Complications of obesity in adults: A short review of the literature

D Segula

Introduction

Obesity, which broadly refers to excess body fat, has become an important public health problem. Its prevalence continues to increase worldwide.[1] As the prevalence of obesity increases so does the burden of its associated co-morbidities.[2] Non-communicable diseases and their risk factors including obesity are now becoming a significant problem not only in affluent societies but also in developing countries.[3-6]

Assessing total body fat accurately requires sophisticated technology which is not readily available for purposes of the epidemiology of the disease.[7,8] The World Health Organisation (WHO) adopted body mass index (BMI), which is calculated by dividing the body weight in kilograms (Kg) by the square of the height in metres (m), as a surrogate measure of total body fat.[4] BMI correlates well with the percentage body fat in the young and middle aged where obesity is most prevalent.[7,8] With this index, obesity is defined when the value is equal to or more than 30Kg/m2.[7,8]

However, not only does the total body fat matter but also the pattern of distribution. Excess visceral fat, also referred to as central obesity, has a stronger association with cardiovascular disease than subcutaneous fat with is deposited mainly around the hips and buttocks. Central obesity produces a characteristic body shape which resembles an apple and thus is also referred to as "apple shaped" obesity as opposed to "pear shaped" obesity in which fat is deposited on the hips and buttocks.[9] This distribution is also reflected in the waist circumference and Waist:Hip ratio (WHR), ie the ratio of the hip circumference to waist circumference.

In this review, data from different studies on complications of obesity are summarized and controversies discussed. Areas of current and future research in obesity and its complications have also been highlighted.

Current evidence linking obesity and mortality

Several large studies have demonstrated increased mortality above a certain threshold of BMI. In the Framingham heart study, a prospective cohort study, male and female non-smokers aged 40 years who were obese lived 5.8 and 7.1 years less than their non-obese counterparts.[10] Another study by Fontaine et al. which used data from the National Health and Nutrition Examination Survey (NHANES I and II) and the NHANES III Mortality Study, found a marked reduction in life expectancy in obese young adults compared to non-obese adults.

There is now evidence that not only does percentage of fat assessed by BMI matter in predicting mortality but also the distribution of fat in the body. The INTERHEART study, among other studies, showed that high hip fat distribution assessed by hip circumference had a negative predictive effect on myocardial infarction (MI) whereas high waist fat distribution again assessed by waist circumference was associated with high rates of MI.[11]

The possible effect of fat distribution on mortality and morbidity cannot be ignored in view of these emerging data. Body fat distribution, assessed using magnetic resonance imaging in leading research institutions, and its effects on mortality and morbidity is currently a research topic of interest.

Morbidities related to obesity

Impaired glucose tolerance and Diabetes mellitus

There is currently no controversy that obesity is associated with impaired glucose tolerance or type 2 diabetes mellitus. The underlying mechanism is thought to be due to insulin resistance. However, there is currently limited data accurately quantifying insulin resistance using the standard hyperinsulinemic euglycemic clamp,[12] largely because the invasive nature of the procedure makes it unsuitable for general epidemiological studies.[12]

The association of obesity with diabetes has been shown in several studies. In one of the biggest cohort studies, in which 84,941 female nurses were followed up for 16 years, there were 3,300 new cases of diabetes mellitus. Importantly, the study revealed that overweight or obesity was the main predictor of type 2 diabetes mellitus.[13] In men, there were similar findings from the Health Professional follow-up study. An age adjusted relative risk of 60.9 for developing diabetes was found in those with a BMI ≥35Kg/m2 in comparison to those with BMI <23Kg/m2.[14]

In Malawi, the prevalence of diabetes in adults aged 25- 64 years is estimated at 5.6%. [3] However, there is limited data on obesity attributable diabetes in Malawian adults.

Hypertension

Data available shows a strong association between obesity and hypertension. In one large cohort study of 82,473 participants, BMI was positively associated with hypertension at age 18 and midlife. There was also marked increase in risk of hypertension with weight gain.[15] In the Framingham study, the relative risk of hypertension in overweight men and women were 1.46 and 1.75, respectively, after adjusting for age.[16] In the same study, reduction of weight in obese women at age 18 reduced the risk of hypertension.

