

INTRODUCTION

The 2016 Global Nutrition Report states that the rates of overweight/obese people are rising in every region of the world, and in nearly every country. The global adult obesity prevalence is 13% as against 4.9% in India, and for overweight, prevalence is 39% global and 22% for India, virtually indicating that one in four Indians has a weight problem of abundance. The World Health Organization (WHO) has declared obesity as the largest global chronic health problem in adults which is increasingly turning into a more serious problem than malnutrition. Obesity is a gateway to ill health, and it has become one of the leading causes of disability and death, affecting not only adults but also children and adolescents worldwide. In 2014, more than 1.9 billion adults (18 years and older) were overweight. Of these over 600 million were obese. 42 million children under the age of 5 were overweight or obese in 2013.¹

Obesity is defined as a disease process characterised by excessive body fat accumulation with multiple organ-specific consequences.² There are two ingredients integral to this definition- (i) excess body fat, and (ii) multiple organ-specific consequences.

MEASURES OF OBESITY

Body fat content can be measured by several methods,³ these are indicated in Table 1. The anthropometric measures are easy to perform, can be used in the field, but none of them is a true reflection of the content of obesity. Body mass index (BMI) is one of the commonest indices used to determine excess body fat. It is easy to measure using the formula- $BMI = (\text{weight in kg})/(\text{height in metres})^2$, and the criteria applied are universally accepted (Table 2). For the South Asians, the cut-off for abnormally elevated BMI is taken as ≥ 23 . However, body mass index can be fallacious specially if the weight of an

Method	Technique
1. Density-based methods	Hydrodensitometry (underwater weighing), Air Displacement plethysmography (ADP)
2. Scanning methods	CT, MRI, DEXA
3. Bioelectrical impedance analysis	
4. Anthropometric methods	Skinfold measurements, Waist circumference, Waist-hip ratio

individual is high because of increased muscle mass or oedema. BMI also does not truly reflect visceral adiposity. Similarly, another commonly used and advocated index is the waist circumference which is a better reflector of central or abdominal obesity. However, it cannot truly assess generalised obesity and can be fallacious in cases of liver disease or ascites. Waist circumference can also not distinguish between visceral adiposity and parietal (subcutaneous fat) adiposity. Waist circumference however can be a valuable adjunct to BMI, and can indicate visceral adiposity even in persons who have normal BMI. A waist circumference ≥ 80 cm (females) and ≥ 90 cm (males) is considered to be abnormal, and indicative of abdominal adiposity. Indians have a smaller body size, have excess body fat and greater truncal and abdominal obesity, and have lower average waist circumference. Therefore, the cut-off for obesity for Indians is $BMI \geq 23$, since even at lower BMIs, Indians (South Asians) carry excess morbidity risks than their western counterparts.

Waist to hip circumference is also employed in various clinical settings, however, it requires two measurements and hip circumference measurement can be an awkward thing to perform, be in a population setting or in clinics. Skin fold thickness measurements are also used in clinical practice, however it requires a trained person for measurement and can have greater inter-observer variability. Though it provides a good measure of the subcutaneous adipose tissue, the visceral adipose tissue is not directly measured. Apart from this, the skin fold callipers is costlier than the non-stretchable tape, weighing machine or the height scale, which are used to measure other anthropometric variables.

Density based methods are very costly, and seldom used

BMI	Classification	Co-morbidity Risk
< 18.5	Underweight	Low, but other problems
18.5-24.9	Healthy weight	Average
25-29.9	Pre-obese state (Overweight)	Increased
30-34.9	Obesity grade I	Moderate
35-39.9	Obesity grade II	Severe
≥ 40	Obesity grade III	Very severe

*For South Asians including Indians, the cut-off for overweight is ≥ 23 , and or obesity should be taken as ≥ 27.5

Table 3: Health consequences attributed to obesity

- Bronchial Asthma
- Gastro-esophageal reflux disease (GERD)
- Pancreatitis
- Osteoarthritis
- Sleep disturbance, sleep-disordered breathing, and obstructive sleep apnoea (OSA)
- Cancers of the
 - Breast
 - Ovaries
 - Endometrium
 - Gall bladder & Pancreas
 - Prostate
 - Colon & Esophagus
 - Renal cells
 - Leukemia
- Coronary heart disease (CHD) & cerebrovascular disease (CVD)
- Dyslipidemia
- Hypertension
- Venous thromboembolism in combined oral contraceptive users
- Stroke
- Pulmonary thromboembolism (PTE)
- Atrial Fibrillation
- Dementia
- Depression
- Diabetes, Metabolic Syndrome (Nonalcoholic fatty liver disease-NAFLD, polycystic ovarian syndrome-PCOS)
- Reduced fertility & reproduction in both sexes
- Pregnancy & birth complications

even in research settings. Imaging modalities are often used, and specially have been employed to assess regional fat distributions, as in visceral adiposity or subcutaneous adipose tissue deposits. Bioimpedance analysis which uses the delivery of an electric current is often used in research settings and can be considered to be a good indicator of the body fat tissue, minimising the handicaps of anthropometry and the huge costs of density-based methods or the radiation side-effects of scanning methods.

