



Obesity As A Cardiometabolic Risk Factor

Ikwu A. N. *

*Senior Registrar, Cardiology Unit, Department of Medicine, OAUTHC, Ile-Ife

INTRODUCTION

Obesity is an abnormal or excessive accumulation of body fat that may impair health¹. Body mass index (BMI) defined as a person's weight in kilograms divided by the square of his height in meters (kg/m^2) is commonly used to classify overweight and obesity in adults. The World Health Organization (WHO) defined obesity as a BMI greater than or equal to 30.

The term 'metabolic syndrome' was coined to refer to a condition in which an overweight person, especially one with abdominal obesity, also has high blood pressure, high blood fats and/or heightened blood

sugar.

Obesity is an important risk factor for cardiometabolic disease including diabetes mellitus (DM), systemic hypertension, dyslipidaemia, coronary artery disease, stroke and overall mortality, independent of other cardiac risk factors^{2,3}.

Cardiometabolic abnormalities associated with obesity are as a consequence of insulin resistance, glucose intolerance, dyslipidaemia, systemic hypertension and a prothrombotic-inflammatory profile².

EPIDEMIOLOGY

In 1997, WHO recognized obesity as a global pandemic. The prevalence of obesity and metabolic syndrome has increased over the past several decades. As of 2005, the WHO estimated that, at least 400 million adults (9.8% of the world population) were obese, with higher rates among women than men⁴. The recent 2012 WHO Statistics Report revealed that 12% of the world population is considered obese.

The prevalence of obesity in Nigeria ranges from 8.1% - 22.2%⁵. A study by Ahaneku et al⁶ in a South-Eastern rural community of Nigeria reported that females had a higher prevalence of all forms of obesity (abdominal: 36.2%; global: 14.8%), compared with males (abdominal: 14.5%, global: 10.1%).

It is estimated from the third National Health and Nutrition Examination Survey-NHANES III (1988-1991) that 33% of the US population is obese, compared with 25% in NHANES II (1976-1980).

Obesity is associated with increased prevalence of cardiometabolic risk factors. Tharkar et al⁷ in a study on effect of obesity on cardiovascular risk factors in an urban population of South India reported increasing cardiometabolic abnormalities with increasing BMI.

In the Heart of Soweto Study⁸ in South Africa, 44% of patients with systemic hypertension were obese. Obesity is frequently but not invariably accompanied by dyslipidaemia.

Again, Obesity, particularly visceral or central, is very common in type 2 diabetes mellitus (T2DM) patients. Mugharbel et al⁹ in a retrospective study of DM patients registered in Primary Health Care Centers in Al-Khobar Saudi Arabia reported that 46.2% of T2DM patients were obese.

Long-term longitudinal studies indicate that, obesity not only relates to coronary heart disease but independently predicts coronary atherosclerosis. A 4-year prospective study by Rimm et al¹⁰ reported that middle aged men with BMI >25 but <29 had a 72% increased risk of non fatal or fatal coronary heart disease.

The association of obesity with stroke remains controversial.

AETIOLOGY

Obesity is a heterogeneous group of disorder. Obesity results from an interaction between environmental influences and an individual's genetic predisposition to weight gain. Recent research has identified more than 41 sites on the genome as possible links to the development of obesity in a favorable environment.

Genetic defects associated with obesity are Leptin (Lep(ob)), Leptin Receptor (Lep R(dp)), Proopiomelanocortin (POMC), Type 4 receptor for Agouti (Agouti), Melanocortin 4 Receptor (MC4R), Dendin (Dn), Carboxypeptidase E etc. Other genes associated with obesity are: Prader-Willi syndrome, Cohen's syndrome, etc.

