A Survey on Knowledge and Management of Childhood Asthma outside Dhaka

Submitted By

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A thesis paper is submitted to the Department of Pharmacy, East West University in the partial fulfillment of the requirements for the Degree of Bachelor of Pharmacy

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This Research Project is Dedicated to My Beloved Parents

DECLARATION BY THE CANDIDATE

I, **Samina Tasnim**, hereby declare that this dissertation entitled **"A survey on Parent's Knowledge and Management of Childhood Asthma outside Dhaka''**,is an authentic and genuine research work carried out by me under the guidance of Nishat Nasrin, Senior Lecturer, Department of Pharmacy, East West University, Dhaka, Bangladesh.

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CERTIFICATE BY THE SUPERVISOR

This is to certify that the dissertation entitled **''A Survey on Knowledge and Management of Childhood Asthma outside Dhaka''**, submitted to the Department of Pharmacy, East West University, in partial fulfillment of the requirements for the degree of Bachelor of Pharmacy was carried out by Samina Tasnim, ID: 2011-3-70-051 under my guidance and supervision and that no part of the research has been submitted for any other degree. I further certify that all the sources of information and facilities availed of this connection is duly acknowledged.

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CERTIFICATE BY THE CHAIRPERSON

This is to certify that, the research work on **"A survey on Knowledge and Management of Childhood Asthma outside Dhaka"**, is a bonafide research work done by Samina Tasnim (ID: 2011-3-70-051) under the guidance and supervision of Nishat Nasrin, Senior Lecturer, Department of Pharmacy, East West University, Dhaka.

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Abstract

Asthma is a common long-term condition that can cause coughing, wheezing, chest tightness and breathlessness**.** Asthma is a chronic condition affecting the lungs which can be managed but not cured. Symptoms associated with asthma are usually controllable and reversible with treatment. Our study was aimed to know the current situation of childhood asthma, parents knowledge on that and prescribing pattern among patients. The study was conducted on a total number of 185 patients by using a structured questionnaire. The location of our study was Chittagong, Mymensingh, Comilla, Narayanganj & Chandpur. This study results showed that the prevalence of asthma increased for those children who have common cold (56.03%), allergy (42.07%) & symptoms oriented with dust, irritants (55.14%). From our study it has shown that family history of asthma was 34.78%. The prescribing pattern among the patients represents that almost 73.51% took antibiotics for respiratory tract infection. Most of the doctors prescribed combined bronchodilator (60.54%) in acute exacerbation of asthma symptoms. To increase consciousness, knowledge, management & adherence to treatment are the best way to reduce the prevalence and risk factors of asthma.

Key word: Asthma, childhood, treatment, management, knowledge**.**

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List of Abbreviation

GINA	Global Intiative for Asthma
WAO	World Allergy Organization
ISAAC	International Study of Asthma and Allergies in Childhood
ICS	Inhaled Corticosteroid
CAMP	Childhood Asthma Management Program
FVC	Forced Vital Capacity
FEV-1	Forced Expiratory Volume
PEF	Peak Expiratory Flow

1.1 Asthma

Asthma is a disorder defined by its clinical, physiological and pathological characteristics. Asthma is a chronic inflammatory disorder of the airway in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness the leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning. These episodes are associated with widespread but variable, airway obstruction within the lung that is often reversible either spontaneously or with treatment (GINA, 2010).

Asthma is a heterogeneous disease resulting from complex interactions of environmental and genetic factors. Though asthma is an immune mediated disease of airways, this immune dysregulation in asthma has been attributed to the involvement of diverse immune cells that contribute to the immunopathology of the disease. According to World Health Organization (WHO) reports from 1950 to the present has increased in countries regardless of whether they had high, intermediate or low rates of asthma. The rise in rates of asthma over a few decades and the differences in rates among countries and in migrating populations suggest an important role of the local environment in the development of asthma. Therefore, it is critical to determine mechanisms for the development of allergy/asthma and identify environmental mediators that regulate the development of allergy in order to identify novel targets for intervention (GINA, 2007).

There is no clear definition of asthma phenotype, researchers studying the development of this complex disease turn to characteristics that can be measured objectively such as atopy (the presence of positive skin prick tests or the clinical response to common environmental allergens), airway hyperresponsiveness (the tendency of airways to narrow excessively in response to triggers that have little or no effect in normal individuals) and other measures of allergic sensitization. There is now good evidence that the clinical manifestations of asthma symptoms sleep disturbance, limitation of daily activity, impairment of lung function and the use of rescue medications can be controlled with appropriate treatment. When asthma is controlled there should be no more than occasional recurrence of symptoms and severe exacerbations should be rare (Reddel *et al*, 2003).

1.2 Pathophysiology of asthma

Inflammation has a central role in the pathophysiology of asthma. Airway inflammation involves an interaction of many cell types and multiple mediators with the airways that eventually results in the characteristic pathophysiological features of the disease: bronchial inflammation and airflow limitation which causes recurrent episodes of cough, wheeze and shortness of breath. The processes by which these interactive events occur and lead to clinical asthma are still under investigation.

1.2.1 Inflammatory cells in asthmatic airway

1.2.1.1 Mast cell: Activated mucosal mast cell release bronchoconstrictor mediators (histamine, prostaglandin D2) (Robinson, 2004). These cells are activated by allergens through high affinity IgE receptors. Increased mast cell number in airway smooth muscle may be linked to hyperresponsiveness (Kay *et al*, 2004).

1.2.1.2 Eosinophils: Present in increased number in airways release basic protein that may damage airway epithelial cell. Increase in inflammatory cell often correlate with greater asthma severity. It has a distinct role in different phases of asthma (Larche *et al*, 2003).

1.2.2.3 T Lymphocytes: Th1 and Th2 with distinct inflammatory profiles effects on airway function. Increased number in airway release specific Th2 cytokines including IL-4, IL-5, IL-9, IL-13 that explain overproduction of eosinophilic inflammation and IgE production by B lymphocytes, development of airway responsiveness (Akbari *et al*, 2006). An increase in Th2 cell activity may be due in part of reduction in regulatory T cell that normally inhibits Th2 cells.

1.2.2.4 Dendritic cells: Sample allergen from the airway surface migrates to the lymph nodes where they interact with regulatory T cells and ultimately stimulate the production of Th2 cell from the naive T cells (Golden, 2004).

1.2.2.5 Macrophage and Neutrophil: May be activated by allergens through low affinity IgE receptors to release inflammatory mediators and cytokines that amplify the inflammatory response (Wenzel S, 2003). Pathophysiological role of neutrophil cell is uncertain and they are increase in number due to glucocorticoid therapy (Chung K.F, 2000).

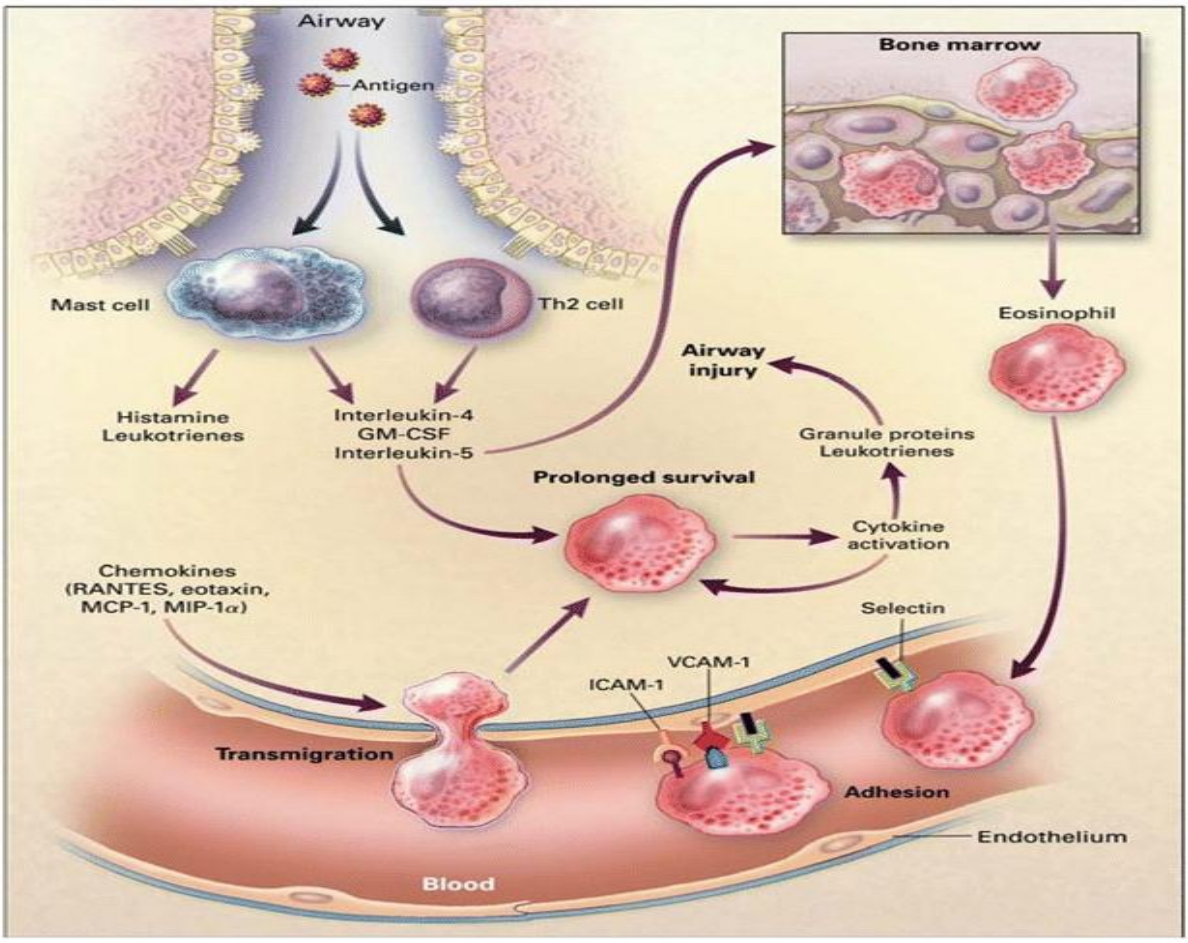

Figure 1.1: Airway inflammation in inhaled antigen

1.2.2 Airway structural cells involved in pathogenesis of Asthma

Airway epithelial cells: Sense their mechanical environment, express multiple inflammatory proteins in asthma and release cytokine, chemokine and lipid mediators.

Airway smooth muscle cell: Express similar inflammatory proteins to epithelial cells.

Endothelial cells of bronchial circulation: Recruiting inflammatory cells from the circulation into the airway.

Fibroblast and Myofibroblasts: Produce connective tissue component such as collagen and proteoglycans that are involved in airway remodeling.

Airway Nerves: Cholinergic nerves may be activated by reflex triggers in the airways and cause bronchoconstriction and mucus secretion. Sensory nerves may be sensitized by inflammatory stimuli (GINA, 2007).

1.2.3 Inflammatory Mediators involved in asthma

1.2.3.1 Chemokines: Are important in recruitment of inflammatory cells into the airways and are mainly expressed in airway epithelial cells (Barnes, 2002). Eotaxin is relatively selective for eosinophils, whereas thymus and activation-regulated chemokines (TARCs) and macrophage-derived chemokines (MDCs) recruit Th2 cells.

1.2.3.2 Cytokines: Direct and modify the inflammatory response in asthma and likely determine its severity. Th2-derived cytokines include IL-5, which is needed for eosinophil differentiation and survival; IL-4 is important for Th2 cell differentiation and IL-13 is important for IgE formation.

1.2.3.3 Cysteinyl-leukotrienes: Are potent bronchoconstrictors derived mainly from mast cells. They are the only mediator whose inhibition has been specifically associated with an improvement in lung function and asthma symptoms (Ricchiardolo *et al*, 2004). Recent studies have also shown leukotrieneB_4 can contribute to the inflammatory process by recruitment of neutrophils (Vignola *et al*, 2003).

1.2.3.4 Nitric oxide (NO): Is produced predominantly from the action of inducible NO syntheses in airway epithelial cells; it is a potent vasodilator. Measurements of fractional exhaled NO may be useful for monitoring response to asthma treatment because of the purported association between FeNO and inflammation in asthma (Vingola *et al*, 2003).

1.2.3.5 Prostaglandin D2: Is a bronchoconstrictor derived from mast cells and involved in Th2 cell recruitment to the airways (GINA, 2010).

1.2.4 Airway Narrowing in the asthma

1.2.4.1 Airway smooth muscle: Contraction in response to bronchoconstrictor mediators and neurotransmitter is the main cause of airway narrowing in asthma.

1.2.4.2 Airway edema: Occurs due to increased micro vascular leakage in response to inflammatory mediators.

1.2.4.3 Airway thickening: Occurs due to structural changes in airway passage (remodeling) which is occur in some severe cases and diseases.

1.2.4.4 Mucus hypersecretion: Leads to mucus plugging and is a product of increased mucus secretion and inflammatory exudates (GINA, 2010).

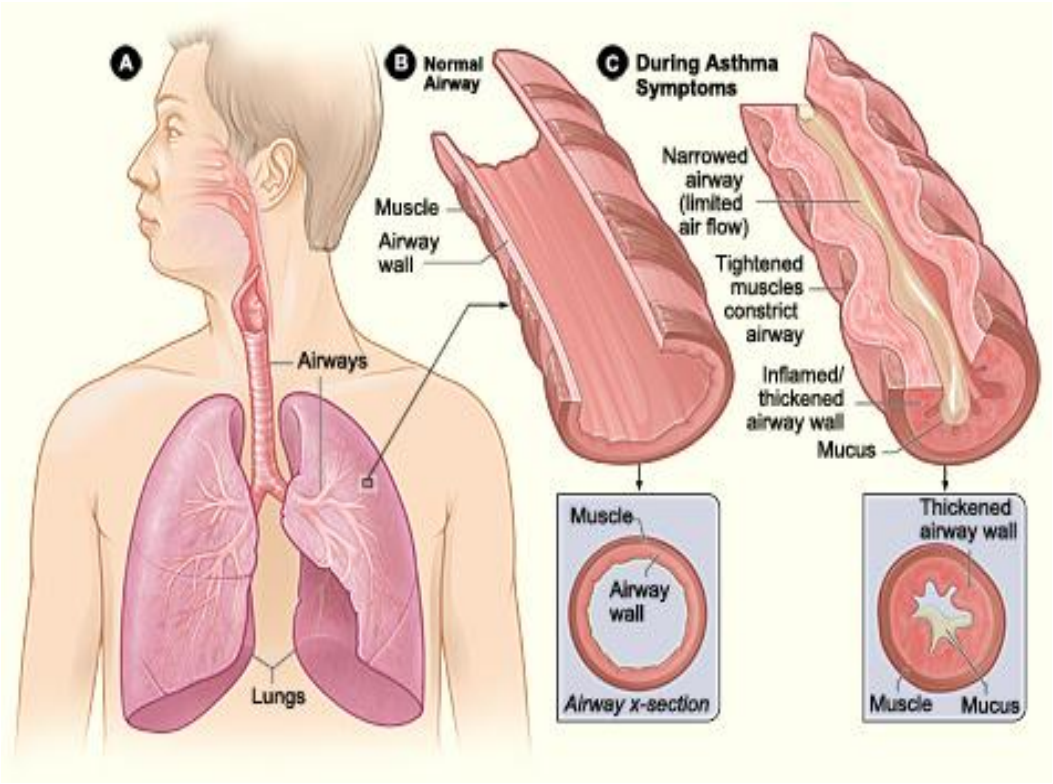

Fig 1.2: Airway narrowing in Asthma

1.3 Asthma Phenotypes in Childhood

Childhood asthma is a heterogeneous condition. Epidemiologic studies have identified three main asthma phenotypes in children.

The Tucson Children's Respiratory Study suggested that transient wheeze is probably related to congenitally small airways and tends to resolve before the age of 3 years as the airways grow in absolute size, although lung function remains low at age 6 when compared with children with no history of wheeze (Turner *et al*, 2000*).* They found that reductions in forced expiratory volume in 1 second (FEV1) had resolved at age 6 in children with reduced maximal expiratory flow at functional residual capacity (Vmax FRC) at 4 weeks and that continuing deficits in maximal mid-expiratory flow rate (FEF25–75) had mostly resolved by the age of 11.

1.3.1 Atopy, wheeze and exposure to allergens

Atopy, defined as the excessive production of specific IgE in response to exposure to common environmental allergens, is a major risk factor for childhood asthma. In addition, early sensitization appears to be an important factor in persistent asthma. Sensitization to an allergen can occur at any time and may be related to dose and individual susceptibility. Atopy appears to be an important risk factor for persistent but not transient wheeze. Exposure to allergen is a prerequisite for the development of atopic sensitization; however, the role of allergen exposure in the development of asthma is still unclear. It is documented that allergen exposure increases asthma severity in sensitized individuals (Tunnicliffe *et al*, 1999).

1.3.2 Atopy, lung function and asthma development

Different factors may be important in the development of atopy that involved in the development of asthma in childhood. Factors independent of allergen exposure, such as genetic or other environmental factors, may influence the growth and elasticity of the airways and lung parenchyma and are more important in the development of the different phenotypes of asthma. The Childhood Asthma Management Program (CAMP) investigated the relationship between allergen sensitization and exposure and lung function in 1041 children with mild and moderate asthma and 88% of the children had at least one positive skin prick test result. No significant difference was found in lung function between sensitized and non

sensitized children; however, pre–bronchodilator FEV1 was lower in atopic children than in non atopic children for all allergens except tree pollens. It is possible that if children with severe asthma had been included in the study, the observed differences may have been magnified (Nelson *et al*, 1999).

1.3.3 Endotoxin, atopy and the lungs

Exposure to endotoxins, soluble lucopolysaccharide (LPS) fragments on the outer membrane of gram-negative bacteria, have been shown to increase the severity of disease in persons with asthma and may prove to be a factor in the initial development of the disease. A study by Park *et al*, showed an increased risk of recurrent wheeze in infants exposed to elevated levels of endotoxin in the home during the first year of life. However, other studies have suggested that exposure to endotoxin may be protective in terms of reducing the risk of atopy and perhaps asthma (Reddel *et al*, 2003).

1.4 Classification of Asthma

1.4.1 Etiology: Many attempts have been made to classify asthma according to etiology with regard to environmental sensitizing agent. Despite this having afforded to identify an environmental cause for asthma should be part of initial assessment to enable the use of avoidance strategy in asthma management. Describing patients as having allergic asthma is usually of little benefit in guiding treatment, unless a single specific trigger agent can be identified (GINA, 2010).

According to GINA documents asthma has been divided by severity basis on the level of the symptoms, airflow limitation and lung function variability into four categories: Intermittent, Moderate persistent, Mild persistent or Severe persistent (WebMD, 2013).

1.4.2 Intermittent asthma

Asthma is considered intermittent if without treatment any of the following are occur

- Symptoms (difficulty breathing, wheezing, chest tightness and coughing) occur on fewer than 2 days a week.
- Do not interfere with normal activities.
- Nighttime symptoms occur on fewer than 2 days a month.

1.4.3 Mild persistent asthma

Asthma is considered mild if the children have the following conditions:

- Symptoms occur on more than 2 days a week but do not occur every day.
- Attacks interfere with daily activities.
- Nighttime symptoms occur 3 to 4 times a month.
- Lung function tests are normal when the person is not having an asthma attack.

1.4.4 Moderate persistent asthma

Asthma is considered moderate persistent if one has the following conditions:

- Symptoms occur daily. Inhaled short-acting asthma medication is used every day.
- Symptoms interfere with daily activities.
- Nighttime symptoms occur more than 1 time a week, but do not happen every day.
- Lung function tests are abnormal.

1.4.5 Severe persistent asthma

Asthma is considered severe persistent if without treatment any of the following will occur:

- Symptoms occur throughout each day.
- Severely limit daily physical activities.
- Nighttime symptoms occur often, sometimes every night.
- Lung function tests are abnormal (60% or less of expected value).

