Introduction
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Obesity is a serious public health problem that results from the imbalance occurring when energy intake exceeds expenditure. It is an abnormal condition by which excess of lipids accumulate in adipose tissue. Obesity is associated with numerous metabolic disorders, including diabetes mellitus, hypertension, hyperlipidemia, stroke, osteoarthritis and certain types of cancer \cite{Lei et al., 2007}. Obesity treatments are namely lifestyle changes, diet control, regular exercise, and pharmacotherapy. Many pharmacological approaches for the prevention and treatment of obesity have been suggested. Therapies for obesity include suppression of nutrient absorption and administration of drugs that control lipid utilization. Obesity is measured through the Body Mass Index (BMI), a simple index of weight-height relationship that indicates the amount of body fat which is used to classify overweight and obesity in adults. Obesity has been evident in the human record for over 20,000 years and it has affected numerous aspects of human life and society. It is a major chronic disorder affecting a large population in the world in 21\textsuperscript{st} century \cite{Barness et al., 2007}. Obesity and its complications are identified by WHO and top 10 countries are listed in Figure 1. The statistics of 2013 revealed that 2.1 billion people are obese in the world.

Obesity is a Universal health problem in both developed and developing countries. Obesity is a multifactorial disease, caused by sedentary life style. \cite{Figure 2} Obesity causes major risk factor for insulin resistance, type II diabetes, atherosclerosis, stroke, hypertension, impaired vascular function, sleep disorders, and some types of cancer including colon and breast cancers. \cite{Nisoli and Carruba, 2004}.

Thousands of years ago obesity was rarely seen. In 1997 the World Health Organization (WHO) formally recognized obesity as a global epidemic. As of 2008, the WHO claimed that 1.5 billion adults are overweight and out of these over 200 million men and nearly 300 million women are obese. In the age of 50- 60 years the rate of obesity is increased. This problem is increased in high income countries and obesity rates are rising worldwide. Overweight and obesity are the fifth leading risk for global deaths. At least 2.8 million adults die each year as a result of overweight or obese.

Prevalence of obesity

Obesity is a most serious health problem in the world. WHO estimated that 75\% are overweight and they are less than 5 year old and children’s with the age of 15
Figure 1: Global Obesity rate

A Hefty Increase

In 1980, 857 million people were overweight or obese; that number rose to 2.1 billion people in 2013, a study shows.

Global obesity rates

- Adults: 12%
- Children and adolescents: 4.9%

Top 10 countries ranked by number of obese people in 2013, in millions:

- U.S.: 86.9
- China: 62.0
- India: 40.4
- Russia: 29.2
- Brazil: 26.2
- Mexico: 24.9
- Egypt: 21.8
- Germany: 17.1
- Pakistan: 16.7
- Indonesia: 15.1

Source: www.wsj.com
Figure 2: Obesity caused by Diet and Sedentary lifestyle

Source: Adipopathy. J. AM coll Cardiol. 2011; 57(25):2461-2473
years and above are more prone to obesity. Hyperlipidemia is a big problem in obese people. The intake of saturated fat is increased, it is associate with the risk of cardiovascular disease and type 2 diabetes, which in turn is associated with the risk of Alzheimer’s diseases (Ohara et al., 2011).

Prevalence of obesity is increased in adolescents and children from 4.1 to 13.9% between 1975 and 1997 in Brazil, from 6.4 to 7.7% between 1991 and 1997 in China, and from 16 to 24% from 2002 to 2007 in New Delhi, India. Also overweight was more common in urban areas compared to rural areas, privately funded schools compared with government funded schools, girls compared with boys in India. In the year 2010 the medical cost for treating obesity was estimated that to be $72 billion and $198 billion, respectively.

Etymology

Obesity is from Latin word “Obesitat”. Obesitat means “stout, fat or plump”.

Global Scenario of Obesity

In 2005 WHO’s study indicated that approximately 1.6 billion adults were overweight and 400 million adults were obese. In 2015 approximately 2.3 billion people were overweight and more than 700 million would be obese. At least 20 million children under the age of 5 years are overweight globally in 2005. Obesity is prevalent not only in high income countries, but now a days, it has spread dramatically in medium and low income countries also (George and Nimmi, 2011).

Indian scenario of Obesity

In the year 1998 and 2005 statistics revealed that 20% people are overweight or obese. Presently women are overweight than men in India. In India obesity rate is increased dangerously to 70 million. Obesity rate in India is shown in Table 1.

Obesity is a disease in which the adipocytes are increased in size and number. Fat and glucose metabolism is mainly involved in obesity. Fat is synthesised and used by muscles for energy. The excess of fat is stored in adipose tissue.

Adipocyte was recognised in 1850 and published in the text book of microscopic anatomy. Growth and development of cells were described by Hassall in 1849 and Hoggan and Hoggan, 1879. They observed that fat vesicle and in certain type of obesity fat cell number is increased.
Adipose tissue

Adipose tissue is a major endocrine organ involved in storage of lipids and synthesis of adipokines. The development of obesity within the adipose tissue takes place by three processes. They are

1. Adipocyte hypertrophy (increase in cell size)
2. Adipocyte hyperplasia (increase in cell number). (Figure 3)
3. Angiogenesis (Avram et al., 2007; Hausman et al., 2001; Smas and Sul, 1995).

Adipose tissue is a major energy reservoir in the body; it stores energy in the form of glycogen and triglycerides and releases it on demand. Adipose tissue is categorized into two types based on the function of adipose tissue

- White adipose tissue (WAT)
- Brown adipose tissue (BAT) (Figure 4)

**White adipose tissue (WAT)**

WAT is one type of adipose tissue. WAT adipocyte diameter is on average 60-100μm (Fonseca-Alaniz, et al., 2007). (Figure 4, 4a) Fat is stored as an energy reserve
in WAT, and released in blood stream as fatty acids to be used by the organs (Cannon and Johansson, 1980). It is also involved in lipolysis (Figure 4b).

Lipolysis is one of the process that taking place in WAT. It is associated with obesity. During this process free fatty acids and glycerol are released from triglycerides by Lipoprotein lipase. Luminal surface of capillary endothelial cells has a site for Lipoprotein lipase (LPL), and it is involved in hydrolysis of triglycerol (Cryer, 1981). This process is stimulated when the energy is needed by organism. It is involved in the development of insulin resistance when stimulation of lipolysis is not activated. (Reynisdottir et al., 1995; Large et al., 1999). It plays an important role in energy metabolism. Insulin is released from the pancreas and insulin receptors of white adipose cells cause a dephosphorylation cascade that lead to the inactivation of hormone-sensitive lipase (HSL). When Glucagon is released from the pancreas, glucagon receptors cause a phosphorylation cascade that activates HSL, causing the breakdown of the stored fat to fatty acids, which are bound with albumin and transported in blood freely. Muscle and cardiac tissue take up free fatty acids as a fuel source and glycerol is

Figure 3: Hyperplasia and Hypertrophic adipocyte formation

from preadipocyte

Source: www.cell.com
taken up by liver for gluconeogenesis process. White adipose tissue secretes adipokines which cause many diseases like, Cardiovascular and metabolic diseases. Adipokines includes leptin, resistin, adiponectin, TNF-α and plasminogen activator inhibitor-1 (PAI-1) (Trayhurn and Beattie, 2001; Friedrichs et al., 1995; do Nascimento et al., 2004).

**Brown adipose tissue (BAT)**

BAT adipocytes are about 30-40μm diameter in size (Figure 4) (Fonseca-Alaniz, et al., 2007). BAT is another type of adipose tissue. BAT is mainly involved in producing heat energy (non-shivering thermogenesis). BAT is brown-reddish colour. This colouration is mainly due to the presence of large number of mitochondria and red cytochromes in large amounts. Major function of BAT is in heat production during fatty acid oxidation, and also involved in maintaining the body temperature and regulation of energy expenditure (Hull and Segall, 1966; Lafontan and Berlan, 1993).

Brown adipose tissue oxidizes free fatty acids to generate ATP and this was explained by Jens Nedergaard and colleagues in 1980 and they discovered a protein named as ‘thermogenin’ (Cannon et al., 1982).

**Morphology of BAT (Figure 4)**

Based on the morphological studies of BAT proved that BAT contains mature brown adipocytes (~40%), endothelial cells (~40%), adipocyte precursors and mast cells (Bukowiecki et al., 1986; Geloen et al., 1990; Himms-Hagen et al., 1992).

Based on the quantitative analysis WAT and BAT is distinguished. Based on the lipid accumulation pattern it is differentiated. BAT is unilocular and due to this nucleus is pushed away. WAT are multilocular that is it contains multiple small triglyceride droplets. BAT function is inactive, which means that lipolysis is not taking place. Another one indication is density of mitochondria. BAT contains more mitochondria density and cristate organisation, whereas in WAT the mitochondria density is much lower. Based on the qualitative method adipocytes are distinguished by the presence of protein uncoupling protein-1 (UCP1) or thermogenin in the inner membrane of brown adipocyte mitochondrion.

