REVIEW OF LITERATURE

Asthma is a major and chronic health problem affecting persons of all ages. The understanding of many aspects of asthma has improved over the past few decades although the fundamental causes of the disorder and the reasons for its increased prevalence remain largely unknown. The increase in asthma prevalence has been associated with a rise in atopic sensitization and a parallel increase in other allergic conditions e.g. eczema and rhinitis. Allergic sensitization appears to begin in utero. There is, undoubtedly, a genetic component to asthma, and it seems possible that changing patterns of environmental influences such as exposure to microorganisms, pollutants, indoor and outdoor allergens, and diet also exert a strong influence on the development of the disease in susceptible individuals (Braman, 2006).

A wide variation in prevalence rates has been documented. Studies of both children and adults have revealed low prevalence rates (2%–4%) in Asian countries especially China and India and high rates (15%–20%) in the United Kingdom, Canada, Australia, New Zealand and other developed countries (International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee, 1998; Janson et al., 2001; Asher et al., 2006 and Zock et al., 2006). Certain ethnic groups such as African Americans and Hispanics have an even higher prevalence (Masoli et al., 2004).
In developing countries, poverty and non-communicable respiratory diseases have long been linked and most of the patients have poor access to health care; this is even true of the poorest minorities in industrialized countries (Colley & Reid, 1970 and Prescott et al., 1999).

In India, few studies on field epidemiology of asthma are available. Vishwanathan et al. (1966) reported its prevalence as 17.6% in an urban population. According to the National Family Health Survey-2 (1998-1999) report, the estimated prevalence of asthma in India is 2468 per 100,000 persons. As per International Institute of Population Studies (2000), the prevalence has been reported to be higher in rural (2649) than in urban areas (1966). The prevalence among males was slightly higher (2561) than among females (2369). Among those below 15 years of age, asthma prevalence has been reported to be 950 per 100,000 persons, 2309 per 100,000 among those in the age group of 15–59 years and 10,375 per 100,000 in those above 60 years of age.

Chowgule et al. (1998) carried out a survey in Mumbai and reported the prevalence of asthma as 3.8% in males and 3.4% in females. Tindal et al. (2000) studied the prevalence of asthma in Chandigarh and reported as 3.94% in urban and 3.99% in rural men. In females of the same age group, the prevalence was 1.27% both in urban and rural areas. According to Matricardi & Bonini (2002) on examining the changes in the prevalence of asthma over a period of time in countries with comparable levels as India, an increase of up to 3% over a period of 10 years has been reported.
Most of the Asian countries including India and China, although reporting relatively lower prevalence rates than those in the West, account for a huge burden in terms of absolute numbers of patients (Wong & Chan-Yeung, 2005; Aggarwal et al., 2006 and Jindal, 2007). There has been a constant and variable increase in asthma prevalence worldwide in the last two decades and the same is being observed in India (International study of Bronchial Asthma and allergies in childhood-ISAAC, 1998); Guidelines for management of asthma at primary and secondary levels in India, 2005 : WHO-Govt. of India Collaborative programme 2004-2005; Barclay, 2007; Pandey et al., 2007; Nickmilder & Bernard, 2007 and Fact sheet: Asthma- A worldwide problem, 2008).

**Pulmonary Functions in Asthma**

Orie (1961) stated that there is an accelerated decline in lung function that is related to bronchial responsiveness and atopy. Fletcher et al. (1976) showed an accelerated decrease in FEV1 (forced expiratory volume in one second) in 17 asthmatics compared with control subjects who were followed from 1961 to 1969. Subsequent to these seminal reports, many investigations have confirmed this accelerated decline. An irreversible decline in lung function does occur in a significant number of asthmatics. Finucane (1985) and Connolly (1988) have reported the development of persistent airway obstruction in some patients with asthma. The magnitude of this decline, of course, varies from patient to patient.

