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REVIEW ARTICLE

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Obesity and Non-Communicable Diseases: Part I Cardiovascular Diseases, Respiratory Diseases, Depression, Liver Diseases

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Abstract

Obesity has become a pandemic. Obesity is associated with a wide array of physical and emotional health ailments. It is associated with a reduced quality of life. Comorbid disorders often result in premature mortality. Although BMI is the widely used standard for defining overweight and obesity, abdominal or visceral obesity has a more significant association with several noncommunicable diseases. Weight loss is beneficial in halting the deleterious effects of excess body weight. Part I of this manuscript, discusses the harmful effects of obesity on cardiovascular diseases, respiratory diseases, depression, and liver diseases.

Keywords: obesity, non-communicable diseases, cardiovascular diseases, respiratory diseases, obesity, depression, liver diseases

1 | INTRODUCTION

Obesity is growing exponentially all over the world[1]. Obesity is recognized and classified according to a person's body mass index (BMI)[2]. BMI is a person's weight [kilograms] divided by the square of his or her height [meters])[2]. According to the World Health Organization (WHO), a BMI between 20 and 25 kg/m2 is normal, a BMI between 25 and 30 kg/m2 is considered overweight, while a BMI of >30 kg/m2 represents obesity[3]. These numbers are different for the Asian population (Asian people have a high risk of type 2 diabetes and CVD at a lower BMI) [3]. Obesity is further divided into 3 classes (class 1, BMI > 30 and < 35; class 2, BMI > 35 and < 40; class 3, BMI > 40)[4]. In the USA in 2017-2018, 42.2% of all adults were obese[5]. Europe has the second highest proportion of overweight or obese people, with obesity rates of over 30% in most countries[6]. Several low- and middle-income countries, like China, India, and Brazil, have also seen a major rise in the prevalence of obesity[7–9]. It has also been increasing at an alarming rate in African countries[10]. The Global Burden of Disease Group reported in 2017 that "since 1980, the prevalence of obesity has doubled in more

than 70 countries and has continuously increased in most other countries"[11]. Excessive weight gain is not limited to adults, it also affects children and adolescents[12]. This puts them at a higher risk to develop major noncommunicable diseases like diabetes and cardiovascular diseases at a younger age[13]. It is estimated that obesity will affect 1.12 billion people by 2030[14].

BMI is unable to specify the type of collection of fat – subcutaneous adiposity or visceral adiposity[15]. The latter represents central obesity or abdominal obesity[15]. Abdominal fat is metabolically active[16], unlike subcutaneous fat – it induces inflammation[17], insulin resistance[18], and a procoagulant state[19], resulting in a high risk of several chronic diseases. Subcutaneous fat, on the other hand, protects the body from lipotoxicity[15,20]. Several anthropometric measurements are now routinely done to objectively diagnose central obesity[21,22]. These include the waist circumference (WC), waist hip ratio (WHR), and the weight height ratio (WHtR)[21,22]. WC is measured to the nearest 0.1 cm at the umbilical level while standing[23]. It should ideally be <102 cm in males and <88 cm in females[23]. The WHR is normal if it is 0.85 or less in women and 0.9 or less in men[24]. The WHtR is calculated by dividing the WC by height (< 0.5 (no central obesity) and > 0.5 (central obesity)[25].

Besides the nine chronic diseases discussed in this two-part manuscript, obesity is also implicated in several other disorders, including gastroesophageal reflux disease[26], pancreatitis[27], osteoporosis[28], infertility[29,30], and can increase complications related to pregnancy[31]. It may lead to psychosocial distress and obese people may have low self-esteem and feelings of rejection[32]. They often have heightened anxiety, body image dissatisfaction, and may face weight bias and sigma[33,34]. Stigma may also be exhibited by health care providers[35]. Obesity may also lead to disqualification from the US military[36]. It reduces the health quality of life[37]. It is associated with an increase in disability and mortality[38,39]. Most of the deaths attributable to obesity occur due to cardiovascular diseases[40]. According to the GBD 2015 Obesity Collaborators, obesity accounted for about four million deaths worldwide[41]. It is a major cause of preventable death, second only after smoking[42]. Obesity care is also expensive[43]. In the US alone, obesity related health care is over $150 billion yearly[44].

