ASSESSMENT OF VALIDITY AND RELIABILITY OF MALAY VERSION OF ASTHMA CONTROL TEST QUESTIONNAIRE

BY

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“The will to conquer is the first condition of victory”

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LIST OF ABBREVIATIONS

ACT : Asthma Control Test

GINA : Global Initiative for Asthma

AIRAP : Asthma Insight and Reality in Asia Pacific Study

AIRE : Asthma Insight and Reality in Europe

ISAAC : International Study of Asthma and Allergies in Childhood

ACQ : Asthma Control Questionnaire

PAQLQ : Paediatric Asthma Quality of Life Questionnaire

ATAQ : Asthma Therapy Assessment Questionnaire

LFT : Lung Function Test

FEV1 : Force expiratory Volume in 1 second

FVC : Force Volume Capacity

Th : T helper cells

IL : Interleukins

ARG : Arginases

IgE : Immunoglobulin E

ABSTRACT

TITLE

Assessment of validity and reliability of Malay version of Asthma Control Test questionnaire

OBJECTIVE

To validate the Malay version of ACT questionnaire for asthma children aged 12 to 18 years old .

METHODS

Pilot test was administered as linguistic validation before proceeding with data collection. The participants completed the ACT questionnaire concurrently while performing the spirometry. Respiratory paediatricians who were blinded to ACT rated their asthma control based on Global Initiative for Asthma (GINA) guideline in order to evaluate validity and reliable of Malay version of ACT.

RESULTS

A total of 60 patients were recruited with median age of 14 years old. The Malay version of ACT has good internal consistency; Cronbach's alpha 0.91.

A significant difference was noted between the different groups of asthma control control as grouped by the GINA - defined classification [F(2,25) =88.16. There was good agreement of ACT with the specialist classification, kappa = 0.84. The study has good sensitivity and specificity for cut off 19 with 92% and 96% respectively. It has fair correlation with FEV1 and PEF (r = 0.41-0.42).

CONCLUSION

The Malay version of ACT is a valid and reliable test for asthma control assessment . Further research for validation needed involving multi centre, bigger sample size and repeated measures to detect the changes over time in order to capture the true picture of asthma control, are required to validate the result of this study.

ABSTRAK

TAJUK

Validiti dan reliabiliti ‘Asthma Control Test’ (ACT) dalam Bahasa Melayu

OBJEKTIF

Untuk menghasilkan ACT dalam Bahasa Melayu yang valid dan dipercayai bagi pesakit asma yang berumur 12 ke 18 tahun

TATACARA

Kajian pilot telah digunakan sebagai validasi linguistik sebelum pengumpulan data dijalankan. Pesakit telah melengkapkan soalan dan menjalankan spirometri. Pakar respiratori menganalisa kawalan asma pesakit berdasarkan garis panduan ‘Global Initiative of Asthma’ (GINA) tanpa mengetahui nilai ACT yang telah diisi bagi menilai validiti dan reliabiliti ACT dalam Bahasa Melayu

KEPUTUSAN

Sejumlah 60 orang pesakit diambil dengan median umur 14 tahun. ACT dalam Bahasa Melayu mempunyai ‘internal consistency’, Cronbach alpha

0.91. Terdapat perubahan yang ketara antara kumpulan asma berdasarkan garis panduan GINA. [F(2,25) =88.16]. Terdapat persamaan antara kumpulan

ACT dan kumpulan analisa pakar dengan nilai kappa 0.84. Kajian ini mempunyai sensitiviti dan spesifisiti yang bagus bagi perantara nilai skor ACT 19 dengan 92% dan 96% secara susunan. Terdapat sedikit korelasi antara ACT dan 'Force Expiratory Volume in one second' (FEV1) dan "Peak Expiratory Flow' (PEF).