Many studies have consistently shown that lung function in patients with clinical asthma is less than predicted (Peat et al., 1987; Lange et al., 1998 and Urlik, 1999). This
may reflect suboptimal treatment at the time of measurement, as well as (depending on the age of the patient) any combination of at least four factors: slower growth of lung-function; lower maximally attained level of lung function; earlier onset of decline of lung function; and accelerated decline of lung function. Even if the magnitude of the excess loss of lung function differs between studies, most studies have reported an excess decline in FEV1 of 5-25 ml/yr in subjects with asthma, when compared to subjects without asthma. Recent studies of patients with asthma selected from the general population have shown increased mortality in subjects with reduced ventilatory function and have thus underlined the importance of preservation of normal lung function (Silverstein et al., 1994; Lange et al., 1996 and Huovinen et al., 1997). Impaired pulmonary function is a predictor of mortality in the general population as well (Schunemann et al., 2000).

Lung function decline may result in persistent airflow limitation for some of the asthmatic individuals. The process of restructuring begins early in the development of the disease, so it can be hypothesized that remodeling may occur in parallel or could even be a prerequisite for the development of airway inflammation (Davies et al., 1998).

Reed (1999) proposed conditions responsible for the loss of lung function in asthmatic subjects: airway remodeling, bronchiectasis, post infectious pulmonary fibrosis, and emphysema and chronic bronchitis. Long-term deterioration of lung function in asthmatic subjects has been described. It has been believed that asthma is characterized by totally reversible airway obstruction. Kupczyk et al. (2004) reported that asthmatic patients develop a progressive decline in pulmonary function.
Airway inflammation, airflow obstruction and bronchial hyper-responsiveness are characteristic phenotypic features of asthma. Clinically, airflow obstruction in asthma often is not fully reversible, and many asthmatic subjects experience an accelerated and progressive loss of lung function over time (Pauscal & Peters, 2005).

Fletcher et al. (1976) studied a group of men with asthma and reported a mean decline in FEV1 of 22 ml per year greater than in healthy volunteers. Also, Peate et al. (1987) found a mean loss of FEV1 in males suffering from asthma of about 50 ml/year compared with 35 ml/year in normal subjects. Urlik et al. (1992) studied patients suffering from asthma and reported an annual decline in the FEV1 level of 50 ml/year in the intrinsic group and a decline in FEV1 of 53 ml per year in patients with moderate-to-severe asthma. In their opinion, this very steep decline in lung function leads to severe nonreversible airflow obstruction.

In one of the largest population-based prospective study, (Copenhagen City Heart Study), subjects who identified themselves as having asthma were found to have an excess FEV1 decline of 16 ml/year over a 15-year follow-up period as compared with subjects with no asthma (Lange et al., 1996). The magnitude of this effect appears remarkable when considering that the average FEV1 decline among subjects with no asthma was 22 ml/year. A subsequent report from the Busselton Health Study (James et al., 2005) reported 4-ml annual excess of FEV1 decline in adult life as compared to Copenhagen study.
In a study carried out by Cibella et al. in 2002 on 142 lifelong nonsmoking, adult, asthmatic outpatients with a well-defined diagnosis of bronchial asthma, FEV1 decay over time, computed for a subject 1.65 m in height, has been reported to be 40.9 ml/yr, with no significant difference between male and female patients.

Both population-based and clinical studies have now clearly demonstrated that, as a group, subjects with asthma show significant lung function deficits as compared with their peers. These deficits appear within normal limits among most subjects with mild disease, but they may lead to impaired lung function and clinically manifest airflow limitation as assessed by reductions in FEV1 and in the ratio between FEV1 and FVC in cases of persistent and severe disease. Indeed, asthma has been shown to account for 30 to 50% of cases of airflow limitation at the population level (Guerra et al., 2008). In addition, in some individuals with asthma, lung function deficits appear also to be accompanied by a decrease in bronchodilator-mediated reversibility of airflow limitation over time (Ulrik et al., 1999; Vonk & Boenzen, 2005 and Van Rensen et al., 2005).

