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Obesity: Causes and Consequences

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"***I guess I don't so much mind being old as I mind being fat and old***" – Benjamin Franklin (1706 – 1790)

Thus said one of the greatest visionaries and founding fathers of the United States of America in the 18th century AD. It is said that at the time of his death, Franklin, aged 84 years, weighed around 300 pounds. The world has changed much since the times of Franklin. But describing a person as 'fat' still carries the same old connotations and more. This is because being 'fat' (which is the everyday term as the lay man knows it) or 'obese' (which is the more scientific term) is not only a cosmetic concern but it is also one of the risk factors to major health problems like heart disease, diabetes, high blood pressure and stroke. Obesity is a condition of excessive fat deposition in the body to an extent that it adversely affects health. The world continues to grow 'fat', so much so that obesity is now prevalent in pandemic proportions. Once considered a malady of affluent nations, obesity is now a major public health concern even in developing and underdeveloped countries.

This write-up is an attempt to sensitize the reader about the rising incidence of obesity and its causes, summarize the associated health problems and discuss the unique features of obesity in the Indian context. A brief outline of the different measures of obesity and the author's opinion about perspectives for the future is also provided.

Causes of obesity:

Obesity is a multi-factorial disorder, and the roles of both genes and environmental factors are recognised. Although obesity tends to run in families, indicating a hereditary component, the classical Mendelian pattern of inheritance (typical of monogenic disorders) is elusive. Genome wide association studies (GWAS) have identified a number of susceptibility loci in the human genome which are supposedly associated with obesity. However, by and large, genes are now thought to set only the stage and provide the backdrop, against which the decisive effects are eventually driven by the environmental and behavioural factors. At the heart of the environmental and behavioural factors are those that influence diet and physical activity. Obesity occurs when a person regularly consumes more calories than needed. The excess calories are stored in the body as fat and manifest as obesity. In that sense, obesity can be thought of as an imbalance between energy intake and energy expenditure. Although rather simplistic, yet most of the cases of obesity in the present times conform to this view. Unhealthy diets (viz. junk foods high in refined grains, red meat, sugary drinks, and unhealthy fats, etc.) and physical inactivity (sedentary jobs, television watching, lack of physical exercise due to increasing automation in all spheres of life, etc.), which are typical of 'urbanization' and the 'modern lifestyle', have contributed enormously to this skewed balance between energy intake and expenditure, thus facilitating the spread of obesity. This sorry situation is often captured by the maxim "passive overconsumption of

energy". Thus, now-a-days it is not uncommon to come across a multitude of children, indulging in junk foods, video games and long hours of television watching who are obese from a very tender age (described in medical parlance by the term 'childhood obesity').

Having said that, it deserves mentioning that there are some conditions where a well characterized genetic defect is the cause of obesity. However, such instances are rare, and they are usually a part of some specific syndrome (e.g. Prader-Willi syndrome, Laurence-Moon-Biedl syndrome, Cushing's syndrome, Ahlstrom syndrome, etc.).

Measures of obesity:

The extent of obesity may be measured using various techniques, such as bioelectrical impedance, hydrostatic weighing, dual energy X-ray absorptiometry (DEXA), air-displacement plethysmography, and so on. But the most popular, convenient and inexpensive measures are perhaps the anthropometric measurements. Two indices are particularly noteworthy in this regard – body mass index (BMI) and waist circumference (WC). BMI, which provides a measure of relative weight adjusted for height, gives an estimate of leanness of the body and thus reflects the extent of overall or generalized obesity. On the other hand, WC is a measure of central or abdominal obesity, which indicates the extent of visceral fat surrounding the internal organs in the abdominal region around the waist.