Triglycerol (TAG) contains three fatty acids esterified to form a glycerol. It is a neutral lipid. The esterification takes place between three hydroxyl groups (-OH) on the
Figure 4: Structure of White adipocyte and Brown adipocyte

Source: www.nature.com

Figure 4a: Adipocyte structure

Source: barbsfitublog.wordpress.com
glycerol and carboxyl groups (-COOH) on all three fatty acid molecules. TAG act to protect the body from heat loss which act as padding for organisms (Budd et al., 1991). TAG plays an important role in transport of free fatty acids to different tissues of the body (Yen et al., 2008). TAG has crucial role for the water barrier on skin surface (Downing et al., 1987) and is involved in energy storage mechanism. It is also one of the promising components of stratum corneum lipids. Excessive amount of TAG accumulation in adipose tissues leads to the condition called obesity (Allison and Saunders, 2000). Excess of TAG accumulation in nonadipose such as liver, heart, skeletal muscle leads to insulin resistance, nonalcoholic steatosis of liver and it is otherwise called as non-alcoholic steatohepatitis and cardiomyopathy (Unger, 2002; Friedman, 2002).

Fat cells

The fat cells estimated is from the total amount of body fat and the average size of the fat cells (Feinstein, 1960) because fat cells differ in size and different regions of
the fat cell in the body. In adults the upper limits of the total normal fat cells range from 40-60x 10^9. The number of fat cells increases most rapidly during late childhood and puberty. It may increase in adult life but 3-5 fold increase in childhood or adolescence. Classification of obesity is based on the number of adipocytes and distribution of body fat or characteristics of localized fat deposits (Stunkard and McLaren-Hume, 1959).

Based on the size and number of adipocytes, obesity is classified into two types they are,

- **Hypertropic obesity**
- **Hypercellular obesity**

**Hypertrophic obesity**

Enlarged fat cells are the important pathological sign to quantify obesity. (Scoville, 1973; Atkinson, 1993) Enlarged fat cells tend to correlate with an android or truncal fat distribution and are often associated with metabolic disorders such as glucose intolerance, dyslipidemia, hypertension and coronary artery diseases.

**Hypercellular obesity**

An increased number of fat cells usually occur when the obesity is in childhood and it might begin in early or middle childhood. This type of obesity tends to be severe (Bray, 1995). It also occurs in adult life and this is to be expected when the BMI is > 40kg/m^2.

Fat accumulation is in the form of Lipomas and lipodystrophy.

**Lipomas and Lipodystrophy**

Fat accumulation includes single lipomas, multiple lipomas, liposarcomas and lipodystrophy. Lipomas vary in size from 1cm to >15cm. Multiple lipomatosis is an inherited disease transmitted as autosomal dominant trait. Liposarcomas are relatively rare representing <1% of lipomas. They tend to affect the lower extremities and it has four types,

- Well differentiated Myxoid
- Poorly differentiated Myxoid
- Rounded cell or adenoid
- Well differentiated Myxoid and poorly differentiated Myxoid
Lipodystrophy

Loss of fat in one or more region of the body is known as lipodystrophy (Rossner, 1992). It can be occur mainly by genetic cause or may be acquired. Familial partial “Lipodystrophy” is a genetic defect due to an alteration in the laminin A/C gene and protein produced by this gene.

On the basis of distribution of excess of body fat accumulation obesity is divided into following three categories.

- Android (Apple Type)
- Gynoid(Pear Type)
- The third type

Android (Apple Type)

Apple shape of obesity is called Android type obesity. This type is most common in both men and women. Females under hormone treatment, for their menstrual abnormalities or after child birth, are more prone to this type of obesity. It occurs in females around menopause due to thyroid gland’s functional disturbance. In this type the patient’s shoulders, face, arms, neck, chest and upper portion of the abdomen are bloated and stomach gives a stiff appearance. The people the arms, shoulders and breast became so stiff. The neck is compressed and back seems to be erect and protruding chest due to the bulk in the stomach. Compared to upper part, lower part of the body like the hips, thighs and legs is so thinner. In this case most of the organs affected are heart, liver, kidneys and lungs. Major risk is cardiac problem due to increased levels of cholesterol (Patidar, 2013).

Gynoid (Pear Type)

In this type the body has extra flesh in lower part. This type is seen in both the sexes but females are more affected. The flesh is flabby in the abdomen, thighs, buttocks and legs, face and neck appears normal. If person grows and become older they have stooping posture and the spine is never erect due to the heavy hips and thighs. Many organs like kidneys, uterus, intestines, bladder and bowls are affected. In this type of exercises or dieting will not at all help for reducing the weight.

The Third Type

Most of the people belong to this type of obesity. Their whole body from head to toe looks like a barrel. Their gait is more like rolling rather than walking. The
movement is affected mainly due to fat tissues hindrance. So such persons should follow a strict diet and do plenty of exercise.

**Childhood and adolescent obesity**

Childhood obesity is a major clinical problem in both developed and developing countries. Prevalence of obesity increases 3 fold. This is emerging pandemic results from genetic and environmental factors, intake of high calories and physical inactivity. 22 million of children under the age of 5 are obese and one in 10% is overweight. National survey of USA from the 1960-1990, the prevalence of childhood obesity and over weight is increased by 5-11%. Physical inactivity and sendentary life style is main reason for obesity. Increased cholesterol and blood pressure is found in 25% of children with the age of 5-10 years. Fibrous plaque in arteries is one in ten of teenagers and young adults. It is studied by autopsy (*Freedman et al., 1999*).

Children consume more soft drinks with high calories diet (55-190 Kcal/day), also consuming lot of candy and sugar added beverages and these are reason for overweight and obesity. The consequences are similar to that of adults.

**Classification of obesity in children and adolescents**

Obesity classification is difficult in both children and adolescents because criteria are similar to adults. Adiposity is associated with morbidity and mortality. BMI and skin method is used to measure the adolescent obesity. Traditionally, weight for height is above the 90\(^{th}\) percentile in growth chart means they are obese. The median is 120 per cent. In case of super obese it is above the 95\(^{th}\) percentile in growth chart and median is 140 per cent. The recent study proved that overweight had BMI value above the 80th percentile while a value greater than the 95\(^{th}\) percentile was indicative of obesity. WHO study showed that overweight is defined as >85\(^{th}\) percentile of BMI, subscapular skinfold for >90th percentile for age adolescent obesity. Hyperlipidemia is the major reason for obesity. Plasma lipids consist of triacylglycerols (16%), phospholipids (30%), cholesterol (14%), and cholesterylesters (36%) and a much smaller fraction of unesterified long-chain fatty acids (4%). This latter fraction, the free fatty acids (FFA), is metabolically the most active form of the plasma lipids.

**Distribution of fat**

Measuring fat distribution of subcutaneous versus visceral compartments is important because visceral fat predicts development of health risks better than total body weight. Body fat distribution is measured by various techniques. The ratio of waist
circumference is divided by hip circumference-waist hip ratio is assessed. Reliable estimation of visceral fat is done by computed tomography (CT) (Munro et al., 1968) or magnetic resonance imaging (MRI) and it is used for the identification of dyslipidemia also (Mathus-Vliegen et al., 1992 and Andersen et al., 1992).

Causes of obesity

Lack of Energy Balance

Energy imbalance most often causes overweight and obesity. Energy balance means that energy or calories got from food and drinks and energy used for breathing, digesting, and being physically active. Both the energy used and energy expenditure must be equal. If energy expenditure is lower than energy intake it causes overweight.

Cushing’s Syndrome

Cushing’s syndrome is another one reason for obesity (Ahlskog and Hoebel, 1973). Different diagnostic methods are available for obesity caused by Cushing’s syndrome and pseudo-Cushing’s syndrome. It is clinically important for therapeutic diagnosis.

Hypothyroidism

Patients with hypothyroidism frequently gain a weight because of less metabolic activity. Some cases gain weight due to fat. This is common in Hypothyroidism of older women. In this condition, measurement of thyroid-stimulating hormone (TSH) is a valuable diagnostic tool (Leibowitz, 1970).

Polycystic Ovary Syndrome (PCOS)

Polycystic ovary syndrome is one of the reasons for weight gain in women. Irregular menstrual cycle is due to congenital adrenal hyperplasia and androgen secreting tumors (Wellman, 2000). The increased level of TSH, Prolactin, Follicle stimulating hormone (FSH), Plasma testosterone, dehydroepiandrosterone, hydroxyl-progesterone is one of the reason for weight gain. 97% weight gain is due to PCOS.

Growth Hormone (GH) Deficiency

Growth hormone is decreased in lean body mass person and increased in obese people. Growth hormone replacement reduces the body fat and visceral fat (Tsujii and Bray, 1992). In case of Acromegaly there will be an opposite effect with reduced body fat and particularly visceral fat. Age also plays a major role in obesity.
Drug Induced Weight Gain

Several drugs can cause weight gain, including a variety of psychoactive agents (Leibowitz, 1970) and hormones. The degree of weight gain is generally not sufficient to cause true obesity, except occasionally in patients treated with high-dose of corticosteroids, some psychoactive drugs, or valproate. Regular treatment with drug may lead to weight gain.

Cessation of Smoking

Obese people stop smoking and this lead to weight gain. Weight gain of 1–2 kg in the first few weeks is often followed by an additional 2- to 3-kg weight gain over the next 4–6 months. Average weight gain is 4–5 kg (Susulic et al., 1995). After cessation of smoking people are prone to eat much more than during smoking and so they become obese.

Sedentary Lifestyle

Sedentary lifestyle lowers energy expenditure and promotes weight gain in both animals and humans. In an affluent society, energy-sparing devices in the workplace and at home reduce energy expenditure and may enhance the tendency to gain weight (Samarin and Garattini, 1993). In children there is a graded increase in BMI as the number of hours of television watching increases (Heal et al., 1998).

