RIVERS STATE UNIVERSITY
PORT HARCOURT

METABESITY –
LIVING IN DEATH, SLOW SUICIDE!

AN INAUGURAL LECTURE

BY

PROFESSOR
CHITURU GODWILL ORLUWENE

B.Med.Sc (UPH); M.B;B.S (UPH); FMCPath, FCAI,)

Department of Chemical Pathology,

Faculty of Basic Clinical Sciences, College of Medical Sciences

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DEDICATION

This inaugural lecture is humbly and graciously dedicated primarily to my "All-Sufficient God" and secondarily to the following: My dear mother Rev (Mrs.) Edith N. Orluwene; My lovely wife, Mrs Ugochi Orluwene and my six lovely gifts(children) from the Almighty God: Diane, Joan, Kelsey, Bonaventure, Mariane and Endwell

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PROTOCOL

The Vice-Chancellor and Chairman of this occasion
Chairman and Members of the Governing Council
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Distinguished Professors and Members of Senate
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Graduate and Undergraduate Students
Ministers of God
Your Royal Majesties and Highnesses
Members of the Fourth Estate of Realm
All Invited Dignitaries
Distinguished Ladies and Gentlemen.

1.0 INTRODUCTION

Vice-chancellor Sir, today and in this hallowed auditorium, I stand presenting the 91st Inaugural Lecture of this great University and the 1st Inaugural Lecture from the Department of Chemical Pathology, of the Faculty of Basic Clinical Sciences of the Rivers State University. This is the 3rd inaugural lecture to be presented from the relatively young College of Medical Sciences of this University.

Let me acknowledge here the two inaugural lectures from the Department of Chemical Pathology, College of Health Sciences, University of Port Harcourt, presented by my fathers and mentors in the field of Clinical Pathology. Today's inaugural lecture shall be the 3rd in the medical field of Clinical Pathology in Rivers State.

The 1st Inaugural Lecture in Clinical Pathology in Rivers Statewas titled: Do you need a check-up? Meet the clinical Pathologist presented as the 46th Inaugural lecture of the University of Port Harcourt – 24th November, 2005 by Prof. Victor C. Wakwe.

The 2nd Inaugural Lecture in Clinical Pathology in Rivers Statewas titled: Life as a Chemical Reaction: The Clinical Laboratory and the Battles for Life – presented as the 160th Inaugural lecture of the University of Port Harcourt on 27th June, 2019 by Prof. Aaron C. Ojule.

Today, I am presenting the topic: **Metabesity – Living in Death, Slow Suicide!**

The first two Inaugural lectures dealt squarely with the general aspects of Chemical Pathology and did enough justice to the introduction of the Department. I should not really spend time

again on the introduction of the Department, but because this is the very first inaugural lecture from the medical department of Chemical Pathology of this University, I will briefly tell you what we do and our relevance in the clinical setting and in the medical care of patients, clients and in medical diagnosis even after death.

1.1 What is Pathology?

Pathology is the scientific study of diseases – it's causes, identification and progression.

Pathology is described as the "**father of Clinical Medicine**". The Pathologist's diagnosis as to the cause of a disease or cause of death is generally regarded as the final(even in court). The Pathologist is thus "**a consultant to other medical doctors**"

Pathology is a very vast field of medicine and for this reason it is subdivided into four very important sections or departments:

1.2 Anatomical Pathology: This is the branch of pathology that practices and teaches how to identify diseases by carefully identifying changes in cells, tissues or organs associated with the disease and or its complications.

1.3 Medical Microbiology: This is the branch of Pathology that practices and teaches how to identify diseases by actually identifying the causative organism of the disease, either in whole or in part.

1.4 Haematology: This is the branch of Pathology that practices and teaches the identification of diseases by specifically detecting significant changes in the blood cells and blood-forming organs.

1.5 Chemical Pathology: This is my own specialty! This is the branch of Pathology that Identifies diseases by detecting and noting the specific biochemical derangement associated or

pathognomonic for the disease and its sequelae.
Chemical Pathology, as the name implies is dealing with body chemistry and thus, quite broad. It has a number of sub-specialties e.g General body Chemistry, Nutrition, Toxicology, Endocrinology & Metabolic Medicine, Trace metals, Immunology etc.
Today, I am delving into the sub-specialty area of metabolic medicine, a subspecialty that attracted my interest and to which I devoted most of my time.
Vice-chancellor Sir, standing before you is a Metabolic Physician.

2.0 WHAT IS METABOLIC MEDICINE?

Metabolic Medicine is a subspecialty of Chemical Pathology which covers overlapping areas of clinical practice, predicating on detailed understanding of basic biochemistry and metabolism. It focuses on diseases where disturbances or perturbations in basic biochemistry have direct effects on human health.
From the above definition, diverse collection of diseases can be assembled as metabolic disorders or diseases:

i. Diabetes
ii. Obesity
iii. Hyperlipidaemia
iv. Lysosomal Storage Diseases
v. Metabolic Bone Diseases
vi. Porphyrias
vii. Endocrinopathies (Endocrine disorders)
viii. Gout etc

Metabolism is the process by which the body makes energy

from the food you eat. It involves proper functioning of the organs of the body especially, liver, kidney, pancreasetc. You develop a metabolic disease or disorder when these organs become diseased or fail to function normally- e.g. Diabetes.
When a person has many of these problems at the same time, it is called "Metabolic Syndrome". A Metabolic Physician is one who is well-versed with the knowledge and management of metabolic disorders. He is primarily a medical doctor who specializes in Chemical Pathology or Internal Medicine and sub-specializes in metabolic disorders.

3.0 METABOLIC SYNDROME (ALSO CALLED SYNDROME X)

This is cluster of conditions that increase the risk of heart disease and/or stroke.
There are five (5) risk factors associated with the metabolic syndrome; $\geq {}^{130}/_{85}\, mmHg$

1. Blood Pressure (BP)
2. Fasting Plasma Glucose (FPG) ≥ 6.1mmol/L
3. Waist Circumference (WC) >102cm (40inch)male and > 88cm (35inch)female
4. Triglyceride (TG) >1.7mmol/L
5. HDL Cholesterol (HDL-C) < 1.0mmol/L (male) and < 1.3mmol/L (female)

The common denominator in all these is insulin resistance (the inability of the body to respond to insulin). Each one of the components of the metabolic syndrome carries a risk of cardiovascular disease but does not define metabolic syndrome. **For you to have metabolic syndrome, you must present with any three or more of the disorders listed above**.

4.0 METABESITY

Metabesity is a new terminology recently coined by Dr. Alexander Fleming (an endocrinologist). It describes not only metabolic syndrome but also all the interconnected non-communicable chronic diseases with root in abdominal obesity. It describes specifically that metabolic syndrome in which abdominal obesity (increased waist circumference) is a component with its co-morbidities. It has a direct relationship with development of multifarious chronic (non-communicable) diseases (figure 1 and Plates 1-3).

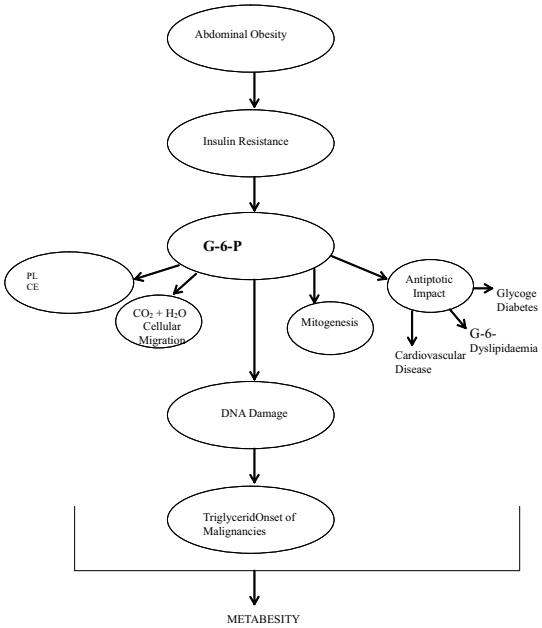
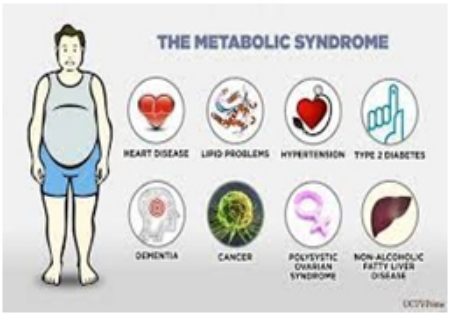


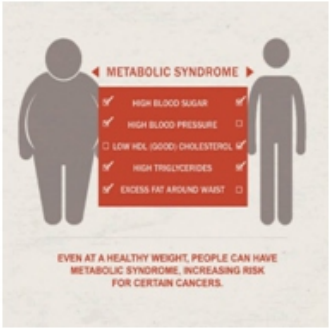
Fig. 1: Relationship between Abdominal Obesity, Metabolic Syndrome and Metabesity

a



b

Plates 2a-b: Pictures of individuals with Metabolic Syndrome



Plates 3a-b: Pictures showing difference between Metabolic Syndrome and Metabesity

Abdominal obesity is the major component of metabesity that differentiates metabesity from normal metabolic syndrome. Metabesity encompasses metabolic syndrome. You can have metabolic syndrome without having abdominal obesity but you cannot be said to have metabesity without abdominal obesity.
Abdominal obesity is thus, the major component of metabesity and one that more than 70% contributes to the development of the co-morbidities associated with this condition. Obesity is implicated in the aetiology of Diabetes Mellitus (Particularly Type 2 Diabetes Mellitus), dyslipidaemia (obesity is one of the known causes of secondary hyperlipidaemia), hypertension and other co-morbidities that will be explained below.

