Obesity and Risk of Pulmonary Infections and Disorders

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Introduction

Obesity is one of the major health challenges of recent time. The prevalence of obesity has increased dramatically worldwide during the last two decades and is only believed to increase over coming years.[1-3] It is well known that overweight and obesity increases risk for a number of adverse health effects, including diabetes, cardiovascular diseases, and multiple cancer types that in turn increases the risk of associated morbidity and mortality. Of late, it has also been shown that obesity increases susceptibility to bacterial and viral infections and infectious agents also have a role in the pathogenesis of obesity.[1,4-6] Intriguingly, less recognized is the fact that respiratory disorders, such as obstructive sleep apnea, pulmonary embolism, chronic bronchitis, and asthma are also associated with obesity. The ensuing paragraphs discuss the complex relationship between obesity and the respiratory systems, and the risk and outcome of infections in obese adults with particular focus on respiratory infections.[1,3]

Pulmonary Infections in the Obese

A number of potential factors have been suggested to predispose obese patients to increased risk and severity of pulmonary infections; these may include alteration of lung mechanics in obese patients including reduced lung volumes, decreased compliance, abnormal ventilation, and respiratory muscle inefficiency (Table 1).[1,7]

Interestingly, emerging data suggest that the risk of respiratory infections in the obese is centered mostly around influenza and pneumonia with almost similar magnitude of increased risk in both infections.[1]

Table 1: Factors influencing the risk of pulmonary infections in obese patients

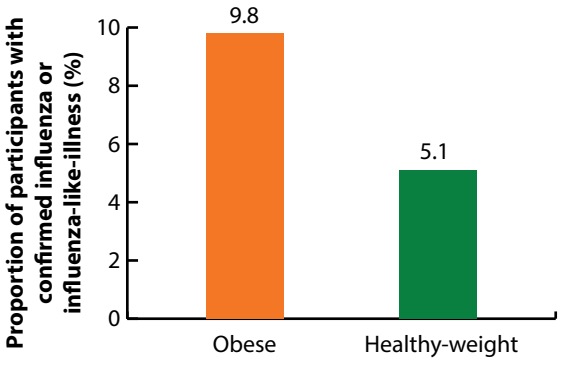
- Alteration in lung mechanics
  - » Abnormal gas exchange
  - » Abnormal ventilation and perfusion
  - » Decreased lung compliance
  - » Reduced pulmonary volumes
  - » Respiratory muscle inefficiency
  - » Pulmonary restriction
- Common medical comorbidities
  - » Chronic heart disease
  - » Chronic kidney disease
  - » Type 2 diabetes mellitus
- Pathophysiology of obesity
  - » Altered cell signaling
  - » Immunomodulation of innate and adaptive responses through adipokine secretion, such as leptin by adipose tissue
  - » Increased pro-inflammatory and pro-thrombotic risk
- Predisposition to aspiration
  - » Increased incidence of gastro-esophageal reflux disease
  - » Swallowing impairment
  - » Weak/absent cough reflex

Influenza

The association between obesity and influenza was first noticed during the early phase of the 2009 influenza A (H1N1) pandemic, when data from various countries across the world suggested that obese persons exhibit greater susceptibility to pulmonary viral infections. Moreover, obese patients admitted to an ICU had longer duration of mechanical ventilation, as well as ICU and hospital length of stay compared with those who were not obese. Importantly, obesity has also been shown to worsen the effect of seasonal influenza on respiratory mortality.[4,8,9]

Although vaccination is the most effective strategy for preventing influenza virus infection and is a major component for pandemic preparedness, vaccines may fail to provide optimal protection in high-risk groups, including overweight and obese individuals.[10] The same was observed in a prospective observational study[11] of trivalent inactivated influenza vaccine in a total of 1022 adults. The results revealed that 9.8% of obese individuals

Figure 1: Incidence of confirmed influenza or influenza-like-illness in obese versus healthy-weight individuals



had either confirmed influenza or influenza-like-illness (ILI) compared with 5.1% of healthy-weight participants (Figure 1). These findings underscore the deleterious effect of obesity on influenza outcomes in that despite robust serological responses, vaccinated obese adults are twice as likely to develop influenza compared with healthy weight adults.

