Study on prevalence of Asthma and COPD at Dhaka city in Bangladesh

A dissertation submitted to Department of Pharmacy, East West University, in Partial fulfillment of the requirements for the Degree of Bachelor of Pharmacy (B. Pharm)

Submitted by

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June, 2016

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Declaration by the Candidate

I hereby declare that this dissertation, entitled **"Study on prevalence of Asthma and COPD at Dhaka city in Bangladesh''** is an authentic and genuine research work carried out by me under the guidance of Meena Afroze Shanta, Lecturer, Department of Pharmacy, East West University, Dhaka.

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This is to certify that the research work on **"Study on prevalence of Asthma and COPD at Dhaka city in Bangladesh"** submitted to the department of pharmacy, East West University, Aftabhnagar, Dhaka in partial fulfillment of the requirements for the degree of Bachelor of pharmacy (B. Pharm) was carried out by Narzis Ahmed (ID: 2012-1-70-024) under our guidance and supervision and that no part of the thesis has been submitted for any other degree. We further certify that all sources of information in this connection are duly acknowledged.

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Certificate by the chairperson

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Dedication

This research work is dedicated to my beloved parents,
honorable faculties and loving friends.

Abstract

The percentage of Asthma and COPD is increasing gradually in the world as well as in Bangladesh due to many reasons. So this current study was aimed to find out the prevalence of Asthma and COPD at Dhaka city in Bangladesh. This was a survey based study where general people were interviewed as per the structured questionnaire. Among 300 subjects both male and female was there aged between 15-65 years. It was found 18% Asthma prevalence and 7% COPD prevalence among those populations. 28% COPD patients were currents smokers taking at least one pack or more than one pack daily. Hypertension was present both in Asthma and COPD. Many undiagnosed Asthma patients were also found who had severe coughing and shortness of breath. Asthma or COPD was present in the family history of 70% patients. Smoke was one of main triggers for asthmatic and COPD patients. Breathless condition and chest tightness both were prevalent for Asthma and COPD. There working and living conditions were the most important factors but only 30% asthmatic and 35% COPD people worked in a well ventilated area. Almost many of them were not concern about taking their medications properly. So, adequate steps should be taken in our country to make people concern and should be made aware of the facts that may reduce the incidence of these types of chronic illnesses, medical conditions as well as to motivate people to take medications and also to manage these diseases.

Key words: *Asthma prevalence, COPD prevalence, Hypertension, Coughing, Shortness of breath, Chest tightness, Triggers.*

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List of Abbreviations

ASM= Airway Smooth muscle

COPD= Chronic Obstructive Pulmonary Disease

CAMP= Childhood Asthma Management Program

FVC= Forced Vital Capacity

FEV-1= Forced Expiratory Volume

GINA= Global Initiative for Asthma

ICS= Inhaled Corticosteroid

ISAAC= International Study of Asthma and Allergies in Childhood

LABA= Long Acting β2Agonist

MDI= Metered Dose Inhaler

PEF = Peak Expiratory Flow

WAO= World Allergy Organization

WHO= World Health Organization

CHAPTER 1
INTRODUCTION

1.1 Overview

Asthma is a common chronic disorder of the airways that is complex and characterized by variable and recurring symptoms, airflow obstruction, bronchial hyper responsiveness, and an underlying inflammation. The interaction of these features of asthma determines the clinical manifestations and severity of asthma, and the response to treatment. Asthma can vary among individuals, and its progression and symptoms can vary within an individual's experience over time. The course of asthma over time, either remission or increasing severity, is commonly referred to as the natural history of the disease. It is known little about the exact causes of asthma or the prevention of asthma, but known how to control the symptoms and inflammation of asthma. Asthma is not currently curable, but it is treatable (Minnesota Department of health,n.d). Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease that makes it difficult to empty air out of the lungs. This difficulty in emptying air out of the lungs (airflow obstruction) can lead to shortness of breath or feeling tired because you are working harder to breathe. COPD is a term that is used to include chronic bronchitis, emphysema, or a combination of both conditions. Asthma is also a disease where it is difficult to empty the air out of the lungs, but asthma is not included in the definition of COPD. It is not uncommon, however for a patient with COPD to also have some degree of asthma (American thoracic society, 2011).

Asthma is a problem worldwide, with an estimated 300 million affected individuals. Despite hundreds of reports on the prevalence of asthma in widely differing populations, the lack of a precise and universally accepted definition of asthma makes reliable comparison of reported prevalence from different parts of the world problematic. Nonetheless, based on the application of standardized methods to measure the prevalence of asthma and wheezing illness in children and adults, it appears that the global prevalence of asthma ranges from 1% to 18% of the population in different countries. There is good evidence that asthma prevalence has been increasing in some countries and has recently increased but now may have stabilized in others. The World Health Organization has estimated that 15 million disability-adjusted life years (DALYs) are lost annually due to asthma, representing 1% of the total global disease burden. Annual worldwide deaths from asthma have been estimated at 250,000 and mortality does not appear to correlate well with prevalence. There are insufficient data to determine the likely causes of the described variations in prevalence within and between populations (GINA, 2006). COPD is a leading cause of morbidity and mortality and results in an economic and social burden that is both substantial and increasing. COPD prevalence, morbidity, mortality vary across countries and across different groups within countries. It is the result of cumulative exposures over decades. Often the prevalence of COPD is directly is directly related to the prevalence of tobacco smoking. Although in many countries outdoor, occupational, indoor air pollution- the latter resulting from burning of wood and other biomass fuels are the major risk factors. A systematic review and meta analysis of

studies carried out in 28 countries between 1990 and 2004 which provide evidence that COPD is appreciably higher in smokers and ex-smokers than in non smokers, in those over 40 years of age than those under 40 and in men than in women (GOLD, 2013). The development of successful preventive strategies requires better elucidation of the untraditional risk factors for COPD besides smoking. In addition, it is likely that other risk factors biologically interact with cigarette smoking and potentiate the development of airflow obstruction. Consequently, there is an urgent need to evaluate the contribution of novel risk factors for COPD at the population level, both in our country and worldwide.

1.2 Comparison between Asthma and COPD

Table 1.1 Comparison between Asthma and COPD

Parameter	Asthma	COPD
1. Age group	At any age, common in childhood	Generally over 40years.
2. Causes	Genetic and environment factors	Usually smoking but also linked to genetics and environment.
3. Diagnosis	Careful history taking, trials of therapy. Lung function and other test.	Spirometry and other tests.
4. Prognosis	Symptoms can be well controlled and patents except severe asthma can maintain activities of daily life.	Symptoms deteriorate over time.
5. Predictability	Disease is not progressive. Moving between levels of severity with little warning	Progression is relatively predictable-function declines with time.
6. Aims of care	To restore and maintain normal lung function and avoid acute attacks.	To manage or slow decline lung functions, maximizing quality of life and reduce the frequency of exacerbations.
7. Management	Largely in primary care. Specialist services for severe asthma.	Requires many different types of input to coordinate care.

8. Treatment	Inhaled steroids, long acting bronchodilators or other agents if necessary.	Regular bronchodilation with high dose inhaled steroids or inhaled corticosteroids and long acting bronchodilators are reserved for severe cases
9. Airway inflammation	Eusinophilic.	Neutrophilic.
10. Spirometry results	Often normalize over time	May improve but do not normalize over time.
11. Co-morbidities	Other allergic conditions; including hay fever.	Smoking related co-morbidities such as coronary heart disease and systemic problems
12. Breathlessness	Variable	Persistent and productive.

1.3 Epidemiology of Asthma and COPD in the world

In 2005, an estimated 22.2 million Americans had asthma: 6.5 million children and 15.7 million adults. The public health impact of asthma is significant. In 2003, asthma accounted for 1.4 deaths/100,000 persons in the USA (NCHS, 2003). According to the National Center for Health Statistics, in 2003, children between the ages of 5 and 17 years with a history of at least one asthma attack in the previous year accounted for 12.8 million missed school days, and adults with a history of at least one asthma attack in the previous year accounted for 10.1 million missed workdays.

GINA estimates that the prevalence of asthma is 300 million persons worldwide. The World Health Organization estimates that 1% of the global disease burden, 15 million disability-adjusted life years, is attributable to asthma. Asthma accounts for 250,000 deaths annually worldwide (GINA, 2015). Mortality does not correlate with prevalence since countries such as Wales and New Zealand have the lowest asthma-related mortality rate, despite a high prevalence of disease.

The epidemiology of asthma differs from that of COPD in that asthma usually presents early in childhood, and atopy is much more prevalent in asthma than in COPD. Asthma is usually not progressive, although exacerbations can be intermittent and variable. Eosinophils and lymphocytes are the major inflammatory cells in asthma. With appropriate therapy, asthma is completely reversible in most patients (Wise *et al.,* 2007).

COPD is the fourth leading cause of death in the USA (Wise *et al.,* 2007). In 2001, the World Health Organization reported that COPD was the fifth leading cause of

death in high-income countries and the sixth leading cause of death in low- and middle-income countries.

COPD usually presents in middle age, is slowly progressive and is associated with history of cigarette smoking in 80-90% of patients (Taussig *et al.,* 2003). Patients usually present with a chronic productive cough, and atopy is not a frequent finding. Clinical symptoms are slowly progressive, and airflow limitation is only partially reversible after tobacco cessation and with bronchodilator use. T lymphocytes, with macrophages and neutrophils, are the predominant inflammatory cell types (Rabe *et al.,* 2005).

1.3.1 Epidemiology of Asthma and COPD in the Asia

Asthma is a chronic inflammatory disorder of the airways characterized by bronchial hyperresponsiveness, reversible airflow limitation, and respiratory symptoms (Sugita, 2005). In the Asia-Pacific region asthma causes considerable morbidity, with 15% of teenagers troubled by exercise-induced symptoms during the past 12 months (Lai *et al.,* 2003). Furthermore, asthma mortality rates in more affluent areas, such as Hong Kong and Japan, are similar to those reported in Western countries (Lai *et al.,* 2003). Studies in Korea also bear witness to these increasing trends (Lee, 2005). The reported prevalence of asthma in Korea ranges from 2 to 13% (Kim, 2002). However, its prevalence in the elderly has been reported to be very high, at 12.7% in those aged 65 or more (Kim, 2002). Indeed, with a population estimated at more than 48 million, and a life expectancy of 72.0 yr for males and 79.5 yr for females, Korea faces an important public health challenge in terms of dealing with chronic diseases such as asthma. In India in a study the prevalence of asthma was reported as 22.78% in an urban population aged 30-49 years (Chowgule, 2011). There are about 3 million asthmatics in Japan of whom 7% have severe and 30% have moderate asthma. India has an estimated 15-20 million asthmatics. In the Western Pacific Region of WHO, the incidence varies from over 50% among children in the Caroline Islands to virtually zero in Papua New Guinea. In Brazil, Costa Rica, Panama, Peru and Uruguay, prevalence of asthma symptoms in children varies from 20% to 30%. In Kenya, it approaches 20%.In India, rough estimates indicate a prevalence of between 10% and 15% in 5-11 year old children (WHO, 2013).

COPD is more likely to be reported as a contributory rather than underlying cause of death or morbidity, or may not be reported at all (Holguin *et al.,* 2001). In Asia-Pacific countries where tobacco smoking and indoor air pollution are highly prevalent the rise of COPD incidence is particularly dramatic contributing to a significant disease burden data from a WHO World Bank study were used to extrapolate a COPD prevalence figure of 3.8% for the entire Asian population, but recent studies suggest that COPD is a more significant problem in the region than has been previously realised. Two major studies conducted in Japan (Takemura *et al.,* 2005) and Korea (Kim *et al.,* 2005) more recently showed a COPD prevalence of 8.55% and 7.5% respectively. The prevalence of COPD in Asia-Pacific has been estimated indirectly

through a risk factor prevalence model, which was mainly driven by varying smoking rates and levels of air pollution. The prevalence of moderate to severe COPD in adults aged 30 years or above in the Asia-Pacific region was estimated to be at approximately 6.3% and for Malaysia at 4.55%.

Consistent with the findings of WHO Global Burden of Disease study (Murray, 2011) both mortality and morbidity rates for COPD in the Asia-Pacific region were reported to be higher in men than in women and increased with increasing age. (NIH, 2004) COPD-related illness was higher in men, with rates of 32.6 to 334 per 10,000 people, compared with rates of 21.2 to 129 per 10,000 for women (Murray, 2011).

1.3.2 Epidemiology of Asthma and COPD in Bangladesh

Asthma in Bangladesh appears to be a substantial public health problem: an estimated 7 million people including2 million people suffer from asthma-related symptoms (Hassan, 2001). The prevalence of asthma (wheeze in the last 12 months) was 6.9% . The prevalence of other asthma definitions were: ever wheeze (lifetime wheeze) 8.0%; perceived asthma (perception of having asthma); doctor diagnosed asthma (diagnosis of asthma by any category of doctor either qualified or unqualified) 4.4% (Kabir, 2003). The prevalence of asthma in children (5–14 years) was higher than in adults (15–44 years). Asthma in children was found to be significantly higher in households with ≤3 people than in larger households. The low-income group and illiterate group were more vulnerable to asthma attacks than the high-income group and more educated people, respectively (Mahmud *et al.,* 2005).

Prevalence of COPD in >40 years population was 21.24%.The total number of COPD patients in Bangladesh is assumed to be 5947200. The overall prevalence of COPD in total population of Bangladesh is estimated to be 4.32%. The prevalence of COPD was found to be highest for rural population 23.15%, followed by urban 22.62% and was lowest for metropolitan population 17.77% of the patients were suffering from moderate- COPD, the prevalence of which in rural areas (48.55%) was higher than that of urban and metropolitan areas (44.30% and 42.53%). In general, males suffer more than females (62.83% vs. 37.17%) (BOLD-BD, 2007).

1.4.1 Definitions of Asthma

Asthma attacks all age groups but often starts in childhood. It is a disease characterized by recurrent attacks of breathlessness and wheezing, which vary in severity and frequency from person to person. In an individual, they may occur from hour to hour and day to day. This condition is due to inflammation of the air passages in the lungs and affects the sensitivity of the nerve endings in the airways so they become easily irritated. In an attack, the lining of the passages swell causing the airways to narrow and reducing the flow of air in and out of the lungs (WHO, 2005).

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation causes an associated increase

in airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. The episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment (GINA, 2004).

Asthma is a disease of the bronchial tubes (the "airways") that typically presents with "wheezing", a high-pitched whistling sound heard during breathing, especially when breathing out. However, wheezing does not always occur, and asthma can also involve shortness of breath or coughing, particularly in children. Asthma most commonly develops in early childhood, and more than three-quarters of children who develop asthma symptoms before age 7 no longer have symptoms by age 16. However, asthma can develop at any stage in life, including adulthood (Pearce *et al.,* 2011).

1.4.1.1 Different types of Asthma

1.4.1.2 Exercise induced asthma

When exercise causes asthma symptoms, this is called exercise induced asthma. The triggering events in exercise induced asthma believed to be rapid breathing and airway cooling associated with vigorous exercise. It can occur almost in everyone, but it is most common in people especially children who already have persistent asthma associated with exposure to allergens such as animal dander, dust mites and molds. The prevalence of exercise induced symptoms in patient with asthma has been reported to range from 40 to 90 percent (Fadden *et al.,* 1994).

1.4.1.3 Nocturnal asthma

Worsening of asthma at night, is very common. Many factors may contribute to the increased symptoms.

- Exposure to allergen in the bedroom; particularly dust mites.
- Delayed allergic response which may occur after 3 to 8 hour of exposure.
- Chronic sinus problem.
- Gastroesophageal reflux.
- Decreased effect of medications during early morning hours.
- Sleep apnea (Warwick, 1988).

1.4.1.4 Occupational asthma

The two categories of asthma in the workplace are occupational asthma and work-aggravated asthma. Occupational asthma is characterized by variable airflow limitation, bronchial hyperresponsiveness, or both, due to conditions in a particular

work environment, not to stimuli outside the workplace. Work-aggravated asthma is preexisting or concurrent asthma that is aggravated by irritants or physical stimuli in the workplace. Occupational asthma may develop in a person with preexisting asthma or concurrent asthma after a workplace exposure.

Two types of occupational asthma can be distinguished, according to whether there is a latency period. Occupational asthma with latency is the most common type. This develops after a period of exposure that may vary from a few weeks to several years. Occupational asthma with latency includes all instances of immunologic asthma, although the immunologic mechanism has not yet been identified for some agents. Occupational asthma without a latency period follows exposure to high concentrations of irritant gases, fumes, or chemicals on one or several occasions (Yeung *et al.*, 1995).

1.4.1.5 Steroid-Resistant asthma

While the majority of patients respond to regular inhaled glucocorticoid (steroid) therapy, some are steroid resistant. Airway inflammation and immune activation play an important role in chronic asthma. Current guidelines of asthma therapy have therefore focused on the use of anti-inflammatory therapy, particularly inhaled glucocorticoids (GCs). By reducing airway inflammation and immune activation, glucocorticoids are used to treat asthma. Furthermore, glucocorticoids do not reduce the eosinophilia (high concentration of eosinophil granulocytes in the blood) or T cell activation found in steroid resistant asthmatics. This persistent immune activation is associated with high levels of the immune system molecules IL-2 (interleukin 2), IL-4 and IL-5 in the airways of these patients (Corrigan *et al.,* 1991).