1.5 Factors influencing the development and expression of asthma

1.5.1. Genetic: Asthma has a heritable component but it is not simple. Multiple genes may be involved in the pathogenesis of asthma (Holloway, Beghe & Holgate 1999). Genes linked for the development of asthma has focused in four major areas: production of allergen specific IgE antibody (atopy), expression of airway hyperresponsiveness, generation of inflammatory mediators such as cytokine, chemokine and growth factors, determination of ratio between Th1 and Th2 immune responses (Strachen, 1989). Variation in genes encoding the beta adrenoreceptor has been linked to differences in subject's responses to β2 agonist (Isreal *et al*, 2004).

1.5.2 Obesity: Asthma is more frequently observed in obese subjects (Body Mass Index>30 kg/m2) and more difficult to control. Obese people with asthma have lower lung function compared with normal weight people with asthma (Weiss ST & Shore S, 2004). The use of secondary glucocorticoid and secondary lifestyle promote obesity in severe asthma patient. It has been proposed that obesity could influence airway function due to its effect on lung mechanics, development of proinflammatory state; in addition to genetic, environmental and hormonal influence (Shore, 2005). Obese patients have a reduced expiratory reserve volume, a pattern of breathing which may alter airway smooth muscle plasticity and airway function.

1.5.3 Sex: Male sex 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 (Horwood *et al*, 1985). By adulthood the prevalence of asthma is greater in women than in men. The reason for this sex related difference is still not clear. However lung size is larger in female than male at birth but smaller in adulthood.

1.5.4 Environmental Factors: There are some important causes of asthma symptoms such as air pollution and some allergens, occupational sensitizers but they are not clearly linked to the development of asthma. Risk factors are discussed in details:

1.5.4.1 Allergens: Indoor and outdoor allergens are involved to cause asthma exacerbation. Birth Cohort Studies showed that sensitization to house dust mite allergens, cat dander, dog dander (Wahn *et al*, 1997). Aspergillus mold are also important risk factor for the symptoms of asthma in children up to 3 years of age. Some allergens that are derived from house dust mites and cockroach appears to be directly correlated with exposure (Wahn *et al*, 2001).

1.5.4.2 Infection: During infancy a number of viruses have been associated with asthma phenotypes such as Respiratory syncytial virus (RSV) and parainfluenzavirus. Symptoms of bronchiolitis are parallel with too many features of asthma (Sigurs *et al*, 2000). The interaction between atopy and viral infection appear to be complex relationship in which the atopic state can influence the lower airway response to viral infections.

1.5.4.3 Occupational sensitizers: Over 300 subjects are associated with the development of asthma. These substances include highly reactive small molecule such as isocyanates, irritants, platinum salts, complex plant and animal biological product known as immunogens that stimulate the production of IgE (Malo *et al,* 2004). Occupations associated with high risk of occupational asthma include farming and agricultural area, painting, cleaning work and plastic manufacturing.

1.5.4.4 Tobacco smoke: Exposure to tobacco smoke both parentally and after birth is associated with measurable harmful effects such as development of asthma symptoms. Tobacco smoking increases asthma severity, declines lung function in people with asthma and less responsive to inhaled and systematic glucocorticosteroid (Strachan & Cook, 1998).

1.5.4.5 Diet: The role of diet, particularly in breast feeding in relation to the development of asthma has been extensively studied and in general data reveal that infants fed formulas of intact cow's milk or soy protein have a higher incidence of wheezing illness in early childhood compared with those breast fed breast milk (Friedman & Zeiger, 2005).

1.6 Maternal factors associated with offspring

1.6.1 Maternal transfer of risk of allergy to offspring

Some studies suggest that the development of allergen responsiveness may occur prenatally (Blumer *et al,* 2005). In reports examining human maternal and paternal asthma associations with the development of allergies in offspring, most associations are with maternal allergy/asthma suggesting that sensitization can occur prenatally or early postnatally. It is suggested that in utero and early exposures to environmental factors are critical for increased risk of allergic disease (Bousquet *et al,* 2011). There is an association of higher risk of eczema, wheezing, and lower respiratory tract infections in early life with human maternal and cord blood C-reactive protein which is an acute phase protein produced during inflammation.

A mouse model for matemal transfer of risk of allergy to offspring has been established. This model reflects many of the parameters of development of allergic disease in humans including increased risk for development of allergies in offspring of allergic mothers.

Moreover, as in humans, in this mouse model, the allergic responses of the offspring are not specific to the allergen of the mother (Bousquet *et al,* 2011).

1.6.2 Breast milk and offspring allergy

The milk of allergic mothers is not necessary for the offspring allergic responses because in utero matemal effects are sufficient for allergic responses by offspring of allergic mothers. Briefly, pups from allergic mothers that are nursed by non-allergic mothers have an allergic response to suboptimal challenge with OVA. Therefore, maternal effects in utero mediate development of allergen responsiveness in offspring of allergic mothers (Leme, 2006). Breast milk is sufficient, but not necessary, for maternal transmission of asthma risk in the offspring because when pups from non-allergic mothers are nursed by allergic mothers, the pups exhibit a response to suboptimal allergen challenge. The breast milk from allergic and non-allergic mothers contained no detectable IFNγ, IL-2, IL-4, IL-5, IL-13, or TNFα, suggesting that other mediators increase the risk of offspring allergy through breast milk (Leme, 2006). It is reported that the mediators, omega-3 and omega-6 polyunsaturated fatty acids, in human milk associate with asthma and atopy but the mechanism is not known.

1.6.3 Transplacental mediators and development of allergic disease

It is not known whether transplacental cytokines influence the matemal effect on the offspring development of allergic responses. Th2 cytokines (IL-4, IL-5, and IL-13) are elevated in the placenta but transplacental crossing of these cytokines has not been demonstrated (Bowen *et al*, 2003). It is reported that only 2 % of matemal GM-CSF crosses the human placenta, whether matemal GM-CSF increases risk of offspring for allergic responses is not known. Understanding mechanisms of matemal transfer of risk for allergy to offspring and mechanisms for regulation of this risk will have an impact on limiting the development of allergic disease early in life (Bowen *et al*, 2003).

1.6.4 Maternal vitamins regulate offspring allergic responses

Environmental factors likely impact allergies and asthma. Environmental factors that regulate allergy and asthma in the mother could affect the risk of development of allergy and asthma in offspring. Exposure to environmental factors, such as chemical irritants or nutrients,

during pregnancy has been associated with allergic disease in offspring (Netting, Middleton & Makrides, 2014). Supplementation with higher levels of vitamin D during pregnancy or in cord blood has been associated with both a higher & lower risk of allergy in early infancy, but adequate vitamin D levels during pregnancy support fetal maturation (Junge, Lehmann & Borte, 2013). An environmental change over the past 40 years, which may contribute to elevating allergic responses, has been an increase in the isoform of vitamin E in the diet and in infant formulas (Uauy, 1994).

1.7 Clinical diagnosis of asthma

1.7.1 Medical history

1.7.1.1 Symptoms: A detailed family history of asthma and allergies can help doctor to make an accurate asthma diagnosis. Childs own personal history of allergies is also important as many are closely linked to asthma.

Information about asthma symptoms is also useful. Be prepared to divulge when and how often they occur and what factors seem to exacerbate or worsen symptoms. Common symptoms and signs include:

- Wheezing
- Coughing
- Breathing difficulty
- Tightness in the chest
- Worsening symptoms at night
- Worsening symptoms due to cold air
- Symptoms while exercising
- Symptoms after exposure to allergens

It is also wise to have knowledge of health conditions that can interfere with asthma management such as runny nose, sinus infections, acid reflux disease, psychological stress and sleep apnea.

It is often somewhat harder to diagnose young children who may develop their first asthma symptoms before age 5. Symptoms are likely to be confused with those of other childhood

conditions, but young children with wheezing episodes during colds or respiratory infections are likely to develop asthma after 6 years of age (GINA, 2010).

1.7.1.2 Cough variant Asthma: Cough variant asthma can be distinguished from so called eosinophil bronchitis in which patients have cough and sputum eosinophil but in normal incidence of lung function when accessed by spirometry and airway hyperresponsiveness (Gibson *et al*, 1989). Other diagnoses to be considered are cough-induced by angiotensin converting enzyme (ACE) inhibitors, gastroesophageal reflex, postnasal drip and vocal cord dysfunction (Irwin & Boulet, 1998).

1.7.1.3 Exercise induced bronchoconstriction: Exercise induced bronchoconstriction typically develops within 5-10 minutes after completing exercise such as running which is a potent trigger of asthma. It may occur in any climatic condition, but it is more common when the patient is breathing dry, cold air and less common in hot, humid condition (Tan & Teoh, 1985). Some children with asthma only show exercise induced symptoms. In that case exercise testing is helpful. An 8 minute running protocol is easily performed in clinical practice and can establish a firm diagnosis of asthma (Anderson, 2002).

1.7.2 Physical Examination: The most usual abnormal physical finding is wheezing on auscultation, a finding that confirms the presence of airway limitation. However in some people with asthma wheezing may be absent or only detected when the person exhaled forcibly. Other clinical signs are only present if the patients are examined during symptomatic periods such as features of hyperinflation which results from patients breathing at a higher lung volume in order to increase outward retraction of airway (GINA, 2010). Physicians will also check for a runny nose, swollen nasal passages, and nasal polyps. Skin will be examined for conditions such as eczema and hives, which have been linked to asthma. Physical symptoms are not always present in asthma sufferers and it is possible to have asthma without presenting any physical maladies during an examination (Anderson, 2002).

1.8 Tests for diagnosis and monitoring of asthma

1.8.1 Measurement of lung function: Measurement of lung function greatly enhance diagnostic confidence cause patients with asthma frequently have poor recognition of their symptoms and poor perception of symptom severity if their asthma is long lasting (Killian *et al*, 2000). It provides an assessment of the severity of airflow limitation, its variability which ultimately provides confirmation of the diagnosis of asthma. Various methods are available to assess airflow limitation but below methods have gained acceptance for use in patients over 5 years of age. These are Spirometry, forced vital capacity (FVC) and peak expiratory flow (PEF) measurement.

Forced vital capacity (FVC) - the maximum amount of air one can inhale and exhale Forced expiratory volume (FEV-1) - the maximum amount of air exhaled in one second.

Predicted values of (FVC), (FEV-1), (PEF) based on age, sex and height. The term reversibility and variability refer to changes in symptoms accompanied by changes in airflow limitation. Reversibility is generally applied to rapid improvement in FEV-1(or PEF) measured within minutes after inhalation of rapid acting bronchodilator. Variability refers to improvement or deterioration in symptoms and lung function occurring over time and it is part of assessment of asthma control (GINA, 2007).

1.8.2 Spirometry: It is recommended method of measuring airflow limitation and establishes a diagnosis of asthma. Measurement of FEV-1, FVC are undertaken during a forced expiratory maneuver using a spirometer. It is reproducible but effort dependent. The normal range of values is wider and predicted values are less reliable in young people (<age 20) and in the elderly (>age 70). A useful assessment of airflow limitation is the ratio of FEV1 to FVC which is normally greater than 0.75 to 0. 80, any possibly greater than 0.90 in children. Values less than these suggest airflow limitation (GINA, 2010).

1.8.3 Peak expiratory flow: Measurements are performed by using peak flow meter and important in diagnosis and monitoring of asthma. Modern peak expiratory flow (PEF) meters are relatively inexpensive, portable, plastic and ideal for patients to use in home settings.

Measurement of PEF is not interchangeable with other measurements of lung function such as FEV-1 in either adult 16 or children (Eid N. *et al*, 2000).

PEF monitoring is valuable in a subset of asthmatic patient and can be helpful:

- To confirm the diagnosis of asthma
- To improve control of asthma particularly in patients with poor perception of symptoms.
- To identify environmental causes of asthma symptoms.

1.8.4 Measurement of airway responsiveness: Measurement of airway responsiveness reflects the sensitivity of the airways to factors that can cause asthma symptoms, sometimes called triggers. These test are sensitive for diagnosis of asthma, but have limited specificity (Cockcroft *et al*, 1992). This means a negative test can be useful to exclude a diagnosis of persistent asthma in a patient who is not taking inhaled glucocorticosteroid treatment but a positive test does not always mean that a patient have asthma (Boulet, 2003). This is because airway hyperresponsiveness has been described in patients with allergic rhinitis (Ramsdale, 2003).

1.8.5 Measurement of allergic status: The presence of allergies in asthma patients (identified by skin testing or measurement of specific IgE in serum) can help to identify risk factors that cause asthma symptoms in individual patients. It is not routinely recommended cause it is rarely useful in establishing a diagnosis, requires expertise (Hoeppner *et al*, 1985). Skin test with allergens represents the primary diagnostic tool in determining allergic status. Measurement of specific IgE in serum does not surpass the reliability of result from skin tests. The positive test does not mean that the disease is allergic in nature or it causing asthma. The relevant exposure and its relation to symptoms must be confirmed by patient history (Hoeppner *et al*, 1985).

1.9 Distinguishing asthma from COPD

Both of them are chronic obstructive diseases that involve underlying airway inflammation. COPD (Chronic obstructive pulmonary disease) is characterized by airflow limitation which is not fully reversible and associated with an abnormal inflammatory response of the lungs to noxious particles or gases. Individual with Asthma exposed to noxious agent may develop fixed airflow limitation and chronic respiratory symptoms. It may be difficult to differentiate the two diseases (GINA, 2010).

1.10 Distinguishing asthma from pneumonia

Asthma and pneumonia in children have some similar symptoms, even though they are different conditions. Asthma is a chronic condition that cannot be cured, although it can be managed by controlling symptoms. Pneumonia, on the other hand, is a condition that is limited to the duration of the infection**.** Asthma is the result of genetic or environmental factors that affect one's ability to breathe. Pneumonia is a respiratory infection caused by a bacterium, virus, fungus or parasite. With pneumonia, as in most infections, child will have a fever, and sometimes a high fever. Other symptoms of pneumonia include feeling sick, with muscle aches, fatigue, headache, sweating or chills. Children with pneumonia might also develop pleurisy, a stabbing chest pain in the rib area that is worse with breathing. Coughing and being short of breath are also symptoms of pneumonia (WebMD, 2015).

1.11 Asthma medication used in children

Medications that are available fall into two general categories.

1.11.1 First category: Includes drugs taken daily to control asthma in the long term and reduce the frequency of asthma attacks (controller or maintenance medications). These can include inhaled corticosteroids like budesonide, fluticasone and leukotriene antagonists like montelukast sodium or zileuton. Less common controller medications include long-acting bronchodilators (in combination with corticosteroids) and theophylline.

1.11.2 Second category: Are medications that provide instant relief from symptoms (rescue medications). These include short-acting bronchodilators like albuterol and levoalbuterol. Short courses of systemic corticosteroids -- drugs like prednisone and prednisolone given,

often used with bronchodilators during asthma attacks. Inhaled ipratropium may be used in addition to inhaled bronchodilators following asthma attacks or when asthma worsens.

Every child needs to follow a customized asthma management plan to control asthma symptoms. The severity of a child's asthma can both worsen and improve over time, so the type (category) of child's asthma can change, which means different treatment can be required over time. Treatment should be reviewed every one to six months, and the choices for long- and short-term therapy are based on how severe the asthma is (WebMD, 2013).

1.12 Treatment of Asthma

1.12.1 Choice of device: Inhaled therapy is a cornerstone of asthma treatment for children of all ages. Almost all children can effectively use inhaled therapy. Different age group require different inhaler for effective treatment. The choice of inhaler should include in consideration of the efficacy of drug delivery, cost, safety, ease of use and convenience (Bisgraard *et al*, 2005).

Table 1.1: Choosing an inhaler device for children with Asthma

Age group	Preferred Device	Alternate Device
Younger than 4 years	Pressurized meter dose inhaler plus dedicated spacer with face mask	Nebulizer with face mask
4-6 years	Pressurized meter dose inhaler plus dedicated spacer with mouthpiece	Nebulizer with mouthpiece
Older than 6 years	Dry powder inhaler or breath actuated pressurized metered dose inhaler or pressurized metered dose inhaler with spacer and mouthpiece	Nebulizer with mouthpiece

1.12.2 Controller medications

Controller medications for children include inhaled and systemic glucocorticosteroids, Leukotriene modifiers, Cromolyn and long acting β2 agonist.

1.12.2.1 Inhaled Glucocorticosteroid

It is most effective controller therapy and recommend for asthma for children of all ages.

Doses of different inhaled glucocorticosteroid administered via different inhalation devices for children older than 5 years shown in the below figure:

Table 1.2: Estimated equipotent daily doses of inhaled glucocorticosteroid for children older than 5 years

Drug	Low Daily dose	Medium daily dose	High daily dose
Beclomethasone dipropionate	100-200	>200-400	>400
Budesonide	100-200	>200-400	>400
Budesonide-Neb	250-500	>500-1000	>1000
Flunisolide	500-750	>750-1250	>1250
Fluticasone propionate	100-200	>200-500	>500

Children 5 years and younger: Treatment with inhaled glucocorticosteroids in children 5 years and younger with asthma generally produces similar clinical effects as in older children but dose response relationship have been less studied.

1.12.2.2 Leukotriene Modifiers

Children older than 5 years: Leukotriene modifiers provide clinical benefits in children older than 5 years at all levels of severity but generally less than that of glucocorticosteroid (Ostrom, 1998). It provides partial protection against exercise-induced bronchoconstriction. Leukotriene modifiers provide moderate clinical improvements in children whose asthma is controlled by low dose of inhaled glucocorticosteroids as an add-on treatment. Combination therapy is less effective in controlling asthma in children.

Children 5 years and younger: Leukotriene modifiers reduce viral induced asthma exacerbations in children ages 2-5 years with a history of intermittent asthma.

1.12.2.3 Long acting inhaled β2 agonists

Children older than 5 years: Long acting inhaled β2 agonists Used as an add-on therapy in children whose asthma is not controlled on low to high doses of inhaled glucocorticosteroid. Add-on treatment with long acting inhaled β2 agonists has not been shown to reduce the frequency of exacerbation (Bisgaard, 2003). Inhalation of single dose of long acting β2 agonist effectively blocks exercise induced bonchoconstriction for several hours (Simons *et al*, 1997). Fixed combination products inhalers ensure that the long acting β2 agonist accompanied with glucocorticosteroid.

Children 5 years and younger: Combination therapy with budesonide and formeterol used as maintenance has been shown to reduce asthma exacerbations in children ages 4 years and older with moderate to severe asthma (Bisgaard, 2006).

1.12.2.4 Theophylline

Effective as monotherapy and as add-on treatment to inhaled or oral glucocorticosteroid in children older than 5 years and more effective than placebo at controlling day and night symptoms and improving lung functions (Kat *et al*, 1985). The use of Theophylline level should be maintained in children within therapeutic range of 55-110μmol/L. Add-on treatment with theophylline has been found to improve asthma control and reduce the maintanence glucocorticosteroid dose necessary in children with severe asthma (Brenner & Berkowit, 1988).

1.12.2.5 Anti-IgE

Omalizumab has proven efficacy in children age 6 to 12 years with moderate to severe and severe persistent allergic (IgE mediated) asthma. Anti-IgE treatment is expensive and requires regular injections and observation after each injection (Brenner & Berkowit, 1988).

1.12.2.6 Cromones: sodium chromoglycate and nedocromil sodium

Sodium chromoglycate and nedocromil sodium have limited role in long term treatment of asthma in children (Trasche *et al*, 2000). Meta analysis concluded that sodium chromoglycate is not significantly better than placebo for management of asthma in children. Nedocromil sodium has been shown to reduce exacerbations but its effect in other asthma outcomes is not superior to placebo.

1.12.2.7 Long acting oral β2 agonists

Treatment with long acting oral β2 agonists such as slow release formulations of salbutamol, terbutaline reduces nocturnal symptoms of asthma (Kuusela, 2000). Long acting oral β2 agonist's therapy suffers little or no protection against exercise induced bronchoconstriction.

1.12.2.8 Systemic glucocorticosteroid

Because of the side effect of prolonged use, oral glucocorticosteroid in children with asthma should be restricted to the treatment of acute severe exacerbations whether viral induced.