The obesity paradox is a phenomenon where obesity is associated with increased survival, especially in hospitalized patients[45]. It has been observed in chronic diseases such as heart failure[46], coronary artery disease[47], and end-stage kidney disease[48]. It has also been observed in acute conditions such as pneumonia[49], sepsis[50], acute respiratory distress syndrome (ARDS)[51], and other critical illness[52]. Several hypotheses have been advanced to explain this phenomenon[53–57].

The health effects of obesity on common chronic medical conditions are discussed in this two-part manuscript. Part I discusses the relationship between obesity and cardiovascular diseases (CVD), chronic obstructive pulmonary disease (COPD), depression, and liver diseases. Part II discusses its impact on cancer, diabetes mellitus, kidney diseases, Alzheimer's disease, and arthritis.

2 | DISCUSSION

The Centers for Disease Control and Prevention (CDC) defines chronic diseases as "conditions that last 1 year or more and require ongoing medical attention or limit activities of daily living or both"[58]. Most chronic diseases are noncommunicable diseases (NCDs) and are gradually replacing infectious diseases as the major health burden in developing countries[59]. Out of the 17 million premature deaths (under the age of 70) due to noncommunicable diseases in 2015, 82% were in low- and middle-income countries[59].

The NCDs discussed in this part include cardiovascular diseases (such as hypertension (HTN), coro-

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nary artery disease, stroke, and heart failure (HF)), chronic respiratory diseases (such as chronic obstructive pulmonary disease (COPD), lung cancer, tuberculosis, lung infections, asthma, and interstitial lung diseases) depression, and liver diseases (such as nonalcoholic and alcoholic hepatitis, viral hepatitis, cirrhosis of liver). Cardiovascular diseases (CVD) are the leading cause of morbidity worldwide[60]. They are also the leading cause of global mortality and were responsible for 17.9 million deaths in 2016 (representing 31% of all global deaths)[61]. Of all the global deaths in 2015, 82% were in low- and middle-income countries[61]. CVDs were responsible for 37% of these deaths[61]. Men and women were nearly equally affected[59]. The most common underlying pathology is atherosclerosis (especially in myocardial infarction, ischemic stroke and peripheral arterial disease)[60]. The most frequent chronic respiratory diseases encountered include chronic obstructive pulmonary disease (COPD), lung cancer, tuberculosis, lung infections, asthma, and interstitial lung diseases (ILD). Chronic respiratory diseases are responsible for about 7.5 million deaths per year, and account for approximately 14% of annual deaths worldwide[63,64]. COPD is the most common cause, and is usually due to tobacco smoking[65]. These patients experience airflow limitation, and COPD can be diagnosed by the FEV1 /FVC ratio of less than 0.70[66]. Asthma is a chronic inflammatory disorder of the airways[67]. Globally, one in two hundred and fifty deaths are due to ashtma[68]. The physical quality of life is impaired by bronchial symptoms[69], while social life is also impaired by rhinitis co-morbidity[70]. Obstructive sleep apnea syndrome results from upper airway obstruction[71]. Periods of reduced or absent airflow through the nose or mouth cause loud snoring and the hypoxemia is usually terminated by arousal[72]. Sleep is especially disturbed in these patients[73]. Major depressive disorder (MDD) is the primary cause of disability worldwide[74]. It can be diagnosed by the presence of at least five of the following symptoms occurring independently of physical illness, normal bereavement, alcohol or drugs: abnormal depressed mood; abnormal loss of interest and pleasure; appetite or weight disturbance; sleep disturbance; disturbance in activity (agitation or slowing); abnormal fatigue or loss of energy; abnormal self-reproach or inappropriate guilt; poor concentration or indecisiveness; and morbid thoughts of death or suicide[75]. The five diagnostic symptoms, which should include abnormal depressed mood or loss of interest and pleasure, are present nearly every day for at least two weeks after the diagnosis[75]. The World Health Organization predicts that depression will generate the greatest global burden by 2030[76]. Liver diseases affect more than 10% of the world population[77]. The leading liver disease globally (40% of all liver diseases) is nonalcoholic fatty liver disease (NAFLD). Other common liver diseases are Hepatitis B virus (HBV) (30%), Hepatitis C virus (HCV) (15%) and excessive consumption (11%)[77]. These patients may progress to cirrhosis of the liver or develop liver cancer[78].

