

Obesity and asthma

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ABSTRACT

Asthma is a chronic disorder affecting millions of people worldwide. The prevalence of asthma is around 300 million and is expected to increase another 100 million by 2025. Obesity, on the other hand, also affects a large number of individuals. Overweight in adults is defined when body mass index (BMI) is between 25 to 30 kg/m² and obesity when the BMI >30 kg/m². It has been a matter of interest for researchers to find a relation between these two conditions. This knowledge will provide a new insight into the management of both conditions. At present, obese asthma patients may be considered a special category and it is important to assess the impact of management of obesity on asthma symptoms.

KEY WORDS: Asthma, body mass index, obesity

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INTRODUCTION

Asthma is a chronic disorder affecting millions of people worldwide. The prevalence of asthma is around 300 million and is expected to increase another 100 million by 2025.^[1,2] Obesity, on the other hand, also affects a large number of individuals. Overweight in an adult, is defined as BMI between 25 to 30 kg/m² and obesity when the BMI >30 kg/m².^[3] It has been a matter of interest for researchers to find a relation between these two conditions. This knowledge will provide new insights into the management of both conditions. At present, obese asthma patients may be considered a special category and it is important to assess the impact of management of obesity on asthma symptoms.

EPIDEMIOLOGY

As per the WHO factsheet,^[3] globally, there are more than 1 billion overweight adults, and at least 200 million men and nearly 300 million women are obese. In the USA, between 1960 and 1994, the prevalence of overweight has increased from 30.5% to 32% and obesity has increased from 12.8% to

22.5%.^[4] In India, the prevalence of overweight individuals is reported to be between 20-40% in various studies, with over 5-10% being obese.^[5,6] The interaction of obesity with asthma is variable. Studies have found a modest correlation between asthma and obesity. Seidell *et al.* (1986)^[7] first described an association of obesity with asthma in a Dutch cohort study, which analyzed the relation between obesity and prevalence of some chronic diseases, followed by Negri *et al.* in 1988.^[8] After these studies, several cross sectional and case control studies has been done since 1999 and most of them have shown a positive correlation between the two conditions.^[7,9-12] These studies included a large number of subjects and have provided new light into the epidemiology of the two disorders. Although certain studies depended on self-reported weight and height to determine BMI, which may be a potential limitation due to inaccuracies or biases related to reporting. However, in studies that use measured rather than self-reported height and weight to define BMI,^[9,11,12] there is still a significant association between elevated BMI and asthma. Although BMI is ideally used, a measure of obesity studies has shown that skin fold thickness, waist circumference and waist to hip ratio are similar or a more accurate predictor of altered lung function.^[13] However, most of the studies use only BMI as a measure of obesity.

Prospective studies done over time have also shown similar results. Shaheen *et al.* (1999)^[12] however did not find a significant association between BMI at age of 10 with asthma symptoms at the age of 26 in follow-up. The Nurse's Health Study II,^[14] included 85,911 women between 26 to 46 years, of which 1596 had asthma and were followed up for 4 years.

Access this article online	
Quick Response Code: 	Website: www.lungindia.com
	DOI: 10.4103/0970-2113.106132

The study found a positive correlation between BMI and asthma incidence. Huovinen *et al.* (2003)^[15] showed that after a 9-year follow-up of 9671 adult Finnish twins (139 had asthma), obese participants had a substantially higher risk of asthma development than participants with a normal body mass index. The National Health and Nutrition Examination Survey I (NHANES I)^[16] was an epidemiologic follow-up study of 9456 participants and found a moderately increased risk for asthma development among obese adults aged 25 to 74 years who entered the study between 1971 and 1975. The National Health and Nutrition Examination Survey III (NHANES III)^[17] was carried out from 1988 to 1994 and showed a strong association between asthma and BMI. However, NHANES II (1976-80)^[18] did not show such a relationship. The relative risk varies from 1.0 to 3.0.^[19] Camargo *et al.* (1999)^[14] monitored 85,911 women for 4 years and found 1596 incidence of asthma cases. In a multivariate model, the relative risk of incident asthma for increasing categories of BMI was 1.0, 1.1, 1.6, 1.7, and 2.7 (p for trend <0.001).