1.4.1.6 Cough-Induced asthma

Cough-induced asthma is one of the most difficult asthmas to diagnose. The doctor has to eliminate other possibilities, such as chronic bronchitis, post nasal drip due to hay fever, or sinus disease. In this case the coughing can occur alone, without other asthma-type symptoms being present. The coughing can happen at any time of day or night. If it happens at night it can disrupt sleep (Corrao *et al.,* 1979).

1.4.2.1 Pathophysiology of Asthma

Airway smooth muscle (ASM) plays an integral part in the pathophysiology of asthma. It is responsible for acute bronchoconstriction, which is potentiated by constrictor hyperresponsiveness, impaired relaxation and length adaptation. ASM also contributes to airway remodeling and inflammation in asthma. Structural and inflammatory changes throughout the airway wall lead to bronchial thickening and edema as well as increased mucus production and bronchoconstriction, all of which contribute to the episodic airflow obstruction typically found in asthma. In recent years, there has been much attention on inflammation in asthma, for example, whether the type of inflammatory cell predominately found in the airway denotes a specific phenotype in asthma or whether targeting antibodies, inflammatory cytokines, and

inflammatory cells is helpful for the treatment of asthma. Although ASM has been implicated in constrictor hyperresponsiveness in asthma for decades, other important roles of ASM have recently been identified. Through impaired airway relaxation and mediation of structural changes and inflammatory signaling, the ASM cell plays multiple diverse roles in the pathophysiology of asthma. This review is meant to update practicing physicians with current knowledge about these less discussed direct effects of ASM on airway narrowing and indirect influences on airway remodeling and inflammation in asthma (Doeing *et al.*, 2013).

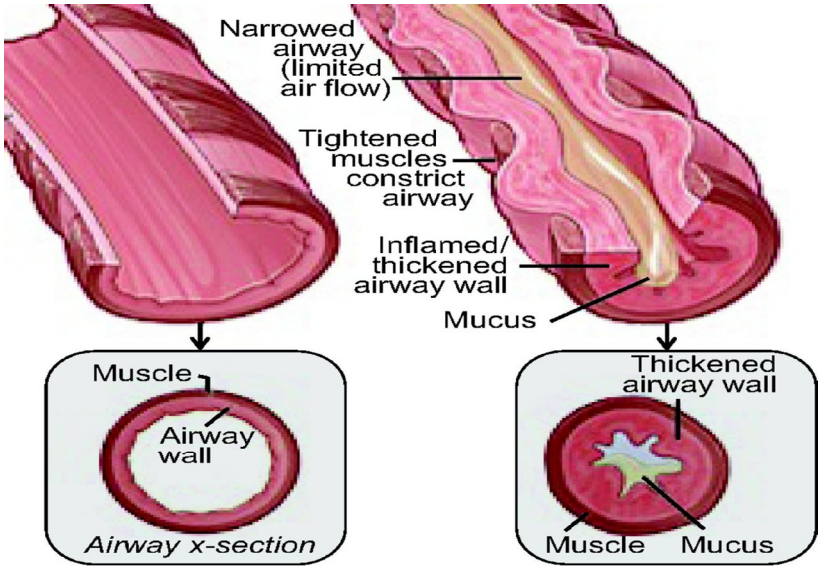

Figure 1.1: Multiple mechanisms of airflow obstruction in asthma, including bronchoconstriction by airway muscle, obstruction of airflow by intraluminal mucus, and inflammation and remodeling of the airway wall.

1.4.2.2 Functional Changes in asthmatic ASM

ASM is most well known for its role in acute bronchoconstriction. Smooth muscle surrounds the airway in a circumferential pattern, reducing the airway luminal diameter as it contracts. It is this function of ASM that causes the acute airflow obstruction, shortness of breath, and wheezing most commonly associated with the clinical syndrome of asthma. In asthma, ASM is primed to contract, often excessively, in response to various stimuli, but in addition, it resists relaxation.

1.4.2.3 Airway hyperresponsiveness

The excessive contractile response of ASM in asthma results in inordinate bronchoconstriction and airflow obstruction in response to relatively little provocation; this phenomenon is denoted as airway hyperresponsiveness. A variety of chemical and physical stimuli can trigger bronchoconstriction. Contractile agonists, like methacholine, can directly activate receptors on ASM cells that initiate myocyte contraction and consequent bronchoconstriction, and this is the basis of the methacholine challenge test sometimes used to diagnose asthma. Substantial

respiratory heat and water loss, as occur during exercise in temperate or cold climates, can also provoke bronchoconstriction, likely mediated by contractile agonists released from mast cells or nerves exposed to a hyperosmolar milieu. Contributing mechanisms include both an increased availability in asthmatic airways of contractile mediators such as histamine from mast cells and increased ASM mass. Mathematical models initially proposed that excessive ASM generates abnormally increased force, but increased dynamic muscle stiffness (due to impaired breathing-induced muscle softening) may actually be the more important mechanism. Other explanations for airway hyperresponsiveness in asthma include increased vagal tone, cytokine-potentiated increases in intracellular free calcium that enhance ASM cell contractility and activation of the procontractile Rho kinase pathway. Increased RhoA protein levels have also been identified in animal models of allergic asthma, and inhibition of the RhoA-Rho kinase pathway can prevent or reverse airway hyperresponsiveness (Soleway, 2013).

1.4.2.4 Impaired Relaxation

Aberrant shortening of ASM in asthma can also partly be explained by inadequate relaxation. There is no direct sympathetic innervation in human ASM. Additionally, β_2-adrenergic receptors may become down regulated when bombarded frequently with β_2-agonist medications, in a fashion that depends in part on genetic polymorphisms. This phenomenon has been observed in a number of cell types, including ASM, and may further potentiate the imbalance of autonomic neurotransmitter influences on the airway in asthma. In fact, patients with asthma can develop tolerance to β-agonist therapy. Inflammatory cytokines further potentiate this effect. Interleukin-1β (IL-1β), a cytokine produced by a variety of lung cells, reduces β-adrenergic responsiveness in cultured human ASM cells. Another important inflammatory cytokine, IL-13, has a similar effect on adrenergic receptors, albeit through a different mechanism Prevention or reduction of β_2-adrenergic receptor desensitization with agents that preserve receptor expression and function, such as ascorbate) or alendronate might conceivably be helpful in the treatment of asthma (Masoli, 2011).

1.4.3 Breathing-Induced Reversal of Bronchoconstriction and Length Adaptation

Other properties of ASM function may also contribute to airway narrowing in asthma. It has long been observed that in normal people, deep breathing can reverse bronchoconstriction. Within the lung, the airways are connected to the lung parenchyma, which is firmly attached to their adventitial surfaces. With each inspiration, the lung parenchyma surrounding each airway expands and pulls radically outward on the airway, stretching it partially during the breath. Isolated ASM that is forcibly lengthened while still contracting reduces its force of contraction, likely due to perturbation of actin-myosin interactions. Furthermore, fluctuations in the force applied to isolated contracting smooth muscle, simulating the tidal stretches that occur

with breathing, cause it to relengthen, even when the mean force is held constant. As a result of these behaviors of ASM, stretching of bronchoconstricted airways by breathing in part reverses the lumenal narrowing that had been present. However, in individuals with asthma, the ability of deep breaths to reverse bronchoconstriction seems blunted; this might stem from increased muscle mass and increased muscle stiffness as noted above or might reflect other mechanisms that are not yet fully understood. Nonetheless, the role of airway distension during a deep breath seems certain, for pronounced bronchoconstrictor responses to methacholine, similar to those of patients with asthma, can be elicited in normal subjects when deep breathing is restricted. Recently, we and others have found pharmacological interventions that potentiate ASM relengthening in response to force fluctuations in vitro. Pharmacologically potentiating the ability of deep inspirations to reverse bronchoconstriction might represent a novel therapeutic approach to relieve or prevent airflow obstruction in the future. Indeed, corticosteroids, a mainstay of asthma treatment, might exert some of their therapeutic effect through this mechanism (Soleway, 2013).

1.4.4.1 Structural changes in ASM in asthma: Remodeling

Remodeling of the airway refers to pathologic changes such as increased ASM mass, basement membrane thickening, and mucus gland hyperplasia These are common features of asthma that contribute to airflow obstruction both by luminal encroachment and by enhancing constrictor hyperresponsiveness. In addition, bronchoconstriction appears to promote airway remodeling thus airway inflammation and bronchoconstriction might participate in a vicious cycle that maintains the structural abnormalities characteristic of asthma. Here it is focused on the pathophysiology of increased ASM mass in asthma.

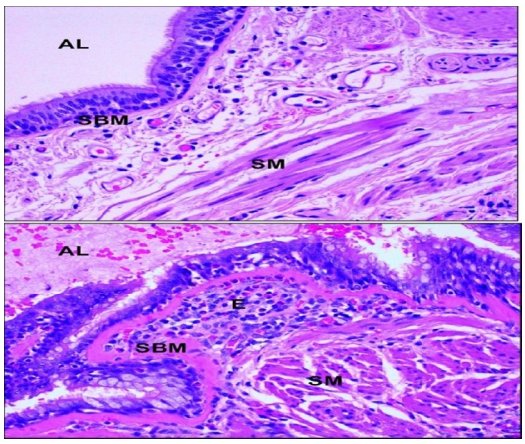

Figure 1.2: Remodeling (Husain, 2003)

1.4.4.2 Increased ASM mass in asthma

Increased ASM mass has been identified as a hallmark of asthma, and its abundance is particularly great in fatal or severe asthma. There is much debate, however, about

the mechanism driving its excess accumulation. Both increased ASM cell size (hypertrophy) and cell number (hyperplasia) have been described, with hypertrophy predominant in some subjects and hyperplasia characteristic of others. One study found that ASM hypertrophy was significantly increased in individuals with severe asthma, and studies in cell culture suggest that the PI3K-Akt-mTOR-p70 kinase pathway is involved. However, most research has focused on the mechanism of ASM hyperplasia. Stimuli that induce hyperplasia in cultured ASM cells include growth factors such as transforming growth factor (TGF-β_1), epidermal growth factor, platelet-derived growth factor, and contractile stimuli acting through G-protein-coupled receptors, including histamine and leukotriene D4. TGF-β_1 is a particularly important growth factor implicated in asthma. It is secreted by both infiltrating inflammatory cells and resident cells native to the airway, and exposure to allergens increases TGF-β_1 in the broncho alveolar lavage fluid of individuals with asthma. Furthermore, cultured ASM cells obtained from endobronchial biopsies of individuals with asthma demonstrate more rapid proliferation than do those from normal individuals. This might be explained by the absence of an antiproliferative transcription factor, C/EBPα . As C/EBPα also mediates the antiproliferative effect of corticosteroids in normal ASM, its reduction in asthmatic ASM may represent the underlying mechanism. Another possible mechanism of increased ASM mass is the migration and differentiation of fibrocytes from bone marrow. Fibrocytes exposed in culture to TGF-β acquire characteristics of smooth muscle cells, and the number of circulating fibrocytes in the peripheral blood of individuals with asthma with chronic airflow obstruction correlates with their rate of decline in lung function over tim. Therefore, interest has developed in TGF-β as a therapeutic target in asthma Animal models of allergen-induced asthma have shown significant reductions in ASM proliferation following TGF-β neutralization or inhibition (Busse *et al.*, 2001).

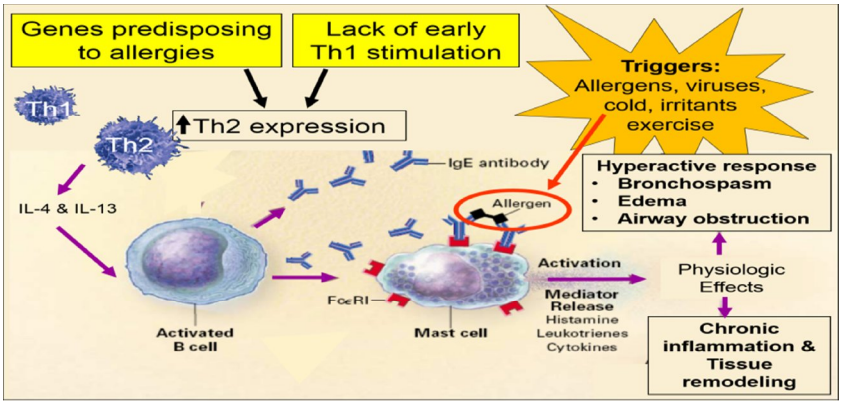

Figure 1.3: Initiation of asthma attack and mediators (Busse *et al.*, 2001)

1.4.5 Symptoms of Asthma

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 allergen.

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).

1.4.6.1 Risk factors of Asthma

1.4.6.2 Genetic

Asthma has a heritable component but it is not simple. Multiple genes may be involved in the pathogenesis of asthma (Holloway *et al.,* 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).

1.4.6.3 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 *et al.,* 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.

1.4.6.4 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.

1.4.6.5 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:

1.4.6.5.1 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).

1.4.6.5.2 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.

1.4.6.5.3 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.

1.4.6.5.4 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 *et al.,* 1998).

1.4.6.5.5 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 *et al.,* 2005).

1.4.7 Diagnosis of Asthma

Primary care doctor will diagnose asthma based on your medical and family histories, a physical exam, and test results. Doctor also will figure out the severity of your asthma—that is, whether it's intermittent, mild, moderate, or severe. The level of severity will determine what treatment need to start on.

It may need to see an asthma specialist if:

- It is needed special test to diagnose asthma.
- Life threatening asthma attack
- If it is needed more than one kind of medicine or higher doses of medicine to control asthma (Busse, 2011).

➢ The initial diagnosis is based on:

- History
- Physical examination
- Considering other diagnoses
- Documenting variable airflow limitation.

1.4.7.1 Medical and Family history

It is needed to ask about:

- current symptoms (both daytime and night-time)
- pattern of symptoms (e.g. course over day, week or year)
- precipitating or aggravating factors (e.g. exercise, viral infections, ingested substances, allergens)
- relieving factors (e.g. medicines)
- impact on work and lifestyle
- home and work environment

- smoking history (tobacco or cannabis, exposure to other people's smoke)
- past history of allergies including atopic dermatitis (eczema) or allergic rhinitis ('hay fever')
- family history of asthma and allergies (Burke, 2003).

1.4.7.2 Physical examination

Physical examination is performed including chest auscultation and inspection of upper respiratory tract for signs of allergic rhinitis (Wahn, 2001).

1.4.8 Tests for Diagnosing Asthma

1.4.8.1 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).

1.4.8.2 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 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).

1.4.8.3 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 *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 perception of symptoms.
- To identify environmental causes of asthma symptoms.

1.4.8.4 Challenge Test

If the spirometer results are normal or near normal, doctor might try to trigger asthma symptoms by having you inhale a substance that causes the airways to narrow in people with asthma, such as methacholine. If appear to have asthma triggered by exercise (exercise-induced asthma), one may be asked to do physical activity to see whether it triggers symptoms. After either action, it is retaken the spirometry test. If the spirometry measurements remain normal, one probably don't have asthma. But if the measurements have fallen significantly, it's possible to have asthma (GINA, 2007).

1.4.8.5 Exhaled nitric oxide test

Breathing into a tube connected to a machine that measures the amount of nitric oxide gas in the breath. Nitric oxide gas is produced by the body normally, but high levels in your breath can mean your airways are inflamed — a sign of asthma (Busse, 2011).

1.4.8.6 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).

1.4.8.7 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).

1.4.9 Treatment and medication of Asthma

There are two types of treatment for asthma. One is non-pharmacological and another is pharmacological.

1.4.9.1.1 Non-pharmacological Intervention

1.4.9.1.2 Provide asthma education

- Basic facts about asthma
- How medication works
- Importance of taking daily controller medications.
- Inhaler techniques.
- Environmental control measures.
- Need for regular follow up visits (Zairina *et al.,* 2013).

1.4.9.1.3 Encourage Patient self management

- **Self monitor symptoms:** Patient monitors symptoms and/or uses a peak flow meter to assess control and signs of worsening. Consider use of a peak flow meter for patients who have moderate or severe persistent asthma or a history of severe exacerbations, or who poorly perceive airflow obstruction and worsening asthma.
- **To follow asthma action plan:** With the provider, the patient develops and follows a written Asthma Action Plan that includes: instructions for daily management, self-monitoring to assess control and signs of worsening (either through symptoms or peak flow), and instructions for managing worsening asthma.
- **To take medication correctly:** To make understand of taking medicines at right time at right dose.
- **To limit or control environmental factors:** Which elements triggers or worsens symptoms, including: tobacco smoke, strong odors or sprays, dust mites, cockroaches, animal dander, pollen, outdoor mold, and indoor mold is Considered referral to allergy and asthma for testing to verify allergen sensitization and for specific advice on allergen avoidance (GINA,2010).