Environmental factors associated with obesity results from a combination of excessive nutrient intake and sedentary lifestyle. Certain physical and mental illnesses and certain drugs predispose to obesity; examples are hypothyroidism, Cushing's syndrome, growth hormone deficiency, steroids, antipsychotics, bulimia nervosa, binge eating disorder, etc. Factors associated with increased visceral adiposity are increasing age, menopause in women, smoking, nutrition factors (high caloric intake), sedentary behavior and race (increased in Asians, decreased in Blacks)².

WHO defined metabolic syndrome as abnormal blood sugar regulation (T2DM, preliminary stages of DM, or impaired insulin sensitivity), plus at least 2 of the following four criteria.

- Blood Pressure (BP) \geq 140/90mmHg, or use of BP medications.
- Triglycerides \geq 1.7mmol/L and/or high density lipoprotein (HDL) cholesterol $<$ 0.9mmol/L in men, $<$ 1.0mmol/L in women.
- BMI $>$ 30 and/or waist-hip-ratio (WHR) $>$ 0.9 in men, $>$ 0.85 in women.
- Albumin discharge in urine.

PATHOPHYSIOLOGY

Body fat distribution is also an important risk factor for obesity-related diseases¹¹. Excess abdominal fat is associated with an increased risk of cardiometabolic syndrome.

The mechanism(s) responsible for the relation between excess abdominal fat distribution and cardiometabolic disease is not known, but several hypotheses have been proposed¹¹.

1. Activation of the central nervous system- adrenal axis by environmental stressors caused both the preferential deposition of adipose tissue in the trunk and the cardiometabolic disorders associated with the deposition¹¹.

2. Limited ability of subcutaneous fat depots to store excess energy results in an "overflow" of chemical energy to intra abdominal adipose tissue and "ectopic" sites, such as liver and skeletal muscle. Excess ectopic fat accumulation then causes metabolic dysfunction in those organs. Increased intrahepatic fat is associated with dyslipidaemia and hepatic insulin resistance and increased intramyocellular fat is associated with skeletal muscle insulin resistance¹¹.

3. Direct effect of omental and mesenteric adipose tissue depots on insulin resistance, lipoprotein metabolism and blood pressure. Also, omental and mesenteric adipose tissue produce specific proteins and hormones such as, inflammatory adipokines, angiotensinogen, and cortisol, which can also contribute to metabolic disease¹¹.

4. Some genes predispose to the preferential deposition of fat in abdominal depots which independently cause cardiometabolic disease¹¹.

There may be interplay between these mechanisms and other unknown mechanisms may be involved in the association between abdominal fat mass and adverse metabolic consequences.

IS OBESITY A RISK MARKER FOR CARDIOMETABOLIC DISEASE?

It is estimated that the average life expectancy of people who are obese is 6-7 years shorter than of people of normal weight¹. Table 1 shows the relative risk (RR) of contracting cardiometabolic diseases and other obesity-related diseases among individuals who are obese compared to people of normal weight.

TABLE 1: INCREASE IN THE RISK OF VARIOUS DISEASES LINKED TO OBESITY.

DISEASE	RELATIVE RISK
Type 2 Diabetes	5-10
Cardiovascular Diseases	2
Stroke	2-3
Systemic Hypertension	3-5
Gall-stones	3-4
Arthrosis	2-3
Respiratory problems including sleepapnea	3-4
Cancer	1.4

Source: WHO. Obesity: Preventing and managing the Global Epidemic. Report on a WHO Consultation 2000. Technical Report Series, No 894.

OBESITY AND TYPE 2 DM

The risk of DM increases with the degree and duration of being overweight or obese and with a more central or visceral distribution of fat. Increased visceral fat enhances the degree of insulin resistance associated with obesity¹². In turn, insulin resistance and increased visceral fat are the hallmarks of cardiometabolic syndrome, an assembly of risk factors for developing diabetes and cardiovascular disease.

OBESITY AND CORONARY ARTERY DISEASE (CAD)

Obesity is an independent risk factor for development of CAD and is an important modifiable risk factor for prevention of CAD. The INTERHEART global case-control study of 6787 women from 52 countries found that abdominal obesity was more predictive of myocardial infarction than BMI alone¹³.