HEALTH CONSEQUENCES OF EXCESSIVE BODY FAT

Obesity translates in to presence of excess body fat, assessment of which has already been outlined. The health consequences of the presence of excess body fat, is the second component in the definition of obesity. Table 3 outlines the several morbidities that can be associated with the presence of excess fat. It is clear from a glimpse of Table 3, that obesity contributes to or worsens

Table 4: Primary Prevention of Excess weight gain (Overweight and obesity)

Reduce

- Energy-dense foods in diet
- Consumption of 'fast foods'
- Alcohol intake
- Reduce sedentary behaviour including watching television/working or playing on computers /Mobile watching

Encourage

- Physical activity and outdoor sport activities

allergic airway disease, cancers, degenerative diseases, inflammatory diseases, heart and cerebrovascular diseases, diabetes, fertility issues, and also sleep disorders and psychiatric morbidities. Therefore, the consequences can be troublesome and disastrous, and can result in even increased mortality. Hence, the need to control excess fat and maintain body weight.

NON-PHARMACOLOGIC MANAGEMENT OF OBESITY

The first part of management of obesity is spreading awareness about the ill-effects of obesity and preventing weight gain. Table 4 outlines the modalities for prevention of overweight and obesity.

However, once obesity or overweight has set in, the goals of management are different (Table 5).⁴ One has to realise that losing weight may not be an easy thing to do for many persons. At other times, some patients may be able to lose weight rapidly, but then they are unable to sustain it, and the lost weight comes back, and at times the weight regained is much more than what was lost. To restrict diet and to curb food intake that satisfies the taste buds, is no mean task. Therefore, management of obesity is a tricky situation. It is important to realise that the foremost thing is to aim at abolishing further weight gain. Once weight gain halts, then it is important to concentrate on gradual weight loss. Then, once the patient starts losing weight, then it is important to ensure that there is no weight regain. The last but not the least important goal in the management of overweight and obesity is that the health consequences of obesity should be curtailed, irrespective of the fact whether weight loss has been achieved or not. Reducing morbidities, or controlling morbidities and reducing risk of diseases will result in a better quality of life and also prolong productive life. Measures adopted to achieve these goals (Table 5) include lifestyle modifications which improve exercise capacity and instil in the patient a new confidence, thus improving the physical and psychological state of the patient's mind and thus improving patient's overall quality of life and longevity, as well. It will be pertinent to mention here that simply looking from the point of view of weight or BMI, a person who is overweight or mildly obese is unlikely to have obesity related co-morbidities and a 5-10% weight loss in such a patient will reduce likelihood of cardiovascular disease and metabolic risks. Patients, who

are moderately or severely obese viz. BMI ≥ 30 , are likely to have obesity related co-morbidities and in such patients 15-20% weight loss is required for sustained improvement in co-morbidities. A 5-15% weight loss over a period of 6 months is realistic and of proven health benefit. A greater

weight loss (20% or more) may be considered for greater degrees of obesity (BMI ≥ 35 kg/m²).⁴

Achieving weight loss requires a concerted effort comprising of physical activity, dietary change and behavioural modification. It is recommended to have at least 30-45 minutes of brisk walk as a physical activity which may be increased to 45-60 minutes of moderate intensity exercise on at least 5 days a week. This will translate into 225-300 min/week, which will be equivalent to 1800-2500 kcal/week. This should be supplanted by dietary changes incorporating calorie reductions inducing 600 kcal/day energy deficit. The dietary changes will need

Table 5: Goals of management in Overweight/obesity

- Prevention of excess weight gain
- Weight loss
- Prevention of weight regain
- Optimising health and reducing risk of disease (whether or not weight loss achieved)

Table 6: Three-pronged non-pharmacological strategy for managing overweight/obesity

- Increasing Physical activity
- Initially at least 150 min/week moderate aerobic exercise
- Combine with 1-3 sessions/week resistance exercise (single set exercise, using major muscle groups).
- Reduce sedentary behaviour
- Individualise programme keeping in mind physical limitations, if any

