Medical and Research Publications
International Open Access

Research Article **Journal of MAR Pediatrics (Volume 4 Issue 3)**

Usefulness of Pediatric Respiratory Assessment Measure Score in Assessing the Severity and Outcome of Acute Exacerbation of Wheeze in Children

Dr. Venugopal Reddy. I *[1], Dr. G. Siva Kartheek Reddy [2], Dr Dinesh Kumar Vuppu [3], Dr Murali Mohan Voona [4]

1. Medical Director and Consultant Pediatrician, Ovum Hospital, Bangalore.

2. Consultant Pediatrician, Best Care Hospital, Andhra Pradesh.

3. Consultant Neonatologist and Pediatrician, Ovum Hospital, Bangalore.

4. Consultant Pediatrician and Neonatologist, Ovum Hospital, Bangalore.

Corresponding Author: Dr. Venugopal Reddy. I, Medical Director and Consultant Pediatrician, Ovum Hospital, Bangalore.

Received Date: May 30, 2023

Published Date: June 15, 2023

DOI: 10.1027/marpe.2023.0184

Introduction

Asthma is one of the most common chronic diseases in the world. It is a major cause of morbidity and mortality throughout the world and there is evidence that its prevalence has increased considerably over the past 20 years, especially in children[1].

Asthma is a worldwide problem, with an estimated 300 million affected individuals'. The global prevalence of asthma ranges from 1% to 18% of the population in different countries. There is good evidence that international differences in asthma symptom prevalence have reduced, particularly in the 13-14 year age group, with decreases in prevalence in regions where prevalence was previously low[2]. The increase in the prevalence of asthma has been associated with an increase in atopic sensititisation, and is paralleled by similar increase in other allergic disorders such as eczema and rhinitis. In India, the reported prevalence of childhood asthma varies from less than 5% to as high as 20% [3].

Asthma is a chronic inflammatory diseases of the lung airways resulting in episodic airflow obstruction. The chronic inflammation is associated with airway hyper responsiveness that leads to 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. Airflow obstruction during exacerbations can become extensive resulting in life threatening respiratory insufficiency [2].

Guidelines for the management of acute pediatric asthma hinge on the objective assessment of asthma severity, generally measured by lung function tests such as peak expiratory flow rate or spirometry[2]. Unfortunately, these lung function test are nearly impossible to obtain preschool aged children because of poor coordination and in 35% to 50% of school aged children, because of severity of illness or poor familiar it with the technique[5]. With preschool aged children representing over half the patients treated for acute asthma[6], it is estimated that three quarters of asthmatic children cannot perform standard lung function test in th emergency setting[7].

Clinical scores can serve as simple and inexpensive tools to assess asthma severity for the entire paediatric age groups. More than 16 different clinical scores have been reported for assessing asthma severity8. In spite of the availability of many asthma scores, information on the clinimetric properties of score in terms of reliability, validity and responsiveness are scarce. Hence emphasis is on evaluating the properties of already existing scores.

The Paediatric Respiratory Assessment Measure (PRAM) score has been found to be an attractive score for assessing asthma severity and response to treatment[9]. The PRAM is a 12 point clinical score rubric that captures a patient's condition in scalene muscle contraction, suprasternal retractions, wheezing, air entry, and oxygen saturation. Birken et al in a study of asthma severity scores in preschool aged children identified PRAM score as one of the scores with good measurement properties [10]. Ducharme et al developed and validated the PRAM score against respiratory resistance and proved this as discriminative and responsive to change". This study aims to determine the performance characteristics of PRAM score in children with acute exacerbation of asthma.

Review of literature

History of Asthma

The term Asthma comes from the Greek verb aazein, meaning "to pant, to exhale with the mouth open, sharp breath". In the Iliad, a Greek epic poem, the expression asthma appeared for the first time.

The Corpus Hippocraticum, by Hippocrates (460-360 BC), is the earliest text where the word asthma is found as a medical term. Hippocrates said spasm linked to asthma were more likely to occur among anglers, tailors and metalworkers. Hippocrates recommended vapour inhalation.

Aretaeus of CappadociaftlOO AD), an ancient Greek master clinician, wrote a clinical description of asthma. Galen (130-200 AD), an ancient Greek physician, wrote several mentions of asthma which generally agreed with the Hippocrates text and to some extent those of Aretaeus.

Moses Maimonides (1135-1204 AD), the rabbi and philosopher who lived in Andalucia (Spain), Morocco and Egypt wrote Treatise of Asthma for Prince Al-Afdal, a patient of his. He noted that his patients symptoms often started as a common cold during the wet months. Eventually the patient gasped for air and couged until phlegm was expelled. He noted that the dry months of Egypt helped asthma sufferers.

During the early 1800's asthma was rarely mentioned in medical literature. In the 19th century, inhalation therapy was introduced to the western world with the use °f Datura stramonium, a congener of atropine. This was available as asthma cigarettes.

There has been an increase in the prevalence of childhood asthma from all over the world and similar trends have been observed in India. Paramesh et al in a hospital based study on the prevalence of Asthma in Bangalore found a 3 fold increase in the prevalence in the last 20 years [13]. The increased

prevalence correlated well with demographic changes of the city. He also identified an increase in incidence of persistent asthma from 20% to 27.5% and persistent severe asthma 4% to 6.5% between 1994-99. The ISAAC study found a wide variation in the prevalence of asthma from different parts of the world and even from different parts of same country**[**14**]**. This regional variation is due to differing levels of pollution, infections, industrialization, socio-economic, educational status, climate and population densities. This study found the prevalence in 6-7 years, 13-14 years in India to be around 6% which is at the lower end of the world wide prevalence range. Within the country, Chennai was one of the high prevalence centres with a prevalence for more than 6% **[**15**]**.

The economic burned of asthma is considerable both in terms of direct medical costs (such as hospital admissions and cost of pharmaceuticals) and indirect medical costs (such as time lost from work and premature death). Although from the perspective of both the patient and society the cost to control asthma seems high, the cost of not treating asthma correctly is even higher. There is every reason to believe that the substantial global burden of asthma can be dramatically reduced through efforts by individuals, their health care providers, health care organizations, and local and national governments1.

Definition

According to the Global Initiative for Asthma (GINA) 2008 guidelines, asthma is defined as **[**2**]**:

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyper responsiveness that leads to 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 within the lung that is often reversible either spontaneously or with treatment.

Factors Influencing the Development and Expression of Asthma

Factors that influence the risk of asthma can be divided into those that cause the development of asthma and those that trigger asthma symptoms; or both. The former category includes host factors (which are primarily genetic) and the latter category usually consists of environmental factors.

Host factors	Environmental factors
Genetic:	Allergens
Genes pre-disposing to atopy, genes pre-disposing to airway hyper responsiveness	Indoor: Domestic mites, furred animals, cockroach allergen, fungi molds, yeasts Outdoor: Pollens, fungi, molds, yeasts
Obesity	Infection
Gender	Tobacco smoke
	Air pollution
	Diet
	Occupational sensitizers

Table 1: Factor influencing the development and expression of asthma

Genetic

Asthma has a heritable components, but it is not simple. Current data show that multiple genes may be involved in the pathogenesis of asthma and different genes may be involved in different ethnic group17 l8. The search for genes linked to the development of asthma has focused on four major areas:

a) Production of allergen specific IgE antibodies (atopy)
b) Expression of airway hyperresponsiveness
c) Generation of inflammatory mediators, such as cytokines, chemokines, and growth factors.
d) Determination of theTatio between Thl and Th2 immune responses (as relevant to the hygiene hypothesis of asthma).

According to the EGEA study (Epidemiological study on the genetics and environment of asthma, atopy and bronchial hyperresponsiveness) analysis showed linkage of asthma severity scores to the locus on chromosome 18p II, 2p33. 1019.

Obesity

Obesity has also been shown to be a risk factor for asthma. Certain mediators such as leptons may affect airway function and increase the likelihood of asthma development20,21.

Gender

Male gender is a risk factor for asthma in children. Prior to the age of 14, the prevalence of asthma is nearly twice as great in boys as in girls. As children grow older the difference between the sexes narrows, and by adulthood the prevalence of asthma is greater in women than in men[22]. The reason for this gender related difference is not clear.

Environmental Factors

Allergens

Although indoor and outdoor allergens are well-known to cause asthma exacerbations, their specific role in the development of asthma is stillnot fully resolved. Birth cohort studies have shown that sensitization to house dust mite, allergens, cat dander, dog dander and Aspergillus mold are independent risk factors for asthma like symptoms in children upto 3 years of age [23, 24]. However, the relationship between allergen exposure and sensitization in children is not straightforward. It depends on the allergen, the dose, the time of exposure, the child's age and probably genetics as well.

Infections

During infancy, a number of viruses have been associated with the inception of the asthmatic phenotypes. Recurrent wheezing episodes in early childhood are associated with common respiratory viruses like respiratory syncytial virus, rhino virus, influenza, parainfluenza, human metapnuemo virus. Injuries viral infections of the airways manifesting as pneumonia or bronchiolitis requiring hospitalization are risk factors for persistent asthma in childhood.

The "hygiene hypothesis" of asthma suggests that exposure to infections early in life influences the development of a child immune system along a "non allergic" pathway, leading to a reduced risk of asthma and other allergic diseases. Early exposure to respiratory infections may favour a Thl type of response and thus switch off Th2 response giving protection against asthma and other allergic diseases[25].

The interaction between atopy and viral infections appear to be a complex relationship, in which the atopic state can influence the lower airway response to viral infections, viral infections can then

influence the development of allergic sensitization and interactions can occur when individuals are exposed simultaneously to both allergens and viruses[26].

Tobacco smoke

Exposure to tobacco smoke, both prenatally and after birth, is associated with measurable harmful effects including a greater risk of developing asthma like symptoms in early childhood.

Outdoor / indoor air pollution

Outbreaks of asthma exacerbations have been shown to occur in relationship to increased levels of air pollution, and this may be related to a general increase in the level of pollutants or to specific allergens to which individuals are sensitized. Similar associations have been observed in relation to indoor pollutants, eg., smoke and fumes from gas and biomass fuels used for heating and cooling, molds, and cockroach infestations.

Diet

Infants fed formulas of intact cow's milk or soy protein have a higher incidence of wheezing illnesses in early childhood compared with those fed breast milk[27].

Path physiology of asthma

- Airway inflammation is associated with airway hyper reactivity or bronchial hyper responsiveness, which is defined as the inherent tendency of the airways to narrow in response to various stimuli (e.g., environmental allergens and irritants).
- Airway inflammation leads to cellular inflammatory infiltrate and exudates distinguished by eosinophils, but also including other inflammatory cell types (neutrophils, monocytes, lymphocytes, mast cells, basophils). These cells fill and obstruct the airways and induce epithelial damage and desquamation into the airway lumen.
- Helper T lymphocytes and other immune cells produce proallergenic, pro inflammatory cytokines (IL-4, IL-5, IL-6, IL-13) and chemokines that mediate the inflammatory process.
- Pathogenic immune responses and inflammation results from a breach in the normal immune regulatory process (Th2 lymphocytes). All these lead to aberrant repair and structural changes in airway[28].

Airway inflammation in asthma may represent a loss of normal balance between two ‘‘opposing” populations of Thl lymphocytes. Thl cells produce interleukin (IL-2) and IFN-a, which are critical in cellular defiance mechanism in response to infection. Th2 in contrast, generates a family of cytokines (IL-4, IL-5, IL- 6, IL-9 and IL-13) that can mediate allergic inflammation. The current “hygiene hypothesis” of asthma illustrates how this cytokine imbalance may explain some of the dramatic increases in asthma prevalence.

Clinical features

Consider asthma if any of the following signs or symptoms is present:

- Frequent episodes of wheezing - more than once a month
- Activity induced cough or wheeze
- Cough particularly at night during periods without viral infections
- Absence of seasonal variation in wheeze
- Symptoms that persists after age of 3 years
- Symptoms occur or worsen in the presence of aerollergens (house dust mites, companion animals, fungi, and cockroach), pollen, respiratory (viral) infections, strong emotional expression and tobacco smoke.
- The child’s colds repeated “go to the chest” or take more than 10 days to clear up.
- Symptoms improve when asthma medication is given.

Making a definite diagnosis of asthma in children 5 years and younger is challenging because episodes of respiratory symptoms such as wheezing and cough are also common in children who do not have asthma, particularly in those younger than 3 years.

The young the child, the greater is the likelihood that an alternative diagnosis may explain the recurrent wheeze. Lung function measurement that are key to the diagnosis of asthma in older children and adults are not reliable in children less than 5 years.

Some children do not have typical symptoms of wheeze. The variants seen are:

Cough variant asthma

Patients with cough variant asthma have chronic cough as their principal, if not only symptoms. It is particularly common in children and is often more problematic at night. Evaluation of these children during day can be normal.