1.12.3 Reliever medications

Rapid acting inhaled β2 agonists and short acting oral β2 agonists. Rapid acting inhaled β2 agonists are the most effective bronchodilators and preferred treatment for acute asthma in children of all ages. The inhaled therapy offers significant protection against exercise induced bronchoconstriction and other challenges for 0.5 to 2 hours. Oral therapy is rarely needed and persevered mainly for young children who cannot use inhalation therapy (GINA, 2007).

1.13 Management of Asthma

1.13.1 General Principles: The long term goal of asthma management is symptom control and risk reduction. The aim is to reduce the burden of patient, risk of exacerbation, airway damage and medication side effects.

1.13.2 Population level Recommendations: Preferred asthma treatments represent the best treatments for most patients in population.

1.13.3 Patient level treatment: Decisions should take into account to any individual characteristics or phenotype that predicts the patient's response to treatment together with patient's preference and practical issues such as inhaler technique, adherence and cost.

1.13.4 Partnership: Between patient and their health care providers is important for effective asthma management. Training health care providers in communication skills may lead to increase patient satisfaction, better health outcomes and reduced use of health care resources.

1.13.5 Health Literacy: The patient ability to obtain process and understand basic health information to make appropriate health decisions (Wahn *et al*, 1997).

1.14 Asthma Control

Asthma control may be defined in a variety of ways. In lay terms, control may indicate disease prevention or even cure. The aim of treatment should be achieve and maintain control for prolonged period with due to regard to the safety of treatment, potential for adverse effect and the cost of treatment required to achieve this goal (Bateman *et al*, 2004).Therefore the assessment of asthma should include not only control of clinical manifestation but also control of the expected future risk to the patient such as exacerbations, accelerated decline in lung function and side effects of treatment (Bateman *et al*, 2004).

1.15 Asthma Prevention

Measures to prevent asthma may be aimed at the prevention of allergic sensitization or the prevention of asthma development in sensitized people. Other than preventing tobacco exposure both in utero and after birth. The role of dieting particularly breast feeding in relation to the development of asthma is extensively studied and showed that infants fed formulas of intact cow's milk or soy protein compared with breast milk have higher incidence of wheezing illnesses in early childhood. Excessive breast feeding during the first months after birth is associated with lower asthma rates during childhood. Exposure to tobacco smokes both prenatally and postnatally is associated with most measurable harmful effects (GINA, 2007).

1.16 Global burden of asthma

Asthma has become more common in both children and adults around the world in recent decades. The increase in the prevalence of asthma has been associated with an increase in atopic sensitization, and is paralleled by similar increases in other allergic disorders such as eczema and rhinitis. The rate of asthma increases as communities adopt with western lifestyles and become urbanized. In many areas of the world persons with asthma do not have access to basic asthma medications or medical care. Increasing the economic wealth and improving the distribution of resources between and within countries represent important priorities to enable better health care to be provided. The number of disability-adjusted life years (DALYs) lost due to asthma worldwide has been estimated to be currently about 15 million per year. Worldwide, asthma accounts for around 1% of all DALYs lost, which reflects the high prevalence and severity of asthma. The burden of asthma in many countries is of sufficient magnitude to warrant its recognition as a priority disorder in government health strategies. Resources need to be provided to improve the care of disadvantaged groups with high morbidity, including certain racial groups and those who are poorly educated (Richard B, 2004). Resources also need to be provided to address preventable factors, such as air pollution, that trigger exacerbations of asthma. It is estimated that asthma accounts for about 1 in every 250 deaths worldwide. Many of the deaths are preventable, being due to suboptimal long-term medical care and delay in obtaining help during the final attack. The economic cost of asthma is considerable both in terms of direct medical costs (hospital admissions & cost of pharmaceuticals) and indirect medical costs (time lost from work and premature death). Novel public health and pharmacological measures become available to reduce the prevalence of asthma, morbidity and mortality are available with asthma worldwide (Richard B, 2004).

2.1 The prevalence of childhood asthma in China: a systematic review

It is well known that the prevalence of asthma has been reported to increase in many places around the world during the last decades. Therefore, the aim of this study was to identify and review studies of asthma prevalence among children in China and address time trends and regional variation in asthma. However, the findings from one large study of children from 27 different cities support an increase in current prevalence of childhood asthma from 1990 to 2000. The lowest current prevalence of childhood asthma was found in Tibet (Yangzong *et al*, 2012).

2.2 The Childhood Asthma Management Program (CAMP): contributions to the understanding of therapy and the natural history of childhood asthma

The Childhood Asthma Management Program (CAMP) has been in continuous existence for almost two decades, which makes it the largest randomized, placebo-controlled clinical trial with extended follow-up for children with mild to moderate asthma. As such, its cumulative data from baseline, active treatment, and post-treatment have proved to be an invaluable resource for not only assessing the efficacy and safety of long-term inhaled corticosteroid therapy in childhood, but for discovery of many other aspects of childhood asthma, including genetics and biomarkers. CAMP investigations have established that long-term use of inhaled corticosteroids (ICS) at a low–medium dose over 4–6 years is safe in children although it does produce a small decrement in height that is not progressive after the first few years. Various phenotypic features and genotypic variants modify both long-term asthma outcomes and response to ICS in childhood asthma (Ronina *et al*, 2012).

2.3 Longitudinal associations between neighborhood walkability and incident childhood asthma

The Institute for Clinical Evaluative Sciences evaluated the association between neighborhood walkability and incident childhood asthma using prospectively-collected administrative data. Among the children living in Toronto, neighborhood quintile of

walkability was reported using a validated walkability index with 4 dimensions: population density, dwelling density, access to services and street connectivity. It results that twenty-one percent of the 326 383 children met the Ontario Asthma Surveillance Information System (OASIS) criteria for asthma. After adjusting for sex, preterm delivery, obesity, atopic conditions and neighborhood income quintile, children with low home neighborhood walkability at birth were at increased risk of asthma development [hazard ratio (HR) 1.11; 95% confidence interval (CI), 1.08-1.14], and the association did not change for children with healthcare visits for asthma in the past year (HR 1.10; 95% CI, 1.04-1.16). When walkability in each year of the child's life was considered, low neighborhood walkability was associated with increased odds of incident childhood asthma (odds ratio 1.12; 95% CI, 1.09-1.15) (Elinor *et al*, 2014).

2.4 Associations between second-hand smoke exposure in pregnancy and age of childhood asthma development

Maternal smoking during pregnancy has been associated with an increased hazard of incident childhood asthma. The work has done in Canada showed that Household second-hand smoke exposure prevalence was 8.3% during pregnancy and 10.6% in the first year of life; 15.5% of children developed asthma. After adjusting for sex, prematurity, being born in Canada and maternal asthma, children exposed to home second-hand smoke during pregnancy were more likely to develop asthma and developed asthma sooner [adjusted hazard ratio (HR) 1.36, 95% confidence interval (CI): 1.09, 1.70], even after excluding children whose mothers smoked in pregnancy (HR 1.53, 95% CI: 1.09, 2.14). The association strengthened (HR 1.88, 95% CI: 1.16, 3.02) after adjusting for home second-hand smoke exposure in the first year. Home second-hand smoke exposure during pregnancy is associated with an increased hazard of childhood asthma development, even if the mother is not a smoker (Elinor *et al*, 2012).

2.5 Prevalence of asthma in Highly polluted Dhaka city & low polluted coastal area in Bangladesh

Bangladesh National Asthma Prevalence Study (1999) states that around 4 million people are suffering from asthma in our country and prevalence is more in rural areas than metropoliton area of Bangladesh. This work was a cross-sectional study and it is a multistage stratified random sampling design,conducted over a population of 6161 (Dhaka 3087 & coastal Area 3029). The results showed that frequency of asthma was significantly higher in coastal area than the Dhaka city and the prevalence of asthma was 6.8%. The common cold,extreme weather, ingestion of cold/food, drink, allergenic food, gas, kerosene stove were possible trigger factors for asthma for residents of dhaka city and coastal area. The first & full moon seems to be important factors for asthma in coastal area (Hasan M.D, 2005).

2.6 Childhood Asthma-A global Problem

According to International Study of Asthma and Allergies in childhood (ISAAC) in urban and rural area in Dhaka district in Bangladesh showed that the prevalence was 9.1% among 6-7 year old and 6.1% among 13-14 year old. The prevalence was increased among children compared to adult (7.3% vs. 5.3%) (Kabir *et al*, 2003). Analysis of the World Allergy Organization (WAO) on Global Allergy Physician and Patient survey (2006) identified that physicians who treat children with asthma are not prescribing treatment according to the Global Initiative for Asthma (GINA) guideline recommendations and a large proportion of children with asthma are not presently receiving of asthma care (Carlos & Baena, 2009).

2.7 Effectiveness of prophylactic inhaled steroids in childhood asthma: a systemic review of Literature

This study has been performed to evaluate the effectiveness of prophylactic inhaled steroids in childhood asthma. In total, 24 of 93 studies retrieved met the inclusion criteria. The overall weighted relative improvement in mean total symptom score (inhaled steroid vs. placebo) was 50% (95% confidence interval [CI]: 49%, 51%), the overall weighted relative decrease in mean concomitant beta2-agonist use (inhaled steroid vs. placebo) was 37% (95% CI: 36%,

38%), and the overall weighted relative decrease in mean concomitant oral steroid use (inhaled steroid vs. placebo) was 68% (95% CI: 66%, 70%). The overall weighted absolute improvement in mean peak expiratory flow rate (inhaled steroid vs. placebo) was 38 L/min (95% CI: 34.3 L/min, 41.7 L/min). Prophylactic inhaled steroids are effective, compared with placebo, in improving both clinical and laboratory outcomes in childhood asthma (Calpin *et al*, 1997).

2.8 Asthma in adults: comparison of adult-onset asthma with childhood-onset asthma relapsing in adulthood

The prevalence of asthma in children and young adults is rising. Although the general features of asthma are similar in children and adults, there are several differences. Studies of the differences between childhood- and adult-onset asthma may provide new insight into the phenotypic heterogeneity of asthma. The aim of this cross-sectional study was to compare the characteristics of asthmatic adults who reported having (***n***=84) or not having (***n***=235) asthma in childhood. The specialists completed a standardized questionnaire, and carried out a clinical examination and spirometric tests. Male sex; greater severity, particularly lower spirometry values related to small airways; greater severity and earlier onset of allergy; and maternal history of atopic dermatitis and perennial rhinitis were found to be associated with reported childhood asthma. This study exhibits highly internally consistent results and indicates that subjects who did have childhood asthma and relapse in adulthood appeared to have a potentially more severe form of asthma (Segela C. *et al,* 2000).

2.9 Evolution of asthma through Childhood

The greatest incidence of childhood asthma is among males under 5 years, with decreasing numbers of new cases with age. Many young children wheeze, but remission is common especially in non-atopic children without a family history of allergy or asthma. Among children born to parents registered in a health maintenance organization in Tucson, Arizona, 34% developed wheezing illness before age 3 years, giving a mean annual incidence in the first 3 years of life of 11.3%, while a further 15% developed wheezing between 3 and 6 years old, giving a mean annual incidence of 5%. Many of these children went into remission, but

nevertheless there was a substantial incidence of wheezing illness in the first 6 years of life. In Sweden, an 11-year follow up of 1654 children revealed a total cumulative incidence of 5.3%, which would average 0.5% per annum, but incidence by age is not documented. In the national cohort study conducted in the UK, the annual incidence of asthma at ages 7, 11, 16 and 23 years was estimated to be 2.6%, 1.1%, 0.7% and 0.8%, respectively a group of almost 3000 children surveyed in Michigan at an interval of 2–4 years, the highest incidence of new asthma over the interval (5.4%) was in young males up to age 4 years. In other age groups, the incidence of new asthma varied between 1.7 and 3.3% per annum, depending on age and sex. The pattern of childhood asthma is variable, depending largely on factors operating at inception of the disease, but modulated by environmental exposures (Sears M.D, 1998).

2.10 Cost-Benefit Analysis of Childhood Asthma Management through School-Based Clinic Programs

Asthma is a leading chronic illness among American children. School-based health clinics (SBHCs) reduced expensive ER visits and hospitalizations through better healthcare access and monitoring in select case studies. The purpose of this study was to examine the cost-benefit of SBHC programs in managing childhood asthma nationwide for reduction in medical costs of ER, hospital and outpatient physician care and savings in opportunity social costs of lowing absenteeism and work loss and of future earnings due to premature deaths. Eight public data sources were used to compare costs of delivering primary and preventive care for childhood asthma in the US via SBHC programs, including direct medical and indirect opportunity costs for children and their parents. The costs of nurse staffing for a nationwide SBHC program were estimated at $4.55 billion compared to the estimated medical savings of $1.69 billion, including ER, hospital, and outpatient care. In contrast, estimated total savings for opportunity costs of work loss and premature death were $23.13 billion. Medical savings alone would not offset the expense of implementing a SBHC program for prevention and monitoring childhood asthma. However, even modest estimates of reducing opportunity costs of parents' work loss would be far greater than the expense of this program. Although SBHC programs would not be expected to affect the increasing prevalence of childhood asthma, these programs would be designed to reduce the severity of

asthma condition with ongoing monitoring, disease prevention and patient compliance (Teressa & Sherry, 2010).

2.11 Recent advances on diagnosis and management of childhood asthma and food allergies

The epidemic of childhood allergic disorders has been associated to the decline of infectious disease. However, exposure to many triggers (airborne viruses, tobacco smoke, pollution, indoor allergens, etc.) contribute to the disease. Breast feeding practices, nutrition, dietary and obesity also play a multifaceted role in shaping the observed worldwide trends of childhood allergies. Guidelines for treatment are available, but their implementation is suboptimal. Then developed countries are slowing learning integrating the development of suitable guidelines with implementation plans. Awareness, psychosocial and family factors strongly influence asthma and food allergy control. Moreover, monitoring tools are necessary to facilitate self-management. By taking into consideration these and many other pragmatic aspects, national public health programs to control the allergic epidemic have been successful in reducing its impact and trace the need for future research in the area. The most recent advances in the field of childhood asthma summarized in this review give an idea of how fast clinical research in this area is making progress. Solid approaches to avoid risk factors and to promote protective factors should be established according to the recent findings (Dani & Salvatore Tripodi, 2013).

2.12 Ketotifen alone or as additional medication for long term control of asthma and wheeze in children

A number of agents with potential anti-inflammatory actions have been identified, including macrolides and ketotifen. Small RCTs of macrolides therapy including one pediatric RCT (n=19), have suggested a beneficial effect, but further studies are necessary to delineate which patients are most likely to benefit. Ketotifen, an antihistamine has been shown to improve asthma control in predominantly atopic, mild to moderate childhood asthma when used alone or in combination with other therapies. Benefits to be weighed against side effects such as sedation and weight gain (Bassler *et al*, 2004).

Significance of the study

Now a day's asthma is a growing Health Problem around the world. As a chronic illness asthma has a major impact on the life of individual as well as their family (Kumar *et al*, 2005). Approximately 300 million people worldwide currently have asthma and its prevalence has been increases by 50% every decade (Braman, 2006). Bangladesh National asthma prevalence Study (1999) states that around 4 million children are suffering from asthma and its prevalence is more in rural area. It is the most concerning matter due to the reason of parent's unconsciousness, correct diagnosis of the diseases, and unhealthy environment of the poor country. Childhood asthma is the major cause of morbidity of children and their prevalence is increasing day by day. Therefore monitoring of the risk factors and treatment practice of childhood asthma would help doctors to think for modification of current asthma guideline.

Several cross sectional studies have been conducted over past 20-30 years that indicate prevalence of allergic respiratory diseases worldwide, particularly among children in western countries (Anderson *et al*, 1994).

In this study we will try to find out the risk factors, practice of medication and treatment process and awareness, knowledge of the parents. Although bronchial asthma cause a great deal of morbidity among children in Bangladesh but epidemiological study on that is very less (Zaman & Yunus, 2007). Study has conducted on childhood asthma in rural areas in Bangladesh which deals with the prevalence of wheezing and its association with environmental and host factors (Takeuchi *et al*, 2007). Another cross sectional study conducted in 2001 among highly populated Dhaka city and coastal areas of Bangladesh which ultimately gives the result that asthma is more prevalent in coastal areas with low outdoor pollution (Hassan M.D. *et al*, 2005). Our study will try to assess the awareness among parents, adherence to treatment to reduce the rate of asthma prevalence. The significance of this study is to reduce mortality from the asthma, to reduce severity and increase patient's compliance and to improve management of asthma.

Aims and Objectives of the study

The aims and objectives of this study were

- to find out the current situation of childhood asthma and parent's knowledge on that.
- to explore the prescribing pattern among the patients.
- to know the treatment pattern of asthma among different child age group and the risk factors prompting its initiation

3.1 Type of Study

This was a survey based study among the parents and patients.

3.2 Place of Study

Chittagong Medical College and Hospital, Chittagong, It is situated at the 2 number gates, adjacent to Chokbajar and the hospital is under the administration of the government of Bangladesh. **Chittagong Halishahar General Hospital** which is situated on Boro pool, Halishaher and this is private hospital. **Chittagong Maa & Shishu Hospital**, which is situated at Agrabad in Chittagong. It can accommodate around 1000 patients (mother & child). This Hospital is not under the administration of government, this is private Hospital.

Comilla Medical College and Hospital, **Comilla** is a government sponsored medical college near kuchaitali in Comilla, Bangladesh. Total 30 departments are running in the college and hospital. Our study population was also collected from another hospital of Comilla named Moon **Hospital (Moinamoti medical college)** which is situated at Jhawtola, Comilla. This is private organization. Majority portion of comilla data were collected from the Comilla Medical College & Hospital.

Mymensingh Medical College & Hospital, Mymensingh which is under Government administration. Our study population was also collected from that Hospital. Few of our study population were collected from Chandpur and Narayanganz also.

3.3 Study Population

This study was performed on 185 respondents among them majority were parents and few of them were patient, interviewed with a questionnaire to know their knowledge about management of asthma. Age eligible for this study was from less than 1 year to 16 year.

3.4 Design

In this study, purposive, sample technique was followed.

3.5 Study tool

The data was collected through a questionnaire which was designed by considering various studies conducted in different countries like India, Hong Kong, Australia, UK and other countries.

3.6 Study period

The study period was about 6 month started from January 2015 to June 2015.

3.7 Method

The study was performed via a questionnaire containing 41 questions which covered monitoring and maintenance treatment of childhood asthma. This questionnaire has several parts. Respondent's parents were asked to indicate their demographical profile and answer questions based on their monitoring of Asthma. For treating acute asthma respondents parents were asked about the medication particularly corticosteroid their child taken.

3.8 Data analysis

The data obtained were categorized according to the qualitative and quantitative variables after interposing the data from excel. All the test was carried out in the MS excel 2007 with respect to the respective parameters.

4.1 Age distribution

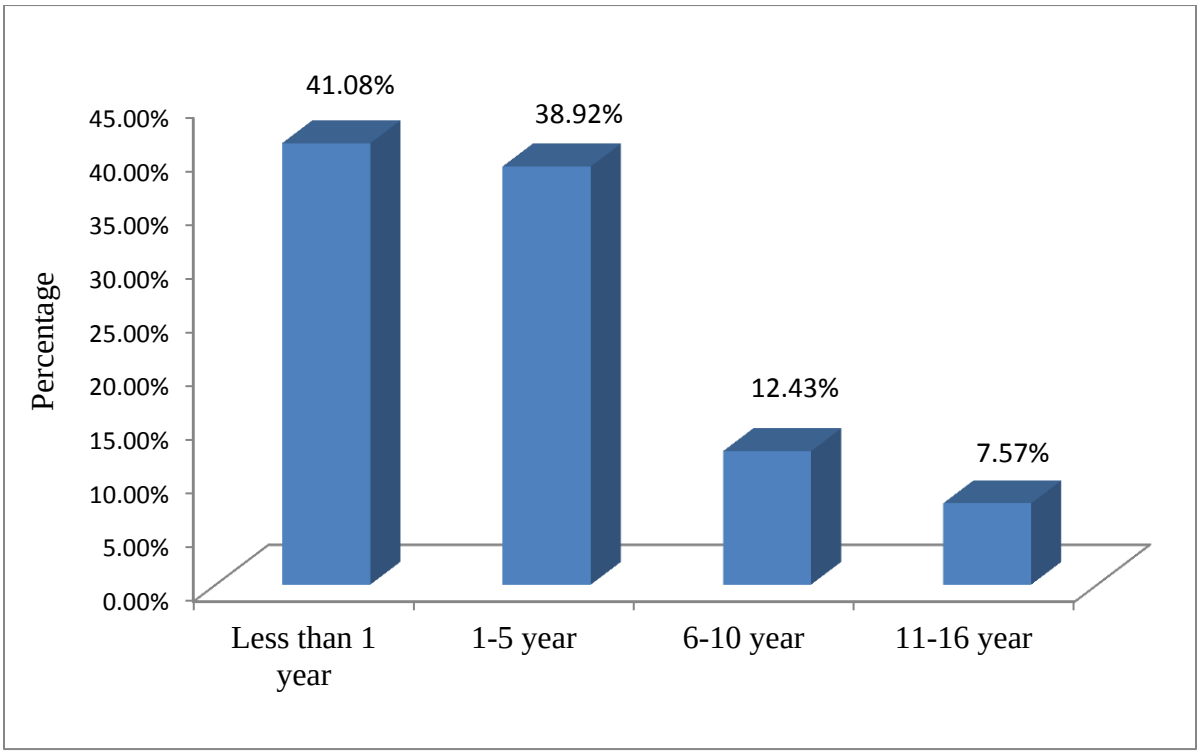

Fig 4.1: Age distribution

From the above graph it can be seen that the majority of our study population was aged less than 1 year (41.08%) and 1-5 years (38.92%).