Diet

The amount of energy intake relative to energy expenditure is the central reason for the development of obesity. However, diet composition is most important in its pathogenesis.

Breast feeding

Lots of recent publication has suggested that breastfeeding may reduce the prevalence of obesity in later life. In a large German study of more than 11,000 children, (Blundell et al., 1995 ; Leibowitz et al., 1987) showed that breast feeding reduced the incidence of overweight, but not obesity. However, the potential that breastfeeding can reduce the future risk of obesity is another reason to recommend breastfeeding for at least 6–12 months.

Overeating

Overeating (repeated ingestion of energy exceeding daily energy needs) can increase body weight in normal weight men and women. When people stop overeating, they lose their weight automatically. Over eating protocol can influence the genetic
pattern in over weight (Dryden et al., 1996). Childhood obesity is mainly due to over eating and less physical activity.

Dietary Fat Intake

High-fat diet is associated with obesity. The relative weight in several populations, for example, is directly related to the percentage of dietary fat in the diet (Kennett et al., 1987). High-fat diet foods into the diet, with a corresponding increase in energy density (i.e., lesser weight of food for the same number of calories) can leads to obesity. This makes over consumption in which glucose stored as glycogen in liver and muscle is limited, and needs to be replenished frequently. This contrasts with fat stores, which are more than 100 times the daily intake of fat. This difference in storage capacity makes eating carbohydrates a more important physiologic need that may lead to overeating when dietary carbohydrate is limited and carbohydrate oxidation cannot be reduced sufficiently.

Dietary Carbohydrate and Fiber

Body weight gain is mainly due to the consumption of high amount of sugar and sugar sweetened beverage which are consumed by children daily and it enhances the risk of rapid weight gain (Hammer et al., 1990). High fiber consumption has a lower prevalence of obesity (Braddon et al., 1986). Fiber intake may also be inversely related to the development of heart disease and diabetes.

Dietary Calcium

Goodall and Silverstone, 1987 reported that there was a negative relationship between BMI and dietary calcium intake in the data collected by the National Center for Health Statistics. More recently Li et al., 1994 found that there was a strong inverse relationship between calcium intake and the risk of having the highest value of BMI. These data suggested that low calcium intake plays a role in the current epidemic of obesity.

Frequency of Eating

The continuous consumption of food intake, high intake of glucose and lipid also increases the obesity. In the case of normal individuals, if they consume lot of small meals for a day they have low serum cholesterol concentrations, if they eat large meals also they maintain the cholesterol level. Blood glucose concentration changes when meals are taken regularly (Nichols, 1986). Insulin secretion is associated with larger meals.
Restrained Eating

Limited food intake pattern is called “restrained” eating (Lemaire et al., 1985). It has also an inverse relationship to body weight and social class. Women of upper socioeconomic status often use restrained eating to maintain their weight. In weight loss, higher restraint scores were associated with lower body weights (Dunn et al., 1978). Weight loss was associated with a significant increase in restraint, indicating that higher levels of conscious control maintain lower weight.

Binge-Eating Disorder

Binge eating disorder is a psychiatric illness characterized by uncontrolled eating, usually in the evening. The patient may respond to treatment with drugs that modulate serotonin.

Night-Eating Syndrome

The night eating syndrome is the consumption of at least 25% (and usually >50%) of daily energy intake between the evening meal and the next morning (Balcioglu and Wurtman, 1998; Gadde et al., 2001). It is related to sleep disturbances.

Psychological and Social Factors

Psychological factors in the development of obesity are widely recognized. The weight gain is seasonal affective disorder (SAD) and depression that occurs during the winter season in some people living in the North and it is for short period. Body weight is increased in these patients in winter. This condition is treated effectively by providing higher-intensity artificial lighting in the winter (Anderson, et al., 2002).

Socioeconomic and Ethnic Factors

Obesity is more prevalent in lower socioeconomic groups. Overweight is found in both adults and children. Paul et al., (1982) reported that socioeconomic and BMI were inversely related. People of higher socioeconomic were more concerned with healthy weight control practices, including exercise and tended to eat less fat food.

Genetic and Congenital Disorders

Leptin and ghrelin influence appetite and ghrelin are produced by the stomach modulating short-term appetitive control. Leptin is involved in long time appetitive control. The leptin deficiency causes obesity and is rare in humans, which correspond to the obese (ob/ob) mouse animal model (Angel et al., 1986; Hauger et al., 1986; Angel et al., 1987). Leptin is a 167–amino acid protein produced in adipose tissue, the
placenta, and possibly other tissues that signals the brain through leptin receptors. Fat children are hypogonadal, are not hypothermic or endocrine deficient. A defect in the leptin receptor may lead to obesity. Discovery of leptin, ghrelin, insulin, orexin, PYY3 36, cholecystokinin, adiponectin have also been studied. The adipokines and cytokines are mediators produced by the adipose tissue for many metabolic pathways.

**Measurement of obesity**

Various methods are used for the measurement of obesity and fat accumulation. There are

**Weight and height**

Weight and height are simple method to measure body size. It is inexpensive than other methods. Weight is highly correlated with body fat, but it also correlates with height. The weight and height is more useful indicator for overweight (Power et al., 1997). Weight and height is categorised into two types, they are

1. Relative weight
2. Power type indices

**Relative weight**

It is a common method to measure overweight children. The average weight of people of the same height requires the use of tables of expected weight for the child’s height and sex (Gibson, 1990).

**Power type weight and height indices**

Other than this the height and weight tables have been used to measure the relative weight to the power of height (wt/ht(n)), such as the ponderal index (ht/wt –1/3), Rohrer index (wt/ ht^3), Benn’s index (wt/ htp) and the Quetelet index or the body mass index (wt/ht^2).

**Skinfold thickness**

This method is used for total body fat prediction at various anatomical sites of the body. It used in both children and adolescents (Rolland-Cachera, 1993). In case of children of adolescence, the most common site for adiposity is the subscapular skinfold measurement, truncal body fat and triceps skinfold is determined by this method. Different types of skinfold measurement is used, and that triceps skinfold correlates positively with artherosclerosis index and systolic blood pressure, and negatively with high-density lipoprotein cholesterol (Kanda et al., 1997). It is also an inexpensive method.
Limitations

- It is not an accurate method.
- Very difficult to measure individuals with a BMI of 35 or higher.

Body mass index

The body mass index (BMI) is the most widely accepted method to determine obesity (Kushner, 1993). BMI is defined as weight in kg divided by height in meters, squared. Since cardiovascular risks begin to increase, when BMI increases above 25, they are clinically overweight individuals. If BMI < 25kg/m² are considered as normal, between 25-29kg/m² are overweight and BMI is >30kg/m² are consider as obese. BMI is proposed both by the major national and international health organisation for obesity measurement. Epidemiologic studies have established relationship between BMI and mortality. Table 2 shows the BMI classification.

\[
\text{BMI} = \frac{\text{Weight (kg)}}{(\text{Height})^2 (\text{m}^2)}
\]

Relationship between body weight and height was explained by Belgian mathematician. It is called as Quetelet index or Body mass index (BMI) (Quetelet, 1994). It is simple method to calculate BMI and it is an excellent screening tool in the assessment of total body adiposity. Total body weight in the numerator does not discriminate lean and fat body mass. Normal weight individuals with excess body fat will not be diagnosed as being overweight and adults with high body mass such as those with increased muscle mass may be classified as obese. WHO reveals statistical analysis that shows comparison with BMI and Obesity. Criteria for obesity (body fat-25% in men and 35% in women as measured by bioelectrical impedance) revealed a pooled sensitivity of 50% to identify excess adiposity and a pooled specificity of 90% indicating that half of the patients with excess body fat were not diagnosed as obese (Romero-Corral et al., 2008). There is evidence that the BMI criteria used for diagnosis of overweight and obesity are not independent of age, gender, and ethnicity (Gallagher et al., 1996).

Obesity in Adult

Obesity in adult is measured by BMI calculation. It is a precise method. Table 2 shows BMI classification of obesity. Waist/hip ratio (WHR) indicates the abdominal fat
accumulation. But it cannot predict the risk. A lower BMI cut off point for over weight is $\geq 23\text{kg/m}^2$ and for Asians it is $\geq 25.0\text{kg/m}^2$.

**In children and adolescents**

BMI, weight for height and skinfold thickness is used. But BMI is the most accepted method to measure adiposity in children and adolescents. WHO reference for BMI in the age 5-19 years are around 17.

**In Elder Patients**

Accumulation of abdominal fat is higher than adult and adolescents. Anthropometric, Waist circumference, Waist hip ratio and sagittal abdominal diameter is most commonly used. They have the common risk of cardiovascular diseases.

**Waist Circumference**

Waist Circumference is another less expensive method to assess obesity. Obesity is correlated with imaging techniques and high association with cardio-vascular disease risk and mortality. But it has some practical limitations including the location of measurement and cut-off values (Pouliot et al., 1994, de Koning et al., 2007). For each measurement site we still need values that predict cardiovascular disease morbidity and mortality.
Hip Circumference

Hip circumference (HC) is not a significant predictor of all types of mortality. It is used to calculate the waist/hip ratio (WHR) (Mason et al., 2008). It is measured at the level of the widest circumference at the buttocks because wider hips imply and provide protection against cardiovascular disease (Snijder et al., 2004).