A difference in prevalence of asthma between obese men and women has been found. However, there are some conflicting results. Coronary artery risk development in a Young Adults study^[20] included 4547 men and women aged 18 to 30 years, of which 310 had asthma and were followed for 10 years. In follow up, only women showed association of obesity with asthma. Seidell *et al.* (1986) surveyed 19,126 Dutch adults and found that women with a BMI of >30 had 1.8 times the risk of having asthma than non-obese women.^[21] Chen and colleagues (2002), in their Canadian National Population Health Survey study, found that the incidence of asthma was associated with a degree of baseline adiposity in women, but not men.^[22] However, Gunnbjornsdottir *et al.* (2004) in their study of relation of obesity, nocturnal GERD and asthma symptoms, included 16,191 participants and found that the association between obesity and asthma is no higher in women compared with men.^[23] Similarly Huovinen *et al.* (2003), in their follow up study, did not find any difference between men and women.^[24]

There is more difference in pediatric epidemiologic literature regarding the strength of the obesity and asthma association. Gold *et al.* (2003) did a prospective study of 9,828 children, aged 6 to 14 years and showed that, after a mean follow-up of 5 years, obesity increased the risk of incident asthma.^[25] Chinn and colleagues (2001) studied 3415 British boys and 3329 girls aged 5 to 6 years; the annualized odds of developing asthma was 1.09 for boys and girls and the risk did not change with adjusted BMI.^[26]

EFFECT OF OBESITY

Physiological consequences

Obesity usually causes a restrictive effect on the lungs. Ricard *et al.* (2006) has shown that there is a linear relation of decreased lung volumes and BMI.^[27] At a BMI of 30 kg/m², functional residual capacity (FRC) was reduced to 75% and

expiratory reserve volume (ERV) reduced to 40% that of a lean individual with a BMI of 20 kg/m². More reduction in lung volumes was seen in overweight and mildly obese individuals. There is a moderate reduction in total lung capacity (TLC) and greater reduction of functional residual capacity (FRC).^[19] A majority of the morbid obese individuals breathe around the closing volume.^[28,29] Moreover, Fredberg *et al.* (1997) and other similar studies showed that decrease in FRC and tidal volumes leads to small cycling rates, leading to the conversion of airway smooth muscle from rapid cycle actin-myosin cross bridges to slow cycle latch bridges.^[30-32] The attainment of the latch state in obese asthmatics, due to an increased frequency of detachment rate of actin-myosin may be considered a reason for persistent obstruction in asthmatic airways.^[30,32] Increased airway responsiveness has been found to be associated with the latch state of airway smooth muscles.^[30-32] Moreover, breathing around the closing volume may enhance these effects.^[32-35] Some studies have shown a decrease in the forced expiratory flow in the mid portion of FVC (FEF₂₅₋₇₅) in obese individuals.^[36,37] Litonjua *et al.*, (1999) in their study, found that the FEF₂₅₋₇₅/FVC ratio is independently associated with increase methacholine responsiveness of the airways.^[38] Reduction in lung volumes is proportionate to the degree of obesity. Moreover, these physiological changes can be reversed on reduction of weight.^[39] Respiratory resistance increases in obese individuals, but when airway resistance is calculated by adjusting for lung volumes, it was found to be within normal limits.^[40] It is possible that other mechanisms, apart from mechanical effect, may lead to increased airway resistance, like airway remodeling, peripheral airway obstruction etc.^[40] This hypothesis needs further studies for confirmation. Therefore, obesity did not cause obstruction of airways and moreover, FEV₁ to FVC ratio remained either normal or increased.^[19] Wang and his colleagues (2006) have shown increased airway hyper responsiveness with increase BMI.^[41] However, Nicolacakis *et al.* (2008) showed that obesity *per se* does not alter bronchial reactivity.^[42] This study stated that obesity and asthma independently affect the function of the lungs.