Exercise induced bronchoconstriction

Physical activity is an important cause of asthma symptoms for most asthma ; patients and for some it is the only cause. Exercise induced bronchoconstruction I, typically develops within 5-10 minutes after completing exercise. Patients experience typical asthma symptoms or sometimes a troublesome cough. Rapid improvement of post exceptional symptoms after inhaled 02 agonist use, or their prevention by pre-treatment with an inhaled 02 agonist before exercise, supports a diagnosis of asthma.

Some children with asthma present only with exercise induced symptoms.

Physical examination

Signs suggestive of generalized airflow obstruction include generalized rhonchi, prolonged expiration and chest hyperinflation.

Investigations

Test	When	What information
Hemogram	As a baseline	May reveal eosinophilia
X-ray chest	As a baseline	Essentially normal hyper aeration
Spirometry	Use in limited to situations where clinical diagnosis of asthma is in doubt, provided: Child can perform the text (age) equipment is available cost is permissible	Establish a diagnosis if FEVI and FEVI/FVC are reduced Improvement in FEVI by >12% after inhaling short acting bronchodilator
Peak expiratory flow	A poor tool for diagnosis, may be used when clinical diagnosis pf asthma is in doubt, spirometry is unavailable, unaffordable or normal at the time of doctor visit	Establish a diagnosis of asthma when: 15% increase in pEfafter bronchodilator 15% decrease in PEF after exercise Diurnal variation of >10% in PEF when not on bronchodilator therapy or diurnal variation of >20% in PEF when on bronchodilator therapy

Serum IgE levels, RAST, skin allergy testing	Not routinely indicated	Indicate atopic state. Skin testing may be required prior to immunotherapy to identify incriminating allergens

Table 2: Investigations

Classification of Asthma Severity By Clinical Features Before Treatment

Mild intermittent	Symptoms less than once a week Brief exacerbations Nocturnal symptoms not more than twice a month FEVI or PEF > 80% predicted PEF or FEV 1 variability <20%
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 FEVI or PEF >80% predicted PEF or FEV 1 variability <20 - 30%
Moderate persistent	Symptom daily Exacerbations may affect activity and sleep Nocturnal symptoms more than once a week Daily use of inhaled short acting P2 agonist FEVI or PEF 60-80% predicted PEF or FEVI variability > 30%
Severe persistent :--------- ------ ----------	Symptom daily Frequent exacerbations Frequent nocturnal asthma symptoms Limitation of physical activities FEVI or PEF < 60% predicted PEF or FEVI variability > 30%

Table 3: Asthma severity by clinical features before treatment

Levels of Asthma Control

Asthma control may be defined in a variety of ways. In general, the term control may indicate disease prevention, or even cure. However, in asthma, where neither of these are realistic options at present, it refers to control of the manifestations of disease. It is recommended that treatment be aimed at controlling the clinical features of disease, including lung function abnormalities.

Characteristic	Controlled (all of the following)	Partly controlled (any measure present in any week)	Uncontrolled
Daytime symptoms	None (twice or less / week)	More than twice / week	3 or more features of partly controlled asthma present in any week
Limitation of activities	None	Any	
Nocturnal symptoms / awakening	None	Any	
Need for reliever / rescue treatment	None (twice or less / week)	More than twice / week	
Lung function (PEF or FEV1)	Normal	<80% predicted or personal best (if known)	
Exacerbations	None	1 or more / year	

Table 4: Levels of asthma control

Acute exacerbation of asthma

Exacerbations of asthma are episodes of progressive increase in shortness of breath, cough, wheezing, chest tightness or a combination of symptoms.

Severe exacerbations are potentially life threatening and their treatment requires close supervision. Most patients with severe asthma exacerbation should be treated in an acute care facility. Patients at high risk of asthma related death also require close attention.

Milder exacerbations, defined by a reduction in peak flow of less than 20% nocturnal awakening, and increased use of short acting b2 agonists can usually be treated in a community setting. If the patient responds to the increase in inhaled bronchodilator treatment after the"first few doses, referral to an acute care facility is not required but further management under the direction of a primary care physician may include the use of systemic glucocorticosteroids. Patient education and review of maintenance therapy should also be undertaken.

Patient a high risk of asthma related death require close attention and should be encouraged to seek urgent care early in the course of their exacerbations. These patients include those:

- With a history of near fatal asthma requiring intubation and mechanical ventilation.
- Who have had a hospitalization or emergency care visit for asthma in the past year.
- Who are currently using or have recently stopped using oral glucocorticosteroids.
- Who are not currently using inhaled glucocorticosteroids.
- Who are over dependent on raid acting inhaled p2 agonists, especially those who use more than one canister of salbutamol (or equivalent) monthly.
- With a history of psychiatric disease or psychosocial problems, including the use of sedatives.
- With a history of non compliance with an asthma medication plan.

Assessment of severity

A brief history and physical examination pertinent to the exacerbation should be conducted concurrently with the prompt initiation of therapy.

The history should include; severity and duration of symptoms, including exercise limitation and sleep disturbance; all current medications, including dose (and device) prescribed, dose usually taken, dose taken in response to the deterioration, and the patients response (or lack thereof) to this therapy; time of onset and cause of the present exacerbation; and risk factors for asthma related death.

The physical examination should assess exacerbation severity by evaluating the patient ability to complete a sentence, pulse rate, respiratory rate, use of accessory muscles, and other signs. In a study by Singhi S et al to identify clinical signs and symptoms that predict hypoxemia in asthma, they found that physical examiantion should include at least accessory muscle use and pulses paradoxus since these predict hypoxemia the best.

Any complicating factors should be identified (eg. Pneumonia, atelectasia, pneumothorax, or pneumomediastinum).

Laboratory Investigations in Acute Asthma

- X-ray chest: Routine X-ray chest is not recommended unless a pneumothorax or physical signs suggestive of parenchymal disease are present.
- ABG: This is useful in severe exacerbations to assess the severity of respiratory acidosis. Usual findings in the early phase are hypoxemia and hypocarbia. In later stage once respiratory ailure ensures PaCO2 will build up and profound decrease in pH occurs. However the decision to intubate should not be made on ABG parameters alone. Assessment of respiratory effort, SpO2 and level of consciousness should guide the decision.
- Pulmonary function test: Spirometry and PEFR are objected measures of assessing the degree of ajrway obstruction. However this is difficult to perform in children <5 years.

Severity of asthma exacerbations

The severity of the exacerbation determines the treatment administered.

Indices of severity, particularly PEF (in patients older than 5 years), pulse rate, respiratory rate, and pulse oximetry, should be monitored during treatment.

	Mild	**Moderate**	**Severe**	**Respiratory arrest imminent**
Breathless	Walking	Talking infant - softer shorter cry: difficulty feeding	At rest. Infant stops feeding	
	Can lie down	Prefers sitting	Words	
Talks in	Sentences	Phrases	Words	
Alertness	May be agitated	Usually agitated	Usually agitated	Drowsy or confused
Respiratory rate	Increased	Increased	Often >30 / min	
Accessory muscles and suprasternal retractions	Usually not	Usually	Usually	Paradoxical thoracoabdominal movement
Wheeze	Moderate, often only end expiratory	Loud	Usually loud	Absence of wheeze

Pulses paradoxus	Absent <10mm Hg	May be present 10-25 mm Hg	Often present >25 mm Hg (adult) 20-40mm Hg (child)	Absence suggests respiratory muscles fatigue
PEF after initial bronchodilat or % predicted or % personal best	>80%	Approximately 60-80%	<60% predicted or personal best or response lasts <2 hrs	
PaO2 (on air) and/ or PaCO2	Normal test no necessary <45mm Hg	>60 mm Hg <45 mm Hg	<60mm Hg possible cyanosis >45mm Hg possible respiratory failure	
SaO2(on air)	>95%	91-95%	<90%	

Table 5: Severity of Asthma exacerbations

Age	Normal rate
<2 months	< 60/min
2-12 months	<50/min
1 -5 years	<40/min
6-8 years	<30/min

Table 6: Normal rates of breathing in awake children

Symptoms	Mild	Severe*
Altered consciousness	No	Agitated, confused or drowsy
SpO2 on presentation	>94%	<90%
Talks in	Sentences	Words
Pulse rate	<100bpm	>200bpm (0-3 yrs) >180 bpm (4-5yrs)
Central cyanosis	Absent	Likely to be present

Wheeze intensity	Variable	May be quiet

Table 7: Initial assessment of acute asthma in children <5 years

Asthma severity scoring systems

Clinical scores can serve as simple and inexpensive tools to assess asthma severity for the entire paediatric age groups. More than 16 clinical scores have been reported for assessing asthma severity8. A good scoring system should be reproducible, obtainable in children of all ages, reflect the severity of underlying pathophysiology and be useful in clinical decision making.

Wood downes - leeks asthma score

In 1972, Wood et al devised a clinical scoring system to detect impending or existing respiratory failure in childhood status asthmatics. It was based on evaluation of oxygenation, gas exchange work of breathing, airway obstruction and cerebral function. A significant correlation was noted between the scores and levels of PaO2 and PCO2.**[**29**]**

	0	**1**	**2**
PaO2 or	>70 mm Hg in room air	<70 mm Hg in room air	<70 mm Hg in 40% oxygen
Cyanosis	None	In air	In 40% oxygen
Inspiratory BS	Normal	Unequal	Decreased to absent
Accessory muscles	None	Moderate	Maximal use
Expiratory wheeze	None	Moderate	Marked
Cerebral function	Normal	Depressed / agitated	Coma

>5 indicated impending respiratory failure, >7 indicated respiratory failure.

Table 8: Wood Downes-Leckes asthma score

Merits: Useful in ICU set up to identify respiratory failure

Demerits:

a. Cannot be used in primary care level as it includes estimation of PaO2.
b. When used on mild to moderately severe acute asthmatic children, and without the cyanosis component, it correlated poorly with arterial oxygen tension.Hence found to be useful only in very sick children
c. Baker et al**[**30**]** evaluated the correlation of the Wood-Downes-Lecks clinical asthma score with outcome in 210 consecutive known asthmatic children presenting to an urban emergency department for treatment of acute asthma. They found that Wood's score alone is not a reliable indicator of severity of acute asthma s judged by subsequent disability (prolonged hospitalization, ongoing disability following ER discharge).

Asthma severity score (SS)

This scoring system consists of 3 variables - wheeze, heart rate, accessory muscle use, each on 0-3 scale.

Score	Wheeze	Accessory muscle	Heart rate
0	Absent	0	<80
1	Expiratory only	+	81-110
2	Inspiratory and expiratory	+++	111-140
3	Audible without stethoscope or silent chest in severe asthma	+++	>141

Table 9: Asthma severity score

Merits

a. Simple objective method which can be used in primary care level

Young et al found ASS to have very good inter observer agreement with a moderate relationship to oxygenation and FEVI. FEV1 correlated with accessory muscle use scores and heart rate correlated with saturation. Bishop et al32 found that an ASS score of moderate or worse (greater than 3) had sensitivity of 97% and specificity of 50% for predication of admission.

Clinical asthma score (CAS)

CAS was developed as a modification of Wood-Downe score. CAS consisted °f five clinical characteristics: respiratory rate, wheezing, in drawing, observed dyspnea, and inspiratory to expiratory ratio which is scored 0, 1 or 2. The score for each variable are added together with a possible total score of 10.

Merits

Parkin Pc et al33 found that CAS was valid, with a strong correlation with length of hospital stay, drug dosing interval, responsive with a significant change in CAS from admission to discharge.

Demerits

- Inspiratory: Expiratory ratio, one of the components of the score is difficult to measure in young children.
- Degree of dyspnea is a subjective assessment. Accurate estimation of degree of dyspnea is difficult in young children.

Score	Accessory	Wheeze	Dyspnea
0	No retractions	No wheezing	No dyspnea
1	Intercostals	End Exp.	Normal activity
2	Intercostals and suprasternal	Insp. & Exp.	5-8 words sentence
3	Nasal flaring	Audible or silent	Rather not speak

Table 10: Clinical asthma score

Pulmonary index (PI)

Becker AB et al34 devised pulmonary index for asthma in 1984. It had 4 components. The PI was derived from respiratory rate, wheezing, inspiratory expiratory ratio, and use of accessory muscles. Becker et al found the PI before treatment correlated significantly with the mean percent of forced expiratory volume •n the first second to force vital capacity ratio (FEV1/FVC). The PI 30 minutes after treatment correlated significantly with all tests of pulmonary function performed.

Score	Respiratory rate	Wheezing	Inspiratory / expiratory ratio	Accessory muscle use

0	<30	None	1:1.5	None
1	30-40	Terminal expiration	1:2.0	1 site
2	41-50	Entire expiration	1:3.0	2 sites
3	>50	Inspiration and entire expiration	>1:3.0	3 sites or neck strap muscle use

Table 11: Pulmonary index

Demerits:

Inspiratory: Expiratory ratio, one of the components of the score is difficulty to measure in young children.

