# "VISCERAL TO SUBCUTANEOUS FAT RATIO DETERMINED USING COMPUTED TOMOGRAPHY AS A PREDICTOR OF MULTIPLE METABOLIC RISK FACTORS IN SUBJECTS WITH NORMAL WAIST CIRCUMFERENCE"

**THESIS**

**Submitted to**

**All India Institute of Medical Sciences, Jodhpur**

**In partial fulfilment of the requirement for the degree of**

**DOCTOR OF MEDICINE (MD)**

**(RADIOLOGY)**

**JUNE, 2022** **DR. THOMAS GEORGE**

**AIIMS, JODHPUR**

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## CERTIFICATE

This is to certify that the thesis titled **"VISCERAL TO SUBCUTANEOUS FAT RATIO DETERMINED USING COMPUTED TOMOGRAPHY AS A PREDICTOR OF MULTIPLE METABOLIC RISK FACTORS IN SUBJECTS WITH NORMAL WAIST CIRCUMFERENCE"** is the bonafide work of Dr. Thomas George carried out under our guidance and supervision, in the Department of Diagnostic and Interventional Radiology, All India Institute of Medical Sciences, Jodhpur.

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## DECLARATION

I hereby declare that the thesis titled **"VISCERAL TO SUBCUTANEOUS FAT RATIO DETERMINED USING COMPUTED TOMOGRAPHY AS A PREDICTOR OF MULTIPLE METABOLIC RISK FACTORS IN SUBJECTS WITH NORMAL WAIST CIRCUMFERENCE"** embodies the original work carried out by the undersigned in All India Institute of Medical Sciences, Jodhpur.

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**Dr. Thomas George**

# ABBREVIATIONS

| | | |
|---|---|---|
| **BMI** | **–** | **Body Mass Index** |
| **DM** | **–** | **Diabetes Mellitus** |
| **HbA1c** | **–** | **Glycated Hemoglobin** |
| **HDL** | **–** | **High Density Lipoprotein** |
| **LDL** | **–** | **Low Density Lipoprotein** |
| **MONW** | **-** | **Metabolically Obese Normal Weight** |
| **MHO** | **–** | **Metabolically Healthy Obese** |
| **MDCT** | **-** | **Multi-Detector Computed Tomography** |
| **SFA** | **-** | **Subcutaneous fat area** |
| **SFM** | **–** | **Subcutaneous Fat Mass** |
| **SFV** | **–** | **Subcutaneous Fat Volume** |
| **VFA** | **–** | **Visceral Fat Area** |
| **VFM** | **–** | **Visceral Fat Mass** |
| **VFV** | **–** | **Visceral Fat Volume** |
| **VSR** | **–** | **Visceral-Subcutaneous fat ratio** |
| **WC** | **–** | **Waist Circumference** |

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# ABSTRACT

**"VISCERAL TO SUBCUTANEOUS FAT RATIO DETERMINED USING COMPUTED TOMOGRAPHY AS A PREDICTOR OF MULTIPLE METABOLIC RISK FACTORS IN SUBJECTS WITH NORMAL WAIST CIRCUMFERENCE"**

**Abstract:**

Prevalence of obesity is rising in both developing and developed countries. The distribution of fat is important in determining metabolic risk. Abdominal fat is stored in superficial and visceral fat compartments. Of these fat compartments, it is increased visceral fat that increases risk of metabolic complications. Multidetector CT can be used to estimate visceral and subcutaneous fat and calculate visceral to subcutaneous fat ratio (visceral fat volume/subcutaneous fat volume). The aim of the study is to see if visceral subcutaneous fat ratio can be used to predict multiple deranged metabolic risk factors in persons with normal waist circumference. A prospective observational study was done with a sample size of 80 cases with hypertension, diabetes, hyperlipidemia and 80 controls with normal metabolic parameters and normal waist circumference from subjects who presented for abdominal CT. Visceral and subcutaneous fat volumes are determined at L4-L5 level with a slice thickness of 5 mm. Visceral to subcutaneous fat ratios were calculated. Relevant blood investigations were obtained. Volume of visceral and subcutaneous fat and visceral to subcutaneous fat ratio is significantly higher in those patients with metabolic risk factors as compared to those without risk factors. Volume of subcutaneous fat and visceral subcutaneous fat ratio is significantly higher in women as compared to men. There is no statistically significant difference in visceral fat volume between men and women.Cut-offs of 7.3 $cm^3$ for visceral fat volume ,16.4 $cm^3$ for subcutaneous fat and 0.55 for VSR can identify subjects who may develop diabetes, hypertension and dyslipidaemia. Multidetector CT can be used to accurately estimate abdominal fat compartments and detect metabolically obese normal weight individuals in patients with normal waist circumference.

# INTRODUCTION

Obesity is defined as an excess of body fat. The high prevalence of obesity has public health significance because of its association with multiple disease conditions and mortality.

**Epidemiology of Obesity**

Obesity is a public health problem with complex multifactorial etiology. According to the WHO Global Health Observatory data (2016) there are 1.9 billion people who are overweight, of which 650 million are obese. This represents a threefold increase in prevalence of obesity between 1975 and 2016. [1]

This increase in obesity has been across all age groups and both sexes and has occurred irrespective of geographical locality, ethnicity and socioeconomic status. Among women, the prevalence of obesity increased from 6% to15% and the prevalence of overweight individuals increased from 23% to 39%. In men, the rates of obesity increased from 3% to 11% and the overweight rates increased from 20% to 39% from 1975 to 2016.

The 2015 Global Burden of Disease Study has shown a prevalence of overweight slightly lower in women than in men among adults aged between 20 and 44 years. However in the age group between 45-49 years the prevalence of overweight is greater in women as compared to men. Obesity prevalence was generally higher in women than in men across all groups with maximum differences between men and women seen between the age of 50 to 65 years. [2]

Early in the 20$^{th}$ century ,obesity was largely confined to populations from the developed world. However over the past 20 years, there is evidence of a nutritional transition[3] happening across both developed and developing nations. This has been accompanied by a demographic transition in which there is a shift from a pattern of high fertility and high mortality to one of low fertility and low mortality. An epidemiological transition has been noted in the pattern of disease affecting the population with a shift from high prevalence of infectious diseases associated with poor nutrition and poor environmental conditions to high prevalence of life style diseases like cardiovascular disease, diabetes and hypertension. The nutritional

transition refers to a change in dietary patterns and activity levels with an increased consumption of fat, sugar, processed foods instead of starchy low fat, high fiber diets and a change from an active labour intensive lifestyle to a more sedentary lifestyle caused by a shift in technology.**(Figure 1)**

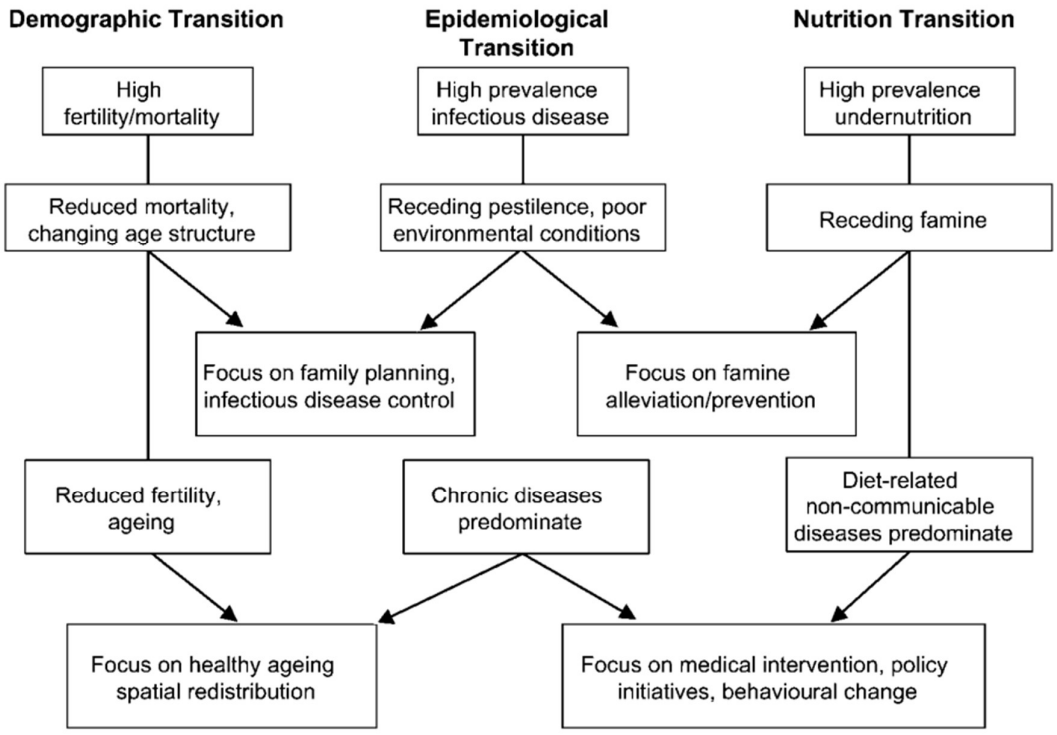



**Figure 1 : Stages of health, nutritional and demographic change**

**Epidemiology of obesity in India**

The prevalence of obesity is rising in India. According to the National Family Health Survey -4 (NFHS-4 Survey), 21% of women and 19% of men between the ages of 15 to 49 are overweight or obese. [4] Prevalence of obesity has increased to 24% in women and 22.9% in men as per the NFHS-5[5].Among women the highest prevalence of obesity was seen in Kerala (54.8%), Goa (53.7%) and Punjab(53.6%).The least prevalence of obesity among women was noted in the states of Jharkhand (20.5%) and Chhattisgarh (23.7%).The NFHS-4 survey data showed that there was wide variation in the prevalence of obesity among men across India with maximum prevalence of obesity seen in Sikkim with 64.8% and Kerala with 59% and the lower prevalence noted in states of Chhattisgarh and Madhya Pradesh at around 25%. Overall the data shows a

rising trend in the prevalence of obesity across most states although the rate of rise of prevalence varies widely between the states. [4]

The NFHS-4 data revealed majority of overweight and obese persons live in urban areas with the most differences noted in prevalence between rural and urban areas among males noted in Orissa and Arunachal Pradesh and lowest difference in Delhi, Meghalaya and West Bengal .In women, the highest rural-urban divide was apparent in Arunachal Pradesh, and Mizoram and lowest was in Haryana, Punjab and Uttaranchal. [4]

**Markers used for measurement of obesity**

The most commonly used marker used to measure obesity is body mass index which is defined as weight in kilogram divided by height in meter squared. Multiple studies have demonstrated a link between BMI and increased risk of developing diabetes[6],hypertension[7], dyslipidaemia [8] ,cardiovascular disease[9],gallstones[10] and cancers[11].

The WHO constituted an Expert Consultation Group in 1993 to classify BMI in well-defined categories. The committee published their findings in 1995.They classified BMI into four categories – underweight , normal, overweight and obese.

In 1997, an International Obesity Task Force described BMI in terms of pre-obesity, class I obesity, class II obesity and class III obesity.[12] A BMI of 25 to 29.9 is referred as "pre-obesity," a BMI of 30 to 34.9 is class I obesity, 34.9 to 39.9 is class II obesity, and a BMI of 40 or greater is class III obesity – **Table 1**.

**Table 1 – WHO Body Mass Index classification**

| | **Class** | **BMI** |
|---|---|---|
| **Overweight** | **Pre-obesity** | **25-29.9** |
| **Obesity** | **Class I** | **30-34.9** |
| | **Class II** | **34.9-39.9** |
| | **Class III** | **40 or greater** |

There is substantial variation in body fat and fat free lean body mass between ethnic groups. A study by Dudeja et al [13] of 123 healthy Asian Indians showed a low sensitivity and negative predictive value of the conventional cut-off of BMI (25 kg/m$^2$) in the identification of overweight individuals and misclassified overweight and obese individuals as normal in approximately 25% of men and approximately 70% of women.

Asian Pacific BMI cut-offs[14]

WHO introduced lower cut-offs for the Asia-Pacific region - underweight (<18.5 kg/m$^2$), normal weight (18.5–22.9 kg/m$^2$), overweight (23–24.9 kg/m$^2$), and obese (≥25 kg/m$^2$).

**Limitations of BMI**

BMI has limitations as an index of obesity in that it cannot distinguish between fat and lean body mass. Therefore a person with high muscle mass and low-fat mass will be classified as having high BMI. [15]

Raised BMI is associated with better survival and fewer cardiovascular events in patients with established cardiovascular disease – the so called obesity paradox. [16]

BMI has limitations in explaining the metabolically obese normal weight (MONW) persons and metabolically healthy obese (MHO) individuals. Ruderman first introduced the concept of metabolically obese normal weight individuals as individuals in the healthy range of standard body weight tables who have metabolic abnormalities commonly associated with obesity like hyperinsulinemia, increased adipocyte size and hypertriglyceridemia, which could be corrected with caloric restriction. [17,18] Goday et al[19] defines MONW as persons of normal BMI (18.5-24.99 kg/m$^2$) with at least three impaired metabolic parameters as defined by National Cholesterol Education Adult Treatment Panel III guidelines which consists of waist circumference, high triglycerides or receiving treatment, low HDL cholesterol, hypertension or previous diagnosis or receiving treatment and high fasting glucose or receiving treatment for diabetes. MONW individuals weigh within the normal BMI range yet have metabolic complications. The prevalence of MONW subjects ranges between 5 and 45%,depending on the criteria used, age, BMI and ethnicity. [20] MONW subjects showed insulin resistance, higher risks for type 2 diabetes mellitus and hypertension,

atherogenic lipid profile and increased risk of cardiovascular diseases. Individuals have BMI of more than 30 kg/m$^2$ but do not have diabetes or dyslipidaemia was postulated that these differences occurred because of the presence of excess visceral adipose tissue. Limitations such as these led to the possibility that it is not adiposity but its distribution can also play a role in determining metabolic risk.

Metabolically healthy obese (MHO) individuals are defined as those with BMI more than or equal to 30 kg/m$^2$ and triglycerides less than or equal to 150 mg/dl, HDL more than 40 mg/dl in men and more than 50 mg/dl in women, systolic blood pressure less than or equal to 130 mm Hg, diastolic blood pressure less than or equal to 85 mm Hg, fasting blood glucose less than or equal to 100 mg/dl and no treatment of dyslipidaemia, hypertension or diabetes and no evidence of cardiovascular disease. [21] MHO patients are having higher levels of subcutaneous fat, lower levels of visceral and liver fat, lower levels of inflammatory markers, greater insulin sensitivity and greater cardiorespiratory fitness and physical activity as compared to metabolically unhealthy obesity. It is estimated that MHO has an age and gender dependent prevalence of between approximately 10% to 30%.[21]

Another limitation of body mass index is it does not account for variation in body fat distribution since it assumes that adipose tissue is distributed evenly over the body.

**Evolution of methods of visceral fat estimation**

Jean Vague[22,23] described “android” (male) and “gynoid” (feminine) patterns of obesity in which fat accumulation in a visceral and upper thoracic distribution is android pattern whereas fat accumulation in lower part of the body (hips and thighs) is gynoid pattern. Ahmed Kissebah and colleagues[24] followed up on these findings with classification as upper versus lower body fat distribution as shown by high or low waist hip circumference ratio respectively.

Krotkiewski et al[25] in a landmark paper proposed that regional differences in fat distribution, body shape and fat cell number and size are factors that are related to the risk of metabolic complications. They reported that men and women with a male abdominal type of obesity are more susceptible to the adverse effect of obesity on lipid and carbohydrate metabolism.

Waist hip ratio was found to correlate with increased risk of cardiovascular disease, type 2 diabetes and death. Waist hip ratio is limited in its utility for follow up studies as both its numerator and denominator changes with treatment. Waist circumference is an alternative to the waist hip ratio for assessing fat distribution. Waist circumference is more strongly associated with visceral fat compartment which is the more metabolically active compartment. [26] The NIH was the first to use the threshold values for waist circumference (≥88 cm in women and ≥102 cm in men) for defining obesity. [27]

Development of cross sectional imaging provided medical professionals with a new tool to assess visceral obesity. Tokunaga et al[28] of the University of Osaka, Japan was the first group to develop techniques to use CT to measure visceral and subcutaneous fat compartments. This was a major advance over clinical methods which did not differentiate between visceral and subcutaneous abdominal fat and enabled study of the specific relationships between body fat compartments and various health outcomes.