4.1 Obesity (Abdominal obesity) can be controlled or prevented through conscious personal principles and discipline in terms of diet, exercise and drugs. It is true that obesity has a genetic (hereditary) component, but even this can be modulated or modified in expression by environmental, behavioural and life style measures.As individuals therefore, we have a significant role to play in prevention or control of obesity, metabesity and the associated morbid conditions.
We are up to 60% responsible for the extension of our "**healthspan**", defined as the portion of life spent free of major diseases. If we deliberately fail to play our part, then we are consciously facilitating our death and there can be no better definition of suicide - that is why my inaugural lecture topic is carefully chosen as "**Metabesity-living in death, slow suicide.**

The Metabolic Physician works from within the body.
Critias, the Athenian Statesman said and I quote: "**If you discipline yourself within, you will be less vulnerable to injury from outside**".

Napoleon Hill said, "**If you do not conquer self, you will be conquered by self**"
In life, you need more than a willing spirit to fulfill destiny, you need a conquered flesh. Self-discipline is the ability to do what is right even if you don't feel like it. Great people are greatly principled. The core secret of winners in the race of life is held up in the belief that there are things to give up. Failure to do this results in slow but steady journey towards suicide.
It is true that the British historian, **Arnold Torynbee** said "**from the moment of birth there is the constant possibility that a human being may die at any moment, and inevitably, this possibility is going to become an accomplished fact**". But any attempt to speed up this process consciously by any individual on himself or herself amounts to suicide.
Plato said "**For a man to conquer himself is the first and noblest of all victories**"

5.0 CARBOHYDRATE METABOLISM & HYPERGLYCAEMIA

Carbohydrates are one of the major classes of food that are broken in the intestine to simple sugar (glucose). The body has three subdivisions of carbohydrates, namely;

1. Monosaccharides
2. Disaccharides
3. Polysaccharides

5.1 Polysaccharides include glycogen and starch. Starch is taken in from plants; glycogen is formed in the liver and muscle tissues of animals, they contain numerous chains of glucose units. The glycogen is highly branched; branching in starch is

more linear.

5.2 Disaccharides consists of two monosaccharide units e.g. sucrose, lactose, maltose.

Sucrose: Glucose + Fructose
Lactose: Galactose + Glucose
Maltose: Glucose + Glucose

5.3 Monosaccharides: These are the simplest forms of carbohydrate e.g. fructose, glucose. galactose. Some of these sugars are able to reduce copper compounds and are accordingly called reducing sugars e.g. glucose, galactose, fructose, maltose and lactose. Sucrose is not a reducing sugar.

Carbohydrates when ingested through diets are broken down into disaccharides by enzymatic action of salivary amylase which acts on cooked starch. Further breakdown of carbohydrates in the intestines takes place in the small intestine where disaccharides and amylases released from the pancreas catalyze the breakdown of disaccharide into monosaccharide (Especially glucose).

Glucose is absorbed into the blood stream through the villi. A number of hormones affect the metabolism of glucose (carbohydrate metabolism). These hormones are:

(a) **Insulin**: Released from the β-cells of the pancreas-from the islets of Langerhans. They stimulate the entry of glucose, potassium, phosphorus, and magnesium into the cells. They are also necessary for the action of certain enzymes e.g. Glucokinase, Hexokinase, Lipoprotein Lipase. Insulin does not directly influence the entry of glucose into the liver and brain. The stimulus for insulin secretion is high plasma glucose levels and it varies directly with blood glucose. Insulin

inhibits gluconeogenesis, glycogenolysis, it encourages glycogenesis; it encourages protein synthesis and lipogenesis and inhibits lipolysis and proteolysis.

(b) **Glucagon:** A polypeptide hormone secreted from the alpha(α)-cells of the pancreas. The stimulus for its secretion is low plasma level of glucose or low insulin level. Its action is aimed primarily at increasing the plasma level of glucose in the body. This it does by:

1. Stimulating gluconeogenesis
2. Stimulating glycogenolysis
3. Stimulating lipolysis
4. Stimulating proteolysis
5. Inhibiting glycogenesis
6. Inhibiting glucose uptake into the cell
7. Inhibiting lipogenesis and protein synthesis

© **Glucocorticoids(e.g. Cortisol):** These are steroid hormones secreted from the adrenal cortex. They increase concentration of glucose in the blood by increasing lipolysis and by decreasing the uptake of glucose by cells.

(d) **Adrenaline:** Synthesized in the adrenal medulla and increases glucose level in plasma by stimulating glycogenolysis in the muscle and enhancing gluconeogenesis and lipolysis.

(e) **Growth Hormone:** A peptide hormone produced from the anterior pituitary gland. It increases plasma level of glucose by increasing lipolysis, glycogenolysis, and it influences protein synthesis. The last four hormones (b-e) are called anti-insulin hormones because rather than decreasing the blood level of glucose like insulin, they increase the blood level of glucose.

The blood glucose level is maintained within a narrow limit of

4.5-11mmol/L. These hormones play regulatory roles in maintaining blood glucose homeostasis. Once in circulation, glucose is taken into the liver and the enzyme that catalyses this uptake of glucose by the liver is called**Glucokinase**. This enzyme has a limited affinity for glucose, such that at low plasma glucose concentration, it is difficult to take up glucose into the liver cell. Plasma glucose is also taken up by other cells of the body like the brain, muscle, adipose tissue. The enzyme involved in these cases is **Hexokinase**. Hexokinase has a very high affinity for glucose, such that even in low plasma glucose concentration, it has the ability to take up glucose into these cells. This is clinically very important for maintaining normal cellular function. The uptake of glucose into the muscle and adipose tissues is directly influenced by insulin but glucose uptake by the brain and liver is not by direct insulin action. Glucose serves as
a source of energy for most cells and is particularly very important for the brain which uses no other energy source apart from glucose and ketones.

6.0 ABNORMALITY IN GLUCOSE METABOLISM (DIABETES MELLITUS)

Deficiency of insulin (absolute or relative i.e. whether due to inability of the pancreas to secrete enough or due to insensitivity of the cells to insulin) leads to high concentration of glucose in the blood (Hyperglycaemia). This situation is abnormal and leads to a metabolic disorder called **Diabetes Mellitus**.
Diabetes Mellitus (Hyperglycaemia state) is a component of Metabesity Syndrome. It is a metabolic disorder characterized by hyperglycaemia resulting from either absolute or relative

insulin deficiency. In Diabetes Mellitus (DM), there is hyperglycaemia (blood glucose level above renal threshold of 10mmol/L). Because of this increase of plasma glucose above renal threshold, glucose will appear in urine. Excess glucose in urine will result in osmotic diuresis because glucose is an osmotically active substance, this leads to the production of large volume of urine (polyuria). Very high plasma concentration of glucose increases plasma osmolality and causes the shift of water from the cells to the extracellular fluid along the osmotic gradient created by the high glucose level in plasma. In the brain, this can cause coma and also stimulate the thirst centre making the individual drink plenty of water (polydipsia). Low insulin level will result in high secretion of glucagon (except in type 2 diabetics) which will increase the rate of lipolysis and protein breakdown. This effect will lead to weight loss and consequent increase in appetite (polyphagia). These symptoms of polyuria, polydipsia, polyphagia and weight loss are the classical presentation of a patient with diabetes mellitus(Plate 4).

Plate 4: Pictures of the Symptoms of Diabetes Mellitus

6.1 Classification of Diabetes Mellitus

The most recent classification of diabetes mellitus is based on the aetiology:

Type 1 (a) Immune based (Autoimmune destruction of the pancreas)
(b) Idiopathic (unknown cause of pancreatic failure)

Type II Receptor associated tissue resistance to insulin
Type III Due to other causes

- Acute Pancreatitis
- Cushing's syndrome
- Phaeochromocytoma
- Drugs e.g. Thiazides

Type IV Gestational Diabetes Mellitus (GDM)

Type 1 affects people younger than 40 years and is associated with the development of ketoacidosis.

Type II affects older persons (usually above 40 years but can affect younger persons especially when it appears as part of the metabesity syndrome). Obesity (especially abdominal obesity) triggers this type of Diabetes Mellitus because of the associated insulin resistance.

6.2 Diagnosis of Diabetes Mellitus

Standard criteria for Diagnosis:

1. Random Blood Glucose $\geq$ 11.1mmol/L (RBG)
2. Fasting Blood Glucose > 7.0 mmol/L (FBG)
3. Oral Glucose Tolerance Test (OGTT) @2hrs >11.1mmol/L
4. GlycatedHaemoglobin (HbA_{1C})> 6.5%

6.3 Complications of Diabetes

Acute Complications:

a. Diabetic Ketoacidosis (Commoner in Type 1)
b. Diabetic Hyperosmolar Non-Ketotic Coma (Commoner in Type 2)

Chronic Complications

a. Diabetic Retinopathy & Cataracts
b. Diabetic Nephropathy
c. Diabetic Neuropathy/Diabetic ulcers

} Due to glucose and lipid deposition in tissues

d. Hypertension → congestive cardiac failure
e. Sexual dysfunction/infertility
f. Depression & psychiatric manifestations

6.4 Insulin-Resistant Conditions

The conditions associated with insulin resistance includes obesity, metabolic syndrome, metabesity, pregnancy etc. Any of these conditions will be accompanied with a number of metabolic chain-reactions (Figure 2 and Plate 5)

Insulin-Resistant Condition
(Obesity, Metabolic Syndrome, Pregnancy etc.)

