

# Obesity: An Epidemic of the 21st Century

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Obesity is an excessive accumulation of fat in the body. It can be assessed by various ways including Body Mass Index (BMI), waist circumference, life insurance tables, CT / MRI and absorptiometry. Body Mass Index (BMI) is the most widely accepted means of assessing obesity (weight in kilograms divided by the square of height in meters). The relationship of BMI to total body and visceral fat, and consequent complications varies between ethnic groups.<sup>1</sup> Asian population particularly those from South East Asia have more fat and co-morbidities for any given BMI, resulting in different suggested BMI cut-off points.<sup>2</sup> Adult BMI cut offs (Table 1) cannot be used in children and adolescents to assess obesity as BMI varies throughout childhood. In children the BMI is higher in 2nd year of life and then drops at ages 4-7 years rising slowly to adult values. BMI for age charts<sup>3</sup> can be used in clinical practice to assess obesity in children. According to these charts a child is overweight having a BMI between 85th - 95th percentiles and obese above 95th centiles. Central obesity particularly visceral fat is a risk factor for metabolic syndrome. Waist circumference cut-offs have been internationally accepted for adults (Table 2) but there are no internationally accepted criteria for waist circumference in chil-

dren.

## **Epidemiology of Obesity**

The prevalence of obesity is steadily increasing across the world particularly in the developed countries. In 1980, 39% of men and 32% of women in UK were overweight or obese and 1991 this figure rose to 53% and 44% respectively.<sup>4</sup>

W.H.O. estimates the prevalence of obesity to be 4.8% in the developing countries, 17.1% in countries in economic transition and 20% in the developed world. More than one billion adults worldwide are overweight and at least 300 million of them are clinically obese.<sup>5</sup>

The increase in prevalence of overweight and obesity is not limited to adults but is also affecting the children even more. In Australian children over the decade 1985 - 1995 the combined prevalence of the two conditions almost doubled while that of obesity on its own more than tripled.<sup>6</sup>

## **Etiology of Obesity**

The etiology of obesity is complex and multifactorial. Both environmental and genetic influences play a role. The recent increase in obesity is clearly due to

**Table 1. Classification of obesity.**

Classification	Caucasian	Asian
Normal range	18.5 - 24.9	18.5 - 22.9
Overweight	25.0 - 29.9	23.0 - 25.9
Obese	>30.0	>26
Class I	30.0 - 34.9	26.0 - 29.9
Class II	35.0 - 39.9	30.0 - 35.0
Class III	>40.0	>35

**Table 2. Waist circumference cutoff for central obesity.**

	Caucasian	Asian
Men	≥102	≥ 90
Women	≥ 88	≥ 80

**Table 3. Examples of changes in energy intake and energy expenditure over the past 50 years.**

Energy Intake	Energy expenditure
Cheaper food:	Increased ownership of cars:
Greater availability of food:	Change in work practices:
Supermarkets	Construction machines
Freezers	Production lines
Fast food outlets	Computers
Change in diet composition:	Labour-saving devices:
Increased fat	Washing machines
Increased refined sugars	Dishwashers
Less complex carbohydrates	Remote controls
More alcohol	Cordless phones
Change in eating patterns:	Sedentary relaxation:
More snacks	Television
Fewer 'family' meals	Computer games
Increased portion size	Lifts
	Escalators
Children:	Children:
Targeted by food industry	Push chairs
Greater autonomy	Fewer walk to school
Greater spending power	Decreased sport at school

environmental factors i.e. easy availability of high-energy food together with major reduction in physical activity that has characterized human existence until recently. Examples of changes in energy intake over the past 50 years are shown in Table 3.

Not everybody who is exposed to obesogenic environment due to affluence become obese, thus indicating that a genetic predisposition is required. In adoption studies it has been shown that adoptees resemble their biological parents in body size more than adoptive parents.<sup>7</sup> Some genes which predispose to obesity have been identified i.e., leptin, leptin receptor, POMC and Melanocortin-4 receptor. Most instances of human obesity are thought to be poly-genic.

### Medical Consequences of Obesity

Obesity is associated with increased morbidity and mortality. This has been known for more than 2000 years and Hippocrates said, "Sudden death is more common in those who are naturally fat than in the lean."

