

## PATHOLOGY OF OBESITY

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### ABSTRACT

Prevalence of obesity worldwide is on an increase at an alarming rate with USA alone showing a 37.5% increase in obese individuals. Obesity is defined by the basal metabolic rate of the individual however off-late waist to hip ratio has gained precedence over simple BMI in diagnosing Obesity. Post mortem in obese is challenging not only due to the logistics involved but also due to the various co-morbid conditions that an obese individual will have. Adipose tissue is now being looked upon as an entire organ in itself rather than a simple inert tissue and this organ is capable of releasing chemicals which control some of the major metabolic functions of the body. Various diseases occurring with obesity as a cause under study are OSA, OSH, Cancer etc. which we will discuss in this article.

**Keyword:** Leptin, adipocytokine, body mass and fertility

### INTRODUCTION

Prevalence of obesity worldwide is on an increase at an alarming rate with USA alone showing a 37.5% increase in obese individuals.<sup>1</sup> Obesity is defined by the basal metabolic rate of the individual however off-late waist to hip ratio has gained precedence over simple BMI in diagnosing Obesity.<sup>2</sup> Obesity is important for the pathologist as somewhere while performing an autopsy or making a diagnosis he or she is bound to come across death or disease due to obesity.

Post mortem in obese is challenging not only due to the logistics involved but also due to the various co-morbid conditions that an obese individual will have for e.g. Cardiovascular disease, metabolic syndrome, thrombo-embolism, obesity hypoventilation syndrome, obstructive sleep apnoea etc. <sup>3</sup> Hence it's important that the role obesity plays in these deaths is acknowledged.

### DISCUSSION

Adipose tissue is now being looked upon as an entire organ in itself rather than a simple inert tissue and this organ is capable of releasing chemicals which control some of the major metabolic functions of the body e.g. adiponectin, leptin etc. Adipose tissue acts as an endocrine organ which for example releases adipokines which are inflammatory cytokines implicated in the development of cancer, atherosclerosis and thrombosis.<sup>4</sup>

### OBSTRUCTIVE SLEEP APNOEA

OSA signifies recurrent episodes of apnea due to upper airway obstruction during deep sleep followed by transient awakening to restore breathing. This occurs

commonly in people with fat necks and is treated by CPAP. Recurrent apnea causes chronic alveolar hypoxia leading to increased pulmonary vascular resistance and hypertension leading to cor pulmonale and heart failure.<sup>5</sup> Hence while doing an autopsy a pathologist can encounter OSA as a cause of death and should keep the entity in mind.

### OBESITY HYPOVENTILATION SYNDROME

Also known as the Pickwickian syndrome, is a condition where severely overweight people fail to breathe rapidly enough or deeply enough, resulting in low blood oxygen levels and high blood carbon dioxide (CO<sub>2</sub>) levels. Patients may stop breathing altogether for short periods of time during sleep (obstructive sleep apnea), resulting in many partial awakenings during the night, which leads to continual sleepiness during the day.<sup>6</sup> The disease eventually leads to the symptoms such as heart failure, leg swelling and various other related symptoms. The most effective treatment for such conditions is weight loss, but it is often possible to relieve the symptoms by nocturnal ventilation with positive airway pressure (CPAP) or related methods.<sup>1-2</sup>

### OBESITY CARDIOMYOPATHY

Obesity produces an increase in total blood volume and cardiac output because of the high metabolic activity of excessive fat. In moderate to severe cases of obesity, this may lead to left ventricular dilation, increased left ventricular wall stress, compensatory (eccentric) left ventricular hypertrophy, and left ventricular diastolic

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dysfunction. Left ventricular systolic dysfunction may occur if wall stress remains high because of inadequate hypertrophy.<sup>7</sup> Right ventricular structure and function may be similarly affected by the morphologic and hemodynamic alterations and by pulmonary hypertension related to the sleep apnea/ obesity hypoventilation syndrome. The term obesity cardiomyopathy is applied when these cardiac structural and hemodynamic changes result in congestive heart failure. Obesity cardiomyopathy typically occurs in persons with severe and long-standing obesity. The predominant causes of death in those with obesity cardiomyopathy are progressive congestive heart failure and sudden cardiac death.

### **SUDDEN DEATH IN OBESE**

The increased risk of sudden cardiac death in obese patients is becoming a major challenge, especially since obesity prevalence has been increasing steadily around the globe. Traditional risk factors and obesity often coexist.<sup>2</sup> Hypertension, diabetes, obstructive sleep apnea and metabolic syndrome are well-known risk factors for CV disease and are often present in the obese patient. Although the bulk of evidence is circumstantial, sudden cardiac death and obesity share common traditional CV risk factors.<sup>8</sup> Structural, functional and metabolic factors modulate and influence the risk of sudden cardiac death in the obese population.

### **LIVER IN OBESE**

While obesity and alcoholism are two very different health issues, their impact on the liver can be quite similar. Both can cause fatty deposits to build up in the liver leading to fatty liver disease. Almost all heavy drinkers develop this condition, but it is climbing quickly among nondrinkers, especially among people who are overweight or have Type 2 diabetes. When it occurs in moderate or nondrinkers, we call it nonalcoholic fatty liver disease, or NAFLD.<sup>9,10</sup>

NAFLD is now the most common cause of chronic liver disease in our country, far surpassing alcohol-related liver disease. An estimated 20 to 30 percent of Americans have NAFLD, although most probably don't know it, because it progresses without symptoms.<sup>9</sup> While the short-term effects are minimal, the potential long-term complications – gastrointestinal bleeding, anemia, encephalopathy (abnormal brain function), cirrhosis, liver cancer and liver failure – are the same serious problems that often occur after decades of alcohol abuse.