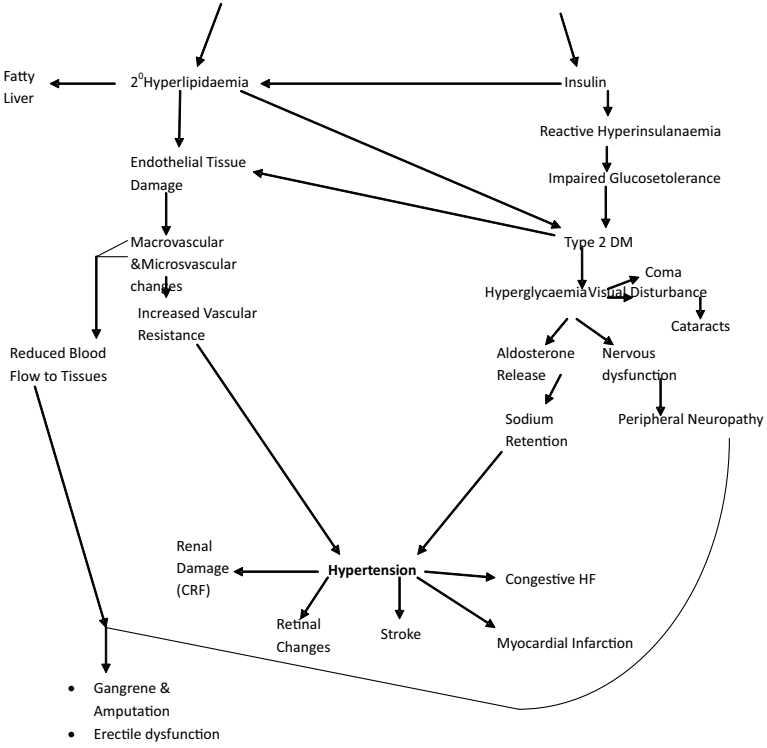


Fig. 2 Insulin Resistant Condition and Sequelae

6.5 Major Complication of Diabetes Mellitus

The major complications of diabetes mellitus (which is one the major co-morbidities of metabesity syndrome) are summarized in Plate 5. The effect of these complications on the quality of life of the affected individual can be appreciated as you see the pictures in (Plates 6a-g).

Plate 5: Major Complication of Diabetes

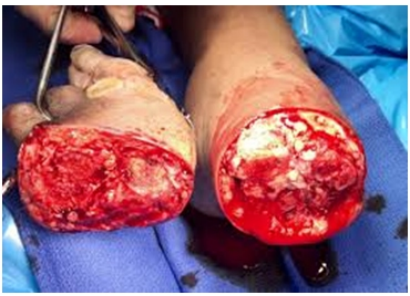


Plate a

Plate b

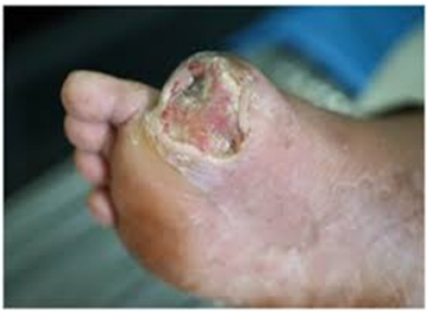


Plate c

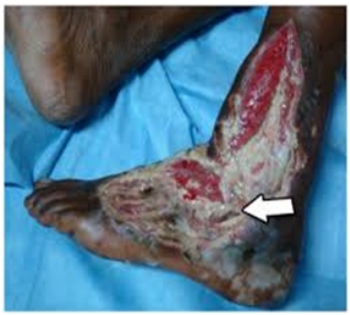


Plate d

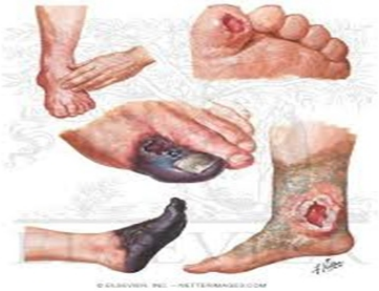


Plate e

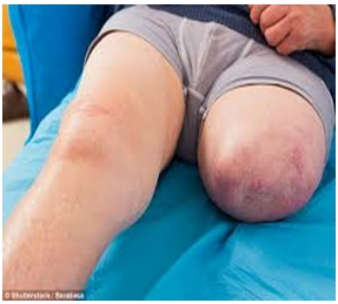


Plate f

Plate g

Plate h

Plate i

Plate 6a-i: Pictures of effect of Complicated Diabetes Mellitus on Livelihood

7.0 LIPID METABOLISM & DYSLIPIDAEMIA

Lipids are substances that are generally insoluble in water but solute in organic solvents like Ether, Chloroform, and Benzene. Four types of lipids exist in the human body:

7.1 Fatty Acids: These are straight chain carbon compounds with the general formulae RCOOH where R is the akyl group. Fatty acids are classified either based on the length of the chain or based on their level of saturation.

Based on the light of the chain, we have;

a) Short-chained fatty acids (2-4 carbon atoms)
b) Medium chained fatty acids (C6-C10 carbon

atoms)

c) Long-chained fatty acids (C12-C26 carbon atoms)

It is the long-chained fatty acids that are present in the human body and it is usually with even number of carbon atoms.

Based on the degree of saturation, we have;

(a) **Saturated Fatty Acids**: These do not contain any double bond

(b) **Mono-Unsaturated Fatty Acids**: These have only one double bond in the chain length.

(c) **Poly-Unsaturated Fatty Acids**: These contain two or more double bonds in their chain length.

Some fatty acids are very important to the body but cannot be synthesized by the body; they are called **Essential Fatty Acids** and include **Linoleic acid** and **Linolenic Acid**. Fatty acids can exist free and are called Free Fatty Acid (FFA) or Non-Esterified Fatty Acid (NEFA). Fatty acids can be esterified with glycerol to form **Triglycerides**. Free fatty acids in plasma are bound to albumin and transported to the tissues.

7.2 Phospholipids: These are complex lipids. They resemble triglycerides but are structurally different from it in that one of the fatty acid chains in triglyceride is replaced with a phosphate group and Nitrogenous base. They are important lipids because they form major constituents of cell membranes and lipoproteins.

7.3 Triglycerides: These are fatty acid esters of glycerol. Their presence in plasma confers turbidity to the plasma because of their ability to scatter light. They form part of the core of lipoproteins. They can be gotten from diet (Exogenous source)

or synthesized from the liver (Endogenous synthesis). They can be hydrolyzed by lipases in the intestines and capillary endothelium to fatty acids and glycerol.

7.4 Cholesterol: These are steroid alcohols. They are very important to the body. They are precursors of steroid hormones, prostaglandins and bile acids (this is evidenced by the fact that all these substances share the same basic skeleton of per-hydrocyclopentanophenanthrene (Sterane nucleus) ring typical of cholesterol.

Cholesterol is synthesized in the liver. The rate limiting enzyme is 3-methy Glutaryl Coenzyme A (HMG-CoA) reductase. The cholesterol formed will either be in the blood (plasma) or tissue. In the plasma, cholesterol is converted by esterification to cholesterol ester by Lecithin Cholesterol Acyl Transferase (LCAT) and in the tissues; the same conversion is catalyzed by Acyl Cholesterol Acyl Transferase (ACAT). Cholesterol ester is a component of the core of lipoproteins. Cholesterol can be secreted unchanged into bile (super saturation of Cholesterol in bile form cholesterol gallstones). Cholesterol can also be catabolized to bile acids (primary and secondary).

7.5 Lipoproteins

Since lipids are generally insoluble in water and plasma contains a high percentage of water, lipids, in their original or traditional forms cannot be found in plasma. For lipids to be carried in plasma, they must be complexed with water-soluble substances (especially proteins). This association of lipid with protein is called **Lipoprotein**. The protein component of a lipoprotein is called **Apoprotein**.

A typical lipoprotein is made up of an **envelope** of hydrophilic substances and a **core** which hides the hydrophobic lipids. The

Core thus contains Triglycerides and Cholesterol ester. The outer covering (Envelope) contains – Proteins (Apoproteins), Phospholipids and Cholesterol.

7.6 Classification of Lipoproteins

Lipoproteins are classified based on their densities (established by ultracentrifugation) or based on their electrophoretic mobility.

Based on Densities, we have (from the least dense to the most dense);

7.6.1 Chylomicron: Least dense, largest in size. Has a lipid-protein ratio of 99:1. In the core, the Triglyceride – cholesterol ester ratio (Tg:CE) is 95:5. This lipoprotein molecule is essentially **Triglyceride-rich.**

7.6.2 Very Low Density Lipoprotein (VLDL): More dense than chylomicron. Lipid- protein ratio of 90:10. In the core, Tg:CE is 85:15. This lipoprotein molecule is **Triglyceride-rich**.

7.6.3 Low Density Lipoprotein (LDL): More dense than VLDL. The Lipid-protein ratio is 80:20. In the core Tg:CE is 10:90. This lipoprotein molecule is essentially Cholesterol-rich. This is a very dangerous lipoprotein because of its atherogenic tendencies. LDL is carried to be deposited on the tissues of the body and not carried away from the tissues. Dumping LDL on tissues, especially the vascular endothelium is the precursor to coronary heart disease with its catastrophic sequelae.

7.6.4 Intermediate Density Lipoprotein (IDL): In normal humans, this lipoprotein cannot be seen

in plasma. Presence of this lipoprotein in plasma, in itself reflects a disease state. Lipid - protein ratio here is 60:40 and the Tg:CE is 50:50. Excess of IDL in plasma give rise to a primary mixed hyperlipidaemia. A condition commonly referred to as **broad-beta disease**.