Moreover, there is reduction of respiratory system compliance.^[43] This may be due to excess soft tissue weight compressing the thoracic cage, fatty infiltration of the chest wall, and an increase in pulmonary blood volume in obese individuals.^[44-47] Cournand *et al.* (1954) shown that there is increased oxygen cost of breathing with decreased lung compliance.^[48] Sin *et al.* (2002) found that increase in obesity is a subjective perception of dyspnea.^[49] Therefore, obesity causes a reduction in respiratory system compliance and lung volumes, leading to alteration in pulmonary blood volume, and a ventilation-perfusion mismatch.

Inflammatory consequences

In obese individuals, adipocytes act as an active endocrine organ, with increased inflammatory activity. Moreover, adipocytes may recruit other inflammatory cells and augment inflammatory responses.

Both asthma and obesity are associated with an inflammatory state. Along with increased inflammatory cells, there is also an increase in inflammatory mediators in obese individuals. Several inflammatory mediators like TNF- α , interleukin-6, interleukin 18, CRP etc., have been found to be increased.^[19] Mohamed-Ali *et al.* (1997) has shown that IL-6 and TNF α were constitutively expressed by adipocytes.^[50] Tsigos *et al.* (1999) showed that increased levels of IL6 and TNF α could be correlated with total fat mass, especially abdominal obesity.^[51] Espostio *et al.* (2003), in their study have shown that medical weight loss in obese women resulted in a decrease of IL-6, IL-18 and CRP levels to a significant extent.^[52] Striz *et al.* (1999) showed that TNF- α increases IL-4 mRNA production while IL-4 subsequently decreases TNF- α production.^[53] Similarly, Salvi *et al.* (1999) found that TNF- α also increases production of IL-5 by bronchial epithelial cells.^[54] Gosset *et al.* (1992) and Yokoyama *et al.* (1995), in their separate studies, showed that IL-6 production increased in asthma and has been related to stimulation with histamine, IL-4, TNF- α , and IL-1.^[55,56] It has been found that IL-6 may be responsible for the IL-4 mediated IgE production.^[57] However, these markers are more closely related to central obesity.^[19] Thuesen *et al.* has shown that insulin resistance in centrally obese patients is more closely related to asthma like symptoms than obesity or BMI itself.^[58]

Hormones

Obesity results in changes in the level of energy regulating hormones from adipocytes. Leptin and adiponectin are two hormones of this type released by adipocytes.^[19]

Leptin, also known as the satiety hormone works as a proinflammatory mediator.^[19] Leptin is coded by the Ob gene. Sierra-Honigmann and colleagues (1998) showed that leptin shares a structural similarity with long-chain helical cytokines, like IL-6, and has been found to be associated with proliferation and activation of T-cells, recruitment and activation of monocytes and macrophages, and promotes angiogenesis.^[59] Shore *et al.* (2005) sensitized and challenged lean BALB/cJ mice with ovalbumin and then infused either saline or leptin subcutaneously. They found that after leptin infusion, serum leptin levels increased, with associated enhancement of airway hyperresponsiveness (AHR), and an increase in serum IgE following inhaled ovalbumin challenge. However, these changes were not observed with saline infusion.^[60] Similar studies in animals have also shown that leptin treatment leads to increase in allergen induced airway hyperresponsiveness. However, there is no increase in eosinophil influx or Th2 cytokine expression.^[42,60,61] This suggests that leptin works through a mechanism that is independent of Th2 response. Studies have also shown increased levels of leptin in patients with asthma. However, certain studies showed that leptin has a significant immunomodulatory role, irrespective of body mass.^[62,63]