KESIMPULAN

ACT dalam Bahasa Melayu adalah valid dan dipercayai bagi mengesan kawalan asma. Kajian validasi yang seterusnya diperlukan yang melibatkan pelbagai pusat, saiz sampel yang lebih besar dan kaedah ulangan untuk mengesan perubahan penyakit mengikut peredaran masa dalam mengenalpasti gambaran sebenar kawalan asma pesakit

CHAPTER 1

INTRODUCTION

1.1 Asthma

Asthma is a chronic inflammatory disorder associated with variable airflow obstruction and bronchial hyperresponsiveness. It presents with recurrent episodes of wheeze, cough, shortness of breath, and chest tightness (Global Initiative in Asthma (GINA), 2009). It is estimated about 30% in all Western countries and almost 235 million people worldwide having asthma. In Asia Pacific, the prevalence of asthma is lower than in Western countries (Christopher, Zainudin et al, 2003). However the percentage of asthma in adolescence in Malaysia is 3 times more than in adult based on the Malaysian National Health Morbidity Survey 2006 (NHMS III, 2006) . The prevalence of children that require hospital admission in fact continues to rise yearly.

Despite all the current treatment modalities and improvement of health care for asthma, the overall effects on patients are still suboptimal (Christopher, Zainuddin et al,2003; Koolen, Verben et al,2011). A significant number of patients continue to have asthmatic symptoms and lifestyle restriction and require recurrent emergency care visits. It is reported in

The Asthma Insights and Reality in Asia Pacific (AIRIAP) study which showed an under achievement of asthma control in Asia Pacific greater than in European countries. Few factors involved include suboptimal management, low awareness to asthma control, underestimation of severity status by patients, caretaker and paediatricians and poor compliance to medications. (Christopher, Zainudin et al,2003). The underestimation of asthma severity by the caretakers, patients and paediatricians can lead to under treatment and poor quality of life of the children and families. (Sande, Riekert et al,2011).

1.2 Justification study

The purpose of this study is to validate the Malay version of the ACT questionnaire in order to provide a valid tool to paediatricians as well as the patients in Malaysia for assessing asthma control. Furthermore, the Ministry of Health has practically used the ACT questionnaire as a tool to assess asthma control in Malaysia. However, the Malay version has not yet been validated.

CHAPTER 2

LITERATURE REVIEW

The recent GINA guideline focuses on achieving and maintaining asthma control rather than asthma severity (Koolen,Verberne et al,2011). It stated that ‘ it is reasonable to expect that in most patients with asthma, control of the disease can and should be maintained’ (GINA, 2009). The definition of asthma control based on GINA guideline is defined as the absence or minimisation of chronic symptoms, reduction of exacerbations, avoidance of asthma related visits to emergency health care facilities, minimal or no requirement for reliever or beta 2 agonist medications, no asthma related limitation of normal physical activities, near normal lung function and minimal or no adverse effects of asthma medication. (GINA,2009) .

2.1 Prevalence

Asthma affects 5-10% of the population worldwide. It predominantly occurs in boys during childhood age with male : female ratio of 2:1 and the ratio is 1:1 by puberty. The prevalence is greater in female after puberty and for adult onset cases diagnosed after 40 years old. The prevalence is higher in the younger age group because of airway responsiveness and lower level of lung

function. The majority of asthma cases are diagnosed before 18 years old which is about 2/3 of asthma population. Half of them are symptom free or improvement by early adulthood. In Malaysia, the rate is increasing based on the latest International Study of Asthma and Allergies in Childhood (ISAAC III, 2012). It had increased from 6.4% to 9.4 % in children aged 6-7years and from 9% to 13 % in children aged from 13-14 years old. A study done by Devi B et al, 2008 showed only 39.2% of asthma patient in Malaysia have controlled asthma whereas the remaining 60% have inadequate controlled of asthma despite being on maintenance therapy. The most frequent characteristic symptoms are nocturnal attacks and exacerbations (Devi, Rosidah et al, 2011).

2.2 Pathophysiology:

The pathophysiology of asthma is complex and it involves three mechanisms, airway inflammation, intermittent airflow obstruction and bronchial hyper responsiveness. The mechanism of airway inflammation can be acute, sub acute or chronic. Few principal cells involved in airway inflammation include mast cells, eosinophils, epithelial cells, macrophages and activated T lymphocytes. T lymphocytes play a major role in the inflammatory mechanism. Two types of Th lymphocytes have been characterized, Th-1 and Th-2. Th-1 involves in response to infection, where as Th2 produces groups of cytokines that mediate allergic inflammation.