L Sjostrom et al[29] of the University of Gothenburg developed methods to determine total visceral adipose tissue using CT and compared it to fat determination using total body water and total body potassium. They determined that fat estimation using CT was as accurate as that using total body water and total body potassium and more reproducible.

The techniques for fat estimation using CT also evolved over time with initial studies utilizing segmentation of the body into multiple fat volumes and multiple scan approaches. There was significant radiation exposure in these approaches and would enable only a limited number of scans for fat estimation in large population based studies. As such the techniques had to be modified in order to reduce radiation exposure. Fujioka et al[30] showed that visceral and subcutaneous fat estimation at the level of L4-L5 showed significant correlation with entire abdominal fat volume. This enabled subsequent studies to utilize a single slice scan taken at the level of L3-L4 or at the level of umbilicus to estimate visceral and subcutaneous fat volume. Lee et al[31] in their 2004 paper showed that while there were differences in the volume of fat at different levels of the abdomen and there were interindividual variations, the ability of single images obtained at L4-L5 level, 5 cm above this level and at L3-L4 levels to measure visceral and subcutaneous fat compartments are comparable.

Fujioka et al[30] was first to establish that higher visceral fat volume and visceral subcutaneous fat ratio measured using CT was correlated with higher levels of fasting blood glucose, fasting serum triglyceride levels and serum cholesterol levels. They determined that a visceral subcutaneous fat ratio of 0.4 can be used to identify individuals at increased risk of metabolic risk factors.

Further studies proved that visceral adiposity was associated with increased risk of hyperlipidaemia, cardiometabolic risk factors, diabetes, proinflammatory prothrombotic profile, hypertension.[32-37]Raji et al[38] showed that Asian Indians had fasting hyperinsulinemia, higher glucose and insulin levels during oral glucose tolerance test, lower HDL, higher LDL and higher PAI-1 (Plasminogen activator inhibitor-1) levels. CT scan done at L2-L3 and L3-L4 levels revealed greater values of total abdominal fat and visceral fat in Asian Indians as compared to Caucasians. It was postulated the raised visceral fat in Asian Indians may be responsible for these abnormalities.

# AIMS OF THE STUDY

The aim of the present study is to see if VSR can be used to predict multiple metabolic risk factors in persons with normal waist circumference in Indian population.

# REVIEW OF LITERATURE

**Kaess et al**[39] studied the relationship between visceral subcutaneous fat ratio and metabolic risk factors in 3223 individuals ( 1,543 women) who were enrolled within the Framingham Heart Study (the Framingham Offspring and Third Generation cohort).Visceral fat, subcutaneous fat and VSR were quantified using CT. Mean age was 51.8 years in women and 49.5 years in men. Mean VSR was 0.39 in women and 0.84 in men. In women, higher VSR was correlated with increased risk of diabetes, hypertension and dyslipidaemia (all with $p<0.0003$). The positive correlation was seen in both pre and post-menopausal women. Men with high VSR showed positive correlation with all metabolic risk factors except diabetes but the risk was less that of women. When adjusted for visceral fat tissue, association of VSR with metabolic risk factors remained significant for lower HDL cholesterol, higher Triglycerides, higher prevalence of hypertension, diabetes and metabolic syndrome in women.

**Oh et al**[40] conducted a cross-sectional study of 535 patients (296 men,239 women) to see if VSR can be used to predict the presence of two or more metabolic risk factors in persons with normal waist circumference. The mean age of men and women was 52.1±9.9 and 50.6±9.7 years, respectively. In men, VSR was significantly raised in patients with metabolic risk factors as compared to those who had normal metabolic parameters except for the group with low HDL cholesterol which did not show any statistically significant difference. Visceral fat and subcutaneous fat volume however did not show any statistically significant differences between those with and without risk factors. In women, statistically significant higher VSR and visceral fat volume was found in those with risk factors as compared to those without risk factors. There was no statistically significant difference in subcutaneous fat volume between the two groups. The study concluded that VSR has diagnostic value in predicting the presence of multiple metabolic risk factors in patients with normal waist circumference with higher accuracy in women over men.

**Fujioka et al**[30] studied the correlation between visceral fat accumulation and glucose and lipid levels in 46 patients (15 males,31 females). The fasting plasma glucose level, area under the plasma glucose concentration curve after oral glucose loading (plasma glucose area), fasting serum triglyceride level, and serum total cholesterol level were

statistically significant higher values in patients with Visceral subcutaneous fat ratio >0.4 as compared to those with a lower V/S ratio. The correlation of higher VSR with metabolic risk factors were seen in both men and women when analysed separately.

**Ryo et al**[41] showed that visceral fat estimated at the level of L4 using CT correlated with total abdominal fat volume. They showed that a single slice can be used to estimate visceral and subcutaneous fat volumes and a VFA more than 100 $cm^2$ is the cut-off to determine risk of obesity related disorders.

**Maurovich-Horvat et al**[42] evaluated 100 Caucasian patients (in the age range: 37–83 years ; of which 49% were women) of the Framingham Heart Study offspring cohort who underwent MDCT. Subcutaneous and visceral adipose tissue volumes (SFV and VFV in $cm^3$) and areas (SFA and VFA in $cm^2$) and waist circumference (WC) and sagittal diameter (SD) were measured by two experienced radiologists and another radiologist one week later to look for interobserver variability. The study showed that inter-reader reproducibility was excellent for VFV and SFV. The mean absolute and relative intra-observer differences were small and nonsignificant for both measurements (SFV: −0.6±6.1 $cm^3$, $P$=0.29; VFV: 0.7±6.0 $cm^3$; $P$=0.26). The mean SFV/VFV ratio was significantly different between participants <60 vs > 60 years (1.971.0 vs 1.570.7; P<0.001) and between men and women (1.270.5 vs 2.270.9; P<0.001).This study showed that MDCT volumetric quantification of abdominal visceral and subcutaneous fat was reproducible. Volumetric based adipose tissue compartment ratios showed expected age and sex related differences in abdominal fat tissue distribution.

**Pickhardt et al**[43] studied 474 patients (217 men, 257 women) with a mean age of 58.3 years (range, 35–92 years) to see if visceral adiposity and hepatic steatosis correlates with metabolic syndrome. The area under the receiver operating characteristic curve (AUC) for visceral fat area was 0.830 (95% CI, 0.784–0.867) in men and 0.887 (0.848–0.918) in women ( p = 0.162). The AUC for subcutaneous fat area was 0.865 (0.823–0.899) in men and 0.762 (0.711–0.806) in women (p = 0.024). The AUC for visceral fat percentage was 0.527 (0.472–0.581) in men and 0.820 (0.774–0.859) in women ( p < 0.001). The AUC for liver attenuation was 0.706 (0.653–0.754). Thresholds of subcutaneous fat area greater than 204 $cm^2$ in men, visceral fat area greater than 70 $cm^2$ in women, and liver attenuation less than 50 HU yielded a sensitivity and specificity of

80.3% and 83.7%; 83.7% and 80.0%; and 22.0% and 96.7%, respectively. The study showed that visceral fat was the best predictor of metabolic risk in women and subcutaneous fat was the best predictor in men. The percentage of visceral fat was a poor predictor for metabolic syndrome in men. Decreased liver attenuation was insensitive but was highly specific for metabolic syndrome.

**Katsuyama et al[44]** studied 29 patients in which visceral fat area (VFA) and subcutaneous fat area (SFA) was measured using CT and brachial ankle pulse wave velocity was measured as a marker of atherosclerosis. Although VFA was positively correlated with waist circumference, body mass index and systolic blood pressure, it was not correlated with lipid markers like high LDL and triglycerides, low HDL and blood glucose parameters like fasting blood glucose and HbA1c.VSR ratio was not correlated with BMI or WC(waist circumference) but showed significant positive correlation with serum triglycerides and brachial ankle pulse wave velocity in obese subjects.

**Gómez-Ambrosi et al[45]** did a cross-sectional study of 6123 Caucasian subjects (4208 females/1915 males) aged between 18 and 80 years in which they assessed the degree of misclassification of obese patients with BMI as compared to direct body fat (BF%) estimation using air displacement plethysmography. They compared cardiovascular and metabolic risk in patients classified as obese and non-obese based on BMI with similar BF% in a subset of 3051 subjects (2213 females/838 males). This subset included a reference group of subjects who were classified as lean using both BMI and BF% (560 women,96 men) and compared it to a group classified as non-obese using BMI (<30 $kg/m^2$ ) and obese by BF% (1208 women,371 men) and a group classified as obese both by BMI and BF% (445 women,371 men). Overweight was defined as BF% between 20.1-24.9% for men and 30.1-34.9% for women and obesity was defined as BF% greater than or equal to 25% for men and 35% for women. The study found that 29% patients who were classified as lean using BMI criteria had BF% in the obese range. The misclassification was higher for women (30% classified as obese by BF% classified as lean by BMI) than for men (25% classified as obese by BF% classified as lean by BMI).The BMI cutoff of 30% had good specificity (89% in men,98% in women) but poor sensitivity (77% in men,65% in women).The level of cardiometabolic risk factors are higher in lean and overweight BMI-classified subjects with BF% within

the obesity range (men 4.3±9.2, women 4.9±19.5 mg $l^{-1}$) as well as in obese BMI-classified individuals (men 4.2±5.5, women 5.1±13.2 mg $l^{-1}$) as compared with lean volunteers with normal body fat % (men 0.9±0.5, women 2.1±2.6 mg $l^{-1}$); p value < 0.01 for both males and females. The study showed that BMI misses patients with raised cardiometabolic risk and elevated body fat%.

**Yoo et al[46]** did a retrospective, cross-sectional, observational study of 369 patients ( 192 females,177 males) to determine the threshold of visceral fat which would predict metabolic syndrome in the patients. The mean age of women in the study was 51.2±14.8 years and the mean age of men was 52.8±15.6 years. Visceral adipose tissue was found to significantly higher in those patients with metabolic syndrome as compared to those without risk factors. There was no statistical difference in subcutaneous fat volume between those with and without metabolic syndrome. Visceral subcutaneous fat ratio adjusted for age was significantly higher in those with metabolic syndrome as compared to those with no metabolic syndrome in men (p=0.027 for men). However the relationship between increased VSR and metabolic syndrome was not statistically significant in women. VSR and VAT was seen to have statistically significant predictive value in determining patients at increased risk of metabolic syndrome. The study determined that the cut-off value of Visceral adipose tissue to predict metabolic syndrome was 132 $cm^2$ for individuals under 50 years living in the UAE.VSR cut-offs in patients less than 50 was 0.293(p<0.01) for women and 0.424(p<0.01) for men. Above 50, the VSR threshold values were higher at 0.647(p=0.422) for women and 0.693(p=0.165) in men. Sensitivity of VSR was 37.2%.

**Fukuda et al[47]** conducted an observational study in which 682 patients aged >/ 20 years with diabetes were enrolled with a mean age of 64 +/-13 years of which 41% were women. Visceral fat area and subcutaneous fat area was determined by dual bioelectrical impedance analyser. They were followed up with a median follow up of 2.5 years with the study end point being the first occurrence or recurrence of cardiovascular disease (CVD). 21 patients reached the end point in the study including 4 events of cerebrovascular accident, 14 events of coronary artery disease and three events of peripheral arterial disease. The study determined that high values of VSR ( AUC 0.66 (95% CI: 0.57–0.76)) was associated with increased risk of CVD and is an independent predictor of incident or recurrent CVD in diabetic patients in Japanese

population V/S ratio. Visceral fat area(VFA), subcutaneous fat area (SFA) and body mass index (BMI) were found to be not predictive of incident or recurrent CVD.

**Porter et al**[48] studied 3001 patients (48.5% women) who had participated in the Framingham Heart Study to determine if subcutaneous adipose tissue (SAT) is protective against cardiometabolic risk factors. The study showed that in patients with the highest visceral adipose tissue, increased subcutaneous fat was associated with lower triglyceride levels suggesting a beneficial effect of SAT on triglyceride levels in the obese.

**Narumi et al**[49] studied 122 patients (40 female) with a mean age of 56.2 ± 8.4 years to determine the relationship of subcutaneous fat area (SFA), the visceral fat area (VFA) and the VFA/SFA ratio with calcium score of the whole aorta (CSWA) (surrogate marker of the severity of atherosclerosis). The mean ± SD of SFA and VFA were 140.1 ± 62.7 $cm^2$ , and 94.2 ± 46.3 $cm^2$ , respectively. VFA showed significant positive correlation with metabolic risk factors like systolic and diastolic blood pressure, fasting blood glucose, HBA1C, triglyceride, LDL-C and HOMA-R and significant negative correlation with adiponectin and high-density lipoprotein (HDL)-cholesterol. SFA did not correlate with fasting blood glucose, HBA1C, triglyceride, HDL-cholesterol, or adiponectin ( $P > 0.05$).SFA was significantly and inversely correlated with log CSWA (p=0.015) but VFA was not correlated ( p=0.25),therefore the VSR was significantly and positively correlated with log CSWA (P=0.015).The study showed that subcutaneous fat had a protective effect against atherosclerosis in asymptomatic patients.

**Dudeja et al**[13] studied 123 healthy volunteers (86 males, 37 females) and assessed their body fat percentage and body mass index. BMI for males was 21.4 kg/m2 with a standard deviation of 3.7 and the BMI for females was 23.3 kg/m2 with a standard deviation of 5.5.Percentage body fat was 21.3 % with a standard deviation of 7.6 for males and the percentage body fat in women was 35.4% with a standard deviation of 5.It was found that using conventional WHO cut-offs misclassified subjects who were overweight or obese especially in women. Receiver operating characteristic (ROC) curve analysis showed a low sensitivity and negative predictive value of the conventional cut-off of the BMI (25 kg/m2) in identifying subjects as overweight or obese as compared to cut-offs based on body fat percentages. Based on the ROC curve,

they suggested adoption of lower cut-offs of 21.5 kg/m2 for males and 19.0 kg/m2 for females for BMI for identifying subjects who are overweight or obese.

**Nazare et al**[50] collaborated in the INSPIRE ME AA trial (International Study of Prediction of Intra-Abdominal Adiposity and Its Relationship With Cardiometabolic Risk/Intra-Abdominal Adiposity) which was an international prospective study of 4504 patients from 29 countries. This study population included 2011 whites, 166 African Caribbean blacks, 381 Hispanics, 1192 East Asians, and 347 Southeast Asians. Computed tomography was used to assess visceral and subcutaneous abdominal fat distribution and its quantification and to estimate liver fat content. Blood pressure, lipid profile, high sensitivity CRP (hs-CRP) and blood sugar values were recorded. It was found that higher ranges of BMI was associated with higher levels of visceral fat and liver fat. East Asians had the highest accumulation of visceral adipose tissue even though they had lower BMI values. This showed that ethnicity significantly affects abdominal adiposity and its distribution. All ethnic groups showed association between visceral fat and hypertension, , type 2 diabetes, hypertriglyceridemia, low HDL-cholesterol concentration, or high C-reactive protein concentration.

**Lear et al**[51] studied the etiology of increased cardiovascular risk in South Asian population among subjects recruited in Multicultural Community Health Assessment Trial (M-CHAT) trial. The study group consisted of 207 South Asians with 201 Caucasians as controls. The study found that South Asians had significantly higher lipid, glucose, insulin and hs-CRP values as compared to Caucasians after adjusting for confounders. These differences got attenuated by 16-52% when adjusted for visceral fat between the two groups. The study concluded that higher levels of risk factors for CVD in South Asians are predominantly because of the unique phenotype of South Asians having greater VAT than Europeans even at the same BMI.