Waist-hip circumference ratio

Waist hip circumference ratio is another method to measure the regional fat distribution in the body and is often used as a marker for intra-abdominal fat accumulation. In adults there are gender differences in accumulation of intra-abdominal fat, which appears to be independent of the total amount of body fat (Lemieux et al., 1993). Caprio et al. (1996) explained about positive correlation between visceral fat mass and triglycerides and inverse relationship with high-density lipoprotein cholesterol in obese adolescent girls. In the case of male android pattern of fat distribution is seen. Where as in females, body fat tends to accumulate in the thighs and buttocks. It results in a peripheral or gynoid pattern of adiposity. WHR ratio increase >1.0 for males and > 0.8 for females. It has greater risk of chronic diseases such as hypertension, stroke and ischemic heart diseases. In children and adolescents, excessive intra-abdominal fat accumulation is associated with cardiovascular risk factors. Waist hip ratio and waist circumference have been significantly associated with intra-abdominal fat (Despres et al., 1991). Recent studies showed waist circumference is the most single anthropometric measurement for assessment of visceral adipose tissue (Pouliot et al., 1994; Lemieux et al., 1996). It correlates well with BMI, intra-abdominal fat mass and cardiovascular risk factors. In case of women who showed reduced waist circumference during weight loss indicates reduced risks of cardiovascular diseases. Brambilla et al., (1994) explained that adiposity in children has subcutaneous pattern and that there is no difference between sexes. MRI technique is used to assess peripheral and intra-abdominal adipose tissue in obese and non-obese 10-15-year-old children.

Limitations

- Lot of error occur during measurement, because it requires two measurements.
- More complex to interpret than waist circumference, since increased waist-to-hip ratio can be caused by increased abdominal fat or decrease in lean muscle mass around the hips.
- Two people with different BMI could have the same WHR.
• May be difficult to measure and less accurate in individuals with a BMI of 35 or higher.

**Dilution Method (Hydrometry)**

Isotope labelled water is given orally to the patients. Body fluids are collected for analysis. Based on the isotope levels fat free body mass, body fat mass and total body water is calculated (*Hu, 2008*). It is accurate, low cost and safe method. It is used if BMI is >40.

**Limitations**

• The ratio of body water to fat-free mass may change during illness, dehydration, or weight loss, decreasing the accuracy.

**Sagittal Abdominal Diameter**

Sagittal abdominal diameter (SAD) can be measured by CT or MRI. This is the better method of abdominal visceral fat, metabolic disorders and coronary arteries disease than WHR (*Iribarren et al., 2006; Onat et al., 2004*). For SAD measurement it has been standardized and validated in normal thresholds. Weight and size is increased in CT.

**Anthropometry**

Muscle mass is determined by measuring the mid-upper arm and mid-thigh circumference. Obese people strongly need to assess the accuracy and reliability of these measurements and their clinical importance is unclear (*Sebo et al., 2008*).

**Dual-Energy X-ray Absorptiometry**

This is used for the attenuation of radiation at two different energy levels to determine fat tissues. It is the best method for assessment of body fat. This method is used to estimate body fat in adults and children (*Van Der Ploeg et al., 2003*). DEXA method is best when compared with CT scan because very little amount of radiation is used for repeated measurement.

**Limitations**

• Equipment is expensive and it cannot be moved from one place to another.
• It cannot be accurate.
• It should not be used with pregnant women, since it requires exposure to a small dose of radiation.
• Most current systems cannot accommodate individuals with a BMI of 35 or higher.
**Bioelectric Impedance Analysis**

This method is influenced by gender, age, disease state, race and ethnicity level of adiposity, environment, menstrual cycle and underlying medical conditions (Rush et al., 2006, Dehghan and Merchant, 2008). Electric conductivity of tissues is used because it depends on their water and dissolved ion content. Fat and bone are relatively nonconductive. A small alternating single frequency current is passed through electrodes attached to body extremities like wrist or ankle and the impedance is measured, and an estimation of total body water estimation is obtained. This method is a reliable method.

**Limitations**

- Hard to calibrate.
- The ratio of body water to fat may be change during illness, dehydration or weight loss, decreasing the accuracy.
- Not as accurate as other methods, especially in individuals with a BMI of 35 or higher.

**Complications of obesity**

Obesity induce many complications like diabetes mellitus, cancer, coronary heart diseases, Gallstone formation, Osteoarthritis, sleep apnoea, respiratory problem, polycystic ovary syndrome, hypertension, steatohepatitis, chronic kidney disease and psychological problem. These complications are shown in Figure 5.

**Diabetes mellitus**

10% of obese patients are diabetic, (Nadler et al., 2000) obesity alone is not sufficient to cause type 2 diabetes. Factors especially islet beta-cell dysfunction can also cause diabetes. (Bell and Polonsky, 2001). 25% risk is due to obesity and BMI over 22 kg/m2(Colditz et al., 1995). Metabolic effects play a major role in increasing insulin resistance and glucose intolerance. Diabetes is the key factor to induce obesity (Figure 6). Insulin resistance may present 10 - 20 years before onset of the disease and this is the best predictor for those who are going to get diabetes mellitus later. Adipocytes secrete adiponectin, interleukin- 6 (IL-6), tumour necrosis factor α (TNF-α), resistin, free fatty acids and cortisol which may control insulin sensitivity (Ahima and Flier, 2000). Obesity leads to increased deposition of triglycerides within skeletal muscle and that the levels of intramuscular triglycerides correlate negatively with insulin sensitivity. It exacerbates metabolic abnormalities of type 2 diabetes including hyperglycaemia, hyperinsulinaemia and dyslipidaemia. Obesity may contribute to excessive morbidity in
type 2 diabetes and as a result it causes risk of developing hypertension and cardiovascular disease (Maggio and Pi-Sunyer, 2003).

**Cancer**

Obesity is related to the risk of gallbladder cancer, particularly among women (Garfinkel, 1986). Obesity increases the risk of endometrial cancer. The risk is three times higher in obese women (BMI ≥30 kg/m²) compared to normal weight women.

**Figure 5: Complications of Obesity**

![Complications of Obesity](surgerytimes.com)
Risk is low when compared to breast cancer, heart disease, and diabetes. Adult weight gain is also related to increased risk (Schottenfeld and Fraumeni, 1996).

Epidemiologic studies showed postmenopausal women to have more risk (Lew and Garfinkel, 1979). But it is inversely related to the incidence of premenopausal breast cancer. A weight gain of more than 20 lb from age 18 to midlife doubles a woman’s risk of breast cancer. This weight gains are positively related to the risk of postmenopausal cancer (Huang et al., 1997).

**Breast cancer**

Approximately 20% of females are affected due to breast cancer, With 80% of cases in postmenopausal stage (Pharoah et al., 1998). The International Agency for Research on Cancer (IARC) statistics showed that 25% of breast cancer cases worldwide are the result of obesity and a sedentary lifestyle (International Agency for Research on Cancer Working Group on the Evaluation of Cancer 2000).
Colon cancer

Many studies proved a positive relation between obesity and colon cancer in men, and women (Giovannucci et al., 1995). Many women with a BMI of > 29 kg/m2 had distal colon cancer as women with a BMI < 21 kg/m2 and a woman with high waist-to-hip ratio was associated with increased risk of colon polyps (Giovannucci et al., 1996). In men, the relationship between obesity and colon cancer was weaker than that for distal colon cancer (Giovannucci et al., 1995).

Obese women and men have a higher risk of developing colon cancer. Studies have shown that when the BMI is greater than 24 kg/m2 chances of developing colon cancer increase if BMI is 30 kg/m2 they have more risk of colon cancer. Colon cancer in men is positively associated with obesity and in the case of women this relationship is weaker (Lew and Garfinkel, 1979). Colon and colon rectal cancer is mainly due to the consumption of dietary fat and animal fat (Lin et al., 2004).

Obese women have a risk of endometrial cancer three times greater than women with normal weight (Schottenfeld and Fraumeni, 1996). Obesity is the major risk for prostate cancer. Cancer in the obese subjects is 25% more in men. Obesity increases the risk of cancer of kidney, gallbladder, pancreas, bladder, cervix, ovary and brain. Higher level of risk of breast cancer is due to increased level of oestrogen.

Obesity increases the risk of diseases like coronary heart disease, Gallstone formation, osteoarthritis, sleep apnoea, Polycystic ovary syndrome, hypertension, steatohepatitis, chronic kidney disease and psychological issues.