It produces interleukins (IL)-3, 4,5, 6 and 13 where the IL-4 promotes the switch from Ig M to Ig E antibodies.The cross linkage of two Ig E molecules by allergen leads to mast cells degranulation, histamine and other mediators release that promote the airway inflammation including oedema of the airways and mucous hyper secretion (Michael, Erika et al, 2006). A study by Gauvreau et al found that IL-13 has a role in allergen-induced airway responses Gauvreau, O'Byrne et al, 2011). Other constituent cells such as fibroblasts, epithelial and endothelial cells contributed to the chronicity of asthma. In gross pathology, asthma displays lung hyperinflation, smooth muscle hypertrophy, thickening of lamina reticularis, mucosal oedema, sloughing of epithelial cells, disruption of cilia cells and mucous gland hypersecretion.

Airflow obstruction results as a complication of acute bronchoconstriction, airway oedema, chronic mucus plug formation and airway remodelling. Upon exposure to aero-allergen, these inflammatory cells induce a rapid early phase immunoglobulin E (IgE) mediated bronchial hyper-responsivenss which is the primary component in early asthmatic response.It is followed by late phase of IgE mediated reaction leading to airway oedema which occurs 6-24 hours following exposure to the allergens. Chronic mucus plug formation may take weeks to resolve. With longstanding inflammation, airway remodelling happen and may affect the reversibility of airway obstruction. As a consequence, airway obstruction may result in hyperinflation due to increase airflow resistance and reduce expiratory flow rates.

Hyperinflation occurs as a compensation to airflow obstruction, however it is limited when the tidal volume approaches the volume of the pulmonary dead space; the result is alveolar hypoventilation. As a result, there are uneven distribution of the air, uneven changes in airflow resistance and alteration in the circulation and further lead to ventilation- perfusion mismatch and vasoconstriction. In the early phase, ventilation perfusion results in hypoxemia. Hypercarbia is prevented by readily diffusion of carbon dioxide through alveolar capillary membrane and as a result of hyperventilation. With prolonged ventilation perfusion mismatch, carbon dioxide retention occurs. Later, the increase work of breathing,increase oxygen consumption and increase cardiac output lead to poor tissue perfusion, respiratory failure, metabolic and respiratory acidosis (Fireman, 2003; Michael K et al, 2006).

2.3 Factors influencing the development of asthma:

Factors that favour the risk of asthma can be divided either those that develop or trigger the asthma symptoms. The factors that influence to the development of asthma are primarily genetics and the latter are usually environmental trigger. There are many gene expression signatures involved that reflect the acute asthma exacerbation. (Aoki T, Noguchi et al, 2009) . Few examples are such as interleukins (IL- 4/IL-13) genetic pathway which strongly influence the development of atopy in asthma (Michael K et al,

2006), arginases, genetic loci through the effects of nitrosative stress that causing up and down regulated asthma risk respectively, (Salam, Frank et al, 2009) , eosinophil counts with atopic asthma (Daniel F, Kari et al, 2009), and epigenetics. This epigenetic mechanism regulate the transcription factors that are involved in the development of mature T cells which is important to the development of Th-2 response. Alteration in epigenetic marks have been influenced by air pollution, tobacco smoke and asthma phenotype. (Ivana, Schwartz, 2012).

Eczema or atopy also have association in asthma. Children with eczema have 3 fold increased odds to the development of asthma whereas children with allergic rhinitis are almost 5 times risk of experiencing severe asthma exacerbation as compared to asthmatic patient alone. (Matia, Adnan et al, 2014).

Environmental factors have also been suggested to contribute to atopic asthma. For instance, maternal smoking and home environment contribute to persistent sensitisation and increasing risk for wheezing in children. Environmental allergens mainly house dust mite doubled the risk of developing asthma exacerbation. Other factors namely viral upper respiratory tract infection, environmental pollutants, pollens or tobacco smoke and emotional stress also influence the asthma exacerbation.