**Kim et al**[56] enrolled 250 subjects aged 27 to 80 years to estimate the relationship between visceral fat volume and metabolic syndrome. They measured the visceral and subcutaneous fat volume from the level of the highest point of the liver dome to the pelvic floor on axial CT images. They also quantified the subcutaneous and visceral fat areas from the lowest to highest part of the umbilicus on axial images. Using dedicated software, SFA,VFA,SFV and VFV were calculated. Taking adipose tissue density as 0.9 g/ml, they also estimated subcutaneous and visceral fat mass. They found that

visceral fat volume and visceral fat mass had the highest predictive value in determining metabolic syndrome in both men and women. They calculated cut-offs for visceral fat volume and visceral fat mass in Korean population to be 4852 $cm^3$ and 4366.8 g for men and

**Pickhardt et al**[57] recruited a cohort of 7785 adults (4361 women and 3424 men) to study the application of fully automated CT based visceral measures to identify metabolic syndrome in asymptomatic adults. They found that L1 total abdominal fat (area under the ROC curve [AUROC] = 0.909; odds ratio [OR] = 27.2), L3-level skeletal muscle index (AUROC = 0.776; OR = 5.8), and volumetric liver attenuation (AUROC = 0.738; OR = 5.1) performed well when compared with abdominal aortic calcification scoring (AUROC = 0.578; OR = 1.6). An L1-level total abdominal fat threshold of 460.6 $cm^2$ was 80.1% sensitive and 85.4% specific for metabolic syndrome. On follow-up, cardiovascular events were found to more frequent in those with metabolic syndrome. They estimated that using thresholds of 204 $cm^2$ in men for subcutaneous fat area, a threshold of 70 $cm^2$ for visceral fat area in women and liver attenuation less than 50 HU detected metabolic syndrome with a sensitivity and specificity of 80.3% and 83.7%; 83.7% and 80.0%; and 22.0% and 96.7%, respectively. They determined that visceral fat area was the best predictor in women and subcutaneous fat area the best predictor in men. The study showed that fully automated quantitative tissue measures of fat, muscle, and liver derived from abdominal CT scans can help identify individuals who are at risk for metabolic syndrome. These visceral measures can be opportunistically applied to CT scans obtained for other clinical indications, and they may ultimately provide a more direct and useful definition of metabolic syndrome.

**Summary of the Review of Literature is listed in Table 2**

**Table 2 : Summary of Review of Literature**

| Author | Year | Sample Size | Conclusion |
|---|---|---|---|
| **Fujioka et al[30]** | 1987 | 46 | The fasting plasma glucose level, area under the plasma glucose concentration curve after oral glucose loading (plasma glucose area), fasting serum triglyceride level, and serum total cholesterol level were statistically significant higher values in patients with Visceral subcutaneous fat ratio >0.4 as compared to those with a lower V/S ratio. The correlation of higher VSR with metabolic risk factors were seen in both men and women when analysed separately. |
| **Dudeja et al[13]** | 2001 | 123 | It was found that using conventional WHO cut-offs misclassified subjects who were overweight or obese especially in women. Based on the ROC curve, they suggested adoption of lower cut-offs of 21.5 kg/m2 for males and 19.0 kg/m2 for females for BMI for identifying subjects who are overweight or obese. |

| Author | Year | Sample Size | Conclusion |
|---|---|---|---|
| **Maurovich-Horvat[42]** | 2007 | 100 | Subcutaneous and visceral adipose tissue volumes (SAV and VAV in $cm^3$) and areas (SAA and VAA in $cm^2$) and waist circumference (WC) and sagittal diameter (SD) were measured by two experienced radiologists and another radiologist one week later to look for interobserver variability. The study showed that inter-reader reproducibility was excellent for VAV and SAV. |
| **Porter et al[48]** | 2009 | 3001 | . The study showed that in patients with the highest visceral adipose tissue, increased subcutaneous fat was associated with lower triglyceride levels suggesting a beneficial effect of SAT on triglyceride levels in the obese. |

| Author | Year | Sample size | Conclusion |
|---|---|---|---|
| **Narumi et al[49]** | 2009 | 122 | VFA showed significant positive correlation with metabolic risk factors like systolic and diastolic blood pressure, fasting blood glucose, HBA1C, triglyceride, LDL-C and HOMA-R and significant negative correlation with adiponectin and HDL-cholesterol. SFA was significantly and inversely correlated with log CSWA and VSR was significantly and positively correlated with log CSWA. The study showed that subcutaneous fat had a protective effect against atherosclerosis in asymptomatic patients. |

CSWA -calcium score of whole aorta – surrogate marker of atherosclerosis

| Author | Year | Sample size | Conclusion |
|---|---|---|---|
| **Kaess et al[39]** | 2012 | 3223 | In women, higher VSR was correlated with increased risk of diabetes, hypertension and dyslipidaemia. The positive correlation was seen in both pre and post-menopausal women. Men with high VSR showed positive correlation with all metabolic risk factors except diabetes but the risk was less that of women. |
| **Gómez-Ambrosi[45]** | 2012 | 6123 | The study found that 29% patients who were classified as lean using BMI criteria had BF% in the obese range. The misclassification was higher for women (30% classified as obese by BF% classified as lean by BMI) than for men (25% classified as obese by BF% classified as lean by BMI). |

| Author | Year | Sample size | Conclusion |
|---|---|---|---|
| **Pickhardt et al[43]** | 2012 | 474 | The study showed that visceral fat was the best predictor of metabolic risk in women and subcutaneous fat was the best predictor in men. The percentage of visceral fat was a poor predictor for metabolic syndrome in men. Decreased liver attenuation was insensitive but was highly specific for metabolic syndrome. |
| **Nazare et al[50]** | 2012 | 4504 | It was found that higher ranges of BMI was associated with higher levels of visceral fat and liver fat. East Asians had the highest accumulation of visceral adipose tissue.This showed that ethnicity significantly affects abdominal adiposity and its distribution. All ethnic groups showed association between visceral fat and hypertension, type 2 diabetes, hypertriglyceridemia, low HDL-cholesterol concentration, or high CRP concentration. |

| Author | Year | Sample size | Conclusion |
|---|---|---|---|
| **Lear et al[51]** | 2012 | 408 | The study concluded that higher levels of risk factors for CVD in South Asians are predominantly because of the unique phenotype of South Asians having greater VAT than Europeans even at the same BMI. |
| **Ryo et al[41]** | 2014 | | They showed that a single slice can be used to estimate visceral and subcutaneous fat volumes and a VFA more than 100 $cm^2$ is the cut-off to determine risk of obesity related disorders |
| **Katsuyama et al[44]** | 2015 | 29 | Although VFA was positively correlated with waist circumference, body mass index and systolic blood pressure, it was not correlated with lipid markers like high LDL and triglycerides, low HDL and blood glucose parameters like fasting blood glucose and HbA1c.VSR ratio showed significant positive correlation with serum triglycerides and brachial ankle pulse wave velocity in obese subjects. |
| **Oh et al[40]** | 2017 | 535 | In men, VSR was significantly raised in patients with metabolic risk factors as compared to those who had normal metabolic parameters except for the group with low HDL cholesterol which did not show any statistically significant difference. Visceral fat and subcutaneous fat volume however did not show any statistically significant differences between those with and without risk factors. In women, statistically significant higher VSR and visceral fat volume was found in those with risk factors as compared to those without risk factors. The study concluded that VSR has diagnostic value in predicting the presence of multiple metabolic risk factors in patients with normal waist circumference with higher accuracy in women over men. |

| Author | Year | Sample size | Conclusion |
|---|---|---|---|
| **Fukada et al[47]** | 2018 | 682 | The study determined that high values of VSR was associated with increased risk of CVD and is an independent predictor of incident or recurrent CVD in diabetic patients in Japanese population. VFA, SFA and body mass index (BMI) were found to be not predictive of incident or recurrent CVD. |
| **Yoo[46]** | 2020 | 369 | Visceral adipose tissue area was found to significantly higher in those patients with metabolic syndrome as compared to those without risk factors. VSR was significantly higher in those with metabolic syndrome in men. |
| **Kim et al[56]** | 2021 | 250 | Kim et al estimated cut-offs for visceral fat volume and visceral fat mass for predicting metabolic syndrome in men and women in Korean population. SFA and VFA were quantified using axial images obtained at the level of the lowest to the highest part of the umbilicus and near the L4 to L5 vertebral interspace. SFV and VFV were quantified from the highest level of the liver dome to the pelvic floor and the highest level of the anal sphincter on axial CT images .The visceral fat volume and visceral fat mass showed the highest AUC values amongst the parameters assessed. They developed cut-off to determine the risk for metabolic risk at 4852 $cm^3$ for visceral fat volume and 4366.8 g for visceral fat mass in men and 3101 $cm^3$ and 2790 g for VFV and VFM in women. |
| **Pickhardt et al[57]** | 2021 | 7785 | They used automated CT biomarkers to determine individuals at increased risk of metabolic syndrome. They obtained visceral and subcutaneous fat areas at L1 level. An L1-level total abdominal fat threshold of 460.6 cm2 was 80.1% sensitive and 85.4% specific for metabolic syndrome. |

# MATERIALS AND METHODS

This prospective observational study was conducted in the Department of Diagnostic and Interventional Radiology, All India Institute of Medical Sciences, Jodhpur.

**Type of study** : Prospective observational study

**Inclusion and Exclusion criteria for the study was as shown in Table 3**

**Table 3 - Inclusion and Exclusion criteria for the study**

| INCLUSION CRITERIA | EXCLUSION CRITERIA |
|---|---|
| Cases -80 patients undergoing routine abdominal CT with a history of DM, Hypertension or Hyperlipidemia with normal waist circumference | Persons with waist circumference more than 102 cm in males and 88 cm in females |
| For the control group, equal number of patients undergoing routine abdominal CT without any metabolic risk factors with age >40 and normal waist circumference | Persons with waist circumference more than 102 cm in males and 88 cm in females |

**Study duration** : 1.5 years

**Sample size** :

The sample size was calculated based on previously published study done by Oh Y.H et al. Assuming a sensitivity of 75 percent for Visceral subcutaneous fat ratio (VSR) and with 90 percent precision and alpha error of 5%, the, the sample size was estimated to be 72. For adequate power for estimation of sensitivity and specificity for VSR on CT, 72 patients was recruited for the study.

Sample Size (n) = $[Z\ (1-\alpha/2)]^2$ x p (1-p) $/d^2$

Z (1-a) = 1.96 standard normal variate at 5% level of significance

P= sensitivity or specificity of new test

80 cases and 80 controls were included in the study.

The patients who present to outpatient facility of All India Institute of Medical Sciences, Jodhpur meeting the inclusion criteria was enrolled in the study after taking written informed consent. A medical history questionnaire was administered which would record any current and past illnesses and any medications they are taking. They would then undergo an anthropometric evaluation (waist circumference), lab tests and CT scan of the abdomen. Waist circumference was taken at the mid-point between the iliac crest and the rib cage in the midaxillary line. Blood pressure was recorded. Lab tests like fasting blood sugar or HbA1c, lipid profile was seen from hospital CPMS and recorded if available.

**Imaging**

**CT Abdomen :**

Images were acquired by SOMATOM Definition Flash dual energy dual source 2x128 slice CT scanner (Siemens Healthcare GmbH, Germany).

Abdominal subcutaneous and visceral fat was determined by a single slice CT scan at the level of L4-L5 vertebral level of 5 mm thickness with patients in supine position. The technique used for adipose tissue measurements in cross sectional CT images has been previously standardized and validated. Visceral and subcutaneous fat compartments were delineated by drawing the inner and outer borders of the abdominal wall and back muscles in the CT slice. In order to separate visceral from subcutaneous fat, the abdominal muscular wall separating the two fat compartments was manually traced. Visceral fat compartment was defined as the intra-peritoneal fat bound by the visceral peritoneum and subcutaneous fat compartment was defined as the area external to the abdominal and back muscles.

Subcutaneous adipose tissue volume (SF) and Visceral adipose tissue volume (VF) was delineated using -200 to - 40 Hounsfield Units as fat attenuation using Syngo.via version VB30 region growing software available on Syngovia advanced multi-modality workstation. VSR was calculated from the obtained data.

**Statistical analysis**

Analysis was done using SPSS version 23 (IBM Corp. Ltd, Newark, USA). For numerical variables, arithmetic means and standard deviation were calculated. Analysis of means was done with independent sample t-test between the groups. Median, range were also calculated. An ROC curve was used to assess the predictive accuracy of visceral fat, subcutaneous fat and VSR in identifying individuals with metabolic risk factors. Area under the curve (AUC) was used to quantify the accuracy of each test. A *p*-value of less than 5 percent ($p<0.05$) was regarded as statistically significant.

**Ethical considerations**

- The study includes patients who are taking CT as part of their standard plan of care. The radiation exposure of a single slice taken at low kV and low mA is equal to a single abdominal X-Ray.
- No additional contrast is being administered
- No added cost burden for the patient
- The study can probably help identify those at increased risk of metabolic disorders which in turn could help them with early diagnosis and treatment

# RESULTS

During the tenure of the thesis, 80 patients with metabolic risk factors and 80 patients who did not have metabolic risk factors who had presented to the Department of Diagnostic and Interventional Radiology at All India Institute of Medical Sciences, Jodhpur for routine abdominal CT were included in the present study.

Analysis of the patients was done and showed the following :

1.**Gender distribution**

Among the 80 cases, there were 48 males and 32 females. Of the 80 controls, 47 were males and 33 were females.**(Figure 2,3)**

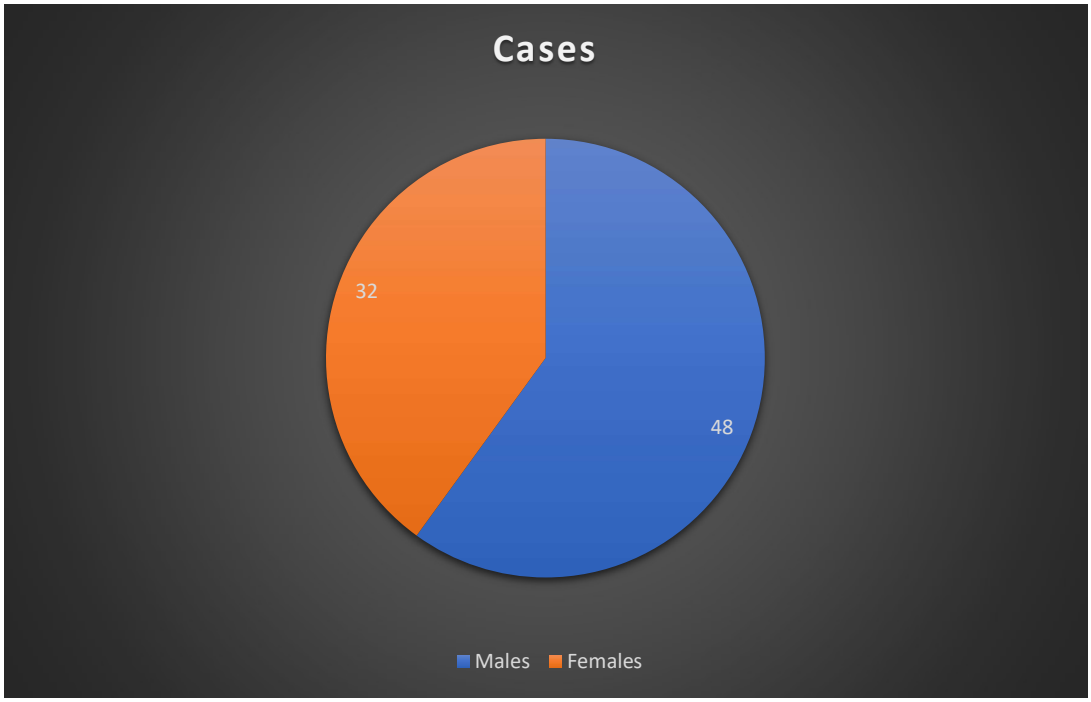



**Figure 2 : Pie chart depicting the gender distribution among cases**

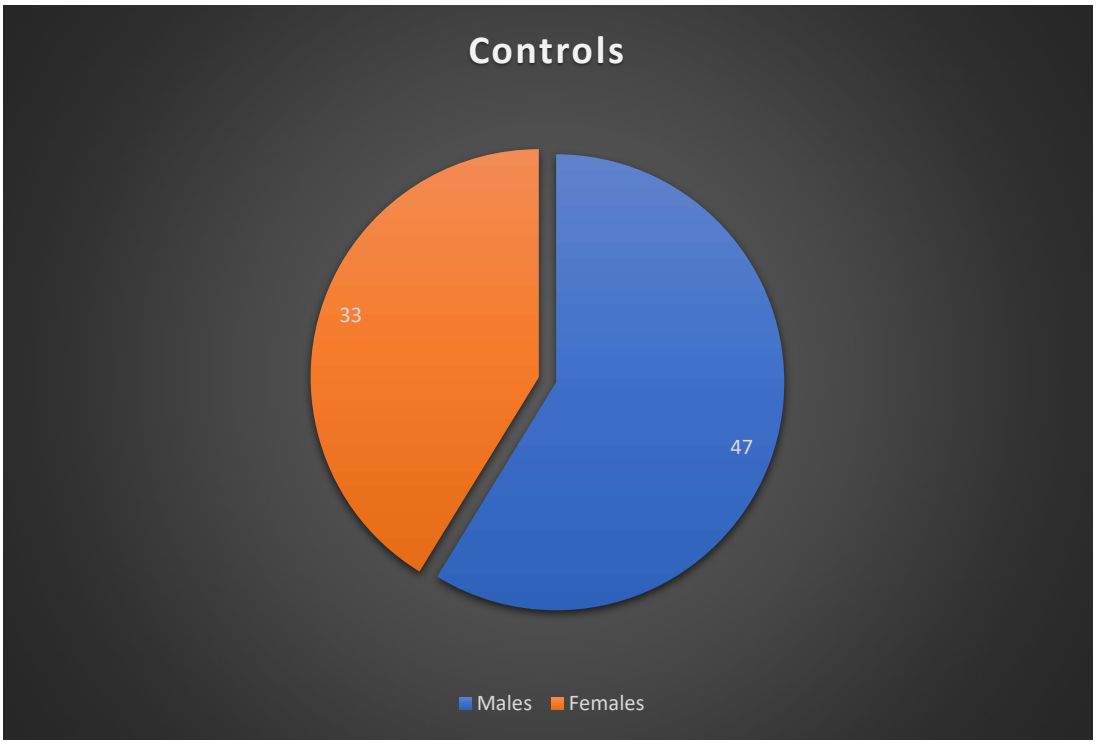



**Figure 3: Pie chart depicting the gender distribution among controls**

**2.Age distribution**

The mean age of patients with risk factors was 60.4 with a standard deviation of 10.3 with a median age of 59 years. The mean age of controls was 56.7 with a standard deviation of 10.2 and a median age of 55 years.