7.6.5 High Density Lipoprotein (HDL): This is the heaviest (most dense) of all the lipoproteins. Lipid-protein ratio is 50:50. The Tg:CE is 30:70. This is essentially a **Cholesterol-rich molecule**. Although HDL is rich in cholesterol, it is not harmful to the body because it carries cholesterol out of the tissues (like a scavenger); it does not dump cholesterol on the tissues like LDL. Therefore, the more HDL-cholesterol you have, the better for you. Low levels of plasma HDL-cholesterol is a measure of poor health and a pointer to high risk of cardiovascular disease.

Based on Electrophoretic Mobility, we have the following lipoproteins:

a. Origin Lipoprotein – Cannot move on the electrophoretic field because of its very large particle size. This lipoprotein is **chylomicron**.

b. Pre-β Lipoprotein: VLDL

c. β – Lipoprotein – LDL (Beta- Lipoprotein)

d. α – Lipoprotein – HDL (Alpha-Lipoprotein)

IDL cannot be found in plasma under normal conditions but when it appears during disease state, it presents between the β band and the α – band. This makes the β band appear very broad;

hence this disease is called **Broad-Beta Disease**.

7.7 Endogenous Metabolism Of Lipoproteins

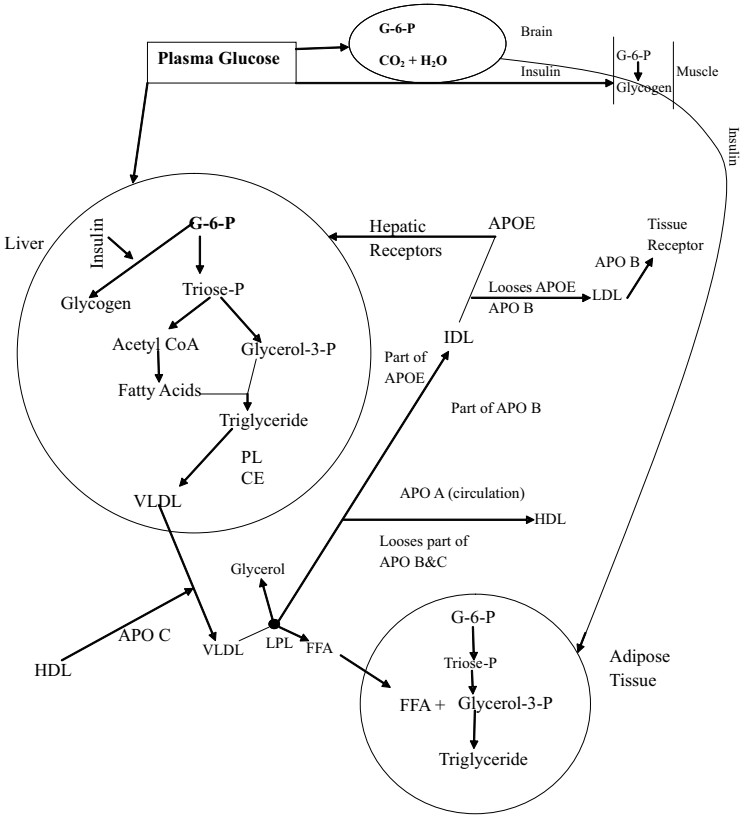


Fig. 3 Endogenous Metabolism of Lipoproteins

Chylomicrons are gotten from dietary consumption of fatty foods; HDL is synthesized during the breakdown of chylomicrons. Control of diabetes (hyperglycaemia) and dyslipidaemia (Hyperlipidaemia) are possible with regulated diet, and lifestyle modification.

8.0 DISORDERS OF LIPID (LIPOPROTEIN)

Metabolism/Hyperlipidaemia (Hyperlipoproteinaemia)
The disorder of lipid/lipoprotein metabolism that is clinically significant is hyperlipidaemia (hyperlipoproteinaemia). Hyperlipideamia can be **Primary** or **Secondary**.
Primary hyperlipidaemias are inherited hyperlipidaemias while secondary hyperlipidaemias are acquired hyperlipidaemias. Secondary hyperlipidaemias are commoner and are preventable or controllable.

Hyperlipidaemias can be:

1. Hypertriglyceridaemias
2. Hypercholesterolaemias
3. Mixed Hyperlipidaemias

8.1 Hypertriglyceridaemias: Here, there is excess triglyceride in the plasma in the form of chylomicron, VLDL or both. The plasma in these individuals appear turbid. Causes include deficiency of Apoprotein C, Deficiency of lipoprotein lipase or it may be due to a secondary cause of hyperlipidaemia. Affected individuals present with skin (tuberous) xanthomatas and severe cases can present with acute abdomen from acute pancreatitis.

8.2 Hypercholesterolaemia: This is due to high plasma

level of cholesterol, usually in the form of LDL or HDL. Causes are due to reduced LDL receptor synthesis, genetically abnormal or deficient Apo B, increased synthesis and breakdown of VLDL or it may be as a result of secondary cause of hyperlipidaemia. Affected individuals may present with tendon xanthomatas, corneal arcus, xanthalesmas (lipid deposition under the lower eyelid). The most dramatic presentation of excess LDL-cholesterol is that suggestive of atherosclerosis. LDL-cholesterol is an atheromatous lipid and so can form atheromatous plaques in the intima of medium and large sized blood vessels. This will progress to coronary heart disease.

8.3 Mixed Hyperlipidaemia: In this case, you have a mixed picture of hypercholesterolaemia and hypertriglyceridaemia. Clinical features are suggestive of both. It is primarily caused by the deficiency of Apoprotein E. Common causes of mixed hyperlipidaemias are secondary. Mixed hyperlipidaemias are thus more commonly seen in clinical practice than isolated hypertriglyceridaemia and hypercholesterolaemia.

8.4 Secondary Cause of Hyperlipidaemia

These are the common causes of the hyperlipidaemias encountered in clinical medicine and especially in our environment.

1. Hypothyroidism
2. Obesity (especially abdominal obesity)
3. Nephrotic syndrome
4. Diabetes Mellitus
5. Alcohol consumption in excess

(Acronym: HONDA); Can be controlled or prevented by regulated diet, exercise and lifestyle modification.

8.5 Lipid Profile

Lipid profile describes a group of tests/investigations carried out to assess the lipid levels in the blood of individuals and use the data obtained to estimate or assess the risk of cardiovascular disease e.g. coronary heart disease, myocardnal infarction.

Before doing a lipid profile:

1. The individual should fast for about 12 hours (especially so if triglyceride must be measured)
2. Individual must be stress-free during venepuncture
3. Serum or blood in EDTA tube is preferred and not lithium heparin tube.
4. Individual should have been on his/her normal diet two weekspreceding the test.

Tests involved:

1. Total Cholesterol (TC) - (Should be < 5.13mmol/L)
2. Total Triglyceride (Tg) - (Should be < 3.13mmol/L)
3. HDL Cholesterol (HDL) - (Should be > 0.8mmol/L
4. LDL Cholesterol can be estimated using the Friedewald's formular:
   LDL = TC - (HDL + Tg/2.2) mmol/L

This formular is valid and reliable provided total triglyceride does not exceed 5mmol/L.

LDL value should be < 3.33mmol/L

LDL value ≥ 4.20mmol/L is highly suggestive of very high risk of coronary heart disease.

Cholesterol Ratio = $TC/HDL \leq 4:1$
Ratio > 4:1 → highly suggestive of high risk of coronary heart disease.

9.0 HYPERTENSION AND ABDOMINAL OBESITY

Abdominal Obesity is waist circumference equal to or above 102cm and 88cm for men and women respectively. Hypertension is blood pressure recording in an individual above 140mmHg systolic and 90mmHg diastolic. Severe hypertension can be complicated by heart failure and / or chronic renal failure. Chronic renal failure is usually preceded by reduction in the glomerular filtration rate (GFR). The GFR can be estimated by measuring the plasma creatinine concentration and using the Cockcroft-Gault Formular:

$$\text{Cockcroft-Gault Formular} = \frac{(140 - Age(years))xWeig\square t\ (kg)}{PlasmaCreatinine\ (mmol/L)\ [x\ 0.85\ if Female]}$$

Interpretation of GFR Values:

> 90	-	Good Renal Status
60-89	-	Mild Renal Disease
30-59	-	Moderate Renal Disease
15-29	-	Advanced Renal Disease
< 15	-	End Stage Renal Disease (ESRD)

In our environment, obesity (especially abdominal obesity) and obesity-related morbidities are becoming problems of increasing importance. Abdominal obesity has been found by several studies to be associated with hypertension. About 300 million people World Wide are estimated to have abdominal obesity and it is projected that about 1 billion adults worldwide

will be obese by 2025.

Normal weight is defined by Body Mass Index (BMI) between 18 and 24.9kg/m^2. Obesity is defined as BMI equal to or above 30kg/m^2. Waist Circumference is better in assessing adiposity and risk of insulin resistance than BMI. The Co-morbidities of obesity are more associated with increasing waist circumference than with increasing BMI.Waist Circumference is better measured in centimeter (cm) using a flexible, non-stretchable tape and the land mark is the midpoint between the lower rib border and the iliac crest (upper rim of the hip bone), after full expiration and with the individual standing upright.

The prevalence of hypertension among individuals with abdominal obesity is 60%. Conscious and determined efforts at reducing waist circumference by physical exercise and dietary modifications (lifestyle changes/measures) greatly diminish the development of hypertension and other co-morbidities in individuals with abdominal obesity.

Obesity as a Metabolic Disorder

Obesity is a metabolic condition arising when the amount of calorie consumed is higher than the calorie expended. It is therefore a metabolic disorder arising from energy imbalance.

Obesity is clinically defined as a condition in which the Body Mass Index (BMI) of an individual exceeds 30.