Pneumonia

Pneumonia is one of the most common infectious diseases and it has been ranked as the third leading cause of death worldwide. Importantly, emerging evidence suggests that obesity is an important risk factor for both community-acquired pneumonia and healthcare-associated pneumonia. Several reasons have been suggested for the association between obesity and increased risk of pneumonia. Obesity has been associated with impairments in host defense mechanisms. In addition, obesity has numerous untoward effects on the respiratory system. Increase in BMI is usually associated with a decrease in forced vital capacity, total lung capacity, functional residual capacity, and expiratory reserve volume. Additionally, obesity can increase the work of breathing due to reduced chest wall compliance and increased respiratory system resistance.[2,12]

Mechanistic Association Between Obesity and Pulmonary Infection

The association between obesity and pulmonary infection is supposed to be multifactorial.[1] Obesity weakens pulmonary host defense against influenza and possibly bacterial and fungal pathogens. This may be attributed in part to the accumulation of excess adipose tissue that in turn may lead to numerous metabolic disturbances that contributes to a chronic state of low grade inflammation.[3,8]

With accumulation of excess adipose tissue, its ability to buffer dietary lipids declines leading to elevated blood triacylglycerol (TAG) and free fatty acids. Consequently, these lipids increase in the peripheral circulation and accumulate in ectopic sites that result in insulin resistance and hyperglycemia. Moreover, adipose tissue also elevates proinflammatory cytokines (TNF-a, IL-6, IL-1b, IL-18, MCP-1), proinflammatory adipokines such as leptin and resistin, and produces less anti-inflammatory adipokines such as adiponectin. Collectively, these alterations result in systemic inflammation that may ultimately impair innate and adaptive immune function against influenza by inducing endoplasmic reticulum stress, lipotoxicity, oxidative stress, and leptin resistance. Moreover, obesity is often accompanied by co-morbid conditions, such as gastroesophageal reflux disease (GERD), diabetes, cardiovascular disease, and liver diseases that are known to impair host defense against viral, bacterial, and fungal pathogens (Figure 2).[2,8,13]

Obesity and Pulmonary Disorders

Obesity is also strongly associated with pulmonary disorders, such as exertional dyspnea, obstructive sleep apnea syndrome (OSA), obesity hypoventilation syndrome (OHS), chronic obstructive pulmonary disease (COPD), asthma, and pulmonary embolism.[14,15]