Among cases the mean age of men was 61.2 with a standard deviation of 10.2 and a median age of 59 years. The mean age of women was 59.2 with a standard deviation of 10.6 and a median age of 59 years.**(Figure 4,5)**

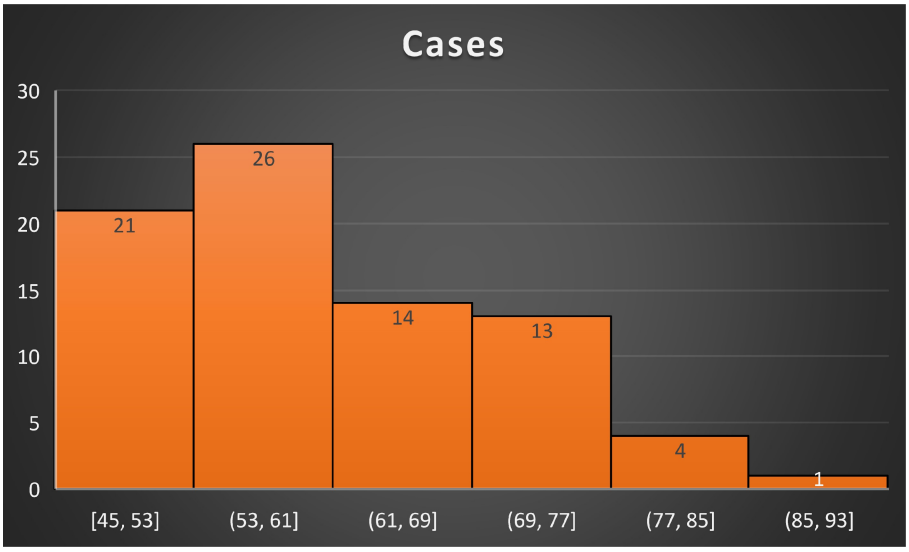



**Figure 4:Histogram showing the age distribution of cases in the study**

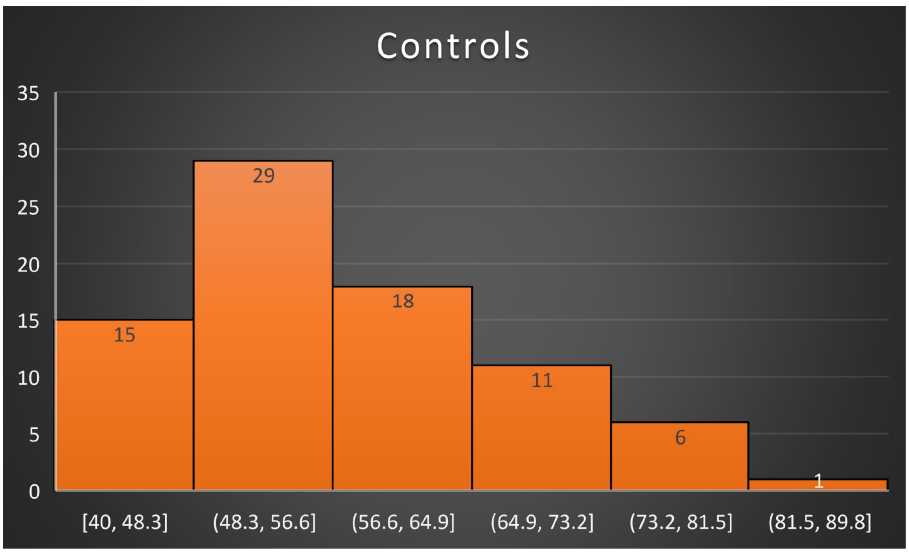



**Figure 5:Histogram showing the age distribution of controls in the study**

### 3. Cases vs controls

Analysis of visceral fat volume, subcutaneous fat volume and visceral subcutaneous fat ratio in cases and controls showed statistically significant differences between cases and controls in all three parameters. Volume of visceral fat ($p$<0.001) and subcutaneous fat ($p$<0.001) is significantly higher in cases as compared to controls. Visceral to subcutaneous fat ratio ($p$=0.025) is significantly higher in cases as compared to controls.

Mean volume of visceral fat was 11.5 $cm^3$,the mean volume of subcutaneous fat was 14.9 $cm^3$ and mean value of visceral subcutaneous fat ratio was 1 in cases.**(Table 4,Figures 6,7,8,9)**

**Table 4 - VF,SF and VSR in cases and controls**

| | Cases/Controls | | | | |
|---|---|---|---|---|---|
| | Controls | | Cases | | *p*-value |
| | Mean | SD | Mean | SD | |
| AGE | 56.7 | 10.2 | 60.4 | 10.3 | 0.026 |
| Volume of visceral fat | 5.2 | 3.6 | 11.5 | 5.6 | <0.001 |
| Volume of Subcutaneous fat | 9.2 | 6.3 | 14.9 | 8.3 | <0.001 |
| Visceral subcutaneous fat ratio | 0.8 | 0.5 | 1.0 | 0.7 | 0.025 |

*p*-value calculated using Independent sample t test.

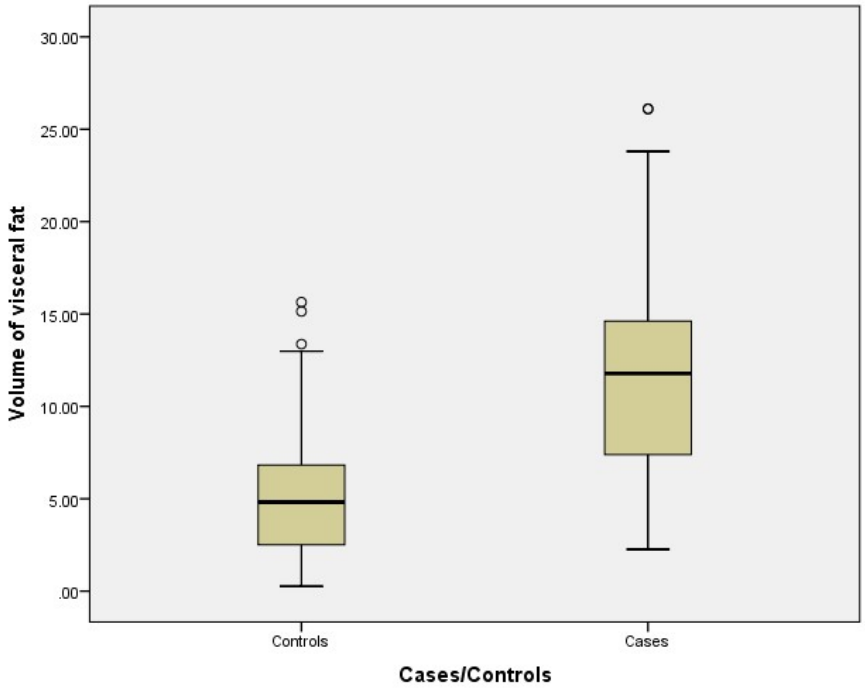



**Figure 6: Box and whisker plot showing increased volume of visceral fat in cases as compared to controls**

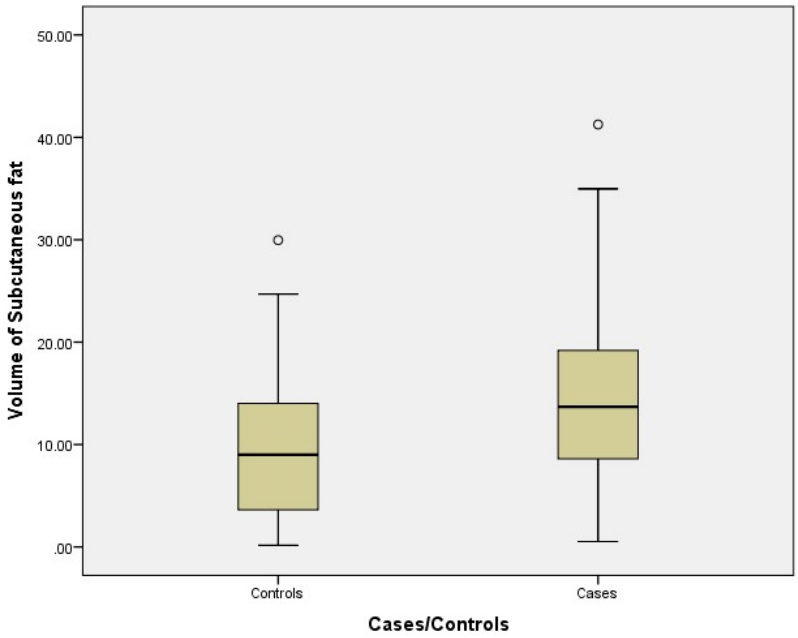



**Figure 7: Box and whisker plot showing increased volume of subcutaneous fat in cases as compared to controls**

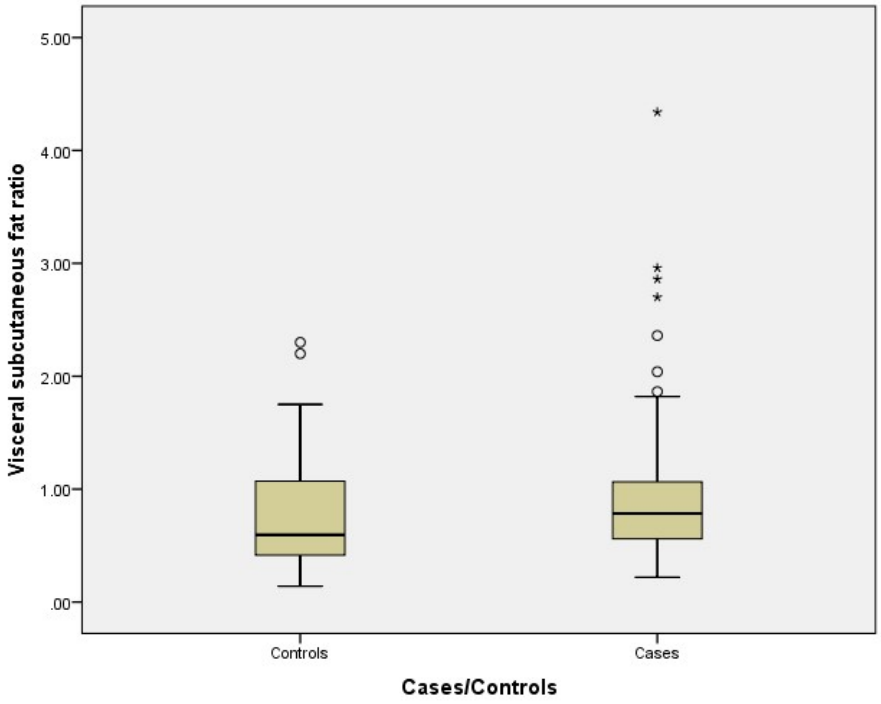



**Figure 8: Box and whisker plot showing increased visceral to subcutaneous fat ratio in cases as compared to controls**

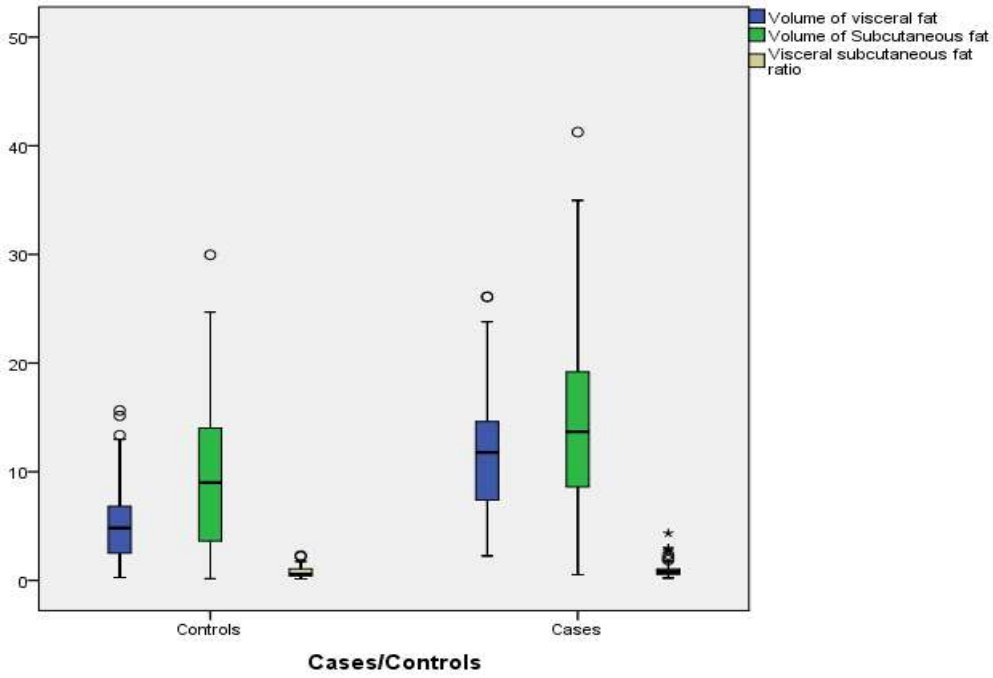



**Figure 9: Box and whisker plot showing increased volume of visceral fat, volume of subcutaneous fat and visceral-subcutaneous fat ratio in cases as compared to controls**

**4.Males vs females**

When analyzed for differences in visceral fat volume, subcutaneous fat volume and visceral subcutaneous fat ratio between men and women, significant differences were seen. Volume of subcutaneous fat and VSR was significantly higher in women as compared to men. There was no statistically significant difference in visceral fat volume between men and women.**(Table 5)**

**Table 5 - VF,SF and VSR in males and females**

| | SEX | | | | |
|---|---|---|---|---|---|
| | F | | M | | *p*-value |
| | Mean | SD | Mean | SD | |
| AGE | 59.2 | 10.6 | 61.2 | 10.2 | 0.386 |
| Volume of visceral fat | 10.4 | 3.8 | 12.2 | 6.5 | 0.165 |
| Volume of Subcutaneous fat | 17.6 | 7.3 | 13.0 | 8.5 | 0.016 |
| Visceral subcutaneous fat ratio | 0.7 | 0.4 | 1.2 | 0.8 | 0.001 |

Mean volume of visceral fat in men was 12.2 $cm^3$ with a standard deviation of 6.5 and mean volume of subcutaneous fat in men was 13 $cm^3$ with a standard deviation of 8.5.Mean volume of visceral fat in women was 10.4 $cm^3$ with a standard deviation of 3.8 and mean volume of subcutaneous fat in men was 17.6 $cm^3$ with a standard deviation of 7.3.Visceral subcutaneous fat ratio in men had a mean of 1.2 with a standard deviation of 0.8 whereas in women the mean VSR was 0.7 with a standard deviation of 0.4.

