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## Introduction

Obesity is a chronic metabolic syndrome associated with high morbidity and mortality. It is now becoming *pandemic* with increasing incidence up to 50%. Obesity has unfavorable effects to the obese subject being a life long source of frustration, to the physician being one of the most challenging disorders with disappointing therapeutic outcomes, and to the community due to the high costs for management of its adverse consequences and loss of productivity (McDermott, 2001).

# **Assessment of obesity**

#### 1-Body mass index (BMI)

It is a measure of excess adipose tissue.

- **BMI: 20-24.9 kg/m<sup>2</sup>→normal**
- **BMI: 25-29.9 kg/m<sup>2</sup>→overweight**
- BMI: 30-34.9 kg/m<sup>2</sup> $\rightarrow$  class I (mild)
- BMI: 35-39.9 kg/m²→ class II (moderate)
- BMI: 40-49.5 kg/m²→ class III (morbid)
- BMI:  $\geq$  50 kg/m<sup>2</sup> $\rightarrow$  class IV (extreme)

Morbid obesity has been defined as BW that is 100% above ideal or BMI  $\geq 40 \text{kg/m}^2$ in association with substantial compromise in health and a ten-fold increase in the mortality rate (McDermott, 2001).

# 2-Waist /Hip (W/H) circumference ratio:

- Body fat distribution has been found to be a more determinant of the health risk consequences of obesity than the BMI.
- Central (android) obesity is associated with a greater risk than lower body (gynoid) obesity.
- Normal W/H ratio is <0.95 in males and <0.85 in females. In android obesity the ratio is > 0.95 in males and >0.85 in females.

#### 3-Waist circumference

- It is the best measure to risk stratify obese patients based on fat distribution because it represents the absolute amount of central body fat.
- It is useful in risk stratify overweight patients with BMI between 25-30 kg/m² where those with high waist circumference deserve greater efforts to prevent further weight gain while increased BW in those with smaller circumference does not pose major health hazards.

#### Waist circumference values (cm)

	Males	Females	
Normal	<94	<80	
Risk I	94-102	80-88	
Risk II	>102	>88	

(McDermott, 2001)

#### **Classification of obesity**

- 1-According to BMI: mild-moderatemorbid-extreme obesity.
- 2-According to fat distribution: android-gynoid. generalized –localized.
- 3-According to fat cell changes hyperplastic-hypertrophic.
- 4-According to the cause
- Interaction between genes and environment.
- Specific syndromes manifested with obesity:

#### a- Cushing's syndrome

b-Laurence-Moon Biedle syndrome (mental retardation-hypogonadism, polydactyly-retinitis pigmentosa, short stature and renal dysgenesis)

c-Pickwickian syndrome (obesityhypoventilation)

d- Hypothrodism.

# **Etiology of obesity**

Obesity arises when caloric intake exceeds energy expenditure leading to a positive caloric balance in addition to disturbance in the centers regulating body weight. Several factors play important roles in the development of obesity:

#### 1-Genetic factors:

A number of studies have shown that the tendency to gain weight in a modern environment is partially genetically determined. However, the prevalence of obesity has dramatically increased in the past 60 years at a time when there has been almost no change in the human gene pool. Therefore, the problem of obesity is a *classic interaction* between genes and environment.

#### **Mutations in the ob gene:**

■ The ob gene is an *odipocyte specific gene that encodes a hormone called leptin*. It was found that animals with ob gene mutations are obese and lose weight when given leptin. In humans, high leptin levels were found to be positively correlated with total body fat, suggesting that obese people are *insensitive to endogenous leptin (leptin resistance)* (McDermott, 2001).

#### Site of action of leptin:

Leptin is taken up by leptin receptors where it interacts with long leptin receptors within the hypothalamus. This interaction results in down regulation of neuropeptide Y expression leading to ↓ food intake.

### 2- Dietary factors:

- consumption of a high fat diet, because this diet produces obesity in experimental animals.
- Bad eating habits.
- Bad cooking habits

#### 3- Increase appetite:

- This plays an important role in obesity.
- Neural pathways regulating food intake are present in the hypothalamus, brain stem and peripheral nervous system, A number of neurotransmitters including norepinephrine, serotonin, cholecytokinin and neuropeptide Y act within specific brain nuclei particularly in the hypothalamus and play an important role in regulating not only total food intake but also preference for fat, carbohydrate or protein.

- 4-Decrease energy expenditure:
- There are 2 components of energy expenditure:
- 1-The basal metabolic rate (BMR).

- 2-The energy expenditure of activity.
- BMR is strongly related to lean body mass and almost no evidence suggests that obesity is caused by \$\dpres\$ BMR.

#### **Adverse consequences of obesity**

- 1- Cardiovascular:
  - HypertensionCAD
  - Stroke
     Thromboembolism
  - ↓ Red cell deformability
- 2- Metabolic:
  - Dyslipidaemia ↑ uric acid
  - Insulin resistance as assessed by insulin resistive index :
- Fasting insulin (mU/ml) x fasting glucose (mmol/L)/22.5
- If < 20 → insulin sensitivity</p>
- If > 20 → insulin resistance

- 3-Respiratory: Sleep apnea
- 4-Gastrointestinal:
- Cholesterol gall stonesGORD
- 5-Oncogenic:
- Male: cancer rectum, colon, prostate.
- Female: cancer breast, uterus, ovary.
- **6-Sex hormone abnormalities:**
- Male : ↓FSH, ↓ testosterone
- Female: ↑ estrogen → endometrial cancer.
- ↑ androgen → hirsutism, anovulatory cycles and dysfunctional uterine bleeding.