Taken together, these observations indicate that, in the long term, a significant proportion of subjects with persistent asthma may be at risk of developing non-fully reversible airway obstruction, the clinical hallmark of chronic obstructive pulmonary disease (Rabe, 2007 and Global Initiative for Chronic Obstructive Lung Disease, 2008).

FEV1 levels are not the only factor taken into account to classify disease severity (Global Initiative for asthma, 2008) they have long been known to be one
of the major predictors of mortality among individuals with asthma (Lange et al., 1998). Lung function deficits, even those with magnitudes insufficient to cause clinically manifest functional impairment, may be related to molecular pathways that, in turn, increase susceptibility to the pulmonary effects of noxious environmental exposures, such as cigarette smoking and occupational hazards. Subjects with asthma who develop non-fully reversible airflow limitation carry a morbidity and mortality burden comparable to that of patients with Chronic Obstructive Pulmonary Disease (Meyer et al., 2002; Shaya et al., 2008 and Blanchette et al., 2008).

**Age and pulmonary functions in asthma**

With regard to the influence of age on lung function decline in asthma, conflicting results have previously been reported. Peat et al. (1987) did not find any influence of age on the functional decline over several years in asthma, but Urlik et al. (1992) reported that aging is associated with a steeper decline in FEV1.

Cibella et al. (2002) reported that in older asthmatics the rate of pulmonary function loss may slow down. In another study it was found that older asthmatics show a lower effect of disease duration on maximum achievable bronchodilatation (Bellia et al., 1998). Therefore, aging per se, unlike the duration of disease, may lower the intensity of the events of remodeling that characterize chronic asthma and thus produce a slower rate of decline in lung function. Moreover, in the same study it was found that after long disease duration (≥ 15 years), the rate of decline of lung function may decrease. Further it is suggested that disease duration and age are not associated and that the two factors may
independently influence lung function. Similar results were obtained by Ulrik and Lange (1994) who showed that men with late-onset asthma presented an increased FEV1 decline with respect to subjects with early-onset asthma. Asthma is a heterogeneous disease with a wide variety of presentations. Hsu et al. (2004) also reported that the pulmonary function of older onset asthma patients was worse than that of early onset patients.

**Asthma and Gender**

Sex affects the development of asthma in a time-dependent manner. Until age 13-14 years, the incidence and prevalence of asthma have been reported to be higher among boys than girls (Crawford & Beedham, 1976; Bronnimann & Burrows, 1986; Weiss et al., 1993; Sears, 1994; Zannolli & Morgese, 1997; Bjornson & Mitchell, 2000; de Marco et al., 2000 and Meurer et al., 2000). Various studies carried out during puberty have shown a greater incidence of asthma among adolescent and young adult females and a greater proportion of males with remission of asthma (Williams & McNicoll, 1969; Bronnimann & Burrows, 1986; Sears et al., 1989; Gerritsen et al., 1989; Kjellman & Hesselmar, 1994; Roorda et al., 1994; Godden et al., 1994; Schwartz & Weiss, 1995; Selroos et al., 1995; Sears et al., 1996; Oswald et al., 1997 and Roche, 1998). In contrast, adult females have more severe asthma than males, with more hospital admissions (Skobeloff et al., 1992; Trawick et al., 2001 and Chen et al., 2003), lower improvement, longer hospital stays and higher rates of readmission.

In the Busselton study carried out by James et al. (2005), in addition to an increased rate of FEV1 decline in adult life, asthma was also associated with
significant FEV1 deficits that were already established by the beginning of adult life. Among males the magnitude of asthma-related FEV1 deficits that were established by age 19 years was greater than the magnitude of the additional deficits that were accumulated over the following 50 years of life as a result of the accelerated FEV1 decline associated with the disease. In other words, according to these findings the greater part of the lung function deficits that a 70-year-old male with asthma has accumulated over his life can be attributed to the tracking of FEV1 deficits that were already established by the time he entered adult life. Interestingly, this proportion appeared substantially smaller for females. Because as compared with their male counterparts females are less likely to have severe asthma in childhood but are more susceptible to adult-onset asthma, a possible explanation for these findings is that lung function trajectories in asthma may differ depending on whether the disease has its onset in childhood or becomes clinically manifest only in adult life.

