

# Review Article

## Health Risks of Obesity

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### Abstract

Obesity epidemic is taking the globe in its stride with the metamorphosed lifestyle. Obesity prevalence is constantly increasing with over a third of population being overweight or obese in India. It contributes in a big way to pathogenesis of chronic non-communicable diseases. Interventions to reduce burden of obesity, partly depend on detecting and understanding the risks complicating obesity. This article summarizes the need for focused clinical skills on obesity related health risks and vigorous validation of benefits possible through interventions toward weight management in patients.

**Key Words:** Obesity, Risks of Obesity, Metabolic Syndrome

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### Introduction

World Health Organization has enabled the classification of individuals as overweight or obese by using a measure of Body Mass Index. Body Mass Index is calculated by dividing body weight in kilogram by square of height in meters. This is essentially the surrogate measure of body fat for specified categories of sex and age<sup>1</sup>. A value equal to or more than 30kg/m<sup>2</sup>, defines state of obesity<sup>2</sup>. Different thresholds are defined by anthropometry (BMI) for overweight and obesity is stated for different ethnicity<sup>3</sup>. Prevalence of obesity increases rapidly in India. Large surveys conducted in different parts, time to time, indicate steady rising trends across all sections of population. In 2004, sample surveyed indicated 20.8% male and 32.3% female population overweight or obese. In 2007, urban males 32.4% and females 41.4% were seen as overweight or obese. Lately, in 2012, 46.6% of urban women above 35 year age and 23.7% of such rural women are overweight. Childhood and pre-pubertal obesity is also fast increasing, particularly in northern part<sup>4</sup>.

The distribution pattern of central obesity is, indicative of excess visceral fat. It exhibits stronger association with cardiovascular diseases than subcutaneous fat deposited around hip. Central obesity is reflected in waist circumference and the waist/hip circumference ratio. The anatomic location profoundly influences biology of adipose tissue. Increased visceral fat associates metabolic dysfunction and cardio-metabolic risk while subcutaneous fat may be protective. The two adipose tissues have embryologically different origins<sup>5</sup>. Visceral adipose tissue and its resident macrophages produce high quantities of proinflammatory cytokines, viz, TNF-alpha, IL-6, and low amounts of protective adiponectin. These changes in cytokines induce insulin resistance, endothelial dysfunction and consequent atherosclerosis<sup>6</sup>.

### Mortality in Obesity

Body mass index (BMI) in excess of certain threshold for specific age/sex groups, is seen to be associated with increased mortality. Six to seven year reduction of longevity was found in a prospective observation cohort<sup>7</sup>. 3457 participants of Framingham Heart study were inducted at 30-49 year age. Substrata were made by sex and smoking status. Life expectancy and probability of death before 70 year age was analyzed using life table. Mortality rates specific for categories of different BMI (normal, overweight and obese at baseline/induction) and age groups were analyzed. Overweight and obesity caused large reductions in life expectancy. The follow up period was 42 years from 1948 to 1990. BMI at ages 30 to 49 years predicted mortality after 50 to 69 years, even upon adjustment for BMI at 50-69 year age<sup>8</sup>.

High waist (central) fat distribution increases while high fat distributed to hip decreases risk of getting myocardial infarction. It was a standardized case control study of acute myocardial infarction with 14037 controls and 12461 cases from multiple countries and ethnicities. The waist to hip ratio showed a graded and highly significant association with risk of myocardial infarction. BMI showed modest association, which disappeared when adjustments were made for waist hip ratio and other risk factors<sup>9</sup>.

### Obesity and Diabetes

Type 2 Diabetes mellitus is the major most prevalent chronic non communicable inflammatory disease, arising as sequel to metabolic syndrome driven by insulin resistance. Overweight and obesity is found to be the main predictor of type 2 diabetes mellitus<sup>10,11</sup>. During 16 year follow up of 84941 healthy female nurses, from 1980 to 1996, 3300 new cases of type 2 diabetes were detected. Overweight or obesity, as per

BMI defined cutoff constituted single most important predictor of diabetes development<sup>10</sup>. Data from cohort of 51529 US male health professionals in age range 40-75 years in 1986 was analyzed following 5 year follow up, in 1992. Persons developing NIDDM numbered 272. Strong positive association of obesity defined by BMI and risk of diabetes development was demonstrated<sup>11</sup>.