Coronary heart disease (CHD)

Coronary heart disease is major risk of obesity. Visceral fat causes endothelial dysfunction due changes in adipokines like adiponectin and TNF-α, which secreted by fat tissue after the macrophages. TNF-α and IL-6 might influence inflammation (CRP) and endothelial dysfunction that are affected which cause insulin resistance, non-essential fatty acid and retinol binding protein 4 induce oxidative stress and causes endothelial dysfunction. This condition leads to risk of premature atherosclerotic process (Figure 7). Increased body mass has mechanical effects on the cardiovascular system. Total body oxygen consumption is increased as a result of expanded tissue mass and the oxidative demands of metabolically active adipose tissue, and this is associated with an absolute increase in cardiac output. Total blood volume is increased in proportion to body weight, and this will contribute to an increase in the left ventricular preload and an
increase in resting cardiac output (de Divitiis, et al., 1981). Increased cardiac output is achieved by an increase in stroke volume while the heart rate remains the same. It increase in diastolic filling of left ventricle (Wikstrand, et al., 1993). The volume expansion and increase in cardiac output causes stress to cardiac wall. Obesity is the main reason for coronary heart disease (CHD). The risk of CHD increases 3- fold when the BMI > 29 kg/m2 compared with the risk in lean subjects (Willett, et al., 1995). Obesity increases the risk of Insulin resistance, hyperinsulinaemia and an increase in atherogenic risk. Visceral adipose tissue, which has been associated with increased insulin resistance, is the strongest predictor of cardiovascular disease. Obesity and excess abdominal fat are directly related to cardiovascular risk factors, including high levels of total cholesterol, low density lipoprotein (LDL), triglycerides, blood pressure, fibrinogen and insulin and low levels of high density lipoprotein (HDL) cholesterol. Studies suggested that adipose tissue secretes a number of proinflammatory cytokines that may lead to coronary heart disease (Poirier and Eckel, 2002).

**Figure 7: Obesity causes Cardiovascular diseases**
Gallstone formation

Gallstones are mainly in gallbladder or bile duct and are composed of cholesterol, calcium bilirubinate and calcium carbonate. The prevalence of gallstones has been found to be high in obese subjects. The probability of gallstone formation is increased 2.7-fold in women with BMIs above 40 kg/m2 compared with women with BMIs less than 24.9 kg/m2, while in men the probability is increased 2.3-fold. The risk of gallstone formation increases about 44% (Jung, 1997).

Osteoarthritis

Osteoarthritis is another big problem. It is most common in older people. Osteoarthritis is characterised by erosion of articular cartilage, either primary or secondary to trauma. In this case cartilage becomes soft, frayed, and thinned with eburnation of the subchondral bone and out growths of marginal osteophytes, pain and loss of function. This mainly affects weight-bearing joints. The risk of developing osteoarthritis is increased by 9 - 13%. Overweight or obesity increases the risk for the development of osteoarthritis (Cicuttini et al., 1996). Obesity and increased fat mass causes production of adipokines and proinflammatory cytokines which affect bone, cartilage and synovial tissue (Figure 8). It is more common in women than in men. The pain in knees and backbone is more common.

Sleep apnoea

Upper body obesity is a risk of sleep apnoea and related severity. The consequences of severe sleep apnoea include arterial hypoxemia, recurrent arousals from sleep, increased sympathetic tone, pulmonary and systemic hypertension, and cardiac arrhythmias (Shepard, 1992). Sleep apnoea people have a BMI > 30 (Chua and Chediak, 1994; Loube et al., 1994). In this case women have large neck. Sleep apnoea is present in about 40% of obese individuals and 70% of sleep apnoea patients are obese.10% increase in body weight was associated with a 6-fold increase in the risk of developing sleep apnoea (Peppard et al., 2000). It leads to arterial hypoxia, increased sympathetic tone, and pulmonary and systemic hypertension is usually associated with severe cases (Millman et al., 1995). Reason for this is the cessation of respiratory airflow caused by occlusion in the upper airway during sleep, with a consequent decrease in oxygen saturation. Obesity is considered to be a very important factor affecting sleep apnoea.
Respiratory problem

Obesity has a negative effect on lung function, due to abdominal and peripheral fat accumulation. Abdominal obesity causes pressure on the diaphragm, decreasing the ability of the lung to expand during inspiration, while accumulation of fat on the chest reduces the chest cavity space (Ray et al., 1983, Lazarus et al., 1997).

Obesity and reproductive function

Obesity is related to menstrual abnormalities, infertility and miscarriage. Obesity is associated with menstrual abnormalities including cycles longer than 36 days, irregular cycles, and virile hair growth with facial hair (Hartz et al., 1978). Obesity in premenopausal women is associated with menstrual irregularity and amenorrhea. It is a great risk for subsequent ovulatory infertility. The most prominent condition associated with abdominal obesity is polycystic ovarian syndrome.

Polycystic ovary syndrome (PCOS)

Polycystic ovary syndrome (PCOS) is another major problem due to obesity. It increases the risk of subsequent ovulatory infertility. It is mainly associated with hyperandrogenism with chronic anovulation in women and also adrenal or pituitary glands are involved. It is mainly due to abdominal obesity (Franks, 1995). Two important factors play a major role in PCOS in obese women. Polycystic ovarian syndrome is endocrine disorder with multiple cysts in the ovaries as well as abnormal level of hormones and its function leads to this condition and also causes insulin resistance (Figure 9). One factor is increased production of oestrogen compared with lean. Another factor is low level of hormones that cannot bind with globulin so that oestradiol level is increased. Direct or indirect reduction in insulin concentrations increase ovarian activity (Pettigrew and Hamilton-Fairley et al., 1997) and the treatment of PCOS patients with insulin-sensitising agents leads to a reduction in androgen levels and improved ovulatory function (Seli and Duleba et al., 2004). Reducing weight showed best result in PCOS.
Figure 8: Obesity causes Osteoarthritis

Source: www.nature.com

Figure 9: Polycystic ovary caused due to Obesity

Source: www.askdrmakkar.com
Hypertension

Obesity is associated with hypertension and this activates renin angiotensin system. It increases the circulating leptin. Due to the activation of Angiotensin II, it secretes angiotensinogen from adipocytes and increases the level of aldosterone which causes the increased glomerular pressure, leading to condition called hypertension (Reaven, 2002) (Figure 10).

Steatohepatitis

In 1979 Non-alcoholic steatohepatitis (NASH) was first described in adults. Liver biopsies from obese prepubertal children with NASH proved fatty change, inflammation and fibrosis, with progression to necrosis and cirrhosis (Manton et al., 2000). Elevated levels of AST and ALT were the reason for cirrhosis of liver.

Non alcoholic fatty liver disease (NAFLD) is a disease ranging from steatosis to steatohepatitis and cirrhosis of liver. The liver enzyme level is increased. It is normal due to life style changes and weight reduction. Waist hip ratio is used to measure the Obesity and in this case abdomen becomes enlarged.

Chronic kidney disease

Obesity is associated with increased prevalence of chronic kidney disease. Mechanism is not clear and may be due to diabetes and hypertension. These people have relative risk of 2.3%. In these cases glomerular filtration rate is decreased.

Psychological Issues

Psychological disturbance is caused due to obesity. In addition, intake of increased food intake and lack of exercise leads to feeling of despair and depression. Immobility and physical incapacity due to back or joint problems and shortness of breath are major contributors to the lifestyle restrictions which are more common consequences that obese individuals face.

Sudden Death

In case of obesity there will be a sudden death due to ventricular hypertrophy. Other risk factors like coronary heart disease is another risk for death, (Hubert et al., 1983) owing to overweight or obese.
Treatment of obesity

Physical activity enhancement

Physical activity is mainly involved in the prevention of overweight and obesity. For the treatment of Children and adolescents should follow less than 60 min of moderate to vigorous physical activity per day and it is helpful for maintaining cardiovascular health (Strong et al., 2005). Moderate exercise like brisk walking is helpful to burn more fat and is excellent for reducing body fat (Poirier and Despres, 2001). Physical activity is the safe method for weight reduction and also has beneficial changes in fat and lean body mass cardiovascular fitness, muscular strength, endothelial function and glucose metabolism. This will be helpful in excess weight reduction (Watts et al., 2005).

Restriction of sedentary behaviour

Children and adolescents are more prone to sedentary life like watching TV, sitting in front of computers and video games. So restrict television viewing during early
childhood. High fat intake, sweet and salty snacks and carbonated beverages during TV watching, reducing the consumption of fruits and vegetables leads to obesity (Coon and Tucker, 2002). So restrict excess of TV watching and snacks intake during TV watching.

**Surgical treatment**

In case of severe adolescent obesity, it is treated by surgical method. Bariatric surgery is done in the case severe obesity (BMI is greater than 40). The bariatric procedure in adolescents is by Roux-en-Y gastric bypass and adjustable gastric banding. Complications like small-bowel obstruction, incisional hernias, weight regain, as well as vitamin and micronutrient deficiencies can arise. But patient must be in medical supervision for life time.

**Pharmacological treatment**

**Appetite Suppressants**

Most common appetite suppressants approved by the food and drug administration (FDA) for weight loss are sibutramine, phentermine, phendimetrazine, and diethylpropion. These medications promote weight loss by decreasing appetite or increasing the feeling of being full. These medications make feel less hungry by increasing the brain chemicals that cause appetite. But these medications have side effects (Table 3).

The drugs like sibutramine, orlistat and metformin are currently used for the treatment of obesity. Sibutramine enhances satiety and it is most effective drug in treating adolescent obesity. It has side effects like increases the heart rate and blood pressure. It is used in obese adolescents with higher blood pressure (Leung et al., 2003). Orlistat is another drug which is a pancreatic lipase inhibitor by increasing the faecal fat loss and is also associated with flatulence, diarrhoea, gallbladder diseases, malabsorptive stools and requires fat-soluble vitamin supplementation and monitoring (Leung et al., 2003, Chanoine et al., 2005). Metformin is an adjuvant to the treatment of obese adolescents with severe insulin resistance, impaired glucose tolerance or polycystic ovarian syndrome (Freemark, 2007) Metformin activates cAMP-activated protein kinase and suppresses hepatic gluconeogenesis activity.