- 7-Musculoskeletal:
- Osteoarthritis.
- 8-Psychological:
- Depression anxiety
- 9-Increase mortality rate
- ↑ mortality in correlation with the severity of obesity due to the forementioned consequences. (Baliga, 2001).

# The new world syndrome (metabolic x syndrome) (Visceral fat obesity syndrome)

This syndrome is applied to obesity with large waist circumference (android pattern) due to 1 visceral fat. Adipose tissue located in the mesenteric bed has been found to be correlated more strongly with the adverse health consequences of obesity due to ↑ delivery of free fatly acids via the portal vein to the liver (Baliga, 2001).

The syndrome is a combination of metabolic, cardiovascular, endocrinal, oncogenic, immunologic and dermatologic manifestations

#### **Metabolic:**

- Insulin resistance or frank type 2 DM
- Android obesity
- Dyslipidaemia
- ↑ uric acid

#### Cardiovascular:

Hypertension

- LVH

- **Endocrinal:** 
  - Polycytic ovary disease
- Hypogonadism

- **Oncogenic:** 
  - High incidence of cancer
- **Immunologic:** 
  - Immunodeficiency
- **Dermatologic:** 
  - Acanthosis nigricans

(Douglas, 2002)

# Treatment of obesity

There are four modalities of treatment:

- Diet, Exercise, Drugs and surgery. The selected modality depends on the severity of obesity and the associated health problems.
- What is the appropriate goal for a weight loss program?
- 1-Mild and sustained weight loss through improving the habits of eating and activity.

- 2-Habit and behaviour changes should be slowly and gradually.
- 3-Any meaningful change in behaviour must be lifelong because of the biological basis of obesity; as soon as the individual stops the weight loss strategy, weight tends to return to its previous level.

# **(1)** Diet

The mainstays of dietary modification in weight loss therapy have been a diet low in fat and reduced in calories. Simple dietary suggestions include eating 3 meals per day, eating only at meal time and eating only one serving. These suggestions help patients to focus on what they are eating, making good food choices and controlling meal size.

Dietary approaches alone are not associated with a high level of success at achieving long-term weight loss (Blasiger et al., 2000).

# (2) Exercise

Exercise plays an important role in a successful weight loss program. Studies of body composition showed that diet plus exercise produce  $\downarrow$  BW with a much ↓ in fat mass and ↑ lean body mass. Although most experts advocate aerobic exercise, recent evidence suggests that a balanced program of strength training and aerobic exercise may be better than either alone (Collazo-Clavell, 1999).

# (3) Drugs

Various medications have been used in the past as amphetamines, thyroid hormone and diuretics to induce weight loss, but they have too many side effects to be acceptable. Recently longterm drug use is recommended where their expected useful effect can be gained and also because if patient lose weight with drug use then stop it, he will regain his weight again (Bray et al., 1999).

Alternatively, some persons use drugs only when they predict that there is difficulty in strict adherance to behavioural program including diet, exercise and smoking. Weight reduction with drug use improves health outcomes as evidenced by ↓ level of glucose, lipids and BP. However, the decision on whether the health benefits outweigh the risks and costs of drugs needs further studies. The commonly avaible drugs in use are given in table (2).

# Table (2): Drugs used in treatment of obesity

Drug	Mechanism of action	Advantages	Side effects
Phenteramine (Adipex P) (Fastin) (Lanomin)	Chemically-related to amphetamine with minimal addiction due to less dopaminergic effect. Acts on norepinephrine to ↓ appetite	Weight loss of 5-10% in 60% of users	-Not used for more than 3 months because of lack of long term study for its safety -Central stimulation leading to insomnia headache and tremors
Sibotramine (Meridia)	Combination of norepinephrine and serotonin reuptake blocker Acts by ↓ appetite - dose: 10-20 mg/d	-Weight loss of 8-10% - Used for one year or longer	- ↑ BP - dry mouth - headache - insomnia - nervousness
Orlistat (xenical)	Pancreatic lipase inhibitor, thus ↓ fat absorption Dose: 120 mg TDS with meals	-Weight loss of 7-8% on long term use - Enforces the subject to take low fat diet to avoid steatorrhea	Steatorrhea due to ↓ fat absorption and sometimes fecal incontinence
Herbal preparation (Ephedra)	<b>↓</b> appetite by acting on norepinephrine like phenteramine	↓ weight without side effects compared to phenteramine	<ul><li>Atrial arrhythmias</li><li>Not FAD approved</li></ul>

## (4) Surgery

#### **Indication:**

For morbidly obese with several medical complications due to obesity after failure of other approaches to  $\downarrow$  BW.

Operations: 1-Gastroplasty: results in small gastric pouch.

2-Gastric bypass: to bypass food absorption.

Results: Surgery offers the best long-term chance to ↓ BW (30%) with improvement of complications as ↑ glucose ↑ BP and dyslipidaemia.

The success rate is 60-70% (Blasiger et al., 2000).