Pulmonary score (PS)

Becker et al34 devised pulmonary index for asthma in 1984. It had 4 components. The pulmonary score is derived from the pulmonary index. The I:E component was removed and the respiratory rate was enhanced by the separating this component into 2 categories by age. Thus PS is the aggregate of 3 items, each scored on a 0-3 scale.

Score	Respiratory rate		Wheezing present*	Accessory muscle usage
	<6 yrs	>6 yrs		
0	<30	<20	None	No apparent activity
1	31-45	21-35	Terminal expiration with stethoscope	Questionable increase
2	46-60	36-50	Entire expiration with stethoscope	Increase apparent
3	>60	>50	During inspiration and expiration without stethoscope	Maximum activity

*If wheezing due to minimal air exc lange: score 3

Table 12: Pulmonary score

Merits

- Simple objective measure
- Can be used in primary care level
- Recommended by IAP respiratory chapter

- Smith SR et al studied the correlation of PS with PEFR in children aged 5-12 yrs and concluded that PS is a practical substitute to estimate airway obstruction in children who are too young or too sick to obtain PEFRs.

Demerits

Does no measure oxygen saturation, which is an important objective Measurement which can predict hospitalization.

Modified pulmonary index score (MPIS)

In the modified pulmonary index score) MPIS), 6 categories are evaluated: oxygen saturation, accessory muscle use, inspiratory to expiratory flow ratio, degree of wheezing, heart rate, and respiratory rate. For each of these 6 measurements or observations, a score of 90 to 3 is assigned. Carol CL et al36 identified MPIS as a highly reproducible and valid indicator of severity of illness in children with asthma. Merits

It includes SpO2 by pulse oximetry, which is an important objective measurement which can predict hospitalzition.

Demerits

Inspiratory: expiratory^ratio is difficult to measure in young children. Paediatric asthma severity score (PASS)

It has six parameters: amount of wheeze, work of breathing as assessed by use of accessory muscles, air entry, tachypnea, presence of prolonged expiration and mental status. For each of these parameters a score of 0 to 2 was assigned.

Score	0	1	2
Wheezing	None	Moderate	Severe or absent
Work of breathing	None	Moderate	Severe
Prolonged expiration	Mildly prolonged	Moderate	Severe

Air entry	Normal or mildly diminished	Moderately diminished	Prolonged or severely diminished
Tachypnea	Absent	Present	-
Mental status	Normal	Depressed	.1

Table 13: Paediatric asthma severity score

Merits

a. It is a simple tool that was developed for use in asthma severity studies. It is a modified version of the pulmonary index, a previously validated clinical asthma severity score. The PASS is less comprehensive but easier to use than the pulmonary index.
b. Gorelick MH et al37 identified that PASS is a reliable and valid measure of asthma severity in children and showed both discriminative and responsive prosperities. They found that the PASS scores correlated with the PEFR and SpO2 measurement in children >6 6 years. S Chu et al38 found that PASS can be used as a predictor of length of stay in the ED for children presenting with an acute exacerbation of asthma.

Merits

Oxygen saturation is an objective measurement which can predict need for hospitalization.

Demerits

a. Degree of dyspnea is difficulty to assess in young children
b. Intercostals in drawing, one of the parameters of this score when present suggests decreased compliance of lung and hence suggests parenchymal lung diseases. Intercostals in drawings are less specific for assessing the severity of asthma**[**29**]**.

Paediatric respiratory assessment measure (PRAM) score

This score consists of 5 variables - suprasternal retractions, scalene retractions, air entry, wheeze, oxygen saturation. It is a 12 point scoring system with the variables scored from 0 to 2 or 3.

The PRAM score was initially described as preschool respiratory assessment measure by Ducharme FM et al11. They elaborated and validated a Preschool Respiratory Assessment Measure that would accurately reflect the severity of airway obstruction and the response to treatment in young patients with asthma. They validated the PRAM scores against concurrent measurement of lung function in

children aged 3-6 years. Subsequent studies by Ducharme FM et al9 showed good performance characteristics of PRAM in all age groups.

Birken CS et al**[**10**]** in an analysis of asthma severity scores in preschoolers concluded that PRAM was one of the scores to demonstrate adequate correlation coefficients between asthma severity scores and clinical measures (length of stay, drug dosing interval, 02 saturation, health professional assessment, PaO2, PaCO2).

They concluded that score such as CAS, PRAM have more rigorously evaluated their measurement properties. Robidas 1 et al**[**40**]** in a study comparing PRAM and PASS scores found both scores to be valid measures of asthma severity in children and show both discriminative and responsive properties with PRAM showing greater responsiveness.

Signs	**0**	**1**	**2**	**3**
Suprasternal indrawing	Absent	-	Present	**[]**
Scalene retractions	Absent	-	Present	-
Wheezing absent	Absent	Expiratory only	Inspiratory and expiratory	Audible without stethoscope / silent chest with minimal air entry
Air entry	Normal	Decreased at bases	Widespread decrease	Absent / minimal
Oxygen	>93%	90-93%	<90%	-

Table 15: PRAM Score

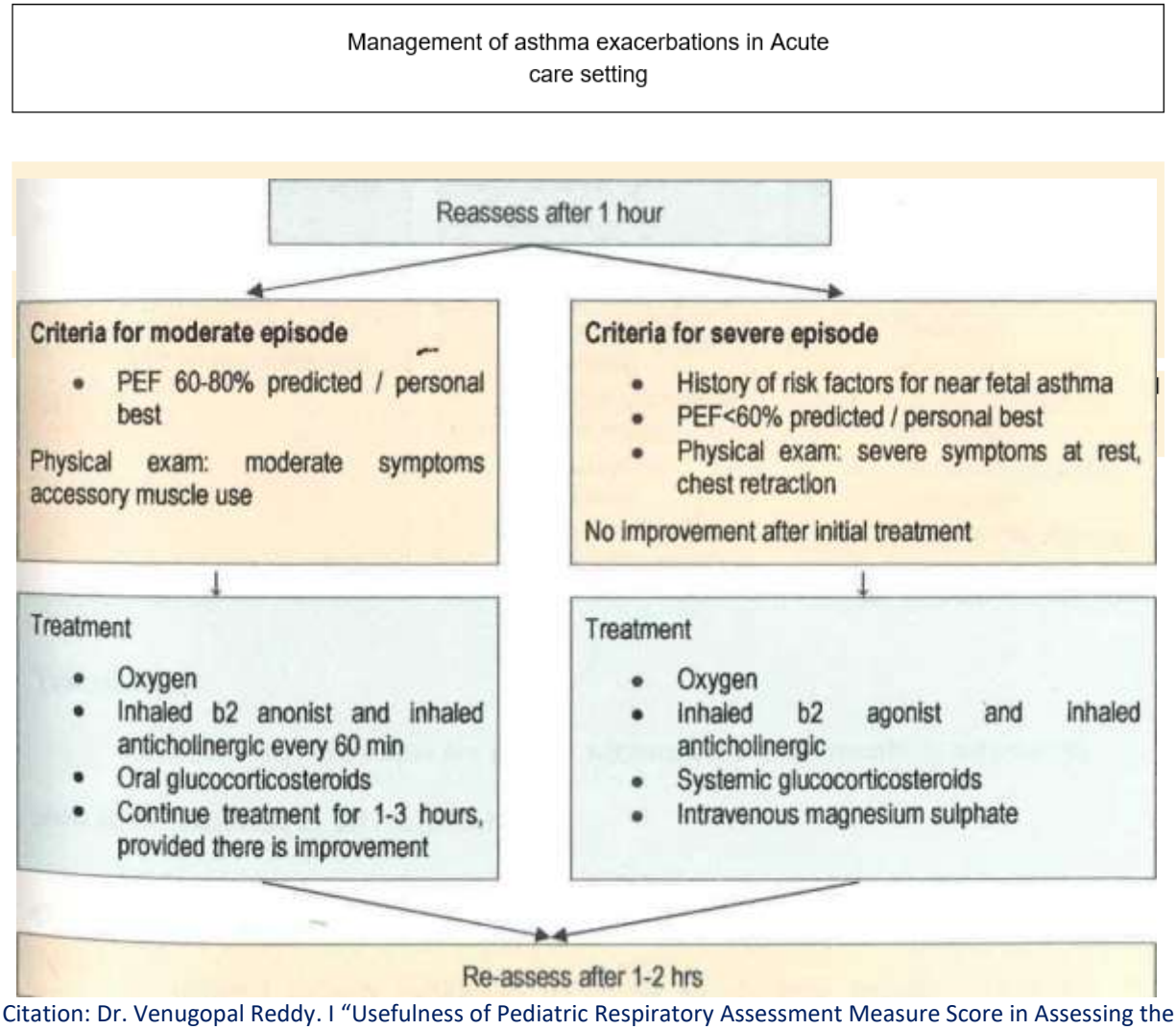
Severity classification	**PRAM score**
Milcb	0-4
Moderate	5-8
Severe	9-12
Impending respiratory failure	12+ following lethargy, cyanosis, decreasing respiratory effort, and / or rising PCO_2

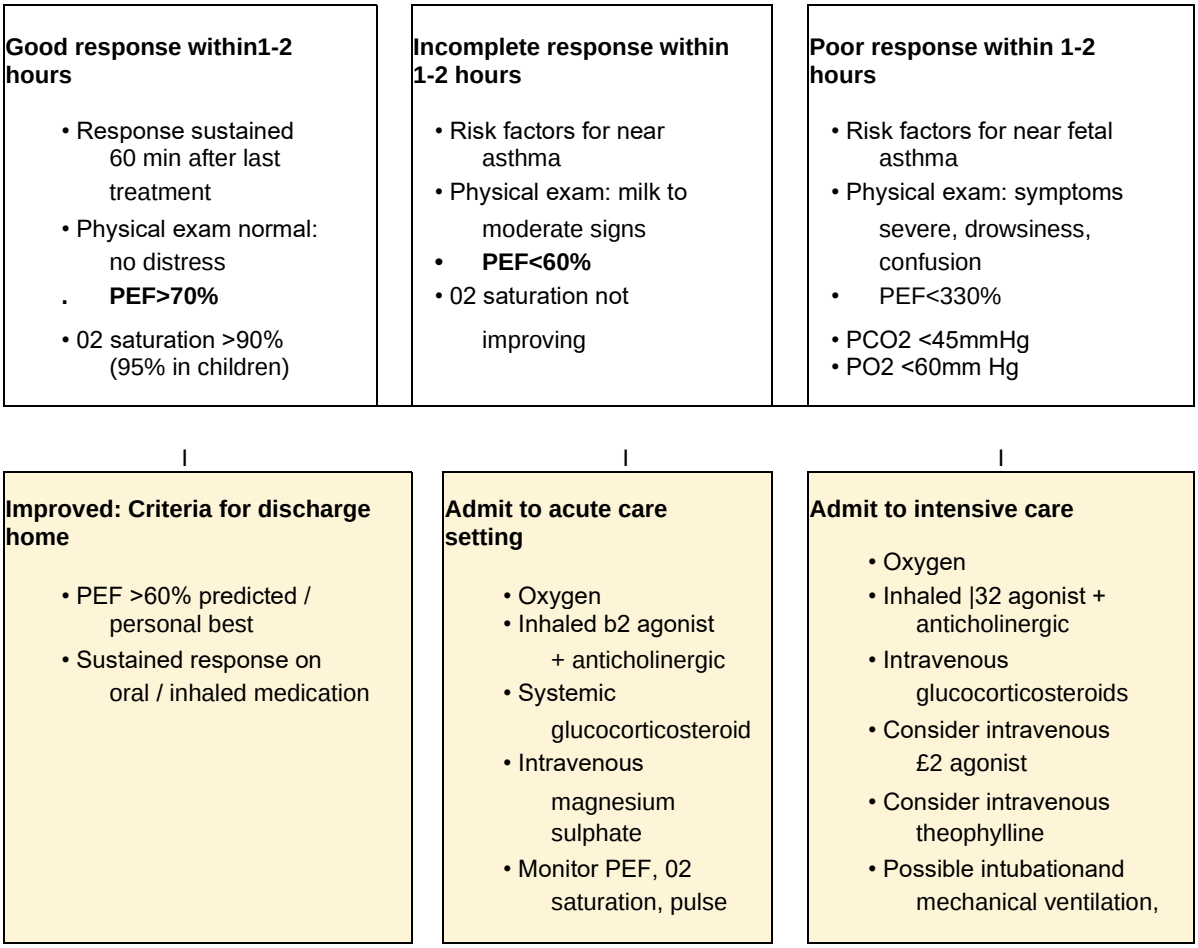
Geelhoed GC et al[43] in another study evaluating the initial SPO2 and outcome of children with asthma concluded that the initial level of SPO2 reflects severity as it predicts the likelihood of poor outcome. This predictive quality of SPO2 is independent of current or past clinical factors. Keogh KA et al[44,46] in study to identify predictors of hospitalization in children factors. Keogh KA et al in a study to identify predicators of hospitalization in children with severe asthma identified several major risk factors - previous ICU admission baseline SPO2 <92%, CAS score of >6 need for hourly salbutamol nebulisation about 4 hrs after steroid therapy. Oxygen saturation has been studied by Mehta SV et al45 as predictor of prolonged, frequent bronchodilator therapy in children with acute asthma. SPO2 <91% was found to predict the need for frequent bronchodilator therapy >4 hrs.