Pharmacotherapy should also be used to treat insulin resistance, impaired glucose tolerance, hepatic steatosis, dyslipidaemia or severe menstrual dysfunction that persist inspite of lifestyle interventions. Rimonabant reduces lipogenesis in liver. They
not only cause weight loss but it has reversed metabolic effects of obesity. But these have side effects and in case of orlistat, it causes Steatorrhoea (oily stools) is common. Metformin has side effect like lactic acidosis and gastrointestinal problems. Rimonabant has side effects. They not only cause weight loss but in addition reverse metabolic effects of obesity. Severe depression and predisposes to neurodegenerative diseases such as Alzheimer’s disease and amyotrophic sclerosis. Hypertension, serotonin syndrome are the adverse effects of Sibutramine. **Table 4** denotes the side effects of medication used for weight loss.

**Prevention of obesity**

Early prevention is better. Individuals should avoid sugar sweetened beverages, reducing daily screen time to less than two hours, watching television and using computers from primary sleeping areas, eating breakfast regularly, limiting eating out especially fast food, encouraging family meals and limiting the portion sizes (*Davis et al., 2007*). Eat fruits and vegetables daily with recommended quantity. A balanced diet rich in calcium and fiber, physical exercise must be followed daily. Bicycles are to be

**Table 3: Appetite suppressants**

<table>
<thead>
<tr>
<th>S.NO</th>
<th>Name of medication</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sibutramine</td>
<td>Increased blood pressure and heart rate</td>
</tr>
<tr>
<td>2</td>
<td>Phentermine</td>
<td>Increased blood pressure and heart rate, sleeplessness, nervousness</td>
</tr>
<tr>
<td>3</td>
<td>Phendimetrazine</td>
<td>Sleeplessness, nervousness</td>
</tr>
<tr>
<td>4</td>
<td>Diethylpropion</td>
<td>Dizziness, headache, sleeplessness, nervousness</td>
</tr>
</tbody>
</table>
Table 4: Drugs used to treat Obesity and it’s side effects

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Mechanism of action</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>Reduces fat absorption from the intestine by inhibiting pancreatic lipase and reduces triglyceride hydrolysis. Low fat diet is generally advised.</td>
<td>Steatorrhoea (oily stools).</td>
</tr>
<tr>
<td>Sibutramine</td>
<td>Centrally acting sympathomimetic amine that enhances satiety by inhibiting nonselective uptake of nor adrenaline, serotonin and dopamine</td>
<td>Hypertension, serotonin Syndrome</td>
</tr>
<tr>
<td>Metformin</td>
<td>It activates cAMP-activated protein kinase and suppresses hepatic gluconeogenesis activity.</td>
<td>Lactic acidosis, Gastrointestinal upset.</td>
</tr>
<tr>
<td>Rimonabant</td>
<td>It is an approved but infrequently used drug. It is a cannabinoid CB1 receptor antagonist. It selectively acts on CB1 receptor in brain and peripheral organs. Reduces lipogenesis in liver. They not only cause weight loss but in addition reverse metabolic effects of obesity</td>
<td>Severe depression and predisposes to neurodegenerative diseases, E.g. Alzheimer’s disease, amyotrophic sclerosis</td>
</tr>
</tbody>
</table>

used by children. So practice regular walking as exercise. Avoid fatty meals which produce high energy.

**Disadvantages of synthetic anti-obesity drugs**

Drugs used for treatment of obesity had altered the basic metabolic process of the human body and so thereby regulate the body weight. These drugs are not long term solution for the treatment of obesity.

Due to the side effects of synthetic drugs there is a need for alternate therapy. So there is growing interest in herbal remedies which contain many bioactive compounds that play a crucial role in treatment of numerous diseases with fewer side effects.

**Reason for herbal drug for Obesity treatment**

Natural ingredients and medicinal plants preparation should enhance satiety, increase metabolism and also increase the weight loss (Larson et al., 2009; Pasman et al., 2008). It is so safe because it is from 100% natural origin, Herbal plants for weight reduction are more effective in the treatment of and obesity related diseases. Herbal drug leads to loss of weight without any side effects. It has less demanding than accepted
lifestyle changes such as exercise and diet, availability. Weight loss efficacy was studied using natural products and based on five mechanism of action like

- Decreasing energy intake.
- Decreasing pre adipocyte differentiation.
- Proliferation of adipocytes.
- Decreasing lipid absorption.
- Increasing energy expenditure and decrease lipogenesis and increased lipolysis. (Yun, 2010).

To alleviate the complications arising due to side effects of synthetic drugs and bariatric surgery, Researchers are turned towards medicinal plants.

**Alternative systems of medicine**

- Traditional Chinese medicine system
- Indian system of medicine
- Ayurveda -The Indian system of medicine
- Siddha system of medicine
- Unani system of medicine
- Homeopathic system of medicine
- Aromatherapy

**Indian system of medicine**

WHO estimates that about 80% of the population living in the developing countries are obese. The need of traditional medicine for primary health care is required. Indian traditional medicine system includes Ayurveda, Siddha and Unani. Indian medicinal system developed an extensive use of medicines from plants from 1000 B.C. This is accepted all over the world for clinical practice. It is oldest method but it is effective in certain cases than modern therapies.

Plants have been used as medicine for thousands of years. These medicines are initially taken in the form of crude drugs such as tinctures, teas, poultices, other powders and other herbal formulations.

**Indian Ayurveda Traditional medicine**

This is accepted all over the world for clinical practice. Ayurveda came into existence in 900 BC. The term “Ayurveda” is derived from Sanskrit word ‘Ayur’ (life) and Veda (Knowledge of science). The origin is from Chinese medicine. This treatment is so good without many side effects. Time taken for the treatment is so long but result is
good. Ancient Greek and middle eastern text refers to concepts and drugs of Indian origin (Magner, 1992). The principles of Ayurvedic medicine and the medicinal uses of plants are contained in thousands of poetic hymns in Rig Veda.

**Medicinal plants in India**

India is endowed with lots of medicinal and aromatic plants. Totally 15000 higher plants and 9000 are commonly useful. 7500 are medicinal and 3,900 are edible. 700 are culturally important, 525 used as a fibre, 400 are fodder, 300 for pesticide and insecticide, 300 for resins and dye and 100 for incense and perfume. 25% of medical drugs are from plants and their derivatives. Medicinal and aromatic plants contain biologically active chemical substances such as saponins, tannins, essential oils, flavonoids, alkaloids and other chemical compounds (Harborne, 1973; Sofowara, 1993). According to the WHO 80% of the world population uses medicinal plant for the treatment of diseases. Phytochemicals like flavonoids, saponins, alkaloids are reported as biologically active molecules. Antiobesity therapeutic products were developed from plants and microbes.

Saponins are major phytochemicals that play an important role in foam industries, beverages industries, agriculture, antibiotic, antiviral and antifungal pharmaceutics. Antitumor potential of saponin was also proved by Agarwal and Rastogi, (1974). It also has cholesterol lowering potential (Messina, 1999), anti-diabetic and antiulcer (Marhuenda et al., 1993) effects. Due to the traditional medicinal uses of *Benincasa hispida* it is used for further study.

*Benincasa hispida* (Thunb.) Cogn. consist of fruit and it belongs to family Cucurbitaceae an extensive trailing or climbing herb cultivated throughout the plains of India and on the hills upto 1200 m altitude. It is used as a vegetable. The genus name is given by famous botanist Gastano Savi in 1818 to honour botanist Giuseppe Benincasa, an Italian paten of botony. *Benincasa cerifera* means “wax bearing” hispida means “rough hairy” as whole plant has rough hair. The seeds are also not having sweet taste after maturity. The melon grows about 80cm length. The common name is winter melon. It is originally cultivated in East Asia and South Asia. It is also called as Ash gourd, Green pumpkin, white gourd. Ayurveda classification of the herb is as “Kshmanda, Pushpaphala, Briatphala and Pitpushpa”.
**Stem**

Stem has more branches with five sided, thick forrowed and covered with sharp bristles.

**Tendrils**

Split at 3cm into 2-3 each into 15cm is slender in shape. It sprawls over the ground.

**Seeds**

Multiple seeds are present in the middle area of fruit (Figure 11).

**Leaves**

Leaves are large, roundish, kidney shaped and base is heart shaped. Upper surface looks rough and lower surface bristly. Blade is 10-25cm long and broad with 5-7 lobes that are ovate and triangular. Edges are scalloped into teeth (Figure 12).

**Flower**

Flower is yellow, flat faced and solitary. Male flowers are 5-15cm long with 3 stamens of 1cm length. Female flowers are 2-4cm long and dividing into 3. Calyx tube is 10-15mm long with dense hair. Lobes are lanceolate. Petals are spreading, blunt but ending in a short point. Filaments of stamens are inflated and hairy at the base, anthers are trilobbed. The flower appearance is shown in Figure 12.