Independent risk factors in asthma include parental history of allergic disease and period of breastfeeding shorter less than 6 months. However, effects of the breast milk feeding towards the expression of inflammatory symptoms and atopy appear to be inconsistent and transient. (Zhang, Holt, 2014). There is no association between sex difference and age dependency in asthma. (Skadhauge,Sigsgaard, 2008)

2.4 Global Initiative for Asthma (GINA)

The 2014 update to the Global Initiative for Asthma (GINA) guideline emphasizes the importance of evaluating asthma control, rather than asthma severity, in order to guide asthma management decisions. Classification of disease severity is a static measure that, whilst useful in initiating treatment, is less helpful in guiding subsequent treatment.

GINA guidelines suggest that classification of asthma control more directly reflects the effectiveness of therapeutic interventions; and thus it may be more useful clinically. Current guidelines define asthma control as absence of limitations of activities, nocturnal symptoms, minimal or no daytime symptoms, minimal or no need for rescue therapy, normal lung function and no exacerbations.

Asthma guidelines indicate that the goal of treatment should be optimum asthma control. In Asthma Insights and Reality in Asia-Pacific study (AIRAP) assessing 8 urban countries, they find out the level of asthma control fell markedly short of goals specified in the international guideline for asthma. Poor asthma control and substantial morbidity of asthmatic patients are due to lacking of the clinical gold standard for determining asthma control, as well as inadequate recognition of asthma control by patients and physician. (Michael M et al, 2012). GINA guideline provides recommendations for the diagnosis and management of asthma in asthmatic patients and is a core component of the National Asthma Programme.

Few studies showed lacking of asthma assessment by medical practitioners in different department. A casual audit of assessment in a study done at Greentown Health Clinic, Ipoh,Malaysia in 2008 revealed inadequate assessment of asthma symptoms by the medical officer in assessing asthma control (Usha, Rosidah et al, 2011).

Another survey done by Kanesalingam et all also found that lacking of asthma assessment occur in Emergency Department and in the ward (Kanesalingam, Loh et al, 2003). Thus, GINA guideline is designed to help medical practitioners in making their decision to achieve and maintain clinical control in the management of asthma. Based on latest GINA guideline, asthma control is classified into 3 categories either controlled, partly

controlled and uncontrolled. It is based on frequency of symptoms (day/ night), limitation of daily activities, frequency of exacerbation and reliever used and degree of airflow obstruction based on Force Expiratory Volume in 1 second (FEV_1). No item in this category is classified as controlled, presence of any parameters considered partly controlled and presence 3 or more features are classified as uncontrolled asthma. (GINA 2014)

2.5 Asthma Control Test

Despite the availability of the guideline, a significant numbers of paediatric asthma patients is still not optimally controlled. In both Asthma Insights and Reality in Europe (AIRE) and AIRIAP, a significant proportion of asthmatic patients have underestimated their asthma control which could be one of the contributing factor for poor asthma control worldwide. Majority of them had daytime and nocturnal symptom and yet considered themselves having controlled asthma. (Christopher, Zainudin et al 2003; Rabe, Maier et al, 2000).

To overcome this matter, there are few standardised questionnaires published in assessing the asthma control based on patients own perception. These questionnaires are the simpler method in assessing asthma control especially in a busy clinic practice with limited time and resources. They also

correlate well with the assessment made by the paediatrician and GINA classification.

These questionnaire are The Asthma Therapy Assessment Questionnaire (ATAQ), Asthma Control Questionnaire (ACQ) and Asthma Control Test (ACT) and Paediatric Asthma Quality of Life Questionnaire (PAQLQ). This study used ACT questionnaire for children aged 12 years and above.

There are 2 types of ACT questionnaire; children- ACT for age 4 to 11 years old and ACT for age 12 years and above. The reason of choosing Asthma Control Test as asthma assessment in this study because it is a short and simple questionnaire, has been widely used, globally validated, easily scored and appropriate in assessing asthma control comparable with the GINA guideline.