In obesity the excess energy is stored in fat cells that enlarge and / or increase in number. Enlarged fat cells produce clinical problems associated with obesity either because of mass of extra fat or because of increased secretion of free fatty acids and numerous peptides from enlarged cells.

Spectrum of medical condition results from obesity some of which are as follows:

### Diabetes Mellitus and Metabolic Syndrome

Type 2 Diabetes is strongly associated with excessive weight in both sexes in all-ethnic population.<sup>8,9</sup> The risk of diabetes increases with duration and degree of obesity and with a more central distribution of body fat. In the Nurses Health Study the risk of diabetes was lowest with BMI less than 22 kg/m<sup>2</sup>. As BMI increased the relative risk increased such that with a BMI of 35, the relative risk increased 40 fold. A similar relationship was observed in men in the Health Professional Follow up study. In the same study it was shown that weight loss or moderating weight gain over years reduces the risk of developing diabetes. Insulin resistance, a hallmark of Metabolic syndrome is very high in overweight and obese. Subsequently all the features of metabolic syndrome are more common in obese subjects.

### Hypertension

Blood Pressure is often increased in obese and overweight subjects.<sup>10</sup> Hypertension in obese subjects appears to be related to altered sympathetic activities. The combination of overweight and hypertension leads to thickening of ventricular wall and larger heart volume with a greater likelihood of cardiac failure.

## **Dyslipidaemia**

A positive correlation between BMI and triglycerides has been repeatedly demonstrated. An inverse relationship of BMI with HDL, the good cholesterol, is more important as a risk factor for coronary artery disease.<sup>11</sup>

## **Heart disease**

Data from the "Nurses Health Study"<sup>12</sup> indicate that the risk of women developing coronary artery disease is increased greater than 3 folds with a BMI greater than 29. Dyslipidaemia, Hypertension and Diabetes all contribute to this increased risk. Aerobic Center Longitudinal Study<sup>13</sup> involving 25714 men who were followed for 1-10 years has shown that the cardiovascular mortality was higher in men with BMI greater than 30 kg/m<sup>2</sup>.

## **Cancer**

Certain cancers are significantly increased in overweight and obese individuals. These include malignant neoplasm of colon, rectum and prostate in men and cancers of breast, uterus and gallbladder in women.

## **Non-alcoholic fatty liver disease (NAFLD)**

It is a disease having liver abnormalities associated with obesity comprising of hepatomegaly, elevated liver enzymes and abnormal liver histology.<sup>14</sup> In a cross sectional study involving liver biopsies in obese subjects have shown steatosis in 75%, steatohepatitis in 20% and cirrhosis in 2%.<sup>15</sup>

## **Gallbladder disease**

The clinical saying "fat, female, fertile and forty" describes the epidemiology of gallbladder disease associated with cholelithiasis. Nurses Health Study has demonstrated this very clearly. It has been shown that the incidence of gallstones gradually increase with increased BMI upto 30 and very steeply with higher BMI. One of the explanations for increased risk of gallstones is the increased cholesterol turnover related to increased body fat.

## **Diseases of the bones and joints**

Osteoarthritis is significantly increased in obese patients. The joints affected are usually the knees and ankles and is directly related to trauma associated with the degree of excess body weight.<sup>16</sup> Increased osteoarthritis of other non-weight bearing joint is also seen in obese patients.

## **Sleep apnoea**

Pulmonary functions are altered in obese patients showing a decrease in residual lung volume associated with increased abdominal pressure on the diaphragm.<sup>17</sup> In addition to this benign effect on pulmonary function obstructive sleep apnoea is also seen more in obese tall-men.

## **Reproductive/Endocrine abnormalities**

Variety of endocrine changes are seen in obese patients but the changes in reproductive system in women are most profound. Irregular, infrequent and an-ovulatory menstrual cycles are common in obese women and the rate of fertility is also reduced.<sup>18,19</sup> Hirsutism is also more commonly seen in obese women who may be suffering from P.C.O.S.

## **Increased mortality/shortened life expectancy**

Framingham Study<sup>20</sup> has shown loss of 3.3 years in overweight women and 3.1 years in overweight men compared with normal weight men and women. In obese women and men these shortened life years are more pronounced reaching 7.1 years and 5.8 years respectively. Despite the fact that obesity is more common in African-Americans than Caucasian-Americans, it is more lethal for whites than blacks.<sup>21</sup> Nurses Health Study<sup>12</sup>, American Cancer Society Cancer Prevention Study II and I<sup>22,23</sup> have all shown increased mortality in both men and women with BMI in the obese range.