**5.Analysis of metabolic risk factors – diabetes, hypertension and dyslipidemia**

**a)Hypertension**

Visceral and subcutaneous fat is increased in hypertensives as compared to normotensive patients. VSR does not show any statistically significant difference.**(Table 6,Figure 10)**

**Table 6 - VF,SF and VSR in hypertensives and normal individuals**

| | Hypertension | | | | | | |
|---|---|---|---|---|---|---|---|
| | No | | | Yes | | | *p*-value |
| | Median | Q1 | Q3 | Median | Q1 | Q3 | |
| AGE | 56.0 | 50.0 | 65.0 | 59.0 | 55.0 | 68.0 | 0.084 |
| Volume of visceral fat | 6.1 | 2.9 | 9.3 | 12.8 | 7.4 | 16.0 | <0.001 |
| Volume of Subcutaneous fat | 10.4 | 4.7 | 15.1 | 13.6 | 8.5 | 20.0 | 0.002 |
| Visceral subcutaneous fat ratio | 0.7 | 0.5 | 1.0 | 0.8 | 0.6 | 1.2 | 0.081 |

*p*-values calculated using Mann Whitney U test

Among patients with hypertension, median visceral fat was 12.8 $cm^3$ and median subcutaneous fat was 13.6 $cm^3$. The median visceral subcutaneous fat ratio in patients with hypertension was 0.8.

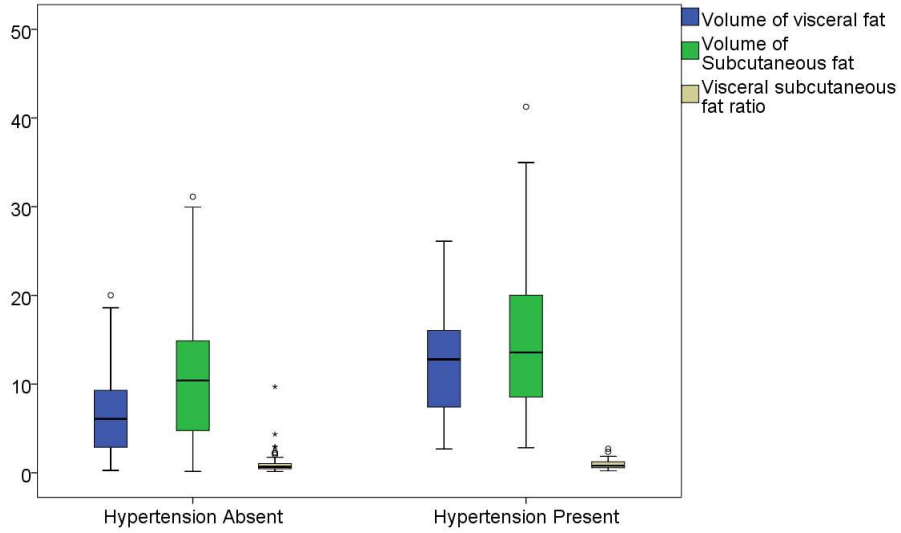



**Figure 10: Box and whisker plot showing increased visceral and subcutaneous fat in hypertensives as compared to normotensives.**

**b)Diabetes**

Volume of visceral fat and subcutaneous fat is significantly increased in those with diabetes as compared to those without diabetes. VSR does not show any statistically significant difference. **(Table 7,Figure 11)**

**Table 7 - VF,SF and VSR in diabetics and normal individuals**

| | Diabetes | | | | | | |
|---|---|---|---|---|---|---|---|
| | Diabetes Absent | | | Diabetes Present | | | *p*-value |
| | Median | Q1 | Q3 | Median | Q1 | Q3 | |
| AGE | 57.0 | 50.0 | 65.0 | 59.0 | 52.0 | 65.0 | 0.51 |
| Volume of visceral fat | 5.9 | 2.8 | 8.7 | 12.0 | 7.4 | 14.5 | <0.001 |
| Volume of Subcutaneous fat | 9.4 | 4.6 | 14.3 | 14.1 | 8.7 | 20.1 | <0.001 |
| Visceral subcutaneous fat ratio | 0.7 | 0.5 | 1.2 | 0.7 | 0.6 | 1.0 | 0.794 |

*p*-values calculated using Mann Whitney U test

Among patients with diabetes, median visceral fat was 12 $cm^3$ and median subcutaneous fat was 14.1 $cm^3$. The median visceral subcutaneous fat ratio in patients with diabetes was 0.7.In those without diabetes, median visceral fat was 5.9 $cm^3$ and median subcutaneous fat was 9.4 $cm^3$. The median visceral subcutaneous fat ratio in patients without diabetes was 0.7.

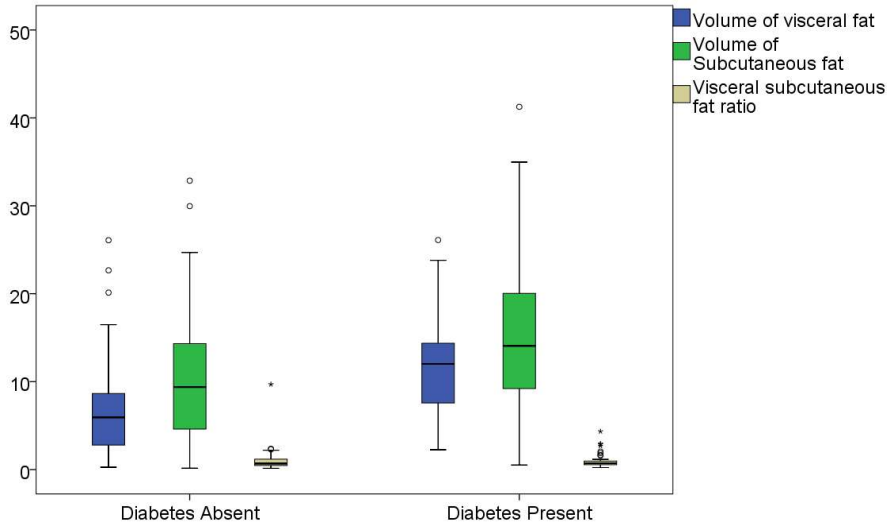



**Figure 11: Box and whisker plot showing increased visceral and subcutaneous fat in diabetics as compared to non-diabetics.**

**c)Dyslipidemia**

Volume of visceral fat is significantly increased in those with high lipid levels. Subcutaneous fat and VSR does not show any statistically significant difference between those with dyslipidemia and those who do not have dyslipidemia.**(Table 8,Figure 12)**

**Table 8 - VF,SF and VSR in dyslipidemic and normal individuals**

| | Hypercholesterolemia | | | | | | |
|---|---|---|---|---|---|---|---|
| | Hypercholesterolemia Absent | | | Hypercholesterolemia Present | | | *p*-value |
| | Median | Q1 | Q3 | Median | Q1 | Q3 | |
| AGE | 57.0 | 50.0 | 65.0 | 62.0 | 54.0 | 71.0 | 0.355 |
| Volume of visceral fat | 6.5 | 3.4 | 12.0 | 12.2 | 9.2 | 13.7 | 0.017 |
| Volume of Subcutaneous fat | 10.7 | 5.5 | 15.9 | 15.8 | 10.8 | 18.7 | 0.092 |
| Visceral subcutaneous fat ratio | 0.7 | 0.5 | 1.1 | 0.8 | 0.6 | 0.9 | 0.471 |

*p*-values calculated using Mann Whitney U test

Among patients with dyslipidemia, median visceral fat was 12.2 $cm^3$ and median subcutaneous fat was 15.8 $cm^3$. The median visceral subcutaneous fat ratio in patients with dyslipidemia was 0.8.In those without dyslipidemia, median visceral fat was 6.5 $cm^3$ and median subcutaneous fat was 10.7 $cm^3$. The median visceral subcutaneous fat ratio in patients without dyslipidemia was 0.7.

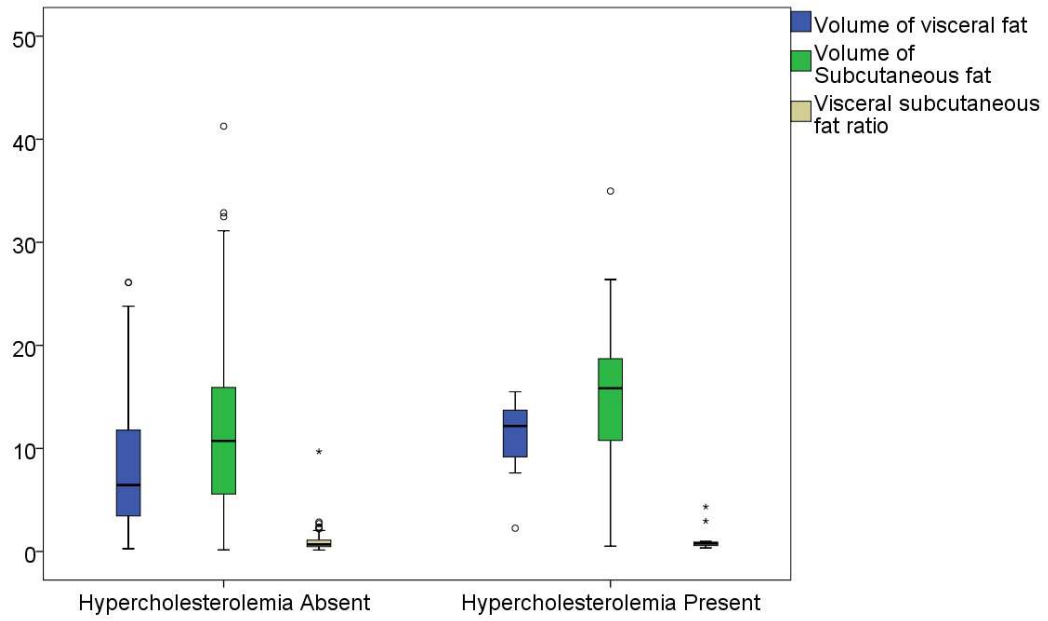



**Figure 12: Box and whisker plot showing increased visceral fat in dyslipidemics as compared to those with normal values.**

## 6. Analysis of cases and controls, males and females for metabolic risk factors

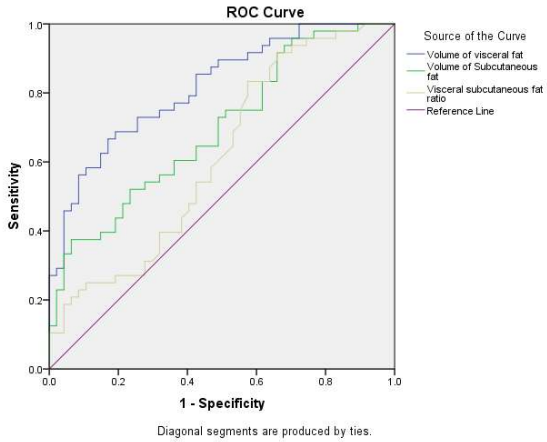



**Figure 13a)ROC curves for VF,SF and VSR in cases and controls**

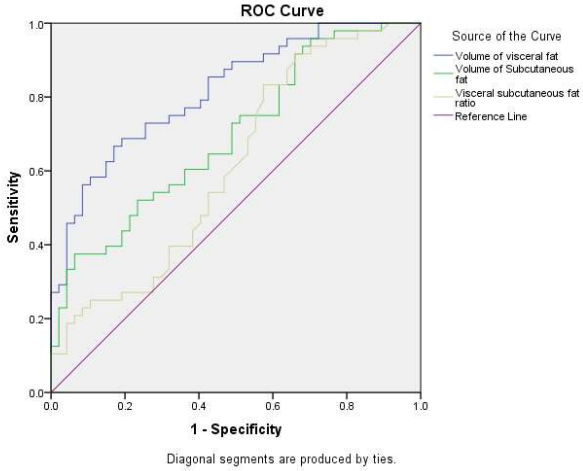



**Figure 13b)ROC curves for VF,SF and VSR in males**

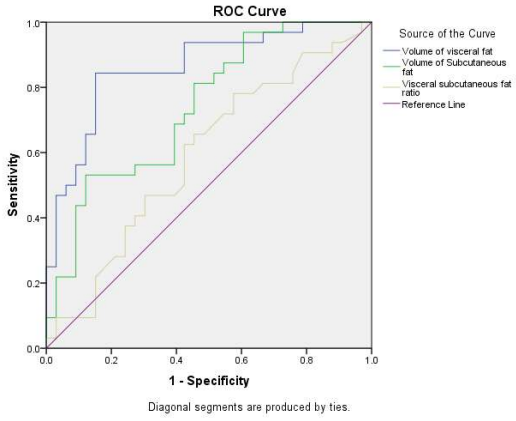



**Figure 13c)ROC curves for VF,SF and VSR in females**

**a) Total cohort**

Analysis of ROC curve as shown in **Figure 13(a)** for all cases and controls showed area under the curve for volume of visceral fat to be 0.828 with a standard error of 0.032, area under the curve for volume of subcutaneous fat to be 0.707 with a standard error of 0.040 and area under the curve for visceral subcutaneous fat ratio to be 0.602 with a standard error of 0.045.

Cut-offs to differentiate subjects at increased risk of developing diabetes, hypertension and dyslipidemia from subjects with no metabolic risk factors in Indian population were calculated. The cut-off for volume of visceral fat was **7.3** with a sensitivity of 76.3% and a specificity of 78.7%, the cut-off for volume of subcutaneous fat was **16.4** with a sensitivity of 41.3% and a specificity of 92.5% and the cut-off for visceral subcutaneous fat ratio was **0.55** with a sensitivity of 80% and a specificity of 43.7%.

**b) Male**

ROC curve analysis for men as shown in **Figure 13(b)** showed area under the curve (AOC) for volume of visceral fat was 0.816 with a standard error of 0.042, AOC for volume of subcutaneous fat was 0.695 with a standard error of 0.053 and AOC for visceral subcutaneous fat ratio was 0.615 with a standard error of 0.058.

The ROC curves for male subjects were analyzed and cut-offs for visceral fat, subcutaneous fat and visceral-subcutaneous fat ratio for differentiating patients with increased risk of developing diabetes, hypertension and dyslipidemia from patients with no risk of metabolic risk factors were calculated. The cut-off for volume of visceral fat in males was calculated to be 8.5 $cm^3$ with a sensitivity of 68.8% and a specificity of 80.9%. The cut-off for volume of subcutaneous fat in males was 15.7 $cm^3$ with a sensitivity of 37.5% and a specificity of 93.6 %. The cut-off for visceral subcutaneous fat ratio in males was 0.61 with a sensitivity of 83.3% and a specificity of 42.6 %.

**c) Female**

ROC curve analysis for women as shown in **Figure 13(c)** showed area under the curve (AOC) for volume of visceral fat was 0.861 with a standard error of 0.046, AOC for volume of subcutaneous fat was 0.739 with a standard error of 0.061 and AOC for visceral subcutaneous fat ratio was 0.590 with a standard error of 0.071.