**Asthma and Smoking**

Smoking has been reported to be the most significant risk factor for developing severe adult onset of asthma. Smoking contributes to decline in lung function in everyone. Althuis et al. (1999) and Gallefoss & Bakke (2003) have reported that smokers with asthma have severe symptoms, greater need for rescue medications, and worse indices of health status in comparison with asthmatics who have never smoked. Asthmatic smokers have an accelerated decline in lung function (Lange et al.,1998; Apostol et al.,2002 and
James et al., 2005) and an increased mortality rate (Marquette et al., 1992 and Ulrik & Frederiksen, 1995) as compared to asthmatic nonsmokers.

Higher levels of smoking have been reported in patients with asthma who attend emergency departments with exacerbations (Silverman et al., 2003). Smoking and tobacco use is related in young, middle aged and the elderly to chronic lung diseases such as asthma and chronic obstructive lung disease (Jha & Chaloupka, 2000 and Gajalakshmi et al., 2003).

Adults and older children with asthma who are active smokers have also worse asthma-specific quality of life compared to asthmatic non-smokers (Siroux et al., 2000; Austin et al., 2005 and Eisner & Iribarren, 2007). In addition, asthmatic patients who smoke appear to have a reduced therapeutic response to inhaled and oral corticosteroids (Chaudhuri et al., 2003; Thomsons & Spears, 2005; Tomlinson et al., 2005 and Lazarus et al., 2007). Recent research has identified genes associated with increased risk for asthma in the presence of tobacco smoke exposure (Bouzigon et al., 2008) and demonstrated that smoking is an important independent risk factor for new onset of asthma in allergic individuals (Polosa et al., 2008).

**Urban –Rural differences**

The global prevalence of asthma, the world's largest respiratory killer, has increased steadily over the past 20 years due mostly to urban development. The processes of urbanization and modernization are part of social and economic development
and are associated with the adoption of a modern lifestyle. Urban populations are growing rapidly throughout the world. Urbanization has a profound effect on people’s living conditions and health status and has been linked to asthma risk. This problem is set to worsen as Asian populations become more urbanized, unless measures are taken now to improve treatment.

The levels of asthma in urban communities have been reported to be higher than in rural areas. Urbanisation has involved so many changes in environment and lifestyle. Environmental factors that contribute to this risk may include changes in diet and physical activity, infectious disease and microbial exposures, increased exposure to antibiotics and vaccines, allergen exposures, exposure to indoor irritants, the effects of industrial and motor vehicle pollution, and psychosocial stress factors including violence (Wright, 2008).

Differences in the prevalence of allergic disease between urban and rural areas have been observed in many parts of the world. Early studies from Africa (South Africa, Ethiopia, Kenya and Ghana) pointed out that populations living in rural areas (i.e. not exposed to the effects of an urban or western lifestyle) experienced a very low burden of allergic disease (Nicolaou, 2005). A series of studies from Asia (China, Japan, Korea, India and Saudi Arabia) confirmed the urban-rural gradient, exploring the role of exposure to different allergens, air pollution, affluence and diet in the development of allergy (Viinanen et al., 2005).
But in India, according to National Family Health Survey -2 report (1998-1999), the prevalence has been reported to be higher in rural than in urban areas. The majority of patients with asthma live in rural areas. Poverty levels are higher in rural areas which once again confirm the role of poor environment in causation of the disease. Ramanakumar & Aparajita (2005) also reported that bronchitis and asthma have been recorded as leading cause of deaths in rural India.