4.2 Incidence of asthma

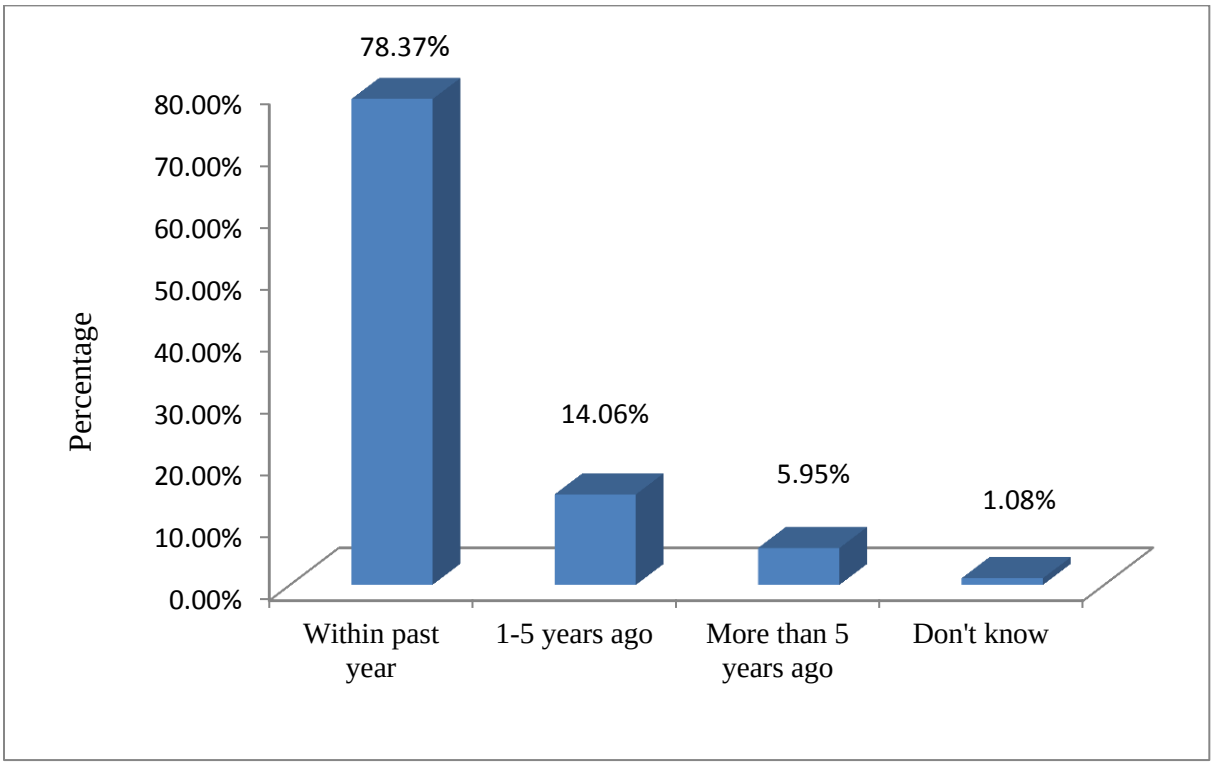

Fig 4.2: Incidence of asthma

As shown from the above graph, most of the Childs' incidence of asthma was within the past year (78.37%) and 1-5 years ago (14.06%). It has also shown that about 1.08% didn't know about their Childs' incidence of asthma.

4.3 Time interval of last asthma symptoms

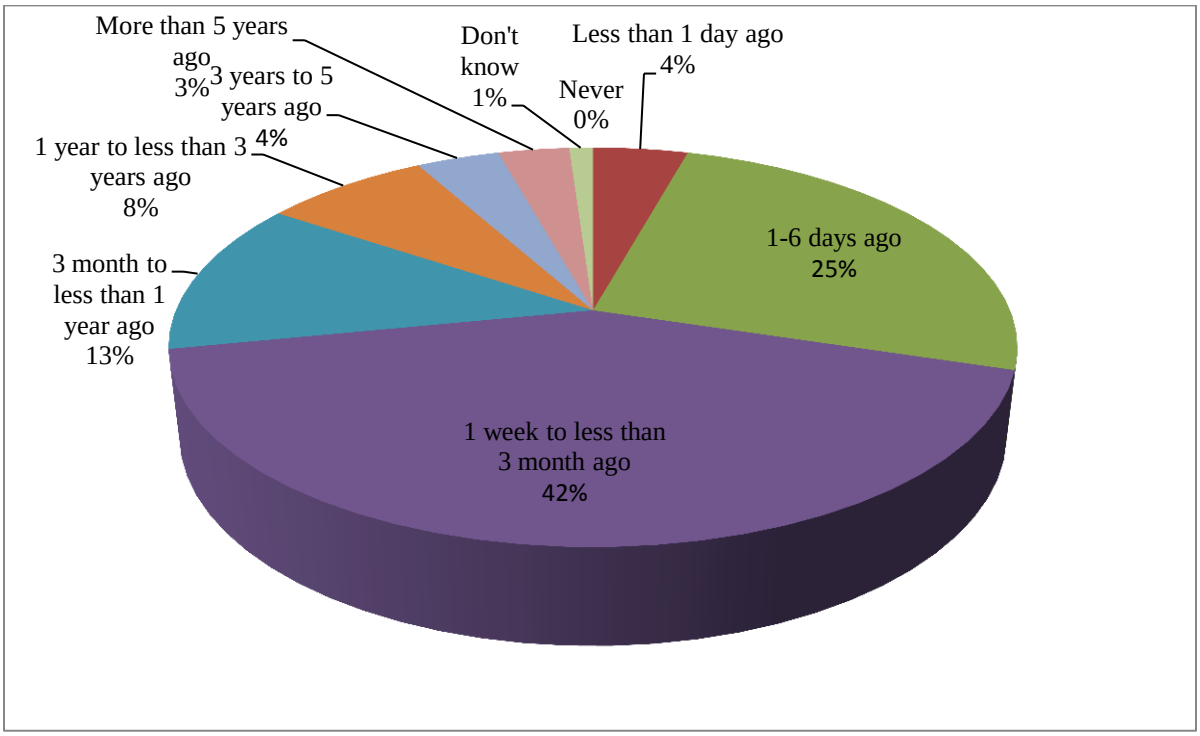

Fig 4.3: Time interval of last asthma symptoms

Above graph represents that 42% of children showed their symptoms of asthma within the range of 1 week to less than 3 months ago. It also represents that 25% of children having their incidence of asthma within the range of 1-6 days ago.

4.4 Time length of last asthma medication

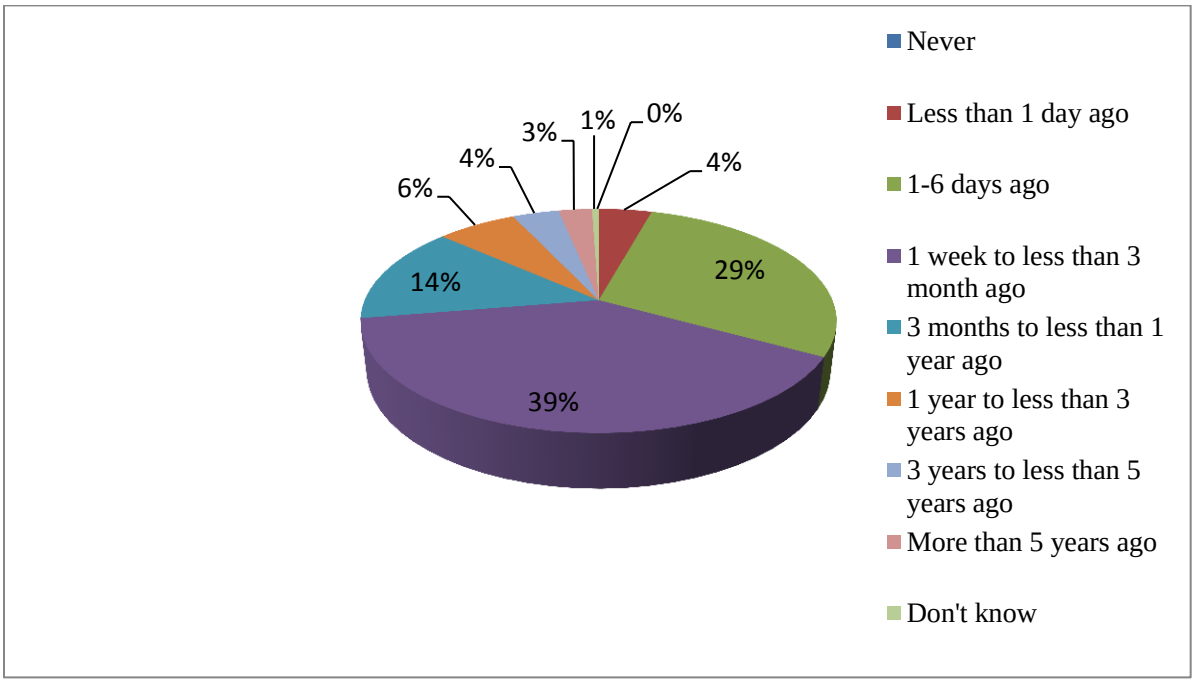

Fig 4.4: Time length of last asthma medication

From the above graph It can be seen that most of the patients (39%) took their last asthma medication within 1 week to less than 3 months ago and the second highest percentage was 29% (within 1-6 days ago) respectively.

4.5 Wheezing symptoms associated with asthma

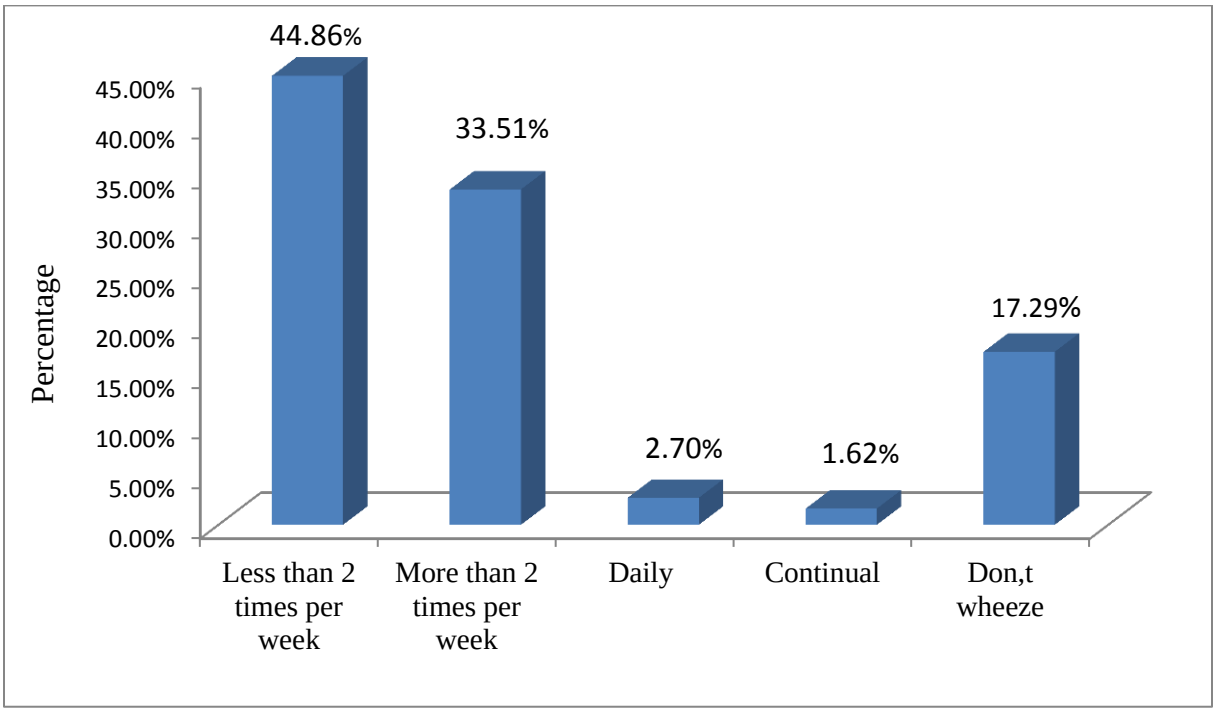

Fig 4.5: Wheezing symptoms associated with asthma

Coughing, wheezing, shortness of breathing helps to predict asthma signs and symptoms, but in case of children under the age of 5, especially in infants it is difficult to predict because wheezing symptoms may also be associated with some other problems (respiratory tract infection, bronchiolitis, pneumonia). It has also shown that not all the children of asthma have wheezing symptoms; child may have only one sign such as lingering cough or chest congestion. In our study that percentage was 17.29%. In the above graph it has been shown that most of the children about 44.86% represent wheezing symptoms in less than 2 times per week which indicates that most of the patients had mild intermittent asthma. Only 1.62% of the patients had severe persistent asthma.

4.6 Seasonal influence

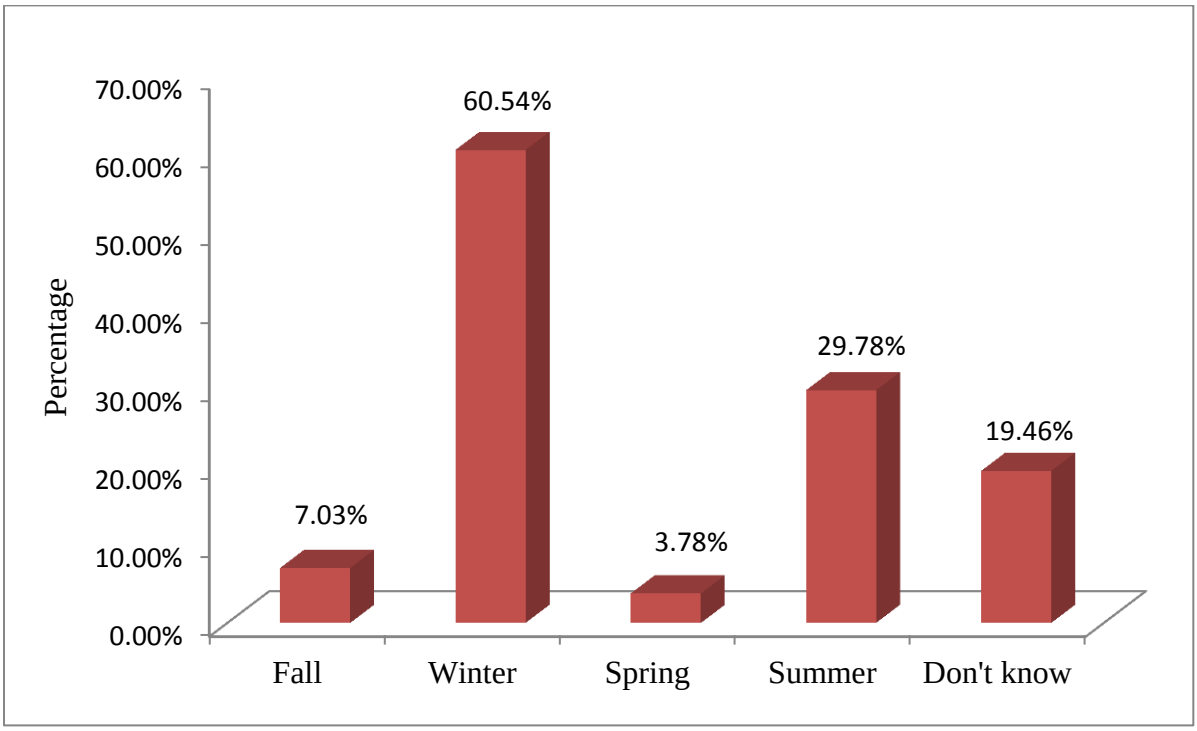

Fig 4.6: Seasonal influence

According to the above graph the seasons which mostly affect children (60.54%) was winter and later on that summer season (29.78%) affect most. Some patients were not sure (19.46%) about the season.

4.7 Continuous symptoms of asthma

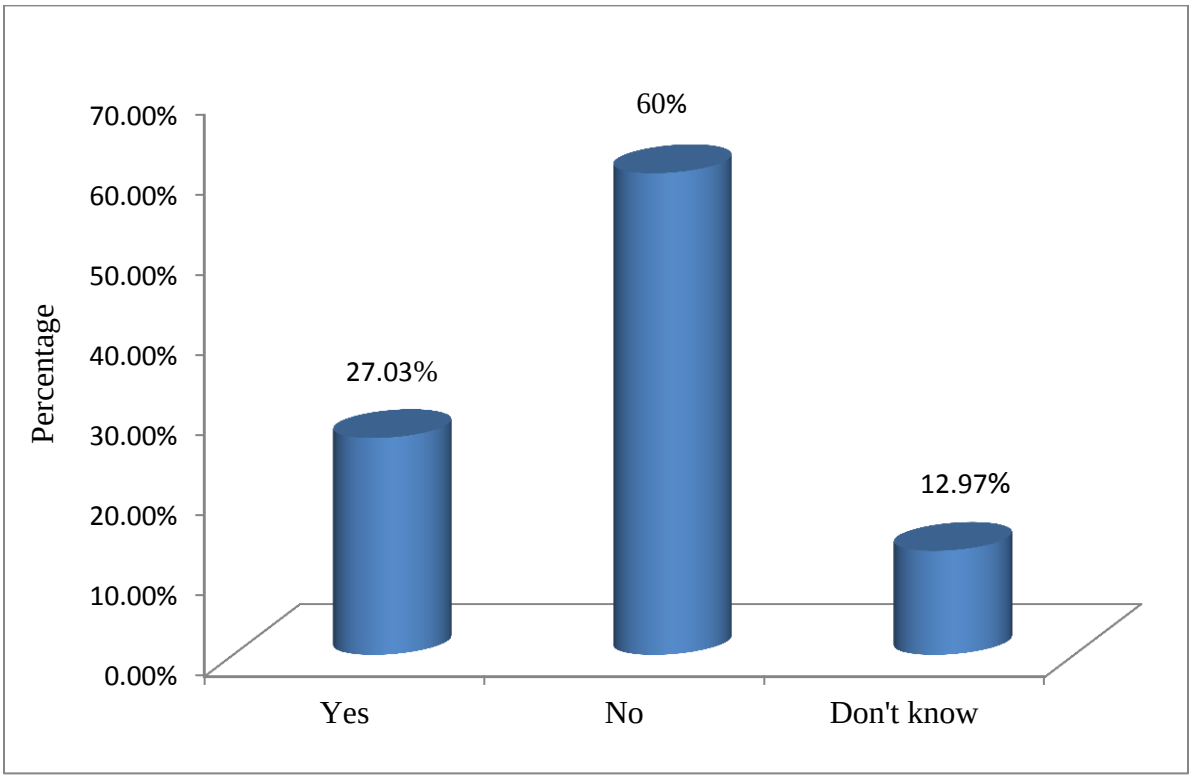

Fig 4.7: Continuous symptoms of asthma

According to the above graph 60% of the child didn't have longer experience of asthma symptoms means that they didn't suffer with the continuation of symptoms of asthma. Around 27.03% of our population suffers with the continuation of process.