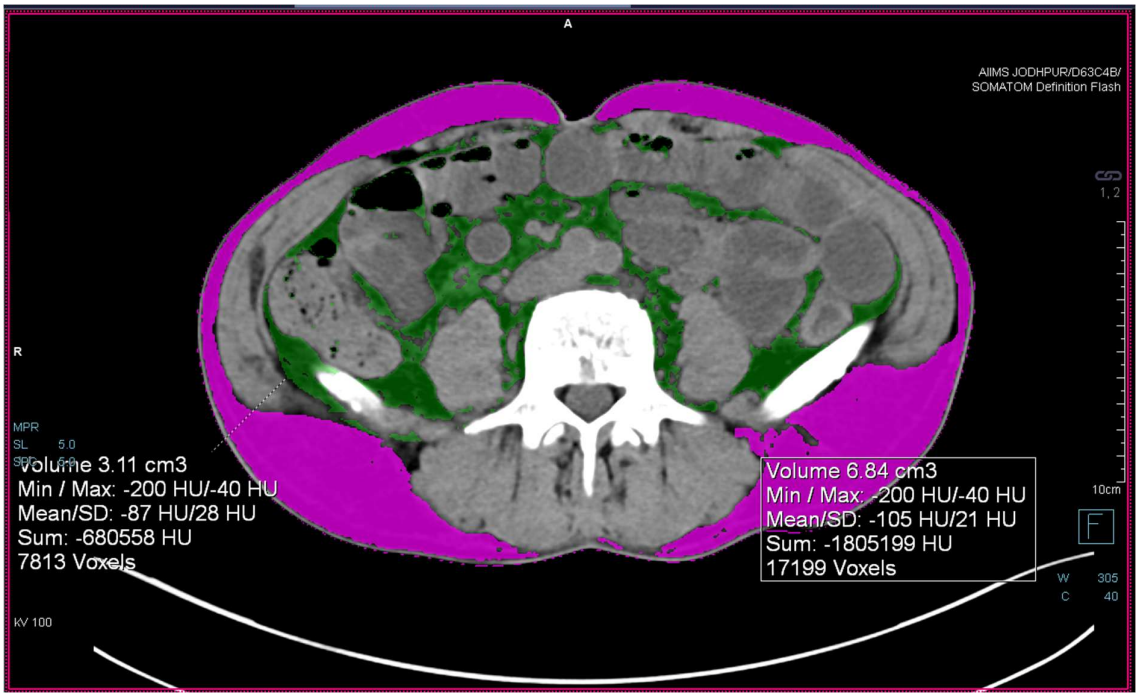
The ROC curves for female subjects were analyzed and cut-offs for visceral fat, subcutaneous fat and visceral-subcutaneous fat ratio for differentiating patients with increased risk of developing diabetes, hypertension and dyslipidemia from patients with no risk of metabolic risk factors were calculated. The cut-off for volume of visceral fat in females was calculated to be 7 $cm^3$ with a sensitivity of 84.4% and a specificity of 84.8%. The cut-off for volume of subcutaneous fat in females was 16.5 $cm^3$ with a sensitivity of 53.1% and a specificity of 87.9 %. The cut-off for visceral subcutaneous fat ratio in females was 0.44 with a sensitivity of 78.1% and a specificity of 42.4 %.

# IMAGE GALLERY

## CONTROLS

### Control 1

63 year old male with no history of hypertension, diabetes, hyperlipidemia




Visceral fat – green  Subcutaneous fat – purple

Visceral fat volume – 3.11 $cm^3$

Subcutaneous fat volume – 6.84 $cm^3$

Visceral subcutaneous fat ratio – 0.45

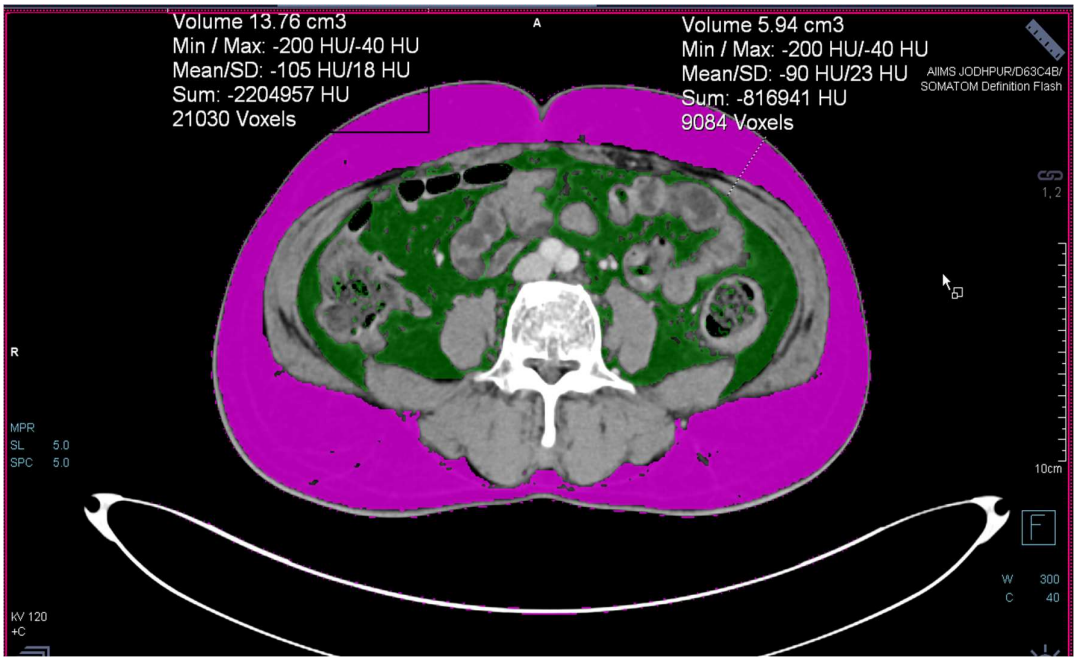
Blood pressure – 120/80 mm of Hg

Normal metabolic parameters

- Visceral fat volume was below the cut-off of 7.3
- Subcutaneous fat volume was below the cut off of 16.4
- VSR was 0.45 which is below the cut off of 0.55

**Control 2**

56 year old male with no history of hypertension, diabetes, hyperlipidemia




Visceral fat – green  Subcutaneous fat – purple

Visceral fat volume – 5.94

Subcutaneous fat volume – 13.76

Visceral subcutaneous fat ratio – 0.43

Blood pressure – 130/70 mm of Hg

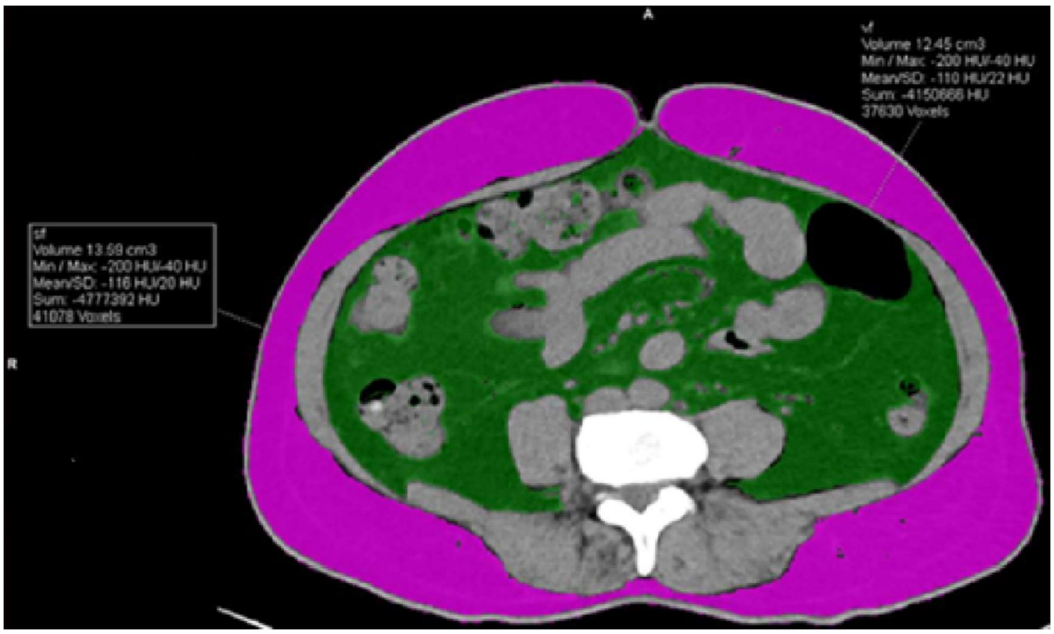
Normal metabolic parameters

- Visceral fat volume was below the cut-off of 7.3
- Subcutaneous fat volume was below the cut off of 16.4
- VSR was 0.43 which is below the cut off of 0.55

# CASES

## Case 1

59 year old female with a history of diabetes and hyperlipidemia




Visceral fat – green

Subcutaneous fat – purple

Visceral fat volume – 12.45

Subcutaneous fat volume – 13.59

Visceral subcutaneous fat ratio – 0.91

Her lab parameters were as follows

HbA1c – 11.9

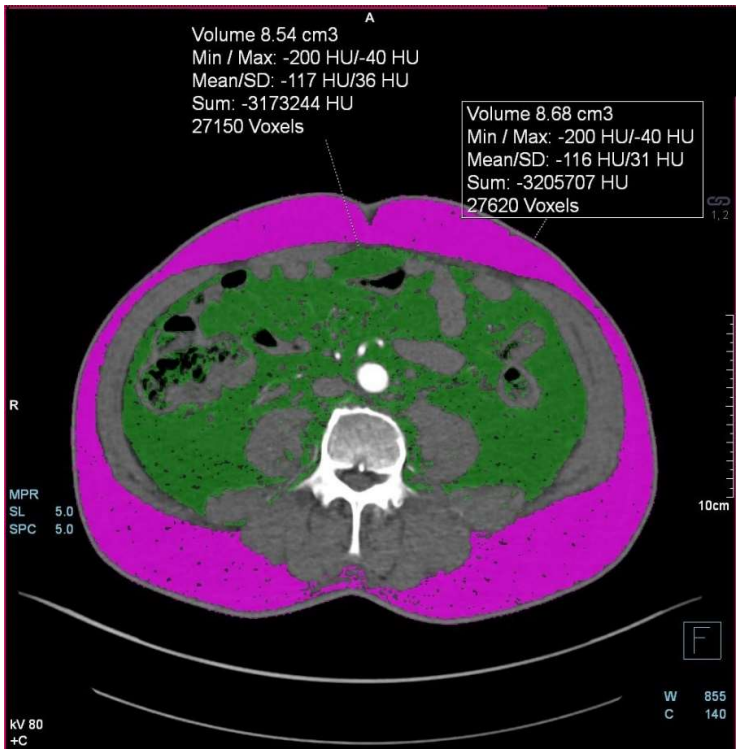
Triglycerides – 387 mg/dl

LDL – 132 mg/dl

- Visceral fat volume was above the cut-off of 7.3
- Subcutaneous fat volume was above the cut off of 16.4
- VSR was 0.91 which is above the cut off of 0.55

**Case 2**

72 year old male with history of diabetes and hypercholesterolemia on irregular treatment




Visceral fat – green Subcutaneous fat – purple

Visceral fat volume – 8.54

Subcutaneous fat volume – 8.68

Visceral subcutaneous fat ratio – 0.98

Her lab parameters were as follows

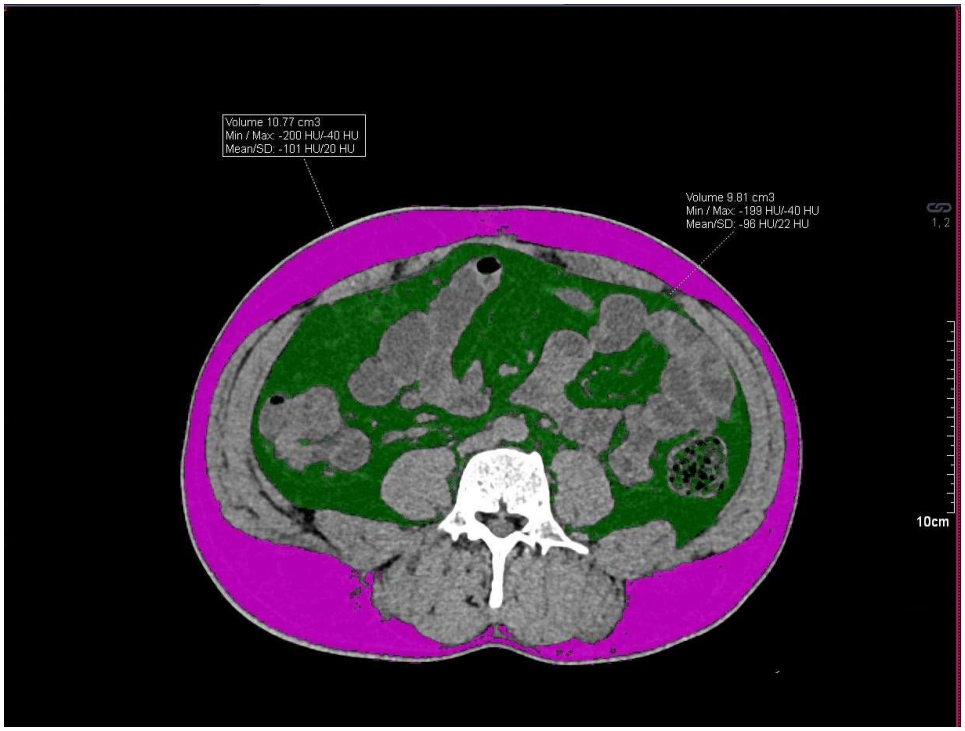
HbA1c – 11.9

Triglycerides – 229 mg/dl. LDL – 123 mg/dl

- Visceral fat volume was above the cut-off of 7.3
- Subcutaneous fat volume was below the cut off of 16.4
- VSR was 0.98 which is above the cut off of 0.55

**Case 3**

48 year old male with history of diabetes and hyperlipidemia on treatment




Visceral fat – green Subcutaneous fat – purple

Visceral fat volume – 9.81

Subcutaneous fat volume – 10.77

Visceral subcutaneous fat ratio – 0.91

Her lab parameters were as follows

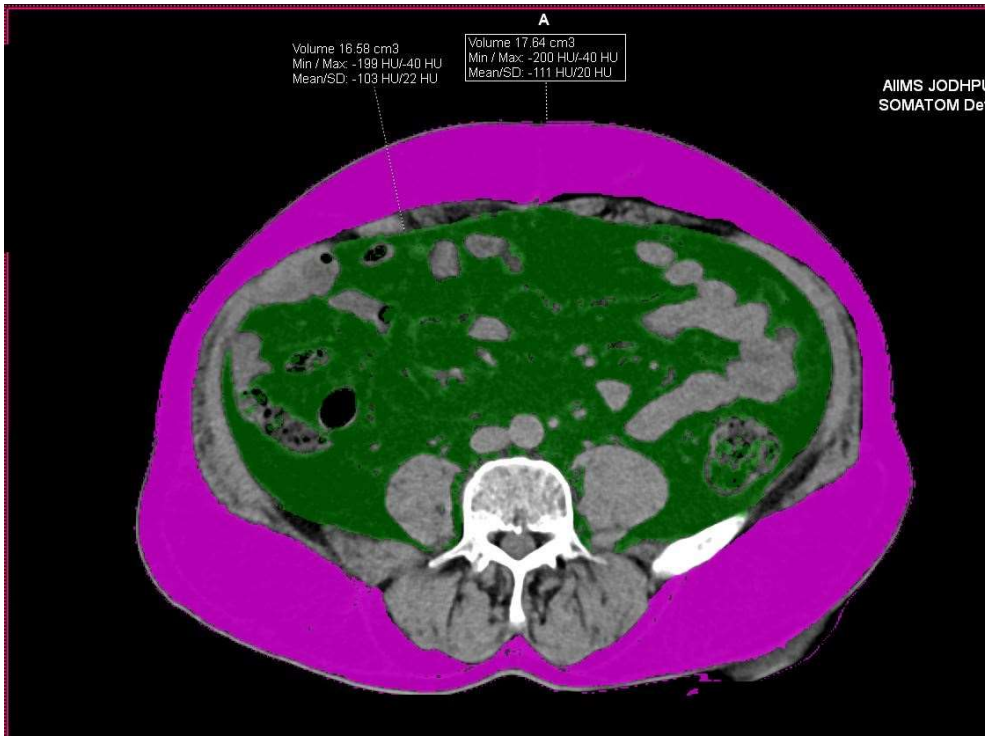
Fasting blood sugar – 106 mg/dl

Triglycerides – 160 mg/dl. LDL – 116 mg/dl

- Visceral fat volume was above the cut-off of 7.3
- Subcutaneous fat volume was below the cut off of 16.4
- VSR was 0.91 which is above the cut off of 0.55