1.4.9.1.4 Promote lifestyle interventions

- Encourage physical activity. Exercise has significant health benefits; exercise-induced asthma symptoms can be controlled and engagement in regular exercise is encouraged.
- Encourage tobacco cessation.
- Encourage weight management (Anderson, 2011).

1.4.9.1.5 Treat comorbid conditions that worsen Asthma

- Environmental allergies.
- GERD.
- Obesity.
- Rhinitis, Sinusitis.
- Obstructive Sleep apnea.
- Stress or Depression.
- Smoking (GINA, 2007).

1.4.9.2 Pharmacological interventions

There are several medications to treat asthma according to their severity.

1.4.9.2.1 Classification of anti-asthmatic drugs

A. Bronchodilators.

- Sympathomimetics:
    i. Short acting beta 2 agonists(Salbutamol)
    ii. Long acting beta 2 agonists(Salmeterol)
- Methyl xanthines (Theophylline)
- Anticholinergic or muscarinic antagonists (Ipratropium bromide)

B. Leukotriene modifiers(monteleukast)

C. Mast cell stabilizers(Sodiun cromoglycate)

D. Corticosteroids:

i. Systemic (prednisolone, hydrocortisone)

ii. Inhalational (Beclomethasone, Fluticasone)

E. Anti IgE antibody (Omalizumab) (Rang *et al.*, 2012)

1.4.9.2.2 Asthma treatment according to the severity

Table 1.2 Asthma treatment according to the severity:

Asthma severity type	**Bronchoconstriction episodes**	**Long term control**	**Quick relief of symptoms**
Mild intermittent	Less than2 per week.	No daily medicine.	Short acting beta 2 agonists.
Mild persistent	More than 2 per week.	Low dose inhaled corticosteroids.	Short acting beta 2 agonists.
Moderate persistent	Daily.	Low medium dose corticosteroids+ long acting beta2 agonist.	Short acting beta 2 agonists.
Severe persistent	Continual.	High dose inhaled corticosteroids+ long acting beta2 agonist.	Short acting beta 2 agonists.

(Lippincott, 2007).

1.4.10 Side effects of Asthma medications

Table 1.3 Side effects of asthma medications

Drug class	**Side effects**
Sympathomimetics	Trembling of hands, nervous tension, palpitations ,muscle cramps, heart attacks and hypokalemia with excessive dose.
Methyl xanthines	Palpitations, arrhythmia,
Anticholinergics	Dry mouth, constipation or diarrhoea.
Leukotriene modifiers	Increased serum hepatic enzymes, eosinophilic vasculitis, dyspepsia.
Mast cell stabilizers	Throat irritation, heart burn.

Corticosteroids	Sore mouth or throat, minor nose bleeding, atopic dermatitis, hypertension.

(Drugs, 2011)

1.4.11 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).

1.5 Definitions of COPD

Chronic obstructive pulmonary disease (COPD) is a lung disease characterized by chronic obstruction of lung airflow that interferes with normal breathing and is not fully reversible. The more familiar terms 'chronic bronchitis' and 'emphysema' are no longer used, but are now included within the COPD diagnosis. COPD is not simply a "smoker's cough" but an under-diagnosed, life-threatening lung disease (WHO, 2005).

COPD is a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with enhanced chronic inflammatory responses in the airways and the lungs to noxious particles or gases. Exacerbations and co morbidities contribute to the overall severity in individual patients (GOLD, 2014).

Chronic obstructive pulmonary disease (COPD) is defined independently of exacerbations, which are largely a feature of moderate-to-severe disease (Burge *et al.,* 2003).

1.5.1 Pathophysiology of COPD

Chronic obstructive pulmonary disease (COPD) is characterised by poorly reversible airflow obstruction and an abnormal inflammatory response in the lungs. The latter represents the innate and adaptive immune responses to long term exposure to noxious particles and gases, particularly cigarette smoke. All cigarette smokers have some inflammation in their lungs, but those who develop COPD have an enhanced or abnormal response to inhaling toxic agents. This amplified response may result in mucous hypersecretion (chronic bronchitis), tissue destruction (emphysema), and disruption of normal repair and defence mechanisms causing small airway inflammation and fibrosis (bronchiolitis) (Macnee, 2006).

These pathological changes result in increased resistance to airflow in the small conducting airways, increased compliance of the lungs, air trapping, and progressive airflow obstruction—all characteristic features of COPD. We have good understanding of the cellular and molecular mechanisms underlying the pathological changes found in COPD.

The pathogenic mechanisms result in the pathological changes found in COPD. These in turn result in physiological abnormalities—mucous hypersecretion and ciliary dysfunction, airflow obstruction and hyperinflation, gas exchange abnormalities, pulmonary hypertension, and systemic effects.

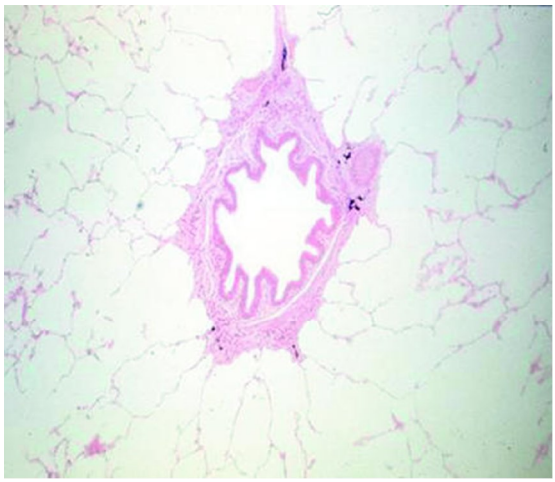

Figure1.4: Normal small airway with alveolar attachments (Macnee,2006).

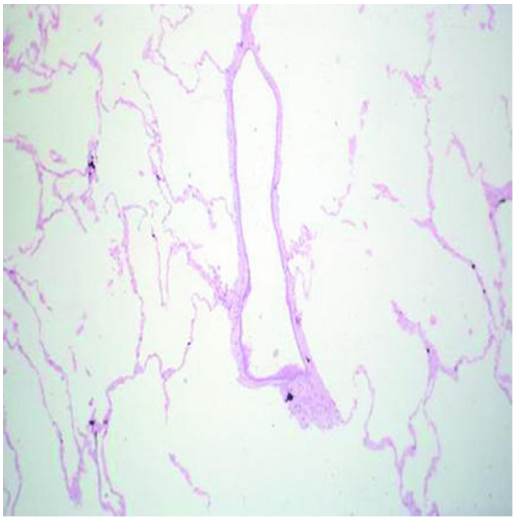

Figure 1.5: Emphysematous airway (Macnee, 2006)

1.5.1.1 Mucous hypersecretion and ciliary dysfunction

Mucous hypersecretion results in a chronic productive cough. This is characteristic of chronic bronchitis but not necessarily associated with airflow obstruction, and not all patients with COPD have symptomatic mucous hypersecretion. The hypersecretion is due to squamous metaplasia, increased numbers of goblet cells, and increased size of bronchial submucosal glands in response to chronic irritation by noxious particles and gases. Ciliary dysfunction is due to squamous metaplasia of epithelial cells and results in an abnormal mucociliary escalator and difficulty in expectorating (Burgel, 2009).

1.5.1.2 Airflow Obstruction and air trapping

The main site of airflow obstruction occurs in the small conducting airways that are < 2 mm in diameter. This is because of inflammation and narrowing (airway remodelling) and inflammatory exudates in the small airways. Other factors contributing to airflow obstruction include loss of the lung elastic recoil (due to destruction of alveolar walls) and destruction of alveolar support (Macnee, 2006). The airway obstruction progressively traps air during expiration, resulting in hyperinflation at rest and dynamic hyperinflation during exercise. Hyperinflation reduces the inspiratory capacity and therefore the functional residual capacity during exercise. These features result in breathlessness and limited exercise capacity typical of COPD. The airflow obstruction in COPD is best measured by spirometry and is a prerequisite for its diagnosis (Garcia, 2009).

1.5.1.3 Gas exchange abnormalities

These occur in advanced disease and are characterised by arterial hypoxaemia with or without hypercapnia. An abnormal distribution of ventilation: perfusion ratios—due to the anatomical changes found in COPD—is the main mechanism for abnormal gas exchange. The extent of impairment of diffusing capacity for carbon monoxide per litre of alveolar volume correlates well with the severity of emphysema (Macnee, 2006).

1.5.1.4 Pulmonary hypertension

This develops late in COPD, at the time of severe gas exchange abnormalities. Contributing factors include pulmonary arterial constriction (as a result of hypoxia), endothelial dysfunction, remodelling of the pulmonary arteries (smooth muscle hypertrophy and hyperplasia), and destruction of the pulmonary capillary bed. Structural changes in the pulmonary arterioles result in persistent pulmonary hypertension and right ventricular hypertrophy or enlargement and dysfunction (cor pulmonale) (Anderson, 2003).

1.5.2 Inflammatory cells in COPD

COPD is characterised by increased numbers of neutrophils, macrophages, and T lymphocytes (CD8 more than CD4) in the lungs. In general, the extent of the

inflammation is related to the degree of the airflow obstruction. These inflammatory cells release a variety of cytokines and mediators that participate in the disease process. This inflammatory pattern is markedly different from that seen in patients with asthma (Rovina *et al.,* 2013).

1.5.2.1 Inflammatory mediators

Many inflammatory mediators are increased in COPD, including

- Leucotriene B_4, a neutrophil and T cell chemoattractant which is produced by macrophages, neutrophils, and epithelial cells
- Chemotactic factors such as the chemokines interleukin 8 and growth related oncogene α, which are produced by macrophages and epithelial cells. These attract cells from the circulation and amplify pro-inflammatory responses
- Pro-inflammatory cytokines such as tumour necrosis factor α and interleukins 1β and 6
- Growth factors such as transforming growth factor β, which may cause fibrosis in the airways either directly or through release of another cytokine, connective tissue growth factor.

1.5.2.2 Protease and anti protease imbalance

Increased production (or activity) of proteases and inactivation (or reduced production) of antiproteases results in imbalance. Cigarette smoke, and inflammation itself, produce oxidative stress, which primes several inflammatory cells to release a combination of proteases and inactivates several antiproteases by oxidation. The main proteases involved are those produced by neutrophils (including the serine proteases elastase, cathepsin G, and protease 3) and macrophages (cysteine proteases and cathepsins E, A, L, and S), and various matrix metalloproteases (MMP-8, MMP-9, and MMP-12). The main antiproteases involved in the pathogenesis of emphysema include α_1 antitrypsin, secretory leucoprotease inhibitor, and tissue inhibitors of metalloproteases (Gadgil *et al.*, 2008).

1.5.2.3 Oxidative stress

The oxidative burden is increased in COPD. Sources of oxidants include cigarette smoke and reactive oxygen and nitrogen species released from inflammatory cells. This creates an imbalance in oxidants and antioxidants of oxidative stress. Many markers of oxidative stress are increased in stable COPD and are further increased in exacerbations. Oxidative stress can lead to inactivation of antiproteases or stimulation of mucous production. It can also amplify inflammation by enhancing transcription factor activation (such as nuclear factor) and hence gene expression of pro-inflammatory mediator (Macnee, 2006).

1.5.3 Symptoms of COPD

At first, COPD may cause no symptoms or only mild symptoms. As the disease gets worse, symptoms usually become more severe. Common signs and symptoms of COPD include:

- An ongoing cough or a cough that produces a lot of mucus (often called "smoker's cough")
- Shortness of breath, especially with physical activity
- Wheezing (a whistling or squeaky sound when you breathe)
- Chest tightness (GINA, 2010).

1.5.4 Risk factors of COPD

1.5.4.1 Genes

Severe alpha-1 antitrypsin enzyme deficiency causes pan lobular emphysema in both smokers and non-smokers. This rare hereditary disease is most commonly seen in individuals of Northern European origin (Blanco *et al.,* 2006). There have been inconsistent reports on the familial risk of airflow obstruction in smoking siblings of patients with severe COPD (McCloskey, 2006).

1.5.4.2 Exposure to particles

1.5.4.2.1 Tobacco smoke

Cigarette smoke causes COPD in susceptible individuals. The risk of COPD in smokers is dose related (Burrow, 2003). Pipe and cigar smokers have greater COPD morbidity and mortality rates than nonsmokers, although their rates are lower than those for cigarette smokers. Environmental tobacco smoke also contributes to respiratory symptoms and COPD by increasing the lungs' total burden of inhaled particles and gases (Leuenberger *et al.,* 1994). Pregnant women are advised to stop smoking as tobacco smoke poses a risk to the foetus by affecting lung growth and development in utero (Tager, 2001)

1.5.4.2.3 Occupational dust and chemicals

Occupational exposures are independently associated with the severity of airflow limitation, respiratory symptoms, and employment status in patients with COPD (Rodriquez, 2008). These exposures include organic and inorganic dusts, chemical agents and fumes. Livestock farmers have an increased risk of chronic bronchitis, COPD and reduced FEV1. Ammonia, hydrogen sulphide, inorganic dust and organic dust may be causally involved, but a role for specific biological agents cannot be excluded. Atopic farmers appear more susceptible to develop farming-related COPD (Eduard *et al.,* 2009).

1.5.4.2.4 Indoor air pollution

Biomass and coal are the main sources of energy for cooking and heating in many communities in the Middle East, Africa and Asia (Smith, 2000). Wood, animal dung, crop residues and coal are burned in poorly functioning stoves, in poorly ventilated rooms and lead to very high levels of indoor air pollution, a well established risk factor of COPD in women (Chan *et al.,* 2004).

1.5.4.2.5 Outdoor air pollution

The role of outdoor air pollution in causing COPD is unclear, but appears to be small when compared with cigarette smoking. However, air pollution from motor vehicle emissions in cities is associated with a decrease in lung function (Abbey *et al.,* 1998).

1.5.4.4 Lung growth and development

Any factor that affects lung growth during gestation and childhood has the potential for increasing an individual's risk of developing COPD. A large study and meta-analysis confirmed a positive association between birth weight and FEV1 in adulthood (Lawlor *et al.,* 2005).

1.5.4.5 Oxidative stress

Oxidative stress results from an imbalance between oxidants (generated by phagocytes during mitochondrial electron transport, air pollutants, cigarette smoke, etc.) and antioxidants. Oxidative stress directly injures the lungs and initiates lung inflammation which plays a role in the pathogenesis of COPD (Macnee, 2005).

1.5.4.6 Gender

The role of gender in determining COPD risk remains unclear. Some studies have suggested that women are more susceptible to the effects of tobacco smoke than men and raise concerns on the increasing number of female smokers in both developed and developing countries (Silverthan *et al.,* 2000).

1.5.4.7 Infections

Infections, both viral and bacterial, may contribute to the pathogenesis, progression of COPD59 and the bacterial colonisation associated with airway inflammation.(Sethi *et al.,* 2006)Infection also plays a significant role in exacerbations associated with deterioration in lung function (Seemungal, 2001).

1.5.4.8 Socioeconomic status

There is evidence that the risk of developing COPD is inversely related to socioeconomic status (Presscott *et al.,* 1999). It is not clear whether this pattern reflects exposures to indoor and outdoor air pollutants, crowding, poor nutrition, or other factors that are related to low socioeconomic status (Tao *et al.,* 1992).

1.5.5 Diagnosis of COPD

1.5.5.1 Initial diagnosis

COPD is significantly underdiagnosed worldwide. Many COPD patients present to their doctors with advanced disease at the time of diagnosis. Early diagnosis with successful smoking cessation interventions reduce the decline in lung function, and early intervention with effective treatment improves symptoms and health status (Anthonisen, 2002). A clinical diagnosis of COPD should be considered in any patient with a history of exposure to risk factors for the disease with symptoms of chronic cough, sputum production or dyspnoea. The diagnosis should be confirmed by spirometry. A post-bronchodilator FEV1/FVC ratio of less than 0.7 confirms the presence of airflow limitation that is not fully reversible and is currently widely accepted as diagnostic of COPD.(GOLD,2011) If spirometry is unavailable, clinical signs and symptoms, such as progressive shortness of breath and chronic cough with low peak expiratory flow rate, can be used to help with the diagnosis.Since peak expiratory flow readings have poor specificity every effort should be made to refer the patient for spirometry to confirm the diagnosis (Kelly *et al.,*1988).

1.5.5.2 Assessment of symptoms

Dyspnoea is the hallmark symptom of COPD and the main reason patients seek medical attention. The dyspnoea is progressive over months or years and is persistent. As lung function deteriorates, the breathlessness interferes with patients' daily activities. Cough is often the first symptom of COPD which may initially be intermittent but later present daily, often with chronic sputum production. Wheezing and chest tightness may also be present. Extrapulmonary effects such as weight loss, signs of cor pulmonale and other co-morbid conditions should also be identified and assessed (Schols *et al.,* 1992). Psychiatric morbidity is common in advanced COPD (Calverly, 1996). COPD patients experience fluctuations in symptoms and general feelings of well-being which can vary from day to day.

1.5.5.2.1 Medical history

A thorough medical history should include the following:

- Current symptoms and the pattern of symptom development including severity of breathlessness.

