal breathing, increased nasal secretions, mucosal swelling, sinusitis, and eczema or other signs of allergic skin problem are strong indicative of asthma.

The use of spirometry or peak flow meter can enhance the diagnosis of asthma. Spirometry which measures the forced expiratory volume in one second (FEV_1) is the preferred method as objective measures are necessary for accurate diagnosis of asthma. Compared to peak flow meter, the measurement of peak expiratory flow (PEF) has significant limitations as it depends on the effort and technique of the child. Bronchial challenge test (e.g. methacholine) and allergy testing (e.g. skin prick) may help to confirm the diagnosis of asthma. Measuring inflammatory markers such as eosinophils level (ECP) is another method to diagnose asthma but it is not routinely used in clinical practice.

The diagnosis of asthma can be more difficult in young children, aged less than 5 years as it is often not possible to perform spirometry. The diagnosis has to be based mainly on clinical judgement, symptoms and physical assessment. In school children (above the age of 7) airway functions and bronchodilator responsiveness may be used to confirm the diagnosis as these children are likely to be able to perform the test more reliably. Diagnosing asthma in children requires clinical judgment as the signs and symptoms vary considerable from patients to patients.

Asthma severity in this section is discussed in the context of previously published guidelines by GINA and the National Asthma Education and Prevention Program (NAEPP). Asthma severity is defined according to the underlying disease process represented by the clinical characteristics before treatment (GINA, 2003; NHLBI, 2002).Based on symptoms and level of airflow limitation, the guidelines classify asthma into four steps; intermittent, mild persistent, moderate persistent and severe persistent as illustrated in Table 2.1.

Severity can be used as a predictor in the limitations of normal daily activities and cost of asthma has been shown to be related to level of severity (Antonicelli et al., 2004). Patients have more symptoms with increasing severity and the overall cost of asthma increases with increasing severity. This cost includes the direct and indirect costs (Godard et al., 2002). Other studies have also reported similar findings although these studies used retrospective data and different criteria to define severity (Weiss et al., 2000; Serra-Batlles et al., 1998; Smith et al., 1997).

Table 2.1: Classification of asthma severity by clinical features before treatment.

Step 1: Intermittent
Symptoms less than once a week
Brief exacerbations
Nocturnal symptoms not more than twice a month
FEV_1 or PEF $\geq$ 80% predicted
PEF or FEV_1 variability < 20%
Step 2: Mild Persistent
Symptoms more than once a week but less than once a day
Exacerbations may affect activity and sleep
Nocturnal symptoms more than twice a month
FEV_1 or PEF $\geq$ 80% predicted
PEF or FEV_1 variability 20-30%
Step 3: Moderate Persistent
Symptoms daily
Exacerbations may affect activity and sleep
Nocturnal symptoms more than twice a week
Daily use of inhaled short-acting $ß_2$ - agonist
FEV_1 or PEF 60-80% predicted
PEF or FEV_1 variability > 30%
Step 4: Severe Persistent
Symptoms daily
Frequent exacerbations
Frequent nocturnal asthma symptoms
Limitation of physical activities
FEV_1 or PEF $\leq$ 60% predicted
PEF or FEV_1 variability > 30%

Notes: PEF = peak expiratory flow; FEV_1 = forced expiratory volume in 1 sec.
Source: GINA, 2003.

In the recent revised version of the GINA and NAEPP guidelines, the concept of severity has been refined and expanded to include the concept of current impairment and future risk (GINA, 2006; NHLBI, 2007). According to the revised guidelines, severity reflects the level and intensity of treatment required to achieve control (Taylor et al., 2008). The severity and control of a patient's asthma can determine the patient's level of impairment and future risk. Impairment is defined as the frequency and intensity of symptoms, low lung function, and current or recent limitations of daily activities. Future risk is identified as the patient's risk of exacerbations, progressive loss of lung function, or adverse reactions from medications. The new guidelines state that patients can still be at high risk for frequent exacerbations even if they experience minimal day-to-day effects of asthma.

Once the diagnosis has been established, the focus is then shifted to classifying asthma severity so that appropriate therapy can be initiated to achieve good control (Taylor et al., 2008). Table 2.2 provides the detail impairment and risk criteria that are used in the guidelines. Level of control is based on the most severe impairment or risk category.

This classification is important because asthma therapy involves a stepwise therapy and appropriate maintenance treatment should correspond to the patient's severity. Higher doses of therapy can be justified for patients with more severe asthma. A reduction in therapy should follow once the asthma control is achieved and maintained for a sufficient period of time.