9.1 Assessment of Obesity

9.1.1 Body Mass Index (BMI): This is the ratio of the weight in kg to the square of the height in meters. $= \frac{Weight\ (kg)}{Height\,(\mathrm{m})^2}$

9.1.2 Waist Circumference (WC): This is a measure of the abdominal girth at the level of the umbilicus, in centimeter (cm). A value of ≥ 102cm in male and ≥ 88cm in female defines obesity and particularly "Abdominal Obesity". The greater the waist circumference (Abdominal obesity) in an obese individual, the more the problems associated with obesity. In other words, the waist circumference has a direct relationship with the co-morbidities of obesity and with the "metabolic syndrome" and particularly "metabesity". This is the most important assessment of obesity, metabolically speaking.

9.1.3 Waist-To-Hip Ratio (WHR): It is a measure of the ratio of the waist circumference to the hip circumference. The hip circumference is measured as the distance around the hip from the largest extension of the buttocks. A ratio of greater or equal to 1.0 and 0.8 defines obesity in male and female respectively.

$$= \frac{WC}{HC} = WHR \begin{pmatrix} Men < 1.0 = safe \\ Female < 0.8 = safe \end{pmatrix}$$

Physical activity refers to any bodily movement produced by skeletal muscles that results in an expenditure of energy:

(a) Occupational Work: Carpentry, Construction work, Farming

(b) House Hold Chores: Washing floors, Window

cleaning, Gardening, Yard work

(c) Leisure Time Activities: Walking, Skating, Biking, Swimming, Dancing, Football, Tennis etc.

Sedentary Lifestyle: A style of life devoid of most or all of the above physical activities.

9.1.4 Classification of Obesity based on BMI and Waist Circumference (see table 1)

Table 1: ***Classification of obesity based on BMI and waist circumference***

			Disease Risk * Relative to Waist Circumference	
Description	**BMI kg/m²**	**Obesity Class**	**Male ≤ 102cm Female ≤88cm**	**>102cm > 88cm**
Underweight	< 18.5	-	-	-
Normal `	18.5-24.9	-	-	-
Overweight	25.0-29.9	-	Increased	High
Obesity	30.0-34.9	I	High	Very high
Severe Obesity	35.0-39.9	II	Very high	Very, very high
Extreme Obesity	≥ 40.0	III	Very, very high	Extremely high

* Type II DM
* Dyslipidemia
* Hypertension
* Coronary Heart Disease

9.2 Pathophysiologic Pathway that Controls Obesity & BMI

Thereare a number of postulations regarding the evolution and progression of overweight and obesity. One of the major postulations have to do with the Leptin pathway (figure 4).

PATHWAY THAT CONTROLS OBESITY & BMI

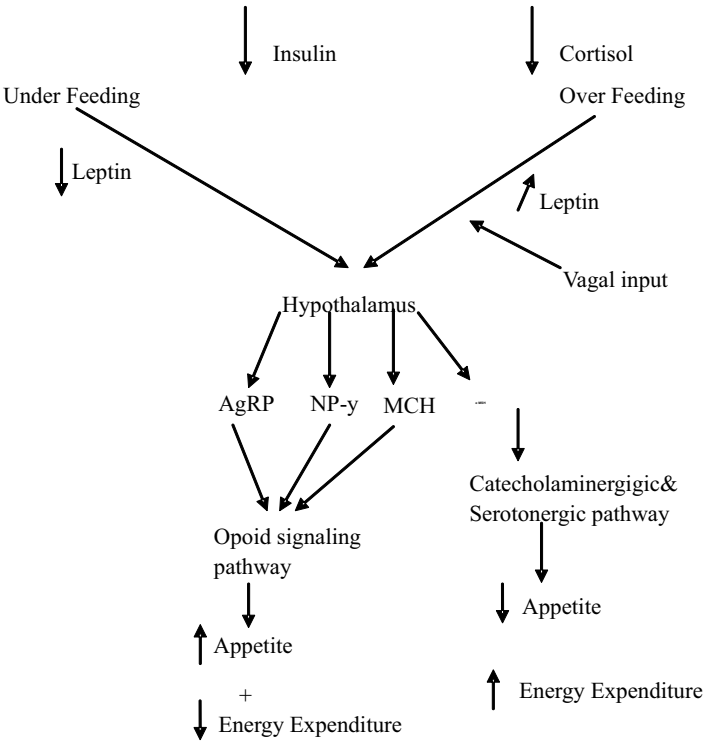


Fig 4: The obesity –Leptin Pathway

Energy Expenditure (Metabolic)

1. Basal Metabolic rate (BMR) – 70%
2. Energy involved in metabolizing and storing food
3. Thermic effect of exercise – 5-10%
4. Adaptative thermogenesis (BAT)

9.2.1 Factors Contributing to Obesity: The adipose tissues secrete the hormone called leptin which is important in the stimulation of neural and endocrine mechanisms involved in the control of appetite. The leptin pathway is believed to be responsible for appetite control acting through the hypothalamus. In obesity, one of the hypothesis has been that there is a disorder of the leptin pathway. In this pathway, when there is underfeeding, there is reduced production of leptin by adipocytes which causes hypothalamic release of neuropeptide-Y (NP-y), Agouti related peptide (AgRP) and melanocyte concentrating hormone (MCH). These three substances increase appetite and reduce energy expenditure acting through the Opoid Signaling Pathway. By this mechanism, appetite is increased in a person that is underfeeding. In states of overfeeding, there is increase in leptin production by the adipocytes; overfeeding itself also causes vagal stimulation. The hypothalamus in response to these stimulations secretesthe α – melanocyte stimulating hormone (α – MSH) which decreases appetite and increases energy expenditure acting through the Serotonergic and Catecholaminergic pathway; a disorder in this pathway is believed to contribute to obesity. Insulin and cortisol exert positive influences on this pathway.

9.2.2 Genetic/Environmental Factors in Obesity: It

has been found that there is a genetic component to obesity. Evidence to support this stems from the fact that children born to obese parents tend to be obese, while children born to lean parents have less likelihood to obesity. Identical twins of obese parents tend to become obese even when they are reared apart. Environmental factors have also been seen to play a part in obesity. They tend to modulate the genetic predisposition. For example, in an environment that is faced with famine, individuals genetically prone to obesity fail to develop obesity.

9.2.3 Behavioural Factors in Obesity: Individuals with sedentary life style are prone to obesity than individuals involved in active work and exercise.

9.2.4 Cultural Factors in Obesity: Certain cultures encourage obesity. Female confinement as practiced in certain parts of Nigeria after delivery of a baby or wives of Alhaji's who are kept in confinement and away from the public. In some parts of Africa, the wealth of a man is assessed by the size of his wife.

9.2.5 Disease and Obesity: Certain disease states tend to encourage or predispose to obesity. In polycystic ovarian syndrome (PCOS) and in Cushing's syndrome, obesity is usually an accompanying feature.

9.2.6 Drugs and Obesity: Steroids and antidepressants have also been implicated in

obesity.

9.3 Co-Morbidities of Obesity

Co-morbidities of obesity are disease states or adverse health conditions associated with obesity. The prevalence of these Co-morbidities increases as the abdominal circumference (WC) increases. In other words, they are brought about more by an increase in abdominal circumference than by just an increase in BMI. These Co-morbid conditions include:

9.3.1 Type II Diabetes Mellitus: Obesity is associated with insulin resistance and Type II Diabetes Mellitus.

9.3.2 Coronary Heart Disease (CHD): This is a major problem in obese individuals. It arises as a result of atherogenic lipids occasioned by increase lipolytic action of abdominal fats; this leads on to atherosclerosis and CHD. In these individuals, the Low Density Lipoprotein (LDL) is abnormally high, Total Cholesterol (TC) is abnormally high and High Density Lipoprotein-Cholesterol (HDL) is decreased.

9.3.3 Osteoarthritis: This is associated with obesity as a result of increasing weight on the joints.

9.3.4 Malignancies: Obesity is associated with increased incidence of certain malignancies. This is thought to be as a result of the increased conversion of androstenedione to estrone. The malignancies often associated with obesity include that of breast, ovary, endometrium in females and in the males prostate, colon, rectum etc.

9.3.5 Fungal Infections: Due to the increase in the friability of the skin in obesity, obese individuals are prone to severe fungal infections.

9.3.6 Gout: Obesity is associated with gout (an inflammatory condition due to deposition of monosodium urate crystals in the joint and soft tissues; commonly complicating severe hyperuricaemia). This is as a result of increase cell turnover and uric acid production.

9.3.7 Psychological Depression: Obese individuals suffer psychological depression resulting from the feelings of not looking like others, this is especially so in those with morbid obesity, metabolic syndrome or "Metabesity".

1 Insulin Resistance
Type II DM } 80%
Glucose intolerance

↑with weight gain
↓with weight loss
↑with intra abd. Fat
TNF – α
FFA↓es Insulin action

2. Hypogonadism in Male:

↓Testosterone
↓SHBG
↑Estrogen

3. Polycystic Ovarian Syndrome (40%) ↑Androgen Anovulation

4. Malignancies e.g. Breast, Endometrium, Cervix, Ovaries, Prostate, Colon, Rectum etc. ↑Androstenedione ↘ Estrogen

5. Cardiovascular Disease: ↑Lipolytic activity of abdominal fat
   ↓
   ↑Atherogenic Lipid Profile

6. Pulmonary Disease: ↓Chest wall compliance
   ↓Work of breathing
   ↑Minute ventilation
   ↓Total Lung Capacity
   ↓Functional Residual Capacity
   (→ Obstructive sleep apnea - obesity hypoventilation syndrome)
7. Gallstones,Cholecystitis, Cholelithiasis:
   →↑Biliary secretion of Cholestrol
   →Supersaturation of fats →Gallstones
8. Bone & Joint Disease:
   →↑ Trauma → Added wt. bearing → Osteoarthritis
9. Fungal/Yeast Infections: ↑ Friability of skin
10. Complications of Pregnancy: Big Babies – C/S
11. Gout: - ↑ Cell turnover/uric acid production
12. Poor female Reproductive Health:
    Menstrual irregularities, Infertility, irregular ovulation
13. Bladder Control Problems: Stress incontinence
14. Psychiatric Problems

Metabolic Syndrome occurs if any three (3) of these are found in one individual:

1. Hypertriglyceridaemia (Triglyceride – Tg> 1.7mmol/L)
2. Abdominal (waist) circumference ≥ 88cm (female), ≥ 102cm (male)
3. High Density Lipoprotein - Cholesterol (HDL) < 1.0mmol/L
4. Hypertension, BP > mmHg $^{130}/_{85}$
5. Insulin resistance, with a fasting plasma glucose of ≥ 6.1mmol/L

If abdominal obesity (WC> 88cm (female), 102cm (male) is one of the three (or more) components of metabolic syndrome in an individual, you can say the individual has "Metabesity syndrome", this poses a higher challenge for the metabolic physician.

