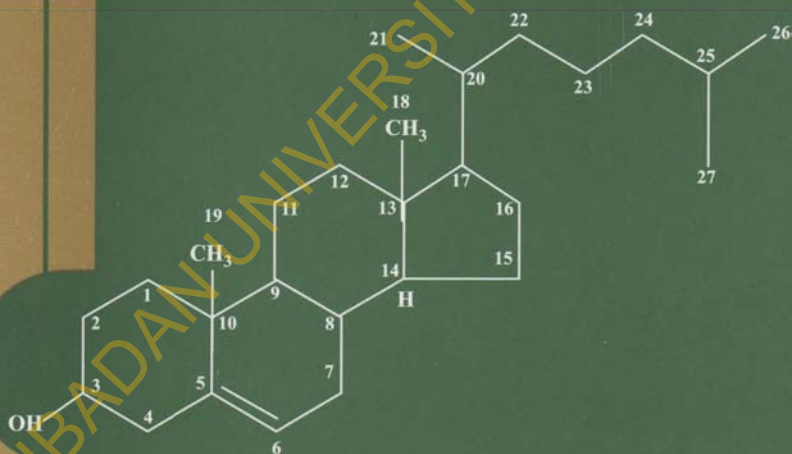


Recent Advances In Nutrition And Metabolism



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RECENT ADVANCES IN NUTRITION AND METABOLISM

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IBADAN UNIVERSITY PRESS
2017

Ibadan University Press,
Publishing House,
University of Ibadan,
Ibadan, Nigeria

© 2017 Department of Chemical Pathology
University of Ibadan, Ibadan

First Published 2017

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ISBN: 978 – 978 – 54045 – 1 – 7

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OVERWEIGHT, OBESITY AND METABOLIC SYNDROME: IMPLICATIONS IN RESOURCE POOR SETTINGS

Mabel A. Charles-Davies and Emmanuel O. Agbedana**

Introduction

ABSTRACT

Overweight and obesity defined as abnormal or excessive fat accumulation that may impair health, result from physical inactivity and adoption of poor nutritional habits. Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. Raised BMI is a major risk factor for non-communicable diseases including cardiovascular diseases (CVD), type 2 diabetes (T2DM), musculo-skeletal disorders and some cancers. However, metabolic abnormalities are absent in some obese individuals while some moderately overweight individuals are characterised by a whole cluster of atherogenic and diabetogenic metabolic abnormalities. It is thought that metabolic complications of overweight and obesity, known as the metabolic syndrome (MS), are more related to excess intra-abdominal fat that increases the risk of CVD and T2DM.

In recent studies high prevalence of overweight, obesity and MS resulting in non-communicable diseases (NCDs), in the continuing presence of under-nutrition, characterises many resource-poor settings including Nigeria. This is a deviation from earlier studies that reported the low prevalence of CVD risk factors in Nigeria. Overweight, obesity and MS are preventable and can be managed by lifestyle changes, diet and physical activity. Improvement in CVD risk factors after 6 and 12 months dietary modification has been reported.

INTRODUCTION

Obesity is epidemic worldwide and is a natural consequence of over-nutrition and sedentary lifestyle (Misra and Khurana 2008).

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Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health. Body mass index (BMI) is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. It is defined as a person's weight in kilograms divided by the square of his height in metres (Kg/m^2) (WHO 2017).

Raised BMI is a major risk factor for non-communicable diseases including cardiovascular diseases (CVD) - mainly heart disease and stroke, the leading causes of death in 2012; type 2 diabetes (T2DM), musculoskeletal disorders (especially osteoarthritis - a highly disabling degenerative disease of the joints) and some cancers (including endometrial, breast, ovarian, prostate, liver, gallbladder, kidney and colon). The risk for these diseases increases with increase in BMI (WHO 2017). The absence of metabolic abnormalities in some obese individuals with excess body fat has been reported. On the other hand, some moderately overweight individuals are characterised by a whole cluster of atherogenic and diabetogenic metabolic abnormalities. It is thought that metabolic complications of overweight and obesity are more related to the location of body fat rather than the amount of total body fat (Despres et al. 2008; Arsenault et al. 2011).

Individuals with excess intra-abdominal or visceral adipose tissue have metabolic abnormalities and are at increased risk of CVD and T2DM. Thus, obesity particularly its abdominal (visceral) component and insulin resistance are important twin components of the MS (Arsenault et al. 2011). There is rapidly increasing prevalence of obesity and MS in developing countries, leading to increased morbidity and mortality due to T2DM and CVD (Misra and Khurana 2008). The MS is present in Nigerians with normal weight, overweight and obesity, and increases with increasing BMI (Charles-Davies et al. 2012).