4.8 Medicines taken on time

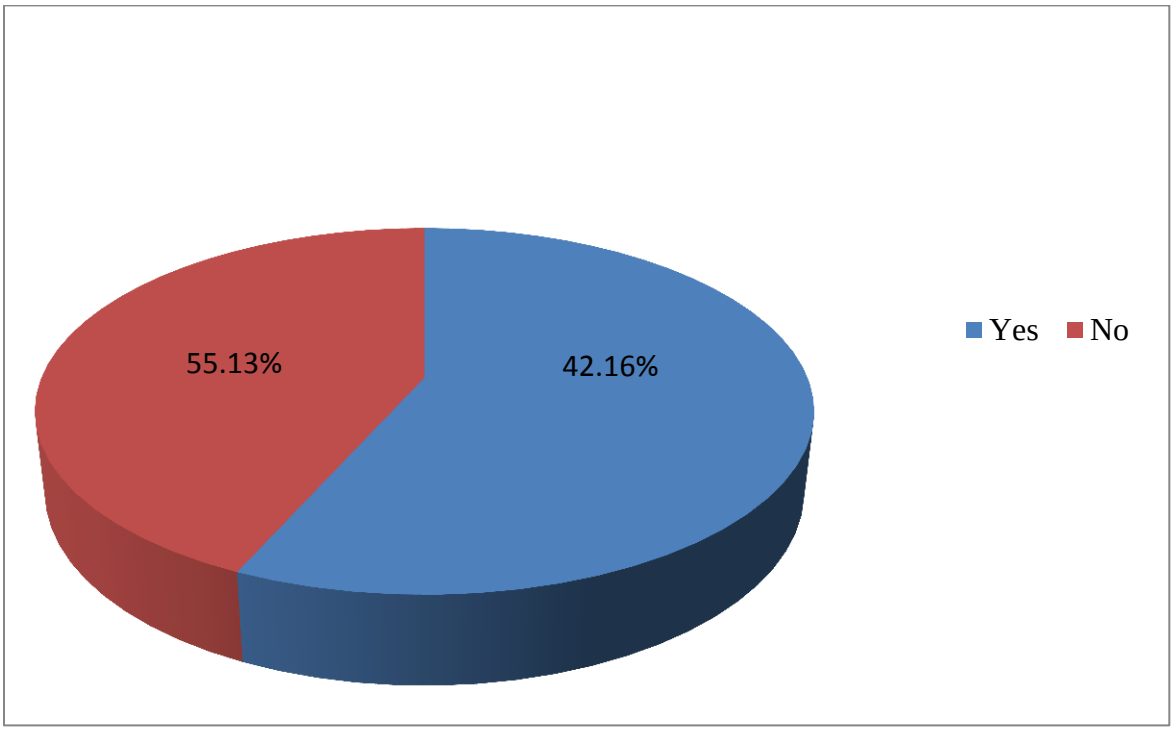

Fig 4.8: Medicines taken on time

Although Bangladesh is a poor country but from our study it has shown that 55.13% of our respondents took their medicines on time and their parents were also careful about that. About 42.16% didn't take their medicine due to some reasons.

4.9 Reasons for non-adherence of medicine

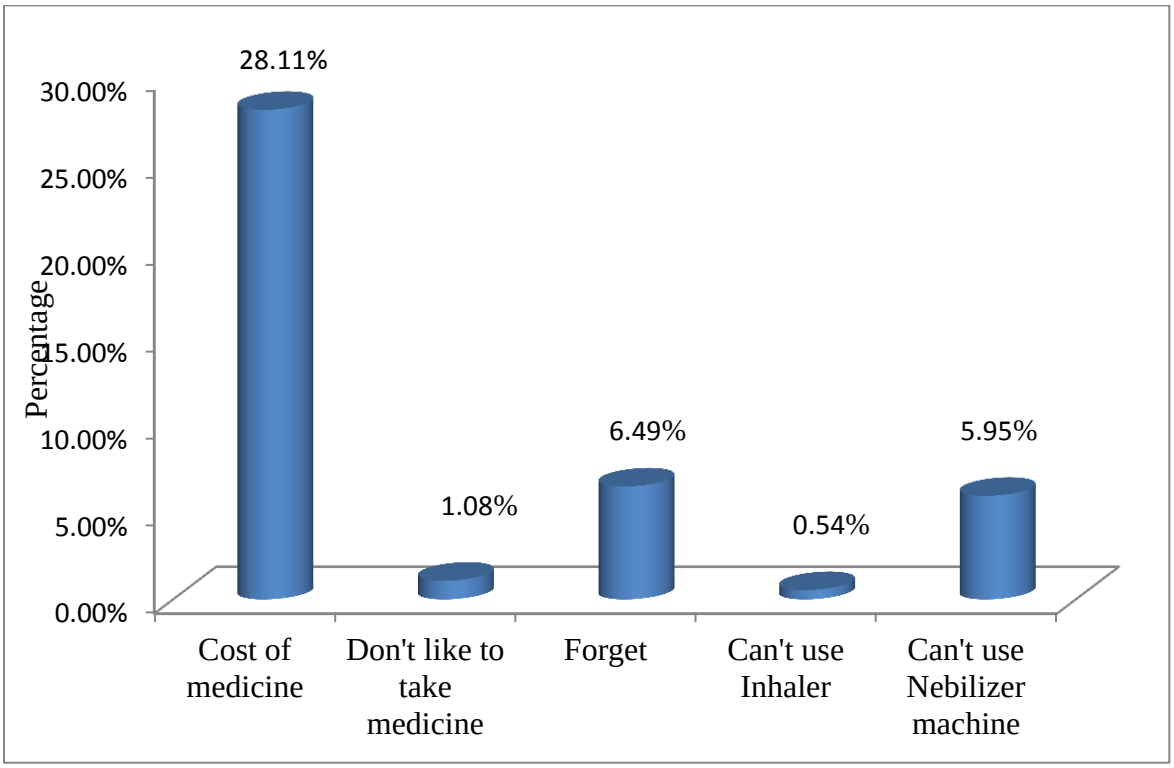

Fig 4.9: Reasons for non-adherence of medicine

Above graph describes that among our study population, 28.11% of child didn't take their medicine on time due to cost as most of the people in our country is poor. Our study also shows that some populations forget to take medicines on time (6.49%) and some (5.95%) didn't know how to operate some special device called Nebulizer.

4.10 Most recent asthma attacks/episodes

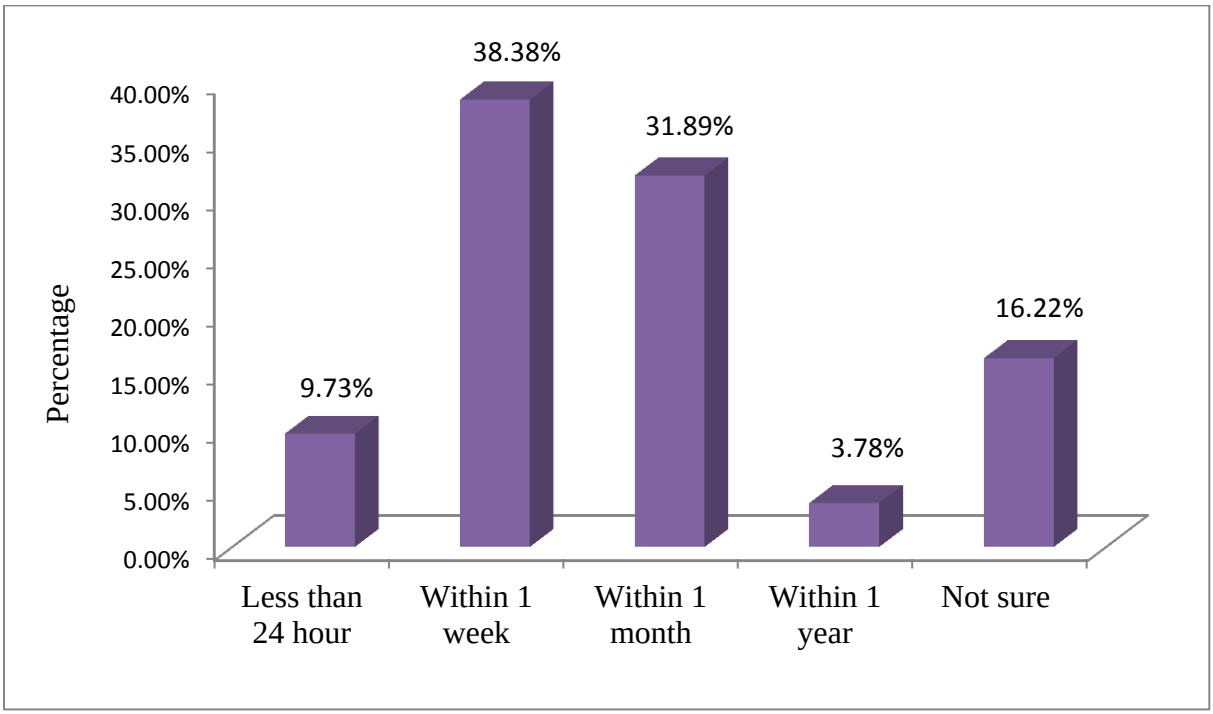

Fig 4.10: Most recent asthma attacks/episodes

According to the above graph most of the child's (38.38%) most recent asthma attacks were within 1 week with some other associated problems (like cold, fever, nasal congestion). The second highest percentage was 31.89% which has shown most recent asthma attack within a month.

4.11 Comparison of recent asthma attack with previous attacks

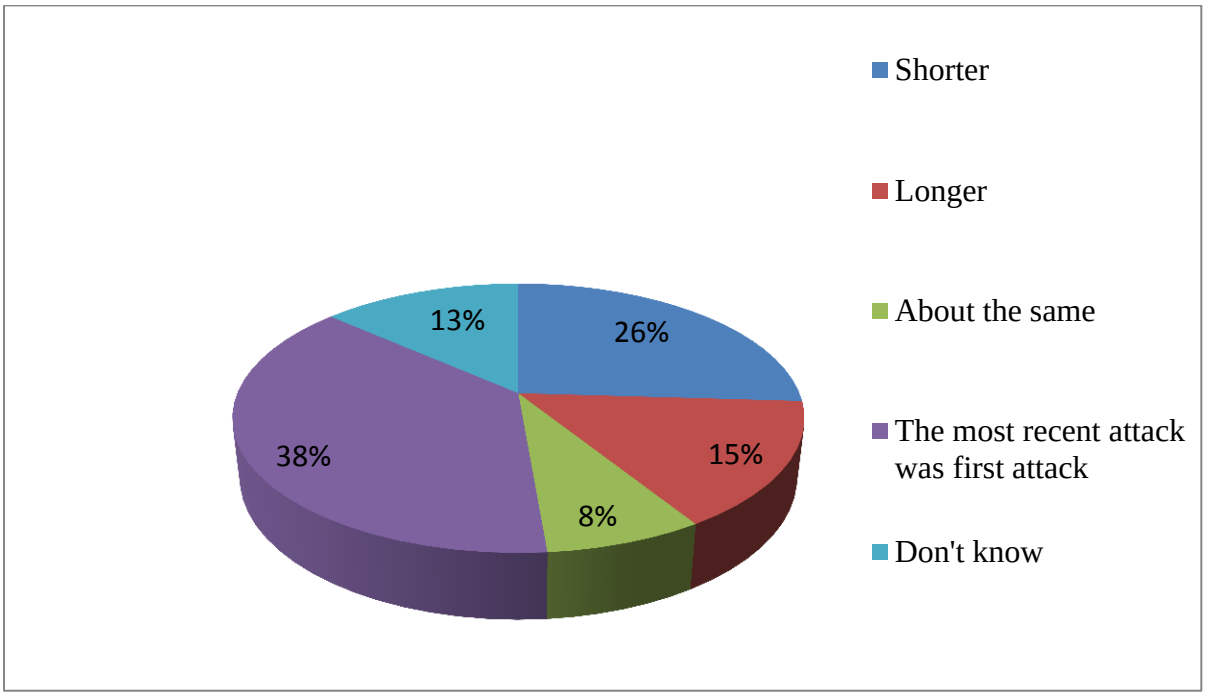

Fig 4.11: Comparison of recent attack with previous attack

According to above pie diagram majority of child's (38%) recent attack was actually their first asthma attack. When compared to previous asthma attacks about 26% had shorter attack and 15% had longer attack.

4.12 Impact of asthma on Childs' routine activity

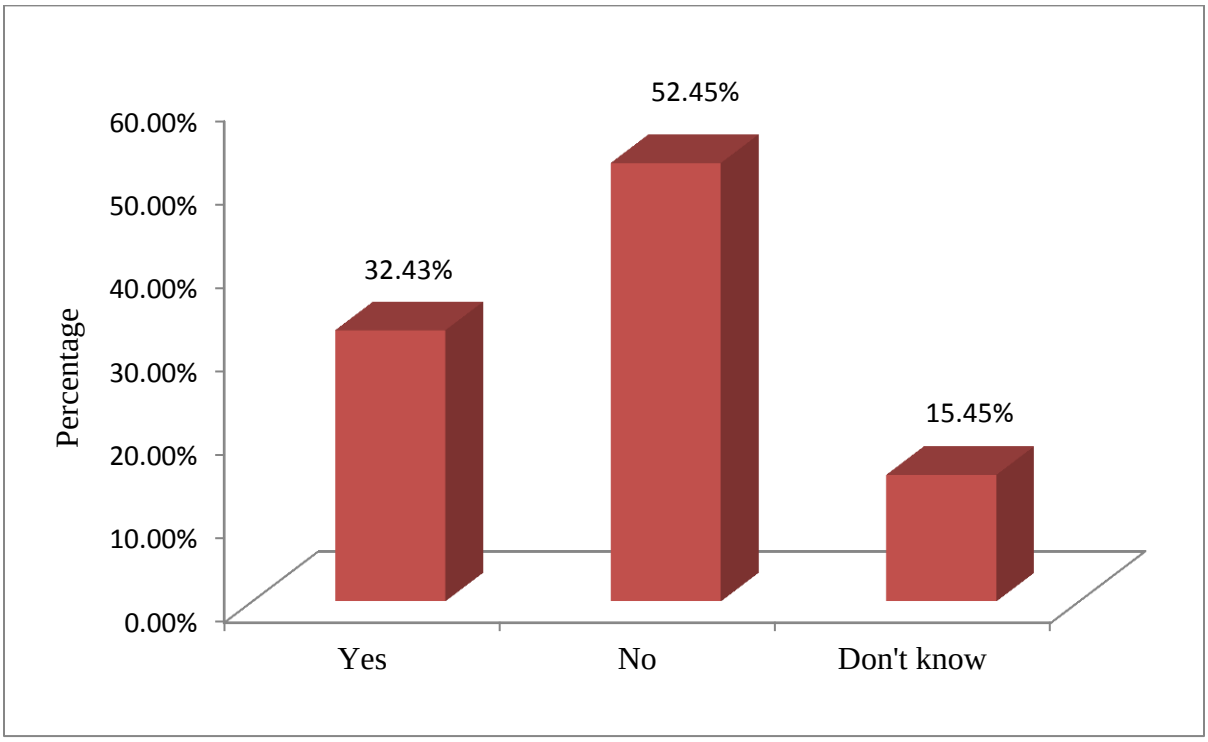

Fig 4.12: Impact of asthma on child's routine activity

In case of our study population (52.45%) usual activities was not hampered due to asthma. Child's (32.43%) activity was hampered due to asthma and 15.45% of the study population was not aware about that.

4.13 Childs' difficulty in sleeping

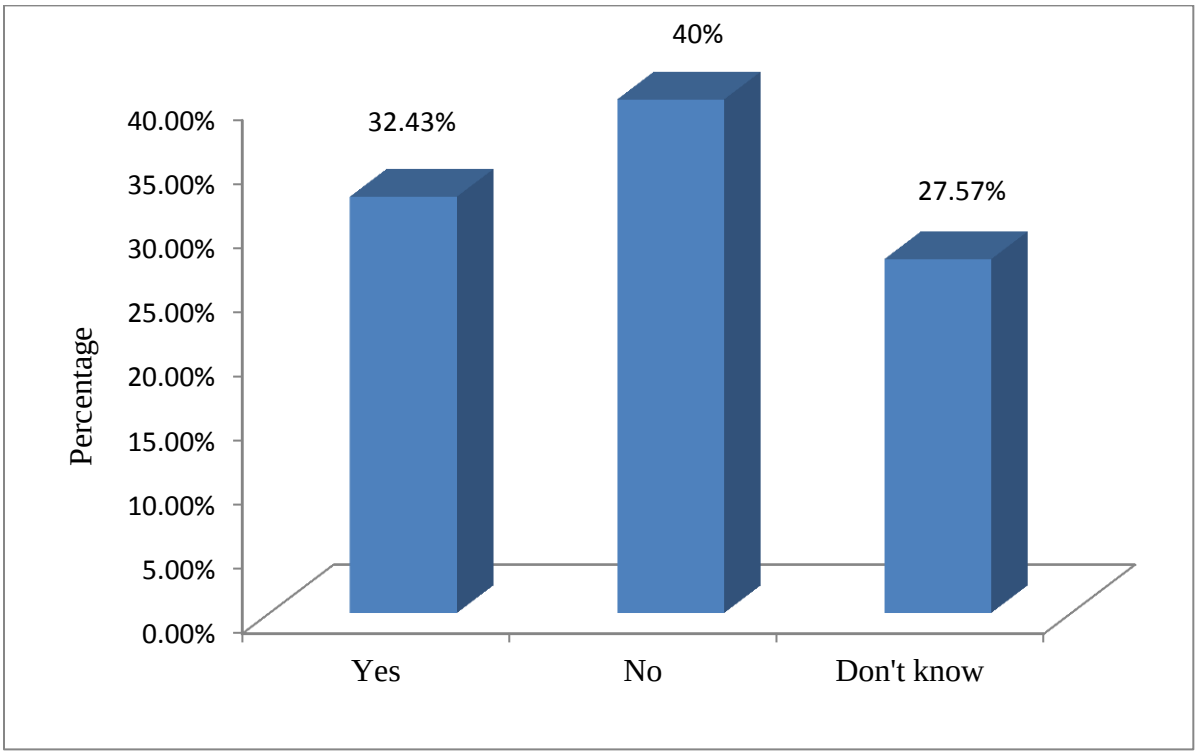

Fig 4.13: Childs' difficulty in sleeping

According to the above graph 40% child didn't have to stay awake due to asthma episodes or attacks whether 32.43% of the child's have to stay awake or difficulty in sleeping due to their asthma symptoms which has shown after several time intervals. About 27.57% parents didn't notice that reason yet.