The development of ACT questionnaire was done by Robert A Nathan in 2003 by collecting 22 items from the survey of 471 asthma patients in specialist clinic. Five items were selected from regression analysis to be produced as final questionnaire. It has a good overall agreement more than 70% and good internal consistency reliability of 0.84. The overall agreement from specialist rating ranged between 71-78% and area under the curve (AUC) was 0.77. It consists of 5 items pertaining to asthma control for the past 4 weeks.

It is self-rated and each item is scored into a 5- point score. All points are totalled. The higher scores indicate better control. A cut off ACT score of 19 suggestive of controlled asthma with 69% sensitivity and 76% specificity. The lower ACT score showed higher sensitivity but lower specificity in diagnosing uncontrolled asthma (Nathan, Pendegraft et al, 2003)

There are few studies evaluating the efficacy of ACT questionnaire. In a study done by the developer in 2006, assessing the validity, reliability and responsiveness in asthmatic patients who were not under specialist follow up. Three hundred and thirteen patients were included in the study. They were compared with specialist rating, lung function test and ACQ at baseline and follow up. The internal consistency reliability of ACT was 0.85 (baseline) and 0.79 (follow up). Test retest reliability was 0.77. There was significant correlation between baseline ACT score and specialist rating of asthma control ($r= 0.52$, $p<.001$) and ACQ scores ($r= -0.89$, $p<.001$). There were also significant correlations between changes in ACT score and specialists' rating ($r=0.44$, $p<.001$), ACQ scores ($r = -0.69$, $p<.001$) and percent predicted FEV1 ($r=0.29$, $p<.001$). The highest area under the curve (ROC) was noted for a cut off score of 19 with sensitivity and specificity of 71.3% and 70.8 % respectively. The positive and negative predictive value were 72.6% and 69.3% respectively and the percentage of patients correctly classified was 71%. (Michael S, Christine A et al, 2006).

The ACT can also be used as a tool to assess asthma control in non specialist centre or even at home. In a cross sectional survey assessing 570 asthmatic patients at home using ACT questionnaire, they found out the questionnaire was reliable with internal consistency 0.85. The optimal cutoff point for controlled asthma was 20 with 78% sensitivity and 83% specificity (Michael,Robert Zeiger et al, 2007) .

Another study evaluated the usefulness of the ACT in a poor setting resource. It showed that ACT can predict GINA guideline -based level of control and gives credence to it usefullness in a poor clinical setting resources. (Kappa= 0.66) (Jumbo, Erhabor et al, 2013).Other than that, the ACT questionnaire was comparable to other asthma questionnaires. ACT score was significantly correlated with the Asthma Therapy Assessment Questionnaire (ATAQ) using Spearman rank correlation of -0.73 ($p<.001$) other than ACQ as mentioned before.

There were few countries that validated the ACT questionnaire into different languages. In the Chinese version, the internal consistency of ACT was 0.854. It also showed the strongest correlation with the specialists rating (r= 0.729), followed by ACQ (r= -0.722), non spirometric ACQ (r= -0.695) and percentage predicted FEV1 (r= -0.657) (Zhou X,Wang CZ,2007).

In the Spanish version, 607 patients were assessed. The internal consistency was 0.84 and intraclass correlation (ICC) of > 0.85. The optimal cut off score was 19 with area under the curve (AUC) of 0.86, 71% sensitivity and 85% specificity. (Vega, Dal-Re et al, 2007).

For the Arabic version, the internal consistency (Cronbach's alpha) was 0.92. There was moderate correlation with the specialists rating (r=0.482, p<. 002) , and with the treatment modification (r= -0.35, p<.027) and low correlation with the FEV1. (H.Lababidi,Zarzour et al, 2008).

The Korean version of ACT questionnaire had the internal consistency of 0.71 and intraclass correlation coefficient of 0.83 between baseline and second visits. There was significant correlation between ACT and specialists rating of asthma control at baseline visit (r= 0.87, p=.001). However, it did not correlate with the baseline percent predicted FEV1 values (r= 0.28, p= 0.004). The Korean version of ACT score also had significant correlation with the ACQLQ at baseline visit (r= 0.70, p< .001). (Hyuok, Yoon-Seok at al, 2008)

The Persian version of ACT questionnaire was validated using 150 patients. From their study, the internal consistency reliability was 0.89. There was significant different between asthma control group; F= 305.3, p<.001 and between treatment recommendations group (F=50.54, p<.001).