The major causative agents reported in rural area are pollen grains, fungal spores, dust mites, insect debris, animal epithelia, several environmental factors like poor housing conditions, dust mite, bed dust allergy etc. Hard and unfavourable occupations like stone crushing, cement and chemical industry, whitewash, carpentry and harvesting are also seen as asthma prone. Gupta & Mangal (2006) identified rural area as significant risk factor for occurrence of asthma. Male sex, low socioeconomic status, other forms of smoking and cooking with kerosene or dung has been reported to be major risk factors to asthma.

**Socioeconomic factors**

Poverty and the broader term socio-economic status are major determinants of overall health status. The incidence of asthma is highest among low-income populations worldwide. Asthma deaths are most common in low and middle income countries. Ekerljung et al. (2010) have reported that low socio-economic status is significantly
associated with an increased risk for prevalent and incident asthma and respiratory symptoms. The increase in risk was most pronounced in manual workers.

Several studies have recently shown an association between low socio-economic status and respiratory symptoms. Many studies have shown increased asthma hospital admissions for those who are materially deprived (Walters et al., 1995 and Watson et al., 1996) and increased asthma severity in low social class groups (Littlejohns & Macdonald, 1993). Community level variables linked to asthma include some factors like air pollution, physical and psychological demands of living in a relatively deprived environment that may potentiate a person’s susceptibility to environmental exposures, characteristics of the community, such as degree of social support or exposure to poverty, that may influence chronic life stress, which has been suggested to affect asthma (Wright & Fisher, 2003).

Like most diseases, asthma also is socially patterned, with lower socio-economic groups, on an average, being more burdened (Wright & Fisher, 2003). Some suggest that the observed social patterning in asthma may simply reflect the disproportionate exposure to adverse environmental factors among lower socio-economic groups (Weiss & Wagener, 1990 and O'Neill et al., 2003). Others have proposed the differential exposure to psychosocial stressors as a direct explanation to account for the social disparities in asthma (Busse et al., 1994; Wright et al., 1998 and Wright & Fisher, 2003).
Most likely due to income and geography, the incidence of and treatment quality for asthma varies among different racial groups. The prevalence of "severe persistent" asthma is also greater in low-income communities than those with better access to treatment. Children of parents with lower socio-economic status have greater morbidity from asthma (Halfon & Newacheck, 1993; Strachan et al., 1994; Erzen et al., 1997; Goodman et al., 1998 and Claudio et al., 1999).

Respiratory disorders are mainly due to unfavourable housing and living conditions. In India, National Family Health Survey (NFHS-II), 1998-99, reveals that only 19% people live in pucca (good) houses and remaining live in kaccha and semi-pucca houses with mud walls and roofs. Another study examined effect of cooking smoke on the reported prevalence of asthma in elderly (>60 years age) based on NFHS-II conducted during 1998-99 revealed that the risk of asthma is 1.59 times (women 1.83 and men 1.32 times) among rural household who use biomass fuel for cooking. This explains the role of biomass fuels on polluting in-house environment, and advocates an urgent need to find a substitute for that. It is very clear that mostly the sanitation and poor hygienic conditions may suffocate an individual due to these environmental shortcomings.

In a study by Pakhale et al. (2008), the prevalence of asthma and wheeze in a rural region in India was similar to that found in the urban but higher in students from lower socioeconomic groups with poor environmental conditions. Hegewald & Crapo (2007)
reported that there is a significant negative correlation between lung function (primarily FEV1 and FVC) and socioeconomic status. This relationship exists even after adjusting for smoking status, occupational exposures and race. The magnitude of the effect of low socioeconomic status on lung function is variable, but FEV1 reductions of >300 ml in men and >200 ml in women have been reported.