Mechanistic links of obesity to diabetes development are hypothesized with partial supportive observations. Genetic and epigenetic predisposition for preferential deposition of fat in abdominal depots is proposed. This process may be added by stress induced hypothalamo-pituitary-adrenal axis activation. The overflow of uncontained fat from omental and mesenteric tissue probably invades organs as liver, skeletal muscles, inflicting metabolic dysfunction. Direct effect of omental and mesenteric adipose tissue depots may be exerted on insulin resistance, lipoprotein metabolism and blood pressure. Metabolic products of omental and mesenteric adipose tissue depots are released in to the portal vein, which provides direct delivery to liver. Lipolysis of omental and mesenteric adipose tissue triacyl-glycerol releases free fatty acids that can induce hepatic insulin resistance and provide substrate for lipoprotein synthesis and neutral lipid storage in hepatocytes. In addition, specific proteins and hormones produced by omental and mesenteric adipose tissue, such as inflammatory adipokines, angiotensinogen and cortisol (generated by local activity of 11 beta hydroxysteroid dehydrogenase), can also contribute to cardio-metabolic disorder<sup>12</sup>.

## Hypertension and Obesity

Obesity increases risk of developing hypertension<sup>13,14</sup>. In a large study, 14924 adult participants were grouped by BMI cutoffs and waist circumference as per NIH criteria. Relative risks of hypertension, dyslipidaemia and metabolic syndrome were higher in overweight and obese. These risks correlated positively with waist circumference. Importantly, risk level associating a given waist circumference was unaffected by differences in BMI, emphasizing major significance of the parameter<sup>15</sup>.

## Obesity and Heart Disease

Number of studies have established regular relation of obesity to increased risk of coronary artery disease<sup>14,16</sup>. The obese are also twice as likely to suffer heart failure as the non obese<sup>17</sup>. Paradoxically, the survival rate of obese heart failure cases is better than the non obese<sup>18</sup>.

## Obesity and Cerebrovascular Disease

Increased BMI associates increased risk of ischemic stroke. Hemorrhagic stroke risk appears to concentrate at either extremes of the BMI<sup>19</sup>. Lean body weight and lower cholesterol level have been linked to increased hemorrhagic stroke risk by a prospective cohort of 21414 male physicians<sup>20</sup>. During 12.5 years of follow-up, 747 strokes (631 ischemic, 104 hemorrhagic, and 12 undefined) occurred. Compared with participants with BMIs less than 23, those with BMIs of 30 or greater had an adjusted relative risk of 2.00 (95% confidence

interval [CI], 1.48-2.71) for total stroke, 1.95 (95% CI, 1.39-2.72) for ischemic stroke, and 2.25 (95% CI, 1.01-5.01) for hemorrhagic stroke. When BMI was evaluated as a continuous variable, each unit increase of BMI was associated with a significant 6% increase in the adjusted relative risks of total (95% CI, 4%-8%), ischemic (95% CI, 3%-8%), and hemorrhagic stroke (95% CI, 1%-12%). Additional adjustment for hypertension, diabetes mellitus, and hypercholesterolemia slightly attenuated the risks for total and ischemic (relative risk 4%; 95% CI, 2%-7%), but not hemorrhagic, stroke. Another study was conducted in Korea, on 2,712 persons (904 cases, 904 hospital controls, and 904 community controls)<sup>21</sup>. Obese men ( $25.0 \leq \text{BMI} < 30.0 \text{ kg/m}^2$ ) had an odds ratios (OR) of 1.39 (95% CI 1.03 to 1.87) a hemorrhagic stroke, compared to men with a normal BMI (18.5 to 24.9  $\text{kg/m}^2$ ). Conversely, women with lower BMI had a higher risk of having hemorrhagic stroke. About a three-fold increase was observed in the risk of intracerebral hemorrhage (ICH) in the highly obese group obesity was identified as one of the risk factors in hemorrhagic stroke, in particular ICH. Conversely, in women, a lean body weight increases the risk of hemorrhagic stroke. Consequently, managing one's weight is essential to reduce the risks of hemorrhagic stroke. Central (truncal) obesity increases stroke related mortality, however<sup>22</sup>.