- Exposure to risk factors and possibilities for eliminating or reducing risk factors.
    - Smoking history Quantification of tobacco consumption: total pack-years = (number of cigarettes smoked per day ÷ 20) x number of years of smoking
    - Occupational and environmental exposures to other lung irritants.
- Impact of disease on psychological well being.
- Past medical history including exacerbations and admissions for respiratory illness.
- Family history of any respiratory disorder.
- Presence of other co-morbidities such as cardiovascular disease, psychiatric illness, malignancy, osteoporosis and musculoskeletal disorders.
- All current medical therapy and its appropriateness.
- Social and family support available to the patient.

1.5.5.2.2 Physical examination

Physical examination is not usually diagnostic of COPD but is an important part of patient care. Physical signs of airflow limitation and air trapping (barrel chest, loss of cardiac and liver dullness, prolonged expiration, reduced breath sounds) are not usually present until the disease is already at an advanced stage. Physical examination may detect co-morbidities or other illnesses and detect the development of complications of COPD such as malnourishment and cor pulmonale (Kelly *et al.,* 2007)

1.5.5.2.3 Measurement of lung function

Spirometry is required to confirm the diagnosis of COPD and to assess the severity of the disease. Spirometry should be performed in people with exposure to risk factors who have chronic cough and sputum production even without dyspnoea as it may help identify patients earlier in the course of the disease (Walker *et al.,* 2006). Peak flow measurements can detect airflow limitation but has poor specificity. The relationship between peak expiratory flow and FEV1 is poor in COPD (Aggarwal *et al.,* 2006).

1.5.5.2.4 Bronchodilator reversibility testing

Bronchodilator testing is required to establish the best attainable lung function at that point of time. Response to a bronchodilator is considered significant if the change in FEV1 is both at least 200 mL and 12% above the pre-bronchodilator FEV1 (Rabe *et al.,* 2007). If there is a marked response to bronchodilators, asthma should be

considered. A proportion of COPD patients may show significant response to bronchodilators (Calverley *et al.,* 2003).

1.5.5.2.5 Assessment of COPD severity

COPD severity is based on the patient's level of symptoms, the severity of spirometric abnormality based on FEV1 and the presence of complications such as respiratory failure and cor pulmonale (Gibson, 2006). Multi-dimensional assessment of severity includes the BODE index (Cote *et al.,* 2008) and the locally developed SAFE index 80 (Shah *et al.,* 2007).

1.5.5.3 Additional investigations

1.5.5.3.1 Six minute Walk Test (6MWT)

This test measures the distance covered during six minutes and is a useful test of exercise capacity (ATS, 2002) and provides prognostic information.Arterial oxygen desaturation can be measured with a pulse oximeter during walking (Casanova *et al.,* 2007).

1.5.5.3.2 Chest Radiograph

A chest radiograph is valuable in excluding other diagnoses such as lung cancer, heart failure, bronchiectasis and tuberculosis. Radiological changes associated with COPD include the presence of hyperinflation (flattened diaphragm and increased lung volume), bullae and hyperlucency of the lungs. High resolution computed tomography scanning is not routinely recommended unless there is diagnostic uncertainty (Gibson, 2006).

1.5.5.3.3 Arterial blood gas analysis

This should be performed in patients with FEV1 < 40% predicted if they have low arterial oxygen saturation (less than 92% on pulse oximetry) or with clinical signs of respiratory failure or cor pulmonale as these patients may benefit from long term oxygen therapy at home (Roberts *et al.,*1993).

1.5.5.3.4 Full blood count

This detects underlying anaemia of chronic diseases. Polycythaemia can develop with chronic hypoxaemia.

1.5.5.3.5 Electrocardiography (ECG)

ECG is useful in detecting pulmonary hypertension in advanced disease and concurrent ischaemic heart disease.

1.5.5.3.6 Alpha 1 antitrypsin deficiency screening

This should be performed in young COPD patients (< 45 years old) or those who have a strong family history of the disease. Other suggested investigations include fasting plasma glucose, serum albumin and serum fasting lipids to detect other common co-morbidities (Casanova *et al.,* 2007).

1.5.5.4 Differential diagnoses

Other potential diagnoses in older patients presenting with progressive breathlessness are (Bronchial asthma, congestive heart failure, pulmonary tuberculosis, diffuse parenchymal lung disease). The major differential diagnosis is chronic asthma. In most instances, the diagnosis can be easily made but occasionally a clear distinction between asthma and COPD may not be possible clinically and physiologically, and it is assumed that both conditions co-exist in these patients (Calverley *et al.,* 2003).

1.5.6 Treatment and Medication of COPD

There are two type treatments for COPD. One is Pharmacological and another is non pharmacological.

1.5.6.1 Pharmacological interventions

1.5.6.1.1 Bronchodilators remain the mainstay of pharmacological therapy.

- They reduce airway smooth muscle tone, improve expiratory flow rate, reduce air-trapping and hyperinflation of the lung.
- They also improve the patient's dyspnoea scores, increase exercise tolerance, reduce disability in daily living and improve overall health status.
- Optimal pharmacotherapy should be guided by the patients' symptoms, level of activity and frequency of COPD exacerbation (Presscott *et al.,* 1999).

1.5.6.1.2 Inhaled short acting bronchodilators

- These include inhaled short-actingβ2-agonists (SABAs) and inhaled short-acting anticholinergics (SAACs)
- Inhaled SABAs(Salbutamol 200 µg, fenoterol 200 µg or terbutaline 500 µg PRN or 4 to 6 hourly). They have been shown to improve lung function, dyspnoea and exercise tolerance.
- Inhaled SAACs(Ipratropium bromide 40 µg 6 hourly) (Roberts *et al.,* 1993).

1.5.6.1.3 Inhaled long acting bronchodilators

- Consist of long-acting β2-agonists (LABAs) and long-acting anticholinergics (LAACs)

- Offer a more sustained relief of symptoms and improvement of lung function
- Also improve patients' compliance to treatment.
- Inhaled LABAs(salmeterol 50 µg twice daily or formoterol 9 µg twice daily)
- Inhaled LAACs(Tiotropium is the only LAAC currently in the market. The dose is 18 µg once daily administered through a Handihaler)

1.5.6.1.4 Inhaled LABA and inhaled corticosteroid (ICS) combination

The combination of LABA/ICS has been shown to improve lung function, quality of life and reduce exacerbations compared with placebo in COPD patients with FEV1 < 65% predicted (Calverley, 2007). In the study, there was a trend towards a reduction in mortality in patients taking LABA/ ICS compared to placebo, though the reduction was not statistically significant (Calverley ,2007). In the same study, the decline in lung function in the patients taking LABA/ICS (39 mL/year) was also slower compared with placebo (55 mL/year) (Celli, 2008). When ICS/LABA was compared with LAAC in the INSPIRE study among patients with severe and very severe COPD with a history of exacerbation, there was no difference in exacerbation rate but the former was associated with better health related quality of life and lower mortality (Wedzicha, 2008). However, this study was not statistically powered to study the mortality outcome. Only Inhaled corticosteroids are fluticasone 500 µg twice daily by budesonide 400 µg twice daily by Turbuhaler (Celli, 2008).

1.5.6.1.5 Oral corticosteroids

- About 10% of COPD patients show significant improvement in lung function (defined as an improvement of at least 20% of FEV1) after oral corticosteroid administration (Piggiaro *et al.,*1998).
- However, chronic systemic corticosteroid usage is known to be associated with potentially serious side-effects such as osteoporosis, premature cataract, muscle weakness, diabetes mellitus and hypertension.
- Indeed, one study showed that in severe COPD patients, maintenance treatment with oral glucocorticoids is associated with increased mortality in a dose-dependent manner. Hence, prolonged courses of systemic corticosteroids for the treatment of COPD should be discouraged (Schols, 2001).

1.5.6.1.6 Methylxanthines

- Oral sustained-release theophylline 125-300 mg twice daily.
- Theophylline is a weak bronchodilator, hence offering only a modest improvement in symptoms and exercise tolerance.

- This potential benefit should be weighed against its side-effects, such as nausea, abdominal discomfort, diarrhoea and risk of cardiac arrhythmias (Schols, 2001).

1.5.6.1.7 Phosphodiesterase-4 (PDE4) inhibitors

- oral roflumilast 500 mg once daily, cilomilast 15 mg twice daily
- Recently, treatment with PDE4 inhibitors has been studied in COPD patients.
- Significant adverse effects in subjects treated with PDE4 inhibitors include nausea, diarrhoea, weight loss and headache (Calverley, 2007).

1.5.6.2 Non pharmacological interventions

1.5.6.2.1 Pulmonary Rehabilitation in COPD

Pulmonary rehabilitation aims to reduce symptoms, decrease disability, increase participation in physical and social activities, and improve the overall quality of life for patients with chronic respiratory diseases. It includes exercise, education, psychosocial and behavioral intervention by an interdisciplinary team of specialists (ATS, 2006).

Benefits of pulmonary rehabilitation include;

- Improvement in exercise tolerance.
- Reduction in the sensation of dyspnoea.
- Improvement in health-related quality of life.
- Improvement in peripheral muscle strength and mass.
- Reduction in number of days spent in hospital.
- Cost effectiveness.
- Improvement in the ability to perform routine activities of daily living.
- Reduction in exacerbations.
- Reduction in anxiety and depression.

1.5.6.2.2 Domiciliary oxygen therapy for COPD

Long-term administration of oxygen of > 15 hours per day to patients with chronic respiratory failure has been shown to increase survival. Home oxygen therapy does not appear to improve survival in patients with mild to moderate hypoxaemia or in those with only oxygen desaturation at night. The goal of long-term oxygen therapy

is to increase the baseline PaO2 to at least 60 mmHg (or 8.0 kPa) at rest, and/or produce an SaO2 of at least 90% (Cranston *et al.,* 2007).

1.5.6.3 Lung volume reduction for COPD

1.5.6.3.1 Lung volume reduction surgery

Lung volume reduction by resection of non-functioning emphysematous areas improves exercise tolerance and decreases 2-year mortality in patients with severe, predominantly upper-lung emphysema who have low baseline exercise capacity after pulmonary rehabilitation (Fishman *et al.,* 2003).

1.5.6.3.2 Bullectomy

Bullectomy has been reported to improve lung function and dyspnoea in selected patients by removal of large bullae compressing on adjacent lung parenchyma was maintained three years post-bullectomy. Surgical techniques used have included thoracotomy, video-assisted thoracoscopy and stapled wedge resection (Schipper, 2004).

1.5.6.3.3 Lung Transplantation

At the present time it is limited to younger patients with other chronic lung diseases. Patients with COPD are considered for lung transplantation (Orens *et al.,* 2006). When life expectancy is not predicted to exceed 24-36 months despite optimal and maximal medical management, < 60 years old with an FEV1 < 25% predicted after bronchodilator therapy or with severe pulmonary hypertension. The 5-year survival after transplantation for emphysema is 45 to 60% in Western series. Lifelong immunosuppressive therapy is required (Studer *et al.,* 2004).

1.6 Significance of the study

Day by day prevalence of Asthma and COPD is increasing in the whole world as well as in Bangladesh. The morbidity and mortality rate also has been increased. Asthma affects both children and adults. Using conservative definitions, it is estimated that as many as 300 million people of all ages and all ethnic backgrounds suffer from asthma. For the past 40 years, the prevalence of asthma has increased in all countries in parallel with that of allergy. It is estimated that asthma accounts for about 250 000 annual deaths worldwide. Chronic obstructive pulmonary disease (COPD) affects 210 million people. It was the fifth cause of death in 2002 and it is projected to be the fourth cause of mortality by 2030. Tobacco smoking is the major risk factor, but the use indoors of solid fuels for cooking and heating also presents major risks.

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

In this study we will try to find out the prevalence of Asthma and COPD in a region for the better understanding of the present situation and to aware people about the diseases and to reduce mortality rate, to reduce severity and increase patient's compliance and to improve management of asthma and COPD.

1.7 Aims and objectives of the study

The aims and objectives of this study were to

- Explore the prevalence of asthma and COPD in Dhaka city.
- To identify how many people have symptoms of asthma or COPD who are still undiagnosed.
- To identify how many people are prone to having asthma or COPD.

CHAPTER 2

LITERATURE REVIEW

2.1 Prevalence of Asthma and COPD in general practice in 1992: has it changed since 1977?

Asthma and COPD are common diseases of the airways which are mainly diagnosed and treated in general practice. Various studies have reported an increase in the morbidity of asthma and COPD. Tirimanna *et al.,* has conducted a study on a sample of 2328 adults from the general population were screened for asthma and COPD. Those screened were then divided into five sub-groups (grades 1-5), according to severity of: (1) respiratory symptoms; and (2) loss in FEV1. The number of patients who were not known to the general practitioner prior to the screening as having asthma or COPD grades 1-5 was also assessed. In 1992, they studied a different sample of 1184 adults of the general population in the same area. They used the same criteria as in 1977 to analyse their results. The number of patients not known to the general practitioner prior to the screening was also studied. The result was overall prevalence (grades 1-5) of asthma and COPD has increased from +/- 19% in 1977 to +/- 31% in 1992 (range 21-42). The main reason for this is an increase in prevalence of very mild to moderate asthma and COPD (grades 1-3) from 17% in 1977 to 27% in 1992. The prevalence of severe cases (grades 4-5) increased from 2% in 1977 to 4% in 1992. In 1992, around 65% of the patients were not known to the general practitioner as having any grade of asthma or COPD. This was only slightly lower than the 72% in 1977. All patients with a severe disease (grade 5) were known to the general practitioner. There is a real increase in the prevalence of asthma and COPD, caused predominantly by an increase in the number of mild cases (Tirimanna *et al.,* 1996).

2.2 Self reported asthma symptoms in children adults of Bangladesh: findings of the National Asthma Prevalence Study

No population-based studies to determine the magnitude of the asthma problem have been carried out in Bangladesh. This study aimed to define the prevalence of asthma as well as to identify the risk factors of asthma in the general population of Bangladesh. A cross-sectional study was conducted from January 1999 to August 1999 on 5642 Bangladeshi people by Hassan *et al.,* Data were collected from randomly selected primary sampling units of 8 municipality blocks of 4 large metropolitan cities, 12 municipality blocks of 6 district towns and 12 villages of 6 districts chosen randomly from all 64 districts of the country. Face-to-face interviews were performed with the housewives or other guardians at the household level using a structured questionnaire. The prevalence of asthma (wheeze in the last 12 months) was 6.9%.The prevalence of other asthma definitions were: ever wheeze (lifetime wheeze) 8.0%,perceived asthma (perception of having asthma) 7.6%,doctor diagnosed asthma (diagnosis of asthma by any category of doctor either qualified or unqualified) 4.4%.The prevalence of asthma in children (5–14 years) was higher than in adults (15–44 years). Asthma in children was found to be significantly higher in households with ≤3 people than in larger households. The low-income group and illiterate group

were more vulnerable to asthma attacks than the high-income group and more educated people, respectively. Asthma in Bangladesh appears to be a substantial public health problem: an estimated 7 million people including 4 million children suffer from asthma-related symptoms (Hassan *et al.,* 2001).

2.3 Global asthma prevalence in adults: findings from the cross sectional world health survey

Asthma is a major cause of disability, health resource utilization and poor quality of life world-wide. The study was set out to generate estimates of the global burden of asthma in adults, which may inform the development of strategies to address this common disease. The World Health Survey (WHS) was developed and implemented by the World Health Organization in 2002-2003. The study was conducted among 178,215 individuals from 70 countries aged 18 to 45 years responded to questions related to asthma and related symptoms. The prevalence of asthma was based on responses to questions relating to self-reported doctor diagnosed asthma, clinical/treated asthma, and wheezing in the last 12 months. The global prevalence rates of doctor diagnosed asthma, clinical/treated asthma and wheezing in adults were 4.3%, 4.5%, and 8.6% respectively, and varied by as much as 21-fold amongst the 70 countries. Australia reported the highest rate of doctor diagnosed, clinical/treated asthma, and wheezing (21.0%, 21.5%, and 27.4%). Amongst those with clinical/treated asthma, almost 24% were current smokers, half reported wheezing, and 20% had never been treated for asthma. This study provided a global estimate of the burden of asthma in adults, and suggests that asthma continues to be a major public health concern worldwide. The high prevalence of smoking remains a major barrier to combating the global burden of asthma. While the highest prevalence rates were observed in resource-rich countries, resource-poor nations were also significantly affected, posing a barrier to development as it stretches further the demands of non-communicable diseases (Stanojevic *et al.,* 2012).

2.4 Changes in asthma Prevalence: two surveys 15 years apart

In 1973 Burr *et al.,* conducted a survey among 12 year old children living in a defined area of South Wales. In 1988 the survey was repeated in the same area, again among 12 year old children. Questionnaires were completed for all 965 children in the population sample; peak expiratory flow rates were performed on them all, and repeated (except for five children) after an exercise provocation test. The prevalence of a history of wheeze at any time had increased from 17% to 22%, while that of a history of asthma at any time had increased from 6% to 12%. Current asthma had increased from 4% to 9%, but wheezing in the past year not attributed to asthma had remained at 6%. The exercise provocation tests suggested that both mild and severe asthma had become more common. Increases had also occurred in the frequencies of a history of eczema (from 5% to 16%) and of hay fever (from 9% to 15%). It was seemed that the prevalence of asthma had risen, and that this could not be wholly explained by a greater readiness to diagnose the disease (Burr *et al.,* 1989).