9.4 Management of Obesity

There are three modalities for the effective management of obesity. The effective management of obesity is multi-disciplinary. In the main, it involves:

9.4.1 Combines Lifestyle Measures: This is by far the most important approach in the management of obesity. It involves dietary regulation (a dietician should be involved here, who will fashion the diet with respect to the food locally available in the environment), exercise and behavioral therapy. All these combined should be able to reduce the weight by about 10% in 6months. Failure to achieve this within the time

period will need addition of drugs to these measures.

9.4.2 Goals of Combined Lifestyle Measures

1. Reduce body weight
2. Maintain a lower body weight over long term
3. Prevent further weight gain

For desired effect: Weight loss of 10% body weight over 6 months is the target.

9.4.3 Other Modalities of Management

(a) **Drugs**: In the treatment of Obesity, drugs must not be used alone. They must be used in conjunction with the combined lifestyle measures. Consider pharmacotherapy to have failed if patient does not lose up to 2kg in first four weeks of treatment. Drugs involved include Dopamine and Serotonine re-uptake inhibitor (e.g. Silbutramine) and Pancreatic Lipase inhibitor (e.g. Orlistat (Xenical)) which decreases fat absorption.

(b) **Surgery**: Surgery is reserved for patients with clinically severe obesity (extreme or morbid obesity) i.e. BMI $\geq$ 40 or a BMI $\geq$ 35 with Comorbid conditions.

There are different modalities of surgery but surgical procedures are complicated by anastomotic leak, subphrenic abscess, splenic injury, pulmonary embolism, wound infection,

stoma stenosis etc.

9.4.4 Nutrient and Recommended Intake

DIETARY GUIDELINE

Nutrient		**Recommended Intake**
Calories		≅500to 1000Kcal/day Reduced from usual intake ♀ 1000 -1200Kcal/day ♂ 1200 -1600 Kcal/day
Total Fat	-	30% or less of total calorie
Sat. Fatty Acid	-	8-10% of total calorie
Mono unsaturated fatty Acid	-	Up to 15% of total calorie
Polyunsaturated Fatty Acids	-	Up to 10% of total calorie
Cholesterol	-	< 300mg/day
Protein (Plant & lean animal sources)		≅15% of total calorie
Carbohydrate	-	55% or more of total calorie
Sodium Chloride	-	No more than 100mmol/day (6g Nacl)
Calcium	-	1000 – 1500mg/day
Fibre	-	20 -30g/day

9.4.5 A Guide To Selecting Treatment

Table 2: Guideline for Choice of Management Modality in Obesity

Treatment	25-26.9	27-29.9	30-34.9	35-39.9	
Diet, Physical Activity, Behavioural Therapy	+	+	+	+	+
Pharmacotherapy	-	With comorbidities	+	+	+
Surgery	-	-	-	With comorbidities	+

10.0 MY CONTRIBUTIONS TO KNOWLEDGE

Metabolic Syndrome (Specifically "Metabesity") is a very important and complex syndrome in metabolic medicine. The syndrome and its various ramifications affect virtually all the systems in the body. This is the reason up till date researchers and medical scientists are still unraveling components and disorders associated with the metabolic syndrome, its components and particularly abdominal obesity. It is to this area of medicine I applied myself and made my modest contributions to knowledge.

A study to evaluate the prevalence of metabolic syndrome among apparently healthy individuals in our environment was carried out using two different criteria for metabolic syndrome (NCEP-ATP III and WHO (2002)).

National Cholesterol Education Programme – Adult Treatment Panel III (NCEP-ATP III) criteria for metabolic syndrome (2005): Fasting Plasma Glucose (FPG) $\geq$ 6.1mmol/L, Waist Circumference (WC) > 102cm (male) and > 88cm (female), Blood Pressure (BP) >130/85mmHg, Triglyceride > 1.7mmol/L, HDL < 1.0mmol/L (male) and < 1.3mmol/L (female), any three or more of the above criteria.

World Health Organization (WHO) criteria for Metabolic Syndrome (1999): Fasting Plasma Glucose $\geq$ 6.1mmol/L or random Plasma Glucose $\geq$ 7.8mmol/L plus any two or more of the following other criteria: BMI > 30kg/m^2, BP $\geq$ 140/90mmHg, Triglyceride > 1.7mmol/L, HDL < 0.9mmol/L (male) and < 1.0mmol/L (female).

The NCEP-ATP III emphasizes abdominal obesity rather than overall obesity in definition of metabolic syndrome (metabesity) while the WHO definition lays emphasis on

abnormalities in glucose homeostasis with high risk of type 2 DM and recognizes overall obesity (increase BMI) rather than abdominal obesity (increase Waist Circumference).

Odum EP and Orluwene CG (2013) found higher prevalence (15.7%) of the metabolic syndrome using the ATP III definition than that with WHO definition (10.9%). The ATP III definition thus identifies greater number of persons at high risk of cardiovascular disease and type 2 Diabetes (Tables 3, 4 and figure 5).

Table 3: Prevalence of risk factors in Total Population and Metabolic Syndrome (MS) individuals

	Total Population (N = 267)			
	NO MS Subjects		**MS Subjects**	
Risk Factors	ATP III (%)	WHO (%)	ATP III (%)	WHO (%)
High BP	41.6	34.8	90.5	72.4
Obesity	35.1	29.1	87.5	75.0
Hyperglycemia	15.4	10.1	57.1	69.0
Low HDL	25.8	12.0	45.2	24.1
High TG	6.0	6.0	23.8	17.2

Table 4: Prevalence of metabolic syndrome components in men and women

	ATP III (%)		WHO (%)	
MS Components	Male	Female	Male	Female
High BP	93	87.1	72.7	72.2
Obesity	83.3	90.1	63.6	88.9
Hyperglycemia	50.5	62.3	72.5	66.7
Low HDL	50.4	38.7	36.4	16.7
High TG	34.5	12.9	18.2	16.5

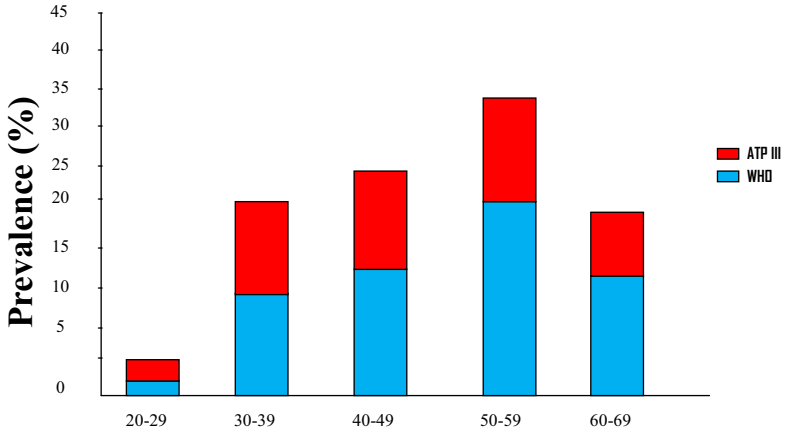


***Figure 5**: Age-Specific Prevalence of Metabolic Syndrome*

In a prospective study involving 195 subjects (comprising 50 obese type 2 diabetics with metabesity syndrome, 45 obese type 2 diabetics without metabesity syndrome, 50 non-obese type 2 diabetics without metabesity syndrome and 50 non-diabetic, non-obese individuals recruited as control)- (Table 1 and 2)Orluwene CG and Ojule AC (2006) found that there was a significant reduction in plasma cholinesterase activity of obese type 2 diabetic individuals with metabesity syndrome (3315 ± 671i.u/L) when compared with the control group (8219 ± 815i.u/L), subjects without metabesity syndrome showed normal plasma cholinesterase activity. The study showed that reduction in plasma cholinesterase activity is associated with the metabesity syndrome. This has important implication in surgery involving general anaesthesis because cholinesterase hydrolyzes succinylcholine which is a potent muscle relaxant used for general anaesthesia. A significant reduction in normal plasma level of cholinesterase will lead to a sustained effect of

succinylcholine and delayed recovery from anaesthesia post-surgery. This study was published and is highly referenced (Tables 5 and 6).

Table 5: Physical measurements of diabetic subjects and control

Group	No of subjects n	Mean Age (yr)	Male (M)	Female (F)	BMI (Kg/M^2)	Waist circumference (cm)	Systolic BP (mmHg)	Diastolic BP (mmHg)
A (Obese Diabetics with M. S.)	50	57(5)	15	35	40(2)	125(4)	145(5)	95(10)
B (Obese Diabetics NO M.S)	45	58(4)	8	37	37(2)	93(3)	125(5)	80(5)
C (Non-Obese Diabetics NO M.S)	50	56(4)	15	35	19(4)	60(7)	120(5)	75(10)
D (Non-Obese, Non-Diabetics NO M.S Control)	50	55(6)	15	35	22(3)	65(8)	115(5)	70(10)

* M. S = Metabolic Syndrome, BMI = Body Mass Index, BP = Blood Pressure
(Orluwene CG and Ojule AC. Plasma Cholinesterase activity in Obese type 2 Diabetics. Port Harcourt Medical Journal 2006; 1:39-43).