## Role of Obesity in Metabolic Syndrome

Metabolic syndrome is defined by presence of any three the following five features: viz. 1) waist circumference above 40 inches in male and 35 inches in female; 2) triglyceride level above 150 mg/dl; 3) High Density Cholesterol (HDL) level below 40mg/dl in male or 50mg/dl in female; 4) Blood pressure above 130/85 mmHg; and 5) Fasting blood glucose level above 100mg/dl<sup>23</sup>. The altered lipid and glucose metabolism appears to be consequent to central obesity and insulin resistance.

## Obesity and Pulmonary Abnormality

Obesity and accompanied increased neck circumference is found to strongly link to the obstructive sleep apnea<sup>24</sup>. Increased fat tissue may impinge upon airway lumen increasing collapsibility<sup>25</sup>. Obesity also increases asthma risk and majority of asthmatic emergency cases are found to be obese or overweight<sup>26</sup>. Obesity asthma linkage may involve decrease in functional and tidal volume, chronic state of sub-acute systemic inflammation including increased production of mediators and the increased hyper responsiveness of airway<sup>27</sup>.

## Obesity and Gastrointestinal Disorders

Obesity is significantly associated to gastro esophageal reflux disease and its late sequel as erosive esophagitis, esophageal cancer etc<sup>28</sup>. Obese men and women both suffer increased incidence of gall stones<sup>29,30</sup>.

## Obesity and Reproduction Disorders

Obesity and insulin resistance typically associate the polycystic ovarian disease that exhibits anovulation and hyper-androgenism. Weight loss and therapeutic remediation of insulin resistance can reverse anovulation and aberrant hormonal profile in these

patients<sup>31</sup>. Obesity negatively impacts male sexual function and fertility, with recovery benefit of weight reduction<sup>32</sup>. Gestational diabetes is likewise more prevalent in the obese with predictable diverse complications for mother and baby<sup>33</sup>.

## Obesity and Late Age Health

Osteoarthritis ensues upon obesity<sup>34</sup>. Besides the extra strain on weight bearing joints, there is evidence of systemic dysregulation of adipokines, to explain increased osteoarthritis in the obese people<sup>35</sup>. Increased incidence of certain cancers in the obese is reported, viz. cancers of gall bladder, esophagus, thyroid, kidney, uterus, colon, breast etc<sup>36</sup>. A lean body weight is known to reduce both incidence and mortality of the cancers<sup>37,38</sup>. Cancers of reproductive and secondary sex organs in females may draw boost from high estrogen synthesis from increased fat<sup>39</sup>. The evidences are most consistent for endometrial cancer, breast cancer among the postmenopausal women, and renal cell cancer. The molecular mechanisms linking obesity to increased cancer incidence have been poorly understood.

## Obesity & Health Related Quality of Life

Several neuropsychiatric maladies like somatization, hypochondriasis, phobias, and obsessive compulsive disorders have shown amelioration in obese patients after undergoing bariatric surgery<sup>40</sup>. Many surgical procedures in the obese carry poor prognoses due to associated ill health. Obesity evidently would increase immobility and access to proper health care.

## Conclusion

Thus, given the magnitude of complications related to obesity, addressing this linkage and revelation of diseases linked to obesity constitute, vital facets of clinical competence and quality care.

Authors declare no conflict of interest.

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