Dietary advice

- Reduce energy intake by 500-1000 kcal/day, although caloric restriction needs to be individualised
- Prefer Low energy dense foods (whole grains, cereals, fruits, vegetables & salads)
- Consume Low-fat, high fibre diet
- Eat more fruits, whole grains, vegetables, salads
- Avoid high energy dense foods (foods containing animal fats, other high fat foods, confectionery, sugary drinks) particularly large portions
- Avoid Sugary drinks and 'Fast foods'
- Consume fewer take-aways
- Decrease the size of food portions
- Avoid snacking between meals
- Do not skip breakfast and avoid eating in the night time
- Minimise alcohol intake

Range of appropriate psychological interventions and strategies includes:

- Self monitoring of behaviour and progress (food intake, exercise, weight)
- Stimulus control (where the patient is taught how to recognise and avoid triggers that prompt unplanned eating)
- Cognitive restructuring (modifying unhelpful thoughts/thinking patterns)
- Goal setting
- Problem solving strategies
- Assertiveness training
- Slowing the rate of eating
- Reinforcement of changes
- Relapse prevention
- Strategies for dealing with weight regain
- Psychological evaluation, counselling, and treatment, if needed
- Education (face-to-face meetings, group sessions, remote technologies)
- Stress reduction
- Motivational interviewing

Table 7: Medications causing weight gain

- Atypical antipsychotics including clozapine
- Beta blockers sp. Ppnl
- Insulin, SU, TZD
- Lithium
- Sodium valproate
- TCA including amitriptyline

to be individualised and the person's dietary preferences need to be taken in to account.

Table 6 outlines the three important facets of Diet alterations, Physical activity and Behaviour therapy which are required for obese patients aiming for adiposity reduction. It is also important to realise that certain drugs used for treating obesity-related co-morbidities, by themselves induce weight gain. Table 7 mentions certain such drugs. Also, it is pertinent to understand that such drugs should not be initiated or if already prescribed, should be possibly withdrawn or substituted. It is also imperative to understand that smoking cessation also causes weight gain, and in fact, it has been observed that trying to restrict weight gain in this subgroup of patients, can result in poor smoking cessation rates. Therefore, at times, weight loss measures may have to be stopped or delayed, depending on the individual case scenario.

PHARMACOLOGIC MANAGEMENT OF OBESITY

Pharmacotherapy for overweight and obesity should be used only as an adjunct to lifestyle therapy. Addition of pharmacotherapy produces greater weight loss and weight-loss maintenance compared with lifestyle therapy alone. Concurrent initiation of lifestyle therapy and pharmacotherapy should be considered in patients with weight-related complications that can be ameliorated by weight loss.

Orlistat is a potent and selective pancreatic lipase inhibitor, which because of its mode of action causes fat malabsorption. It is administered in dosages of 60-120 mg tid to be taken before each meal. Faecal fat loss and related gastrointestinal symptoms are common. Staining of undergarments and faecal leakage can at times be troublesome, and deficiency of fat-soluble vitamins is known to occur. Orlistat is contraindicated in pregnancy.

Phentermine is a sympathomimetic amine anorectic, approved for short-term (few weeks) weight management. The maximum adult dose is 37.5 mg once a day to be taken in mid-morning. Caution should be exercised since it can cause rise in blood pressure. It is contraindicated for use in patients with a history of cardiovascular disease and in pregnancy.

Phentermine/Topiramate extended release combination is available in four separate doses (3.75mg phentermine/23mg topiramate ER and 11.25mg/69mg are titration doses, while 7.5mg/46mg and 15mg/92mg are therapeutic doses. Initial dose of 3.75mg/23mg is prescribed as a 2-week course following which it is increased to the

'mid-range' maintenance dose of 7.5mg/46mg, which needs to be discontinued or escalated if people have not lost 3% weight after 3 months. At the maximum dose of 15mg/92mg, drug discontinuation should be tapered by taking a dose on alternate days for a week or more, before the treatment is stopped (if weight loss is < 5% of body weight with the maximum dose). Dose-dependent side-effects are known to occur viz. paresthesiae, dry mouth, constipation, dysgeusia, insomnia and dizziness. Topiramate has teratogenic risk and the preparation is contraindicated in pregnancy.