Chronic exposure to a low-income environment from birth was associated with the development of persistent asthma. There has also been reported a protective effect against asthma among those children whose families had moved out of poverty (Kozyrskyj et al., 2010). Other studies in poor urban US communities (Lewis et al., 1995) and in urban centers and suburban areas in Belgium (Wieringa et al., 1997) support these findings. Another explanation for the socioeconomic differences could be that poor patients are more likely to have poorly controlled asthma (Conolly et al., 1989; Clark et al., 1990 and Duran-Tauleria & Rona, 1999), possibly because of less recognition of or concern regarding symptoms (Ernst et al., 1995).

Asthma and Obesity

The parallel increase in the prevalence of obesity and asthma in the past three decades has led some researchers to postulate a causal relationship between the two conditions (Shaheen et al., 1999; Sekar et al., 2005; Thomas et al., 2007 and Mathew et al., 2009). A number of studies have found a positive association between obesity and asthma in adults (Chen et al., 1999 and Celedon et al., 2001; Nystad et al., 2004 and Ford,
and in children (Von Mutius et al., 2001). Obesity has also been linked with impaired pulmonary function and airway hyper responsiveness (Gibson, 2000 and Litonjua et al., 2002), but not in all studies (Sin et al., 2002). A recent prospective study of 10,597 adult twins in Finland followed for 9 years has found obesity to be associated with the risk of adult-onset asthma (Huovinen et al., 2003).

The cross-sectional relationship existing between weight (and body mass index, BMI) and lung function in healthy individuals was first revealed very long time ago in 1846 by Hutchinson and later replicated by Schoenberg et al. (1976). These studies showed that lung function, as measured by the Vital Capacity, increased with weight until a certain value e.g. 107% of average weight, and decreased slightly with further increase in weight. The explanation of this relationship between weight and lung function was that the increase of lung function with weight may reject increasing muscle force (muscularity effect), whereas the decrease with further increase in weight probably reflects “the mere circumstance of fat preventing the mobility of the thoracic boundaries (obesity effect). Recently, the detrimental effect of weight gain on lung function decline has been shown in the general population (Chinn et al., 2005). Several mechanisms have been advocated to explain the negative effect of obesity and weight gain on lung function (Shore & Fredberg, 2005 and Shore, 2008). The first of these possibilities rests on simple mechanical considerations, where both static and dynamic factors come into play. Concerning static factors, increased abdominal and chest wall mass in the obese causes lower than normal functional residual capacity (FRC). Because lung volume is a major
determinant of airway diameter, it is therefore likely that obesity-related changes in FRC unload the airway smooth muscle and thereby allow it to shorten excessively when activated (Ding, 1987).

Concerning dynamic factors, the tidal action of spontaneous breathing imposes tidal strains on airway smooth muscle, and these tidal strains happen to be the most potent of all known bronchodilating agencies (Gump et al., 2001). The obese individual breathes at higher frequencies but substantially smaller tidal volume compared with the lean individual, (Sampson & Grassino, 1983) and as a result, this potent bronchodilating mechanism is compromised and predisposes toward increased airway responsiveness compared with the lean individual.

The most convincing evidence of a causal link between obesity and asthma in adults is provided by a large prospective cohort study of 85,911 nurses followed during 1991 and 1995 in which obese women had a much greater risk of asthma and weight gain (Camargo et al., 1999).

Increase in body weight leads to worsening of pulmonary function. The reasons for this include the mechanical effects of truncal obesity and the metabolic effects of adipose tissue (McClean et al., 2008). Obesity affects respiratory mechanics. Patients with BMI 30–35 kg/m2 have significantly lower forced vital capacity (FVC), total lung capacity (TLC), and residual volume (RV) than lean subjects. FRC is significantly reduced, even in overweight subjects (BMI 25-30 kg/m2). Central obesity (excess weight located mostly
in the abdomen and a waist-to-hip ratio of > 0.95) has more impact on pulmonary function than when excess weight is distributed more around the hips (waist-to-hip ratio ≤ 0.95) (Collins et al., 1995). However, the evidence of a relationship between obesity and asthma is not fully conclusive among adults. Several studies have found the relationship between obesity and asthma only in females, but not in males (Chen et al., 2002 and Del-Rio-Navarro et al., 2003). Some found no relationship (Brenner et al., 2001) or fail to link increase in obesity to increase in asthma (Chinn & Rona, 2001). Some have also suggested a reverse relationship between asthma and obesity (Epstein et al., 2000).