**Fruit**

Fruit is hairy and fuzzy like appearance, when it is young. After it ripens it become dark green with a white wax. Outer layer is so hard. Immature fruit skin colour has shades like light green to purple blue, depending on the variety of fruits. The flesh is white in colour and with downy hairs. The shapes of fruit also differ with spherical or rounded. The fruit weight is 2.2-4.5kg and is 30-38cm long (Figure 13).
Vernacular names of *Benincasa hispida*

<table>
<thead>
<tr>
<th>Language</th>
<th>Common Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanskrit</td>
<td>Kusmanda, Brihatphala, Pushpaphala, Pitapushpa etc.</td>
</tr>
<tr>
<td>Assamese</td>
<td>Kumra</td>
</tr>
<tr>
<td>Bengali</td>
<td>Chal Kumra</td>
</tr>
<tr>
<td>English</td>
<td>Ash gourd (Chinese), Winter melon, fuzzy melon, Green pumpkin, wax gourd, white gourd, Hairy melon</td>
</tr>
<tr>
<td>Gujarati</td>
<td>Safed Kohalu, Bhuru, Koha, Bhuru Kolu</td>
</tr>
<tr>
<td>Hindi</td>
<td>Kushmand, Petha</td>
</tr>
<tr>
<td>Kannada</td>
<td>Boodi Hambala</td>
</tr>
<tr>
<td>Malayalam</td>
<td>Kumbalanga</td>
</tr>
<tr>
<td>Marathi</td>
<td>Kohala</td>
</tr>
<tr>
<td>Oriya</td>
<td>Kakiaru, Panikakharu</td>
</tr>
<tr>
<td>Punjabi</td>
<td>Petha</td>
</tr>
<tr>
<td>Tamil</td>
<td>Pooshanikkai</td>
</tr>
<tr>
<td>Telugu</td>
<td>Boodida Gummadi</td>
</tr>
<tr>
<td>Urdu</td>
<td>Petha</td>
</tr>
</tbody>
</table>

**Figure 11: *Benincasa hispida* seeds**

*Source: www.agefotostock.co*
Figure 12: *Benincasa hispida* flower

Source: lepidoptera.butterflyhouse.com.au

Figure 13: *Benincasa hispida* fruit

Source: ranchiexpress.com
Nutritional value of *Benincasa hispida* fruit (100g)

<table>
<thead>
<tr>
<th>Energy</th>
<th>54 kJ (13 kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates</td>
<td>3 g</td>
</tr>
<tr>
<td>Dietary fiber</td>
<td>2.9 g</td>
</tr>
<tr>
<td>Fat</td>
<td>0.2 g</td>
</tr>
<tr>
<td>Protein</td>
<td>0.4 g</td>
</tr>
</tbody>
</table>

**Vitamins**

| Thiamine (B1)   | (3%) 0.04 mg   |
| Riboflavin (B2) | (9%) 0.11 mg   |
| Niacin (B3)     | (3%) 0.4 mg    |
| Pantothenic acid (B5) | (3%) 0.133 mg |
| Vitamin B6      | (3%) 0.035 mg  |
| Vitamin C       | (16%) 13 mg    |

**Trace metals**

| Calcium      | (2%) 19 mg    |
| Iron         | (3%) 0.4 mg   |
| Magnesium    | (3%) 10 mg    |
| Manganese    | (3%) 0.058 mg |
| Phosphorus   | (3%) 19 mg    |
| Sodium       | (7%) 111 mg   |
| Zinc         | (6%) 0.61 mg  |

**Folk medicine**

The folk medicinal practitioners, locally called as Kavirajes or Vaidyas, use simplest form of treatment with medicinal plants. Ancient medicinal practitioners of traditional medicine use this for primary health care for rural and urban poor population.
in the country. Cucurbitaceae family comprises about 960 species and 125 genera. These family plants are used in the folk and tribal medicinal system. Fruit is used in the treatment of fever, epilepsy, respiratory diseases and certain types of neurological diseases. The seeds are used in the urethrorrhea, syphilis and hyperdipsia.

**Ayurveda**

Ayurveda literature says that the plants named as different names like Gandari, ugmaptra and karbudara. It is reported to have kasaa rasa, Ruksha guna, Shita virya and katu vipaka.

**Seeds**

Seeds are used traditionally for the treatment of fever and diuretics (Prajapati *et al.*, 2007). The seeds are useful in dry cough, fever, urethrorrhea, syphilis and hyperdipsia conditions. This also used in the treatment of expelling tapeworms and curing urination and bladder stones.

**Fruit**

A fruit juice of *Benincasa hispida* was given to the asthma patients to cure asthma, (Prajapati *et al.*, 2007) 50ml of fruit juice is given for 3 days consecutively for jaundice, (Hemadri and Rao, 1984). It was main ingredient in ʿkushmanda lehyam, which is used in the numerous nervous disorders in the ayurvedic system of medicine. The fruits were used for epilepsy, fever, cough, diabetes, haemoptysis, hemorrhages from internal organ, epilepsy and fever. It was also useful in insanity, burning sensation, dyspepsia and neurological diseases. Respiratory and heart diseases were also treated using this fruit. The important formulations are *Kusmandarasayana, Himasagaratala, Dhatryadighrita, Vastyamantakaghrita, Mahaukusmandakaghrita*, etc. (Sivarajan *et al.*, 1994).

*Benincasa hispida* belongs to Cucurbitaceae family. Many ayurveda researchers have turned their attention towards the family because the fruits of this family are eaten by human in the form of salads or dessert or pickle.

**Rai *et al.*, (2015)** explained the antiobesity polyherbal formulation containing *Terminalia arjuna, Lagenaria siceraria* and *Piper nigum*. Rats were treated with various polyherbal tablets formulations of *Lagenaria siceraria* alone or combination with other extracts like *Terminalia arjuna* and *Piper nigrum* (400mg/kg body weight) for 14 days. The results showed reduction in food intake, body weight and organ weights, Total
cholesterol, Triglycerides, LDL and increases the locomotor activity and HDL level in HFD treated rats.

*Momordica charandia* or bitter melon had an impact on lipid accumulation and adipocyte differentiation transcription, Cytotoxicity, lipid accumulation and adipogenic genes expression was measured by RT-PCR. 0.5-2.0% of *Momordica charandia* juice concentration was used for the study. The result showed that adipocytes treated with *Momordica charandia* juice for 48hrs reduced the lipid content, perilipin mRNA expression and increased lipolysis and glycerol release. It acts as an effective alternate therapy to reduce adipogenesis in humans (*Nerurkar et al., 2010*).

*Cucumis melo* fruit peel extract in triton induced hyperlipidemia in rats was proved by *Bidkar et al., (2012)*. Chloroform (250mg, 500mg/kg), Methanolic (250mg, 500 mg/kg) and aqueous extracts (250mg,500 mg/kg) were administered to the triton X-100 induced hyperlipidemic rats for 7 days to study antihyperlipidemic activity. The methanolic extract (500 mg/kg) had antihyperlipidemic activity in Triton X-100 induced hyperlipidemia model and was compared with Atorvastatin treated group. It inhibits the serum cholesterol biosynthesis and decreases the serum triglycerides.

*Benincasa hispida* belongs to hispida species. The reviews of this species for antihyperlipidemia are,

Antihyperlipidemic activity of the methanolic plant extract of *Ficus hispida* Linn. leaves was evaluated by *Pandit et al., (2011)* against Triton-WR1339 induced hyperlipidemic mice model. Extract of 125, 250 and 500mg/kg was given orally. It was compared with simvastatin induced mice. Leaf extract showed significant reduction of serum lipids like cholesterol, Triglycerides, VLDL and LDL. This study suggested that administration of methanol extract at 500 mg/kg of *Ficus hispida* was more effective for managing hyperlipidemia.

*Spermacoce hispida* was used as a treatment of hyperlipidemia. This was studied by *Sivaelango et al., (2012)* and ethanolic extract of spermacoce hispida was administered orally at 200mg/Kg against 400mg/kg triton WR-1339 induced hyperlipidemicrats. Results suggested that 200mg/Kg of extract had better activity against hyperlipidemia.

**Diuretic effect**

The experiment designed by *Jayasree et al., (2011)* to evaluate the diuretic effect of chloroform extract of *Benincasa hispida* rind (Pericarp) in guinea pigs.
Urine sample was collected every 5 hours intervals by placing animal in metabolic cages. The urinary pH, exertion of urine was measured and electrolytes like sodium, potassium and chlorine was measured which is compared with control. This study reveals that extract possesses a significant diuretic activity with potassium sparing effect.

- **Antioxidant and antimicrobial activity**
  
  *Abdullah et al., (2012)* showed that *in vitro* antioxidant and antimicrobial activities of peel, pulp and seed extract of *Benincasa hispida*. Antioxidant activity like DPPH, FRAP and antimicrobial activity of *Benincasa hispida* was tested using gram positive and gram negative microorganisms. The result of the study suggested that seed extract of *Benincasa hispida* act as a strong antioxidant and showed antimicrobial activities.

- **Anxiolytic evaluation**

  *Ethanolic extract of Benincasa hispida* fruit extract was used to find the anxiolytic activity in animal model by both light and dark reaction. GABA is responsible for this activity without any sedative, myorelaxant or amnestic effects *Nimbal et al., 2011*.

- **Antinociceptive effect**

  *Hemamalini and Varma (2007)* explained about the methanolic extract of *Benincasa hispida* which was used for analgesic effects on pain (antinoception). Flavonoid is target for prostaglandins, which is involved in late phase of acute inflammation and pain perception. It may be responsible for analgesic activity.

- **Antidiarrheal activity**

  *Swamy et al., (2005)* evaluated the antidiarrheal activity. The extract reduced diarrhoea by inhibiting intestinal peristalsis, gastrointestinal motality and PGE2 induced enter pooling. The extract was a relief from the diarrhoea.