2.1 | CARDIOVASCULAR DISEASES

Obesity has a strong detrimental relationship with CVDs[79,80]. An increased CVD risk of 6% for each 1.1 kg/m2 increase in BMI was noted by Emberson et al. among 6452 British men[81]. Weight loss, on the other hand, reduces CVDs[82]. In the Look AHEAD trial, with a median follow-up of 10.2 years, weight loss decreased CVD outcomes[82]. A 10% body weight reduction in the first year of the study resulted in a 21% lower risk of the primary CVD outcome and a 24% reduced risk of the secondary outcome compared with individuals who were weight stable or gained weight[82].

Obesity has been associated with an increased risk of HTN[83], coronary artery disease[84],stroke[85,86], HF[87],cardiac arrhythmias[88], and sudden cardiac death (SCD)[89]. It is estimated that obesity may result in a 3.5-fold increase in the likelihood of being hypertensive, and obesity may be responsible for about 70% of HTN in adults[90,91]. An increase in weight by 5% appears to increase the incidence of hypertension by 20–30%[92]. On the other hand, weight loss is effective in lowering blood pressure (BP)[93]. Studies indicated that a 10 Kg weight loss would result in a 6 mmHg in BP[94]. Obese patients are twice as likely to have coronary artery disease and their lesions are more complex[95,96]. They do not heal well after coronary artery bypass grafting[97] and have a higher mortality[98]. Obesity is

an independent risk factor for heart failure (HF)[99]. In the Framingham Heart Study of 5881 patients,**an increase in BMI of 1 kg/m2 increased the risk of heart failure by 5% in men and 7% in women**[100]**. They also do not do well after a l**eft ventricular assist device **implantation**[101] **or heart transplant surgery**[102]**. Bariatric surgery induced weight loss in HF patients resulting in a significant reduction in their New York Heart Association classification**[103]**. Ischemic stroke risks are also increased in obese patients**[104]**. In the Physicians' Health Study, men with BMI >30 kg/m2 had a >2-fold increase in risk for stroke**[105]**.** In a prospective study of >39,000 healthy women, those with BMI >35 kg/m2 had a 3-fold increase in the risk of ischemic stroke compared with women with BMI <20 kg/m2[106]. It is estimated that for each 1-U increase in BMI, there is an increase of 4% in the risk of ischemic stroke[107,108]. **Obese patients also have a higher risk of atrial fibrillation, with the risk being 1.52 times compared to that of the normal weight population**[109]**. Obesity increases the risk of SCD**[110]**. There is also a detrimental association noted between obesity and several other CVDs, including aortic stenosis**[111]**, peripheral artery disease**[112]**, erectile dysfunction**[113]**, and venous thromboembolism**[114]**. Obesity is also associated with diabetes mellitus, dyslipidemia, and sleep apnea syndrome – disorders that further increase the risk of cardiovascular disorders**[115]**.**

Obesity results in several pathophysiological mechanisms that damage the cardiovascular system. The adipose tissue releases proinflammatory adipokines, elevates free radicals, causes endothelial dysfunction, and activates macrophages, T cells, and B cells within fat deposits leading to atherosclerosis[116]**.**