Demerits

Difficulty in measuring SPO2 in a primary care centre.

Management of acute asthma





Treatment

The following treatments are usually administered concurrently to achieve the most rapid resolution of the exacerbation:

Oxygen

To achieve oxygen saturation of >95% in children oxygen should be administered by nasal cannulae, by mask or rarely by head box in some infants. Oxygen therapy should be titrated against pulse oximetry to maintain satisfactory OxYgen saturation.

Rapid acting inhaled £2 agonists

Rapid acting inhaled 02 agonists should be administered at regular intervals. A reasonable approach to inhaled therapy in exacerbations, therefore, would be the initial use of continuous therapy, followed

by intermittent on demand therapy for hospitalized patients. There is no evidence to support the routine use of intravenous 02 agonists in patients with severe asthma exacerbations.

Ipratropium bromide

A combination of nebulized 02 agonist with an anticholinergic (ipratropium bromide) may produce better bronchodilation than either drug alone. Combination 02 agonist / anticholinergic therapy is associated with lower hospitalization rate and greater improvement in PEF and FEV1.

Systemic glucocorticosteroids

Systemic glucocorticosteroids speed resolution of exacerbations and should be utilized in the all but the mildest exacerbations especially if:

02 - agonist: Consider aminophlline in an high dependency unit (HDU) or PICU with severe of life threatening bronchospasm unresponsive to maximal doses of other bronchodilators and systemic steroids with close and careful monitoring. Aminophylline is used in a loading dose of 5mg/kg as an infusion over 30 minutes followed by. lmg/kg/hr as continuous infusion. The loading dose is omitted if chid is already on theophylline.

Intravenous terbutaline infusion in acute severe asthma:

Terbutaline is recommended as a useful adjunct in asthma in those patients who fail to respond to standard initial therapy. Terbutaline was found to be effective and safe at doses of 1-5 ug/KG/min. side effects of the drug reported were increase in heart rate, significant fall in diastolic blood pressure which may also require inotropes and hypokalemia.

Heliox:

Heliox, a blend of helium and oxygen, reduces airway resistance and may be a therapeutic option for severe refractory asthma in intubated patients as there is a decrease in peak inspiratory pressure and paCO2.0 the mixture may improve the distribution of inhaled agents and lead to a faster rate of resolution of obstruction. But there is insufficient evidence to establish the utility of heliox in routine emergency room treatment.

Sedatives:

Sedation should be strictly avoided during exacerbations of asthma because of the respiratory depressant effect of anxiolytic and hypnotic drugs.

Ventilation in asthma:

Ventilator assistance can be lifesaving. Both non-invasive and invasive techniques are available. The generally accepted indication are progressive CO2 retention, obtundation and impending cardiopulmonary collapse. The goal of ventilator support is maintain adequate gas exchange until bronchodilators and corticosteroids relive the airflow obstruction vantilatory strategies that provide the longest possible expiratory time are desired sa that dynamic lung inflation is minimized. This goal is accomplished by combining the smallest tidal valume with the slowest ventilatory rate and fastest inspiratory time to keep a static end inspiratory pressure (plateau pressure) of less than 30cm H20.

Aims and Objectives

Aim of study

To study the usefulness of PRAM score in assessing the severity and outcome of an acute exacerbation of wheeze in children aged 1 - 12yrs.

To identify the PRAM score predicting the need for hospitalization and ICU care.

Materials and Methods

Period of study

Dec. 2013 to Aug. 2015 (22 months)

Study design:

This is a prospective cohort study done for a period of two years in the hospital Aarupadai Veedu Medical College of Pondicherry.

Sample size

100 children in the age group 1-12 years presenting with acute exacerbation of wheeze to the emergency room.

Study population:

Inclusion criteria:

1. Children diagnosed to have asthma on treatment / follow up (asthma diagnosis based on GINA guidelines 2008) in the age group of (1-12) yrs presenting to the ER with acute exacerbation of wheeze were enrolled in the study
2. Chidren aged (1-12) yrs who had past history of at least 3 episodes of airway obstruction which improved with bronchodilator therapy, presenting to the ER with acute exacerbation of wheeze were also included in the study.

Exclusion criteria

I- Children less than 1 year.

II. Children with pre-existing pulmonary, cardiac or neurologic disease.

Those children who re-admitted after the initial ER management and discarged on the same day were not included in the study.

Results

Introduction and key objectives

Data for the study was collected over the period December 2013 to August 2015 by me as a single observer.

They key objectives of the study were:

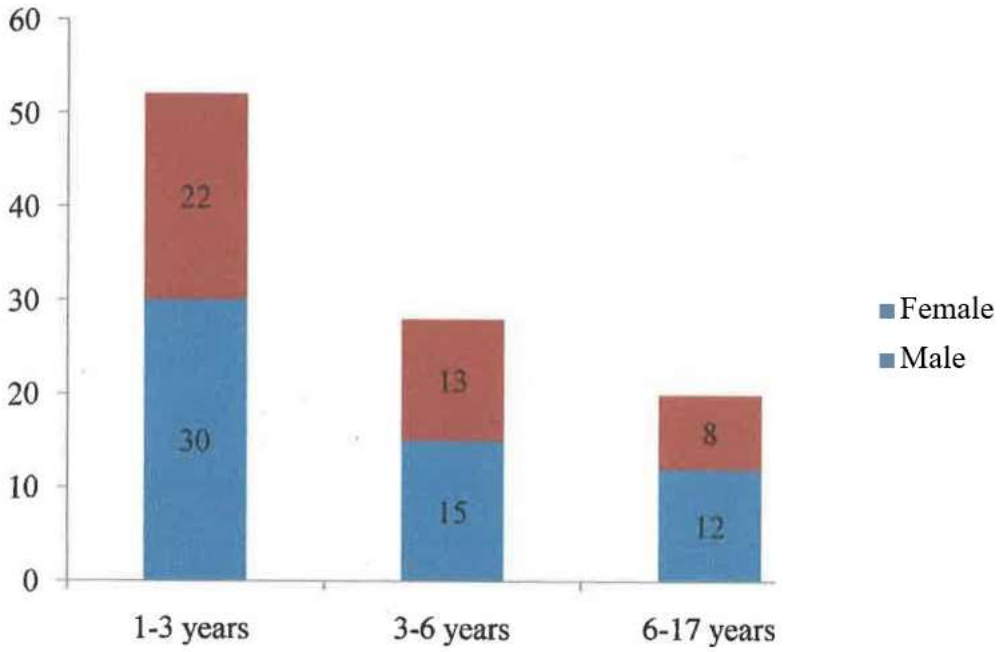
a) To evaluate the usefulness of PRAM score in assessing the severity and outcome of an acute exacerbation of wheeze in children aged 1-12 yrs (H2).
b) To identify the PRAM score predicting the need for hospitalization and ICU care.

The following commentary in this section presents the data collected and analyze the data set. That is followed by results of statistical analyses undertaken to prove whether PRAM scores meet the objectives that have been set out above.

Age and sex distribution of the sample

52% of patients were between the ages of 1-3 years, 28% between the ages of 3-6 years and 20% between the ages of 6-12 years.

57% were male patients and 43% were female patients.



Graph 1: Age and sex distribution

Distribution of asthma severity in our study

In our study moderate persistent asthmatics were the maximum number studied (39%).

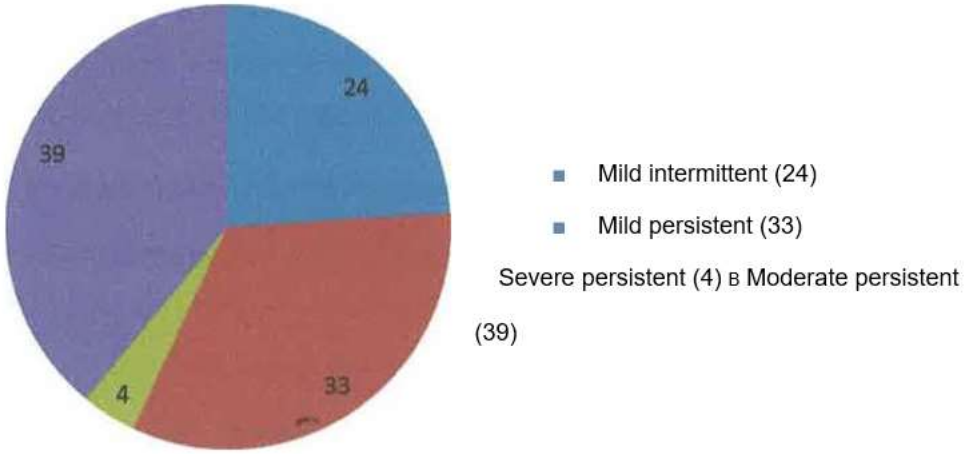


Figure 2: Distribution of asthma severity

PRAM scores by severity classification

Asthma severity	No. of patients	Mean initial PRAM scores	Standard deviation	P value between groups
Mild intermittent	29	5.36	2.69	
Mild persistent	33	6.72	2.31	0.003
Moderate persistent	39	6.99	2.33	
Severe persistent	4	11.00	1.00	

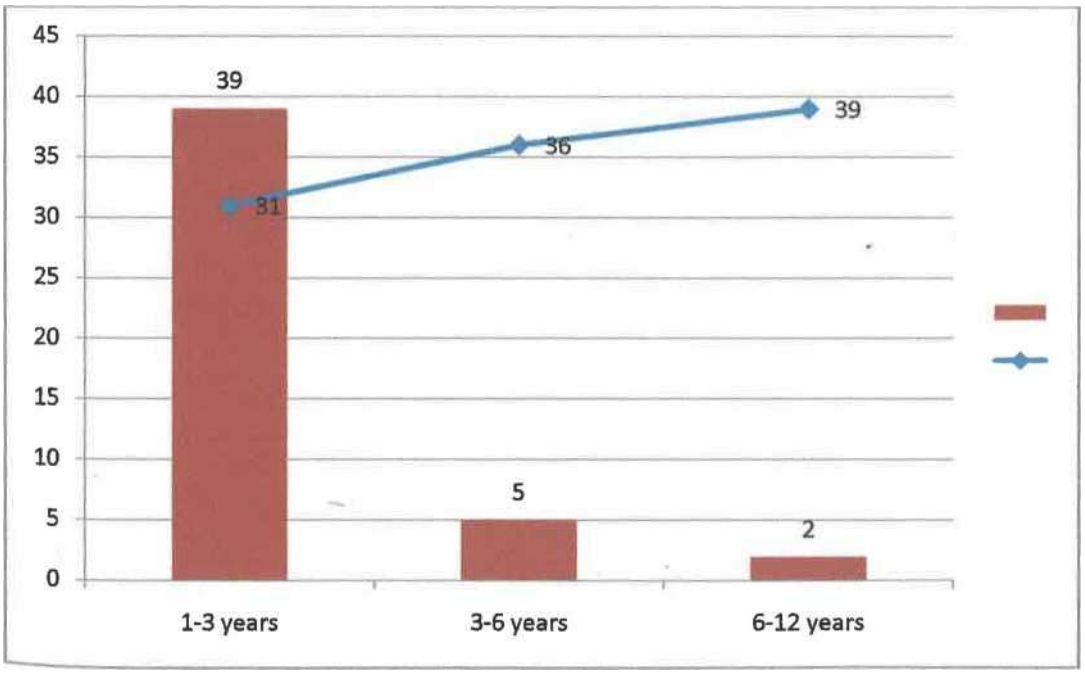
Table 16: PRAM scores by severity classification

From the above table it can be seen that there is a correlation between asthma severity and the mean initial PRAM scores. It was found that patients with severe persistent asthma had high initial PRAM scores when compared to other groups. This correlation should be seen as an incidental observation

and more likely underscores the fact that the patients with severe asthma in our study had uncontrolled asthma.