2.5 Interpreting COPD prevalence Estimates: What is the True Burden of Disease?

The study objective was to summarize the available data on COPD prevalence and assess reasons for conflicting prevalence estimates in the published literature. Halbert *et al.,* reviewed published studies that estimated COPD prevalence for a population, and clearly described the methods used to obtain the estimates. Thirty-two sources of COPD prevalence rates, representing 17 countries and eight World Health Organization-classified regions, were identified and reviewed. Prevalence estimates were based on spirometry (11 studies), respiratory symptoms (14 studies), patient-reported disease (10 studies), or expert opinion. Reported prevalence ranged from 0.23 to 18.3%. The lowest prevalence rates (0.2 to 2.5%) were based on expert opinion. Sixteen studies had measured rates that could reasonably be extrapolated to an entire region or country. All were for Europe or North America, and most fell between 4% and 10% was considerable variation in the reported prevalence of COPD. The overall prevalence in adults appears to lie between 4% and 10% in countries where it has been rigorously measured. Some of the variation attributed to differences in risk exposure or population characteristics may be influenced by the methods and definitions used to measure disease. Spirometry is least influenced by local diagnostic practice, but it was subject to variation based on the lung function parameters selected to define COPD (Halbert *et al.,* 2003).

2.6 The prevalence of COPD: Using Smoking Rates to Estimate Disease Frequency in the General Population

The study objective was to develop and validate a model based on smoking rates that provided reliable estimates of the true prevalence of COPD that include both clinically detected and undetected patients. Model based on literature review. Age- and gender-specific rates of lung impairment by smoking status were applied to US smoking data. Resultant estimates were compared to the actual prevalence of obstructive airway disease as estimated by US national surveys. The model then was applied to estimate the prevalence of COPD in several European countries, where national data on undiagnosed lung disease do not exist. The model was adapted from both a literature review and health-care data, and the analysis was applied to the United States and Europe. Using smoking rates, it was estimated from the model that 15.3 million people who were > 40 years of age in the United States had COPD. The prevalence estimate, based on spirometric definitions for COPD in the same age group using the Third National Health and Nutrition Examination Survey (NHANES III), is 17.1 million people. NHANES III and other US national health-care surveys further suggested that only between 2.4 and 7 million people actually had COPD diagnosed; thus, the proportion of COPD that was currently being diagnosed in the United States is between 14% and 46% of all cases. Using smoking rates and our model, which was developed and validated for the United States, it was calculated the prevalence of COPD for Germany (2.7 million people), the United Kingdom (3.0

million people), Spain (1.5 million people), Italy (2.6 million people), and France (2.6 million people) in those people > 45 years of age. Smoking rates appeared to provide a useful method of estimating current COPD prevalence in those countries where more objective data were unavailable. These results were important because recognition of the true burden of disease and corresponding efforts to increase early identification of COPD could help to reduce the morbidity and mortality associated with COPD in populations at risk (Stang *et al.,* 2000).

2.7 International variation in the prevalence of COPD (The BOLD Study): a population-based prevalence study

Chronic obstructive pulmonary disease (COPD) is a growing cause of morbidity and mortality worldwide, and accurate estimates of the prevalence of this disease are needed to anticipate the future burden of COPD, target key risk factors, and plan for providing COPD-related health services. Buist *et al.,* aimed to measure the prevalence of COPD and its risk factors and investigate variation across countries by age, sex, and smoking status. Participants from 12 sites (n=9425) completed postbronchodilator spirometry testing plus questionnaires about respiratory symptoms, health status, and exposure to COPD risk factors. COPD prevalence estimates based on the Global Initiative for Chronic Obstructive Lung Disease staging criteria were adjusted for the target population. Logistic regression was used to estimate adjusted odds ratios (ORs) for COPD associated with 10-year age increments and 10-pack-year (defined as the number of cigarettes smoked per day divided by 20 and multiplied by the number of years that the participant smoked) increments. Meta-analyses provided pooled estimates for these risk factors. The prevalence of stage II or higher COPD was 10·1% .Overall, 11·8% (7·9) for men, and 8·5% (5·8) for women. The ORs for 10-year age increments were much the same across sites and for women and men. The overall pooled estimate was 1·9 per 10-year increment. Site-specific pack-year ORs varied significantly in women,but not in men. This worldwide study showed higher levels and more advanced staging of spirometrically confirmed COPD than had typically been reported. However, although age and smoking were strong contributors to COPD, they did not fully explain variations in disease prevalence—other factors also seemed to be important. Although smoking cessation is becoming an increasingly urgent objective for an ageing worldwide population, a better understanding of other factors that contribute to COPD is crucial to assist local public-health officials in developing the best possible primary and secondary prevention policies for their regions (Buist *et al.,* 2007).

2.8 Global burden of COPD: systemic review and meta-analysis

The aim of this study was to quantify the global prevalence of chronic obstructive pulmonary disease (COPD) by means of a systematic review and random effects meta-analysis. Halbert *et al.,* was searched for population-based prevalence estimates published during the period 1990–2004. Articles were included if they: 1) provided total population or sex-specific estimates for COPD, chronic bronchitis and/or emphysema; and 2) gave method details sufficiently clearly to establish the sampling strategy, approach to diagnosis and diagnostic criteria. Of 67 accepted articles, 62 unique entries yielded 101 overall prevalence estimates from 28 different counties. The pooled prevalence of COPD was 7.6% from 37 studies, of chronic bronchitis alone (38 studies) was 6.4% and of emphysema alone (eight studies) was 1.8%. The pooled prevalence from 26 spirometric estimates was 8.9%. The most common spirometric definitions used were those of the Global Initiative for Chronic Obstructive Lung Disease (13 estimates). There was significant heterogeneity, which was incompletely explained by subgroup analysis (*e.g.* age and smoking status). The prevalence of physiologically defined chronic obstructive pulmonary disease in adults aged ≥40 yrs is ∼9–10%. There were important regional gaps, and methodological differences hinder interpretation of the available data. The efforts of the Global Initiative for Chronic Obstructive Lung Disease and similar groups should helped to standardise chronic obstructive pulmonary disease prevalence measurement (Halbert *et al.,* 2006).

CHAPTER 3

METHODOLOGY

3.1 Type of study

It is survey based study among general population.

3.2 Study design

In this study data were collected through interviews with a structured questionnaire. The study protocol was reviewed and approved by the supervisor.

3.3 Study population

A total 300 peoples were included and interviewed as per the questionnaire. Age eligible for this study was in between 15 to 65 years old.

3.4 Study area

The study area was mainly farmgate and its surroundings in the Dhaka city.

3.5 Inclusion criteria

The following was included-

- Any male or female subject.
- Any person having age between 15 to 65 years.

3.6 Exclusion criteria

The following was not included in the study-

- Any respondents having age less than 15 years.
- Any respondents having age more than 65 years.

3.7 Study period

The study period was about 6 month started from January 2016 to June 2016**.**

3.8 Data collection method

During February 2016 to April 2016, in the study period, peoples were interviewed as per the questionnaire and it was made understood to them in Bengali. In the questionnaire some generalized questions including their age, gender, living area, weight, height, working and living area's condition and questions of symptomatic conditions on asthma and COPD were there.

3.9 Data analysis

Data were organized, tabulated and aggregated using Microsoft excel 2007.

CHAPTER 4

RESULTS

4.1 Gender distribution

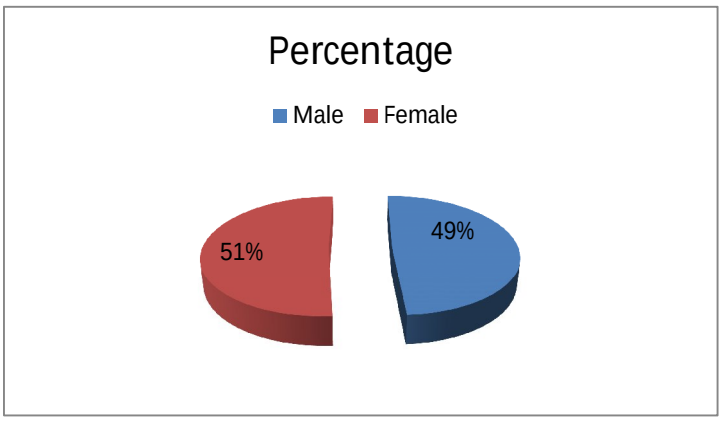

Figure 4.1: Gender distribution

Among the sample of 300 population 51% were found female and 49% male.

4.2 Age range of the respondents

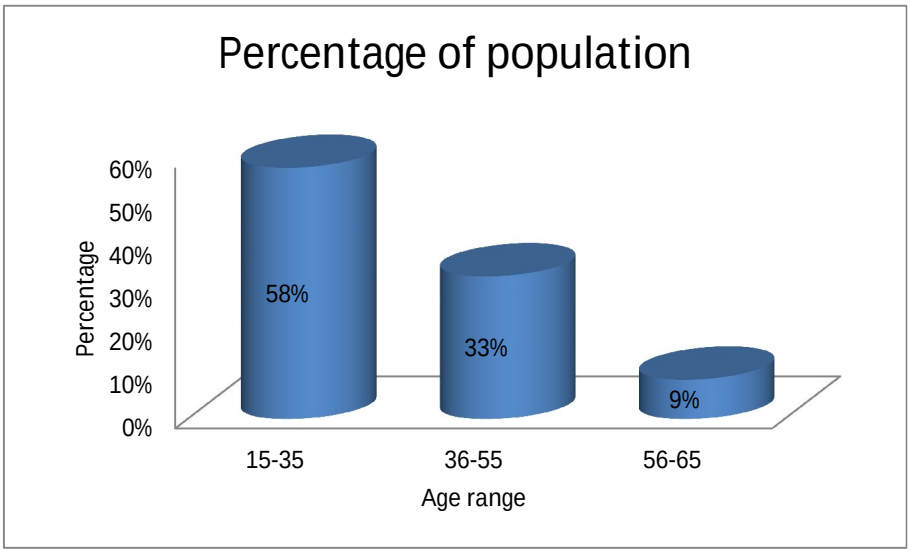

Figure 4.2: Age range of the respondents

58% population were in the range of (15-35) years. 33% population were in the range of (36-55) years and 9% population were in the range of (56-65) years.

4.3 Educational status

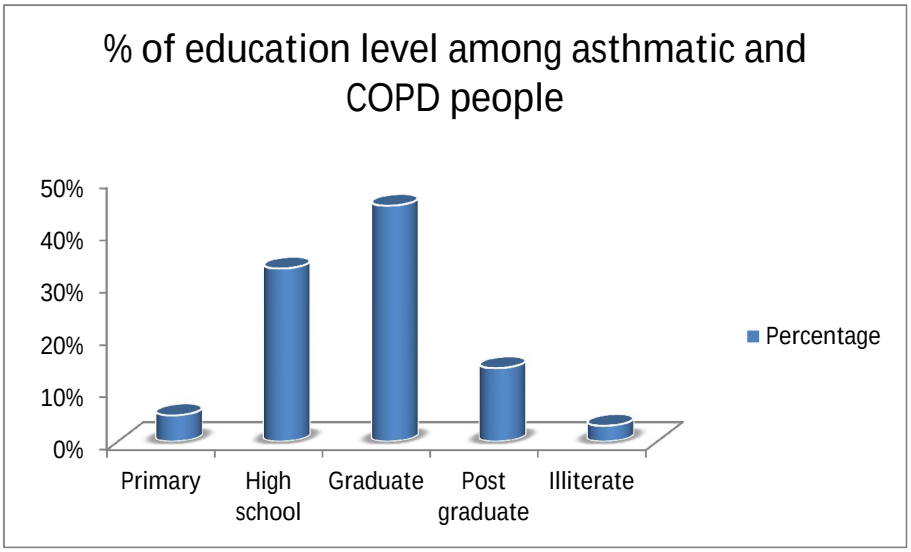

Figure 4.3: Education level among asthmatic and COPD people

Among the people who had asthma or COPD it was found that, 5% were in the primary level, 33% were in the secondary level, 45% were in the under graduation or graduation level, 14% were in the post graduation level and 3% were illiterate.

4.4 Occupational level

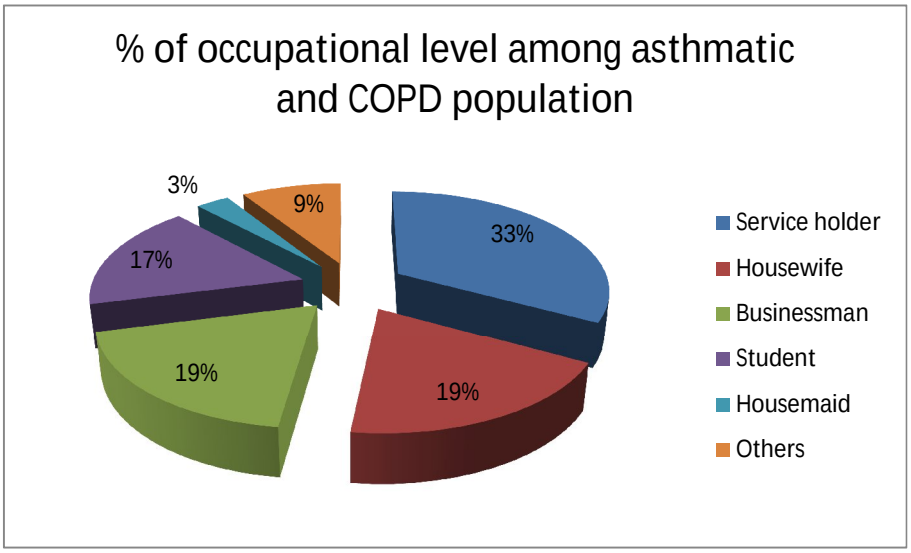

Figure 4.4: Occipational level among asthmatic and COPD people

Among the asthmatic and COPD people 33% were service holder, 19% were housewife, 19% were businessman, 17% were student, 3% were housemaid and 9% were from other occupation.

4.5 Family history of asthma or COPD

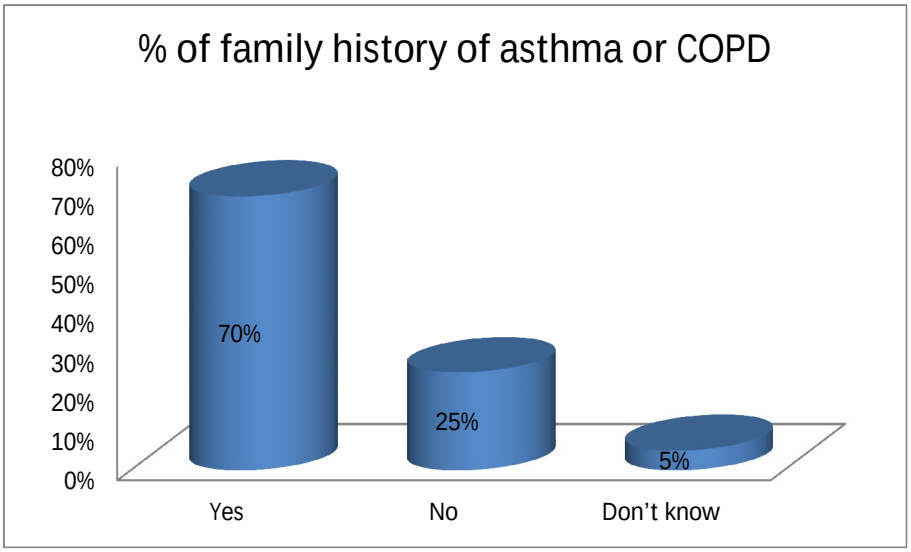

Figure 4.5: Percentage of having family history of asthma or COPD

When the family history were taken from the respondents it was found that 70% had asthma or COPD in their family, 25% had no asthma or COPD and 5% had no idea whether they had in their family or not.

4.6.1 Age distribution of the asthmatic people

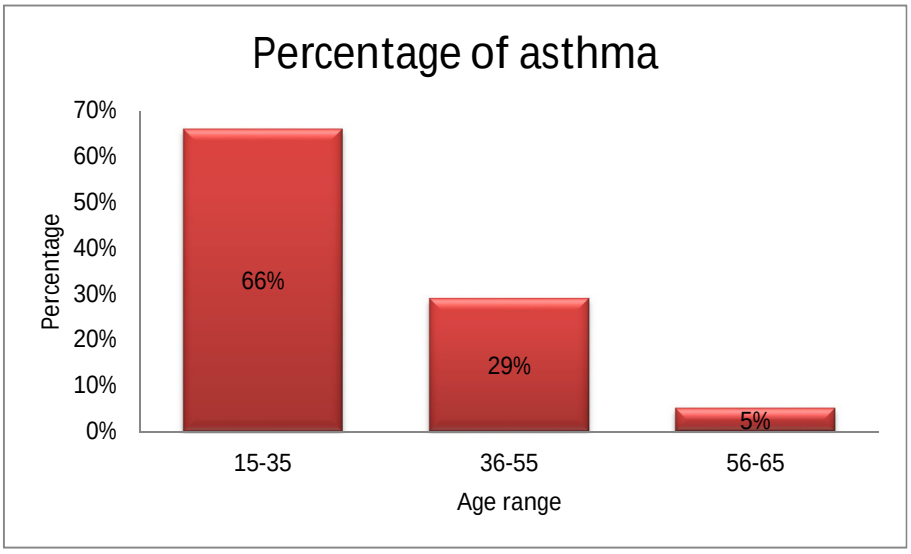

Figure 4.6: Age distribution of the asthmatic people

66% asthmatic people were in the range of (15-35)years, 29% were in the range of (36-55) years and 5% were in the range of (56-65) years.