Adiponectin is an insulin sensitizing hormone released by adipocytes. It has anti-inflammatory effects and its levels decrease in obese individuals.^[61] Adiponectin acts on macrophages and monocytes to inhibit production of proinflammatory cytokines and to augment IL-10 and IL-1 receptor antagonist expression.^[64] Shore *et al.* (2006) in their animal study in mice showed that exogenous administration of adiponectin results in an almost complete suppression of allergen-induced AHR, airway inflammation, and Th2 cytokine expression.^[65] Decline in the mRNA expression of all 3 adiponectin receptors in the lungs, after allergen sensitization and challenge in mice, suggests that asthma may be a adiponectin resistance state.^[65] Kadowaki *et al.* (2008) and similar studies showed obesity-related decline in adiponectin.^[64,66] Shore *et al.* (2006) showed additional decline in serum adiponectin with allergen challenge.^[65] Therefore, obese patients with asthma may have defects in this important immunomodulatory pathway that augments the effects of an allergen challenge.^[61]

Some studies have shown an increased association of obesity with asthma among women, compared to men. This may be due to hormonal differences, mostly attributable to the sex hormone estrogen. Troisi *et al.*, in their study of the relation between menopause, postmenopausal hormone replacement therapy (HRT) and asthma has shown significantly increased relative risk of incident asthma in women on HRT (RR 1.49).^[67] Moreover, studies have shown that estrogen increases IL-4 and IL-13 production and increases eosinophil recruitment and degranulation,^[68-70] which are also observed in asthma patients.

Co-morbidities

Several co-morbidities have been associated with obesity and it is supposed to be a contributing factor in asthma symptoms.

Obesity is commonly associated with dyslipidemia. Animal studies^[71,72] have shown that a high-cholesterol diet promotes Th2 inflammation in mouse models of asthma. However, this can be reversed by a lipid lowering agent.^[71,72] Al-Shawwa and colleagues (2006), in their study, showed a higher prevalence of asthma in children with high serum cholesterol.^[73] However, the study population was small and the results need further confirmation.

GERD and sleep disordered breathing (SDB) are also important co-morbid conditions in obesity. GERD and SDB are thought to increase the risk for asthma. Gunnbjornsdottir *et al.* (2004) and Sluit *et al.* (2005), in separate studies, showed that habitual snoring, or SDB did not substantially affect the relationship between obesity and asthma, when adjusted for GERD.^[74,75] Therefore, an increased risk of asthma in the obese may be independent of GERD and SDB. When a person adopts the supine posture, there is further reduction of FRC in the obese which may thus exacerbate asthma symptoms.^[61] Moreover, continuous positive airway pressure, a treatment used extensively in the treatment of

SDB, elevates the FRC, improving the quality of life in an asthma patient.^[76,77] More studies are required in this context to confirm or refute this relation.

Al-Shawwa and colleagues (2007) reported a higher prevalence of insulin resistance among obese children with asthma, compared with obese children without asthma.^[78] The study included a small number of subjects and needs further confirmation. Moreover, studies have shown that only the subset of obese individuals with central adiposity and insulin resistance demonstrated enhanced systemic inflammation.^[61] Thuesen *et al.* (2009) showed that insulin resistance was associated with incident wheezing (OR 1.87, 95% CI 1.38-2.54) and asthma-like symptoms (OR 1.61, 95% CI 1.23-2.10), and was a stronger risk factor for asthma than obesity.^[58]

GENETIC BASIS

Several genes have been associated with both obesity and asthma. Genes related to the β adrenergic receptor (locus 5q, gene ADRB2), insulin-like growth factor (locus 12q, gene IGF1), interleukin 1 α (locus 12q, gene IL1A), leukotriene A4 hydroxylase (locus 12q, gene LTA4H), glucocorticoid receptor (locus 5q, gene NR3C1), signal transducer and activator of transcription gene (locus 12q), tumor necrosis factor (locus 6p, gene TNF), uncoupling protein (locus 11q13, gene UCP2 and 3) etc., have been postulated to be relevant to both obesity and asthma.^[42]

Hallstrand *et al.* (2005) studied genetic pleiotropy between asthma and obesity among twins.^[79] The study included 1001 monozygotic and 383 dizygotic same sex twin pairs. They detected substantial heritability for asthma (53%) as well as for obesity (77%). 8% of the genetic component of obesity is shared with asthma patients.^[79] Murphy *et al.* (2009) found that single-nucleotide polymorphisms (SNPs) of the protein kinase C alpha gene (PRKCA) were associated with both BMI and asthma,^[80] suggesting a genetic association between the two conditions.^[81]