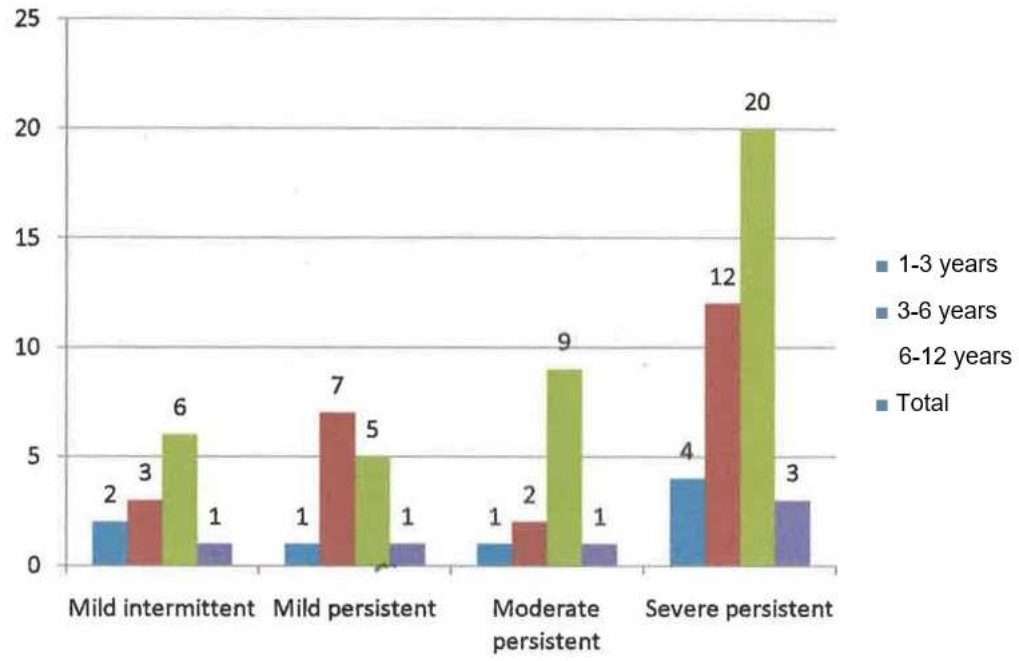
Patients with past history of wheeze

Of the total no of 100 patients studied, 62(62%) were known asthmatics and 38(38%) had previous history of wheeze responding to bronchodilation. Among the patients with previous history of wheeze maximum number of patients 78% were in the 1-3 year age group



Group 3: Patients with past history of wheeze

Patients Using Metered Dose Inhalers and Their Compliance

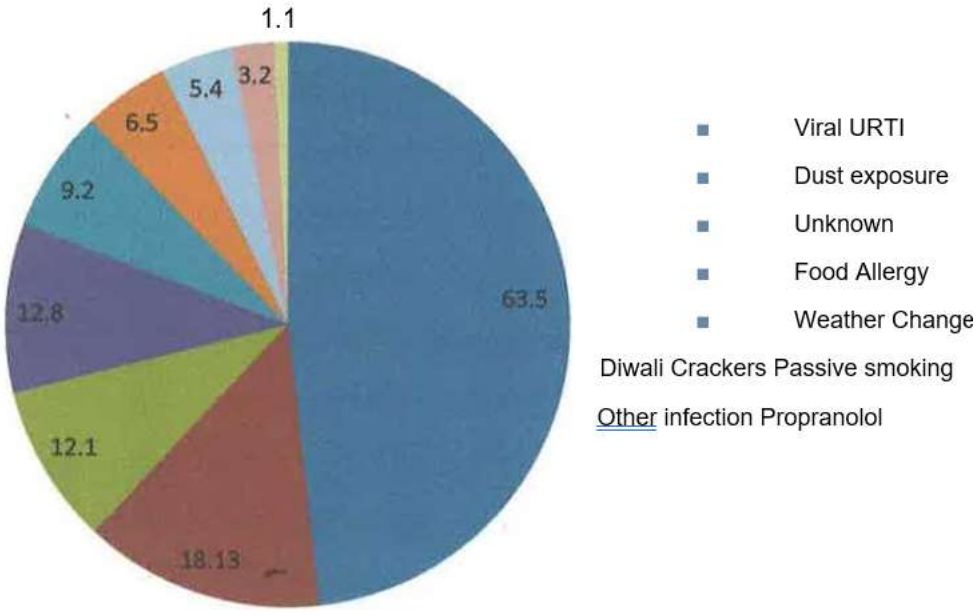


Group 4: Patients using MDI and their compliance

62% (39) of the known asthmatics were using MDT with 54% having good compliance according to the data collected in the study.

Common trigger factors

The common trigger factors leading to exacerbation of wheeze was studied.



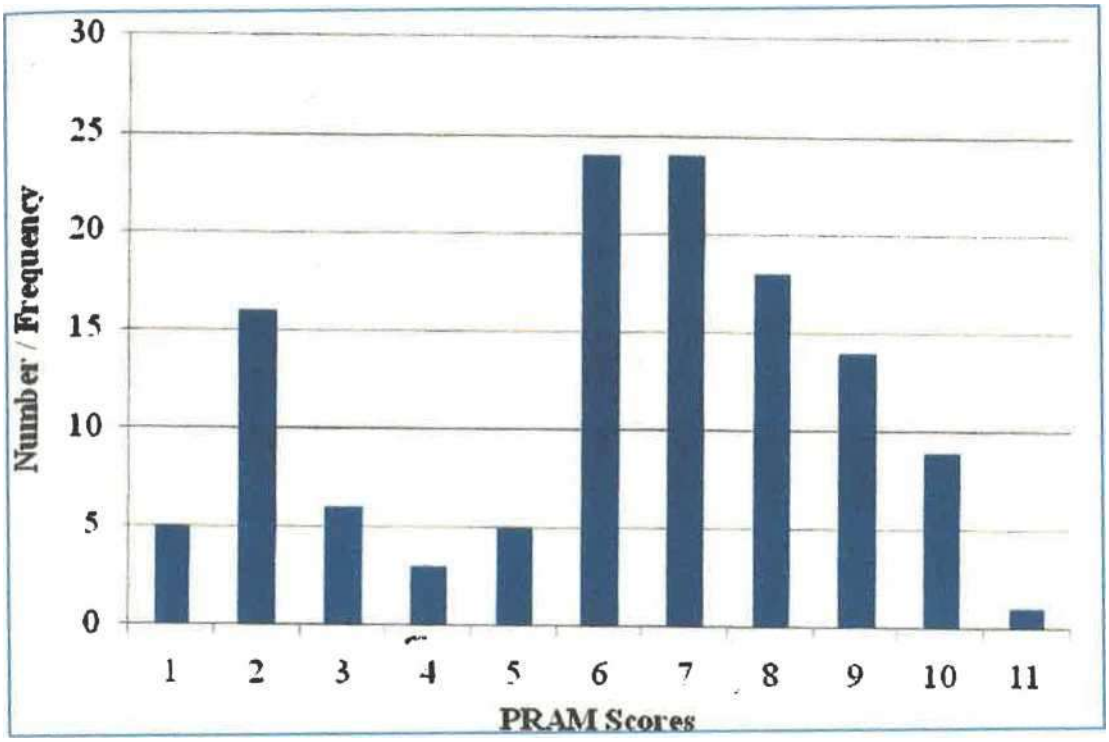
Group 5: Trigger factors

The most common trigger according to our study was viral upper respiratory tract infection (63.5%) followed by exposure to dust (18.13%).

Number of patients with family history of asthma, atopy, allergic rhinitis, etc

59.1% of patients had a positive family history according to our study.

Frequencies of Scores Observed in Our Study

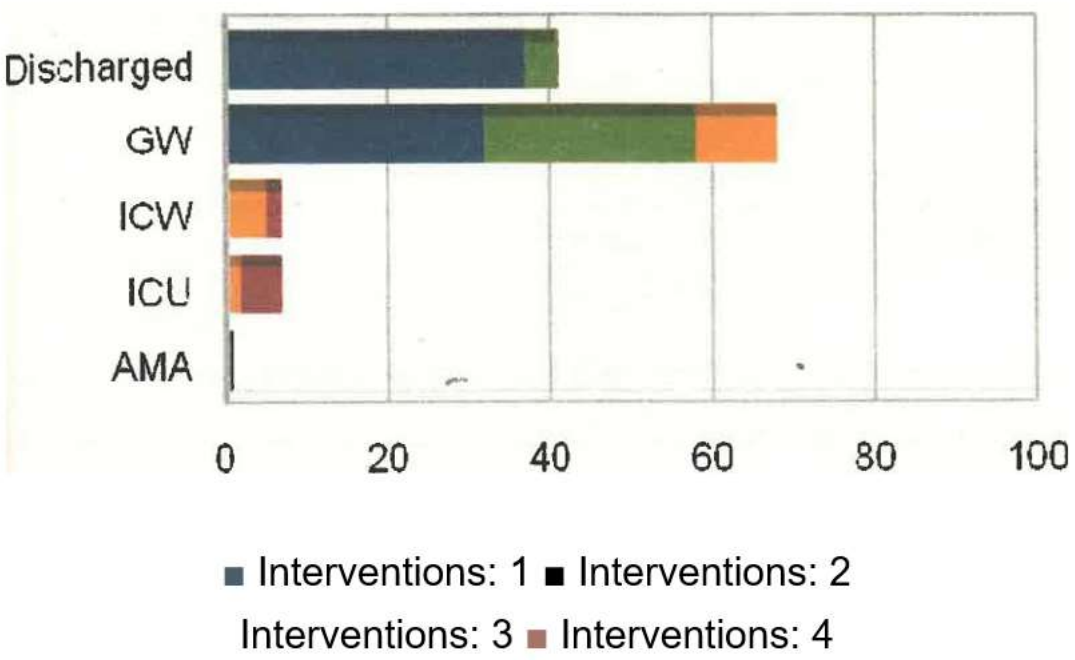


Graph 6: Frequencies of scores observed

The maximum number of patients were seen with PRAM scores of 6 and 7 (19.0%) in our study.

Outcomes of ER management

In our study of 100 patients, 32 were discharged from the ER after treatment, 52 were admitted to the general ward, 5 were admitted in the ICW (Intermediatry care ward) 6 were admitted to the ICU (Intensive care unit) and 5 patients discontinued treatment against medical advice (AMA).



Graph 7: Outcomes of ER management

Outcome	No. of patients	No. of interventions			
Discharged	32	29	3	-	-
General ward	52	22	23	8	-
ICW	5	-	-	4	1
ICU	6	-	-	2	4
AMA	5	5	-	-	-

Table 17: Outcomes of ER management

Interventions in the ER - nebulisationwithb2 agonist + anticholinergics, oral / iv steroids, iv management sulphate, subcutaneous terbutaline.

As can be seen from th?‘above table, patients who were admitted to the ICU had the maximum number of interventions given before shifting to ICW/ICU. Most discharged patients were sent home after 1 or 2 interventions. The table below presents a more detailed overview of PRAM scores and outcome of ER management at different stages / numbers of intervention.

	Count	Avg.Initial PRAM	TA 1 PRAM	TA 2 PRAM	TA 3 PRAM	TA 4 PRAM
ER	100					
Stages						
Discharge	29	3.86	1.36			
AdmGW	22	5.75	3.72			
Adm	1	8.00	6.00			
Adm	**0**	-	-			
LAMA	2	7.50	6.00			
Stage 1	**58**	**4.86**	**2.62**			
Discharge	3	6.25	3.50	0.67		
AdmGW	22	7.31*“-	5.96	4.81		
Adm	1	10.00	9.00	6.00		
Adm	1	12.00	11.00	11.00		
LAMA	2	8.00	6.50	6.00		
Stage 2	**25**	**7.44**	**5.94**	4.73		
Discharge	0	-	-	-	-	
AdmGW	7	9.00	7.86	6.86	5.57	
Adm	5	8.80	7.60	7.20	5.80	
Adm	5	9.80	9.20	9.20	7.80	
LAMA	0	-	-	-	-	
Stage 3	**14**	**9.18**	**8.18**	7.65	**6.29**	
Discharge	**0**	-	-	-	-	-
AdmGW	3	9.00	6.67	7.00	5.67	5.33
Adm	**0**	-	-	-	-	-
Adm	1	10.00	10.00	10.00	8.00	7.00
LAMA	**0**	-	-	-	-	-
Stage 4	**5**	**9.25**	**7.50**	7.75	**6.20**	**5.75**

Table 18: Outcomes of ER management with PREM scores

TA 1 - nebulisation with |32 agonist = anticholinergics

TA 2 - oral / iv steroids.

TA 3 - iv magnesium sulphate

TA 4 - Sc terbutaline.

Stage 1- patients received TA 1 only

Stage 2- patients received TA 1 and TA 2 only

Stage 3- patients received TA 1. TA and TA3 only

Stage 4- patients received TA 1, TA 2, TA 3 and TA 4.

As can be seen from the above table of the total of 100 patients, 28 had one intervention, 14 had three and 5 patients have four.