**Case 4**

77 year old male with a history of hypertension and diabetes on treatment




Visceral fat – green Subcutaneous fat – purple

Visceral fat volume – 16.58

Subcutaneous fat volume – 17.64

Visceral subcutaneous fat ratio – 0.92

Her lab parameters were as follows

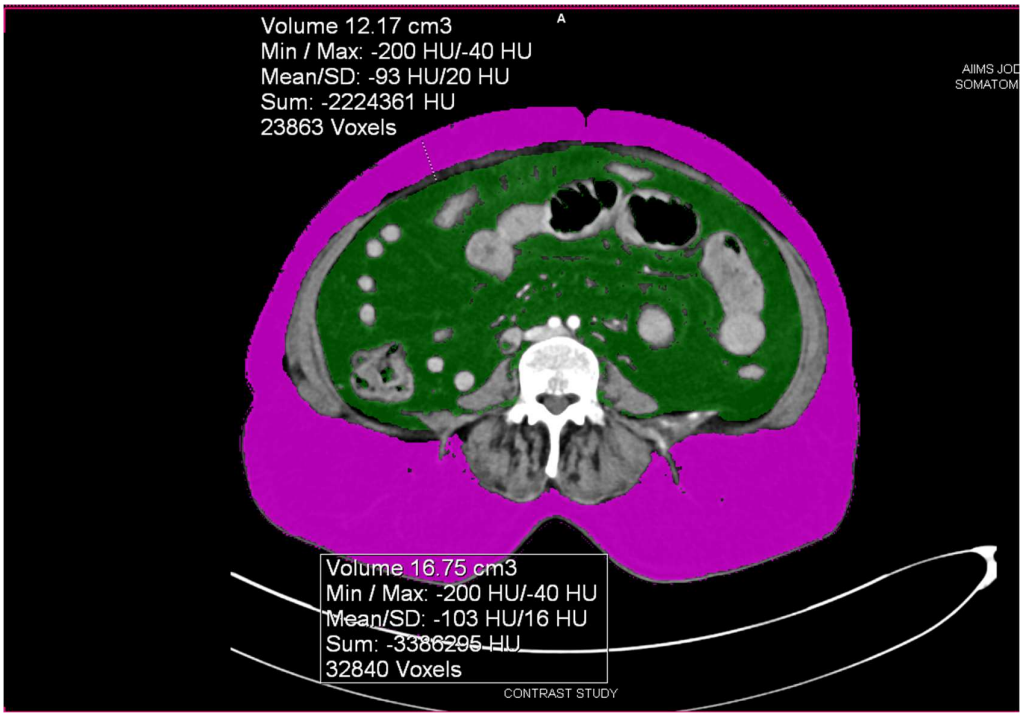
Blood pressure – 140/90 mm Hg

HbA1c – 13.9%

- Visceral fat volume was above the cut-off of 7.3
- Subcutaneous fat volume was below the cut off of 16.4
- VSR was 0.92 which is above the cut off of 0.55

**Case 5**

71 year old female with history of diabetes and hyperlipidemia




Visceral fat – green Subcutaneous fat – purple

Visceral fat volume – 12.17

Subcutaneous fat volume – 16.75

Visceral subcutaneous fat ratio – 0.72

Her lab parameters were as follows

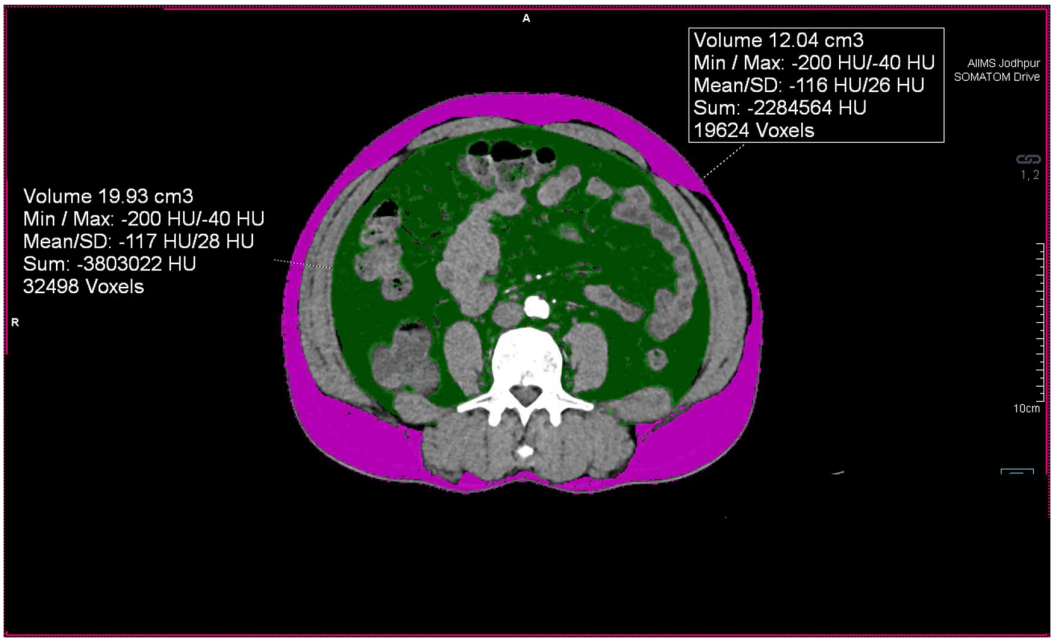
HbA1c – 7.5 %

Triglycerides – 181 mg/dl. LDL – 145 mg/dl

- Visceral fat volume was above the cut-off of 7.3
- Subcutaneous fat volume was above the cut off of 16.4
- VSR was 0.72 which is above the cut off of 0.55

**Case 6**

55 year old male with hypertension and diabetes on treatment




Visceral fat – green Subcutaneous fat – purple

Visceral fat volume – 19.93

Subcutaneous fat volume – 12.04

Visceral subcutaneous fat ratio – 1.65

Her lab parameters were as follows

HbA1c – 5.7 % (on treatment)

Blood pressure – 130/80 mm of Hg

- Visceral fat volume was above the cut-off of 7.3
- Subcutaneous fat volume was above the cut off of 16.4
- VSR was 1.65 which is above the cut off of 0.55

**Case 7**

52 year old male with history of diabetes and hypertension


Visceral fat – purple  Subcutaneous fat – green

Visceral fat volume – 11.15

Subcutaneous fat volume – 17.33

Visceral subcutaneous fat ratio – 0.66

Her lab parameters were as follows

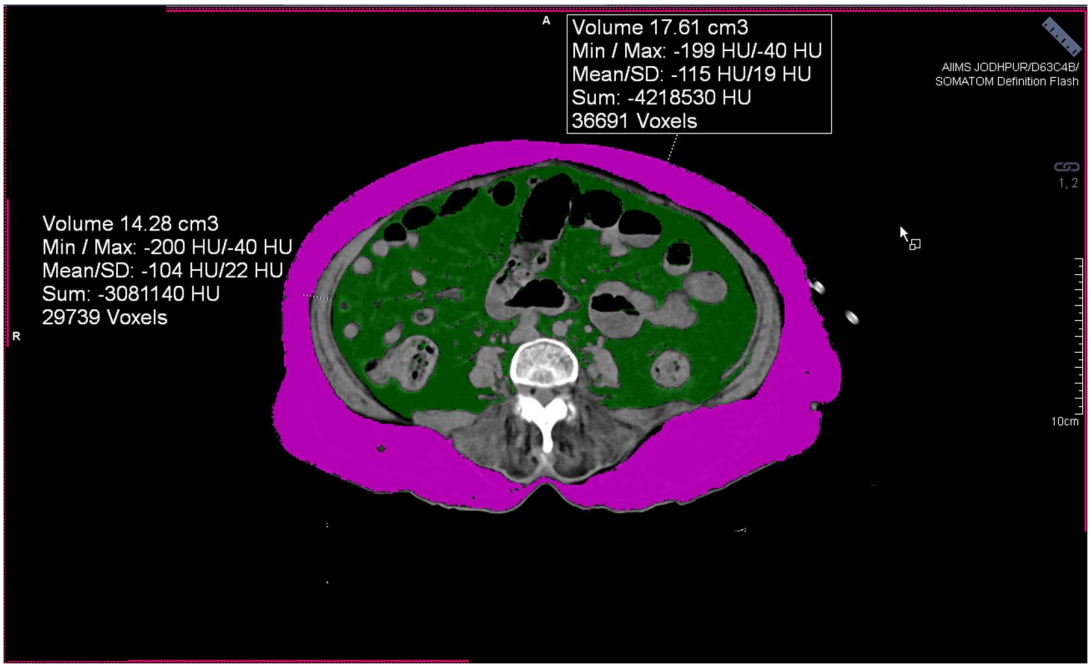
HbA1c – 6.9%

Blood pressure – 150/80 mm of Hg

- Visceral fat volume was above the cut-off of 7.3
- Subcutaneous fat volume was above the cut off of 16.4
- VSR was 0.66 which is above the cut off of 0.55

**Case 8**

77 year old female with history of diabetes and hypertension




Visceral fat – green  Subcutaneous fat – purple

Visceral fat volume – 14.28

Subcutaneous fat volume – 17.61

Visceral subcutaneous fat ratio – 0.81

Her lab parameters were as follows

HbA1c – 6.7%

Blood pressure – 140/80 mm of Hg

- Visceral fat volume was above the cut-off of 7.3
- Subcutaneous fat volume was above the cut off of 16.4
- VSR was 0.81 which is above the cut off of 0.55

# LIMITATIONS OF THE STUDY

1. The subjects were enrolled from a single tertiary care center in Western India which limits the generalizability of the findings to other populations.
2. Standardisation of CT scanners from various manufacturers may be required.

# DISCUSSION

Obesity defined as an excess of body adiposity has become a major public health problem not just in the developed nations but also in developing nations as food habits and exercise habits change. This has led to considerable interest in understanding and tackling obesity which the WHO declared a global epidemic.

The most commonly used measure of obesity is body mass index which has been classified by the WHO into underweight, normal weight, overweight and obesity.[12]

But BMI has several shortcomings in measuring obesity. BMI cannot distinguish persons with high lean body mass who would be misclassified as obese based on their weight.[15] BMI fails to detect metabolically obese normal weight (MONW) individuals and metabolically healthy obese (MHO) individuals.[20,21] This is because BMI is unable to distinguish the metabolically active visceral fat from metabolically inactive subcutaneous fat. The WHO cut-offs were also found to mis-categorize overweight and obese subjects in Indian population especially among women.[13] Waist circumference has proposed as an easily measured clinical tool to assess obesity and it has been shown to be strongly associated with visceral obesity.[26]

The development of cross sectional imaging methods using computed tomography enabled researchers to study the visceral and subcutaneous fat compartments separately, quantify them and correlate each compartment with metabolic parameters.[28-30]

The present study showed that visceral fat volume, subcutaneous fat volume and visceral-subcutaneous fat ratio was significantly higher in individuals with metabolic risk factors as compared to controls. This is in line with previous studies which showed a higher visceral fat volume in those patients with metabolic risk factors.[30,32-37]

Schorr et al[54] concluded that men had higher visceral adipose tissue and visceral subcutaneous fat ratio as compared to women. Subcutaneous adipose tissue was found to be higher in women. Lemieux, S et al showed that although women has higher levels of total body fat, women have lower areas of visceral fat and lower ratio of abdominal visceral to mid-thigh adipose tissue as compared to men. In the present study, the volume of visceral fat, subcutaneous fat and VSR were calculated separately for men

and women and showed statistically significant differences in subcutaneous fat and VSR with greater subcutaneous fat volumes and visceral-subcutaneous fat ratios in men as compared to women. Visceral fat volume was higher in men than in women but the difference was not statistically significant. This differs from previous studies in which visceral fat is significantly higher in males as compared to females.[54,55]

Oh et al[40] had shown that there was no difference in visceral and subcutaneous fat between those with metabolic risk factors and those with normal metabolic parameters [40]. Visceral to subcutaneous fat ratio was found to be raised in men and women with diabetes, hypertension and dyslipidemia. On analysis of patients in the present study who have hypertension and diabetes, visceral and subcutaneous fat are higher as compared to normal individuals with no metabolic risk factors. The VSR did not show any statistically difference between those with diabetes and hypertension and those with normal blood sugar and blood pressure. In subjects with elevated lipid levels, the volume of visceral fat was significantly increased as compared to subjects with lipid level within normal range.

Yoo et al[46] showed that visceral adipose tissue was significantly higher in those patients with metabolic risk factors as compared to those without risk factors. There was no significant difference in subcutaneous fat volume in subjects with and without metabolic risk factors. Visceral subcutaneous fat ratio adjusted for age was significantly higher in those with metabolic syndrome as compared to those with no metabolic syndrome in men. However the relationship between increased VSR and metabolic syndrome was not statistically significant in women. VSR and VAT was seen to have statistically significant predictive value in determining patients at increased risk of metabolic syndrome.

Pickhardt et al[43] had shown that subcutaneous fat area was the best predictor of metabolic risk in men and visceral fat was the best predictor of metabolic risk in women.

Kaess et al[39] showed that in women, higher VSR was correlated with increased risk of diabetes, hypertension and dyslipidaemia .The positive correlation was seen in both pre and post-menopausal women. Men with high VSR showed positive correlation with all metabolic risk factors except diabetes but the risk was less that of women.

The present study showed a statistically significant difference between cases and controls with respect to volume of visceral fat, volume of subcutaneous fat and visceral subcutaneous fat ratio. Volume of visceral fat, volume of subcutaneous fat and visceral subcutaneous fat ratio were significantly higher in those with metabolic risk factors than those who had normal metabolic parameters and this can be used to differentiate between those with metabolic risk factors and those who do not have metabolic risk factors. This is in line with previous studies.[39,40,43,46]

Pickhardt et al[43] measured visceral and subcutaneous fat area at the level of the umbilicus using single slice CT and liver attenuation and estimated that using thresholds of 204 $cm^2$ in men for subcutaneous fat area, a threshold of 70 $cm^2$ for visceral fat area in women and liver attenuation less than 50 HU detected metabolic syndrome with a sensitivity and specificity of 80.3% and 83.7%; 83.7% and 80.0%; and 22.0% and 96.7%, respectively. They determined that visceral fat area was the best predictor in women and subcutaneous fat area the best predictor in men. In the present study, the visceral fat volume was the best predictor of metabolic risk in both women and men. The results cannot be directly compared as the study had used visceral and subcutaneous fat areas and the present study used visceral and subcutaneous fat volumes.

In a later study, Pickhardt et al[57] measured total adipose tissue area and visceral fat at the level of L1 along with skeletal muscle index at L3, volumetric liver attenuation and abdominal aortic calcification scoring. They found out that total adipose tissue area and visceral fat area were highly predictive of metabolic syndrome with total adipose tissue area showing greater predictive value. Using cut-offs of 189 $cm^2$ for visceral fat area, sensitivity of 80.1% and specificity of 74.7% was achieved. Higher cut-off of 205.4 $cm^2$ for visceral fat area increased the specificity to 80%. An L1-level total abdominal fat threshold of 460.6 $cm^2$ was 80.1% sensitive and 85.4% specific for metabolic syndrome. The results cannot be directly compared as the study had used visceral and subcutaneous fat areas and the present study used visceral and subcutaneous fat volumes. In the present study, visceral fat volume was found to have the highest predictive value for detecting metabolic risk.

Kim et al[56] estimated cut offs for visceral fat volume to predict metabolic syndrome in Korean population. They estimated that the metabolic syndrome can be predicted using cut-offs of 4852 cm3 for men with a sensitivity of 76.6% and specificity of 80.7% and 3101 cm3 for women with a sensitivity of 100% and a specificity of 72.6%. They measured visceral fat volume by measuring visceral volume and subcutaneous fat volume from the highest level of the liver dome to the pelvic floor and the highest level of the anal sphincter on axial CT images. But this method would increase total radiation exposure and increase the complexity of fat estimation. Single slice CT measured have been shown to correlate with visceral fat volume.[41,43] They found the visceral fat volume, visceral fat mass and visceral fat area correlated with increased risk of metabolic syndrome. Similar to the study by Kim et al, in the present study, the highest AUC was found for visceral fat volume at 0.828 showing the strongest association with increased risk of developing metabolic risk factors.

Cut-offs to differentiate subjects at increased risk of developing diabetes, hypertension and dyslipidemia from subjects with no metabolic risk factors in Indian population were calculated. The cut-off for volume of visceral fat was **7.3 $cm^3$**with a sensitivity of 76.3% and a specificity of 78.7%, the cut-off for volume of subcutaneous fat was **16.4 $cm^3$** with a sensitivity of 41.3% and a specificity of 92.5% and the cut-off for visceral subcutaneous fat ratio was **0.55** with a sensitivity of 80% and a specificity of 43.7%.