Dewar *et al.* (1997) showed that polymorphisms of the β 2 adrenergic receptor are associated with specific asthma phenotypes and response to treatments.^[82] The Gln27 to Glu polymorphism of this receptor has been found to be associated with increased serum IgE levels.^[82] Turki *et al.* (1995) showed that the Agr16 to Gly polymorphism is associated with nocturnal asthma.^[83] Similar studies showed that this polymorphism is also associated with treatment response to β agonist agents.^[84,85]

Albuquerque *et al.* (1998) showed that the polymorphism of TNF α and LT α gene complex is associated with asthma.^[86] Chagani *et al.* (1999) have also shown a similar relation between TNF α polymorphism and asthma.^[87] Moreover, Norman *et al.* (1995) showed that the TNF α gene is linked to obesity in a population of Pima Indians.^[88] Similarly, polymorphisms at the TNF α -308 region have been found to

be associated with BMI^[89] and obesity^[90] in separate studies.

There is polymorphism in the glucocorticoid receptor gene in obesity.^[91-93] On the other hand, there is increase in glucocorticoid receptor beta activity in asthmatics with increased disease severity and fatality.^[94,95] Several candidate genes in regions chromosomal areas of 5q, 6p, 11q, and 12q have been linked with asthma.^[96] Several studies have shown that there is overlap of genetic foci between asthma and obesity,^[4,91-93] therefore suggesting a common genetic predisposition to both conditions.

RELATION WITH FETAL DEVELOPMENT

Barker and his colleagues proposed that fetal programming can affect the subsequent development of chronic disease.^[97-100] This is also known as the Barker hypothesis. This fetal origin hypothesis proposes that these diseases originate because of adaptations by an undernourished fetus. Fetal programming and birth weight have been associated with the subsequent development of obesity. Hediger *et al.* (1998) has shown that low birth weight is associated with increased percentage of body fat.^[101] Subsequently, Malina *et al.* (1996) studied central fat distribution in children in relation to low birth weight.^[102] NHANES III data showed that low birth weight has also been associated with change in body fat distribution.^[103] Barker *et al.* (1991) showed that lower birth weight was associated with decreased lung function and increased risk of death from obstructive airways disease in adults.^[104] Svanes *et al.* (1998) has shown that asthma symptoms in young adults were inversely associated with birth weight (odds ratio wheeze = 0.82).^[105] Several other studies have also shown similar results.^[106-110]

ASTHMA CONTROL AND SEVERITY

Asthma control is not similar among obese and non obese individuals. Lessard *et al.* (2008) studied 88 asthmatic patients and has shown that obese asthmatics had poorer asthma control than non obese asthmatics, inspite of having similar symptom perception.^[111] Obese asthmatics have a higher ACQ score, more activity limitation and wheezing compared to non obese asthmatics.^[112] Mosen *et al.* (2008), in a study, involving 1113 adult asthmatics showed that there was reduced asthma specific quality of life (OR 2.8), poor asthma control (OR 2.7) and increased hospitalization (OR 4.6) in obese patients, compared to the non-obese.^[112] Peters-Golden *et al.* (2006), in their *post hoc* analysis of 3000 subjects with moderate asthma, found that BMI can influence the natural history of asthma control and response to asthma treatment medication.^[113] Saint-Pierre *et al.* (2006), in their study with 400 asthmatics also showed that obese asthmatics have poor asthma control.^[114] However, Wenzel *et al.* (2007) analyzed data from the Severe Asthma Research Program, which included nearly 800 asthmatics and did not find any difference in BMI, with milder and severe asthma.^[115] Pakhale and colleagues (2010), in their recent study which included

496 asthmatics (242 obese and 254 non obese) showed that asthmatics who were obese tend to have lower lung function, more co-morbidities than normal weight asthmatics.^[116] They also mentioned that obese individuals are more likely to get a misdiagnosis for asthma on their emergency visits due to respiratory symptoms.