## **Treatment of Obesity**

### **Lifestyle modification**

Lifestyle modification remains a cornerstone of obesity treatment. It comprises of dietary modification, increased activity and exercise and behavioral/cognitive therapy. Aim of treatment is to produce clinically valuable weight loss of 5 - 10% that is maintainable long term. Even this modest weight loss is associated with significant benefits as shown in Table 4 on the basis of data from Scottish Intercollegiate Guidelines Network.<sup>24</sup>

Current dietary advice to obese patients is healthy eating principles of reducing fat intake and to limit carbohydrates especially those having a high glycaemic index, as high insulin levels can encourage weight gain.<sup>25,26</sup> A fixed caloric deficit of 600 calories from the stable prior intake is generally advised. This energy deficit can lead to a weight loss of 0.5-0.6/wk.<sup>24</sup> Very low energy diet (VLED) of 800 kcal can be tried in the initial weight loss plan but cannot be maintained long term. The advice of a trained dietitian can be of great help in this regard.

Increased physical activity is an important component of lifestyle modification. A modest initial target of 30 minutes of brisk walking five days per week, which can be increased gradually to 80 minutes of moderate intensity activity per day.

### **Drug Therapy**

Pharmacotherapy should be considered in over-

## Drug Therapy

Pharmacotherapy should be considered in overweight / obese subjects with BMI greater than 27kg/m<sup>2</sup> in the presence of co-morbidities such as Type 2 Diabetes and Hypertension when life style modification has not resulted in desired weight loss. In the absence of co-morbidities a BMI of 30 and above is the cutoff to consider drug therapy.<sup>27</sup> Only two drugs Sibutramine (Meridia, Reductil, Abbott laboratories) and Orlistat (Xenical, Hoffman-Laroche) are licensed for use in obesity by the Food and Drug Administration for long-term use.

**Table 4. Benefits of a 10kg weight loss (based on data from Scottish Intercollegiate Guidelines Network).**

<b>Mortality</b>	<b>Lipids</b>
Reduction	Reduction:
>20% total mortality	10% total cholesterol
>30% diabetes-related deaths	15% LDL
>40% obesity-related cancer deaths	30% triglycerides
	Increases:
	8% HDL
<b>Blood pressure</b>	
Reduction:	<b>Respiratory</b>
10mmHg systolic	Reduced sleep apnoea
20mmHg diastolic	Decreased breathlessness
<b>Diabetes</b>	<b>Gynaecological</b>
Reduction	Improved ovarian function and fertility in PCOS
50% fasting glucose	

Sibutramine is a centrally acting drug that inhibits nor epinephrine and serotonin re-uptake enhancing satiety and suppressing hunger. It also attenuates the fall in metabolic rate, which comes with weight loss. More than 10 prospective randomized controlled trials have supported its efficacy.<sup>28,29</sup> STORM trial<sup>30</sup> of 2 years duration showed that 69% of those receiving sibutramine achieved 5% weight loss and 46% achieved 10% weight loss. On an average systolic blood pressure increases by 4 mmHg and diastolic by 2-4 mm Hg and heart rate increases by 4 beats/min on patients taking sibutramine. It is therefore recommended that the blood pressure and the pulse rate be monitored regularly (2 weekly in the first 3 months, monthly between 4-6 months and quarterly thereafter).

Orlistat, an inhibitor of pancreatic and gastrointestinal lipases prevents absorption of approximately 30% of dietary fat. More than 11 prospective randomized trials have demonstrated its efficacy.<sup>28</sup> Orlistat reduces LDL,

decreases the progression to diabetes and leads to better glycemic control in diabetics.<sup>29</sup> It has no systemic side effects due to its lack of absorption. Gastrointestinal side effects due to its mode of action include loose stools, increased defecation, faecal urgency and oily anal discharge. Fat-soluble Vitamins Supplementation is recommended 2 hours before or after taking Orlistat.

Some antidepressant including SSRI'S and SSNRI affect body weight.<sup>31</sup> Fluoxetine is the most studied drug from this group and shows moderate weight reduction. These drugs are not approved for treating obesity but should be considered when treating depression in obese and overweight patients.