There was significant good correlation observed between ACT and GINA - guided specialist assessment (r =0.86, p<.001) and moderate correlation with percentage predicted FEV1 (r =0.39, p<.001) (Naseh, Shilan Mohammadi et al, 2011)

Vietnamese ACT showed good internal consistency of 0.83. The kappa coefficient showed moderate agreement with the specialist assessment with a correctly classified rate of 75%. (Kappa 0.55). It had a sensitivity of 70%, specificity of 93% and positive predictive value of 89% for the optimal cut off score of 19. (Nguyen, David et al, 2011).

In Japanese study assessing the efficacy of Japanese ACT (J- ACT) for determining their asthma control, 2233 patients were assessed. They found out the J-ACT had good internal consistency (Cronbach's alpha of 0.78) with optimal cut of points of 24 for controlled and 20 for the uncontrolled asthma. (maximum Youden index 0.503 and 0.699 respectively). (Takashi, Eiichi et al, 2012).

Another study done in Uganda assessing 88 patients based on GINA and ACT. From the ACT questionnaire, they found out the ACT has 95% sensitivity (95% CI 87-98) , 92% specificity (95% CI 65-99) with positive and negative predictive value of 99% and 73% respectively for the diagnosis of inadequately controlled asthma (for ACT score less or equal to 19). (Serugendo, Okot- Nwang et al,2013).

Validation study in North African assessing 624 patients in 3 dialectal Arabic version. There were only moderate internal consistency (Cronbach's alpha ranging 0.58 - 0.67), however well correlated test- retest score (r= 0.704) and good face and discriminant validity. (Abdelkader, Adam et al, 2009)

ACT is now routinely incorporated as outcomes in clinical trials of pharmacological treatment and patient perception strategies. It has been established for the use of clinical practice as part of assessment in asthmatic patient worldwide. In Malaysia, limited study assessing the ACT questionnaire and there is still no proper validation study done in Bahasa Melayu. (Chin Yow wen)

CHAPTER 3

OBJECTIVES

3.1 General Objective

To assess validity and reliability of Malay version of ACT questionnaire for children aged 12 years old to 18 years old with bronchial asthma.

3.2 Specific objectives

i. To determine the construct validity and reliability of Malay version of ACT
ii. to determine the known group validity of ACT controlled, partly controlled and uncontrolled asthma by comparing mean score ACT between the groups
iii. To determine agreement between ACT (as classified by ACT in guideline using cutoff point) and GINA (the gold standard) guideline in asthma in asthma control classification

3.3 Research hypothesis

i. Malay version of ACT questionnaire is valid and reliable

ii. Mean score of ACT are different between controlled, partly controlled and uncontrolled ACT groups

iii. There is a very good agreement between Malay version of ACT score and GINA guideline in classifying asthma groups

CHAPTER 4

METHODS

4.1 Study design

Cross sectional study

4.2 Population description

4.2.1 Reference population

Asthmatic patients aged 12 - 18 years old

4.2.2 Source population

Asthmatic patient aged 12 - 18 years old on follow up at Respiratory Clinic in Hospital Universiti Sains Malaysia (HUSM) and Hospital Raja Perempuan Zainab II (HRPZ II)

4.2.3 Sampling frame

Patients aged 12-18 years with diagnosis of asthma within the previous 6 months prior to the study and follow up at Respiratory Clinic HUSM and HRPZ II

4.3 Study duration

One year (May 2014 to May 2015)

4.4 Inclusion criteria

i. Age between 12 to 18 years old
ii. Established diagnosis of asthma based on clinical findings and lung function test as defined by GINA guideline in all severity and asthma control within the previous 6 months prior to the study
iii. The patients did not experience acute exacerbation on recruitment and were receiving standardised asthma treatment prior to the study
iv. Able to comprehend and provide answers to all contents of the questionnaire.
v. Able to speak Bahasa Melayu and understand Malay language.