DIFFERENT PHENOTYPE

With increasing evidence of a relation between obesity and asthma, and a difference between non-obese and obese asthmatics, obesity and asthma may be considered as a different phenotype altogether. Several associations have been found between the two conditions. Firstly, epidemiological studies have shown a significant association between them.^[7-14] Secondly, obesity and asthma both affects the function of the lungs^[29-51] and share some similar inflammatory markers.^[50-58] Moreover, certain co-morbid conditions are more commonly associated with both conditions like dyslipidemia, GERD, SDB etc.^[71-78] Thirdly, obesity and asthma have some similar genetic mechanisms.^[79-92] Hallstrand *et al.* has shown that the co-relation between obesity and asthma was predominantly caused by shared genetic risk factors for both conditions.^[79] Genes have been identified that are associated with both obesity and asthma. The β adrenergic receptor gene, located on chromosome 5q31-q32 and a genetic mutation in the β adrenergic receptor gene result in an increased capacity to gain weight. On the other hand, in asthmatic patients, polymorphisms in the β adrenergic receptor gene have been associated with severity and response to beta-agonists. Fourthly, there have been several hypothesis linking asthma, obesity and fetal development.^[97-110] Finally, asthmatics who are obese have a different level of asthma control and severity.^[111-116] There is strong evidence, because of all these factors, that obesity with asthma can be considered a different phenotype.

MANAGEMENT

Obesity with asthma has thus emerged as a separate phenotype of asthma. This suggests that there may be a difference in response to asthma medications.

Inhaled corticosteroids

Peters-Golden *et al.* (2006) did a post-hoc analysis of four clinical trials which included 3073 asthma patients.^[113] They showed a decreased response to inhaled corticosteroids with increasing BMI. Boulet and Franssen (2007) studied the effect of obesity on the response to fluticasone with or without salmeterol in moderate asthmatics.^[117] These included 1242 asthmatics, not on current inhaled corticosteroids. They concluded that fluticasone propionate combined with salmeterol was more effective in controlling asthma than fluticasone alone in both obese and non-obese asthmatics. However, obese patients especially with a BMI of ≥ 40 kg/m² were

not able to attain asthma control adequately, compared to non obese patients. The study by Sutherland and colleagues (2008), of an analysis of BMI and glucocorticoid response in asthmatics, showed that overweight and obese asthmatics demonstrated an impaired biologic response to glucocorticosteroid.^[118] This suggests that the effect of the inhaled corticosteroids got blunted with obesity.

Monteleucast

Peters-Golden *et al.*^[113] did a *post hoc* analysis of the effect of monteleucast, beclomethasone and placebo in asthmatics in relation to the BMI. The analysis showed that obese asthmatics with increased BMI have better asthma control days when on monteleucast. On the other hand, they show decreased asthma control, when on beclomethasone and placebo.

Weight loss

Stenius-Aarniala and colleagues (2000) in a non blinded randomized clinical trial analyzed the effects of medical weight loss on a variety of asthma outcome measures.^[119] They included obese subjects with asthma from Helsinki, Finland and were assigned to either an intensive dietary programme or to a control group. Asthma was defined during a run in period by the presence of either diurnal peak flow variability or by a bronchodilator response of at least 15%. The mean change from baseline Forced Expiratory Volume in 1 second (FEV₁) and forced vital capacity (FVC) was significantly greater at all time periods. The treatment group demonstrates less dyspnoea, use of rescue medications, and overall symptoms, impact, activity, and total health status scores. At the end of the 1 year follow up period, the treatment group continued to have fewer symptoms and better total health status scores than the controls. Dixon *et al.* (1999) evaluated symptom scores from 32 obese asthmatic subjects before and after gastric bypass surgery; mean BMI decreased from 45.7 kg/m² preoperatively to 32.9 kg/m² at the time of follow up and 26 of the 32 patients reported decreased medication usage postoperatively.^[120] The mean scaled asthma symptom score decreased from 44.5 to 14.3 ($P < 0.001$). Of the 10 patients with "severe" asthma before surgery, none remained in this category at follow up. Macgregor and Greenberg *et al.* (1993) also showed similar improvements in symptoms, medication usage, and asthma severity postoperatively in a study of 40 obese asthmatics.^[121]

No other study assessing the effect of other asthma medications in obese asthmatics is available in literature.