- **Spasmolytic activity**

  The aqueous extracts of fresh fruit juice of *Benincasa hispida* has a spasmolytic activity, that confirming that it has been used in the treatment of intestinal disorders. Acetylcholine causes the contraction of rat ileum *Bharade et al., 2014*.
**Bioactive proteins from *Benincasa hispida***

*Churiyah and darusman, (2009)* isolated and characterized the bioactive proteins from seeds, fruit and roots to analyse the toxicity and cytotoxicity of the proteins. The cytotoxicity test of root protein showed that it was a better inhibitor of Hela cell proliferation than fruit and seeds.

**Anticompulsive effect**

The methanolic extract of *Benincasa hispida* exhibited significant anti-compulsive effect in mice using behaviour test and serotonergic function (*Girdhar et al., 2010*).

**Antihistamic activity**

Antihistamic activity of methanolic extract of *Benincasa hispida* fruit caused reduction in spontaneous motor activity with no muscle relaxant activity. It significantly potentiated the barbiturate induced hypnosis, and this showed that it had significant antihistaminic activity (*Babu et al., 2003*).

**Anticonvulsant activity**

*Punniyakotti et al., (2013)* worked on anticonvulsant properties of *Benincasa hispida* fruit using alcoholic extract. Pentylentetrazole and strychnine was used to induce seizures in mice. Maximal electroshock test was used for this study. *Benincasa hispida* fruit showed better anticonvulsant activity against pentylentetrazole-induced convulsion in mice.

**Antidepressant activity**

*Dhingra and Joshi, (2012)* studied the antidepressant activity of methonolic extract for 14 days in Swiss male albino mice. It was compared with classical antidepressant drugs like imipramine 15 mg/kg, fluoxetine 20 mg/kg, and phenelzine 20 mg/kg. The methanolic extract of *Benincasa hispida* showed significant antidepressant-like activity in mice probably by inhibiting MAO-A, and through interaction with dopaminergic, α1- adrenergic, serotoninergic, and GABAergic systems. The juice of *Benincasa hispida* showed best activity against symptoms of morphine withdrawal. The results showed that *Benincasa hispida* was active in preventing the development of morphine addiction and suppression of opioid withdrawal in animals.
Alzheimer’s disease

Roy et al., (2008) explained about the management of colcicines induced rat model of Alzheimer's disease. It is also increased the antioxidants level in different brain areas. The aqueous extract of *Benincasa hispida* pulp (400mg/kg body weight) was studied for its effect on Alzheimer’s disease.

Effects on gastrointestinal system

Evaluation of free radical scavenging and antiulcer potential of methanol extract of *Benincasa hispida* seeds was studied. Rat model was used to assess the antiulcer activity. Pyloric ligation, water immersion stress and indomethacin were used for ulcer induction. Petroleum ether and methanol extracts were administrated orally at a dose of 300 mg/kg bw, and omeprazole (standard) at the dose of 20 mg/kg body weight was used for the study. Both extracts produced significant reduction in ulcer index (Rachchh and Jain, 2008).

Anthelmintic activity

This study proved that the ethanolic extract of fruit peel of the *Benincasa hispida* displayed a significant anthelmintic activity in dose dependent manner. The assay was performed *in vitro* using adult earthworm (*Pheretima posthuma*) owing to its anatomical and physiological resemblance with the intestinal roundworm parasites of human beings (Muley et al., 2012).

Antioxidant effects:

Mandana et al., (2012) described about antioxidant activity and total phenolic content (TPC) of *Benincasa hispida* seeds extract using conventional Soxhlet extraction. Extract like ethanolic, n-hexane and ethyl acetate extract was used. The ethanolic extract showed the highest phenol content than other extracts.

Rana and Suttee, 2012 investigated the free radical scavenging potential of aqueous and methanolic extract of dried ripe peels of *Benincasa hispida* against DPPH (1,1-diphenyl-2-picryl-hydrazyl). The extracts showed significant potential in a dose dependant manner when compared with the ascorbic acid. The highest scavenging activity of methanol extract was found to be 87.87% at a concentration of 100μg than the aqueous (86.5%) at concentration of 100 μg /ml.

Anti-inflammatory and analgesic effects

The aqueous extract of *Benincasa hispida* exhibited anti-inflammatory properties. Petroleum ether and methanolic extract of *Benincasa hispida* fruit, at the
dose of 300 mg/kg body weight, produced dose dependent and significant inhibition of carrageenan-induced paw edema, histamine induced paw edema and cotton pellet induced granuloma in rat model. Petroleum ether and methanolic extracts showed maximum inhibition in inflammation in histamine-induced paw edema and both extracts showed (62.86% and 54.84% respectively) inhibition as compared to control. The effects were comparable with that of standard drug cetirizine (95.24%). Petroleum ether and methanolic extracts showed insignificant reduction in granuloma tissue formation in cotton pellet implanted rats (Rachchh et al., 2011).

- **Anti vascular inflammatory activity**

  The anti-vascular inflammatory activity of an aqueous extract of *Benincasa hispida* (ABH) in human umbilical vein endothelial cells (HUVECs) was investigated. ABH inhibited high glucose-induced cell adhesion molecules (CAMs) surface and protein expression, resulting in reduced adhesion of U937 monocytes. ABH also inhibited the mRNA expression level of monocyte chemoattractant protein-1 (MCP-1) and interleukin-8 (IL-8). ROS production was also inhibited by ABH. NF-kB activation was blocked via phosphorylation and degradation of its inhibitory protein, IκB-α. ABH also reduced NF-kB promoter activity. This study was carried by Moon et al., 2009.

Both species and family of *Benincasa hispida* has many pharmacological activities.
Aim and Objectives
AIM AND OBJECTIVES OF THE PRESENT STUDY

Aim

To investigate the anti-obesity potential of *Benincasa hispida* fruit and its active fraction to prevent or suppress the obesity and obesity associated complications with high fat diet fed animal model and inhibits lipogenesis via down regulation of AMPK and PPARγ in 3T3-L1 cells.

Objectives of the study

- To perform physicochemical, pharmacognostic and preliminary phytochemical analysis of *Benincasa hispida* fruit.
- To quantify the phytochemicals present in *Benincasa hispida* fruit.
- To assess the *in vitro* antioxidant activity of ethanol extract of *Benincasa hispida* fruits.
- Phytochemical analysis by HPLC.
- Purification of ethanolic extract of *Benincasa hispida* by silica gel column chromatography.
- To quantify the phytochemicals present in the active fractions.
- To profile the bioactive compounds through HPTLC fingerprint analysis.
- To study the constituents of active fraction by GC-MS analysis.
- To identify the active fraction by MTT assay using 3T3-L1 cell lines.
- To study the active fraction for Glyceraldehyde 3 phosphate dehydrogenase activity using 3T3-L1 cell lines.
- To study the active fraction for HMG CoA reductase activity using 3T3-L1 cell lines.
- To assess the role of active fractions on the expression of various gene in 3T3-L1 cell lines by RT-PCR.
- To study the effect of active fractions on the expression of various proteins by immuno blotting.
- To study the effect of *Benincasa hispida* on High fat diet induced obesity rats.
- To study the physical parameters, biochemical assays, *in vivo* antioxidant and histopathological studies using experimental animals.
Plan of the study

Chapter I - Analysis of Phytochemicals

Chapter II - Antioxidant potential of Benincasa hispida fruit extracts

Chapter III - Bioactivity guided fractionation of active principle using chromatographic techniques

Chapter IV - Effect of active fraction of Benincasa hispida fruit on gene expression in 3T3-L1 cell line

Chapter V - Antiobesity effect of active fraction and ethanolic fruit extract of Benincasa hispida in HFD fed wistar albino rat model
Scope
SCOPE OF THE STUDY

Since ancient day’s human beings used plants as a natural source for the treatment of many diseases, among them medicinal herbs have been widely used and have fewer side effects. In current scenario focus on plant research has increased throughout the world and a huge amount of evidences have been collected to show during the last five years period. Recently scientists are using these renewable resources to produce a new generation of therapeutic compounds. Many natural compounds, the most efficient drugs available are from plant kingdom. The plant made pharmaceuticals can be easily produced and also cost effective. Hence bioactive compounds from natural products played a vital role in the treatment of diseases. So treating obesity patients with natural ingredients is a significantly beneficial strategy to suppress the lipid accumulation in adipose tissue as well as in liver by reducing the lipid parameters in serum. Therefore, a search for plants which can suppress the lipid accumulation could be economical and inexpensive. This research was thus initiated in view of serving humanity.

The scope of the study was as follows:

- To determine the presence of phytochemicals present in the extracts of Benincasa hispida fruit.
- To determine the antioxidant capacity of Benincasa hispida fruit extracts in an in vitro condition.
- To purify the ethanolic extract of Benincasa hispida by silica gel column chromatography and to assess the compounds present in active fraction by HPTLC and GCMS analysis.
- To study the effect of Active fraction of Benincasa hispida on the genes and proteins responsible for the obesity in an in vitro model.
- To ascertain the antiobesity effect of Active fraction of Benincasa hispida and ethanolic extract of Benincasa hispida on wistar albino rats an in vivo condition by inducing obesity using high fat diet and studying the biochemical parameters and histopathological observations as well as its effect on oxidative stress.