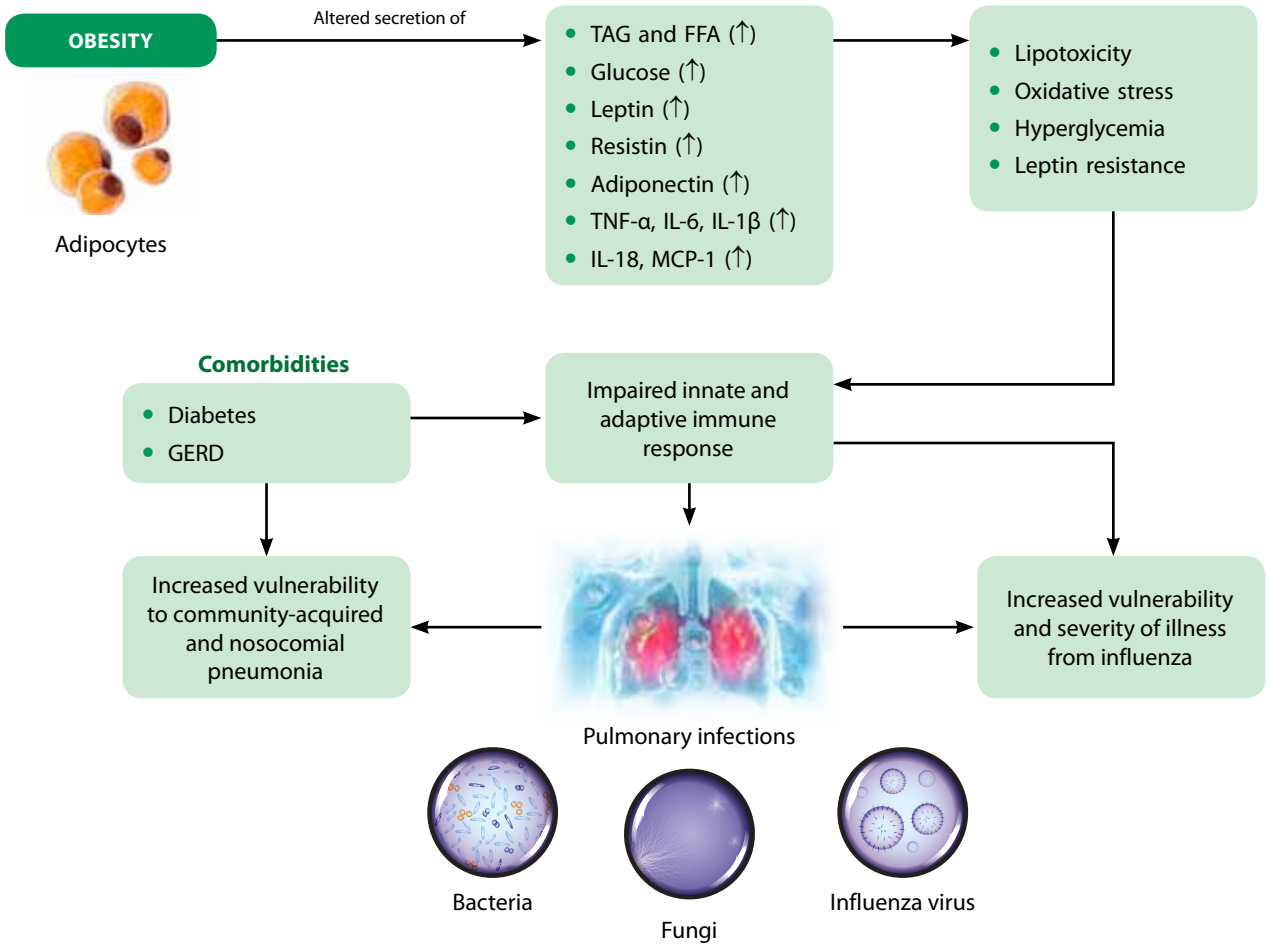
Obstructive Sleep Apnea

OSA is arguably the most common and well known respiratory disease associated with obesity. The risk of developing OSA is shown to increase considerably at a higher BMI; for a morbidly obese individual, the risk of developing OSA lies between 55% and 90%. Studies have revealed that moderate OSA [Apnea–Hypopnea Index (AHI) > 15 events per hour] and severe OSA (AHI > 30 events per hour) are associated with an increased mortality. Reducing disease severity to an Apnea–Hypopnea Index (AHI) < 15 events per hour (mild OSA) through weight loss can help in achieving improved outcomes in OSA patients.[1,15]

Obesity Hypoventilation Syndrome

Obesity is also shown to play a key role in the pathogenesis of OHS. The diagnosis of OHS requires a BMI of more

Figure 2: Mechanistic association between obesity and pulmonary infections



than 30 kg/m^2 (clinical obesity) together with daytime hypercapnia (PaCO2 > 6 kPa). [C] Many OHS patients suffer from sleep-disordered breathing (SDB) and frequently present with a history of snoring and witnessed apneas. Epidemiological studies suggest that the prevalence of OHS might be almost 10% of OSA patients. On evaluating the association between the increased PaCO2 and severity of obesity, it has been found that the prevalence increase with an increase in BMI.[15]

Asthma

Obesity is one of the most common comorbidities of asthma and is associated with increased risk for asthma exacerbations, worse respiratory symptoms and poor control.[16] Obese patients with asthma are known to suffer from more acute attacks, increased use of asthma medication, frequent visits to the emergency department, and more hospital admissions than the non-obese patients with asthma.[15]

The mechanistic association between obesity and asthma are probably multifactorial, stemming from mechanical alterations of the airways and lung parenchyma, to systemic and airway inflammatory and metabolic dysregulation that adversely influences lung function and or response to therapy.[16] A large slew of studies have tried to examine the possible relationship between obesity and asthma and data have revealed an increased prevalence of obesity in the asthma group (from 21.3% to 32.8%) compared with the non-asthma group (from 14.6% to 22.8%).[17] Alarmingly, obese patients with asthma show disparities in response to therapy and have a nearly fivefold risk of hospitalizations due to exacerbations.[18]

Obesity and Respiratory Mechanics

Abdominal obesity has been associated with worsening lung function and respiratory symptoms. Available data suggest that elevated waist-to-hip ratio and abdominal height has good correlation with impaired lung function. Excess weight on the anterior chest wall due to obesity is shown to lower chest wall compliance and respiratory muscle endurance with increase in work of breathing and airway resistance. Moreover, the accumulation of adipose tissue in the anterior abdominal wall and in the intra-abdominal visceral tissue obstructs diaphragmatic movement, lessens basal lung expansion during inspiration, and with the closure of peripheral lung units, causes ventilation–perfusion abnormalities and arterial hypoxemia. These alterations contribute markedly to an increase in prevalence of respiratory problems in obese individuals, mostly on exertion and in the supine position such as during sleep.[15]

Importantly, weight reduction has been shown to be effective in improving the symptoms and severity of several pulmonary disorders, including OSA and asthma. Indeed, weight management for overweight and obese patients with pulmonary disorders appears to be an important component in the medical care of these patients.[14,17]

Conclusion

Obesity increases susceptibility to bacterial and viral infections and infectious agents also have a role in the pathogenesis of obesity. The risk of respiratory infections in the obese is centered mostly around influenza and pneumonia with almost similar magnitude of increased risk in both infections. Moreover, obesity is also strongly associated with pulmonary disorders, such as exertional dyspnea, obstructive sleep apnea syndrome, obesity hypoventilation syndrome, chronic obstructive pulmonary disease, asthma, and pulmonary embolism.

Obesity weakens pulmonary host defense against influenza and possibly bacterial and fungal pathogens. This may be attributed in part to the accumulation of excess adipose tissue that in turn may lead to numerous metabolic disturbances that contributes to a chronic state of low grade inflammation. In addition, abdominal obesity has been associated with worsening lung function and respiratory symptoms. Importantly, weight reduction has been shown to be effective in improving the symptoms and severity of several pulmonary disorders. Therefore, weight management for overweight and obese patients with pulmonary disorders appears to be an important component in the medical care of these patients.

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