Many compounds are currently undergoing clinical trials as an anti-obesity agent including:

- ♣ Leptin or leptin receptor analogues that activate leptin signaling cascade distal to leptin receptor
- ♣ Rimonabant, an inhibitor of the cannabinoid - 1- receptor
- ♣ Amylin, a protein secreted by pancreatic beta cells
- ♣ Anti Ghrelin
- ♣  $\alpha$  MSH and MC4 receptor agonist
- ♣ GLP - 1 agonist
- ♣ CCK agonist

## Surgery

Life style modification has limited success resulting in no more than 10% of total body weight. Bariatric surgery is the only effective modality for long-term weight loss for severely obese patients.<sup>32</sup> They produce weight loss and maintenance of 30 - 40%.

The indications for bariatric surgery are morbidly obese patients with BMI >40 or obese patients with BMI > 35 with associated co-morbid.<sup>33</sup> Bariatric surgeries are of different types:

- ♣ Restrictive and Malabsorptive
  - Gastric bypass (open or laproscopic)
  - Biliopancreatic diversion with duodenal switch
- ♣ Restrictive
  - Vertical banded gastroplasty (stomach stapling)
  - Laparoscopic adjustable gastric band

A comparison of different bariatric surgeries is shown in Table 5.<sup>34</sup> These surgeries are associated with significant morbidity and mortality in inexperienced hands and in centers not geared for it. Peri-operative mortality of 1% and a complication rate of 10% are reported from experienced centers across the world. Adjustable laproscopic gastric banding is becoming the favoured approach because

**Table 5. A comparison of weight loss operation.**

	Gastric bypass	Biliopancreatic diversion with duodenal switch	Gastric Band
Duration of procedure	1 - 4 hours	2 - 5 hours	0.5 - 2 hours
Length of day	2 - 3 hours	2 - 4 days	1 - 2 days
Postoperative supplements	MVI, iron, calcium	MVI,iron,calcium,ADEK	MVI, calcium
Estimated weight loss	50 - 75% EBW	60 - 80% EBW	40 - 60% EBW
Side effects	dumping syndrome	diarrhea, excessive flatus, body odor changes	Vomiting
Short-term complications	DVT / PE, anastomotic leakage, pouch leakage, gastrointestinal bleeding	DVT / PE, anastomotic leakage, pouch leakage, gastrointestinal bleeding	DVT / PE, port-site infection, esophageal perforation
Long-term complications	gastrojejunostomy stenosis, iron deficiency anemia, calcium deficiency, B12 deficiency, marginal ulcer, internal hernia	iron deficiency, calcium deficiency, protein malnutrition, need for common channel revision, internal hernia	band slippage, device leakage, erosion into stomach/esophagus, pouch enlargement, device infection
Mortality rate	0 - 1 %	0.5 - 2.5 %	0 - 1 %

laproscopic gastric banding is becoming the favoured approach because of its reversibility and low morbidity. Excellent results have been reported for Europe and Australia. For unclear reasons the results of this surgery in USA is not very good.<sup>35</sup>

### Conclusion

Obesity is a chronic condition that predisposes patients to multiple serious health disorders and premature deaths. Body Mass Index is the most widely accepted measure of obesity in adults. BMI though established measure of obesity; waist circumference is gaining importance as it measures central obesity, which is an important risk factor for metabolic syndrome.

The prevalence of obesity is steadily increasing across the world particularly in developed countries. This epidemic will continue to plague our society for many years with all its medical consequences. Although influenced by genetics, the current obesity epidemic appears to be driven principally by environmental factors. Lifestyle factors of high-energy food intake and lack of physical activity are the greatest contributors to the energy imbalance that causes obesity. Treatment of obesity involves

dedicated and sustained lifestyle modification assisted by anti-obesity drugs, which has modest effect in losing weight of 5-10%. Our growing understanding of the complex mechanism of energy balance in our body will allow the development of newer and safe drugs in this field. Bariatric surgery is the only effective modality for long-term weight loss for morbidly obese patients.

Major efforts are needed to curb the escalating incidence of obesity globally. Prevention strategies should be targeted which involves lifestyle interventions. Individual and collective efforts at community and population levels are needed if we are to stem this epidemic. Despite prevention strategies, various treatment methods, eradication of obesity does not appear to be on the scene in the foreseeable future.

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