Health consequences of obesity:

Obesity is a chronic medical condition. It can lead to several untoward health effects, involving different organ systems. Obesity is an important risk factor for hypertension (high blood pressure), coronary heart disease (responsible for heart attacks) and cerebrovascular diseases (responsible for strokes). It is strongly linked with dyslipidemia or derangements in lipid profile (such as increased low density-lipoprotein cholesterol, increased triglycerides, increased very low density-lipoprotein cholesterol, decreased high density-lipoprotein cholesterol) which favour atherosclerotic changes on the walls of blood vessels. Atherosclerosis constitutes the basic pathology of hypertension and coronary heart disease, and also a sizeable proportion of cerebrovascular diseases. Obesity (particularly central obesity) also has strong links with diabetes mellitus (DM). Increased intra-abdominal fat impairs insulin action. It promotes insulin resistance and predisposes to type 2 diabetes. In fact, central obesity is a major component for defining metabolic syndrome – a clinical entity, characterized by the presence of interrelated metabolic risk factors which predispose the affected individual to cardiovascular disease (CVD), DM and atherogenic dyslipidemia.

Obesity may also be associated with respiratory problems like 'obstructive sleep apnea' and 'obesity hypoventilation syndrome'. Obese individuals generally exhibit reduced chest wall compliance, increased work of breathing, decreased total lung capacity and functional residual capacity.

Obesity can impair the functioning of hepato-biliary system, as well. Obese individuals have a higher incidence of gall bladder stones, particularly cholesterol gallstones. Obese and overweight individuals are also at risk of developing fatty changes in liver, a condition termed non-alcoholic fatty liver disease (NAFLD). A healthy liver contains little or no fat. NAFLD occurs when fat molecules accumulate inside liver cells, frequently a consequence of obesity and excess fat tissue in the abdomen. In advanced stages, NAFLD can lead to serious liver injury, including cirrhosis (where the liver shrinks, becomes scarred and permanently damaged, subsequently causing liver failure).

Obesity is thought to increase the risk of cancer and cancer-associated mortality too. In males, this includes cancer of the oesophagus, colon, rectum, pancreas, liver and prostrate; while in females it includes cancer of the gall bladder and biliary tract, breasts, endometrium, cervix and ovaries. In addition, obesity can lead to gynaecological problems like abnormal menses and infertility.

Further, obesity is associated with problems of bones and joints like osteoarthritis and gout. It can lead to skin problems as well, viz. acanthosis nigricans (manifested by darkening and thickening of the skin folds on the neck, elbows and interphalangeal spaces), enhanced friability of skin, and increased risk of fungal infections.

To summarize, the adverse effects of obesity on health are multiple. It can compromise the normal physiology of different organ systems and produce far-reaching effects.

Obesity – the Indian scenario:

India is currently undergoing a major epidemiological transition, where nutritional deficiencies and infectious diseases, which were once the dominant health problems, are now being replaced by obesity and obesity associated conditions like diabetes, CVD, etc., largely due to demographic and lifestyle changes. Improvements in sanitation, nutrition, infectious disease control and advances in critical care have led to an enhancement of overall life expectancy. On the negative side though, these improved standards of living have brought about a detrimental shift towards inappropriate dietary patterns and a reduction of physical activities; hence the rising prevalence of obesity. The trends are alarming. A recently conducted phase-wise study by the Indian Council of Medical research (ICMR) revealed very high prevalence of both generalized and abdominal obesity. Projections for the whole country indicated 135, 153 and 107 million individuals with generalized obesity, abdominal obesity and combined (i.e. both generalized and abdominal) obesity, respectively. Further, a recent systematic review compiling data from 52 studies available from **16 states** of India revealed a combined prevalence of 19.3% for childhood overweight and obesity (i.e. roughly one in every 5 children). This is considerably higher than the earlier reported prevalence of 16% in 2001. This is of concern because childhood obesity is a precursor to obesity and other associated disorders in adulthood.