4.14 Urgent treatment for worsening of asthma attacks

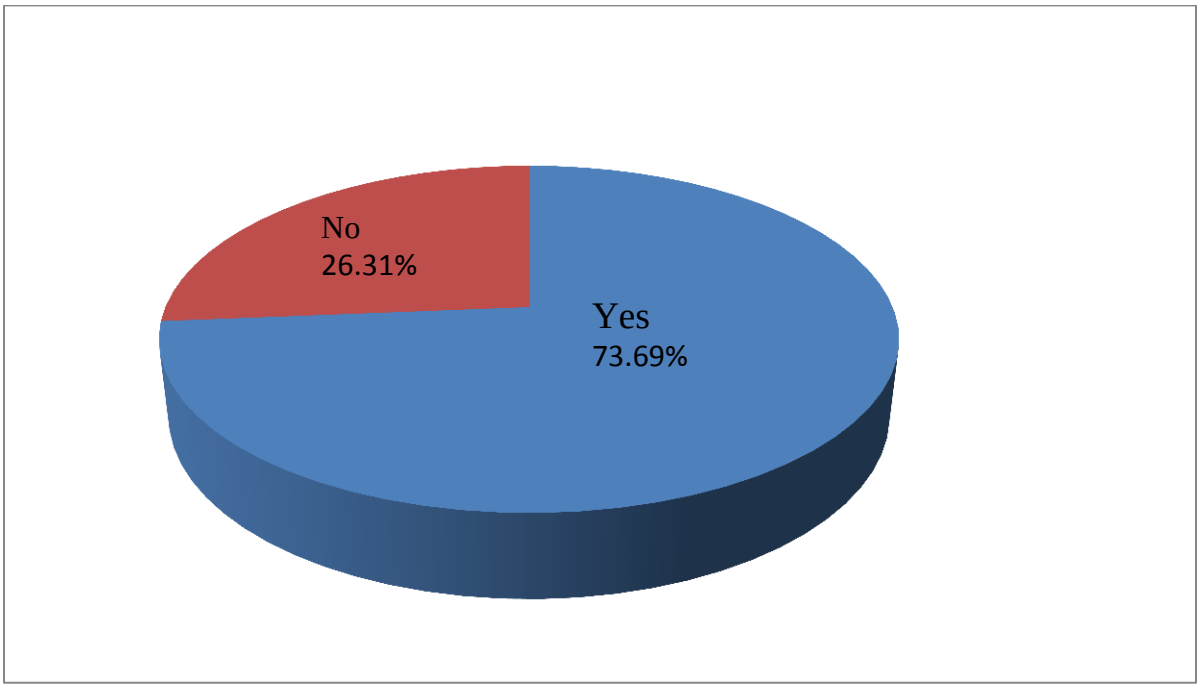

Fig 4.14: Urgent treatment for worsening of asthma attacks

The above diagram represents that majority of child's (73.69%) were admitted into hospital due to worsening of asthma symptoms and taken urgent treatment for acute exacerbation of asthma (such as oxygen inhalation). About 26.31% respondents didn't get admitted to hospital.

4.15 Routine checkup for asthma

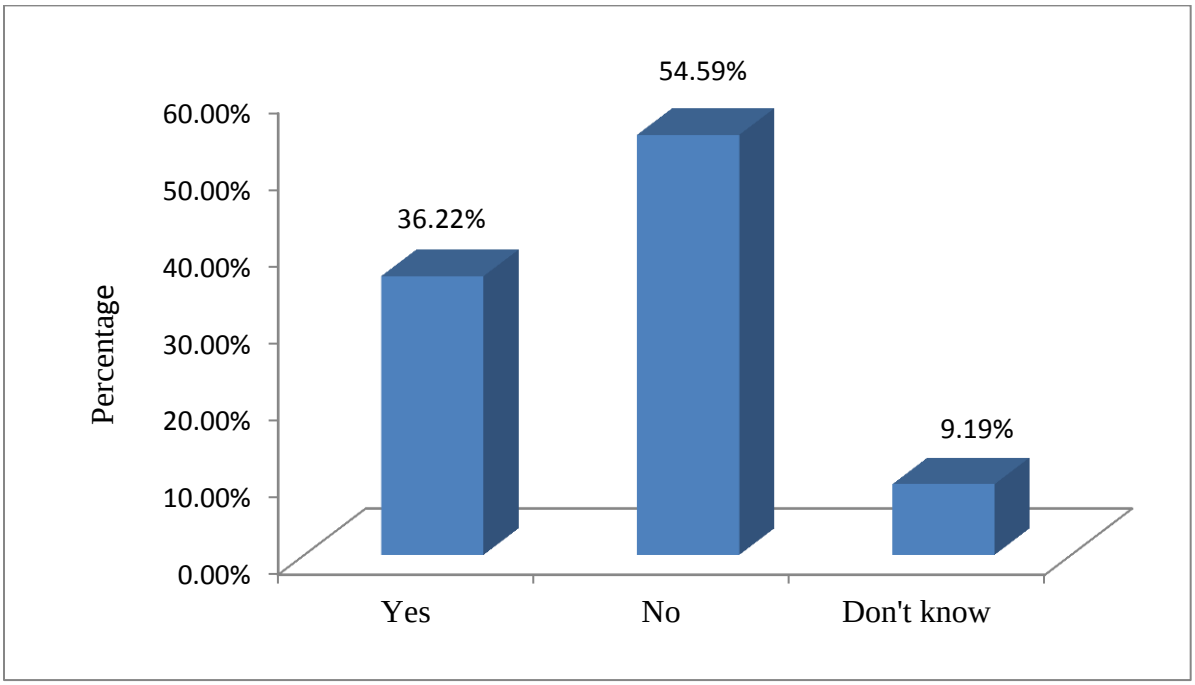

Fig 4.15: Routine checkup for asthma

As most of our study population recent asthma attacks was actually their first asthma attack so rate of routine checkup for asthma was less in our study about 54.59% population. About 36.22% has gone to doctor for routine checkup. Some (9.19%) were confused about the time interval.

4.16 Recognize early signs and symptoms of asthma

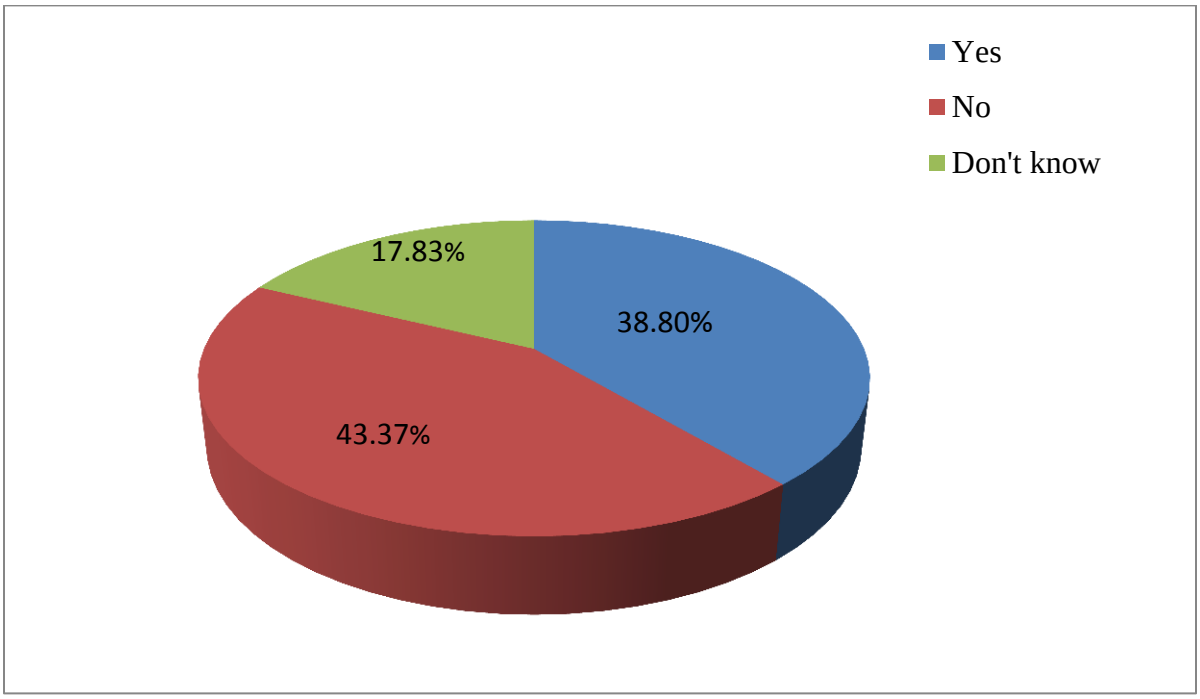

Fig 4.16: Recognize early signs and symptoms of asthma

From the above graph it has shown that despite of their Childs' having asthma most of the parents (43.37%) didn't have any knowledge or lack of knowledge about the early signs and symptoms of asthma. About 38.38% of them recognized the signs and symptoms of asthma.

4.17 Knowledge about asthma attack/episodes

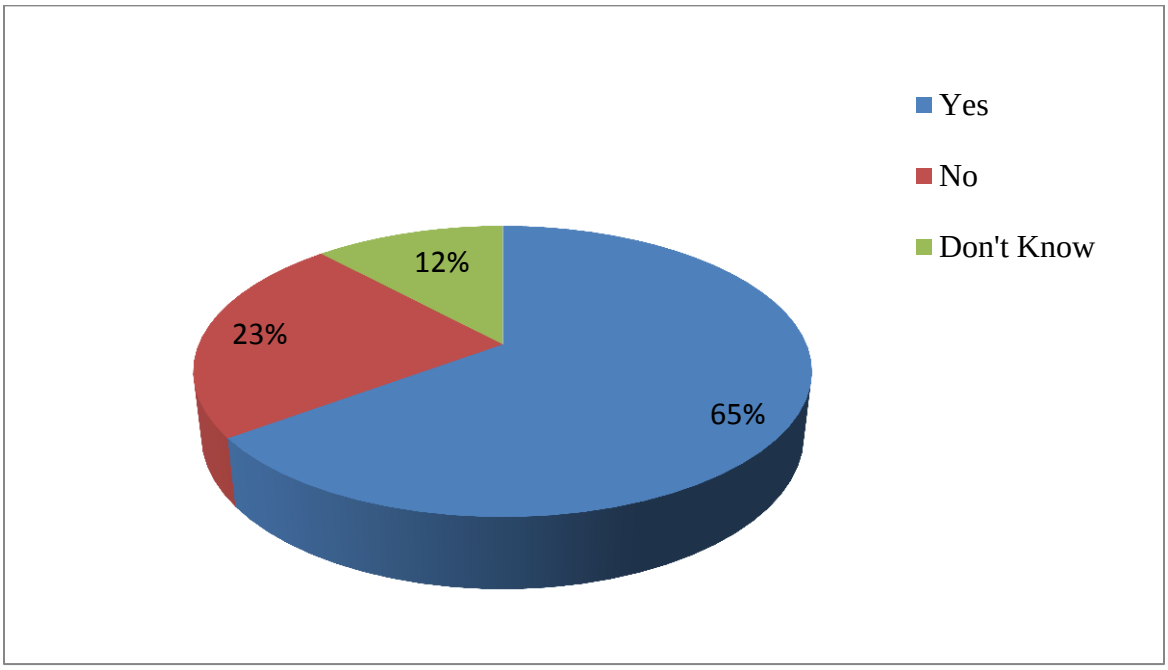

Fig 4.17: Knowledge about asthma attacks/episodes

According to the graph, about 65% of our study population has given information about the asthma attacks. Parents (23%) didn't have any knowledge on asthma attacks and 12% were not interested to answer the question.

4.18 Parent's perception about asthma symptoms caused by external factors

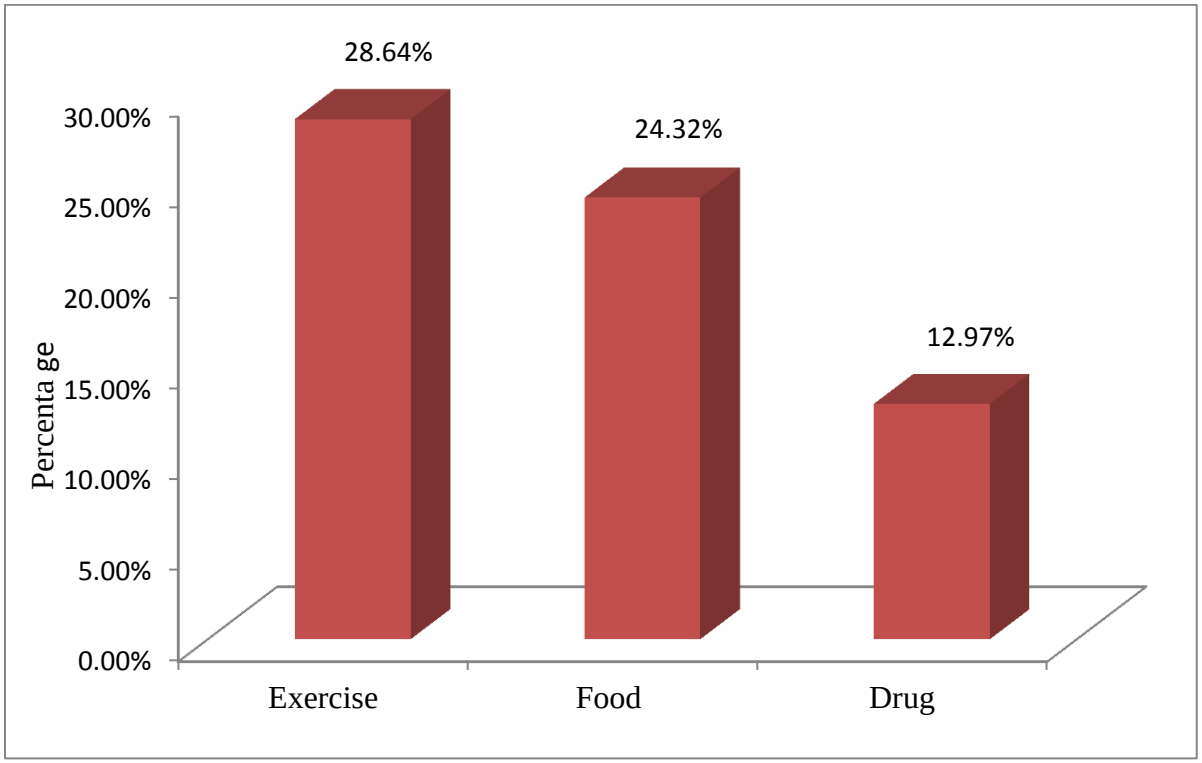

Fig 4.18: Parents perception about asthma symptoms caused by external factors

For asthma exercise, food and drug factors are considered as the major symptoms but our study result find out that majority of the parents were not considered this factors as major factors. From our observation it has shown that only few parents were concern about that factors and their percentage was respectively 28.64% (exercise), 24.32% (food) and 12.97% (drug). Our study result also represents that about 15.68% (exercise), 36.22% (food), 50.81% (drug) can't even say anything regarding these factors.

4.19 Parent's perception about symptoms associated with allergy, irritants and common cold

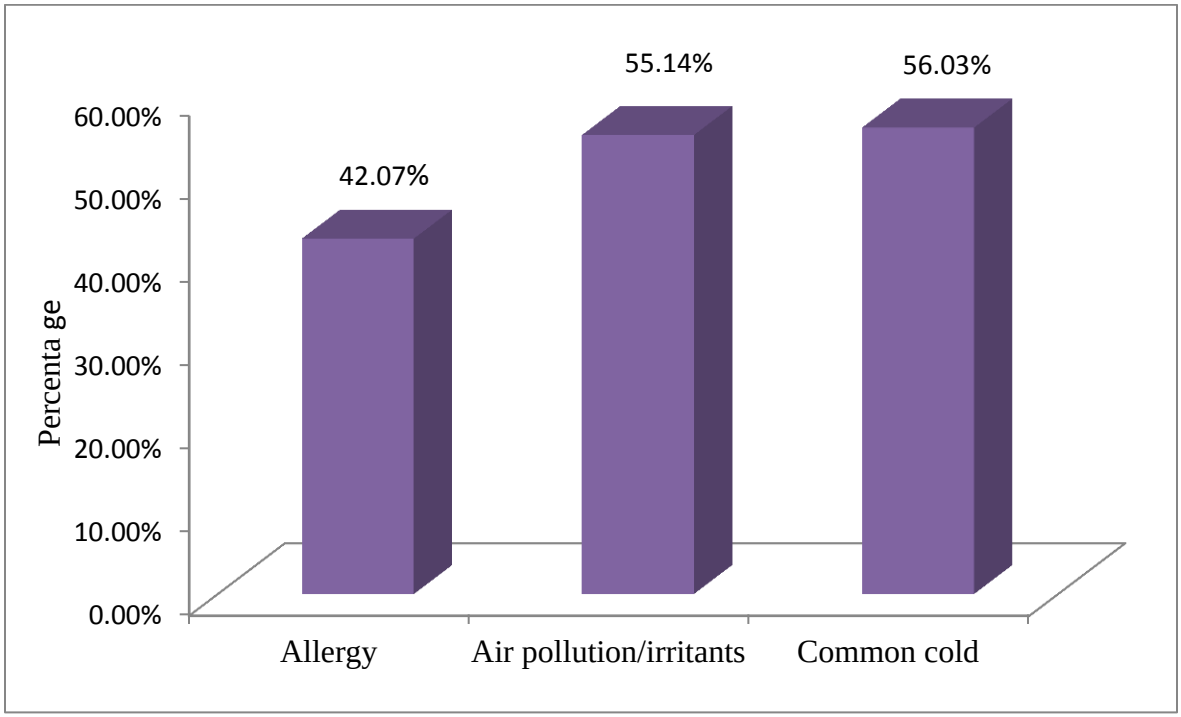

Fig 4.19: Parents perception about symptoms associated with allergy, irritants and common cold

According to the above data about 42.07% of Childs' parents claimed that their child having allergy problem, 55.14% having problems with dust, fumes or any other type irritants and 56.03% of having common cold and nasal problems. About 33.52% (allergy), 16.21% (air pollution/irritants) and 5.21% (common cold) of our population didn't have any idea about these factors.

4.20 Family history of asthma

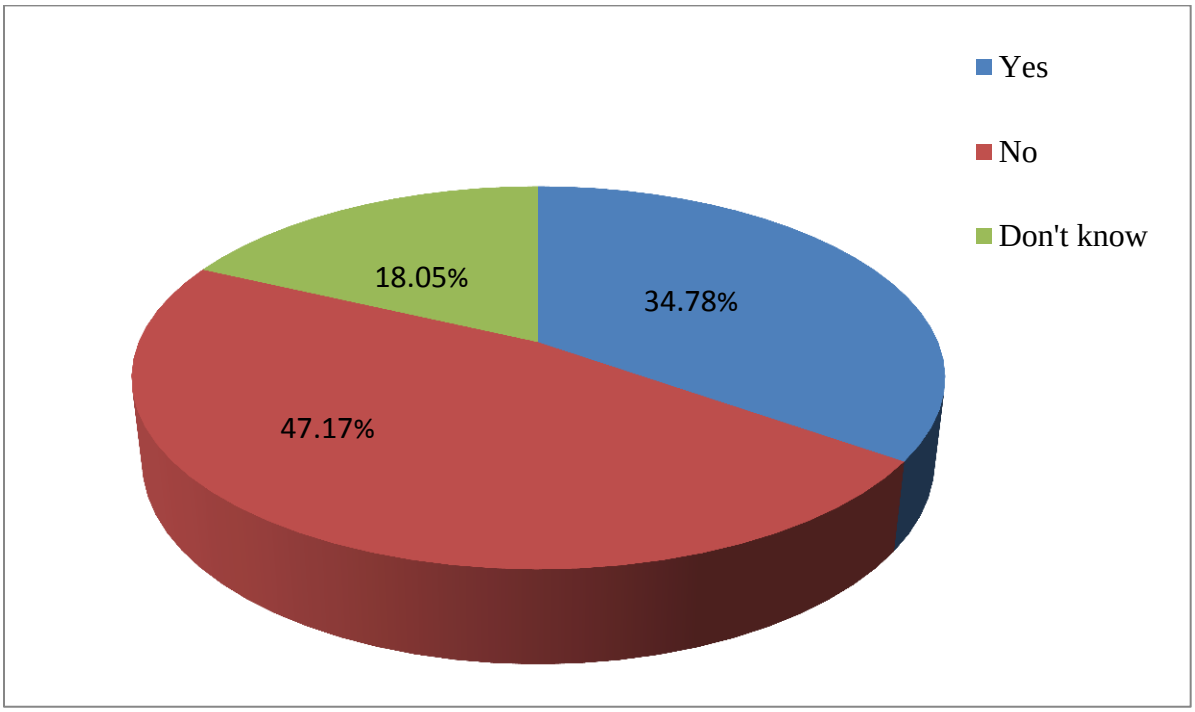

Fig 4.20: Family history of asthma

From the study result it has been shown that about 47.17% had no family history of asthma and 34.78% of children had family history. About 18.05% can't say about the family history of asthma.