Table 6: Laboratory Measurements of diabetic subjects and control

Group	TG (mmol/L	HDL-C (mmol/L	FBG (mmol/L	PCHE (mmol/L
A (Obese, Diabetics with M. S.)	5.72 (1.21)	0.63 (0.1)	9.3 (1.5)	3315 (671)
B (Obese, Diabetics NO M.S)	1.50 (0.61)	1.75 (0.81)	8.5 (1.0)	8183 (1101)
C (Non-Obese, Diabetics NO M.S)	1.92 (0.82)	1.62 (0.11)	11.2 (3.1)	7992 (967)
D (Non-Obese, Non-Diabetic NO M.S Control)	1.70 (0.51)	2.33 (0.23)	4.3 (0.9)	8291 (815)

TG = Triglyceride, HDL-C = High Density Lipoprotein-Cholesterol, FBG- Fasting Blood Glucose
PCHE = Plasma Cholinesterase(Orluwene CG and Ojule AC. Plasma Cholinesterase activity in Obese type 2 Diabetics. Port Harcourt Medical Journal 2006; 1:39-43).

In another study carried out among oil company staff in Port Harcourt, we also found association between Microalbuminuria Evidence of renal dysfunction) and metabesity syndrome.

Microalbuminuria is defined as a rate of excretion of albumin in the urine that is between normal and overt proteinuria. This precedes and is highly predictive of diabetic nephropathy. It is urinary albumin excretion ≥ 20mg/min for timed collection or ≥ 30mg/g (albumin: creatinine).

The study showed a strong association between metabesity syndrome and microalbuminuria. Individuals with metabesity syndrome are thus prone to development of renal dysfunction (Orluwene CG and Ojule AC). Microalbuminuria and the Metabolic Syndrome in Obese type 2 diabetes. Port Harcourt Medical Journal 2007; 2:61-66.

Orluwene CG and Nnatuanya I. (2010) carried out a study on the effect of metabesity on serum prostate-specific antigen (PSA) values of adult males in this environment. We recruited 75 subjects into this prospective study comprising 38 males who satisfy the criteria for metabesity and 37 age-matched males as control. All subjects had no obvious prostate pathology and were not overtly diabetic.

The tables below depicts the results of the study (Tables 7 and 8).

Table 7: Physical characteristics and measurements of individuals with metabesity and control

Group	No of subjects	Mean Age yr)	Mean BMI (Kg/m2)	Waist circumference (cm)	Systolic BP (mmHg)	Diastolic BP (mmHg)
Subjects without Metabesity	37	50(2)	24.6(1.3)	82(2)	128(3)	82(2)
Subjects with Metabesity	38	51(1)	32.1(0.9)	110(4)	143(5)	94(1)
P-Value	P = 0.08	P = 0.10	P = 0.02	P = 0.03	P = 0.03	P = 0.03

Table 8: Laboratory parameters of individuals with metabesity and control

FBG	PCHE (mmol/L	Mean TG Age yr)	Mean HDL-C (mmol/L	Mean FPG (mmol/L)	Mean PSA Value (ng/ml)
Subjects without Metabesity	37	1.61(0.33)	) 1.62(0.20)	4.01(1.20)	2.3(0.6)
Subjects with Metabesity	38	4.25(1.12)	0.68(0.10)	6.71(0.11)	5.8(1.4)
P-Value	P = 0.08	P = 0.01	P = 0.015	P = 0.035	P = 0.01

The subjects with metabesity had a mean PSA value of 5.8 ± 1.4ng/ml while subjects without metabesity had mean PSA value of 2.3 ± o.6ng/ml. this was a statistically significant difference. This implies that care must be taken when interpreting the prostate specific antigen (PSA) results in individuals with metabesity. These group of individuals may need a different "reference interval" for PSA. The result of this study was published and referenced.

Orluwene CG; Mommoh MO (2012) carried out a study to evaluate thyroid hormone levels in Oil Company (NNPC) workers with metabesity in Port Harcourt. A total of 93 industrial workers were recruited comprising 48 that satisfied the diagnostic criteria for metabesity and 45 age-matched controls. The result of this study showed that metabesity is also associated with sub-clinical hypothyroidism, with females being at increased risk of this association (Tables 9,10 and 11).

Table 9: Study group characteristics of individuals with metabesity compared with the control group

Parameters	Study Group (Subjects with Metabesity n = 48)	Study Group (Subjects without Metabesity n = 48)	P- Value
Men	16(33%)	15 (33%)	0.66
Women	32 (67%)	30 (67%)	
Age	41 (5.2)	42 (6.3)	0.59
Waist circumference	103 (3.66)	81.7 (5.1)	0.002
Systolic BP (mmHg)	139.2 (4.8)	122.4 (2.7)	0.001
Diastolic BP (mmHg)	90.5 (6.1)	83.3 (2.2)	0.001
Total Cholesterol (mmol/L)	5.7 (0.7)	4.6 (0.8)	0.015
Triglyceride (mmol/L)	1.85 (0.4)	1.28 (0.6)	0.001
Fasting Plasma Glucose (mmol/L)	6.5 (0.6)	4.9 (0.5)	0.029
High Density Lipoprotein-Cholesterol (mmol/L)	0.8 (0.2)	1.2 (0.1)	0.030
Low Density Lipoprotein-Cholesterol (mmol/L)	3.4 (0.6)	2.7 (0.5)	0.025
Thyroid stimulating hormone (thyrotropin)	5.8 (3.7)	3.7 (3.2)	0.026
Free Thyroxine (ng/dl)	1.09(0.5)	1.38 (0.7	0.038

Table 10: Thyroid function (TSH & FT_4) in individuals with metabesity syndrome compared with the control group

Mean	Study Group (Metabesity n = 48)	Study Group No Metabesity n = 48	P-Value
Overt Hypothyroidism (High TSH + Low FT_4)	0 (0%)	0 (0%)	
Sub-Clinical Hypothyroidism (High TSH + Low-Normal FT_4)	42 (87.5%)	8 (18%)	0.0001
Euthyroid (Normal TSH + Normal FT_4)	6 (12.5%)	37(82%)	0.0001
Hyperthyroidism (Low TSH + High FT_4)	0 (0%)	0(0%)	

Table 11: Association between Patient characteristics and sub-clinical hypothyroidism in the metabesity study group using multiple regression analysis

Parameters	Odds Ratio	Confidence Interval	P- Value
Age	0.401	0.421-1.102	0.234
* Gender	7.521	1.950-13.212	0.025
Systolic BP	0.651	0.540-1.320	0.087
Diastolic BP	0.288	0.280-2.988	0.250
Waist Circumference	2.110	0.590-1.920	0.320
Total Cholesterol	1.520	1.620 – 1.949	0.318
Triglyceride	0.200	0.150 – 1.124	0.071
High Density Lipoprotein Cholesterol	1.301	0.521 – 3.994	0.421
Fasting Plasma Glucose	0.298	0.650 – 2.501	0.385

* Logistic regression analysis recognized the association between female gender (P + 0.025, CI: 1.950 – 13.212) and Sub-clinical hypothyroidism.

From our discussion so far, it is clear that obesity (particularly abdominal obesity) precedes the development of many of the cardiovascular risk factors, including type 2 diabetes mellitus, hypertension and chronic kidney disease. Labile iron has been shown to be associated with these chronic diseases. Orluwene CG andOdum EP (2012) worked on the hypothesis that labile iron may be one of the links between abdominal obesity and these disorders.

We evaluated urinary labile iron in industrial workers with abdominal obesity in Port Harcourt. The result of the study showed that abdominal obesity is associated with increased urinary labile iron. Urinary labile iron is a useful marker of oxidant stress.

Orluwene CG and Isaac NN (2012) were able to show through a prospective study of 72 individuals with metabesity syndrome that a new macrophage-derived biomarker, soluble CD163, is

associated with metabesity and that increasing fasting serum concentration of soluble CD163 in individuals with metabesity predicts increased risk of type 2 diabetes. The data suggest that fasting serum CD163 is a marker for adipose tissue inflammation, and thus for detection of groups at high risk of development of type 2 diabetes especially among individuals with metabolic syndrome (Tables 12, 13, 14 and 15).