Lorcaserin- serotonin 2C receptor agonist, in a dose of 10 mg bid, independent of meals can be prescribed for weight management. If the recipient fails to lose $\geq 5\%$ of his weight 3 months after initiating lorcaserin, medication should be stopped considering the recipient to be a non-responder. Responder rate at 1 year was 48% compared to placebo (20%), and 68% subjects maintained the weight loss after a further year of lorcaserin treatment. Side-effects include headache, dizziness, nausea, fatigue, constipation, dry mouth and 2.3% had cognitive impairment. Symptomatic hypoglycaemia was reported in diabetes patients and hence, dose adjustments of diabetes medications may be required when prescribing lorcaserin to diabetes patients.

Naltrexone-Bupropion combination (8mg/90mg tablet)- Naltrexone is an opioid receptor antagonist while bupropion is a catecholamine reuptake inhibitor. These agents synergistically stimulate central melanocortin pathways and antagonise inhibitory feedback loops that limit weight reduction, leading to improved energy expenditure and reduced appetite. Maximum recommended dose is two tablets bid, and the weight loss effect should be assessed at 12-16 weeks and failure to lose 5% of the baseline body weight should warrant withdrawal of the drug. Side-effects include nausea, headache, vomiting, dizziness and constipation; the former three are the commonest causes for discontinuation.

Liraglutide 3.0 mg, a GLP-1 analogue, is approved for long-term weight management. GLP-1 is a physiological regulator of appetite and energy intake via GLP-1 receptors in the periphery and brain. Liraglutide-induced weight loss is mediated by its effects on appetite regulation (increased satiety, reduced hunger) and reduced energy intake. Common adverse effects are nausea, diarrhoea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain and increased lipase.

NEWER PHARMACOTHERAPEUTIC AGENTS UNDER INVESTIGATION

Bupropion/Zonisamide- Zonisamide is an anticonvulsant drug and its combination with bupropion is being tested in Phase II-III studies wherein the combination has resulted in 7.5% weight loss over baseline, with common adverse effects being headache, insomnia and nausea.⁵

Beloranib- belongs to a novel drug class that influences metabolism because of its selective methionine aminopeptidase-2 inhibition, resulting in reduced fat

biosynthesis and increased fat oxidation and lipolysis.⁵ Drug is being tested in Phase II-III trials with results indicating 5-10% weight loss over baseline. Adverse events witnessed were sleep disturbance, nausea and vomiting.

GLP-1 agonists other than liraglutide have also been tested for their efficacy in inducing weight loss. SGLT-2 inhibitors also induce weight loss in diabetics and are independently being investigated for inducing weight loss in obese individuals. Metformin, for a long time has been known to cause weight loss, and off-label has been used as a weight-reduction agent, because of its mode of action and safe side-effect profile.

BARIATRIC SURGERY

Although touted as a permanent cure for obesity, it is important to realise that active lifestyle interventions need to be continued even after the bariatric surgery procedure. The decision for this modality needs to be taken up on a case-to-case basis, evaluating the risk and the benefits for the individual. Bariatric surgery should be offered to severely obese patients with BMI ≥ 40 kg/m² in absence of coexisting medical problems and for BMI ≥ 35 kg/m² in the presence of one or more severe comorbidities which are expected to improve significantly with weight reduction (viz. mobility problems, arthritis, type 2 diabetes mellitus).^{2,4} Bariatric surgery should only be offered to patients who have failed to achieve success despite completing a structured weight management programme. Patients who regain excess weight ($\geq 25\%$ of the lost weight) and who do not respond to intensive lifestyle intervention, should be started on liraglutide 1.8-3.0 mg or phenteramine/topiramate ER, if they are not candidates for re-operation.

CONCLUSION

Obesity has gained pandemic proportions and increased adiposity in any form has adverse impact on morbidity and mortality. Body mass index combined with waist circumference, remain the most effective anthropometric parameters of use in the clinical practice and for taking decisions on when to intervene. Lifestyle management

remains the cornerstone for prevention of obesity and also for its management. Lifestyle measures include dietary modifications, increased physical activity and behavioural modification. Pharmacotherapeutic options can be valuable adjuncts to lifestyle intervention, but are ineffective alone. The long-term efficacy of pharmacotherapeutic agents (orlistat, lorcaserin, liraglutide, phentermine, phentermine-topiramate and naltrexone-bupropion) remains questionable and under investigation. Newer agents bupropion-zonisamide and beloranib are presently being investigated and appear promising. However, many agents have come in the market and have been withdrawn later because of serious adverse effects, rimonabant and sibutramine are some recent withdrawals from the market. Bariatric surgery can also be offered to severely obese patients who have failed to reduce weight despite adopting vigorous lifestyle interventions. Obesity management remains complex, but needs to be addressed with an open mind and an individualised approach, with emphasis on lifestyle interventions.

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