In older populations, hypertension and obesity continue to relate in a predictable manner as has been shown in the Honolulu Heart Program and Japanese data survey.[17, 18]

Recently, waist circumference (WC) has been shown to be important in assessing obesity and the risk of hypertension. When WC and BMI were compared as continuous variables in the same regression model, WC was found to be a better predictor for obesity related risk, including hypertension, than BMI.[19] However, when WC was used as a categorical variable (normal or high), BMI was a better predictor. WC may be a valuable means of quantifying the risk of hypertension in the obviously obese individuals as it is cheap, easier and faster to apply than BMI which, in addition to a stadiometer, requires a weighing scale and calculation of the index.

Following a recent survey in Malawi, hypertension was estimated at 32.9% in adults aged 25-64 years.[3] The survey also found that 29% of the population in this age range were either overweight or obese possibly indicating that obesity may have played a role in hypertension. However, the

association of obesity and hypertension was not interrogated in this survey.

Heart Disease

There is unequivocal evidence that there is an increased risk of coronary artery disease (CAD) in obesity. In the Asian Pacific Cohort Collaboration study in which more than 300, 000 participants were followed, there was a 9 percent increase in events of ischaemic heart disease for a unit change in BMI. Increased risk of CAD was has also been found in the Framingham and Nurses Health Studies.[16,20]

When the risk of heart failure (HF) was evaluated in the Framingham study, the risk of HF was found to be 2-fold in the obese group than in the non-obese group.[21] However, it appears that having a higher BMI improves survival in patients with congestive heart failure (CHF). In a retrospective analysis of 7,767 patients with CHF who were categorised into 4 BMI ranges including obesity (BMI>30kg/m2), there was reduced crude all case mortality with consecutively higher BMI groups in an almost linear fashion. After further analysis, overweight and obese patients had a hazard ratio of 0.88 compared to healthy weight patients (taken as the reference group) whereas underweight patients with stable CHF had a 1.21 risk of death when they were compared to the same reference group.[22]

The reason for this is not clear. The authors argue that other cardiovascular morbidities associated with obesity and overweight may have lead to the diagnosis of HF in its earlier stages in the obese group than in the group with lower BMI, therefore, reducing the risk of death from CHF.22 However, the cardiopulmonary testing results of overweight and healthy weight patients, with CHF have been found to be similar.[23, 24] Therefore, the foregoing argument is unlikely to account for this difference.

Clearly, with the known adverse effects of obesity and in the absence of knowledge on the mechanism of this 'paradox', recommending overweight or obesity for purposes of reduction of CHF associated mortality is not an option. Elucidating the mechanism of this paradox is currently an area of research interest.

Dyslipidaemia

Dyslipidaemia, manifested by reduced high density lipoprotein (HDL) and increased triglycerides, is associated with obesity.[25] The underlying mechanism is largely due to insulin resistance. Very low density lipoprotein (VLDL) clearance in plasma is dependent on the rate of hepatic synthesis and catabolism by lipoprotein lipase, an enzyme which is also involved in formation of HDL.[25,26] In obesity, insulin resistance is associated with increased hepatic synthesis of VLDL and impaired lipoprotein lipase.[26,27] There is evidence that dyslipidaemia can still occur in the absence of insulin resistance in obesity. In 1998, a study by Gary et al. showed a significant association between obesity, particularly central obesity, and dyslipidaemia after adjusting for insulin resistance.

Cerebrovascular Disease

Currently available evidence shows that the risk of haemorrhagic and ischaemic stroke, in relation to obesity, is increased in men. In women this relation is true with ischaemic stroke but not haemorrhage stroke. In the Korean prospective study involving 234,863 men who were followed up for 9 years, a significant positive association was found between BMI and the risk of ischemic stroke whereas, with haemorrhagic stroke, a J-shaped association was found showing that the risk increased more than that of ischaemic stroke at the upper and lower extremes of BMI.[28] Controlling for confounding factors attenuated the association but still yielded significant association.