These statistics aside, obesity in Indians has some peculiar features too. For instance, the international cut-off points for anthropometric indices of obesity (BMI and WC) are not applicable for Indians and other south Asians (Pakistani, Bangladeshi and Sri Lankans). The recommended range for these indices in these populations is much lower than Western populations (Table 1). This is because people from Indian subcontinent are prone to develop obesity associated morbidities at lower levels of BMI and WC values as compared to other ethnic groups. Further, Indians also have an increased tendency to accumulate subcutaneous and intra-abdominal fat. Thus, Indians are at greater risk to develop obesity associated non-communicable diseases like DM and CVD. Infamously dubbed as the ‘diabetes capital’ and ‘heart disease capital’ of the world, Indians tend to deposit more fat in ectopic sites (e.g. liver) as well. Thus, conditions like NAFLD are also highly preponderant in Indians. Moreover even as neonates, Indian babies have smaller lean mass, but higher abdominal obesity in comparison to Caucasian babies – a phenotype referred to as ‘thin-fat Indian baby’.

Obesity indices	Cut-offs for Asian Indians	Cut-offs for other populations
BMI (kg/m^2)	Normal BMI: 18.0 – 22.9 Overweight: 23.0 – 24.9 Obesity: > 25	Normal BMI: 18.5 – 24.9 Overweight: 25.0 – 29.9 Obesity: > 30
WC (cm)	Abdominal obesity: males: > 90, females: > 80	Abdominal obesity: males: > 102, females: > 88

Table 1. Cut-offs for BMI and WC

While heredity, environmental influences and behavioural factors all seem to play important roles and work in tandem in the Indian context, a comprehensive explanation for the same is lacking. An interesting approach in that direction is examining the 'thrifty genotype' and 'thrifty phenotype' hypotheses. The former attributes the rising burden of obesity and diabetes to thrifty genes, which enhanced chances of survival in the past when food supplies were scarce and intermittent, but have become detrimental in the modern conditions of plentiful food and sedentary lifestyles. On the other hand, the 'thrifty phenotype' hypothesis subscribes to the view that the seeds for obesity and associated complications are sown right during the intra-uterine period. It suggests that foetal undernutrition leads to persistent metabolic and/or structural changes in the developing foetus (foetal origins of disease) – a phenotype that can sustain in the face of thrifty nutrition. Such a phenotype is advantageous if the nutrition stays poor in the post-natal period, but leads to obesity, insulin resistance and diabetes if food supply is surplus. This proposition is particularly attractive for the Indian scenario. This is because people in the Indian subcontinent have faced famines and undernutrition for multiple generations in the past, but now undergoing major lifestyle changes, improved standards of living and easy access to nutrition. In fact, studies in animal models suggest that multigenerational undernutrition leads to foetal metabolic programming such that subsequent nutrient recuperation does not reverse these metabolic changes, but increases the risk of obesity and diabetes instead. Epigenetic modifications in crucial positions of the genome are thought to underlie these changes.

Future perspectives:

Future challenges to biomedical researchers working on obesity are two-pronged. The first challenge is to come up with an integrative understanding of the biological mechanisms involved in obesity predisposition and causation. Relevant lines of investigation in this context include identifying susceptible genetic loci, finding hitherto unknown environmental and behavioural triggers, dissecting the gene-environmental interactions and relevant epigenetic changes, and characterizing the neurobiological regulation of appetite and caloric homeostasis completely. The second challenge is developing effective strategies for preventing and treating obesity. Although there are a number of options for tackling obesity, ranging from lifestyle management (dietary modification and exercise), pharmacological agents and bariatric surgeries, the results are often disappointing. Thus, it is not unsurprising to find people relating to one another the experience of "gaining weight is so easy, but losing weight is so hard". Exploring newer avenues of obesity management (e.g. non-exercise activity thermogenesis, shortly NEAT) is necessary. It is imperative that researchers, physicians, policy-makers, and various stake-holders join their hands and gear their efforts to address these challenges. With rapid urbanization and improved standards of living, it may be expected that the burden of obesity and the looming threat of its associated health consequences will increase even further.

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