### **KIDNEY DAMAGE IN OBESE**

For many years, it has been known that obesity is associated with focal and segmental glomerulosclerosis, yet the degree of the association and its pathogenesis were unknown. Recently, its incidence has increased in association with increased obesity.<sup>10</sup> Insulin resistance/hyperinsulinemia with hypertension and associated abnormalities in the renin-angiotensin system has long been known to contribute to the rate of progression of renal disease. Recent data indicate that the subset of individuals who have hypertension, who are nondippers and have elevated insulin levels and microalbuminuria, are the ones who develop significant renal and vascular disease.<sup>11</sup> The relationship of this risk to obesity and abnormalities in lipids, insulin resistance, and function of the PPAR system has recently been elucidated.<sup>12</sup> It is well recognized that the presence of microalbuminuria in patients with diabetes predicts future development of overt diabetic nephropathy.

### **CANCER IN OBESE**

According to the most recent 2014 Cancer Progress Report from the American Association for Cancer Research (AACR), overweight/obesity is responsible for nearly 25% of the relative contribution to cancer incidence, which ranks second only to tobacco use.<sup>3</sup> Obesity is combined with other related behaviors, including a lack of physical activity and poor diet, the relative contribution rises to 33% of newly diagnosed cancer cases in the U.S. Obesity is strongly tied to many of the most common types of cancer, including post-menopausal breast cancer, colorectal cancer and cancers of the endometrium, kidney, thyroid and gallbladder. There is also evidence to suggest a link to cancers of the liver, cervix, multiple myeloma and Non-Hodgkin's lymphoma.<sup>13</sup> However, evidence is less convincing and somewhat controversial for prostate cancer, lung cancer and pre-menopausal breast cancer; several studies report an inverse relationship between obesity and these particular cancers.

### **METABOLIC SYNDROME**

It comprises of clustering of at least three of the five following medical conditions—abdominal (central) obesity, elevated blood pressure, elevated fasting plasma glucose, high serum triglycerides, low high-density lipoprotein (HDL) levels

Metabolic syndrome is associated with the risk of developing cardiovascular disease and type 2 diabetes.<sup>1,2</sup> Some studies has shown the prevalence in the USA to be an estimated 34% of the adult

population,<sup>3</sup> and the prevalence increases with age. Insulin resistance, metabolic syndrome, and prediabetes are closely related to one another and have overlapping aspects. The syndrome is thought to be caused by an underlying disorder of energy utilization and storage.

## **BARIATRIC SURGERY**

Bariatric surgery includes a variety of procedures performed on people who have obesity. Weight loss is achieved by reducing the size of the stomach with a gastric band or through removal of a portion of the stomach (sleeve gastrectomy or biliopancreatic diversion with duodenal switch) or by resecting and re-routing the small intestine to a small stomach pouch (gastric bypass surgery).

Long-term studies show the procedures cause significant long-term loss of weight, recovery from diabetes, improvement in cardiovascular risk factors, and a reduction in mortality of 23% from 40%.<sup>1</sup> However, a study in Veterans Affairs (VA) patients has found no survival benefit associated with bariatric surgery among older, severely obese people when compared with usual care, at least out to seven years.<sup>2</sup>

The U.S. National Institutes of Health recommends bariatric surgery for obese people with a body mass index (BMI) of at least 40, and for people with BMI 35 and serious coexisting medical conditions such as diabetes.<sup>1</sup> However, research is emerging that suggests bariatric surgery could be appropriate for those with a BMI of 35 to 40 with no co morbidities or a BMI of 30 to 35 with significant co morbidities. The most recent ASMBS guidelines suggest the position statement on consensus for BMI as an indication for bariatric surgery. The recent guidelines suggest that any patient with a BMI of more than 30 with co morbidities is a candidate for bariatric surgery.<sup>1</sup>

Procedures can be grouped in three main categories.<sup>8</sup>

This complex operation is termed biliopancreatic diversion (BPD) or the Scopinaro procedure. The original form of this procedure is now rarely performed because of problems with malnourishment. Part of the stomach is resected, creating a smaller stomach (however the patient can eat a free diet as there is no restrictive component). The distal part of the small intestine is then connected to the pouch, bypassing the duodenum and jejunum.

Jejunioileal bypass

This procedure is no longer performed. It was a surgical weight-loss procedure performed for the

relief of morbid obesity from the 1950s through the 1970s in which all but 30 cm (12 in) to 45 cm (18 in) of the small bowel was detached and set to the side.

Endoluminal sleeve

A study on humans was done in Chile using the same technique<sup>9</sup> however the results were not conclusive and the device had issues with migration and slipping. A study recently done in the Netherlands found a decrease of 5.5 BMI points in 3 months with an endoluminal sleeve. Complications from weight loss surgery are frequent. Common complications faced are gastric dumping syndrome in about 20% (bloating and diarrhea after eating, necessitating small meals or medication), leaks at the surgical site (12%), incisional hernia (7%), infection (6%) and pneumonia (4%) where the mortality was 0.2%.<sup>14</sup> As the rate of complications appears to be reduced when the procedure is performed by an experienced surgeon, guidelines recommend that surgery be performed in dedicated or experienced units.<sup>15</sup> It has been observed that the rate of leaks was greater in low volume centres whereas high volume centres showed a lesser leak rate. Leak rates have now globally decreased to a mean of 1-5%.

## **CONCLUSION**

Hence we can conclude that obesity is not merely a lifestyle disease but an all encompassing problem which can lead to increased morbidity and mortality and hence it needs to be monitored and researched upon in greater detail.

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