In a prospective study of 39,053 participants (all women) followed up for an average of ten years, 432 strokes occurred. Three hundred and seven were ischaemic, 81 hemorrhagic and 4 undefined. In obese subjects (BMI > 30kg/m2), the hazard ratios (95% CI) for total stroke, ischaemic stroke and hemorrhagic stroke were 1.5 (1.16 to 1.94), 1.72 (1.30 to 2.28) and 0.82 (0.43 to 1.58), respectively. This was in comparison with the group of women with BMI less than 25kg/m2.[29]

The reason for the discrepancy in risks of hemorrhagic stroke between men and women is not clear. Following findings from other studies that have shown higher incidence of hemorrhagic stroke in Asian populations in the setting of low cholesterol and lean body weight,[30,31] the authors argue that these factors (low cholesterol and lean body weight) may explain the observed findings in the latter studies. However, this still remains a hypothesis which needs investigating. Further, with this hypothesis one would expect men in the Korean and Physicians' studies to have shown increased risk of hemorrhagic stroke as well with the group with BMI towards lean body weight who presumably would have had low cholesterol levels.[28,32]

Lately, central obesity (where fat is preferentially distributed around the trunk) has been shown to be important in predicting stroke mortality. In the Israel heart disease study, stroke mortality was predicted by trunk obesity alone independent of BMI, hypertension, diabetes and socioeconomic status.[37,33]

Metabolic syndrome

According to the National Cholesterol Education Program's Adult Treatment Panel III (NCEP: ATP III), the metabolic syndrome is defined when an individual has any 3 of the following 5 features: (i) waist circumference above 40 inches for men and >35 inches for women, (ii) Triglycerides above 150mg/dl, (iii) HDL cholesterol above 40mg/dl for men and 50mg/dl for women, (iv) Blood pressure above 130/85 mmHg, (v) Fasting glucose above 100mg/dl.

Central obesity and insulin resistance, which leads to altered lipid and glucose metabolism, appear to be the basis for the features seen in metabolic syndrome.[34] The syndrome was originally intended for prediction of the risk of cardiovascular disease, however, this has recently been questioned as the sum of the combined risk factors appears not to offer more than the sum of individual factors.[35]

Pulmonary abnormalities

Several studies have linked obesity and obstructive sleep apnea (OSA). In the Wisconsin Sleep Cohort study, obesity had a strong association with OSA.[36] In another study, increased neck circumference, which was also shown to correlate very well with obesity, had been shown to correlate with obstructive sleep apnea.[37] There have been two mechanisms that have been thought to contribute to OSA. Firstly, is the direct effect of increased fat tissue along the airway which impinges on the lumen.[38] Secondly, increased fat tissue has been implicated in increasing the collapsibility of the airway.[39]

Asthma is another condition that may occur as a complication of obesity. There is evidence that obesity increases the risk of asthma. In one prospective multicentre study, the prevalence of asthma was observed to increase in obese patients. Seventy five per cent that presented with an asthmatic emergency were either obese or overweight.[40] Further prospective studies have shown that obesity predicts asthma.[41] The mechanism linking obesity and asthma includes increased airway hyper-responsiveness, decreased functional and tidal volumes, chronic systemic inflammation driven by increased inflammatory cytokines and chemokines, adipocytes derived factors leptin, adiponectin and plasminogen activator inhibitor.[42]

Gastrointestinal abnormalities

Most epidemiological studies have found an association between obesity and increased risk of Gastroesophageal reflux disease (GORD). In one large cross-sectional population study, which was part of a randomized trial, involving 10, 537 subjects, the adjusted odds ratios for heart burn and acid regurgitation occurring once in a week in obese patients were 2.91 (95% CI 2.07 – 4.08) and 2.23 (95% 1.44-1.99) respectively, compared with those with normal BMI.46 Recent evidence from a meta-analysis involving data from studies between 1966 and 2004 has shown obesity to be significantly associated with GORD, esophageal cancer and erosive esophagitis and that these disorders appear to increase with increasing weight.[43]

Another gastrointestinal condition that has been studied in relation to obesity is cholelithiasis. Data from the Nurses' study showed that females with BMI of more than 45Kg/m2 had a seven-fold increase in risk of gallstone disease compared to those with BMI of less than 24Kg/m2.[44] Men have had similar results.[45]