In developing countries also some studies have been carried out which have associated overweight conditions with wheezing and asthma. In a high-altitude area in Korea linked high BMI to wheezing among the elderly (Jang et al., 2002). In the Anhui Province in China overweight condition has been linked to asthma in adults (Celedon et al., 2001) and a study among Mexican adults linked measured obesity to asthma in both men and women (Santillan & Camargo, 2003). Mishra (2004) reported the effect of obesity among adult Indian women using data from India’s Second National Family Health Survey (NFHS-2) conducted in 1998-99 and observed a strong positive association between obesity and asthma among adult Indian women.

In a study of adults in families of subjects with asthma in rural China, U-shaped relationship between BMI and asthma in women and an association between underweight and asthma in men have been reported. Extreme BMI is associated with different lung
function impairment. High BMI in both sexes was associated with low FEV1/FVC and low BMI in males are associated with poor Peak Expiratory Flow and Forced expiratory Flow 25–75% and contributed to the symptoms of asthma (Chu et al., 2009).

An inverse relationship between abdominal obesity and lung function has been reported in few studies, mostly cross-sectional (Collins et al., 1995; Carey et al., 1999; Chen et al., 2001; Harik-Khan et al., 2001; Canoy et al., 2004; Ochs-Balcom et al., 2006 and Chen et al., 2007) of middle-aged subjects. Abdominal obesity may mechanically affect the diaphragm and chest wall compliance with decreased lung volumes (Sutherland et al., 2008). Lower levels of ventilation at the lung base may lead to the closure of peripheral lung units, ventilation-to-perfusion ratio abnormalities, and arterial hypoxemia, particularly in the supine position (McCLean et al., 2008). Waist Circumference is correlated with both subcutaneous adipose tissue and intra abdominal adipose tissue, but it is a better predictor of intra abdominal adipose tissue—deleterious fat deposition—than BMI (Klein et al., 2007). Chen et al. (2007) have reported that waist circumference is negatively associated with pulmonary function. An important observation of their study is that WC consistently had a negative association with the pulmonary function testing variables in all BMI categories, whereas BMI was positively associated with FVC and FEV1 in normal-weight subjects. The distribution of body fat may be an important determinant of lung function, and this may account for the more pronounced association that central adiposity has with lung function (Li et al., 2003; Wannamethee et al., 2005; Lin et al., 2006 and Ochs-Balcom et al., 2006).
The reduction in functional residual capacity and in expiratory reserve volume is detectable, even at a modest increase in weight. However, obesity has little direct effect on airway caliber. Spirometric variables decrease in proportion to lung volumes, but are rarely below the normal range, even in the extremely obese, while reductions in expiratory flows and increases in airway resistance are largely normalized by adjusting for lung volumes (Salome et al., 2009).

In India, overweight and obesity are more prevalent among affluent persons living in large cities and underweight more frequent in rural populations (WHO Expert Committee, 1995 and International institute of populations Sciences, 2000).

Pednekar et al. (2007) have also reported that though concerns are raised that the epidemiological transition in India and in other low-income countries might result in a double burden of diseases related to both under- and over-nutrition, but the findings from their large prospective study suggest that currently under-nutrition remains the main problem in urban India. Subramanian & Smith (2006) have reported that the BMI distribution among Asian populations tends to shift towards the low level, with a high proportion of underweight and a smaller proportion of overweight and obese persons.