Escalating over-nutrition in the continuing presence of under-nutrition characterises many resource-poor settings including Nigeria (Misra and Khurana 2008). Under-nutrition and obesity co-existing within the same country, the same community and the same household is now common. Globally, more overweight and

obese individuals die than underweight individuals in every region except parts of sub-Saharan Africa and Asia (WHO 2017). However, in a cohort study of 534 traders in Ibadan, Western Nigeria, 23.4% were overweight, 33.0% were obese while 3.3% were underweight showing a 56.6% contribution to CVD and other non-communicable diseases risk (Charles-Davies et al. 2012).

The economic cost of obesity and related diseases in developing countries, having meagre health budgets is enormous (Misra and Khurana 2008). Many low- and middle-income countries are now facing a “double burden” of disease. While these countries continue to deal with the problems of infectious diseases and under-nutrition, they are also experiencing a rapid upsurge in non-communicable disease risk factors such as obesity and overweight, particularly in urban settings (WHO 2017).

Overweight and Obesity

Globally, 39% and 13% of adults aged ≥ 18 years were overweight and obese respectively in 2014 (WHO 2017). The WHO defines overweight as a BMI greater than or equal to 25 Kg/m^2 while obesity is a BMI greater than or equal to 30 Kg/m^2 . BMI values are age-independent and the same for both sexes. However, BMI may not correspond to the same degree of fatness in different populations due, in part, to different body proportions. The health risks associated with increasing BMI are continuous and the interpretation of BMI grading in relation to risk may differ for different populations. Table (11.1) shows the international classification of adult underweight, overweight and obesity. Additional cut-off points accommodate ethnic variations, indicate public action and facilitate international comparisons (WHO 2006).

Table 11.1: The International Classification of Adult Underweight, Overweight and Obesity According to BMI

Classification	BMI (kg/m ²)	
	Principal cut-off points	Additional cut-off points
Underweight	<18.50	<18.50
Severe thinness	<16.00	<16.00
Moderate thinness	16.00 - 16.99	16.00 - 16.99
Mild thinness	17.00 - 18.49	17.00 - 18.49
Normal range	18.50 - 24.99	18.50 - 22.99 23.00 - 24.99
Overweight	≥25.00	≥25.00
Pre-obese	25.00 - 29.99	25.00 - 27.49 27.50 - 29.99
Obese	≥30.00	≥30.00
Obese class I	30.00 - 34.99	30.00 - 32.49 32.50 - 34.99
Obese class II	35.00 - 39.99	35.00 - 37.49 37.50 - 39.99
Obese class III	≥40.00	≥40.00

Source: WHO 2006

Metabolic Syndrome

Metabolic Syndrome is the concurrence of disturbed glucose and insulin metabolism, overweight and abdominal fat distribution, mild dyslipidaemia and hypertension, associated with subsequent development of T2DM and CVD (Al-Sarraj et al. 2010) (fig. 11.1). It was first described as a clinical entity in 1988 by Reaven, though of much older origin having been observed as early as 1923 by Kylin (Zimmet et al. 2005). From its first description, it has been called various names; Reaven's syndrome, syndrome X, dysmetabolic syndrome, cardiometabolic syndrome, plurimetabolic syndrome, insulin resistance syndrome and the deadly Quartet (Tokin 2004).

Assuming great prominence in clinical discourse in the past decade, the MS has undergone different diagnostic modifications by various organisations over the years (Olaniyan et al. 2016).

These include the WHO, National Cholesterol Education Programme (NCEP): Adult treatment Panel III, American Association of Clinical Endocrinologists and the International Diabetes Federation (IDF). Zeno et al. (2010) showed that guidelines for MS including the IDF criteria were appropriate in excluding healthy individuals if diagnosis of metabolic syndrome was intended for early recognition of CVD risk and slowing CVD development. Ethnic differences in these guidelines were eliminated in their study when percentage body fat (PBF) was included as a criterion.

In 2009, the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity proposed a Joint Interim Statement (JIS) with a view to harmonizing the various criteria used for the diagnosis of MS. The Joint Interim Statement criteria include any three of the following five risk factors: Elevated waist circumference (WC) (≥ 94 cm for males and ≥ 80 cm for females), elevated serum triglycerides (≥ 1.7 mmol/L or ≥ 150 mg/dL), reduced serum high density lipoprotein cholesterol (HDL) (< 1.0 mmol/L or < 40 mg/dL for males and < 1.3 mmol/l or < 50 mg/dL for females), elevated blood pressure (BP) (systolic blood pressure of ≥ 130 mmHg and/or diastolic blood pressure of ≥ 85 mmHg) and elevated fasting blood glucose (FBG) (≥ 5.6 mmol/l or ≥ 100 mg/dL) (Olaniyan et al. 2016).

