INTRODUCTION

Obesity is a major public health problem. Being obese and overweight is associated with substantial increased risks of mortality and morbidity. Obesity and related non-communicable diseases are recognized as imposing a major burden on health systems ***(Pitanga and Lessa, 2005).*** Increased health care costs, activity limitations, and reduced productivity ***(Webb et al., 2010)***, are also associated with a relevant impairment of health related quality of life ***(Mannucci et al., 2010).***

The most widely used anthropometric measure of obesity is body mass index (BMI) and it has been applied into both public health and clinical practice. However, BMI does not consider the distribution of body fat. Other measures which are being increasingly used are waist circumference (WC) ***(Cherqaoui et al., 2012)***, waist-hip circumference ratio (WHR) ***(Kaur and Mogra, 2006)*** and conicity index (Ci) ***(Cordeiro et al., 2010).*** The Ci estimates fat accumulation in the abdomen which leads to a deviation of body shape from a cylindrical to a double-cone shape, i.e. two cones with a common base at the waist level ***(Flora et al., 2009).***

This abnormal deposition of fat in the abdomen has been described as the type of obesity that greatly threatens the individual's health leading to metabolic derangements, coronary disease ***(Hodge et al., 2010)***, increased mortality ***(Liu et al., 2011)***.

In the case of chronic kidney disease patients (CKD), it has been hypothesized that overweight (BMI ≥25 <29.9 kg/m^2) is a sign of a healthy and a better nutritional status ***(Cordeiro et al., 2010).***

The most frequent nutrition disorder of CKD patients is now excessive obesity instead of weight loss. However, WC may be a better predictor of mortality than BMI in adults with CKD ***(Zoccali et al., 2011).***

Abdominal fat has been associated with inflammation, insulin resistance, hyperadipokinaemia, dyslipidaemia, and oxidative stress, each of which may predict malnutrition, increased mortality, and the development of protein-energy wasting ***(Moutsert et al., 2008).***

Hemodialysis is the most common treatment for end-stage renal disease (ESRD). Several studies, but not all, have suggested that the effect of obesity in patients with ESRD undergoing maintenance dialysis is paradoxically in the opposite direction, showing that a high BMI is

associated with improved survival (the so-called obesity paradox) ***(Pellicano et al., 2010).***

Conicity index (Ci), Body mass index (BMI), and waist hip ratio (WHR) are used to predict the risk of obesity related diseases. However, it has not been examined whether these indicators can predict the comorbidities in hemodialysis subjects.

AIM OF THE WORK

1. To measure the frequency of the central obesity in hemodialysis patients in our study group.

2. To investigate the relationship between obesity assessed by the anthropometric variables as Ci, and WHR and morbidity amongst hemodialysis patients.

CHAPTER (I): OBESITY

The World Health Organization defines obesity as "abnormal or excessive fat accumulation in adipose tissue, to the extent that health is impaired". The degree of health impairment is determined by three factors: the amount of fat, the distribution of fat, and the presence of other risk factors ***(World Health Organization, 2000)*.**

Hill et al. (2005) summarized the guidelines for classifying weight status by BMI. Large epidemiologic study has established that there is a strong relationship between BMI and mortality. Obese persons have higher risk for adverse health consequences than those who are overweight ***(Ross and Katzmarzyk, 2003)***.

Table (1): Weight Classification by Body Mass Index.

Status	Obesity Class	Body Mass Index (kg/m^2)	Risk of Disease
Underweight		< 18.5	Increased
Normal		18.5-24.9	Normal
Overweight		25.0-29.9	Increased
Obesity	I	30.0-34.9	High
	II	35.0-39.9	Very high
	III	> 40.0	Extremely high

(Hill et al., 2005)

Obesity is caused by an excessive intake of calories in relation to energy expenditure over a long period of time. Large increases in body fat can result from even minor but chronic differences between energy intake and energy expenditure. In one year, the ingestion of only 5% more calories than expended can promote the gain of approximately 5 kg in adipose tissue. Over 30 years, the ingestion of only 8 kcal/day more than expended can increase body weight by 10 kg ***(Friedman, 2003)*.**

Several factors influence BMI-related health risk. For example, obese persons with excess abdominal fat are at increased risk for diabetes, hypertension, dyslipidemia, and ischemic heart disease than obese persons whose fat is located predominantly in the lower body ***(Berggren et al., 2004)***. Visceral adiposity can be measured in a number of ways: by MRI scanning or CT scans of the abdomen or by dual X-ray absorptiometry (DEXA) with a specific abdominal window.