**Effect of Duration and Severity of Asthma on Pulmonary Functions**

The duration of the disease seems to be associated with lung function decline in a non-linear way. Both newly diagnosed asthma and long-standing asthma appear to be
associated with unfavourable longitudinal changes in lung function, possibly reflecting increased airway vulnerability initially, possibly owing to unopposed inflammation, and progressive airway remodeling due to chronic inflammation (Urlik, 1999). In fact, several studies have found that adult asthmatics may have an excessive annual decline in lung function prior to the time of diagnosis, and also in the first years following the onset of asthma (Postma & Lebowitz, 1995 and Holgate, 2008). However, in adult asthmatics, the degree of lung function impairment seems to be related to the duration of previous asthma. In other words, longer duration of the disease may be associated with increasing decline in lung function (Ulrik et al., 1992 and Kupczyk et al., 2004). Accordingly, incomplete reversibility of airflow obstruction may be found in some, most probably a minority, and patients with long-standing disease (Backman, 1997 and Lee et al., 2007). These observations suggest that long-standing airway inflammation may lead to, perhaps nonreversible, structural changes in the airway wall.

Rivera et al. (2007) have reported that a close relationship between the duration of disease and loss of lung function exists, supporting the concept of asthma as a slow, progressive disease at least among those patients with a mild-to-moderate degree of airflow limitation. A substantially greater loss in lung function over time has been reported in adult female asthmatics, associated with the inability of inhaled corticosteroids to reduce the decline of lung function (Dijkstra et al., 2006).

Cassino et al. (2000) reported that subjects with longstanding asthma had greater degree of hyperinflation than subjects with short duration asthma. This profound degree of
Severe asthma, broadly defined as asthma that is poorly controlled chronically and refractory to treatment, includes only 5–10% of persons with asthma but accounts for disproportionate asthma-related morbidity, mortality, and utilization of health care resources (Miller et al., 2005; Wenzel, 2005; Moore & Peters, 2006 and Strek, 2006). In both Western and developing countries, patients with severe asthma are responsible for approximately 50% of all direct and indirect costs (Beasley, 2002).

Patients requiring hospitalisation for acute asthma and those requiring courses of oral corticosteroids probably have the most severe (and prolonged) worsening of airway
inflammation. Therefore, increased frequency of hospitalisations and severe exacerbations might be associated with an enhanced rate of lung function decline and a greater prevalence of nonreversible airflow limitation (Bai, 2005).

Severe asthma subjects may have more airway obstruction as measured by spirometric variables compared with asthma subjects not classified as severe (Fitzpatrick et al., 2006 and Moore et al., 2007). Patients with asthma are at risk of developing persistent airflow limitation secondary to structural changes in the airways. Significant obstruction only occurs in a subset of patients and is related to age of onset, disease duration, disease severity, environmental exposures, under-treatment and genetic predisposition (American Thoracic Society, 2000; Bumbacea et al., 2004 and Brown et al., 2006).

Kim et al. (2009) reported that previous exacerbation, duration of disease, and decrease in lung function were important clinical indices associated with asthma severity in the Cohort for Reality and Evolution of adult Asthma in Korea (COREA) study patients. It has been proposed that worsening of airway inflammation associated with asthma exacerbations represents periods of enhanced structural airway changes, usually termed airways remodeling.

Bai (2007) reported a decline in mean FEV1 of 14.6 ml per year in patients with infrequent exacerbations and 31.5 ml per year in asthmatics with frequent exacerbations, the difference between the groups being 16.9 ml per year. After 11 yrs,
FEV1 was 64.3% predicted in the group with frequent exacerbations, compared with 77.2% predicted in those with infrequent exacerbations. A higher exacerbation rate was associated with an excess decline in FEV1, such that one severe exacerbation per year was associated with a 30.2 ml greater annual decline in FEV1.

The strong relationship between the degree of airflow obstruction and the duration and severity of asthma, suggests that chronic poorly controlled asthma causes irreversible narrowing of airways and raises the possibility that improved control of asthma may prevent irreversible obstruction. So, one of the aims of treatment in chronic asthma should be to maintain airway function as near normal as possible.