Using the IDF criteria, Charles-Davies et al. (2014) in their study showed that 1% of the apparently healthy individuals who had 3 metabolic syndrome components (excluding elevated waist circumference) were left out from the MS group. These individuals met JIS criteria for MS diagnosis. This is particularly important because reduced HDL (and not WC) was the most prevalent component in males in Ibadan.

Metabolic syndrome (Syndrome X)

- Central obesity
- High blood pressure
- High triglycerides
- Low HDL-cholesterol
- Insulin resistance



Fig. 11.1: The Metabolic Syndrome (Source: drug discovery.com)

Adipose Tissue

Adipose tissue (fat) is an endocrine organ made up of adipocytes, various stromal cells including many immune cells, and an endothelial network. It develops in several distinct anatomical depots within the body. Both lean and obese adults have a wide range of body fat distribution and various fat depots have unique characteristics. Regional fat gain and loss appear influenced by strong genetic factors. Selective dysregulation of these depots probably plays an important role in the metabolic complications of obesity. Visceral fat distribution in obesity most strongly correlates with insulin resistance and cardiovascular disease in humans and animals. Conversely, subcutaneous fat distribution does not appear to have similar negative systemic consequences on metabolism. Dramatic loss of adipose tissue (lipodystrophy) on the other hand, triggers a high degree of insulin resistance as well as signs of other metabolic dysregulation that are similar to visceral fat (Charles-Davies et al. 2012).

Obesity Measures

Several approaches have been used to measure obesity. Body mass index is a measure of general adiposity. WC, waist-hip ratio (WHR) and waist-to-height ratio (WHT) are reliable proxy

measures of abdominal fat. Although, variation in WC for a given BMI has been found to be a strong predictor of all-cause mortality, WC is a crude measure of visceral adipose tissue and does not discriminate intra-abdominal from subcutaneous abdominal adiposity. WC does not adjust for body stature and different WC thresholds may be needed for different ethnic groups (Charles-Davies et al. 2012).

WHR and WHT provide a measure of abdominal obesity that adjusts for an individual's body shape. WHR is positively and independently related to the occurrence of arterial HTN. An increased WHR may reflect either a relative abundance of abdominal fat (increased WC) or a relative lack of gluteal muscle (decreased hip circumference) (Garg et al. 2012). WHR may be important in the detection of MS in Nigerians since it correlated with all metabolic risk factors studied. This may be specific to the Nigerian and necessary in the early detection and management of CVD and probably T2DM (Charles-Davies et al. 2014). WHT (an improved index over WC) is a simple and practical index for assessing central fat distribution and metabolic risk in men and women (Charles-Davies et al. 2013). Hip circumference (HC) measures subcutaneous adipose tissue. Large HC after adjusting for WC and BMI is protective for metabolic risk factors in Caucasians. These measures are influenced by age, sex, ethnicity or the disease being studied (Charles-Davies et al. 2012; 2013).

BMI, WC, WHR, WHT are independently associated with cardiovascular and metabolic risk including T2DM. A combination therefore, of general adiposity and central adiposity has been recommended as both are independently related to the risk of death (NOO1, NOO2), (Chakraborty and Bose 2009). All adiposity measures indicated above increased with increasing BMI in Nigerians in a cohort study in Ibadan (Charles-Davies et al. 2012), indicating their importance as risk factors for metabolic diseases. This finding is in agreement with other cohort studies with no single adiposity measure best predicting MS (Bosy-Westphal et al. 2006; Taylor et al. 2010; Knowles et al. 2011).

Components of the Metabolic Syndrome

The components of the MS are WC, BP, FPG, triglycerides and HDL-C. In a cohort study of traders in Ibadan, Nigeria, both WC

and BP increased significantly with increasing BMI from normal weight to overweight to obesity classes. FPG, triglyceride and HDL-C were however significantly indifferent among normal weight, overweight and obesity (Charles-Davies et al. 2012). These observations indicate poor association of general obesity with dyslipidaemia and T2DM while its association with hypertension is high (23-30%) as reported previously in sub-Saharan Africa ((Ezenwaka et al. 1997; Sodjinou et al. 2008). The development of T2DM in individuals with excess adipose tissue mass is currently believed to be related to many factors including genetic predisposition and ethnicity (Hansen et al. 2010).