4.6.2 Age distribution of the COPD population

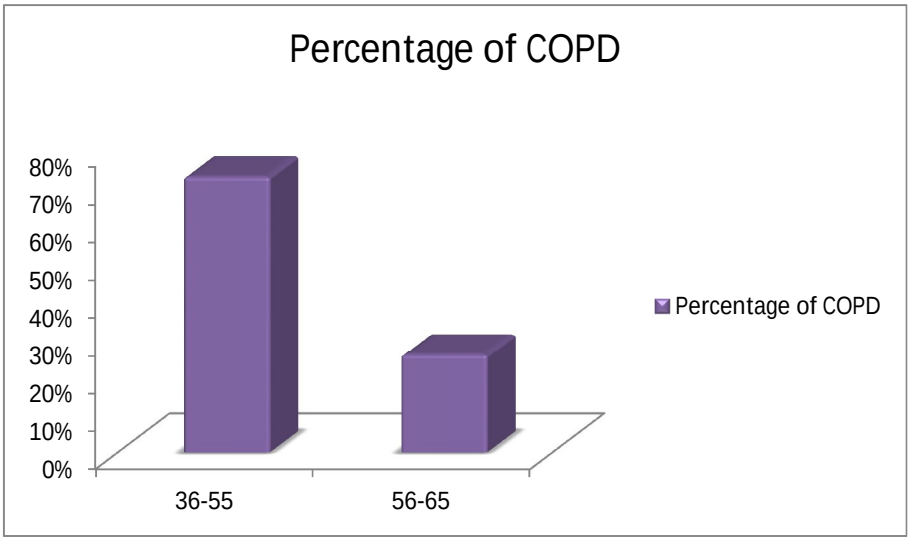

Figure 4.7: Age distribution of the COPD population

73% of COPD people were in the age range of (36-55) years and rest of the 26% were in the range of (56-65) years.

4.7.1 Hypertension among asthmatic people

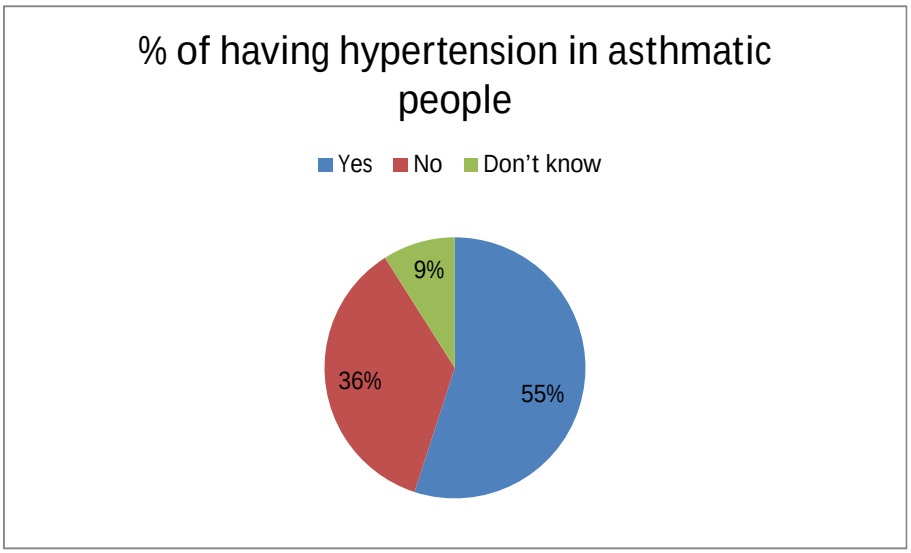

Figure 4.8: Presence of hypertension among asthmatic people

55% people had both asthma and hypertension. Hypertension was not present among 36% asthmatic people and 9% asthmatic people did not know whether they had hypertension or not.

4.7.2 Hypertension among COPD people

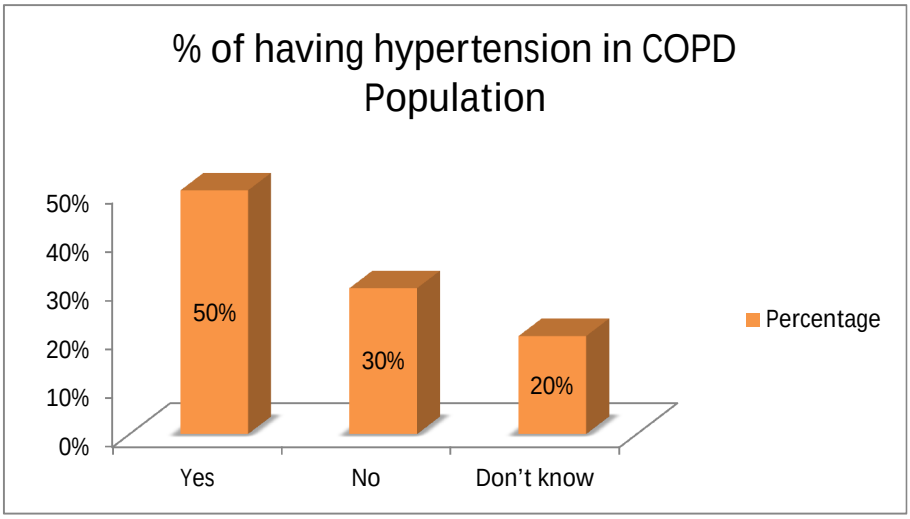

Figure 4.9: Percentage of having hypertension

50% had both COPD and hypertension and 30% had only COPD and 20% did not know about having hypertension.

4.8 Atopic dermatitis in asthmatic people

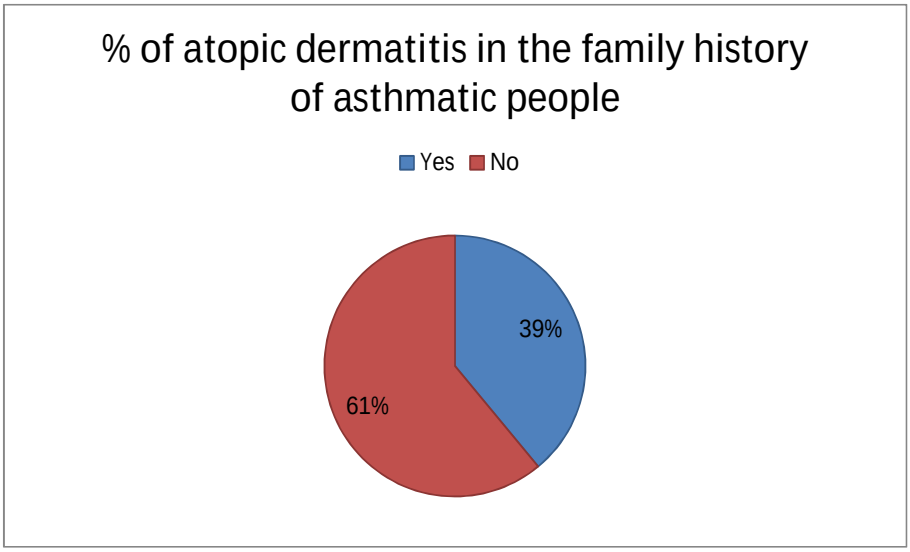

Figure 4.10: Presence of atopic dermatitis in the family history asthmatic people

In the family history of asthmatic people atopic dermatitis which is one type of skin disorder was found in the family history of 61% asthmatic people.

4.9 Duration of Asthma among asthmatic people

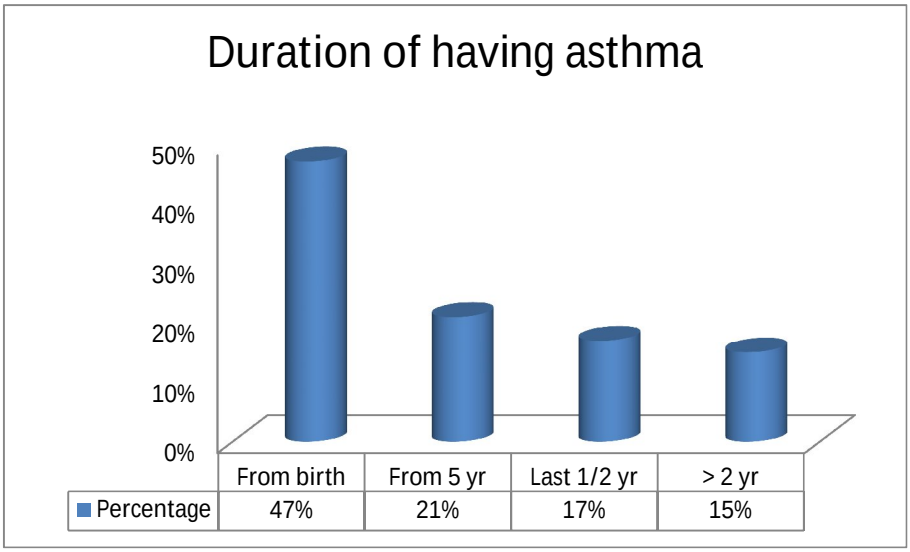

Figure 4.11: Duration of having asthma

It was found that 68% asthmatic people had asthma from their childhood and 32% had adult onset asthma.

4.10.1 Smoking status of asthmatic people

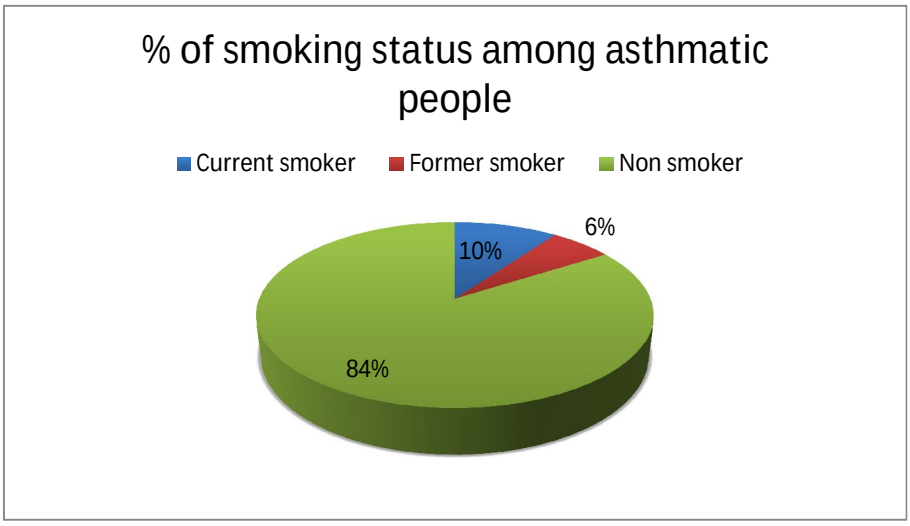

Figure 4.12: Smoking status of the asthmatic people

Among asthmatic people 84% were non smoker,10% were current smoker and 6% were former smoker.

4.10.2 Smoking status of COPD population

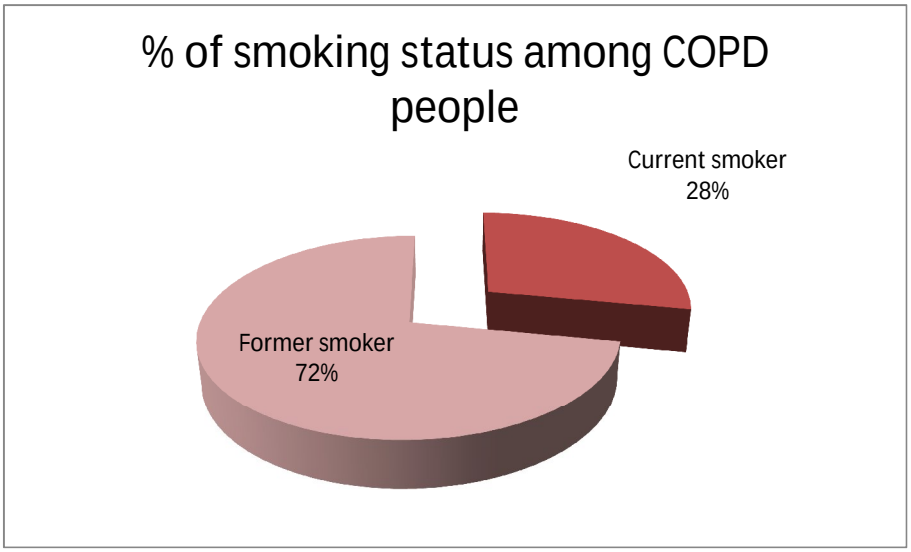

Figure 4.13: Smoking status of COPD population

Among COPD population 28% were current smoker and 72% were former smoker

4.11.1 Percentage of taking cigarettes among asthmatic people

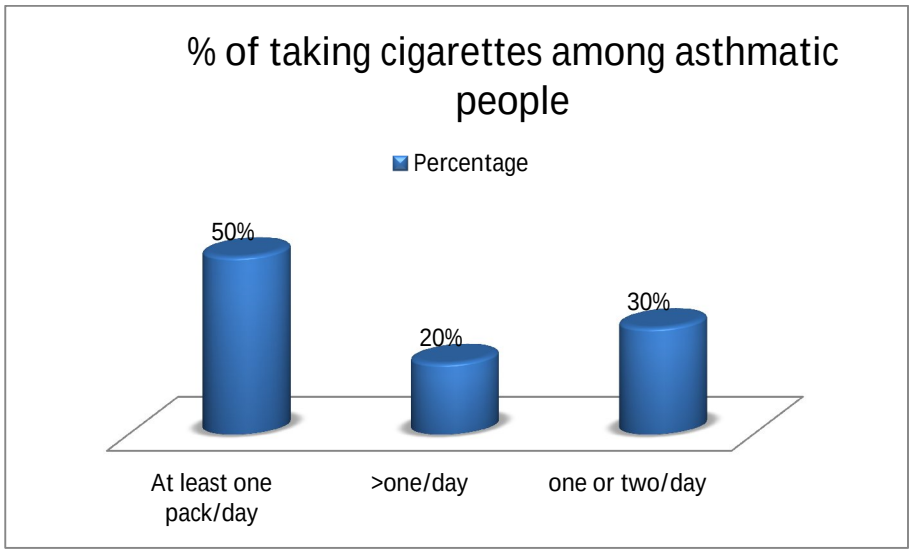

Figure 4.14: Percentage of current smoker taking cigarettes

Among 10% asthmatic current smoker 50% took atleast one pack per day,20% took more than one pack per day and 30 took one or two cigarettes in a day.

4.11.2 Percentage of taking cigarettes among COPD people

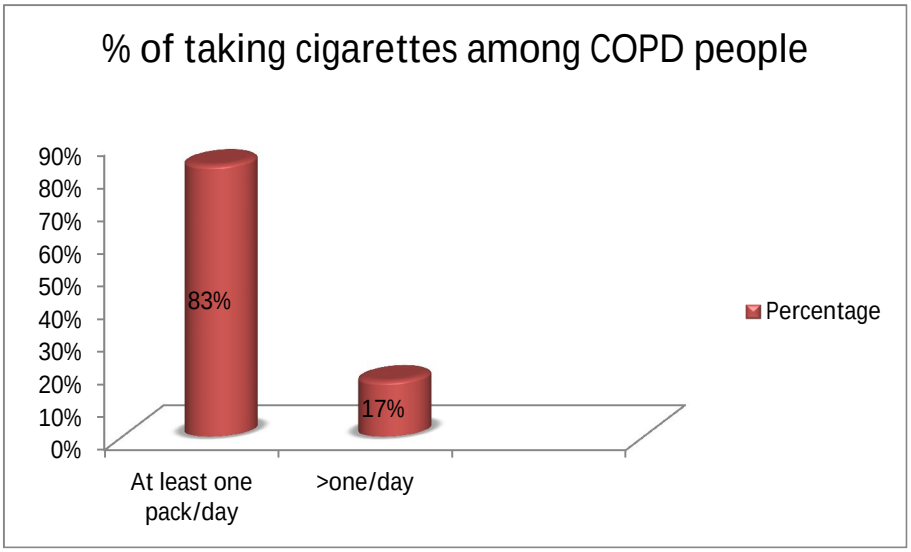

Figure 4.15: Percentage of taking cigarettes of the current smoker

Among 28% current smokers 83% took atleast one pack per day and 17% took more than one pack per day.