Table 12: Parameters of individuals with metabolic syndrome and control recruited for study

Parameters	Age Groups (yrs) 20–40	41–60	P-Value
Number of Subjects	30	42	
Age (yr)	29 (4.5)	52(6.1)	<0.001
Waist circumference	108(4.5)	111(6.2)	0.03
Men	11	15	
Women	19	27	
SBP (mmHg)	128(7.2)	132(8.3)	0.02
DBP (mmHg)	86(5.6)	93(4.8)	0.001
Glucose (mmol/L)	6.2(0.4)	6.3(0.2)	0.45
Total Cholesterol (mmol/L)	5.4(1.2)	5.6(1.8)	0.31
Triglyceride (mmol/L)	1.9(0.3)	1.8(0.7)	0.25
HDL (mmol/L)	0.8 (0.2)	0.7(0.4)	0.34
LDL (mmol/L)	3.0(0.9	3.6 (0.4)	0.02
FsCD163	1.4 (1.2)	1.7 (1.6)	0.03

Table 13: Levels of FsCD163 and Percentage distribution by gender in the age groups

	Age group (Yr)			
	20 – 40		41 – 60	
Parameters	M	F	M	F
Number of Subjects	11(36.7%)	19(63.3%)	15(35.7%)	27(64.3%)
Subjects with FsCD163 <1.0mg/L	3(10%)	1(3.3%)	4(9.5%)	2(4.8%)
Subjects with FsCD163 (1.0-1.5mg/L)	2(6.7%)	8(26.7%)	4(9.5%)	11(26.2%)
Subjects with FsCD163 (>1.5mg/L)	4(13.3%)	12(40%)	7(16.7%)	14(33.3%)

Table 14: Number and percentage of the individuals with metabolic syndrome (metabesity) among the two groups and in the various levels of FsCD163 that developed frank type 2 DM after 5 years of follow-up

Parameters	Age Group (yrs.) 20 – 40 M	F	41 – 60 M	F
Number of Subjects	11(36.7%)	19(63.3%)	15(35.7%)	27(64.3%)
Subjects lost to follow-up (by Death)	0(0%)	0(0%)	0(0%)	2(4.8%)
Subjects with FsCD163 <1.0mg/L that got DM	0(0%)	0(0%)	0(0%)	0(0%)
Subjects with FsCD163 (1.0-1.5mg/L) that got DM	0(0%)	1(3.3%)	1(2.4%)	2(4.8%)
Subjects with FsCD163 (>1.5mg/L) that got DM	2(6.7%)	7(23.3%)	5(11.9%)	11(26.2%)

Table 15: Adjustment made for Covariates using Multiple Regression Model

Variable	Parameter estimate	SE	t	Pr>|t|
Intercept	- 0.32	1.65	-0.18	0.72
*FsCD163	1.30	0.36	3.14	0.001
Gender	-0.52	2.15	-0.19	0.63
Age	-0.82	1.96	-0.13	0.82
*Waist circumference	3.12	2.31	2.44	0.02

* After adjusting for covariates using multiple regression analysis, only FsCD163 and waist circumference remained associated with type 2 DM.

The Vice – Chancellor Sir, an integrated antioxidant defence system exists in plasma and cells of human beings to protect the individual against free radical-induced damage – a mechanism that underlies some chronic disease states in the body (e.g. type 2 Diabetes, cardiovascular disease etc.).This integrated antioxidant defence system is measured as the Total antioxidant status (TAS). Vitamin C and Vitamin E contributes to this total defence system. Odum EP, Orluwene CG, Ejilemele AA and

Wakwe VC (2012) carried out a study in this environment to show that plasma total antioxidant system (TAS) and Vitamins C and E are significantly lower in individuals with metabolic syndrome (metabesity).

This may be as a result of oxidative stress and may aggravate impaired insulin action and endothelial dysfunction and then predispose to diabetes (type 2) and cardiovascular disease. The implication of or inference from this study is that

adequate dietary antioxidants and supplementation could be beneficial in preventing or delaying the consequences of metabesity.

Found a strong association between Metabolic Syndrome (metabesity), Sub-clinical Hypothyroidism, Total Plasma Homocysteine and High Sensitivity C-Reactive Protein. We also found that females have more of this association than males. Individuals with metabesity need to be screened for Sub-clinical Hypothyroidism, Total Plasma Homocysteine and High-Sensitivity C - Reactive Protein. If these four risk factors are found in one individual, there is an increased risk for and accelerated progression for cardiovascular disease. These individuals may benefit from aggressive proactive therapy (Orluwene CG and Mommoh MO(2013)).

In another study carried out in Port Harcourt using female industrial workers as our subjects, Orluwene CG and Mommoh MO (2013) found that associated with thyroid dysfunction (which is a feature of metabesity syndrome) are abnormalities of serum phosphorus and ionized/total serum calcium concentration in the body, thus predisposing these females to early osteoporosis (metabolic bone disease) and necessitating the supplementation of these to prevent severe bone complications.

11.0 Other Contributions to Knowledge

Other academic contributions to knowledge are shown below;

1. **Orluwene CG,** Ojule AC**,** Microalbuminuria and the Metabolic Syndrome in Obese Type 2 Diabetes. *Port Harcourt Medical Journal 2007; 2:61 – 66.*

2. **Orluwene CG**, Mommoh MO: Screening for Microalbuminuria in Newly Diagnosed Type 2 Diabetics at a staff clinic in Port Harcourt. *Port Harcourt Medical Journal 2008; 3: 10 – 14.*

3. **Orluwene CG**, Nnatuanya I: Association of metabolic biomarkers of cardiovascular disease in overweight and obese children in Emohua Local Government Area of Rivers State, Nigeria. *IOSR Journal of Dental and Medical Sciences (JDMS), 2012;1(3): 40 – 46.*

4. **Orluwene CG,** Mommoh MO**:** Plasma total homocysteine, High-sensitivity C-reactive protein and thyroid function in metabolic syndrome patients. *The Nigerian Postgraduate Medical Journal, 2013, Vol. 20; (4), 286-290.*

5. **Orluwene CG,** NkoyoN**.** Use of Serum Cystatin C in Assessment of Early Deterioration of Renal Function in Type 2 Diabetic Industrial Workers in Port Harcourt, Nigeria. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), 2013, Vol. 8 (2); 27-35.*

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12.0 CONCLUSION

Hebrews chapter 12 verse 1b states (Amplified Bible Version), "Lay aside every weight and the sin which so easily entangles us and let's run with perseverance the race that is set before us"
Life is a race and to be able to run this race effectively, there are certain weights (habits/principles/idiosyncrasies) we just must consciously relief ourselves of. When we deliberately fail to do this or through our conscious actions and inactions add-on these "weights" to ourselves, we run the race of life to a halt much faster than we are destined to, thus committing suicide slowly.
Race is very strenuous, Race is exhausting if you add letter "G" to Race, it turns Race to "Grace"
GRACE is easier to run than Race
GRACE is less exhausting
The "G" that will turn RACE to GRACE stands for:

1. Good personal principles (You can never neglect the effect of this on longevity)
2. God-Factor (The closer you get to God the more you turn RACE to GRACE)

Running Grace is like being carried on "Eagle's wings"
Vice-Chancellor Sir, Ladies and Gentlemen, while we still live, let us make conscious efforts to "RUN GRACE and not RACE") BY:

A. Checking these 4 things as often as possible:

1. Your BP
2. Your Blood Glucose
3. Your LDL
4. eGFR

B. Minimizing these 6 things in your Diet as much as possible:

1. Salt
2. Sugar
3. Canned meat and food
4. Roasted red meat
5. Dairy products
6. Starchy products

C. Deliberately increasing these 4 things in the food:

1. Greens/vegetables
2. Beans
3. Fruits
4. Nuts

D. Deliberately trying to forget these 3 things:

1. Your age
2. Your past
3. Your grievances

E. Endeavour to keep these 4 things, no matter how endowed you are:

1. Friends who really love you
2. Caring family
3. Positive thoughts
4. A warn home

F. Doing these 5 things to keep healthy:

1. Fasting
2. Smile/Laugh

3. Trek/Exercise
4. Reduce your weight

G. You don't have to do these 6 things:

1. Waiting until you're hungry to eat
2. Waiting until you're thirsty to drink
3. Waiting until you're sleepy to sleep
4. Waiting until you're tired to rest
5. Waiting until you're sick to medical check-ups
6. Waiting until you have a problem to pray to God

You need to "TAKE CARE OF YOURSELF".

12.2 Recommendations

1. Government should increase funding to the educational sector and make it easier for educational institutions in this country to access these funds and enhance quality research which is the catalyst to development of any society. Metabesity is one area that needs increased research, especially to find out the most appropriate therapies for metabolic syndrome which is becoming very common in our environment with increasing westernization of our population.

2. Government at all levels, institutions, corporate organizations and individuals should begin to lay more emphasis on preventive than curative medicine. Periodic medical checks should be encouraged and made necessary not just for employment but also for

progression and promotion in the employment. Staff should regularly check their waist circumference, blood pressure, fasting plasma glucose, renal function (estimate GFR), Lipid profile, (assess cardiovascular risk). The metabolic clinic should be established at our teaching hospitaland made to be fully functional. Staff should undergo periodic metabolic assessments and not just when sick. The metabolic clinic can run once a week. If adequately utilized, apart from treating patients with metabolic disorders, individuals at risk of cardiovascular disease, type 2 diabetes and other non-communicable chronic diseases and malignancies could be detected and necessary preventive measures put in place to avertuntoward outcome.

3. Health institutions should appropriately engage dieticians and observe general dietary recommendations following established guidelines of low intake of saturated fats (intake of mono unsaturated fatty acids like olive oil is beneficial in preventing metabolic syndrome and its co-morbidities), reduced consumption of sugars, increased intake of fruits, vegetables and whole grains, quitting smoking (very beneficial), moderate alcohol consumption in the form of red wine is not injurious to cardio-metabolic health (alcohol-red wine, Champaign's – contains polyphenols which helps carbohydrate metabolism and increase HDL-C levels. Moderate alcohol is < 20g/d for women and < 40g/d for men).

4. The University should incorporate lectures and possible practical sessions on lifestyle measures in all faculties (just as we have the GES courses). The University should have agymnasium that should be fully equipped and utilized. Standard exercise recommendation is a daily minimum of 30minutes of moderate intensity physical activity e.g. brisk walking, swimming, jogging, biking, golfing, team sports. On a wider scale, a department of lifestyle medicine is strongly advocated.

5. We have to deliberately reduce common sedentary activities in our leisure time (television watching and computer games). We can purchase simple exercise equipment for the home (e.g. treadmills). Vice-Chancellor Sir, Distinguished Academics, Ladies and gentlemen, I AM DONE: Thank you for your attention.

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