Elevated WC, reduced HDLC and high BP are prevalent components in apparently healthy Nigerians and may enhance the determination of negative cardiovascular profile in MS. About 90% of these individuals had 1-5 metabolic syndrome components. All adiposity indices and lipids except total cholesterol were significantly different amongst individuals with varying number of metabolic syndrome components. Although elevated FPG and TG were the least metabolic syndrome components in this study, they should be included in screening programmes in order to include the few with these components. HDLC and FPG appear to correlate with few metabolic risk factors and may explain some unclear underlying mechanisms. Metabolic screening of Nigerians is thus recommended (Charles-Davies et al. 2014).

Pathophysiology of Overweight, Obesity and the Metabolic Syndrome

Overweight and obesity progress to MS through pathophysiological mechanisms, which are still largely unclear. Overweight and obesity are thus fundamentally due to energy imbalance between calories consumed and calories expended (WHO 2017). The prevalence of MS in Africa is due to departure from traditional African to Western lifestyles (Tsang et al. 2007).

Persistent obesity dysregulates metabolic processes including action of insulin on glucose-lipid-free fatty acid metabolism and severely affects processes controlling blood glucose, blood pressure and lipids. The resultant cluster of conditions:

dysglycaemia, dyslipidaemia, hypertension, and procoagulant state known as MS culminates in CVD and T2DM (Misra and Khurana 2008). Dyslipoproteinaemia, a cardinal feature of the MS is also thought to be the major mediator of atherogenicity observed in MS (Alexander et al. 2003; Glinesberg and Stalenhoef 2003).

Recent mechanisms put forward are the inflammatory state and oxidative stress with more complications than were earlier imagined. Firstly, it is hypothesised that overfeeding is the starting signal of obesity, which results in a proinflammatory state starting in the metabolic cells (adipocyte, hepatocyte, or myocyte) and also recruiting immune cells with the consequent release of inflammatory cytokines (TNF- α , IL-6, adiponectin etc.). This inflammatory process may lead to complications such as hypertension, atherosclerosis, dyslipidaemia, insulin resistance, and diabetes mellitus which characterize the metabolic syndrome (Faloia et al. 2012).

Oxidative stress is a condition in which an imbalance results between the production and inactivation of reactive oxygen species characterize MS (Sindhu et al. 2009), its components and progression (Hutcheson and Rocic 2012). Reactive oxygen species, short-lived molecules are highly reactive derivatives of oxygen metabolism. They play an essential role in multiple physiological systems such as gene expression and signal transduction but contribute to cellular dysfunction under conditions of oxidative stress. Oxidative stress is thought to play a major role in the pathogenesis of ageing and a variety of human diseases, including atherosclerosis, diabetes, hypertension, Alzheimer's disease, kidney disease and cancer (Hutcheson and Rocic 2012; Sindhu et al. 2012). Alterations of both inflammatory and oxidative stress biomarkers were observed in individuals with MS in a study in Ibadan, Nigeria (Rahamon et al. 2014).

Cardiovascular Risk Factors in the Nigerian (Past and the Present)

Cardiovascular disease is the most common preventable, cause of death in developed world but has now become important in developing countries (Fabian et al., 2015). It was evident from earlier studies that the distribution of cardiovascular risk factors

among Nigerians aged above 20 years was low and thus explained the low incidence of coronary heart disease among the Nigerian population. A survey of the profile of some risk factors for coronary heart disease in 557 and 325 Nigerian males and females respectively aged 20 years and above belonging to low and medium income groups showed differences among the socio-economic groups (WHO 1990; Taylor et al. 1996). The more affluent Nigerians had higher total cholesterol than the low income group. Smoking and alcohol consumption were commoner among high income subjects and the higher percentage of the smokers and alcohol consumers were male. Blood pressure was correlated with age, smoking and body fat. Also waist to trochanter ratio and PBF were significantly related to plasma total cholesterol level.

These risk factors were also related to income status and socio-economic difference. Some of the lifestyle changes that include: higher intake of calories, fat and salt, smoking, drinking and physical inactivity can contribute to the increase in the level of risk factors for coronary heart diseases. Thus affluent Nigerians and their offspring might have a higher level of risk factors for coronary heart disease if preventive measures were not initiated.

The prediction of these earlier studies that atherogenic risk factors abound in Nigerians and the prevalence might be influenced by disease and lifestyle changes including diet, physical inactivity became obvious about 2 decades ago. Over the years, the burden of CVD has increased considerably and it is suggested that at least three quarters of world death from CVD will occur in low-significant lifestyle changes, including diet and secondary lifestyle. Most recent studies in MS actually indicate a changing trend of risk factors among Nigerians (Charles-Davies et al.2014).