4.21 Use of exhaust fan in kitchen

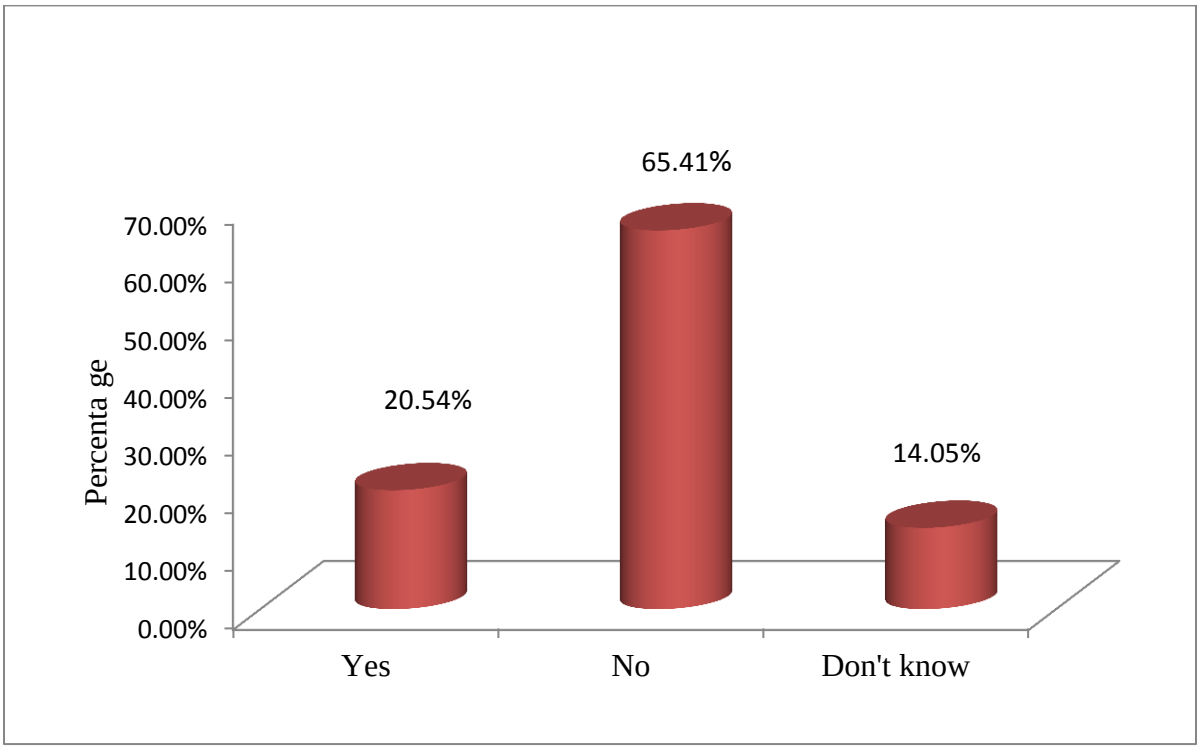

Fig 4.21: Use of exhaust fan in kitchen

From the graph it has shown that about 65.41% didn't use exhaust fan in their kitchen to remove the dust or fumes from the kitchen (As majority of them used wood burning fireplace or stove). 14.05% of populations don't even hear about the exhaust fan.

4.22 Household pets (dogs, birds or feathered pets,) in indoors

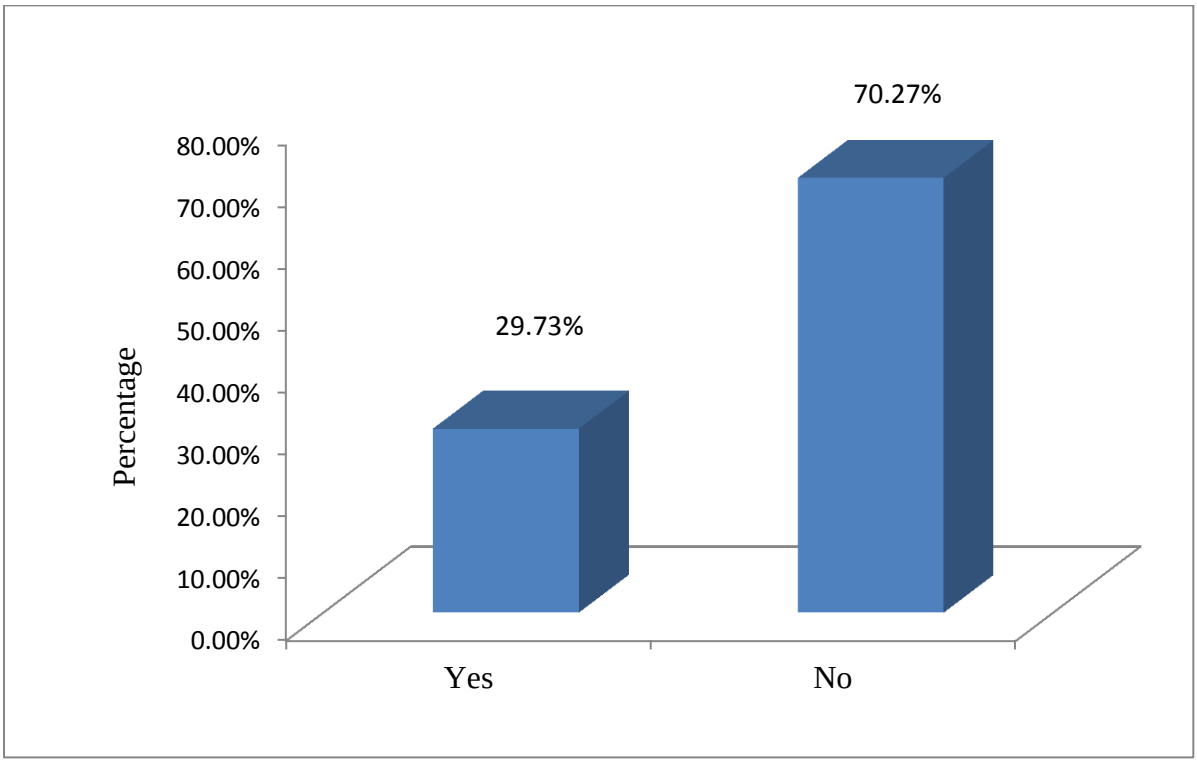

Fig 4.22: Household pets in indoors

The above pie diagram represents that majority of population (70.27%) didn't allow their pets to spent time in indoors as well as household area. About 29.73% allow pets to spend time in indoors.

4.23 Use of carpets and rugs in house

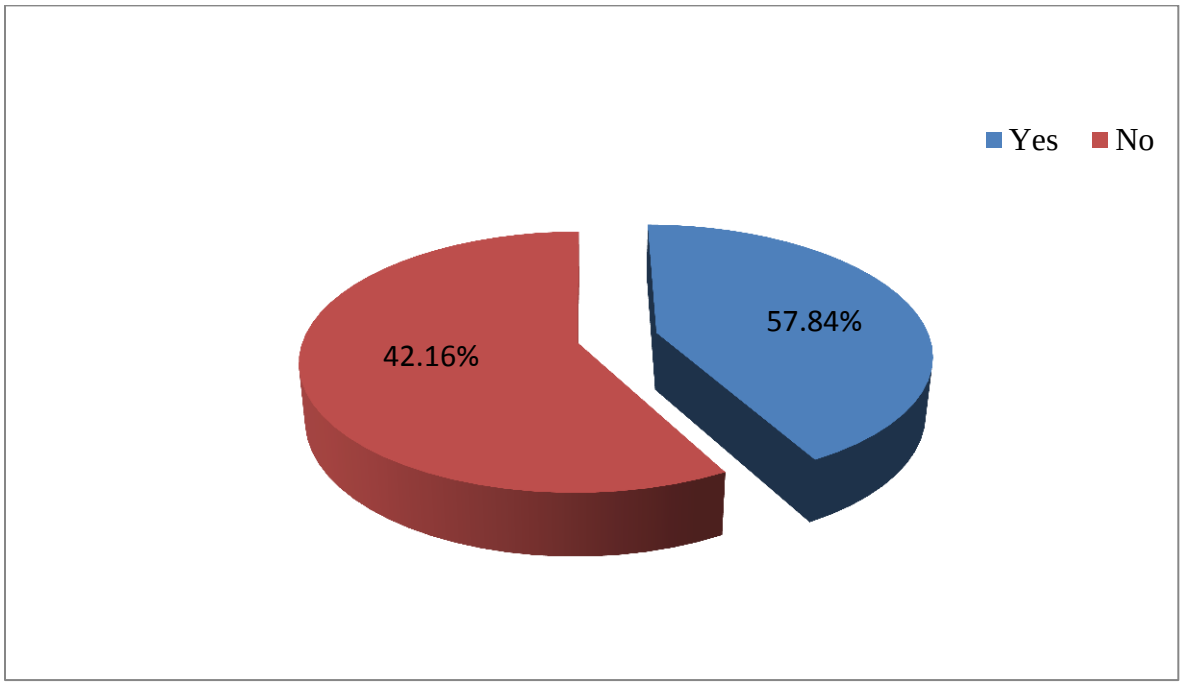

Fig 4.23: Use of carpets and rugs in house

Majority of our study population (42.16%) didn't use carpets but maximum used rugs in their house and 57.84% of our study population didn't use either carpets or rugs in their house.

4.24 Medications taken by children

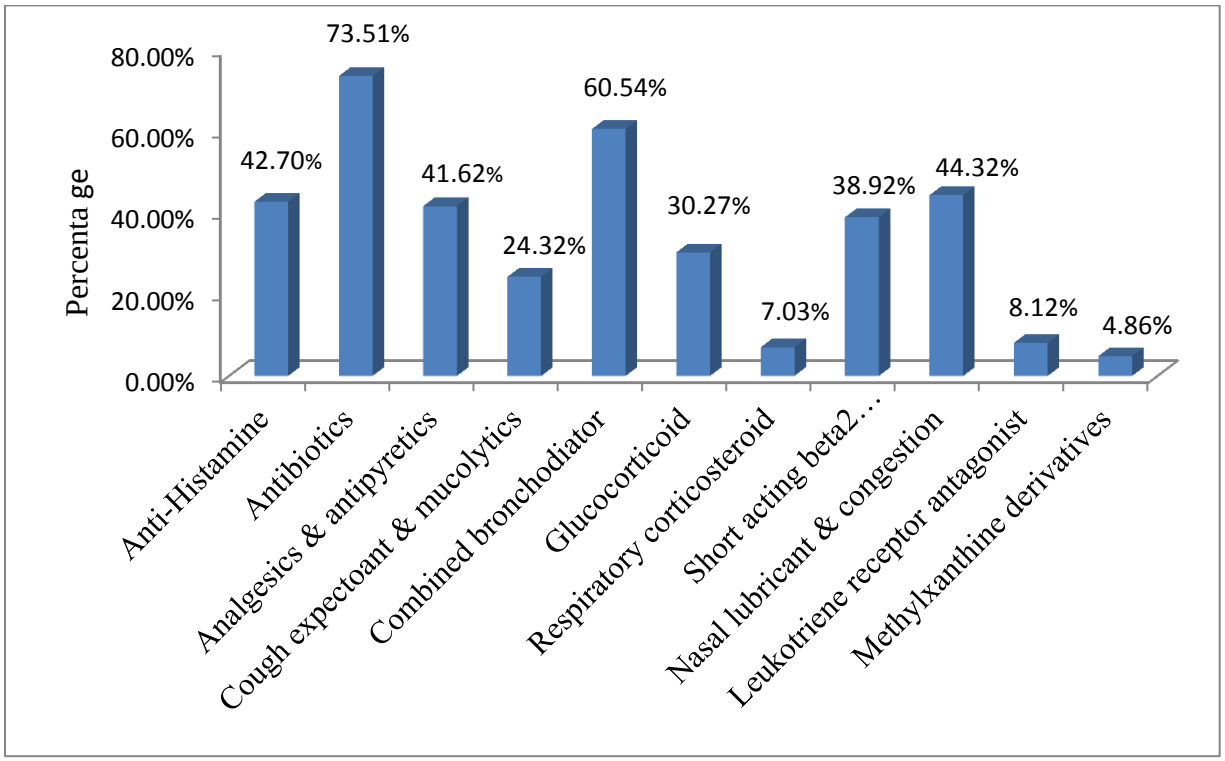

Fig 4.24: Medications taken by children

From the above diagram it has shown that majority of population take medicines not only for asthma symptoms but also for the respiratory tract infections. Among the above graph 73.51% were used Antibiotics (such as cftraiaxone, Meropenem, Flucloxacillin, Cefotaxim). Antihistamine (such as diphenhydramine, fexofenadine HCL and dexamethasone) used to diminish the release of histamine and in some inflammatory conditions, contain the percentage of 42.70%. About 60.54% population have shown to use Combined bronchodilators. Among the Glucocorticoid (30.72%) most of the physician prescribed Prednisolone as in oral and syrup form. Nasal spray or lubricant (44.32%) used for stuffy nose. Short acting β2 agonist (38.92%). 24.32% cold remedies used to remove cough and cold associated with asthma. From the analysis it has also shown that Children about 27% with life-threatening asthma or SpO_2 <94% should receive high-flow oxygen via face mask or nasal cannula at sufficient flow rates to achieve normal saturations of 94-98%.

4.25 Use of prescription inhaler

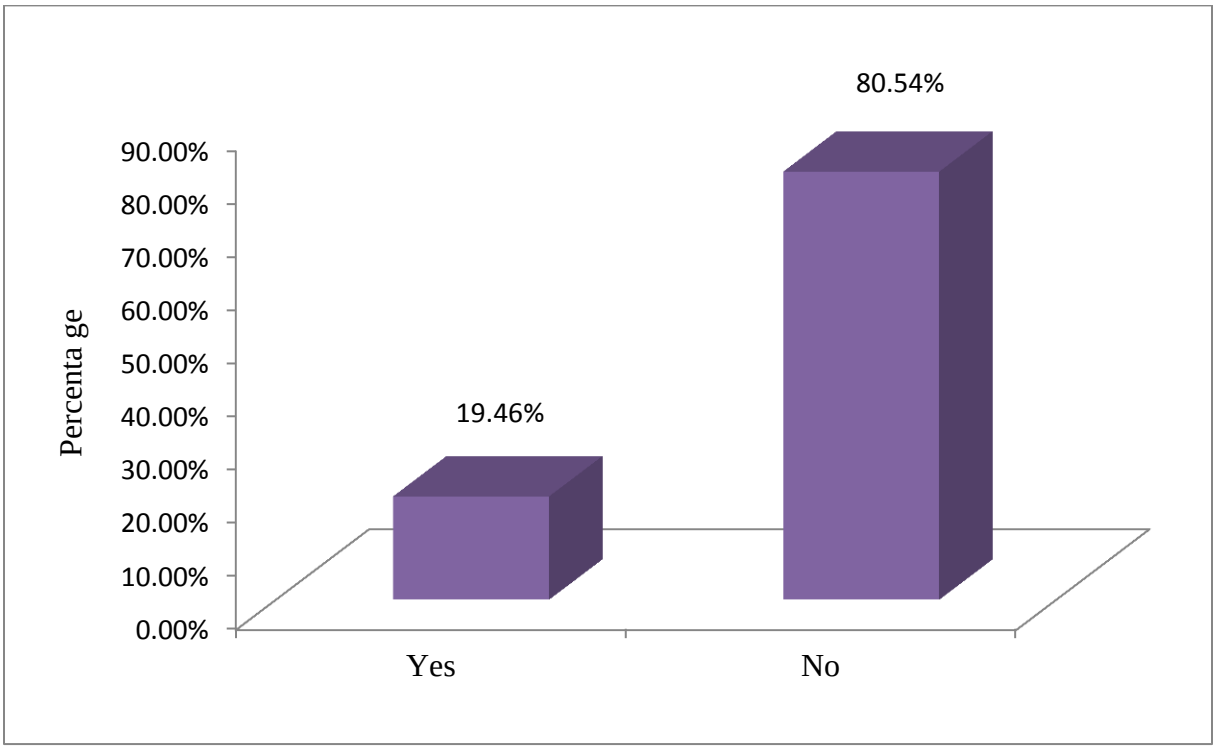

Fig 4.25: Use of prescription Inhaler

As the majority of our population was under the age of 5 year so most of them took medication with the nebulizer (80.54%) and less used inhaler (19.46%).

4.26 Inhaler/puffs taken by children

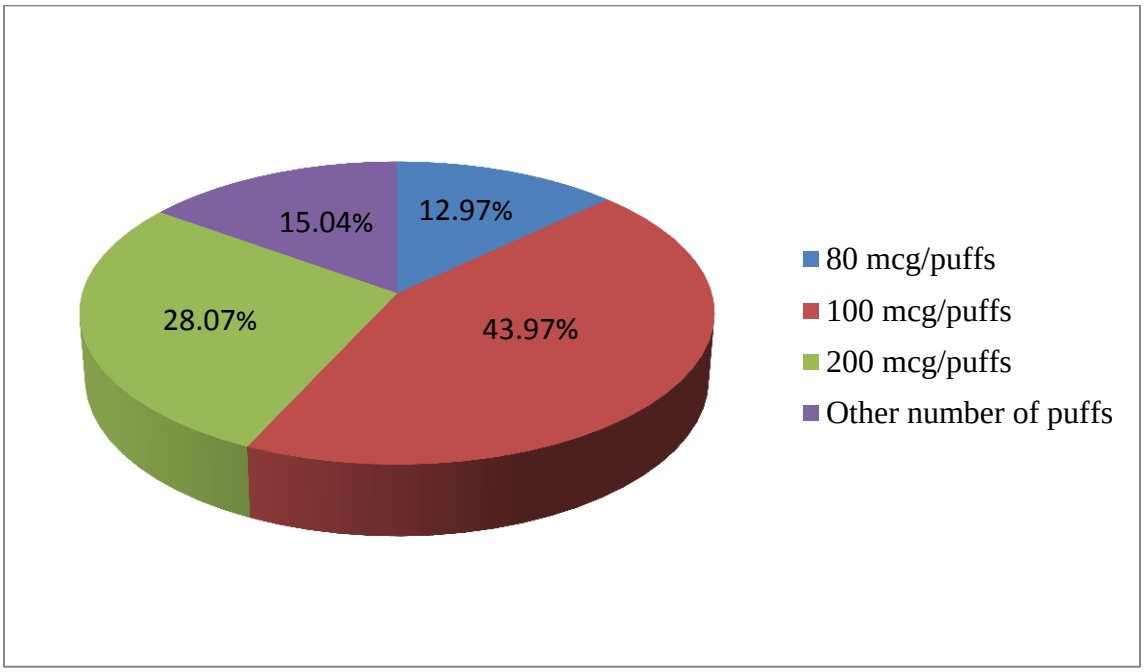

Fig 4.26: Inhaler/puffs taken by children

According to the above data majority of respondents (80.54%) in our study didn't use inhaler. 100 mcg/puffs were taken by 43.97% of the population and 28.07% used 200 mcg/puffs. On average 1-2 puffs was taken each time by child, more puffs 3-4 was taken in certain case like exercise or severe attacks.