1. The PRAM scores of the 56 patients who were administered just one intervention dropped from an average of 4086 to 2.62 after the intervention.
2. The PRAM scores of the 25 patients who were administered just two intervention dropped from an average of 7.44 to 5.94 (1st intervention) and then to 4.73.
3. The PRAM scores of the 14 patients who were administered just three intervention dropped from an average of 9.18 to 8.18 (1st intervention) to 7.65 (2st intervention) and 6.29 (3rd intervention)
4. The PRAM scores of the 4 patients who were administered just four intervention dropped from an average of 9.25 to 7.5 (1st intervention) to 7.75 (2st intervention) and 6.25 (3rd intervention) and 5.75 (4th intervention)

Those patients who requires lesser number of intervention and those who responded to the treatment administered (lower observed PRAM scores) on average were either discharged or admitted to general ward. While those patients who failed to respond to the ER treatment (PRAM scores remain high) on average needed higher level of care and were admitted to the ICW / ICU. While these results broadly tend to show the utility of PRAM scores as a tool predicting asthma severity, in later sections we test the same data using statistical analyses to infer whether these observed correlations stand up to acceptable statistical testing.

Statistical Testing and Analyses

At the beginning of this chapter, the key objectives were identified. In this section on statistical testing and analysis, we test the data for the following:

a) Is the PRAM score an effective tool across the three identified age groups, i.e., does the tool remain unbiased with of the patient in identifying the severity of asthma?

Distribution of Scores Across Age Groups

The patients included in the study were divided into 3 age groups: 1-3 years, 3-6 years, 6-12. The initial PRAM scores across the 3 age group were as follows:

Age Groups	No of patients	Mean Initial scores
1-3 yrs	52	5.79
3-6 yrs	28	6.63
6-12 yrs	20	7.00
Total	100	6.27

Table 19: Distribution of scores across age groups

It is not expected that the scores recorded should very meaningfully across the different age groups. But from a quick glance at the above data, an increase in the mean values of initial examination PRAM scores is observed. We have used the single factor of variance (ANOVA) to answer the question whether the observed differences in the mean values of the three different age groups are meaningful (i.e.. are they statically significant?)

ANOVA identifies whether sufficient evidence is there to say that PRAM scores of one age group differ significantly from at least one other.

We use the single factor ANOVA in our testing (single factor here is the age group)

Anova: single factor

Summary

Groups	Count	Sum	Average	Variance
1-3	52	382	5.181879	7.862005
3-6	28	232	6.628571	5.799748
6-12	20	182	7	5.52

Anova

Source of variation	Ss	Df	MS	F	p-value	F crit
Between groups	33.69591	2	16.84795	2.471772	0.088587	3.069286
Within groups	845.2017	124	6.816143			
Total	878.8976	126				

Table 20: ANOVA for Initial PRAM scores for age groups

We have used the observed initial examination PRAM scores for the 100 patients ahd rum the single factor ANOVA test. The questions being asked is whether the observed differences in the means (average PRAM score at initial examination) of the three different age groups are meaningful.

In statistical language we propose a 'null hypothesis' that states that the three means are equal

Mean of group l-3yrs = mean of group 4-6yrs =mean of group 6-12yrs

From the above table, P-valus is 0.90 which is greater than 0.05 (the 5% significance level that we have chosen), which is interpreted to the null hypothesis that all means are equal stands.

The observed F* value is less than f critical and hence again the null hypothesis stands and is valid.

In summary, the null hypothesis that the means of the three groups are the same and the observed increasing trend with age groups ((table 6-4: distribution of scores across age groups) is not statistically

meaningful. This answers the first key objective of whether the PRAM score is a tool that can be used across different ages.

a) In the below section we analyse statistically whethwr PRAM scores can be used assess the severity of asthma?

Distribution Of Scores Across Discharged And Admitted Groups Of Patients

The initial PRAM scores (shown in the 3 age groups for convenience) in the discharged and the admitted patients are compared to understand if there are any meaningful inferences that can be made. The basic data set is shown below: F value is a ratio. It is the ratio between the "variability observed in the group due to the ages of the patients" to the "variability within groups due to random errors"

Age group	No of patients	Mean Initial scores	Standard deviation	Standard Error	P value within & between groups
Discharged patients					
l-3yrs	16	3.5	2.090	0.47	0.10
3-6 yrs	8	4.0	2.366	0.71	
6-12 yrs	8	54	2.413	0.76	
Total	32	4.1	2.322	0.36	
Admitted patients					
1 -3 yrs	32	6.7	2.548	0.39	0.04
3-6 yrs	19	7.8	1.154	0.241	
6-17 yrs	15	8.0	1.713	0.428	
Total	64	7.3	2.150	0.237	

Table 21: PRAM scores for discharges and admitted patients

The mean initial PRAM scores of discharged patients in all the 3 age groups varied between 3.5 and 5.4 and the average of the entire set of discharged patients (32 patirnts) is 4.1.

The mean initial scores of admitted patients in all the 3 age groups varied between 6.7 and 8 and the average PRAM score for admitted patients (64 patients) was 7.3.

We run a statistical test to understand whether the observed difference in the initial examination pram scores of discharged patients and patients who were admitted are meaningful. Like before we begin with the null hypothesis that:

• Mean of discharged group = mean of admitted group

Anova : Single Factor **Initial PRAM**

Summary

Groups	Count	Sum	Average	Variance
Discharged Initial PRAM Score	32	168	4.1	5.39
Admission Initial PRAM Score	64	597	7.28	4.62

Anova

Source of variation	Ss	Df	MS	F	p-value	F crit
Between groups	176.91	1	276.91	56.78	9.80X10’^{12}	3.92
Within groups	590.16	121	4.88			
Total	867.07	122				

Table 22: ANOVA for discharged and admitted patients

From the above table, p-value is very low (9.80X10'12) which is lesser than 0.05 (the 5% significance level that we have chosen), which is interpreted to the null hypothesis that the means of the two groups are equal has to be rejected.

The observed F value is greater than F critical and hence again the null hypothesis is invalid.

In summary, the null hypothesis that means of the two groups, admitted and discharged patients are the same is rejected and the observed difference in PRAM scores on initial examination is statistically

meaningful. This answers the second key objective of whether the PRAM score is a tool that can be used to assess severity of asthma.

b) In the next section, we try and assess whether the PRAM score can be used to differentiate between patients who were discharged, those who were admitted in the general ward those who require a higher level of care(i.e. ICU and ICW)

Comparison of Initial Pram Scores with Observed Outcomes - Discharged, General Ward and ICU/ICW

Outcome	No of patients	Mean Initial scores
Discharged	32	4.10
General ward	52	6.82
ICE	5	8.86
ICU	6	10.14

Table 23: PRAM scores of patients with different outcomes

This table shows that the initial scores varied with severity at presentation to the ER. Patients with severe exacerbation who did not improve with treatment needing ICU care had high score (10.14) when compared to discharged patients who had a less severe exacerbation which improved with treatment (mean score 4.1)

We run a statistical test to understand whether the observed difference in the initial examination PRAM scores of discharged patients and patients who were admitted are meaningfukLike before we begin with the null hypothesis that:

Mean of discharged group = mean of general ward group = means of ICW/ICU group

General ward and ICU/ICW patients

Anova: Single Factor IE PRAM

Summary

General ward and ICU/ICW patients		General ward and ICU/ICW		General ward and
Anova: Single Factor	IE PRAM	Anova: Single Factor	IE PRAM	Anova: Single
SUMMARY		SUMMARY		SUMMARY
General ward and ICU/ICW patients		General ward and ICU/ICW patients		General ward and ICU/ICW patients

Anova

Source of variation	**Ss**	**Df**	**MS**	**F**	**p-value**	**F crit**
Between groups	360.08	2.00	180.04	42.61	0.00	3.07 11 j
Within groups	506.99	120.00	4.22			
Total	867.07	122.00				

Table 24: ANOVA for Discharged

From the above table, p-value is very low (9.80X1 O'12) which is lesser than 0.05 (the 5% significance level that we have chosen), which is interpreted to the null hypothesis that the means of the two groups are equal has to be rejected.

The observed F value is greater than F critical and hence again the null hypothesis is invalid.

In summary, the null hypothesis that means of the two groups, discharged patients, patients admitted to general ward and patients to ICW/ICU are the same is rejected and the observed difference in PRAM scores on initial examination is statistically meaningful. This answers the second key objective of whether the PRAM score is a tool that can be used to assess severity of asthma and we can safely conclude that the tool effective to differentiate between case that require a higher level of care as wall.

Comparison Of Scores After Initial Bronchodilatation Across Different Outcome Groups

Outcomes	Mean initial score	Standard deviation	P value between groups	Mean scores after treatment	Standard deviation	P value between groups
Discharged	4.09	5.3	0.000	1.5	2.7	0.000
Admitted	7.28	4.62		5.7	6.7	

Table 25: Change in scored after initial bronchodilatation

This table shows the change in PRAM scores after initial nebulisation. 60% change in scores after initial nebulisation was seen in the discharged group when compared to the 22.3% in the admitted group. The mean scores after treatment in the discharged group was 1.5 when compared to 5.7 in the admitted group continued to require further treatment.

We can run same test again on the observed PRAM scores after initial bronchodilatation (stage 1).

Anova : Single Factor stg 1 Exam

Summary

Groups	Count	Sum	Average	Variance
Discharged Initial PRAM Score	31	63.00	1.58	2.76
Admission Initial PRAM Score	63	469.00	5.72	6.75

Anova

Source of variation	Ss	Df	MS	F	p-value	F crit
Between groups	461.81	1.00	461.81	84.69	0.00	3.92
Within groups	654.32	120.00	5.45			
Total	1.116.13	121.00				

Table 26: ANOVA for discharged and admitted patients (after bronchodilatation)

From the above table, p-value is very low (1.3X1 O'15) which is lesser than 0.05 (the 5% significance level that we have chosen), which is interpreted to the null hypothesis that the means of the two groups are equal has to be rejected.

In summary, the null hypothesis that the means of the two groups, admitted and discharged patients are the same is rejected and the observed difference in PRAM scores on initial examination is statistically meaningful. This test again supports the test on initial examination PRAM score. The scores at this stage post 1st intervention probably have a higher level of patients that are admitted. Again, the test answers the second key objective of whether the PRAM score is a tool that can be used to assess severity of asthma.

Comparison of Disposition Scores with Outcomes Observed

The disposition score here refers to the PRAM score measured at the end of treatment in ER, prior to the outcome of discharge or admission. Mean scores at sisposition of patients admitted in general ward was 5.3 = 2.08 (mean = std. dev) compared to disposition scores of discharged patients which was 1.59 = 1.68 with a significant p value of < 0.0001.

Receiver operator curve (ROC) analysis-

The ROC curve was used to identify a disposition score above which most patients were admitted. According to our study a score of 5.5 and above had 89% sensitivity and 64% specificity for admission. So a score of 5.5 was taken as a predictor for admission. *- Area under curve was 0.83 with a standard error of 0.038.

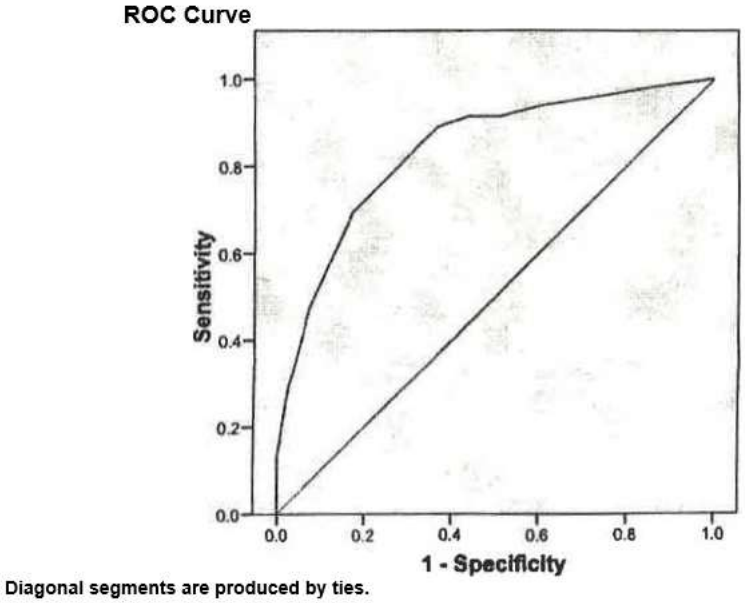


Figure 8: ROC Curve

+if>**	Sensitivity	1 -sqecificity
0.00	1.000	1.000
1.50	0.988	0.902
2.50	0.939	0.610
3.50	0.915	0.512
4.50	0.915	0.439
5.50	0.890	0.366
6.50	0.695	0.171
7.50	0.476	0.073
8.50	0.293	0.024
9.50	0.134	0.000
10.50	- 0.024	0.000
11.50	0.012	0.000
13.00	0.000	0.000

Table 27: Co-ordinates of the curve: test result(s) variable IE PRAM scores

** the test result variable(s); initial examination PRAM score hat at least one tie between the positive actual state group and negative actual state group. The smallest cut-off value ia the minimum observed test minus 1, and the largest cut-off value is the maximum observed test plus 1. All the other cut off values are the averages of two consecutive ordered observed test values.