4.12.1 Presence of asthmatic symptoms in Asthma

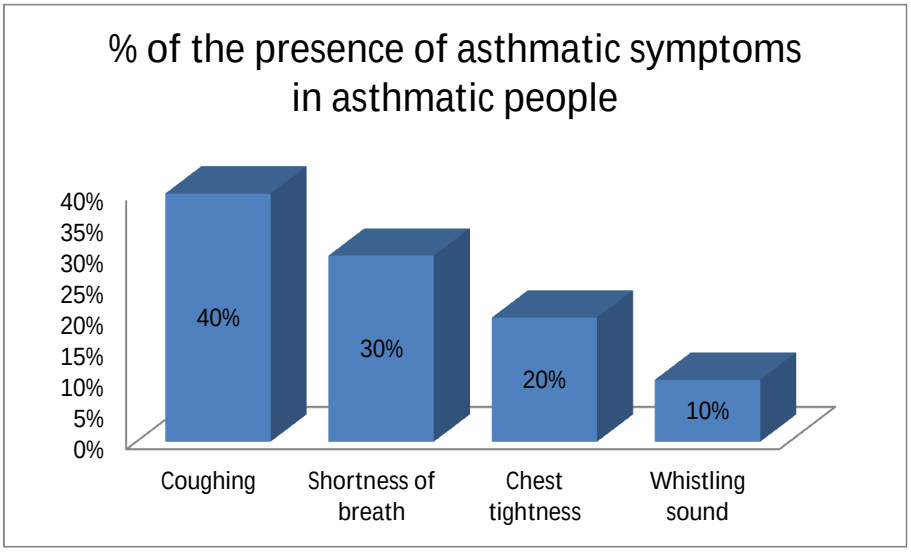

Figure 4.16: Presence of asthmatic symptoms among asthmatic people

Among asthmatic population 40% were suffering from cough, 30% were suffering from shortness of breath, 20% were suffering from chest tightness and 10% were suffering from whistling or wheezing sound in their chest.

4.12.2 Presence of asthmatic symptoms in COPD

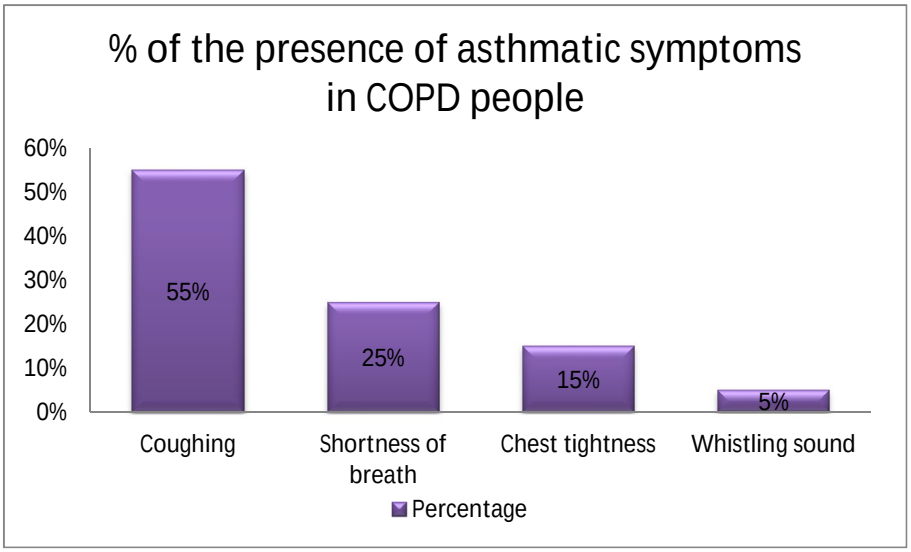

Figure 4.17: Percentage of the presence of asthmatic symptoms

55% COPD people were suffering from coughing, 25% were suffering from shortness of breath and 15% were having chest tightness and 5% having whistling sound in their chest.

4.13.1 Trouble in sleeping of Asthmatic people

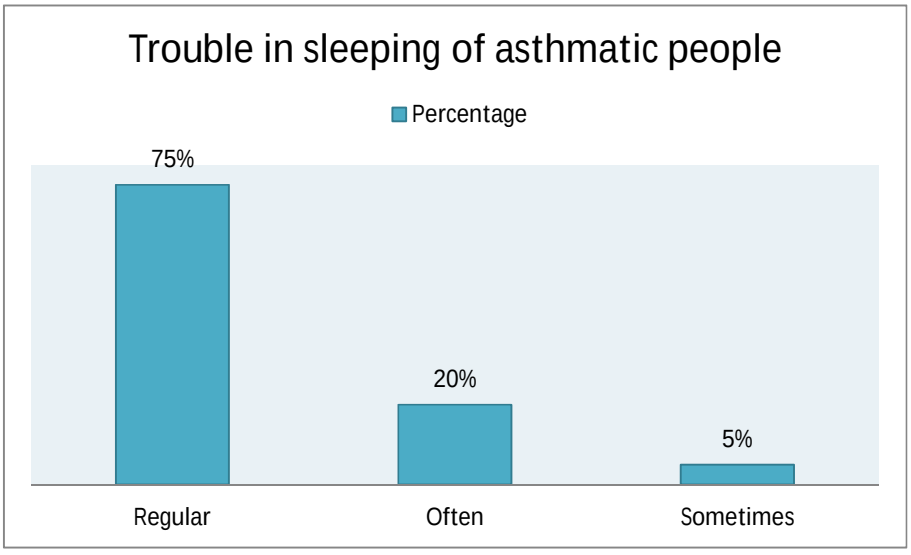

Figure 4.18: Trouble in sleeping due to coughing

75% asthmatic people felt regular problem due to coughing at the time of sleeping, 20% felt trouble often and 5% felt sometimes.

4.13.2 Trouble in sleeping of Asthmatic people

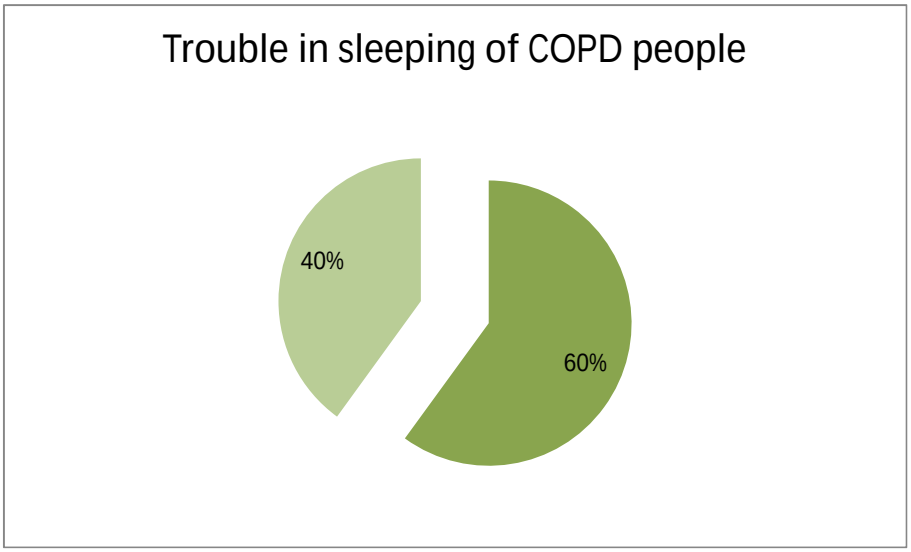

Figure 4.19: Trouble in sleeping due to coughing

60% of the COPD people had regular trouble in sleep due to coughing and 40% had often.

4.14 Breathlessness condition of asthmatic people

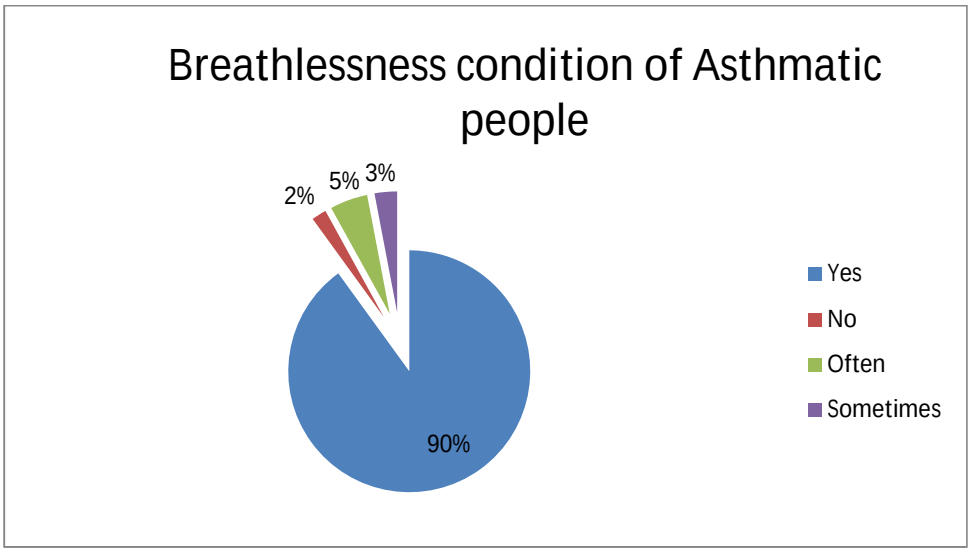

Figure 4.20: Percentage of breathlessness condition

90% asthmatic people felt breathless when climbing up from ground level or at the time of heavy physical activity, 2% did not feel breathlessness, 5% felt often and 3% sometimes.

In COPD, breathlessness condition was found among 100% of people.

4.15.1 Chest tightness among asthmatic people

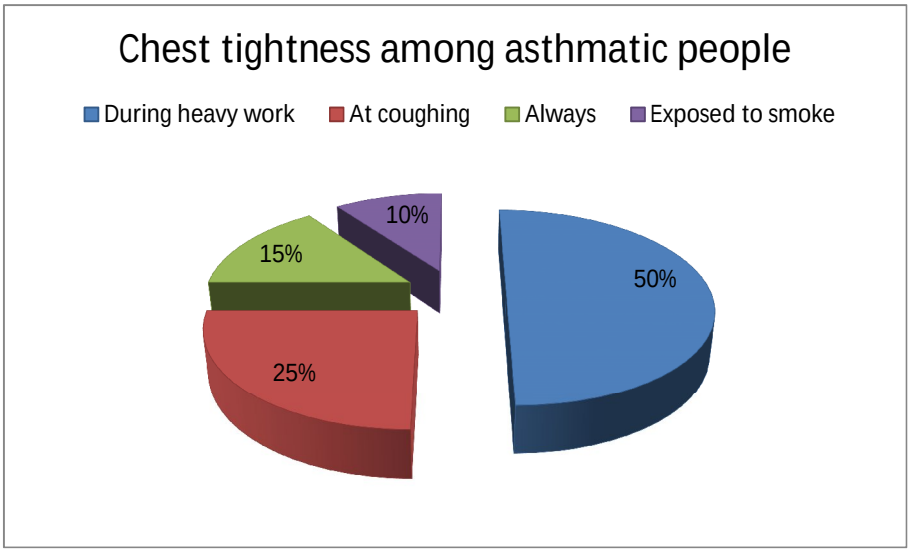

Figure 4.21: Presence of chest tightness

50% asthmatic people felt chest tightness during heavy work, 25% asthmatic people felt chest tightness at the time of coughing, 15 felt always and 10% when they exposed to smoke.

4.15.2 Chest tightness among COPD people

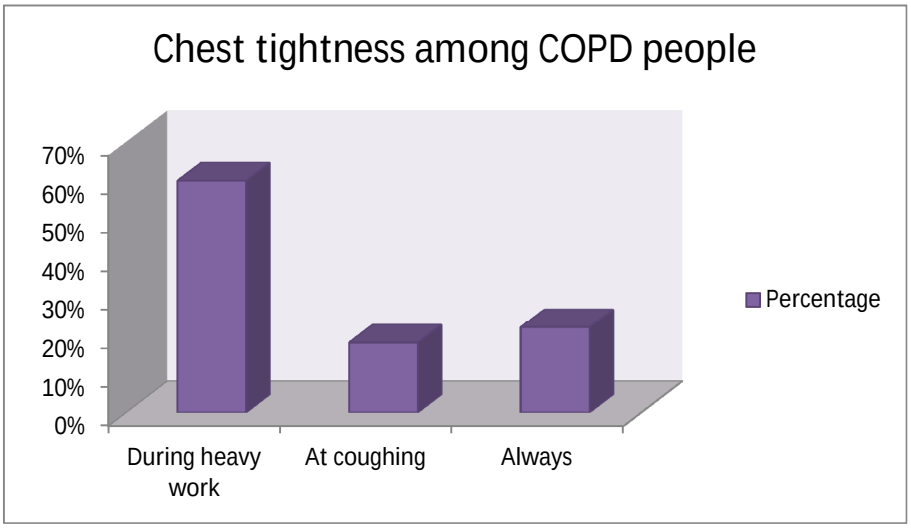

Figure 4.22: Percentage of chest tightness among COPD people

60% of COPD people had chest tightness during heavy work, 18% had at the time of coughing and 22% had always.

4.16.1 Presence of triggers in Asthma

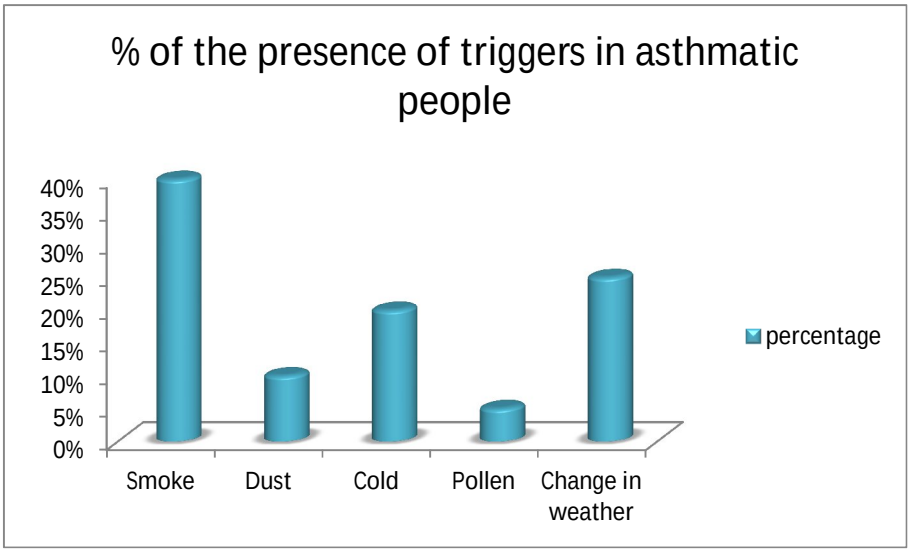

Figure 4.23: Presence of triggers in asthmatic people

40% asthmatic people were sensitive to smoke,dust made the condition worse about 10% people, 20% were sensitive of cold and only 5% were sensitive to pollen. Changes in weather creates problem among 25% population

4.16.2 Presence of triggers in COPD

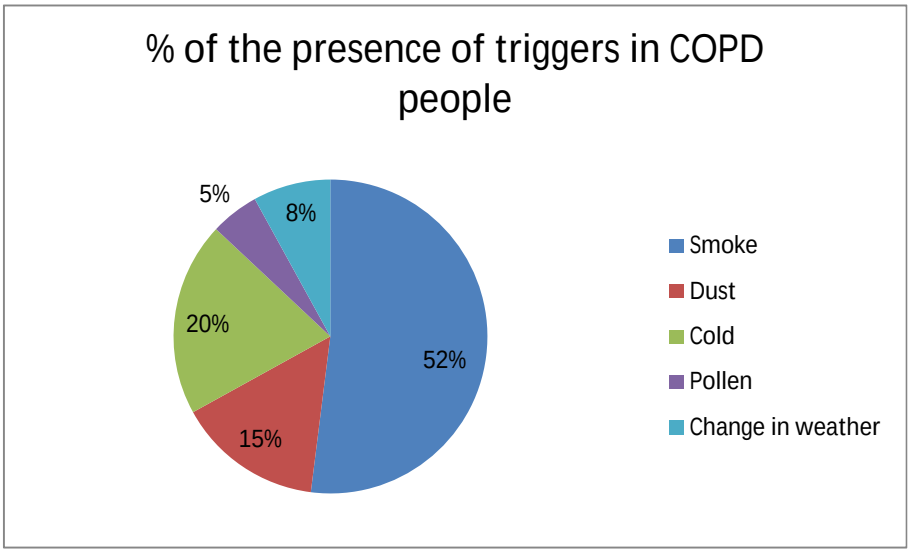

Figure 4.24: Percentage of the presence of triggers

52% were sensitive to smoke, 15% were sensitive to dust and 20% were to cold. Only 5% were sensitive to pollen and changes in weather creates problem among 8%.