4.27 Medication taken in syrup form

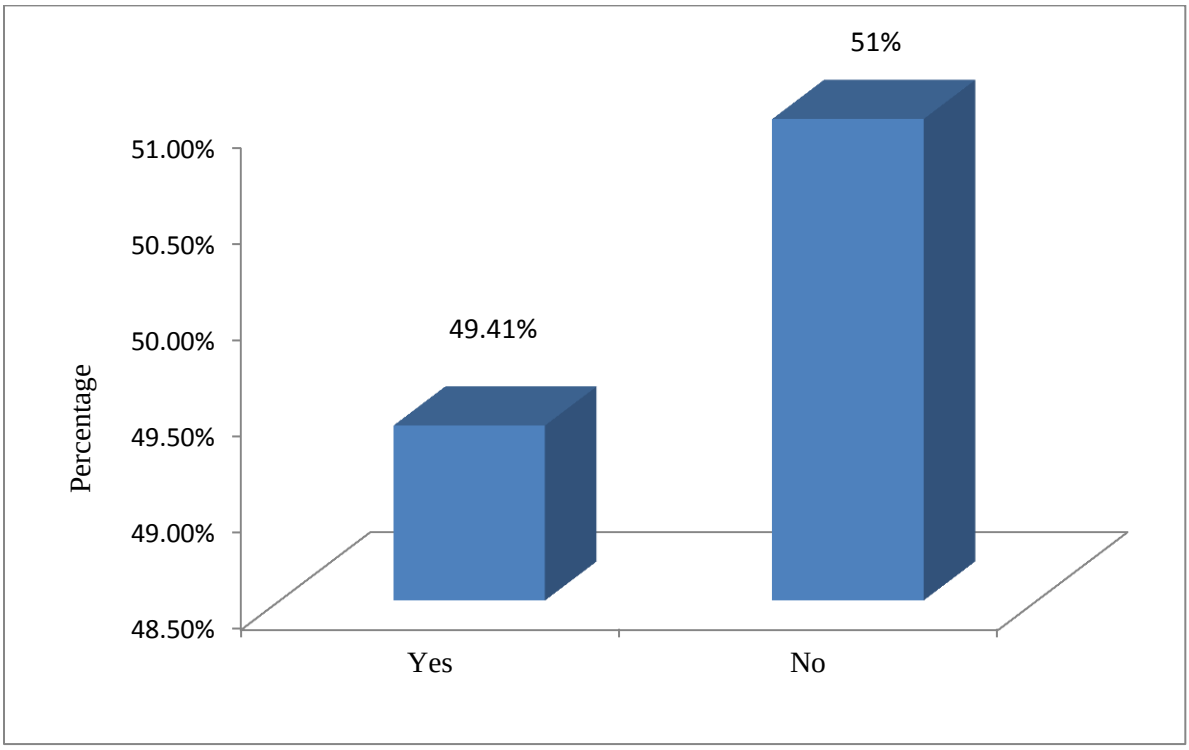

Fig 4.27: Medication taken in syrup form

From the above graph it has shown that 49.41% child took medicines in syrup form and 51% were not prescribed to take medicine in syrup form.

4.28 Medication taken with the nebulizer

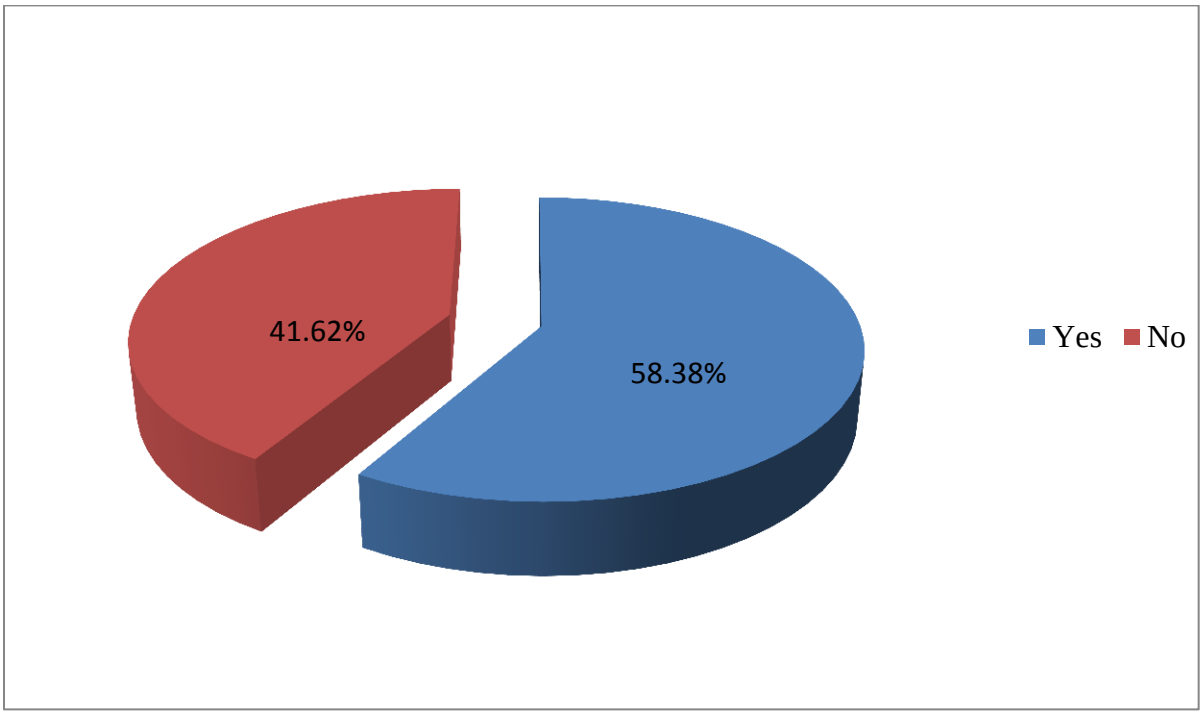

Fig 4.28: Medication taken with nebulizer

Among the respondents majority of our study population around 58.38% took asthma medication with the help of nebulizer. About 41.62% were not taken medicine with the help of nebulizer. They used either syrup or inhaler.

5.1 Discussion of the study

With childhood asthma the lungs and airways become easily inflamed when exposed to certain triggers, such as airborne pollen. In other cases, childhood asthma flares up with a cold or other respiratory infection. Asthma in children is a leading cause of emergency department visits, hospitalizations. Unfortunately, childhood asthma can't be cured, and symptoms may continue into adulthood. In this study our main goal was to find out the parents knowledge and parents perception about asthma attacks, treatment pattern of asthma attacks for children in several districts (Comilla, Chittagong, Mymensingh, Narayanganj, and Chandpur) of Bangladesh. In our study we worked on different ages (>1 year to 16 year) of children which is comparable to a cross sectional survey of knowledge, attitude of parents conducted in 29 cities of China where respondents had an age of 0-14 years (Jing Z. *et al*, 2013).

According to our study prevalence of asthma wheezing symptoms was 44.96%. A study on childhood asthma in Bangladesh (1997) showed 11.18% prevalence of asthma wheezing symptoms in the coastal region (Kabir *et al*, 1999). It has been reported that the history of pneumonia in early life is strongly associated with bronchial asthma (Gern *et al*, 2005). The incidence of wheezing is greatest in first few year of life (Strachen *et al*, 1985). The highest incidence of asthma attacks in our study is 78.37% (0-5 years) and majority of them shown incidence within the last year of our study interval.

For asthma exacerbation symptoms we considered several factors in our study like common cold, seasons, allergic food, dust, kerosene/gas stove and air pollutants such as fumes of motor vehicles. In relation to fumes of motor vehicle similar finding were reported from Germany (Duhme & Weiland, 1996).

From our Study it has shown that many doctors or health care professionals did not use peak flow meters and spirometry and don't give any knowledge to patients or parents about this and these result is comparable to similar study in China (33%) (Frinkelstein *et al*, 2000). A study performed in Taiwan a similarly has a large number of respondents not using these methods (Yeh *et al*, 2006).

Our results have shown that 42.16% of pregnant women exposed to passive smoking during their pregnancy. Longitudinal and case control study over 4 countries suggest that parental smoking or exposed to smoking during pregnancy is more strongly associated with wheezing among non-atopic children and increased incidence of wheezing illness up to age 6, but less strongly thereafter (Strachan & Cook, 2005).

In terms of management of acute asthma exacerbation most doctors act appropriately in accordance with GINA guidelines by administering a beta agonist (GINA 2007). This result is also similar to practices in other nations with established medical care (Civelek & Sekerel, 2004). It is encouraging that 40%-60% of doctors prescribed oral or inhaled corticosteroids in the outpatient setting. These have been shown to decrease hospitalization in large scale (Smith *et al*, 2003). According to our study a good portion of doctors used oral or intravenous steroids (prednisolone) in acute asthma. Short courses of oral steroids have been shown to have minimum side effects in children (Ducharme *et al*, 2003). According to AIRE (The Asthma insights and reality in Europe) study more patients used prescription quick relief medication (63%) than inhaled corticosteroids (23%) (Rabe and Maire, 2003).

From our study it was shown that the patient going to hospital was 73.6%. A majority number of doctor prescribed antibiotics in case of pneumonia, respiratory distress, bronchiolitis associated with fever & suspected with asthma which is comparable with the study of Taiwan (Belle *et al*, 2007).

In our study we have seen that most of the physicians preferred nebulization with Salbutamol and Ipratropium bromide (60.54%) with a certain percentage of normal saline and prescribed short term steroid (30.27%) and short acting beta2 adrenoreceptor agonist (38.92%) levosalbutamol syrup .In acute exacerbation child are inhaled with saturated oxygen. Montelukast is similarly not recommended as monotherapy. The use of theophylline is discouraged. However physicians of Turkey preferred short acting beta agonist as their first choice for acute asthma and preferred nebulized corticosteroids than systemic corticosteroid. The use of theophylline and Ipratropium bromide has received lower scores by turkey physicians (Ozge U.S. *et al*, 2008). In the maintenance treatment of asthma most

doctors prescribed inhaled corticosteroids or a combination of this with long acting beta adrenoreceptor agonist (LABA). Although LABA are not encouraged for most asthmatic patient only recommended for a selective group of patients as on add-on therapy if their symptoms are not controlled by steroids. Whether in Turkey Corticosteroid received highest grade but leukotriene received a comparable score (Ozge U.*S et al*, 2008).

5.2 Conclusion

In this study, consistencies between parents' knowledge, awareness and patient's adherence to treatment have been identified. This indicates that improved asthma knowledge and attitudes can encourage parents to correctly monitor their child's asthma condition and better manage and adhere to their medication regimen. In this survey, parent education is considered as a positive value. Education level will affect the parents' ability to acquire knowledge. Regular physician visits, when asthma is controlled, can bring more opportunities for asthma education to parents. Governmental influence are also requires in that case. Several social organizations can increase awareness among parents by arranging free campaign, free seminar and by recognizing them with the early signs and symptoms of asthma. In the current situation asthma prevalence can be reduced by giving proper guidelines to monitor the asthma condition.

References

Akbari, O., Faul, J.L., Hoyte, E.G., Berry G.J. & Umetsu, D.T. (2006), CD+invariant Tcell receptor+natural killer T cells in bronchial asthma. *N Engl J Med*, 354(11), 1117-29.

Alvarez, M.J., Olaguibel, J.M. & Acero, S. (2000), Effect of current exposure to Der p 1 on asthma symptoms, airway inflammation and bronchial hyperresponsiveness in mite-allergic asthmatics**.** *Allergy*, 55**,** 185–190.

Anderson, S.D. (2002), Exercise induced asthma in children: a marker of airway inflammation. *Med J Aust*, 177, 61-3.

Anderson, H.R., Butland, B.K. & Strachan, D.P. (1994), Trends in prevalence and severity of childhood asthma. *Br Med J*, 308, 1600-04.

Barnes, P.J. (2002), Cytokine modulators as novel therapies for asthma. *Annu Rev Pharmacol Toxico*l, 42,91-98.

Bel, E.H. (2004), Clinical phenotypes of asthma. *Curr Opin Pulm Med*, 10, 44-50.

Bowen, J.M., Chamley, L., Mitchell, M.D. & Keelan, J.A. (2002), Cytokines of the placenta and extra-placental membranes: biosynthesis, secretion and roles in establishment of pregnancy in women .*Placenta* ,2, 239–56.

Bisgaard, H. (2000), Long acting Beta 2 agonists in management of childhood asthma:A critical review of literature. *Paediatre Pulmonal*, 29, 221-34.

Braman, S.S. (2006), the global burden of asthma. *Chest J*, 130, 4-12.

Carlos, E., Baena, C.M.D. (2009), Childhood asthma-A global Problem. *World allergy day*, 80,7.

Chung, K.F. (2000), Airway smooth muscle cells:Contributing & regulating airway mucosal inflammation. *Eur Respire J*, 15(5), 961-8.

Calpin, C., Macarthur, C., Stephens, D., Feldmen, W., Parkin, P.C. (1997), Effectiveness of prophylactic inhaled steroids in childhood asthma:A systemic review of Literature. *J Allergy Clin Immunol*, 100(4), 452-7.

Covar R.A., Fuhlbrigge, A.L., Kelly H.W. & William, P. (2012), The Childhood Asthma Management Program (CAMP): contributions to the understanding of therapy and the natural history of childhood asthma . *Current Respiratory Care Reports*, 1(4), 243-250.

Dani, H. & Salvatore, T. (2013), Recent advances on diagnosis and management of childhood asthma and food allergies. *Italian Journal of Pediatrics*, 39, 40.

Elinor, S., Teresa, T.O., Rahim, M., David S. & Sharon, D.(2012), Associations between second-hand smoke exposure in pregnancy and age of childhood asthma development. *Allergy, Asthma & Clinical Immunology,* 8, A4.

Elinor, S., Sharon, D., Rahim, M. & Teresa.(2014), Longitudinal associations between neighbourhood walkability and incident childhood asthma. *Allergy, Asthma & Clinical Immunology,* 10, A8.

Gibson, P.G., Dolovich, J., Denburg, J., Ramsdale, E.H. & Hargreave, F.E. (1989), Chronic Cough:eosinophil bronchitis without asthma. *Lancet*, 1, 1346-8.

Gern, J.E., Rosenthal, L.A. & Sorkness, R.L. (2005). Effects of viral respiratory infections on lung development and childhood asthma. *J Allergy Clin Immunol*, 115,668-674.

GINA, 2010, *Pocket Guide for asthma management & prevention* [Online] Available At: www.ginasthma.org/local/uploads/files/GINA_Pocket_2010_pdf. [Accessed 3 july,2015].

Hoeppner, V.H., Murdock, K.Y., Kooner, S., Cockcroft, D.W. (1985), Severe acute occupational asthma caused by accidental allergen exposure in an allergen challenge laboratory. *Ann Allergy* , 55, 36-7.

Holloway, J.W., Beghe, B. & Holgate, S.T. (1999), The genetic basis of atopic asthma. *Clin Exp Allergy* ,29(8), 1023-32.

Hendeles, L. & Sherman, J. (2003), Are inhaled corticosteroids effective for acute exacerbations of asthma in children. *J Pediatre*, 142, 26-32.

Isreal, E., Chinchil, V.M., Ford, J.G., Boushey, H.A. & Cherniack, R. (2004), Use of regularly scheduled albuterol treatment in asthma:Genotype Stratified,randomized,placebo controlled cross over trail. *Lancet*, 364(9444), 1505-12.

Joan, M., Cook, M. (2015), Maternal influences over offspring allergic responses, *Basic and Applied Science.* 44, 47.

Junge K.M., Lehmann, I. & Borte, M. (2013), Can vitamin D intake during pregnancy affect the risk of allergy in children? *Expert Rev Clin Immunol*, 9, 699–701.

Kay, A.B., Phipps, S., Robinson, D.S. (2004), A role for eosinophils in airway remodeling in Asthma. *Trends Immunol*, 25(9), 447.

Kabir, M.L., Rahman, F. & Hassan, M.Q. (2006), Asthma,Atopic eczema,allergies and rhinoconjunctivities in school children. *Mymensingh Med J*, 14, 41-45.

Larche, M., Robinson, D.S. & Kay, A.B. (2003), The role of T Lymphocytes in the pathogenesis of asthma. *J Allergy Clin Immunol*, 113(3), 450-63.

Lesley, L., Adnan, C. & Ashley, W. (2003), Childhood Asthma. *Current allergy and Asthma reports*, 3, 109-114.

Leme, A.S. (2006), Role of breast milk in a mouse model of maternal transmission of asthma susceptibility. *J Immunol*, 172, 762–9.

Livestrong.com, (2015), *the difference between asthma & pneumonia symptoms in children.* [Online] Available At:http://www.livestrong.com/article/556842-the-difference-between-asthma-pneumonia-symptoms-in-children [Accessed 03 July, 2015].

Malo, J.L., Lemiere, C., Gautrin, D., Labrecque M. (2004), Occupational Asthma. *Curr Opin Pulm Med*, 10(1), 57-61.

Nelson, H.S., Szefler, S.J.& Jacobs, J. (1999), The relationships among environmental allergen sensitisation, allergen exposure, pulmonary function, and bronchial hyperresponsiveness in the Childhood Asthma Management Program**.** *J Allergy Clin Immunol*, 104, 775–785.

Netting, M.J., Middleton, P.F. & Makrides, M. (2014), Does maternal diet during pregnancy and lactation affect outcomes in offspring? *A systematic review of food-based approaches Nutrition*, 30, 1225–41.

Peters, G.M. (2004),The alveolar macrophage:the forgotten cell in asthma. *AM J Respir Cell mol Biol*, 31, 3-7.

Robinson, D.S. (2004), The role of the mast cell in asthma:induction of airway hyperresponsiveness by interaction with smooth muscle. *J Allergy Clin Immunol*, 114(1), 58-65.

Ricciardolo, F.L., Strek, P.J., Gaston, B. & Folkarts, G. (2004), Nitric oxide in health and disease of the respiratory system. *Physiol Rev*, 84(3), 731-65.

Rosalind, L.S. (2014). Asthma, *Pediatric Health issue*, 32,43.

Simpson, A., Custovic, A., Pipis, S., Adisesh, A., Faraquer, B. & Woodcock A. (1999), Exhaled nitric oxide, sensitization and exposure to allergens in asthmatics not taking inhaled steroids. *Am J Respir Crit Care Med*, 160**,** 45–49.

Strachan, D.P. (1989), Hay fever,hygiene and household size. *BMJ*, 299(6710) , 1259-60.

Strachan, D.P. & Cook, G.D. (1999), Health effects of passive smoking:Parenteral smoking & allergic sensitization. *Thorax*, 53(2), 117-23.

Ségala, C., Priol, G., Soussan, D., Liard, R., Neukirch, F., Touron, D. & Lepage, T. (2008), Asthma in adults: comparison of adult-onset asthma with childhood-onset asthma relapsing in adulthood. *Allergy*, 55(7), 634-40.

Sears, M.R. (1998), Evolution of asthma through childhood. *Clinical & experimental Allergy*, 28(5), 82-89.

Turner, S.W., Palmer , L.J., Rye, P.J., Gibson, N.A., Judge, P.K., Young, S. & Landau, L.I. (2002), Infants with flow limitation at 4 weeks: outcome at 6 and 11 years**.** *Am J Respir Crit Care Med,* 165(9)**,** 1294–8.

Tunnicliffe, W., Fletcheh, T., & Hammond, K. (1999), Sensitivity and exposure to indoor allergens in subjects with differing asthma severity**.** *Eur Respir J,* 13**,** 654–9.

Tan, W,C., Tan, C.H. & Teoh, P.C. (1985), The role of climatic conditions and histamine release in exercise-induced bronchoconstriction, *Ann Acad Med Singaphore*, 14(3), 465-9.

Teresa, T. & Sherry, I. B. (2010), Cost-Benefit Analysis of Childhood Asthma Management Through School-Based Clinic Programs. *Journal of Community Health,* 36, 9305.

Uauy, R.,Hoffman, D.R., Birch, E.E., Birch D.G., Jameson, D.M. & Tayson, J. (1994), Safety and efficacy of omega-3 fatty acids in the nutrition of very low birth weight infants: soy oil and marine oil supplementation of formula. *J Pediatr*. 124(4), 612–20.

Vignola, A.M., Mirabella, F., Coastanzo, G., & Bellia, V. (2003), Airway remodeling in asthma. *Chest* , 123(3), 417-22.

Wenzel, S. (2003), Mechanisms of severe asthma. *Clin Exp Allergy*, 33(12), 1622-8.

Wenzel S.E. (2006), Asthma: defining of the persistent of adult phenotype. *Lancet*,368,804-13.

Weiss, S.T. & Shore, S. (2004), Obesity and asthma:directions for resreach. *Am J Respir Crit Care Med*, 169(8), 963-8.

Wahn, U., Lau, S., Bergmann, R., Kulig M., Forster, J. & Bergmann, K. (1997), Indoor allergen exposure is a risk factor for sensitization during the first 3 years of life. *J Allergy Clin Immunol*, 99, 763-9.

WebMD, (2013), *Classification of Asthma-Topic overview*. [Online] Available At: http://www.webmd.com/asthma/tc/classification-of-asthma-topic-overview [Accessed 10 july,2015].

Yangzong, Y., Zumin, S., Per, N., Lise. & lund H. (2012), The prevalence of childhood asthma in China: a systematic review. *BMC Public Health*, 12, 860.