Such techniques are expensive and difficult to apply to the assessment of central obesity in most clinical practice. However, assessment of visceral fat by a single CT slice at L4/L5 has become a recognized reference measure and is often used in obesity studies ***(Caterson and Gill, 2002)*.**

Other inexpensive and practical methods to accurately localize body fat distribution in humans include:

Waist circumference (the narrowest circumference midway between the lower border of the ribs and the upper border of the iliac crest, taken from the side) is highly correlated with abdominal fat mass and is therefore often used as a surrogate marker for abdominal (upper body) obesity. Waist circumference values denoting increased risk for metabolic diseases have been proposed on the basis of epidemiologic data. For men, a waist circumference greater than 102 cm (40 inches) and, for women, a waist circumference greater than 88 cm (35 inches) have been proposed as cutoff values for increased risk ***(Stewart et al., 2003).***

The waist to hip ratio (WHR). A WHR of more than 1.0 in men and 0.85 in women identify subjects with abdominal fat accumulation ***(Kopelman, 2000).***

The Ci estimates fat accumulation in the abdomen which leads to a deviation of body shape from a cylindrical to a double-cone shape, i.e. two cones with a common base at the waist level ***(Flora et al., 2009).*** This abnormal deposition of fat in the abdomen has been described as the type of obesity that greatly threatens the individual's health leading to metabolic derangements, coronary disease, increased mortality ***(Hodge et al., 2010).***

Another factor that modifies the risk of obesity-related complications is weight gain during adulthood. In both men and women, weight gain of 5 kg or more since age 18 to 20 years is associated with an increased risk of diabetes, hypertension, and coronary heart disease, and the risk of disease increases with the amount of weight gained ***(Koh-Banerjee et al., 2004)***.

Prevalence of Obesity:

The worldwide prevalence of obesity has increased dramatically over the last several decades. In the United States alone, an estimated 60% of adults 20 to 74 years of age are now considered overweight or obese. According to national population surveys conducted since 1960, the prevalence of overweight in the United State increased only slightly but the prevalence of obesity (BMI >30 kg/m^2) more than doubled.

In the United States, the prevalence of obesity increases progressively from 20 to 50 years of age but then declines after 60 to 70 years of age ***(Hedley et al., 2004)***.

The prevalence of obesity has risen in children and adolescents. As defined by a BMI greater than the 95^{th} percentile for age and gender from the revised National Center for Health Statistics growth charts, 10% to 15% of

6- to 17-year-old children and adolescents in the United States are overweight ***(Flegal and Troiano, 2000)***. These data indicate that overweight prevalence rates for children and adolescents, reported by earlier surveys, have doubled. Diseases commonly associated with obesity in adults, such as type 2 diabetes mellitus, hypertension, hyperlipidemia, gallbladder disease, nonalcoholic steatohepatitis, sleep apnea, and orthopedic complications, are now increasingly observed in children ***(Reaven et al., 2004)*****.** Overweight in childhood and adolescence does "track" into adulthood, and this means that the next generation has a far greater chance of developing metabolic disease ***(Caterson and Gill, 2002)*****.**

Complications of Obesity:

Obesity is strongly associated with many serious medical complications that impair quality of life and lead to increased morbidity ***(Reaven et al., 2004)*****.**

▪ Metabolic Disease:

The Metabolic Syndrome:

In the metabolic or insulin resistance syndrome, also known as ***syndrome X***, the specific phenotype of abdominal obesity is associated with a cluster of metabolic risk factors for coronary heart disease (CHD). The diagnostic criteria include a waist circumference >40

inches in men and 35 inches in women, triglycerides >150 mg/dL, and a HDL cholesterol <40 mg/dL in men or <50 mg/dL in women. Additionally, a blood pressure >130/85 mmHg and a fasting plasma glucose >110 mg/dL is required. The diagnosis of the metabolic syndrome requires at least three of the five major criteria for qualification ***(Hill et al., 2005).***

Abdominal obesity has also been associated with the metabolic risk factors of increased serum levels of apolipoprotein B, small dense low-density lipoprotein (LDL) particles ***(LaMonte et al., 2003)*** and plasminogen activator inhibitor-1 with impaired fibrinolysis ***(Skurk and Hauner, 2004).*** The metabolic syndrome does not affect only those with frank obesity; it has also been reported in persons of normal weight, who presumably have an increased amount of abdominal fat ***(Karelis et al., 2004).***

The metabolic syndrome was originally identified and defined on the basis of epidemiologic associations. The underlying pathogenesis and the interrelationships between the individual features have not been completely elucidated. Insulin resistance has been hypothesized to be the common underlying pathogenic mechanism ***(Reaven, 2004).***

Abdominal obesity is clearly associated with insulin resistance. It is not clear whether the visceral (omental and mesenteric) or subcutaneous depots of abdominal fat are more closely related to insulin resistance. In addition, it is difficult to define the relationship between each abdominal adipose tissue depot and insulin resistance because the size of the depots is closely correlated. Furthermore, it is not known whether visceral fat and abdominal fat actually participate in the pathogenesis of the metabolic syndrome or merely serve as markers of increased risk for the metabolic complications of obesity ***(Appel et al., 2004)*.**

Type 2 Diabetes Mellitus:

The marked increase in the prevalence of obesity has played an important role in the 25% increase in the prevalence of diabetes that has occurred in the United States. According to data from the Third National Health and Nutrition Examination Survey (NHANES III), two thirds of the adult men and women in the United States with a diagnosis of type 2 diabetes had a BMI of 27 kg/m^2 or greater. The risk of diabetes increases linearly with BMI; the prevalence of diabetes increased from 2% in those with BMI 25 to 29.9 kg/m^2, to 8% in those with 30 to 34.9 kg/m^2, and finally to 13% in those with BMI greater than 35 kg/m^2 ***(Hill et al., 2005)***. In addition, the risk of

diabetes increases with increments in abdominal fat mass, waist circumference, or ratio of waist to hip circumference at any given BMI value ***(Pi-Sunyer, 2004)***.

Dyslipidemia:

Visceral obesity is associated with several serum lipid abnormalities; including hypertriglyceridemia, reduced HDL cholesterol levels, and an increased proportion of small, dense LDL particles ***(LaMonte et al., 2003)***. The prevalence of hypercholesterolemia (total cholesterol greater than 240 mg/dL) increased progressively with BMI in men. In women, the prevalence was highest at a BMI of 25 to 27 kg/m^2, and did not increase further with increasing BMI ***(Hill et al., 2005).***

- **Cardiovascular Disease:**

Hypertension:

There is a linear relationship between hypertension and BMI. In NHANES III, the age-adjusted prevalence of hypertension (defined as systolic blood pressure > 140 mm Hg, diastolic blood pressure > 90 mm Hg, or the need for antihypertensive medication) in obese men and women was 42% and 38%, respectively. These prevalence rates are more than twice as high as the prevalence rates of hypertension in lean men and women ***(Martins et al., 2003).***

The risk of hypertension also increases with weight gain. Weight gain increased the risk of developing hypertension independent of age and blood pressure level among relatively lean men and women ***(Lee et al., 2004)*.**

Obesity raises blood pressure by increasing renal tubular reabsorption, impairing pressure natriuresis, and causing volume expansion due to activation of the sympathetic nervous system (SNS) and renin-angiotensin aldosterone system (RAAS), and by physical compression of the kidneys, especially when visceral obesity is present. The mechanisms of SNS activation in obesity are still unclear but may be due, in part, to hyperleptinemia that stimulates the hypothalamic pro-opiomelanocortin (POMC) pathway ***(Wofford and Hall, 2004)*.**

Coronary Heart Disease:

The risk of CHD is increased in obese persons, particularly in those with increased abdominal fat and those who gained weight during young adulthood. Moreover, CHD risk starts to increase at the normal BMI levels in both men and women.

The risk of fatal and nonfatal myocardial infarctions was greater in women with the lowest BMI but highest ratio of waist to hip circumference than in women with the

highest BMI but lowest ratio of waist to hip circumference ***(Nicklas et al., 2004).***

Although obesity is a risk factor for the occurrence of clinical coronary events, the link between angiographically determined coronary atherosclerosis and obesity still remains controversial. It has been found that abdominal fat may be predictive of an increasing number of coronary vessels involved among male patients, but not among female patients ***(Auer et al., 2005).***

Obesity-related CHD risk factors, particularly hypertension, dyslipidemia, impaired glucose tolerance, and diabetes, are largely responsible for the increase in CHD. However, even after adjustments for other known risk factors, it was found that overweight and obesity increased the risk of CHD ***(Zhou et al., 2002).*** As a result, the Framingham Heart Study classified obesity as a major preventable risk factor for CHD ***(Rashid et al., 2003).***

Cerebrovascular & Thromboembolic Disease:

The risk of both ischemic and hemorrhagic stroke is approximately twice as great in obese as in lean persons and increases progressively with increasing BMI ***(Song et al., 2004).*** Abdominal obesity is an independent, potent risk factor for ischemic stroke in all race-ethnic groups. It is a

stronger risk factor than BMI and has a greater effect among younger persons ***(Suk et al., 2003)*.**

The risks of venous stasis, deep vein thrombosis, and pulmonary embolism are also increased in obesity, particularly in persons with abdominal obesity ***(Juhan-Vague et al., 2002)*.** Lower extremity venous disease may result from increased intra-abdominal pressure, impaired fibrinolysis, and the increase in inflammatory mediators ***(Skurk and Hauner, 2004)***.

- **Pulmonary Disease:**

Bronchial Asthma:

The risk for developing asthma was associated with increased body weight and abdominal circumference. The increase in asthma morbidity in the overweight subjects was found almost exclusively in the non-atopic asthma patients ***(Ronmark et al., 2005)*.** It has been shown that there is a linear relationship between obesity and the severity of the asthma.

This suggests that obesity may be a potentially modifiable risk factor for asthma or asthma-like symptoms ***(Akerman et al., 2004)*.**