Other risk factors that can lead to CVD are now known. The modifiable risk factors include high blood cholesterol, high triglycerides, low high density lipoprotein, smoking, physical inactivity, overweight/obesity, hypertension and diabetes, while the non-modifiable factors are age, sex and family history of cardiovascular disease. Aside from the classification or traditional risk factors, novel or emerging risk factors include hyperhomocysteinemia, LP(a), markers of oxidative stress, endothelial dysfunction, pro-inflammation and adipose tissue factors. Risk factors that are currently attracting attention are MS, markers of

vascular dysfunction, oxidative stress, pro-inflammation and adipose tissue factors. Our most recent studies have addressed the prevalence of these risk factors in a well-defined population within the city of Ibadan, Nigeria. Individuals with MS are at increased risk for developing T2DM and CVD (Sarraj et al. 2010; Fabian et al. 2015; Rahamon et al. 2014; 2017).

The significant elevation in measures of adiposity (body weight, BMI, HC, PBF, lipid accumulation product, visceral adiposity index, (conicity index), triglycerides, total cholesterol and low density lipoprotein cholesterol suggest that measures of adiposity in addition to dyslipidaemia might be important risk factors for metabolic disease in Nigerians. Others also confirm significant correlation between measures of adiposity and cardiovascular risk (Bosy-West phal et al. 2006, Taylor et al. 2010; Chakaborty and Bose 2009).

The importance of the MS lies in the fact that each individual component carries a grave risk for severe vascular event and the combination has synergistic effect. Among the market women, obesity, MS and its components were widely spread, and thus indicating the huge burden of these cardiovascular risk factors in Nigerians. For example, 23.4% were overweight, 33% were obese, while 3.4% and 23.4% were underweight or normal weight respectively (Charles-Davies et al. 2012).

The prevalence of MS and obesity were 33.1% and 23.4% with significant associations between BMI, MS and gender, showing higher prevalence among females with increasing BMI (Charles-Davies et al. 2012, 2013, 2014). Also, many of the traders had stages 1 and 2 hypertension. The results indicate high prevalence of MS and obesity. It appears female gender, dyslipidaemia, hypertension, increasing age, general and abnormal obesity are now important metabolic risk factors of CVD in non-diabetic Nigerian traders. In addition, the distribution of the metabolic syndrome components indicate that 60.1% had 2 or 3 components, 1.0% had all the five components while only 10% had no components. Elevated waist circumference (70%), reduced high density lipoprotein cholesterol (63%) and high blood pressure (48%) were more frequent metabolic components, while elevated fasting plasma glucose (11%) and high triglyceride (2%) were less

frequent in both metabolic syndrome and non-metabolic syndrome groups (Charles-Davies et al. 2013, 2014).

Prevention and Management of Overweight, Obesity and Metabolic Syndrome

Overweight and obesity, as well as their related non-communicable diseases, are largely preventable. Supportive environments and communities are fundamental in shaping people's choices, by making the choice of healthier foods and regular physical activity the easiest choice (the choice that is the most accessible, available and affordable), and therefore preventing overweight and obesity. The WHO has specific recommendations at individual, societal and food industry levels (WHO 2017).

Appropriate diet, lifestyle changes, weight reduction and increased physical activity are effective lifestyle strategies to reduce cardio-metabolic risk factors in metabolic syndrome individuals in resource-poor settings such as Democratic Republic of Congo. A dietary intervention was initiated among the individuals with metabolic syndrome by interacting with a trained dietician who advised all to:

- (a) Avoid food high in saturated fatty acid or cholesterol (fat, meat, butter, cream).
- (b) Eat moderate amount of food containing appreciating quantities of saturated and mono-saturated fatty acid (e.g. lean meat).
- (c) Substitute with foods high in poly-saturated fatty acid (e.g. sun flower seed oil, fish).
- (d) Increase daily intake of fruit and vegetables.
- (e) Consume whole grain cereals and legumes.

From dietary history, the total calorie intake obtained from protein, total fat and carbohydrate was calculated and pegged at 20%, 30%, and 50% respectively. Short term (6 months) dietary intervention impacted positively on the cardio-metabolic risk factors, oxidative stress markers and pro-inflammation factors) and long term (12 months) shows positive effects on the cardio-metabolic, adiposity measures and oxidative stress markers and inflammatory markers (Rahamon et al. 2014, 2017).

Conclusion

Over the years, the prevalence of the cardiovascular disease risk factors has increased and the need for screening and life style intervention is urgent to prevent a rise in cardiovascular disease as the Nigerian population ages. Monitored dietary modification of Nigerian diet could be a viable therapeutic regime to arrest the increasing burden of cardiovascular risk factors in metabolic syndrome.

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