Similarly children with initial PRAM score of 8.5 and above had a 100% sensitivity and 85% specificity for ICU admission according to ROC curve analysis. Area under curve was 0.96 with a standard error of 0.021.

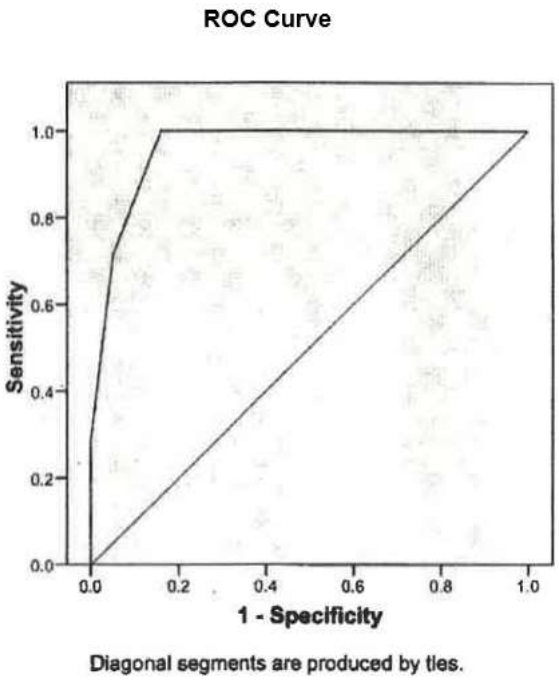


Figure 9: ROC curve

+if>**	Sensitivity	1-sqecificity
0.00	1.000	1.000
1.50	1.000	.958
2.50	1.000	.825
3.50	1.000	.775
4.50	1.000	.750
5.50	1.000	.708
6.50	1.000	.508

7.50	1.000	.308
8.50	1.000	.158
9.50	.714	.050
10.50	.286	.000
11.50	.143	.000
13.00	.000	0.000

Table 28: Co-ordinates of the curve: test result(s) variable IE PRAM scores

** The test result variable(s); initial examination PRAM score hat at least one tie between the positive actual state group and negative actual state group. The smallest cut-off value is the minimum observed test minus 1, and the largest cut-off value is the maximum observed test plus 1. All the other cut off values are the averages of two consecutive ordered observed test values.

The PRAM score obtained from the ROC curve analysis helps to alert the ER physician about the severity of airway obstruction and the possible need for ICU admission.

Changes in scores with treatment

In this section we analyzed the responsiveness of the PRAM score to change. Responsiveness refers to changes over time with in patients. With the use of treatment of known efficacy (nabulisation with bronchodilators, steroids) change in scores with treatment is assumed to be a clinically relevant change.

Change in scores with treatment in the different outcome groups was analyzed using paired t test.

TA 1 - initial bronchodilatation 02 agonist = anticholinergics

TA 2 - oral / IV steroids.

TA 3 - intravenous magnesium sulphate

TA 4 - Subcutaneous terbutaline.

Discharged patients:

	Mean scores	Std deviation	P value between groups
Pre-treatment	4.00	2.294	
TA 1	1.59	1.681	.000
TA 2	1.00	.816	.025

Table 29: Change in scores with treatment in discharged patients

41 patients who improved with initial bronchodilatation and steroids were discharged in our study. The mean initial score of these patients was 4.0 and with treatment improved to 1.0 the change in scores with treatment was found to be statistically significant (p value .025).

General ward patients:

	Mean scores	Std deviation	P value between groups
Pre-treatment	6.82	2.022	
TA 1	5.12	2.366	.000
TA 2	5.64	1.502	.000
TA 3	5.64	1.502	.000

Table 30: Change in scores with treatment in discharged patients

Most patients admitted in general ward required 2 or 3 treatment interventions with marginal improvement in wheeze requiring hospitalizations. The mean PRAM scores initially was 608 and following treatment was 5.6 showing that the patient continued to have clinical signs needing continuing treatment. Statistically also the difference in the group was found to be significant.

Discussion

Accurate assessment of the severity of asthma exacerbation is an important guide to initial treatment and to monitor the response to subsequent therapy. Pulmonary function tests can provide reliable and objective information on the severity of airways obstruction but require cooperation and may not be feasible in young children **[**7**]**. Further, pulmonary function test are difficult to perform at the primary care level.

Pediatric asthma scores, consisting of a combination of clinical symptoms and signs, are frequently used to estimate the severity of acute airways obstruction, to guide treatment decisions, and to evaluate treatment results. Van der Windt et al8 in a review of literature on clinical'asthma scores found 16 different scores. They found that most scores were designed in an ad hoc manner based on clinical experience and face validity only. Information on clinimetric properties of the scores in terms of reliability, validity, and responsiveness was scarce.

The evolution of a clinical scoring system is done based on the properties of the score like reliability, reproducibility **[**47**]**. The study of these clinimetric properities is not without pitfalls. There appears to be little consensus in the literature regarding definitions and methods, especially concerning responsiveness.

Kischner and Guyatt **[**49**]** and Guyatt et al **[**50**]** defined responsiveness as the ability to detect a clinically important change over time. Responsiveness refers to changes over time within patients, whereas validity or reliability usually refers to cross- sectional differences between patients. Reliability refers to cross-sectional differences between patients. Reliability refers to the degree of inter-rater correlation of scores.

Validity refers to the internal consistency (degree to which each individual item contributes to the score) and predictive validity (ability of scores to predict outcome). A variety of statistical methods have been described for the assessment of responsiveness, including receiver operating characteristic curves, responsiveness rations, size etc.

In the evolution of asthma scorce, several external criteria for asthma severity have been used, including pulmonary function (forced oscillation techniques), a treatment of known efficacy, and an general judgment of severity by professionals. The pulmonary function tests are difficult to perform in children less than 5 years of age. A general clinical judgment may not be the best option, because clinical signs and symptoms that make up the score will also form an important part of the general evaluation. In the treatment of known efficacy (nebulized bronchodilators, oral or intravenous steroids)

approach, improvement in asthma score after therapy is assumed to be a clinically relevant change. If this change can be detected over the random measurement error, the asthma score is considered to be responzxive **[**47**]**

Final, clinimetric properties of a scorce depends on the setting and patient population in which the study was conducted. The properties should be analyzed in all age groups and in patients with different severity of asthma

Some of the clinical scores validated include -

1. Paediatric Respiratory Assessment Measure (PRAM)
2. Clinical Asthma Score (CAS)
3. Asthma Severity Scale (ASS)
4. Pulmonary Index (Pl)
5. Pulmonary Score (PS)
6. Modified Pulmonary Index Score (MPIS)
7. Peadiatric Astma Severity score (PASS)

Characteristics of validated paediatric asthma score:

Score	Population Characteristics	Validity construycts
Asthma severity scale	6mo - 12yrs setting-ER N=60	Physician severity of of judgement Oxygen saturation PEFR
Clinical Asthma Score	1-5 yrs Setting - inpatients N=30	Hospital length of stay Drug dosage interval Change in scores from admission to discharge
Peadiatric Respiratory Assessment Measure	2-12yrs Setting - ER N=964~.	Change in scores with treatment Correlation of scores with ER outcome
Pulmonary Index	6-12yrs Setting - ER N=40	Spirometry ER disposition Change in scores with treatment
Pulmonary Score	5-12yrs Setting - ER N=46	PEFR Change in scores with treatment

Modified Pulmonary Index Score	5-12 yrs setting — inpatients N = 30	Correlation of scores to ICU admission Hospital Length of stay Drug dosage interval
Peadiaric Asthma Severity Score	1-12 yrs setting - ER N (ER 1) =852 N(ER2) = 369	PEFR Oxygen saturation Correlation with ER outcome

Validated paediatric asthma scores

Ducharme FM et al**[**11**]** introduced the preschool respiratory assessment measure (PRAM). Was developed by relating prtentially relevant items, such as wheezing and retractions, to a measure of pulmonary function (espiratory resistance), in children aged 3-6 yrs. The validation constructs of PRAM studied were resistance to forced oscillation, clinician and parent severity judgments, and change in score correlation with change in resistance to forced oscillation"

Subsequently the preschool respiratory assessment measure was evaluated by

Ducharme FM et al across all age groups and found to be reliable, responsive and valid. They suggested that the score could be called as paediatric respiratory assessment measuree **[**9**]**.

In our study we evaluated the properties of PRAM score in 6-12 years in the ER setting with a sample size of 100. Patients with varying severity of exacerbation of wheeze were included. The responsiveness and validity of the score was assessed.

The inter-rater reliability was not assessed.

Comparison With Other Studies

Mean age

Mean age of children included in our study was 3.002+ 2.64 which was lower than other comparable studies. In the PRAM study by Ducharme dt al **[**9**]** the mean age was 5.8 PASS study by Gorelick et al **[**37**]** mean age was 7.0 and 5.9 and in the MIPS study by Caroll et al36 the mean age was 7.0.

Sex

Male children predominated in our stue (57%) which was similar to the PASS \ study (60%)**[**37**]** and the PRAM study (63%)**[**9**]** whereas female children predominated in the MPIS study (60%) **[**37**]**.

Chronic asthma severity

Our study had maximum number of children with moderate persistent asthma (39%) which was comparable t the study by Scribano VP et al **[**51**]** (51%) The PASS study37 had more number of children with mild intermittent asthma (66%).

MDI use and compliance

Our study showed 62% of asthmatics using MDI with 54% having good compliance. This was similar to the PASS study which had 78% of children using MDI **[**37**]**.

No of children studied and outcomes

In our study 32% of patients studied were discharged and 68% were admitted. Among the patiets admitted, 80°/^jvere admitted in the general ward, 10% in ICW and another 10% in ICU. The greater percentage of admitted patients in our study reflects a increased severity of airway obstruction studied. This helps to study the ability of PRAM scores to assess the severity.

The distribution of patients in the ED2 of PASS study by Gorelick et al **[**37**]** had 38% discharged and 62% admitted, which was similar tour study. In the Scribano VP et al study of pulmonary score the distribution of patienbts was discharge 38% general ward 38%, ICU 24% **[**51**]**.

Validity of scores across all the age groups

In our study the PRAM scores in the different outcome groups across the studied age groups was analysis using Analysis of Variance (ANOVA) and the p value was found to be statistically noOt significant not significant implying that no difference in scores in tea e groups was observed. The PRAM scores were found to be valid across all age groups (1 -12yrs)

The PRAM study by ducharme FM et a![9] found a similar association between scores and the admission rate in both preschool (2-6yrs) and school age (7-12yrs) children with r value of 0.37 in preschool and 0.43 in school age children.

Predicative validity

In our study percentage of admitted patients with scores of 0-3, 4-7, 8-12 was 8.5%,43.9%, 47.6% respectively implying that maximum numbers of admitted patients had score of 8-12. Similarly the maximum number of admitted patients had score 0-3. The PRAM scores of different outcome groups was also analysed by ANOVA in our study and found to have significant p values showing the predictive validity of the score.

Predictive in the Ducharme et al[9] study of PRAM score found a strong association between rate PRAM score (r=0.4,P<0.0001). The association was stronger with scores after initial bronchodilatition. Similar results were found in our study when scores after bronchodilation where compared in different outcome groups.

ROC analysis of our scores showed a score of 5.5 and above had maximum sensitivity and specificity for admission. Area under curve (AUC) was 0.83. The Ducharme et al study had a similar AUC for admission (0.78) [9]

In the PASS atudy by Gorelick et al37 the AUC for admission was 0.82.

Robidas J et al40 in a study comparing the PRAM and PASS in the same patients found AUC for admission was 0.59-0.79 in PREM and 0.6-0.8 in PASS.

Responsiveness of score:

In our study the change in scores with each of the treatment given in the ER was analysed to assess the responsiveness. The change in scores with initial mobilization, steroids, magnesium sulphate, terbutaline administration was found to have statistically sinnificant P vales.

In our study discharged patients had a 60% change in scores after initial bronchodilatation in comparison to 22.3% in admitted patients. The change in scores was maximal in the discharged group reflection the ability of the scores to respond to change (improvement). Our results were similar to

results of the PASS study where Gorelick et al[37] found a 51-79% change in scores in the discharged patients in comparison to 25-32% in the admitted patients.

The robidas et al[40] study found a 26.7% increase in PREM scores and 26.9% in PASS scores after initial bronchodilatetion. Our study showed similar results with a 29.8% increase in PRAM scores. The PRAM scores showed both discriminative and responsive properties.