4.5 Exclusion criteria

i. Children with other medical problem including lung and cardiac disease (bronchopulmonary dysplasia, cystic fibrosis, congenital or acquired heart disease).
ii. Patients who could not cooperate with the performance of spirometry

4.6 Sample size

Sample size was calculated for all the objectives.

For objective 1, to determine the sample size for assessment of construct validity, a rule of 5 subjects per item was used (Costello and Osborne, 2005), thus a sample of 25 patients was required. After taking into account 10% dropout rate, 28 patients were needed.

In addition, to determine the sample size for construct reliability, an online sample size calculator prepared by Chang (2014) was used (available from https://www.statstodo.com/SSiz1Alpha_Pgm.php). Using hypothesized and expected internal consistency Cronbach alpha of 0.6 and 0.8 , number of ACT items of 5 ,- with type 1 error of 0.05 and power of study of 80%, the sample size needed to answer this objective was 43. After taking into account 10% dropout rate, 48 patients were needed.

For objective 2, to determine the sample size for comparison of mean scores of ACT between the groups (controlled, partly controlled and uncontrolled), partly controlled and uncontrolled were considered as a group just for the purpose of sample size calculation due to anticipation that the number of uncontrolled patients would be limited. The sample size needed was 26 patients per group at significance level of 0.05 and power 80%, with large

effect size (Cohen, 1992). After taking into account 10% dropout rate, 29 patients per group were needed, or a total of 58 patients.

For objective 3, to assess agreement between ACT grouping and GINA grouping of asthma severity, the sample size was calculated using an Excel file prepared by Arifin (2014) available from http://medic.usm.my/biostat/. The sample needed was 47 including 10% drop out with the lowest limit kappa required of 0.4, expected level kappa of 0.8, proportion of controlled of 0.55 (Lenoir et al, 2006), power of 0.8, alpha 0.05 and non centrality parameter of 7.849.

Hence, the minimum sample size to answer all objectives, the study required 58 patients with asthma children age 12-18 years old with the inclusion of 10% drop out.

4.7 Sampling method

Simple random sampling

4.8 Measurement tools

4.8.1 Asthma Control Test

The patient-based index ACT score was developed by Robert A Nathan et al in 2004 as a screening tool to identify poorly control asthma patients. Five items were selected from 22 items . It has good overall agreement more than 70%, good internal consistency reliability of 0.84 and discriminant validity between the group. The overall agreement from specialist rating ranged between 71-78% and area under the curve (AUC) was 0.77.

It consists of 5 questions pertaining to asthma control for the past 4 weeks. It is self rated, and each item is scored into 5- point score and are totalled. The lower the score indicates poor controlled and higher score indicates better control. The patients rated the extent of their asthma symptoms causing limitation to their daily activities over the past 4 weeks.

The 5 questions consist of:

i. Frequency of asthma exacerbation (defined as unscheduled doctor's visit for asthma symptoms or need for extra oral steroid therapy)
ii. Exercise induced symptom
iii. Nocturnal symptoms
iv. Need for rescue treatment
v. self- assessment /rating for asthma control

ACT score of 25 indicates well controlled asthma, 20-24 for partly controlled and score 19 or less are uncontrolled asthma. Refer appendix 1

4.8.2 Specialist rating using GINA guideline

There were 2 asthma paediatricians involved in assessing the patients during follow up. The ratings were according to their symptoms, physical examinations, medications and lung function. Blinded of the questionnaire outcome, the specialist rated the patient based on GINA classification into 3 groups: controlled, partly controlled or uncontrolled groups.

Controlled asthma is defined as absence of limitation of activities and nocturnal symptom, minimal or no daytime symptom, minimal or no need for rescue therapy, normal lung function and no asthma exacerbation.

Uncontrolled asthma is defined as:

1) frequent exacerbation, defined as 2 or more bursts of systemic corticosteroids (3 days each) in the previous year,

2) serious exacerbation, defined as at least 1 hospitalization, intensive care unit stay or mechanical ventilation in the previous year,

3) airflow limitation, i.e force expiratory volume in 1 second (FEV_1) 80% predicted (in the presence of reduced FEV_1/FVC less than the lower limit of normal value) following a withhold of both short and long- acting bronchodilators.