Management of co-morbid conditions

Several comorbid conditions are associated with obesity and asthma. Management of these co-morbid conditions may improve the outcome in patients with obesity and asthma.

Type 2 diabetes

It has been observed that metformin, an oral hypoglycemic agent, reduces expression of proinflammatory

and proliferation gene expression in airway smooth muscles.^[122] Moreover, the thiazolidinediones group of drugs used in type 2 diabetes, are shown to increase adiponectin levels^[123] and reduce airway inflammation.^[124] Since type 2 diabetes is an obesity related condition, managing patients of obesity and asthma with type 2 diabetes as a co-morbid condition by drugs like metformin, thiazolidinediones may lead to improved outcome.

Statins

Statins have been shown to reduce Th2 inflammation in mouse model of asthma.^[125,126] However, their application in clinical practice needs to be evaluated.

SLEEP DISORDERED BREATHING AND NON INVASIVE VENTILATOR

Sleep disorder breathing is known to increase the risk of asthma. In obese individuals, when they adopt the supine position, there is significant reduction of FRC. This increases airway parenchymal uncoupling.^[61] Continuous positive airway pressure (CPAP) elevates the FRC and improve the quality of life in patients with SDB and asthma.^[127,128] The role of CPAP in management of obesity and asthma, with or without SDB, needs further evaluation.

OBESITY, ASTHMA AND THE INDIAN PROSPECTIVE

Both prevalence of obesity and asthma is increasing worldwide. In India, there are studies relating obesity with diabetes, hypertension, and heart disease,^[129-132] but there are few studies relating obesity and asthma. The national family health survey-2 in India collected anthropometric data from a nationally representative sample of more than 90,000 ever-married women of reproductive age.^[133] The survey also collected data on reported asthma prevalence, and on a number of behavioral, demographic and socioeconomic factors. Mishra *et al.* (2004) analyzed this data and found a strong positive association between obesity and asthma among adult Indian women.^[134] To validate this relationship and to establish causality, prospective epidemiological studies, with better measures of overweight conditions and clinical measures of asthma, are needed in developing-country settings. Moreover, obesity in Indian people is different from that of other countries. Several studies in India have shown that Indian populations are at risk of obesity related co morbidities at a lower level of BMI and waist circumference than that recommended by WHO.^[135-137] Therefore, recently, a consensus statement published in the Journal of Association of Physicians, India (JAPI) has recommended different cut-offs for defining obesity in the Indian population.^[138] In Indian circumstances, obesity is defined in the review as follows; normal BMI: 18.0-22.9 kg/m², overweight: 23.0-24.9 kg/m² and obesity: >25 kg/m². This new cutoff will give an additional 10-15%

increased diagnosis of overweight or obese individuals. Therefore, in the light of this new information, further studies are required to explore the relation between asthma and obesity in India.

CONCLUSION

Several epidemiological studies have shown increasing evidence of a relation between obesity and asthma. The incidence of both these conditions has been increasing and they share common risk factors. One condition affects the other. Obesity and asthma due to its unique relation has emerged as a different phenotype of asthma. A clinician has to look into the broader aspect of managing both obesity and asthma together, which may lead to improved outcomes. Due to the new classification of obesity in the Indian population, there will be greater number of obese individuals, which may eventually bring up these conditions together more frequently than before. From a research prospective, newer studies are required, in context of the new obesity classification in India, undiscovered issues and the relationship between obesity and asthma.

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How to cite this article: Baruwa P, Sarmah KR. Obesity and asthma. *Lung India* 2013;30:38-46.

Source of Support: Nil, **Conflict of Interest:** There is no conflict of interest.

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