OBESITY AND HYPERTENSION

Overweight and obesity are established risk factors for hypertension. Hypertension is approximately twice as prevalent in the obese, than in the non-obese. Obesity-associated hypertension is characterized by activation of the sympathetic nervous system, activation of renin-angiotensin system and sodium retention among other abnormalities.

OBESITY AND STROKE

The association of obesity with stroke remains controversial. In the most recent Guideline Statements from Stroke Council of American Heart Association (AHA), obesity was categorized as a "less well documented or potentially modifiable risk factor for stroke". However, in the Framingham Heart Study, an association between metropolitan relative weight and atherothrombotic stroke was found in women but not in men¹⁴. In contrast, the Northern Manhattan Stroke Study, however, reported that abdominal obesity is an independent, potent risk factor for ischemic stroke in all race-ethnic groups¹⁵.

OBESITY AND DYSLIPIDAEMIA

Obesity is characterized by increased triglycerides, decreased HDL levels and abnormal low density lipoproteins (LDL) composition. The pathogenesis of dyslipidaemia in obesity is closely related to insulin resistance in obese individuals. Dyslipidaemia plays a major role in the development of atherosclerosis and cardiovascular disease in obese individuals.

A number of other cardiometabolic risk factors are associated with metabolic syndrome beyond these criteria, such as impaired fibrinolysis and a hypercoagulable state, chronic low grade inflammation, and the presence of atherogenic small protein¹⁶.

Other obesity-related diseases are gout, infertility, intrauterine death, fetal macrosomia, musculoskeletal pain, depression, sleep apnea, cancer, etc.

INVESTIGATIONS

A. Physiological Assessment of Obesity-

1. Body Mass Index (BMI) - Defined as individuals body weight in kilograms (kg) divided by the square of their height in meters (m).

Underweight	08.5kg/m ²
Normal weight	18.5- 24.9kg/m ²
Overweight	25- 29.9kg/m ²
Obesity	30-34.9kg/m ²
Severe Obesity	35- 39.9kg/m ²
Extreme Obesity	≥40 kg/m ²

Author details

Dr Amanze N Ikwu
Cardiac Care Unit, Department of Medicine,
Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife,
Osun State, Nigeria.
amanzeikwu@yahoo.com

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- Body Fat Mass
 - Skin-fold measurement
 - Underwater weighing
- Waist-to-Hip ratio (WHR): Is the ratio of the circumference of the waist to that of the hip.
- Body Fat Percentage
 - Dual energy X-ray absorptiometry
 - Body water measurement
 - Body average density measurements
 - Bioelectrical impedance analysis
 - Anthropometric methods (skin-fold method, height and circumference method)
 - Imaging methods: - Computer Tomography (CT) and Magnetic Resonance Imaging (MRI)

B. Assessment of Cardiometabolic Risk Factors

- * Assessment of Blood Pressure (office BP measurement, Ambulatory BP measurement)
- * Fasting Blood Sugar and 2-hour postprandial blood sugar measurement.
- * Hemoglobin A1c (HbA1c)
- * Fasting Lipid profile
- * Carotid Doppler Ultrasound
- * Magnetic Resonance Angiography
- * Thyroid Function Test/ other hormonal assay

MANAGEMENT

Goals of Management:

1. Identification and treatment of secondary causes of obesity
2. Identification and treatment of co-morbid cardiometabolic risk factors.
 - * Lifestyle modification
 - improved diet
 - increased physical activity
 - * Pharmacological treatment
 - * Surgical treatment

CONCLUSION

Several studies have implicated obesity as a potent factor for elevated cardiometabolic risk. Prevention of obesity and counseling obese patients on the broad negative effects of obesity is of utmost importance in tackling this global pandemic. This may be achieved through health education and institution of weight reduction programs by government agencies, clinicians and non-governmental interest groups.

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