Reproductive disease

Polycystic ovary syndrome (PCOS), characterized by anovulation, hyperandrogenism and a polycystic ovary, is associated with obesity as well as insulin resistance. It has been noted that increased visceral fat assessed by waist circumference of more than 88cm is associated with hyperandrogenemia in patients with PCOS and that reduction of insulin resistance by weight loss or drugs that increase peripheral sensitivity of insulin leads to improve hormonal aberrations and ovulation.[46]

In men, abdominal obesity has been associated with impotence and infertility. In one single blinded randomised controlled trial of 110 obese men with erectile problems but no other risk factors namely diabetes, hyperlipidemia or hypertension, there was improvement of sexual function associated with decreased BMI.[47]

There are other reproductive complications of obesity that occur in pregnancy and labour. These include gestational diabetes, macrosomia, dystocia and increased rates of caesarean sections.[48]

Pyschosocial problems

Obesity in the affluent society has been associated with several untoward outcomes in terms of psychosocial or socioeconomic wellbeing. Obese females for example were found to be less likely to complete school, had a 20% less chance of getting married, earned less and had more household poverty in comparison to females that were not overweight.[49] However, the direction of causality can be either way since status causes obesity and obesity causes status.[50]

Several psychiatric disorders have been linked to obesity. In one study involving psychiatric evaluation of 294 patients before bariatric surgery, the prevalence rates were as follows: somatization (29.3%), phobia (18%), hypochondriasis (18%) and obsessive-compulsive disorders 13.6%. Follow up of these patients after surgery showed that these psychopathologies had been reduced significantly.[51]

Osteoarthritis

Osteoarthritis (OA) appears to follow obesity. In the Framingham cohort study, data from 1420 participants indicated that obesity was an important independent risk factor for OA after adjusting for age, physical activity and the levels of uric acid.[52] Other studies looking at the effect of weight reduction on obesity have shown a significant reduction in the odds of developing OA overtime, further providing evidence for this link.[53]

OA involving weight bearing joints is common later in life and the prevalence is above 50% in both men and women by age 65 years.[54] The mechanism of OA has been presumed to be due to direct chronic strain on the joints related to the overweight.[55] However, there are now notions that non-mechanical mechanisms may contribute to OA in obesity as the same changes of OA seen in weight bearing joints have also been seen in non-weight bearing joints. There is growing evidence that dysregulation of adipokines (hormones from adipose tissue) such as adiponectin, visfatin and resistin may explain the link between obesity and OA – suggesting that osteoarthritis may be a systemic disease in obesity.[56]

Cancer

There is considerable evidence of an association between obesity and some cancers.[57] These include cancer of gallbladder, esophagus (adenocarcinoma), thyroid, kidney, uterus, colon and breast.[58] This link has further been strengthened by the observation that there is reduced incidence of cancer and mortality with weight loss.[59,60] However the underlying mechanism linking these cancers to obesity is not clear. For uterus and breast cancers, it is thought to be due to higher oestrogen levels synthesized from fat tissue in obese women.[61,62]

Access to care

Obesity prevents certain medical procedures being done either due to the physical weight itself, or due to the increased risk of complications (including infections).[63,64] For example, most Computer Tomography scan tables and Magnetic resonance imaging machines have a weight limit of 450 Ib (204Kg).[63] Physical immobility due to obesity may also lead to restricted access to care. Surgical mortality is increased in obese patients and these patients may not be operated on purely due to surgical mortality risk associated with obesity. Obesity is also obstetric risk and is associated with increased risk of certain infectionswhich may require tertiary level care which may not always be accessible.[65]

Conclusion

Obesity and other risk factors of non-communicable diseases (NCDs) are now emerging problems not only in affluent societies but also in developing countries like Malawi. In Malawi, the prevalence of obesity in adults is currently estimated at 4.6% (3). Obesity is predicted to rise over the coming years (4-6). Interventions to reduce the burden of

obesity partly depend on recognising and understanding the complications of obesity. Clinicians are reminded to look for these complications in obese patients and institute interventions emphasizing the benefits of weight loss in obese patients.

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