Predictive validity for ICU admission:

In our study a score of 8.5 and above had 100% sensitivity and 85% specificity for ICU admission. In the MPIS study by carol CL et al a score of 12 was identified as a cut off for ICU admission.

	PRAM score	**PASS score**
Clinical parameters	Suprasternal retractions, scalene retraction, air entry, wheeze, oxygen saturation total range (0-12)	Degree of wheeze, work of breathing prolongation of expiration. Total range (0-6)
No of cases	100	ED 1-852 ED2 -369
Age	4.0 = 2.8	ED 1-7.0= 4.3 ED 2-5.9+ 4.3sss
Gender	Male -58%, female -42%	Male -60%, female -40%
Chronic asthma severity	Mild intermittent - 24%, Mild persistent - 33%	Mild intermittent - 44%, Mild persistent - 22%
Disposition ,	-Admitted - 67% Discharged - 33%	EDI ED2 Admitted 32% 62% Discharged 68%
Mean initial scores	Admitted - 7.2 Discharged - 4.0	Admitted-3.0 Discharged - 0.5
ROC analysis for admission	Area under curve (AUC) - 0.83	AUC-0.82
Change in scores with initial bronchodilatation	Discharged - 60% Admitted - 22.3%	Discharged - 51 -79% Admitted - 25-32%
Inter observer variability	Not studied	Highly reliable among different observers

Comparison of our study with the PASS study [37]

References

1. Global burden of asthma. Developed for global initiative fir asthma available from www. Ginasthma. Org

2. Global initiative for asthma (GINA). Global strategy for asthma management and prevention 2008 (update). Available from www.Kinasthma.org

3. Guglani L, Lodha R$, Kabra SK. Epidemiology, risk factors and natural history of asthma. In Kabra SK, Lodha R, eds. Essential pediatric pulmonology. 1st ed. Delhi; noble vision 2006; 123-143.

4. Lin ah, Covar RA, Spahn DJ, Leung DY. Childhood asthma, nelson textbook of paediatrics, 15th edition; chapter 143:953-970.

5. Ducharma FM, Davis GM. Measurement of respiratory resistance in the emergency department: feasibility in young children with acute asthma. Chest 1997;111:1519-25.

6. Canny GJ, Reisman J, Healy R, Schwartz C, Petrou C, Rebuck AS, et al. acute asthma: observation regarding the management of a pediatric emergency room. Peadiatrics 1989;507-12.

7. Gorelick MH, Stevens MW, Schultz T, Scribano PV. Difficult in obtaining peak expiratory flow measurements in chidren with acute asthma. Pediatr Emerge care 2004.

8. Van Der Windt DA, Nagelkerke AF, Bouter LM, Danker-Roelse JE, Veerman AJ. Clinical scores for acute asthma in pre-school children. A review of the literature .J clin epidemiology. 1994;635-46.

9. Ducharme FM, Chalut D, Plotnick L, Savdie C Kudirka D, Zheng X Meng L, Mcgillivray D, the pediatric respiratory assessment measure: a valid clinical score for assessing scute asthma severity from saddlers to teenagers: J pediatr. 2008 apr: 152(4): 476-80

10. Birlen CS, Parkin PC, Macarthur C. asthma severity, validity, and responsiveness. J clin epidemiology 2004;57:117-81.

11. Chalut DS, DUcharme FM, Davis GM. The preschool respiratory assessment measure (pram): a responsive index of acute asthma severity, J pediatrics 2000, 137: 762-8.

12. Asher MI, Montefort S, Bjorksten B, CK, Strachan DP, weiland SK, Williams h. worldwide time trend in tfie prevalence of sympotoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases one and three repeat multi-country cross-sectional surveys. Lancet. 2007 sep 29;370(9593): 1128.

13. Paramesh H. the epidemiology of asthma in India. India j pediatr. 2002 apr; 69(4): 309-12.

14. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjuctivitis and atopic eczema: ISAAC. Lancet 1998;351:1225-32.

15. Shah JR, amdekar YK, Mathur RS. Nationwide variation in prevalence of bronchial asthma- (part of the international study of asthma and allergies in childhood - ISAAC)Indian J med sci 200;54:213-20

16. Chaoying L, Feekery C. Can Asthma Education Improve Clinical Outcomes? An Evaluation of a Pediatric Asthma Education Program. Jounal of Asthma 2001;38:269-278.

17. Holloway JW, Beghe B, Holgate ST. The genetic basis of atopic asthma. J Allergy Clin Immunology 1999;29(8): 1023-32

18. Wiesch DG, Meyers DA, Bleecker ER. Genetic basis of asthma. J allergy Clin Immunology 1999; 104(5):895-901.

19. Bouzigon E, Siroux V, Dizier MH, Lemainque A, Scores of asthma and asthma severity reveal new regions of linkage in EGEA study families. Eur respire J 2007;30:253-25.

20. Shore SA, Fredberg JJ. Obesity, smooth muscle, and airway hyper responsiveness.

J Allergy Clin Immunol 2005;l 15(5):925-7.

21. Beuther DA, Weiss ST, Sutherland ER. Obesity and asthma. Am j respire crit care med 2006; 174(2): 112-9.

22. Horwood LJ, Fergusson DM, Shannon FT. Social and familial factors in the development of early childhood asthma. Pediatrics 1985 ;75(5):859-68

23. Wahn U, Lau s, Bergmann R, kulig M, forster J, Bergmann K, et al Indoor allergen exposure is a risk factor for sensitization during the first three years of life. J allergy clin Immunol 1997;99(6 pt l):763-9.

24. Sporik R, Holgate ST, plats-mills TA, cogswell JJ. Exposure to house-dust mite allergen (DER p I) and the development of asthma in childhood. A prospective study. N Engl J Med 1990;323(8):502-7.

25. Anderson WJ, Watson L. Asthma and the hygiene hypothesis. N Engl J med. May 24 2001:344(21): 1643-4.

26. Zambrano JC< carper HT, rakes GP, patrie J Murphy DD, plats MILLS ta, et al. Experimental rhinovirus challenges in adults with mild asthma: response to infection in relation to IgE. J Allergy clin immunol 2003; 111(5): 1008-16

27. Friedman NJ, Zeiger RS. The role of breast-feeding in the development of allergies and asthma. J allergy clin Immunol 2005; 115(6): 1238-48.

28. Bousquet J, Jeffery PK, Busse WW, Johnson M, Vignola AM. Asthma. From bronchocostrivtion to airways inflammation and remodeling. AM J respire crit care Med. May 2000; 161(5): 1720-45.

29. Wood DW, Downes JJ, Leeks HI. A clinical scoring system for the diagnosis of respiratory failure. Am J Dis Child 1972;123:227-228.

30. Baker MD. Pitfalls in the Use of clinical asthma scoring. Am J dis child. 1988; 142(2): 183-185.

31. Yung M, South M, Byrt T. Evaluation of a asthma severity score. Journal of paediatrics and child health ISSN 1034-4810.

32. Bishop J, Carlin J, Nolan T. Evaluation of the properties and reliability of a clinical severity scale for acute asthma in children. J clin Epidemiol. 1992 Jan; 45(l):71-6.

33. Parkin PC, Macarthur C, Saunders NR, Diamound SA, Winders PM. Development of a clinical asthma score use in hospitalized children between 1 and 5 years of age. J clin Epidemiol. 1996;49(8):821-5.

34. Smith SR, Baty JD, Hodge D. Validation of the pulmonary sere: an asthma severity scare for children. Aced Emerg med 2002;9:99-104.

35. Becker AB, nelson NA, simons ER. The pulmonary Index: Assessment of a clinical score for Asthma. Am J Dis child. 1984; 138(6):574-5 76.

36. Carroll CL, Sekaran AK, Larer TJ, Schramm CM. A modified pulmonary index score with predictive value for pediatric asthma exacerbations. Ann allergy asthma immunol. 2005 mer;94(3):355-9.

37. Gorelick MH, Stevens MW, Schultz TR, scribano PV. Performance of a novel clinical score, the paediatric asthma severity score (PASS) in the evaluation of acute asthma. Emerg med 2004; 11:10-8.

38. Chu s, tan J, Seabrook JA, Rieder MJ. Peadiatric asthma severity score and length of stay in patients presenting tfTa paediatric emergeny department. Paediatric and perinatal Drug therapy 2008;8:150-153.

39. Maheshg Babu. Approach to a child with respiratory distress. Indian journal of practical paediatrics. 2006;8(2): 110.

40. Robidas I, Gounin S, gravel J, Guimont C, Chaput G, Chalut D, Amre D. comparison pf Two clinical scores in the evaluation of acute asthma in pre-school Children. Canadian pediatric society 2007 abstracts.

41. Geelhoed GC, Landau LI, Lesouef PN. Predictive value of oxygen saturation in emergency evaluation of asthmatic children. Br Med J 1988;297:395-6.

42. Mower WrR, Sachs C, Nicklin El, Barff LJ. Pulse oximetry as a fifth pediatric vital sign. Pediatrics 1997;99:681-6.

43. Geelhoed GC, Landau LI, Lesouef PN. Evaluation of SaO2 as a predicter of outcome in 280 childten presenting with acute asthma. Ann emerg med 1994;23:1236-41.

44. Keogy KA, macarthur C, parkin PC, stephens D, arseneault R, tennis O, bacal L, schuh s. predictors of hospitalization in children with acute asthma. J pediatrics 2001:139:273-277.

45. Mehta S, Parkin PC, Stephens D, Keogh KA, Schuh S. Oxygen saturation as a predictor of prolonged, frequent bronchodilator therapy in children with acute asthma. J paediatrics 2004;145:641-5.

46. Keahey L Bulloch B, Becker AB, Pollack CV, Clark S, Camargo CA. Initial oxygen saturation as a predictor of admission in children presenting to the emergency department with acute asthma Ann Emerg med 2004;40:300-307.

47. Van Der Windt DA. Promises and pitfalls in the evaluation of pediatric asthma scores. J paediatrics 200; 137:744-6.

48. Gorelick M, Scribano PV, Stevens MW, Schuultz T, Shults J. predicting need for hospitalization in acute pediatric asthma. Pediatr emerg care. 2008;24(11):735-44.

49. Kirschner B, Guyatt GH. A methodological framework for assessing health indices. J chron dis 1985;38:27-36

50. Guyatt G, Walter S, Norman G. measuring change over time: assessing the usefulness of evaluative instruments. J chron dis 1987;40:171-8.

51. Scribano VP, Lerer T, kennedy M, Cloutier M. provider adherence to a clinical practice guidelines for acute asthma in a pediatric emergency department. Acad emerg med 2001; 12:1147-1152.

52. Thompson WT, Patterson JL, Shapiro W. Observation on the scalene respiratory muscles. Arch intern med. 1964; 113(6):856-865.

53. Wildhaber JH, Sznitman J, Harpes P, Straub D, Mo“ller A, Basek, Sennhauser FH. Correlation of spirometry and symptom scores in childhood asthma and the usefulness of curvature assessment in expiratory flow- volume curves. Respir care 2007;52(l 2): 1744-1752.

54. Angelilli ML, Thomas R. inter-rater evaluation of a clinical scoring system in children with asthma. Ann allergy asthma Immunology 2002feb,88(2) :209-14.

55. Rahnama’I MS, Geilen Rp, Singhi S, van den akker M, chevannes NH. Which clinical signs and symptoms predict hypoxemia in acute childhood asthma? Indian J pediatr 2006;73(9):771-775.

56. Chugh K, Arora G. Acute asthma. Indian journal of practical paediatrics. 2006;8(2): 116-122.

57. Lin RY, Sauter D, Newman T, Sirleaf J, Walters J, Tavakol M. continuous versus intermittent albuterol nebulization in the treatment of acute asthma. Ann emerg med 1993;22(12): 1847-53.

58. Rodrigo G, Rodrigo C, Burschtin O. A meta-analysis of the effects of ipratropium bromide in adults with acute asthma. Am J med 1999; 107(4):363-70.

59. Rowe BH, Spooner C, Ducharme Fm, Bretzlaff JA, bota GW early emergency department treatment of acute asthma with systemic corticosteroids. Cochrance database syst rev 2000;2.

60. Gluck EH, Onorato DJ, Castriotta R. helium-oxgen mixtures in intubated patient with status asthmaticus and respiratory acidosis. Chest 1990;98:693-698.

61. Kamabalapalli M, Nilchani S, Upadhyayula S. safety of intravenous terbutaline in acute severe asthma, a retrospective study. Acta paediatr 2005;94:1214-1217

62. Cheuk DKL, Chau TCH, Leesl. A meta analysis of intravenous magnesium sulohate for treating acute asthma. Arch dis child 2005,;90:74-77.

63. Slutaky AS. Mechanical riVetilation: American college of chest physicians’ consensus conference. Chest 1993; 104:-l859.