4.17.1 Condition of working area of asthmatic people

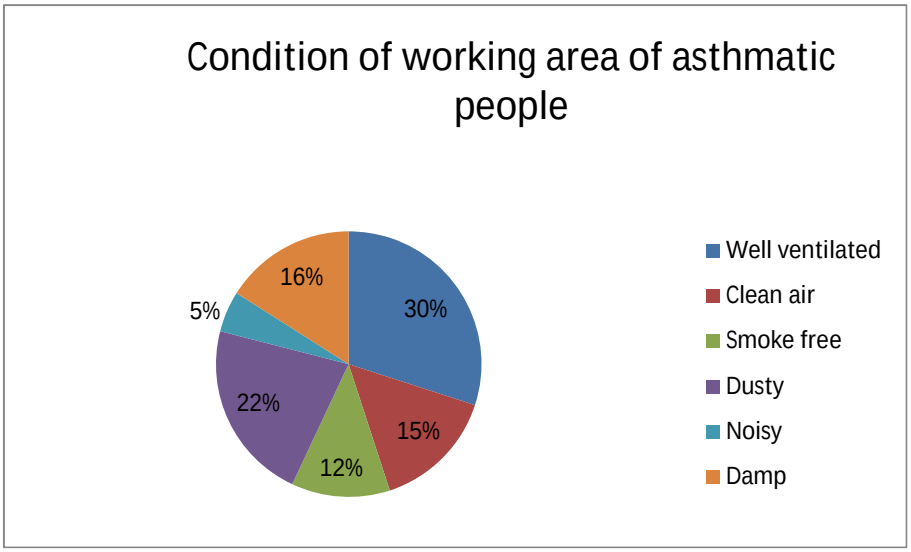

Figure 4.25: Condition of working of asthmatic people

30% asthmatic people worked in a well ventilated area, 15% worked in clean air containing area, 12% worked in smoke free condition, 22% worked in a dusty and 5% worked in a noisy condition and 16% people working condition is damp.

4.17.2 Condition of working area of COPD people

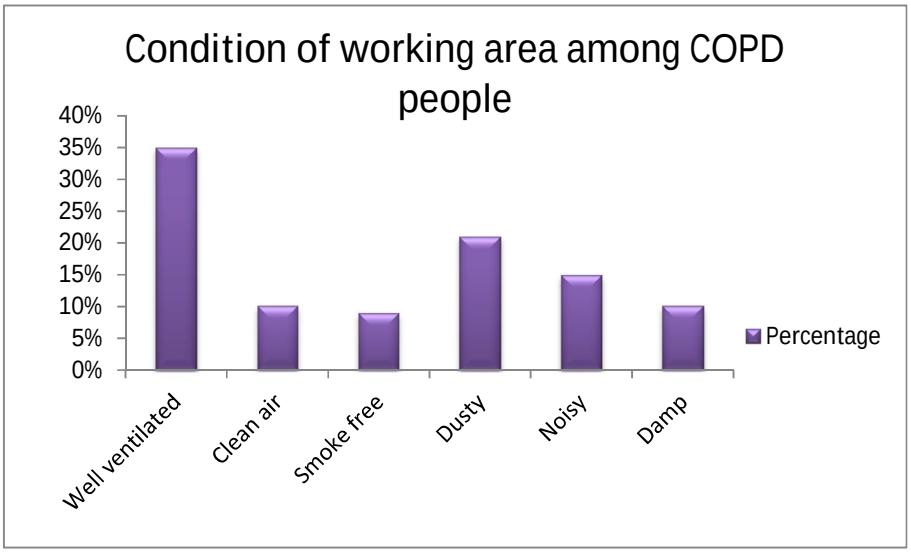

Figure 4.26: Condition of working area among asthmatic people

35% COPD people worked in a well ventilated area, 10% in clean air and 9% in smoke free condition, 21% worked in a dusty environment, 15% in a noisy and 10% in a damp condition.

4.18.1 Condition of living area of asthmatic people

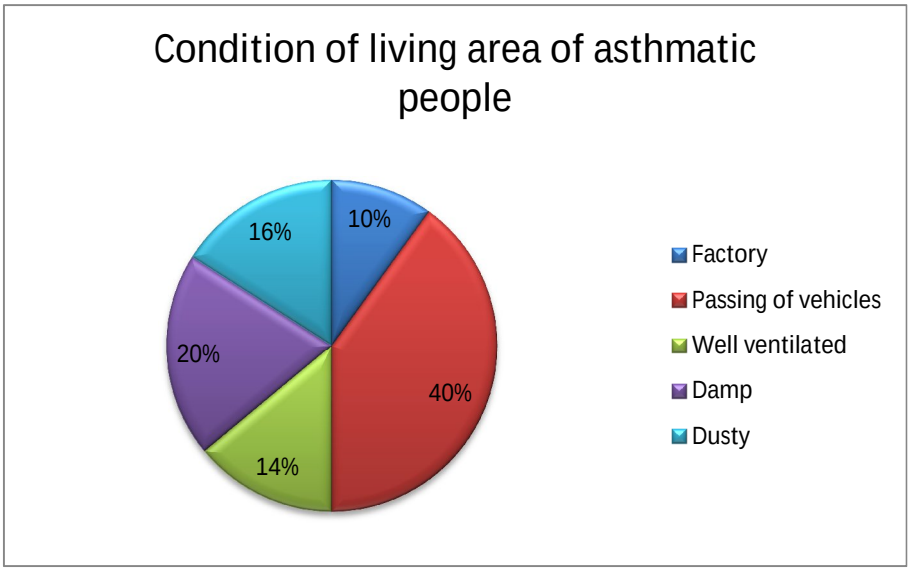

Figure 4.27: Condition of living area of asthmatic people

10% asthmatic people lived beside factory, 40% people lived where passing of cars and heavy vehicles is frequent.Only 14% asthmatic people lived in a well ventilated condition, 20% lived in a damp condition and 16% lived in dusty condition.

4.18.2 Condition of living area of COPD people

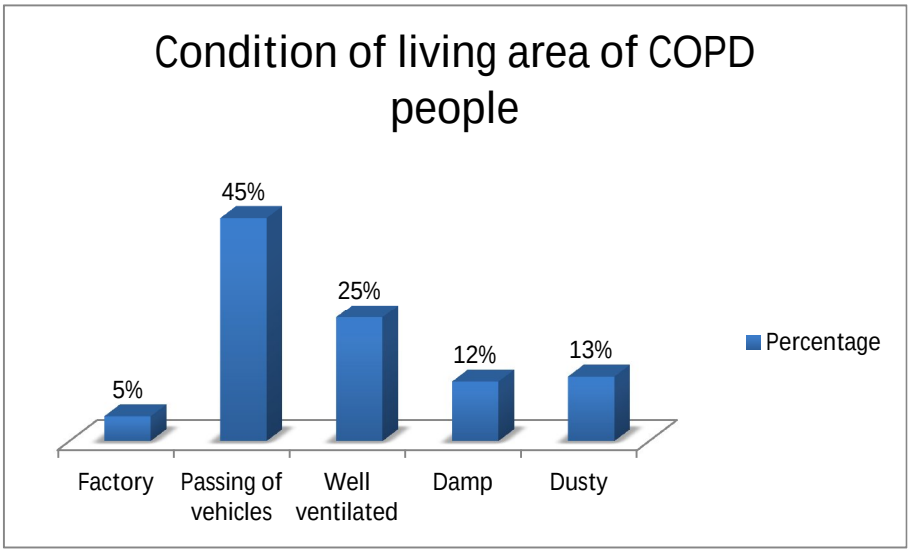

Figure 4.28: Condition of living area of COPD people

5% COPD people lived beside factory, Passing of cars and heavy vehicles is frequent to 45% and 0nly 25% lived in a well ventilated area. 12% lived in a damp condition and 13% in a dusty environment.

4.19.1 Frequency of taking medications in Asthma

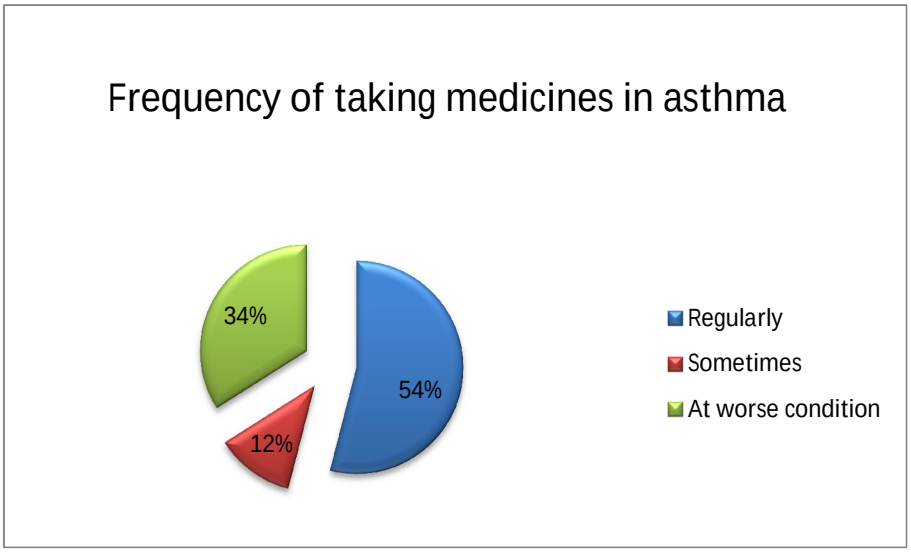

Figure 4.29: Frequency of taking medicines in asthma

54% asthmatic people took medicines regularly,12% took sometimes and 34% people took when their health condition got worse.

4.19.2 Frequency of taking medications in COPD

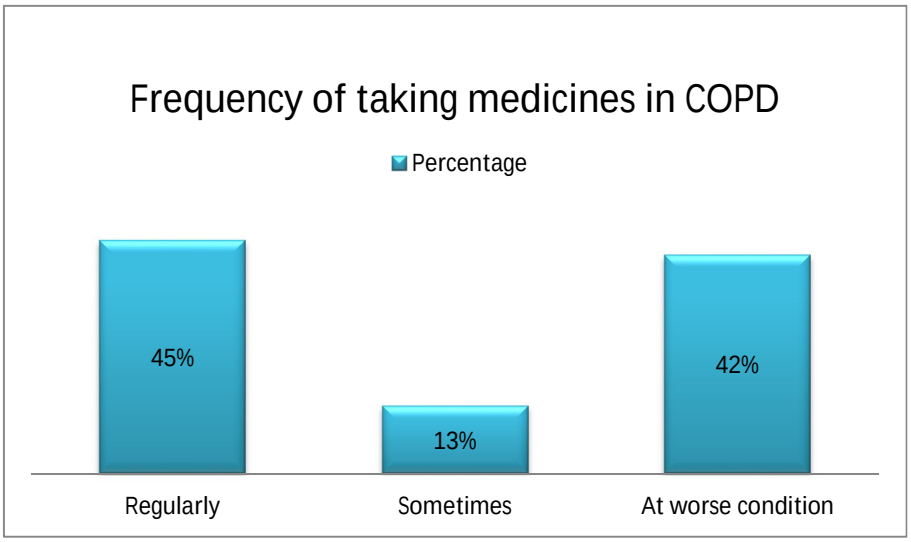

Figure 4.30: Frequency of taking medications of COPD population

45% took their medications regularly,13% sometimes and 42% when their health is at worse condition.

4.20 Medicines used in asthma and COPD treatment

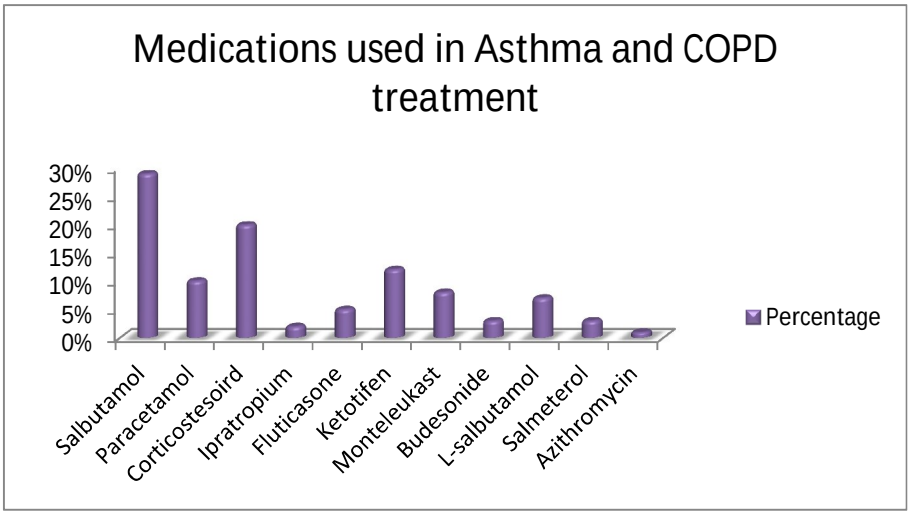

Figure 4.31: Medicines used in asthma and COPD treatment

The medicines that were commonly used in asthma and COPD treatment:

- Salbutamol (short acting beta 2 agonists)
- Paracetamol (analgesic and antipyretic)
- Salmeterol (long acting beta 2 agonists)
- Ipratropium bromide (Anticholinergic or muscarinic antagonists)
- Fluticasone, Budesonide, Beclomethasone(Cortocosteroid)
- Monteleulast (leukotriene modifier)
- Azithromycin (antibiotic)
- Ketotifen (antihistamine)

CHAPTER 5

DISCUSSION

Discussion

Asthma in Bangladesh appears to be a substantial public health problem: an estimated 11.6 million people including 2.1 million suffer from asthma-related symptoms (Hassan *et al.,* 2010). The situation of COPD is also severe in Bangladesh among the aged people. The prevalence of COPD was 13.5% by GOLD criteria.

In this study it has been shown both the prevalence of Asthma and COPD in an area in the Dhaka city. On different ages of population the work is done where the age range was not less than 15 and not more than 65. Same cross sectional study was also conducted in different countries (Richard, 1998).

The study was conducted on 300 populations where 51% were female and 49% were male. Among this population 18% were asthmatic and COPD was found among 7%, the greater asthmatic people were found the age range between (15-35) years. In a previous study it was observed that Asthma in Bangladesh remains almost static over last 10 years although at present prevalence is slightly more in children than adults (Hassan *et al.,* 2010). 73% of COPD people were in the range of (56-65) years.

In our study hypertension was found among 55% asthmatic people and 50% among COPD people. This incidence is the greatest in also many countries due to asthma medications and so on (Stephanie, 1997). Factors contributing to pulmonary hypertension in these diseases include vasoconstriction, endothelial dysfunction, remodeling of pulmonary arteries and destruction of the pulmonary capillary bed.

Family history of asthma or COPD was found in the 70% population who has Asthma or COPD and atopic dermatitis (one type of skin disorder) was prevalent among 61% of asthmatic population's family history. In a study high prevalence figures were found for atopic disease in Asthma (Mortz *et al.,* 2001).The researchers found that cells in damaged skin can secrete TSLP (thymic stromal lymphopoietin), a compound capable of eliciting a powerful immune response,and because the skin is so effective in secreting TSLP into the blood system, the substance travels throughout the body. When it reaches the lungs, it triggers the hypersensitivity characteristic of asthma (Kopan *et al.,* 2009)

A population based survey was done in Spain by good-quality postbronchodilator spirometry to find out COPD prevalence and 10.2% was found. Among them 15.1% were male and only 5.6% were female. The prevalence of COPD increased with age and with cigarette smoking and was higher in low educational levels (Francisco *et al.,* 2009). In this study among the 7% COPD people 72% were former smoker and 28% were current smoker. Among the current smokers 70% had the severe smoking habit, in fact more than one pack or at least one pack is taken by them daily. 10% current smokers were found among asthmatic people.

According to our study the coughing symptom is very much prevalent in both Asthma and COPD. A study on asthma in Bangladesh showed 11.18% prevalence of asthma

coughing symptoms (Kabir *et al.,* 1999). Breathless condition was found among 90% asthmatic people and almost all the people having COPD had this problem. In Asthma, Chest tightness was found 50% during heavy physical activity, 25% at the time of coughing and 15% always had this symptom. In COPD, 22% people always had chest tightness, 60% during heavy work and rest of the 18% at the time of coughing.

Sleep disturbance is a common phenomenon in Asthma and COPD so people with asthma and/or COPD may have sleep issues that can lead to nighttime awakenings and daytime sleepiness (American Thoracic Society). We have found 75% people who had regular disturbance in sleep in Asthma 60% people in COPD.

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

Development of Occupational asthma is shown due to the poor working condition and in our study only 30% asthmatic people and 35% worked in a well ventilated area. It is found that lack of clean air, smoke free environment, dust and damp condition also lead to Asthma and COPD.

In terms of management of acute asthma exacerbation and COPD 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 *et al.,* 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 short acting beta 2 agonists and corticosteroids.

CHAPTER 6

CONCLUSION

Conclusion

Based on this study the prevalence of asthma and COPD is quite higher.The environment condition is poor here which aggravates the diseases more rapidly. Asthma and COPD both of them is chronic illness but medications are not taken regularly. If we consider the limitation of this study, the whole Dhaka city is not covered by which the prevalence can be understood better. Asthma and COPD control is the most important factor, in the current situation these diseases prevalence can be reduced by giving proper guidelines and monitoring the conditions of these patients especially in remote areas by forming medical teams which should be initiated by the government. Therefore it is suggested that if a conclusive result about the prevalence is desired, further large scale researches should be conducted.

CHAPTER 7

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