2.2 | RESPIRATORY DISEASES

Increased BMI results in reduced lung function, with reductions in forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC)[117,118]. Obesity is detrimentally associated with obstructive sleep apnea (OSA)[119] and bronchial asthma[120]. Obesity promotes OSA by causing enlargement of soft tissue structures within and surrounding the airway[121]. An excess of fat deposition has also been observed under the mandible and in the tongue, soft palate, and uvula[122]. Further, obesity may reduce lung volumes by a combination of increased abdominal fat mass[123] and disturbed neuroanatomic interactions[124]. Several longitudinal epidemiological studies have shown that obesity is a major risk factor for asthma in children[125,126]. Obesity and weight gain during pregnancy in the mother are both associated with an increased risk of asthma in the offspring[127]. Several prospective studies in adults have also found a relationship between obesity and incident asthma[128,129.] Obesity in adults with asthma has been associated with reduced response to asthma medications, resulting in worse disease control, higher risk of hospitalization and lower quality of life, when compared to lean asthma patients[130,131]. Weight loss intervention by caloric restriction[132] or bariatric surgery leads to an improvement in asthma outcomes[133]. Abdominal or central obesity, even with a normal BMI, appears to be linked with an increased risk of lung cancer[134]. Yu et al estimated this increased risk to be 40% greater in these patients [135]. Carreras-Torres et al, using Mendelian randomization, recently reported that genetically predicted BMI, WHR, and insulin resistance increased the risk of lung cancer, especially for squamous cell and small cell lung cancer[136]. An obesity paradox has been noted in COPD patients, especially those with severe disease[137]. Patients with a higher BMI survive longer when compared to those with low or normal BMI[138]. It has been suggested that the severity of COPD may be overestimated in obese patients, as when CO2 levels and muscle mass and exercise capacity are looked at, there appears to be no obesity paradox[139].

2.3 | DEPRESSION

Several studies have found that obesity and mental health problems are linked[140−142]**. Simon et al concluded that there was an approximately 25% increase in mood disorders and anxiety in obese patients**[143]**. Obesity and depression also frequently co-exist**[144,145] **and the presence of one not only increases the risk of the other, but also causes significant adverse health outcomes when they co-occur**[146,147]**. The** preva-

lence of depression in obese individuals is estimated to be twice as high as in those of normal weight[148]. **Negative body image, and low self-esteem are common in obese patients[149]. They also face stigma in social and professional lives[150,151].** These factors contribute to the development and maintenance of depression[152,153]. **Other pathophysiological processes may also play a role in this connection[154,155].** Depression also increases weight gain and obesity[156−160]. Depressed individuals may be less physically active and indulge in excessive 'comfort' eating[156−158]. Certain antidepressant medications can also contribute to weight gain[159,160]. **The relationship between obesity and depression is therefore bidirectional[161]. The biological pathways include genetic influence[162], HPA axis disturbances[163,164], immuno-inflammatory dysregulation166, and insulin** abnormalities[167].

2.4 | LIVER DISEASES

NAFLD is prevalent in obese individuals[168]. Obese individuals have a prevalence of 30% to 37% of NAFLD[169]. In those who have undergone bariatric surgery, the prevalence rises to 84% to 96%[170]. Li et al. estimated that obesity produced a 3.5-fold increased risk of developing NAFLD[171] and is more closely related to waist circumference[172]. Pang et al. in a meta-analysis, concluded that for each 1 unit increase in waist circumference, the odds ratio of NAFLD increased by 1.07, and for each 1 unit increase in BMI, the odds ratio increased by 1.25[173]. Obesity also worsens the prognosis in patients with hepatitis[174]. Obese patients with alcoholic hepatitis, are twice as likely to die in the short term, compared to those who are nonobese[174]. Obesity is also common in chronic HCV infected individuals[175]. This increases their risk of developing serious liver related complications and dying early[176]. Antiviral treatment in these patients may sometimes result in weight gain[177].

3 | CONCLUSIONS

The increasing epidemic of obesity has resulted in a greater development, aggressive progression, and poor outcomes for many common chronic diseases and ailments. The evidence for the preventive and therapeutic effects of a BMI of 25 or more on NCDs is strong. Weight loss, including that with bariatric surgery, helps most obesity related conditions.

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