In men, a cut off of 8.5 $cm^3$ can be used for visceral fat volume with a sensitivity of 68.8% and a specificity of 80.9%. In women, a cut off of 7 $cm^3$ can be used for visceral fat volume with a sensitivity of 84.4% and a specificity of 84.8%.Due to differences in methodology, the results cannot be directly compared but visceral fat volume cut-off determined was seen to be predictive of metabolic risk with high sensitivity and specificity both in men and women as in the previous study by Kim et al.

The cut-offs that we obtained in our study was higher than that determined by Fujioka et al [30]and used in the study by Oh et al. [40] Yoo[46] had obtained smaller values for VSR in those with and without metabolic syndrome which was due to the higher levels of subcutaneous fat in the Middle Eastern population.

These differences can be explained by the **Adipose tissue overflow hypothesis** proposed by Sniderman et al as shown in **Figure 14**.[52] They proposed that the subcutaneous adipose tissue compartment in South Asians were smaller as compared to Caucasians. As a result, the subcutaneous fat compartment gets filled up quickly and fat accumulates in the visceral compartment in obese subjects. South Asians have higher visceral fat as compared to Caucasians. Among Asians, Indians have the highest body fat percentage followed by Malays and Chinese.[53] It could be because of the higher visceral fat that South Asians have due to adipose overflow that higher cut-offs are needed to identify those who are risk of developing diabetes, hypertension and dyslipidemia in the Indian population.

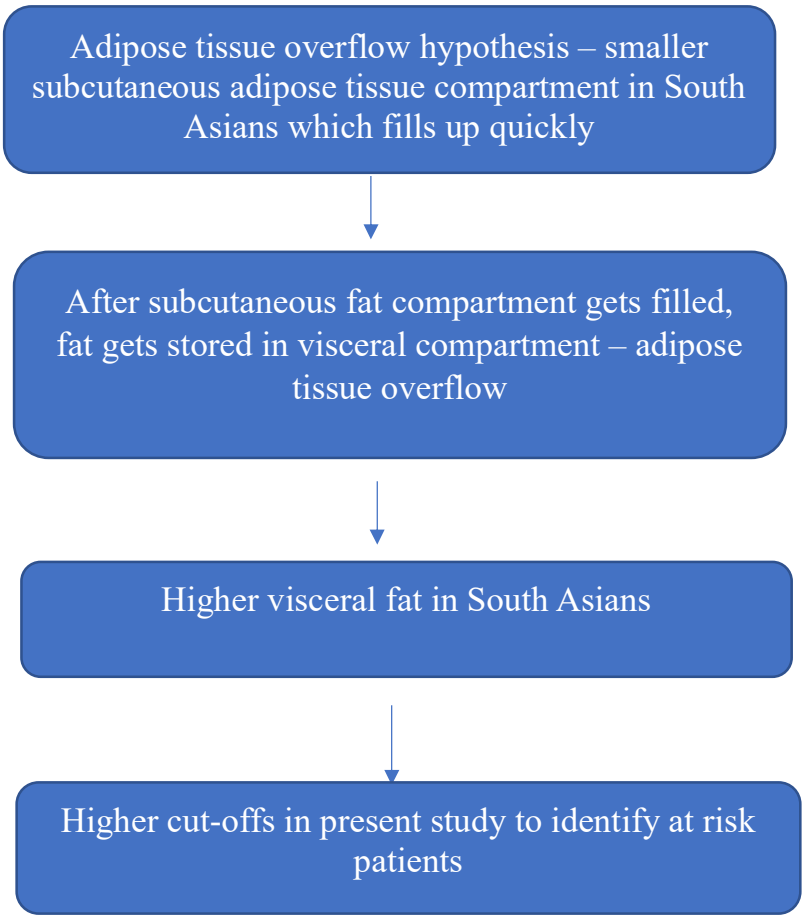



**Figure 14: Adipose tissue hypothesis proposed a smaller subcutaneous fat compartment in South Asians leading to higher visceral fat accumulation.**

# IMPORTANCE OF VISCERAL FAT ESTIMATION

## Relevance of the measurement of visceral and subcutaneous fat using CT

According to the NFHS-5, obesity is a fast growing public health problem in India, with a prevalence of 24 percent in women and 22.9 percent in men.[5] South Asians have higher levels of visceral fat which increases the risk of developing metabolic syndrome. Traditional measures of fat estimation like BMI and waist circumference cannot estimate visceral and subcutaneous fat compartments separately which would enable risk stratification. They also fail to detect patients with normal waist circumference with increased metabolic risk (the metabolically obese normal weight cohort).Cross sectional imaging offers a non-invasive method to accurately estimate abdominal fat compartments and detect Metabolically Obese Normal Weight (MONW) individuals. In a recent study, Pickhardt et al[57] used quantitative tissue measures of fat, muscle and liver using abdominal CT scans to identify individuals at risk for metabolic syndrome. They were able to entirely automate the risk measurements by using deep learning algorithms for fat estimation. **Visceral fat estimation can be used as an opportunistic screening tool to detect metabolic syndrome in CT scans done for other indications facilitating the early detection and subsequent management of metabolic syndrome.**

# CONCLUSION

The prevalence of obesity is rapidly rising in India making it a major public health problem. Early detection and management of obesity can reduce morbidity and risk by reducing the risk of developing complications like cardiovascular disease, cerebrovascular accidents, diabetes, hypertension and cancers associated with obesity.

Measurement of visceral and subcutaneous fat is a easy non-invasive method to detect patients at increased risk of metabolic risk especially in those with normal waist circumference who will not be detected using traditional anthropometric measures of obesity.

Our present study on visceral and subcutaneous fat estimation to detect metabolic risk in patients with normal waist circumference showed :

- **Visceral fat volume, subcutaneous fat volume and visceral subcutaneous fat ratio obtained using single slice estimation at the level of L4 can be used to detect patients at increased risk of metabolic risk in Indian population**
- **In the present study, cut-offs were calculated for visceral fat, sub-cutaneous fat and visceral-subcutaneous fat ratio to identify those with metabolic risk in Indian population**
- **Visceral fat volume showed the highest predictive value in both males and females in determining those at increased risk of developing metabolic risk factors**
- **Visceral fat volume was found to significantly higher in hypertensives, diabetics and those with dyslipidemia as compared to those with normal parameters.**
- **Subcutaneous fat volume and visceral-subcutaneous fat ratio was significantly higher in women as compared to men. There was no significant difference in visceral fat volume between men and women.**

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# अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
# All India Institute of Medical Sciences, Jodhpur
## संस्थागत नैतिकता समिति
## Institutional Ethics Committee

No. AIIMS/IEC/2020/2078 Date: 01/01/2020

## ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2019-20/999**

Project title: **"Visceral to subcutaneous fat ratio determined using computed tomography as a predictor of multiple metabolic risk factors in subjects with normal waist circumference"**

| | |
|---|---|
| Nature of Project: | **Research Project** |
| Submitted as: | **M.D. Dissertation** |
| Student Name: | **Dr.Thomas George** |
| Guide: | **Dr.Binit Sureka** |
| Co-Guide: | **Dr. Pushpinder Singh Khera, Dr.Mahendra Kumar Garg, Dr.Mithu Banerjee, Dr.Surender Deora & Dr.Ravinder Shukla** |

This is to inform that members of Institutional Ethics Committee (Annexure attached) met on **23-12-2019** and after through consideration accorded its approval on above project. Further, should any other methodology be used, would require separate authorization.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma

**Enclose:**

1. Annexure 1



**Basni Phase-2, Jodhpur, Rajasthan-342005, Website:** www.aiimsjodhpur.edu.in, **Phone:** 0291-2740741 Extn. 3109
**Email:** ethicscommittee@aiimsjodhpur.edu.in

Annexure I

# Institutional Ethics Committee
# All India Institution of Medical Sciences, Jodhpur

Meeting of Institutional Ethics committee held on **23-12-2019 at 10:00** AM at Committee Room, Admin Block AIIMS Jodhpur.

Following members were participated in the meeting:-

| S/No. | Name of Member | Qualification | Role/Designation in Ethics Committee |
|---|---|---|---|
| 1. | Dr. F.S.K Barar | MBBS, MD (Pharmacology) | **Chairman** |
| 2. | Justice N.N Mathur | LLB | Legal Expert |
| 3. | Dr. Varsha Sharma | M.A (Sociology) | Social Scientist |
| 4. | Mr. B.S.Yadav | B.Sc., M.Sc. (Physics), B.Ed. | Lay Person |
| 5. | Dr. K.R.Haldiya | MD (General Medicine) | Clinician |
| 6. | Dr. Arvind Mathur | MBBS, MS (General Medicine) | Clinician |
| 7. | Dr. Surajit Ghatak | MBBS, MS (Anatomy) | Basic Medical Scientist |
| 8. | Dr. Vijaya Lakshmi Nag | MBBS, MD (Microbiology) | Basic Medical Scientist |
| 9. | Dr. Sneha Ambwani | MBBS, MD (Pharmacology) | Basic Medical Scientist |
| 10. | Dr. Kuldeep Singh | MBBS, MD (Paediatric), DM (General Medicine) | Clinician |
| 11. | Dr. Abhinav Dixit | MBBS, MD (Physiology), DNB (Physiology) | Basic Medical Scientist |
| 12. | Dr. Pradeep Kumar Bhatia | MBBS, MD (Anaesthesiology) | Clinician |
| 13. | Dr. Tanuj Kanchan | MBBS, MD (Forensic Medicine) | Basic Medical Scientist |
| 14. | Dr. Pankaj Bhardwaj | MBBS, MD (CM&FM) | Clinician |
| 15. | Dr. Praveen Sharma | M.Sc., Ph.D. (Biochemistry) | Member Secretary |

**Dr. Pravesh Sharma**

**Annexures-2**

**Informed Consent Form**

Title of the project : _____

Name of the Principal Investigator : _____Tel. No. _____

Patient/Volunteer Identification No. : _____

I, _____ S/o or D/o _____

R/o _____

give my full, free, voluntary consent to be a part of the study **"VISCERAL TO SUBCUTANEOUS FAT RATIO DETERMINED USING COMPUTED TOMOGRAPHY AS A PREDICTOR OF MULTIPLE METABOLIC RISK FACTORS IN SUBJECTS WITH NORMAL WAIST CIRCUMFERENCE"** the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions.

I understand that my participation is voluntary and am aware of my right to opt out of the study at any time without giving any reason.

I understand that the information collected about me and any of my medical records may be looked at by responsible individual from _____(Company Name) or from regulatory authorities. I give permission for these individuals to have access to my records.

Date : _____ _____

Place : _____ Signature/Left thumb impression

This to certify that the above consent has been obtained in my presence.

Date : _____ _____

Place : _____ Signature of Principal Investigator

**Annexures-3**

**All India Institute of Medical Sciences, Jodhpur, Rajasthan**

**Informed Consent (Hindi)**

- थीसिस / निबंध का शीर्षक: _____
- पीजी छात्र का नाम: _____ टेल न: _____
- रोगी / स्वयं सेवक पहचान संख्या: _____

मैं, _____ एस / ओयाडी / ओ _____

आर / ओ _____

अध्ययन " एक भारतीय आबादी में कई चयापचय जोखिम कारकों के भविष्यवक्ता के रूप में चमड़े के नीचे के वसा अनुपात का दौरा " का एक भाग बनने के लिए मेरी पूर्ण, स्वतंत्र, स्वैच्छिक सहमति दें, जिसकी प्रक्रिया और प्रकृति मुझे अपनी पूरी संतुष्टि के लिए अपनी भाषा में समझाई गई है। मैं पुष्टि करता हूं कि मुझे प्रश्न पूछने का अवसर मिला है।

मैं समझता हूं कि मेरी भागीदारी स्वैच्छिक है और मुझे किसी भी कारण दिए बिना किसी भी समय अध्ययन से बाहर निकलने के मेरे अधिकार की जानकारी है।

मैं समझता हूं कि मेरे और मेरे मेडिकल रिकॉर्ड के कत्रित की गई जानकारी को _____ (कंपनीनाम) याविनियामक प्राधिकरणों से जिम्मेदार व्यक्ति द्वारा देखा जा सकता है।मैं इन व्यक्तियों को अपने अभिलेखों तक पहुंच के लिए अनुमति देता हूं

तारीख : _____

जगह: _____ हस्ताक्षर / बाएं अंगूठे का छाप_____

यह प्रमाणित करने के लिए कि मेरी उपस्थिति में उपरोक्त सहमति प्राप्त की गई है

तारीख : _____

गवाह1: : _____

हस्ताक्षर: _____

तारीख : _____

जगह: _____ पीजी छात्र के हस्ताक्षर_____

**Annexures-4**

# Patient information sheet

1. Risks to the patients: There's no risk of death or any disability resulting directly due to imaging.
2. Confidentiality: Your participation will be kept confidential. Your medical records will be treated with confidentiality and will be revealed only to doctors/ scientists involved in this study. The results of this study may be published in a scientific journal, but you will not be identified by name.
3. Provision of free treatment for research related injury. Not applicable.
4. Compensation of subjects for disability or death resulting from such injury. Not Applicable
5. Freedom of individual to participate and to withdraw from research at any time without penalty or loss of benefits to which the subject would otherwise be entitled.
6. You have complete freedom to participate and to withdraw from research at any time without penalty or loss of benefits to which you would otherwise be entitled.
7. Your participation in the study is optional and voluntary.
8. The copy of the results of the investigations performed will be provided to you for your record.
9. You can withdraw from the project at any time, and this will not affect your subsequent medical treatment or relationship with the treating physician.
10. Any additional expense for the project, other than your regular expenses, will not be charged from you.

**Annexures-5**

# रोगी सूचना पत्रक

1. रोगियों के लिए जोखिम: इमेजिंग के कारण सीधे मौत या कोई विकलांगता का कोई खतरा नहीं है। कोई हस्तक्षेप या जीवन-धम की प्रक्रिया नहीं की जाएगी।

2.गोपनीयता: आपकी भागीदारी को गोपनीय रखा जाएगा। आपके मेडिकल रिकॉर्ड को गोपनीयता के साथ इलाज किया जाएगा और केवल इस अध्ययन में शामिल डॉक्टरों / वैज्ञानिकों को पता चलेगा। इस अध्ययन के परिणाम एक वैज्ञानिक पत्रिका में प्रकाशित हो सकते हैं, लेकिन आपको नाम से पहचाना नहीं जाएगा।

1. अनुसंधान संबंधी चोट के लिए नि: शुल्क उपचार की व्यवस्था। लागू नहीं।

2. ऐसी चोट से उत्पन्न विकलांगता या मृत्यु के लिए विषयों का मुआवजा लागू नहीं है

5.किसी भी समय दंड या लाभों के नुकसान के बिना किसी भी समय भाग लेने के लिए व्यक्ति को स्वतंत्रता लेने और अनुसंधान से वापस लेने के लिए स्वतंत्रता, जिसके तहत विषय अन्यथा हकदार होगा

6.आपको जुर्माना या लाभ के नुकसान के बिना किसी भी समय भाग लेने और अनुसंधान से वापस लेने की पूरी आजादी है, जिस पर आप अन्यथा हकदार होंगे।

7. अध्ययन में आपकी भागीदारी वैकल्पिक और स्वैच्छिक है।

8. प्रदर्शन की जांच की परिणामों की प्रति आपके रिकॉर्ड के लिए आपको उपलब्ध कराई जाएगी।

9.आप किसी भी समय परियोजना से वापस ले सकते हैं, और यह आपके बाद के चिकित्सा उपचार या उपचार चिकित्सक के साथ संबंध को प्रभावित नहीं करेगा।

10. परियोजना के लिए कोई भी अतिरिक्त व्यय, आपके नियमित खर्चों के अलावा, आप से शुल्क नहीं लिया जाएगा।

# Patient proforma

**Demographic details**

Date:

Name:

Age:

Gender :

Address:

Personal history of metabolic disorders

1.Diabetes mellitus (Yes/No) :

2.High blood pressure (Yes/No) :

3.High serum cholesterol (Yes/No) :

Medication History

1. Are you taking medications for treating high blood pressure ? – (Yes/No)
2. Are you taking medications for treating high blood sugar ? – (Yes/No)
3. Are you taking medications for treating high serum cholesterol ? – (Yes/No)

Clinical examination:

Waist circumference in cm

Blood pressure in mm of Hg

Lab results

1. Serum triglycerides
2. Serum HDL
3. Fasting blood sugar / HbA1c

## Radiological imaging proforma

**CT scan**

Date of examination:

Name of the patient:

VFA in cm2:

SFA in cm2:

VSR: