"CORRELATION OF INSULIN RESISTANCE IN LEAN AND OBESE PATIENTS WITH TYPE 2 DIABETES MELLITUS"

By:

DR S. DEEPA M.B.B.S

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DR LAKSHMAIAH .V M.D

PROFESSOR
DEPARTMENT OF GENERAL MEDICINE

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Date:

Place: Kolar

DR. S. DEEPA

Post Graduate
Department Of General Medicine
Sri Devaraj Urs Medical College
Tamaka,Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION &RESEARCH TAMAKA, KOLAR, KARNATAKA.

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled "CORRELATION OF INSULIN RESISTANCE IN LEAN AND OBESE PATIENTS WITH TYPE 2 DIABETES MELLITUS" is a bonafide and genuine research work carried out by DR. S. DEEPA in partial fulfillment of the requirement for the degree of DOCTOR OF MEDICINE (M.D.) in General Medicine

Date:
Place: Kolar

DR. LAKSHMAIAH .V
Professor
Department of General Medicine
Sri Devaraj Urs Medical College
Tamaka,Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION &RESEARCH TAMAKA, KOLAR, KARNATAKA.

ENDORSEMENT

This is to certify that the dissertation entitled "CORRELATION OF INSULIN RESISTANCE IN LEAN AND OBESE PATIENTS WITH TYPE 2 DIABETES MELLITUS" is a bonafide research work done by **Dr. S.DEEPA** under the guidance of **Dr LAKSHMAIAH.V**, professor, Department of General Medicine Sri Devaraj Urs Medical College, Kolar, in partial fulfillment of the requirement for the degree of M.D. in General Medicine

DR. RAVEESHA
Professor & HOD
Department of General Medicine

Date:
Place: Kolar

DR. SREERAMULU P.N.
Principal

Date:
Place: Kolar

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This is to certify that the Ethical committee of Sri Devaraj Urs Medical College, Tamaka, Kolar, has unanimously approved Dr S. DEEPA Post graduate student, in the department of General Medicine at Sri Devaraj Urs Medical College, Tamaka, Kolar, to take up the dissertation work titled "CORRELATION OF INSULIN RESISTANCE IN LEAN AND OBESE PATIENTS WITH TYPE 2 DIABETES MELLITUS" to be submitted to the Sri Devaraj Urs Academy Of Higher Education and Research, Kolar.

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Place: Kolar **Dr S. DEEPA**

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Name of Supervisor	Dr. LAKSHMAIAH. V
Department	GENERAL MEDICINE
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ABSTRACT

Background: Insulin resistance is a precursor of type diabetes mellitus. The most common risk factor related to insulin resistance is obesity. Obesity is one of the various factors which contributes considerably greater to prevalence of diabetes mellitus. However, the non-obese population have also shown a predisposition to the risk of insulin resistance due to genetics. Hence this study aimed to accesses the relationship between insulin resistance in lean and obese type 2 diabetes mellitus patients.

Materials and methods: This study was a cross-sectional, hospital-based study conducted in the department of General Medicine at R L Jalappa hospital, Kolar, studied for a period of 1.5 years. The study population were grouped in two groups containing lean and obese in the ratio of 1:4. Insulin resistance of patients was calculated from both groups using HOMA-IR (Homeostasis Model Assessment). Chi square test was used to test statistical significance. P value < 0.05 was considered statistically significant.

Results: A Total of 106 subjects were involved in the study with mean age of 53.88 ± 9.21 years. There was male preponderance 65 (61.3%) among the study population compared to females 41 (38.7%). The percentage of obese diabetic subjects 84 (79.2%) was greater compared to lean diabetics 22 (20.8%). The difference in lean/obese across the age groups, genders and insulin resistance was found statistical insignificant with a P- value of >0.05.

Conclusion: The association of obese and lean type diabetics to insulin resistance should be further researched.

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LIST OF ABBREVIATIONS

GLOSSARY	ABBREVIATIONS
ADA	American diabetic association
BF	Body fat
CAD	Coronary artery disease
CHD	Coronary heart disease
CRP	C-reactive protein
CT	Computed tomography
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DM	Diabetes mellitus
FFA	Free fatty acid
FM	Fat mass
GK	Glucokinase
GLUT2	Glucose transporter 2
GS	Glycogen synthase
HDL	High-density lipoprotein
ICMR	Indian council of medical research
IDF	International diabetes federation
IFG	Impaired fasting glucose
IGFBP-1	Insulin growth factor binding protein-1
IGT	Impaired glucose tolerance
IR	Insulin resistance
IRS	Insulin resistance syndrome
NAC	North america and caribbean region
NCT	National capital territory
PKCb	Protein kinase c b
SSPG	Steady-state plasma glucose

STR	Subscapular-to-triceps skinfold
TG	Triglycerides
TNF	Tumour necrosis factor
UTs	Union territories
VFA	Visceral fat area
WHO	World health organisation
WHR	Waist to hip ratio

INTRODUCTION

INTRODUCTION

Diabetes mellitus (DM) is one of the most widespread chronic diseases in the world. According to the International Diabetes Federation, 425 million people have diabetes in the year 2017, and by the year 2045, the numbers will rise to 629 million.[1] The Global Burden of Diseases study 2017 estimated that diabetes emerged as the fourth most leading cause of disability.[2] The extreme figure of cases of diabetes mellitus is recorded in the age group between 20 and 64 years of age. With a national DM prevalence of 9.3% of adults and 463 million people with DM, India is known as the "Diabetes capital" of the world and stands second to China in relation to the burden of DM.[3]

The prediabetic state is a long-standing condition in which the blood sugar levels are little above the threshold but can be measured to be normal and below the threshold for diagnosis of diabetes.[4] The valuation of impaired glucose tolerance and impaired fasting glucose levels should be abided by the use of guidelines provided by WHO and ADA(American diabetic association).These two guidelines define the same threshold levels for IGT, but ADA further recommends a lower value of IFG compared to WHO principle.[5]

Worldwide, overweight and obesity has become an epidemic with 2 times increase in the incidence since 1980, later reaching to 1.9 billion overweight and 600 million obese adults in 2014. The report by WHO has predicted that about 66.7% of the world's population will be burdened by chronic non-communicable diseases, especially with diet-related.[6] According to WHO 2006,type 2 diabetes, high blood

pressure and cardiac disease were found at a very young age among the population who were malnourished at a young age and overweight during the adult period.[7]

Diabetes mellitus is categorized by a pathological condition called Insulin Resistance (IR) in which cells become unable to retort customarily to the hormone insulin. Resistance to insulin occurs due to an imbalance in the metabolism of glucose causing least sensitivity of adipose, muscles, liver and other body tissues to insulin, in spite of blood insulin levels being normal or above in concentration. The initial event of glucose-stimulated insulin secretion is glucose sensing. The glucose transporter 2 (GLUT2) and glucokinase (GK) are key molecules which affect various processes of glucose sensing in pancreatic β-cells.[8] Impairment in glucose sensing contributes to pancreatic β-cell dysfunction. Therefore, it is essential to uphold adequate expression levels of GLUT2 and GK to ensure normal β-cell function. The prime offender of resistance to insulin is obesity, which has reached epidemic proportions worldwide, because of improved life quality and ever-increasing inactive lifestyles, the prevalence of obesity increased dramatically over the past decade in India.[9] Previous studies have also indicated that with subcutaneous fat, visceral fat accumulation, known as releasing more proatherogenic and proinflammatory factors, leads to the insulin resistance worsening and oxidative stress, and thus contributes to cardiovascular disease (CVD).

Increased high fat accumulation is generally associated to an elevated risk of the development of diseases, like hypertension, dyslipidaemia, and diabetes mellitus (DM),arterial hypertension, hypercholesterolemia, obesity, and hypertriglyceridemia.[10]

Insulin resistance and beta-cell function can be computed by the homeostatic model known as HOMA. The name HOMA was coined Matthews et al in 1985.[11] This model is a mathematical model which helps in assessing the IR and β cell function from the fasting glucose concentration.[11]

Evolving countries like India are observing a gradual increase in the frequency of obesity in recent decades.Though insulin resistance does not develop in all obese persons, and genetic background backs strongly to insulin resistance, even in nonobese persons. So, the present study is undertaken to find out the correlation between insulin resistance (by HOMA-IR) in obese and lean type 2 DM patients.

The source for Insulin resistance is obtained by the thought that it is strongly related to the obese type of diabetic population. It is theorized that the relation of insulin resistance in obese diabetics is owing to factors like a number of pro-inflammatory cytokines released from adipose tissue along with fatty acids. This rises insulin resistance and causes endothelial dysfunction.[12]

Few studies have shown that South Asians are more insulin resistant compared to other populations, though having similar levels of BMI and total body fat percent. This tells us there are other factors causing insulin resistance other than obesity. Factors like early β-cell function impairment, high visceral fat deposition as in neonates and in adult life, higher levels of plasma leptin and low levels of plasma adiponectin also can play a significant role in causing insulin resistance.[13, 14]

Lean type 2 DM is an emerging entity while differs largely from classical obesity-related type 2 diabetes mellitus. In insulin resistance and body fat distribution in lean type 2 diabetes persons genetic polymorphisms are appraised to play a chief role.[15]

People with diabetes who are lean have a younger age of onset, high prevalence in the male population, poor glycemic control and higher mortality rates.[16]

Need of the study

This study was aimed to assess and associate insulin resistance among lean and obese type 2 diabetes mellitus. We aimed to study the status of insulin resistance in lean as well as obese type 2 diabetes subjects which is an important therapeutic target for oral antidiabetic drugs. HOMA is a simpler way to estimate insulin sensitivity. It is a simple mathematical model which can estimate an individual's insulin sensitivity and beta-cell function from concurrent measurements of fasting insulin and fasting plasma glucose.

OBJECTIVES

AIMS AND OBJECTIVES

1. To estimate insulin resistance (by HOMA-IR) in obese and lean type 2 DM patients.
2. To compare insulin resistance in lean and obese type 2 diabetes mellitus patients.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

GLOBAL BURDEN OF DIABETES MELLITUS: INTERNATIONAL DIABETES

Among the top 10 causes for mortality across the globe, diabetes ranks the top most along with other 3 major non-communicable diseases. Out of the 56.9 million deaths, globally,40.5 million deaths were due to NCDs in 2016. Diabetes killed 1.6 million people in 2016, up from less than 1 million in 2000.[17]

The new edition of the IDF Diabetes Atlas anticipated the prevalence of diabetes and impaired glucose tolerance (IGT) for the years 2017 and 2045. The estimates were provided for 221 countries and territories, grouped into seven IDF regions. The North America and Caribbean region (NAC) had the highest age-adjusted comparative prevalence 20-79 years in 2017 and 2045 (11.0% and 11.1%). The Africa region had the lowest prevalence in 2017 and 2045 (4.2% and 4.1%), likely due to underdevelopment, malnutrition, decreased obesity and higher rates of communicable diseases.The largest numbers of people with diabetes from age 20-79 years were in the United States, India and China in 2017.[18]

High-income countries, presented with type 2 DM contributing to about 87% to 91% of the people. And around 7% to 12% were typed 1 diabetes with 1% to 3% with other types of diabetes.[19] Worldwide around 425 million people that may be about 8.8% of adults of age between 20-79 years were estimated to have diabetes, with about 79% living in emerging countries. It is noticed that the incidence of the population living with diabetes have augmented to 451 million if the age is expanded to 18-99 years. If these trends continue, by 2045, 693 million people 18-99 years, or

629 million of people 20-79 years, will have diabetes.[18] There is a marked increase in the occurrence of diabetes in the employed age (20-64 years) groups accounting for about 326.5 million people. And this number might increase up to 438.2 million by 2045 in the working-age groups, while the frequency of individuals with diabetes 65-99 years may increase to 253.4 million by 2045. Thus increasing the financial burden of diabetes in the next decades among the elder age groups (70-99) with an increase of United States Dollar bill USD 104 billion from 2017-2045.[18]

The frequency of diabetes in females with age 20-79 years was projected to be 8.4% and somewhat lower in males (9.1%). There are about 17.1 million more males than females with diabetes (221.0 million men vs 203.9 million women). The diabetes frequency is anticipated to increase to 9.7% in women and to 10.0% in men, the age group 65-79 years shows the peak diabetes prevalence in both women and men.[18]

Burden of diabetes in India:

The alarming conditions in the incidence of diabetics is increasing across the majority of nations in particular the developing and developed countries. India is one among the country which houses greater inhabitants of diabetes. The low and middle income regions of developing countries hold about 66.6% of the worlds diabetic population.[20] India ranks second with a maximum number of people around 69.2 million with diabetes in the world and these figures are likely to increase to 123.5 million by 2040.[18]

A large population-based study was conducted by The Indian Council of Medical Research–India Diabetes (ICMR–INDIAB) to addresses the need and provide an

accurate and comprehensive state- and national-level data on the prevalence of diabetes and other metabolic NCDs in India. This study is an ongoing national survey directed in adults of both genders, aged ≥20 years and above from all 29 states, National Capital territory (NCT) of New Delhi and 2 union territories (UTs) namely Chandigarh and Puducherry in the mainland of India in a phased manner. A multi-stage sampling method were designed to each state and among 4,000 individuals, 2,800 individuals in rural areas, and 1,200 individuals in urban areas were studied. This resulted in large sample size thus, it was designed in a phased manner.[21]

The results of phase 1 presented the frequency of diabetes to be 10·4% in Tamil Nadu: (Urban-13.7: Rural- 7.8%), 8·4% in Maharashtra: (Urban-10.9%: Rural- 6.5%), 5·3%in Jharkhand:(Urban-13.5%: Rural- 3.0%) and 13·6% in Chandigarh (Urban-14.2%: Rural 8.3%). The prevalence of self-reported diabetes among urban residents of Tamil Nadu, Maharashtra, Jharkhand and Chandigarh were 8·5%, 3·7%, 8·4% and 6·6% while that among rural residents was 4·1%, 1·7%, 0·7% and 3·1% respectively. The Phase I results of the ICMR-INDIAB study showed the prevalence of diabetes was seen highest in Chandigarh followed by Tamilnadu, Maharashtra and Jharkhand. The occurrence of prediabetes was seen highest in Chandigarh followed by Maharashtra, Tamilnadu and Jharkhand.[21]

The frequency of newly diagnosed diabetes among urban residents of Tamil Nadu, Maharashtra, Jharkhand and Chandigarh were 5·2%, 7·2%, 5·1% and 7·6% and that among rural residents, 3·8%, 4·9%, 2·3% and 5·2% respectively. This translated to 4.8 million individuals with diabetes in Tamil Nadu. In Maharashtra, an estimated 6.0 million had diabetes, Jharkhand ,0.96 million and in Chandigarh, 0.12 million had

diabetes in 2011. The ICMR-INDIAB study projected the number of persons with diabetes in India in 2011 to be 62.4 million.[22] The figure for diabetes from the ICMR-INDIAB study was accepted by the International Diabetes Federation (IDF) for India in 2011, which reported a figure of 61.3 million people with diabetes in India in the age group of 20-79 years.[18]

TYPE 2 DM PATHOPHYSIOLOGY: ROLE OF INSULIN REESISTANCE

Insulin resistance is described as a "glucose homeostasis disorder involving a decreased sensitivity of muscles, adipose tissue, liver and other body tissues to insulin, despite its normal or increased concentration in blood".Insulin resistance can be without symptoms or be presented with various complaints such as diabetes type 2, hypercholesteremia, obesity, hypertriglyceridemia or increased arterial pressure.[23]

An insulin receptor is a heterodimer consisting of two alpha-subunits, situated extracellularly, and two beta-subunits which are transmembrane proteins. The cytoplasmic part of the beta-subunit is gifted with tyrosine kinase activity and comprises a region with autophosphorylation capability. When the insulin binds with alpha subunits, there is phosphorylation of beta subunit leading to triggering of several pathways within the cell in repose to the hormone.[24]

Three mechanisms involved in insulin resistance: pre-receptor, receptor and post-receptor

Type A-Receptor:

- Less number of insulin receptors
- Due to mutations of insulin receptors, its affinity to bind to insulin is decreased.

Type B- Pre receptor:[24]

- Genetic variations in the molecular assembly of insulin which is known as "mutant insulin syndrome".
- Augmented Insulin degradation.
- Autoantibodies such as IgG in the blood binding typical insulin.
- Coexistence of Insulin antagonists in the blood such as glucagon, cortisol, growth hormone, androgen and thyroid hormone.

Type C-Post receptor:

- Due to disorders present within the cell, the signaling process to help in binding the insulin to the receptor is disturbed.
- Any aberrations involving the function and structure of glucose transporters carrying glucose into the cell.
- Excessive breakdown of lipid causes hiked number of free fatty acids which in turn leads to hinderance in the breakdown of glucose.

Hepatic and peripheral are the two exemplified types of insulin resistance. The former type of IR comprises gluconeogenesis, glycogenolysis and making of triglycerides and very low-density lipoprotein. The later type of IR is usually is seen in fat tissue and skeletal muscles where there is an irregularity in the uptake and utilization of glucose by the muscles and excessive breakdown of lipids in the fat tissue leading to free-fatty acids production.[25]

Monocytes become extremely sensitive if glucose blood levels increase. This increased blood glucose is sensed by the monocytes by the insulin receptors present on them and further, rapidly eliminates the glucose. In addition, all the iso-forms of

GLUT is shown to be expressed on the plasma membrane of monocytes of adipose and muscle tissue. Hence monocytes can be considered as a consistent model in the study of metabolic disorder.[26]

METABOLIC CONSEQUENCES OF INSULIN RESISTANCE

In early 1970s IR was considered as a classic feature of type 2 diabetes.[3] A progressive inability of the β cells to compensate for the dominant IR by sufficient hyperinsulinemia, heralds the clinical onset of this disorder. The morbidity of the disorder conveys, the severity of improved blood glucose and the significances of glucose metabolism. The main defects in insulin action appear to be in muscle and fat cells, with diminished GLUT 4 translocation resulting in impaired insulin-mediated glucose transport. The metabolic consequences are as follows:[27]

Metabolic Syndrome

Jean Vague's early comments in the 1950s were rediscovered some three decades later, when in 1988 it was planned that individuals with glucose intolerance, elevated triglycerides, low HDL cholesterol and essential hypertension were at significantly augmented for cardiovascular risk.[28]

Their diagnostic criteria for metabolic syndrome require three of the following:[29]

- Waist circumference: greater 40 inches in males and 35 inches in women
- Elevated triglycerides: greater or150 milligrams per deciliter of blood (mg/dL)
- Reduced high-density lipoprotein cholesterol (HDL) less than 40 mg/dL in men or less than 50 mg/dL in women
- Elevated fasting glucose of l00 mg/dL or greater

- Blood pressure values of systolic 130 mmHg or higher and/or diastolic 85 mmHg or higher.

DYSLIPIDAEMIA

The lipid irregularities associated with IR affect all lipid fractions. They are characterised by elevated fasting triglyceride levels, elevated postprandial triglyceride-rich remnant lipoproteins, low HDL cholesterol, and small dense LDL particles.[30]

HYPERTENSION

Essential hypertension is related to insulin resistance in an about of 50 % of the cases. There is a strong association of blood pressure with body weight. Proposed mechanisms have included increased renal sodium retention and augmented sympathetic nervous system activity from compensatory hyperinsulinemia.[31]

Cancer

IR with compensatory hyperinsulinemia has been concerned in the etiology of certain cancers, including colon, endometrial, possibly pancreatic and renal-cell cancers and breast cancer.[32]

NAFLD

NAFLD may progress to non-alcoholic steatohepatosis, steatohepatitis, fibrosis or cirrhosis, representing increasing damage to the liver. IR of peripheral type in muscle

and fat lead to the augmented distribution of free -fatty acids to the liver, increasing triglyceride synthesis.[33]

INSULIN RESISTENCE:ASSOCIATION WITH VARIOUS MICRO AND MACROVASCULAR COMPLICATIONS

The longstanding vascular complications of insulin resistance include retinopathy, nephropathy, neuropathy, and macrovascular disease. The outcomes are the following:

Diabetic Retinopathy causes visual weakening and loss of sight. It is the most common microvascular complication of diabetes. Oxidative tension stages a vital role in cellular damage from increased glucose levels. Hyperglycemia causes an increase in the formation of reactive oxygen species and free radicals which ultimately leads to a complication involving vascular components and further progress to retinopathy.[34]

Diabetic Nephropathy causes renal failure and increased blood pressure. It is defined by proteinuria > 500 mg in 24 hours in the setting of diabetes, but preceded by lower degrees of proteinuria, or "microalbuminuria". End stage renal failure may occur many years later and requires dialysis or kidney transplantation.[35]

Diabetic Neuropathy causes pain, paresthesia, muscle weakness, and autonomic dysfunction due to peripheral nerve damage. According to the American Diabetes Association (ADA), diabetic neuropathy is diagnosed based on excluding other causes of peripheral nerve damage except for diabetes as the reason for damage. The exact mechanism involved in peripheral nerve damage due to hyperglycemia is not well

recognized. However, it is stated that the mechanism such as polyol build up, oxidative strain and injury due to AGEs may be the etiology of peripheral neuropathy.

The diabetic manifestations of peripheral neuropathy include sensory: focal, multifocal and autonomic neuropathies. Diabetic neuropathy also leads to nearly 80% of amputation of a foot due to ulceration.[36]

Macrovascular disease includes cardiac sicknesses, Peripheral vascular disease and stroke. The central pathological mechanism in macrovascular ailment is the course of atherosclerosis, which causes the tapering of arterial walls throughout the body. Atherosclerosis is thought to result from chronic inflammation and injury to the arterial wall in the peripheral or coronary vascular system.

Among macrovascular diabetes problems, coronary heart disease has been associated with diabetes in numerous studies beginning with the Framingham study. Diabetes is also a strong independent forecaster of risk of stroke and cerebrovascular disease, as in coronary artery disease. Population with type two diabetes have greater risk rate (150-400%) for stroke.[37]

LABORATORY ESTIMATION OF INSULIN RESISINANCE:

Numerous methods to assess IR are basically done on simultaneous measures of serum insulin and glucose levels. The IR is based on the starting point measures of insulin and glucose or either the measure taken later to intravenous infusion of a set on a measure of insulin or glucose. IR assessing methods can be categorised into indirect and direct.[23]

Direct method:

- The ‘gold standard’: Metabolic clamp technique
- Endogenous insulin suppression test
- Insulin tolerance test

Indirect method:

- Insulinemic/glycemic index
- QUICKI index
- Intravenous glucose tolerance test
- Bergman method
- Matsuda index
- HOMA-IR index
- Double intravenous glucose challenge test

HOMA IR technique

Mathews et al in 1985 was the first to pioneer HOMA method. This technique measured the IR and function of the beta-cell from the fasting glucose and insulin levels. This model showed the connotation of glucose and insulin properties that foresees the constant fasting state of glucose and insulin levels in cases of several possibilities of IR and beta-cell function. The levels of insulin are usually dependable on Beta-cell to glucose levels while the glucose levels are controlled by the insulin-mediated glucose production through the liver. Therefore, poor β-cell function leads to a weakened response of β-cell to glucose-stimulated insulin secretion. Likewise, IR is echoed by the reduced repressive consequence of insulin on hepatic glucose

manufacture. This model has shown to be a simple and a strong tool in assessing IR at both clinical and epidemic levels.[38]

CLINICAL MARKERS OF INSULIN RESISTANCE

Through ongoing intensified research, many newer inflammatory markers are gaining attention as proxy markers in the valuation of IR.

Insulin growth factor binding protein-1

Current research has recommended insulin growth factor binding protein-1 (IGFBP-1) as a new potential plasma marker to assess IR. IGFBP-1 is shown to have a good correlation with FSIVGTT estimation of insulin sensitivity, chiefly in children younger than 10 years.[39]

Soluble CD36

Hyperglycemia and altered macrophage insulin signalling in insulin resistance lead to increased expression of CD36. Soluble CD36 has been reported to be noticeably raised in people with IR and type 2 diabetes.[40]

C-reactive protein

C-reactive protein (CRP) is the best-studied markers for systemic subclinical inflammation and may have prognostic value in predicting the upcoming risk of cardiovascular events. In cross-sectional studies, highly sensitive - CRP has shown to correlate with increased triglyceride, decreased HDL, increased blood pressure and augmented fasting plasma glucose concentrations, suggesting its association with amplified prevalence metabolic syndrome associated with IR.[41]

Ferritin

Ferritin is the chief intracellular iron storage protein. Lately, ferritin is suggested that when markers of the iron metabolism are elevated, the metabolic syndrome incidence is raised. Ferritin has shown to be associated to both hyperinsulinemia and hypertriglyceridemia.[42]

Adiponectin

Adiponectin is a multifunctional protein that exerts pleiotropic insulin-sensitizing effects and hence is considered as a key molecule in the pathogenesis of the metabolic syndrome. It lowers hepatic glucose production and rises glucose uptake and fatty acid oxidation in skeletal muscle.[43]

Tumour necrosis factor-alpha

Numerous studies have been showed to explore the role and use of tumour necrosis factor (TNF) to aid in assessing the IR. TNF has been established to have a connection to insulin resistance measured by HOMA-IR or insulin clamp and to metabolic syndrome status.[44]

C3 complement

The chief activation fragment of C3, C3a desArg (acylation stimulating protein) favours glucose transmembrane transport and the synthesis of triglycerides in fat cells. This recommends that it has insulin-like properties. C3 is sturdily connected with IR and is autonomous to the metabolic syndrome components.

Glycosylated hemoglobin

Glycosylated hemoglobin (HbA1c) is used to analyse the long-standing glycaemic control in diabetics. HbA1c is anticipated as a measure of substitute assessment of

metabolic syndrome, thereby estimating IR because of various factors. HbA1c reflects long-term glycaemic control in diabetic persons and is a important predictor of chronic complications of diabetes.[45]

Protein kinase C in microangiopathy

It has been speculated that activation of the protein kinase C b isoform (PKCb) which is mediated by hyperglycaemia play as a potential surrogate marker for microangiopathic diseases, and diabetic retinopathy in particular.[46]

OBESITY ASSOCIATION WITH INSUIN RESISNTANCE

Increased adipose tissue, especially that in an upper body was initially related with diabetes and vascular disease was given by French endocrinologist Jean Vague in 1956.[47] Insulin resistance increases with increasing body mass index, waist circumference and in particular waist-hip ratio. These reflect increased adiposity, especially greater levels of visceral fat tissue. Visceral adipose tissue refers to intra-abdominal fat around the intestines and correlates with liver fat. Visceral fat tissue has metabolic characteristics which differ from that of subcutaneous fat. It is more metabolically active with consideration of free fatty acid turnover; the higher fluidity of free fatty acids encourages IR at a cellular level and increases hepatic VLDL production. Omental pre-adipocytes have increased 11-β hydroxysteroid dehydrogenase type 1 activity, initially thought to endorse IR by the effects of locally produced active glucocorticoid, via conversion of cortisone to cortisol, though the consequence of these findings in vivo is debated.[48]

Adipose tissue harvests numerous cytokines that are connected with insulin resistance, along with pro-inflammatory activity, e.g. TNFα, interleukins, and PAI-1. There are regional differences in adipocyte cytokine production. Insulin resistance of muscle is connected with increased intramyocellular triglyceride, derived from adipose tissue lipolysis.

The insulin resistance seen in obesity is believed to involve and liver and primarily muscle, with greater fat cell-derived free fatty acids promoting triglyceride collection in these tissues.[49] Insulin resistance is aggravated with weight gain, and weight loss improves the condition.

PRACTICAL IMPLICATIONS:

CHOICE OF TREATMENT

Persons with Type 2 diabetes should undergo screening at the time of diagnosis and yearly thereafter. Every individual with diabetes must have serum creatinine measurement performed annually. Blood pressure should be measured routinely. Goal blood pressure is < 130/80 mmHg. Population with a blood pressure ≥ 140/90 mmHg should be treated with medication, along with diet and remodeling of lifestyle. Population with a blood pressure of 130-139/80-89 mmHg may attempt a trial of lifestyle and behavioral therapy for 3 months and then receive pharmacological therapy if their goal blood pressure is not achieved. Initial drug therapy should be with a drug shown to decrease CVD risk, but all people with diabetes and hypertension should receive an ACE inhibitor or ARB in their antihypertensive regimen.

Lipid testing should be performed in people with diabetes at least annually. Lipid goals for adults with diabetes should be an LDL < 100 mg/dl (or lesser than seventy mg/dl in population with overt CVD), HDL > 50 mg/dl, and fasting triglycerides < 150 mg/dl. All subjects with diabetes should be encouraged to limit consumption of saturated fat, trans fat, and cholesterol. Statin therapy to lower LDL by 30-40% regardless of the baseline is suggested to reduce the chance of CVD in patients greater than 40 years of age. Patients lesser than 40 years of age may also be considered for therapy. In people with overt CVD, special attention should be paid to treatment to lower triglycerides or raise HDL. Combination therapy with a statin plus other drugs, such as fibrates or niacin, may be necessary to achieve ideal lipid control, nevertheless individuals should be monitored closely for possible adverse reactions of therapy.[50]

Most Relevant Studies:

Graham TE et al[51], conducted a study to correlate RBP4 serum levels with IR, as well to find whether elevated serum RBP4 levels are related to reduced expression of glucose transporter 4 (GLUT4) in adipocytes. They measured insulin resistance, serum RBP4, and mechanisms of the metabolic syndrome in three groups of subjects. GLUT4 protein was measured in isolated adipocytes. Serum RBP4 levels, interrelated with the degree of IR in persons with type 2 diabetes, obesity and in nondiabetic, impaired glucose tolerance, nonobese patients with a solid family history of type 2 DM. Elevated serum RBP4 was linked with mechanisms of the metabolic syndrome, including increased body-mass index, waist-to-hip ratio, serum triglyceride levels, and systolic blood pressure and decreased high-density lipoprotein cholesterol levels. Workout training found to be related to a decrease in serum RBP4 levels only in

subjects in whom insulin resistance improved. Adipocyte GLUT4 protein and serum RBP4 levels were inversely correlated. RBP4 is an adipocyte-secreted molecule that is elevated in the serum before the development of frank diabetes and appears to recognise insulin resistance and related cardiovascular risk factors in subjects with varied clinical presentations.

Mathews et al[52], determined the accuracy and precision of the approximation of IR and beta-cell function using hyperglycaemic and euglycaemic clamps and an intravenous glucose tolerance test. The estimation of IR was attained by HOMA model was correlated to estimates obtained by use of the euglycaemic clamp ($R\sim=0.88$, $p< 0.0001$), and the hyperglycaemic clamp, ($Rs=0.69$, $p< 0.01$). There was no correlation with any aspect of insulin-receptor binding. The estimate of deficient β - cell function obtained by homeostasis model assessment correlated with that derived using the hyperglycaemic clamp ($R\sim = 0.61$, $p< 0.01$) and with the estimate from the intravenous glucose tolerance test ($R\sim = 0.64$, $p < 0.05$). The low precision of the estimates from the model (coefficients of variation: 31% for insulin resistance and 32% for β-cell deficit) limits its use, but the correlation of the model's estimates with patient data accords with the hypothesis that basal glucose and insulin interactions are largely determined by a simple feedback loop.

Abbasi et al[53], defined the relation between insulin resistance in 314 nondiabetic body mass index (BMI) and normotensive, healthy volunteers; and determined the relationship between each of these two variables and CHD risk factors. IR was resolved by the steady-state plasma glucose (SSPG) concentration. In addition, nine CHD risk factors: systolic blood pressure, age, diastolic blood pressure (DBP), total

cholesterol, triglycerides (TG), high-density lipoprotein (HDL) cholesterol and low-density lipoprotein cholesterol concentrations, and glucose and insulin responses to a 75-g oral glucose load were measured in the volunteers. The SSPG concentration and BMI were significantly related. The BMI and SSPG were both independently related with individually to nine risk factors. In multiple regression analysis, SSPG concentration added modest to substantial power to BMI with regard to the prediction of DBP, HDL cholesterol and TG levels, and the glucose and insulin responses. They determined that obesity and IR are both powerful predictors of insulin resistance. CHD risk at any given degree of obesity highlights the risk of CHD and type 2 diabetes.

Mckeigue et al[54], gave a hypothesis that the high death rate from coronary heart disease (CHD) in South Asians settled overseas compared with other populations is due to metabolic disturbances correlated to IR. The study was done on a population survey of 3193 men and 561 women aged 40-69 years in London, UK. In contrast with the European group, the South Asian group had a greater prevalence of diabetes (19% vs 4%), higher blood pressures, higher fasting and post-glucose serum insulin concentrations, higher plasma triglyceride. And lower HDL cholesterol concentrations. Mean waist-hip girth ratios and trunk skinfolds were higher in the South Asian than in the European group. Within each ethnic group,the waist-hip ratio was correlated with glucose intolerance, insulin, blood pressure, and triglyceride. These results concluded that the presence of an IR syndrome, prevalent in South Asian inhabitants and related with a pronounced tendency to central obesity in this group.

Mckeigue et al[55],gave a hypothesis that IR and Type 2 (non-insulin-dependent) diabetes mellitus are linked with centrally-distributed obesity and are especially prevalent in people of South Asian (Indian, Pakistani and Bangladeshi) descent. They examined the relationship of glucose intolerance to body fat pattern in a population survey of 2936 men and 537 women of South Asian and European origin living in London, UK. In both groups, glucose intolerance (defined as diabetes or impaired glucose tolerance) was more sturdily related with waist-hip girth ratio than with BMI or skinfolds. In European males with normal glucose tolerance, fasting insulin levels were more strongly related with body mass index than with waist-hip ratio. Physical activity scores were lower in South Asians than in Europeans, but no statistically significant associations between glucose intolerance and low physical activity were detectable. They concluded that the waist-hip ratio is the most valid anthropometric index for identifying individuals whose obesity and they are more predisposed to glucose intolerance.

Knight TM [56]conducted a cross-sectional study to validate that IR associated with centralised adiposity is the underlying mechanism that predisposes Asian immigrant communities to both diabetes mellitus and ischaemic heart disease, in Bradford, West Yorkshire. They examined Male manual workers of Asian (110) and non-Asian origin (156) aged 20-65 yearsin two textile factories. Diabetes was almost 3 times more prevalent in the Asian group. Setting- after an oral glucose load, Asian man had double the serum insulin concentrations of non-Asian men ($p < 0\ 0001$). Asian men also had significantly lower concentrations of plasma total cholesterol ($p < 0\ 03$), high density lipoprotein cholesterol (HDL) (HDL2, $p < 0\text{-}0001$; HDL3, $p < 0\text{-}0001$), and apolipoprotein AI ($p < 0\ 0001$). Fasting plasma triglyceride concentrations were

slightly higher (p = 0 072) in the Asian men; thus, the ratio of triglyceride cholesterol was higher (p = 0 006). They found that the risk marker profile in the Asian men was therefore quite different from that of their non-Asian complements were related with a greater tendency to centralised adiposity.

Bogardus et al[57], compared the insulin action and maximal aerobic capacity in obese subjects and lean controls. They studied 55 male Pima Indians and 35 male Caucasians with normal glucose tolerance. In vivo insulin action was measured using the hyper insulinemic, euglycemic clamp technique at a plasma insulin concentration of approximately 100 microU/ml. Body composition was determined by densitometry, and maximal aerobic capacity was estimated using a graded exercise test. The results showed that the degree of obesity was nonlinearly related to in vivo insulin action. In both Indians and Caucasians, there was a significant decline in insulin action with increasing obesity up to a percent body fat of approximately 28-30%. Maximal aerobic capacity was positively linearly correlated with insulin action over the entire range of insulin action in both racial groups. They found that the degree of overweight and maximal aerobic capacity was each independently related with insulin action and were of marginal significance in the Caucasians.

Kissebah et al[58], studied the status of body fat distribution as an important prognostic marker for glucose intolerance. They evaluated in 9 nonobese and 25 obese, apparently healthy women. And glucose levels and plasma insulin during oral glucose loading were significantly greater in females with predominantly upper body segment obesity than in females with lower body segment obesity. Fasting plasma triglyceride levels were also significantly higher in the upper body segment of obese women. The

site of adiposity in the upper body segment obese women was comprised of large fat cells, while in the lower body segment obese subjects, it was formed of normal size cells. In both types of obesity, abdominal fat cell size correlated significantly with PPBS and insulin levels. Thus, in women, the sites of fat predominance are important predictors of hyperinsulinemia and hypertriglyceridemia.

Pederson et al[59], investigated the relative importance of total fat mass versus localisation of adipose tissue in insulin-stimulated glucose disposal (R_d) and skeletal muscle glycogen synthase (GS) activity in obese individuals. Twenty obese women with an average BMI of 37.8 ± 1.3 kg/m^2 and a waist to hip ratio (WHR) ranging from 0.78 to 1.02 were examined during basal conditions and following hyperinsulinemia (hyper insulinemic euglycemic clamp). anthropometric measurements, dual-energy x-ray absorptiometry scanning (DEXA-scan), and bioelectric impedance measurements were taken. Insulin-stimulated glucose R_d was negatively correlated with WHR ($R = -.52, P < .025$) whereas there were no correlations with BMI or percent fat ($R = .16$, NS and $R = .16$, NS, respectively). Furthermore, a negative correlation between WHR and insulin stimulation of GS activity in skeletal muscle was found ($R = -.62, P < .005$). In contrast, BMI and percent fat were not correlated with the insulin effect on GS activity in skeletal muscle ($R = .34$, NS and $R = -.35$, NS, respectively). Finally, NEFA concentrations during hyperinsulinemia were negatively correlated with insulin-stimulated glucose R_d ($R = .73, P < .0009$. They found that DEXA-scan and bioelectric measurements were not superior to BMI and WHR in predicting IR in this group of obese women.

Jenson et al[60], determined whether the alterations in body fat distribution result in specific inconsistency of free fatty acid (FFA) metabolism, palmitate turnover, a measure of systemic adipose tissue lipolysis. It was measured in 10 women with upper-body obesity, 9 women with lower body obesity, and 8 nonobese women under overnight postabsorptive (basal), epinephrine stimulated, and insulin suppressed conditions. Upper body obese women had greater ($P < 0.005$) basal palmitate turnover than lower body obese or nonobese women (2.8±0.2 vs. 2.1±0.2 vs. 1.8±0.2), but a reduced ($P < 0.05$) net lipolytic response to epinephrine (59±7 vs. 79±5 vs. 81±7 Mmol palmitate/kg LBM, respectively). Both types of obesity were associated with impaired suppression of FFA turnover in response to euglycemic hyperinsulinemia compared to nonobese women ($P < 0.005$). They found that specific differences in FFA metabolism may reflect adipocyte heterogeneity, which may in turn affect the metabolic aberrations associated with different types of obesity.

Goodpaster et al[61], measured insulin sensitivity, body composition and aerobic fitness within a cohort of sedentary in good physical shape men ($n = 26$) and women ($n = 28$). The subjects, who ranged from lean to obese (BMI 19.6-41.0 kg/m^2), underwent dual-energy X-ray absorptiometry (DEXA) to measure fat-free mass (FFM) and fat mass (FM), computed tomography to measure cross-sectional abdominal subcutaneous and visceral adipose tissue, and computed tomography (CT) of mid-thigh to measure muscle cross-sectional area, muscle attenuation, and subcutaneous fat. Insulin sensitivity was measured using the glucose clamp technique (40 mU · m$\sim^2$ · min^{-1}), in conjunction with [3-^{3}H] glucose isotope dilution. Insulin-stimulated glucose disposal (R_d) ranged from 3.03 to 16.83 mg · min^{-1}· kg^{-1} FFM. R_d was negatively correlated with FM ($r = -0.58$), visceral fat ($r = -0.52$), subcutaneous

abdominal fat (r = -0.61), and thigh fat (r = -0.38) and positively correlated with muscle attenuation (r = 0.48) and Vo_{2max} (r = 0.26, $P < 0.05$). They concluded that subcutaneous abdominal fat has a strong association with IR as visceral fat, and altered muscle composition, suggestive of increased fat content, is an important autonomous marker of insulin resistance in obesity.

Abate et al[62], conducted this study to determine if NIDDM patients accumulate excess intraperitoneal fat, and whether this contributes significantly to their IR. In the present study 31 men with mild NIDDM with a wide range of adiposity were compared with 39 nondiabetic, control subjects for insulin sensitivity (measured using euglycemic-hyper insulinemic clamp technique) and total and regional adiposity (assessed by hydro densitometry and by measuring subcutaneous abdominal, intraperitoneal, and retroperitoneal fat masses using magnetic resonance imaging [MRI], and truncal and peripheral skinfold thicknesses using calipers). MRI analysis showed that NIDDM patients, had increased truncal-to-peripheral skinfolds thickness ratios. In NIDDM patients, as in control subjects, amounts of truncal subcutaneous fat showed a stronger correlation with glucose disposal rate than intraperitoneal or retroperitoneal fat; however, NIDDM patients were more insulin resistant at every level of total or regional adiposity. They found that NIDDM subjects do not have excess intraperitoneal fat, but that their fat distribution favors more truncal and less peripheral subcutaneous fat.

Yin et al[63], aimed to assess the sensitivity of WC cut-off values for predicting metabolic risk factors in middle-aged Chinese. The study involved 923 subjects aged 40-65 years. WC cut-off values are 85-90 cm and ≥90 cm for central pre-obesity and

central obesity in males, respectively, while WC 80-85 cm and ≥85 cm was used as cut-off values of central pre-obesity and central obesity in females. WC values equivalent to BMI 24 kg/m2 and visceral fat area (VFA) 80 cm2 were 88.55 cm and 88.51 cm in males, and 81.46 cm and 82.51 cm in females respectively. ROC curves showed that the optimal WC cut-off of value was 88.75 cm in males, higher than that in females (81.75 cm). The subjects with higher WC values were more likely to have accumulating metabolic risk factors. The prevalence of metabolic risk factors increased linearly and significantly in relation to WC levels. They found thatvarious metabolic risk factors can be predicted by WC cut-off values of central pre-/central obesity.

Haffner et al[64], conducted a population-based study of diabetes and assessed BMI, the ratio of subscapular-to-triceps skinfold (STR), the ratio of waist-to-hip circumference (WHR), lipids, lipoproteins, and glucose tolerance in 738 Mexican Americans (ages 25-64 yr). In general, STR and WHR were associated with high NIDDM rates, low HDL cholesterol levels, and high triglyceride levels, although WHR was somewhat more predictive of these than STR. In females, BMI, WHR, and STR all made independent contributions to estimate of NIDDM and HDL cholesterol; in males, WHR and STR both made independent contributions to the prediction of triglyceride levels. This proposes that both indices may measure different aspects of body-fat distribution. They found that amongst the indicators of body-fat distribution in studies of diabetes and other cardiovascular risk factors, WHR seems to be preferable.

Indian studies

Dudeja et al[65], Asian Indians are at increased risk for the progress of atherosclerosis and related complications, possibly initiated by higher body fat (BF). The present

study aimed to establish appropriate cut-off levels of the BMI for defining overweight, considering percentage BF in healthy Asian Indians in northern India as the standard. A total of 123 healthy volunteers (eighty-six males aged 18±75 years and thirty-seven females aged 20±69 years) participated in the study. Clinical examination and anthropometric measurements were performed, and percentage BF was calculated. BMI for males was 21´4 (SD 3´7) kg/m2 and for females was 23´3 (SD 5´5) kg/m2. Percentage BF was 21´3 (SD 7´6) in males and 35´4 (SD 5´0) in females. A comparison of BF data among Caucasians, Blacks, Polynesians and Asian ethnic groups (e.g. immigrant Chinese) revealed noticeable differences. ROC curve analysis showed a low sensitivity and negative predictive value of the conventional cut-off value of the BMI (25 kg/m2) in identifying subjects with overweight as compared to the cut-off value based on percentage BF (males .25, females .30). This observation is particularly obvious in females, resulting in significant misclassification. Based on the ROC curve, a lower cut-off value of the BMI (21´5 kg/m2 for males and 19´0 kg/m2 for females) displayed the optimal sensitivity and specificity, and less misclassification in the identification of subjects with high percentage BF. Furthermore, a novel obesity variable, BF: BMI, was tested and should prove useful for interethnic comparison of body composition. In the northern Indian population, the predictable cut-off level of the BMI undervalues overweight and obesity when percentage BF is used as the standard to define overweight. These preliminary findings, if confirmed in a larger number of subjects and with the use of instruments having a higher accuracy of BF assessment, would be crucial for planning and the inhibition and treatment of various obesity-related metabolic diseases in the Asian Indian population. Moderate expansion of body fat is mainly due to FCW enlargement, which is subsequently followed by increased FCN. Men and women

with a male abdominal type of obesity are more liable to the effect of excess body fat on lipid and glucose metabolism.

Chandalia et al[66], conducted a study to evaluate whether Asian Indians are more insulin resistant than Caucasians and to define the role of generalised and truncal adiposity, they performed hydro densitometry, skinfold measurements, and euglycemic-hyper insulinemic clamps in 21 healthy Asian Indian men and 23 Caucasian men of similar age and body fat content. The glucose disposal rate (Rd) was significantly lower in the Asian Indians than in the Caucasians (3.7 ± 1.3 *vs.* 5.3 ± 2.0 mg/min·kg lean body mass, respectively; $P = 0.003$). Despite similar total body fat content, Asian Indians had higher truncal adiposity than Caucasians (sum of truncal skinfolds, 117 ± 37 and 92.4 ± 38 mm, respectively). In both Asian Indians and Caucasians, the insulin sensitivity index (Rd/plasma insulin concentrations) was inversely correlated with both total body fat ($r = -0.49$; $P < 0.03$ and $r = -0.67$; $P < 0.001$, respectively) and sum of truncal skinfold thickness ($r = -0.55$; $P < 0.001$ and $r = -0.61$; $P < 0.002$, respectively). After adjustment for total body fat and truncal skinfold thickness, Asian Indians still had a significantly lower glucose disposal rate ($P = 0.04$). These results show that Asian Indian men are more insulin resistant than Caucasian men independently of generalised or truncal adiposity. The severe insulin resistance in Asian Indians is probably a primary metabolic defect and may account for the increased morbidity and mortality from diabetes and coronary heart disease in this population.

Ramchandran et al[67], assessed the prevalence of NIDDM and IGT in the urban and rural areas in southern India. Two populaces of the same ethnic background, but different socioeconomic background was chosen for this study. Nine-hundred urban

people and 1038 rural subjects were studied. Fasting and 2-h post-glucose capillary blood samples after a 75 g oral glucose load (WHO criteria) were obtained in these randomly selected adults (>20 yr of age). RESULTS — Using the WHO criteria, the prevalence of NIDDM, adjusted to the age of the respective general population, was 8.2% in the urban and 2.4% in the rural populations. The prevalence was 8.4 and 7.9%, respectively, in urban men and women, and 2.6 and 1.6% in rural men and women. The age-adjusted prevalence of IGT was 8.7 and 7.8% in the urban and rural areas, respectively. The prevalence of IGT was 8.8% in urban men and 8.3% in women; the corresponding values for rural men and women were 8.7 and 6.4%. The prevalence of NIDDM increased with age, markedly so in the urban people. The urban-rural difference was significant for NIDDM ($x2 = 29.4$, $P < 0.001$) but not for IGT. In the urban population, 65% of the NIDDM patients were known cases, whereas in the rural area, the known cases accounted for only 24%. Bivariate analysis showed an association of BMI, STR, and WHR with the prevalence of NIDDM plus IGT. In the multiple logistic regression analysis, age, BMI, STR, and WHR were associated significantly with glucose intolerance in the urban population, whereas only age was significant in the rural population. The best predictors of NIDDM were age, BMI, WHR, and urbanisation. This study showed an increased prevalence of NIDDM among the southern Indian population.

Singh RB et al.[68] Central obesity in association with insulin resistance is a strong predictor of coronary artery disease (CAD) in South Asians; however, the prevalence of central obesity and insulin resistance in Indians are unknown. Anthropometric measurements, dietary intakes, physical activity and prevalence of risk factors and CAD were obtained in 152 adults between 26-65 years of age (80 males, 72 females)

selected by random sampling from the urban population of Moradabad. The overall prevalence of central obesity was 539 per 1000 adults including 56.2% in males and 51.3% in females. The prevalence of glucose intolerance, diabetes mellitus, hypertension, hypertriglyceridemia and CAD were significantly higher in the higher quintiles of WHR above 0.88 compared to lower quintiles. Fasting and postprandial glucose, plasma insulin and triglycerides as wells total cholesterol and blood pressure were significantly higher in each of the upper quintile of WHR with an increase in WHR compared to the lowest quintile of WHR below 0.81. These findings indicate the existence of an adequate degree of insulin resistance with a modest tendency to central obesity in the urban population of North India. The prevalence of CAD was significantly ($p < 0.01$) higher among subjects with central obesity than in non-obese subjects (21.5 vs 3.2%). Underlying these findings, the prevalence of central obesity was significantly greater among sedentary and mild activity group compared to moderate and heavy activity group and per day energy expenditure during activity in the upper quintiles with WHR > 0.88 was significantly less compared to energy expenditure in lower quintiles of WHR. Similarly, dietary fat intake in the upper quintiles of WHR was also significantly higher than in the lower quintiles of WHR. These findings suggest that populations with a higher prevalence of central obesity and CAD may be benefited with an aim to decrease central obesity.

Gupta et al.[69] Epidemiological study among urban subjects in western India to determine the prevalence of diabetes, insulin resistance syndrome (IRS) and their risk factors. Randomly selected adults ≥20 years were studied using stratified sampling. The target sample was 1800 (men 960, women 840). 1123 subjects (response 62.4%) were evaluated and blood samples were available in 532 men and 559 women

(*n*=1091, 60.6%). Measurement of anthropometric variables, blood pressure, fasting blood glucose and lipids was performed. Atherosclerosis risk factors were determined using current guidelines. Diabetes was diagnosed when the subject was a known diabetic or fasting blood glucose was ≥126 mg/dl, impaired fasting glucose(IFG) diagnosed when fasting glucose was 110–125 mg/dl. IRS was diagnosed when any three of–IFG, high triglycerides >150 mg/dl, low HDL cholesterol (men<40 mg/dl, women<50 mg/dl), central obesity (men>102 cm, women>88 cm), or high normal blood pressure (>130/>85 mmHg) or hypertension-were present. Diabetes was present in 70 men (13.2%) and 64 women (11.5%). Age-adjusted prevalence of diabetes was 9.3% in men (95% confidence intervals (CI) 6.7–11.8), 8.1% in women (CI 5.8–10.4) and 8.6% overall (CI 6.9–10.3). IFG was in 28 men (5.3%) and 29 women (5.2%). IRS was present in 52 men (9.8%) and 114 women (20.4%) with the age-adjusted prevalence of 7.9% in men (CI 6.7–9.1) and 17.5% in women (CI 14.4–20.6) with an overall prevalence of 12.8% (CI 10.8–14.8). Other metabolic abnormalities of IRS in men and women were high triglycerides in 32.1 and 28.6%, low HDL cholesterol in 54.9 and 90.2%; central obesity in 21.8 and 44.0%, and high normal blood pressure or hypertension in 35.5 and 32.4%. IFG subjects had similar atherosclerosis risk factor profile as normal subjects while those with IRS and diabetes had a significantly greater prevalence of obesity, central obesity, hypertension, high triglycerides and low HDL (*P*<0.01). There was a momentous prevalence of diabetes and IRS in this urban Indian population. Subjects with diabetes as well as IRS have a greater prevalence of obesity, central obesity, hypertension, hypertriglyceridemia and low HDL as compared with normal subjects.

LACUNAE OF LITERATURE:

The incidence and prevalence of diabetes mellitus is increasing over the years globally. Insulin resistance is a presumptive state of type 2 diabetes and literature gathered in regards to IR in relation to the obese population is enormous. However, the IR studied among the lean population is least and its associated factors are still very primitive. Studies till date which have gathered evidence on the lean subjects with IR are usually associated with a strong genetic predisposition, but further research should be encouraged to find the associated factors of IR among lean subjects.

METHODOLOGY

MATERIALS & METHODS

Study site: This study was conducted in the department of General Medicine at R L Jalappa hospital, Kolar.

Study population: All lean and obese type 2 diabetic patients presenting to the medicine department of RL Jalappa Hospital were considered as the study population.

Study design: The current study was a cross sectional study

Sample size: Prevalence of 50% is assumed, and an absolute error of 5 is taken. Z alpha value at 95% confidence interval is 1.96. From the above calculation, a sample size of 106 is obtained. Of these lean and obese type, 2 diabetic patients will be taken in the ratio of 1:4. Of these 20% of the total sample size will be lean type 2 diabetic patients.

Sampling method: All the eligible subjects were recruited into the study consecutively by convenient sampling till the sample size is reached.

Study duration: The data collection for the study was done between January 2018 to July 2019 for a period of 1.5 years.

Inclusion Criteria:

- Patients more than 18 years of age with type 2 diabetes mellitus.

Exclusion criteria:

- Known cases of thyroid, pituitary or adrenal disorders.
- Patients who are taking beta-agonists, thiazides, hydantoins and steroids.

Ethical considerations: Study was approved by institutional human ethics committee. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of

participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained.

Data collection tools: All the relevant parameters were documented in a structured study proforma.

Methodology:

The study was conducted among lean and obese type 2 diabetic patients presenting to the medicine department of RL Jalappa Hospital. A written informed consent was obtained from the patients or their relatives.

BMI of type 2 diabetic patients was calculated. Diabetic patients with a BMI value of less than 19 were categorized as group 1 (lean diabetic patients) [6] and those with BMI more than 30 were categorized as group 2 (obese diabetic patients).

Laboratory investigations included fasting insulin level, fasting glucose level and c-peptide level in plasma are measured. Insulin resistance of patients was calculated from both groups using HOMA-IR (Homeostasis Model Assessment).

Investigations:

- Fasting glucose levels
- Fasting insulin levels
- C-peptide

Statistical Methods:

Insulin resistant was considered as the primary outcome variable. Lean/Obese was considered as Primary explanatory variable. Age, gender, GHB, FBs etc., were considered as Other explanatory variables.

Descriptive analysis: Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like a bar diagram, pie diagram.

Categorical outcome:

The association between explanatory variables and categorical outcomes was assessed by cross tabulation and comparison of percentages. Odds ratio along with 95% CI is presented. Chi square test was used to test statistical significance.

P value < 0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.[70]

RESULTS

RESULT

A total of 106 subjects were included in the analysis.

Table 1: Descriptive analysis of age in the study population (N=106)

Parameter	Mean ± SD	Median	Minimum	Maximum	95% C.I	
					Lower	Upper
Age	53.88 ± 9.21	54.50	32.00	70.00	52.10	55.65

The mean age was 53.88 ± 9.21 in the study population, ranged between 32 years to 70 years (95% CI 52.10 to 55.65). (Table 1)

Table 2: Descriptive analysis of gender in the study population (N=106)

Gender	Frequency	Percentages
Male	65	61.3%
Female	41	38.7%

Among the study population, 65 (61.3%) were participants male and remaining 41 (38.7%) participants were female. (Table 2 & Figure 1)

Figure 1: Pie chart of gender in the study population (N=106)

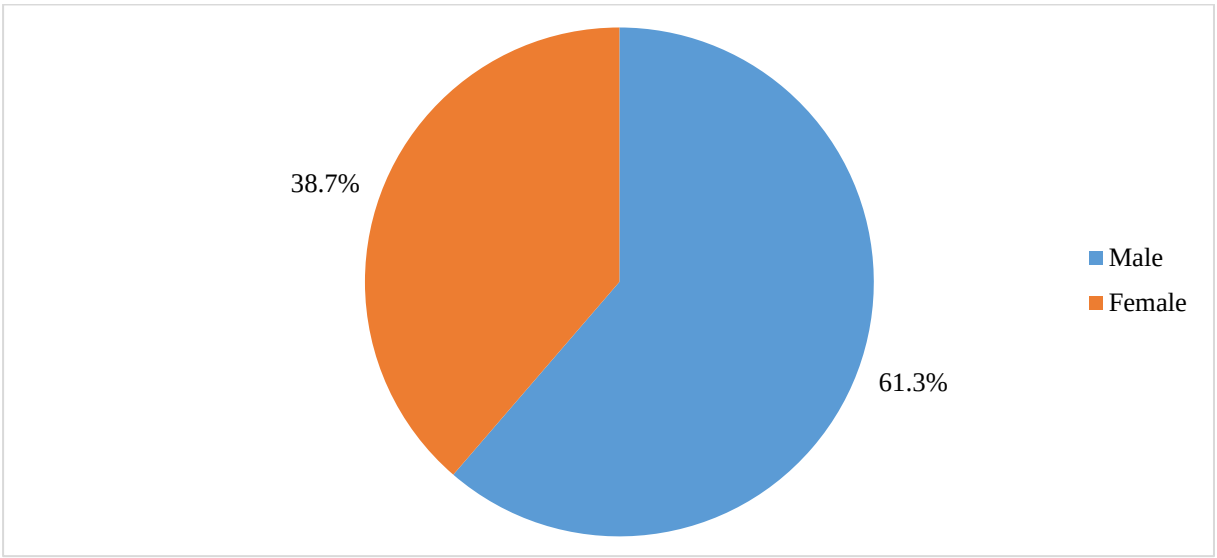

Table 3: Descriptive analysis of BMI in the study population (N=106)

Parameter	Mean ± SD	Median	Minimum	Maximum	95% C.I	
					Lower	Upper
BMI	29.27 ± 5.84	31.00	17.90	38.00	28.14	30.39

The mean BMI was 29.27 ± 5.84 in the study population, ranged between 17.90 to 38 (95% CI 28.14 to 30.39). (Table 3)

Table 4: Descriptive analysis of lean/obese diabetes in the study population (N=106)

Lean/Obese Diabetes	Frequency	Percentages
Lean	22	20.8%
Obese	84	79.2%

Among the study population, Majority of the 79.2% participant were obese, remaining 20.8% were lean. (Table 4 & Figure 2)

Figure 2: Bar chart of lean/obese diabetes in the study population (N=106)

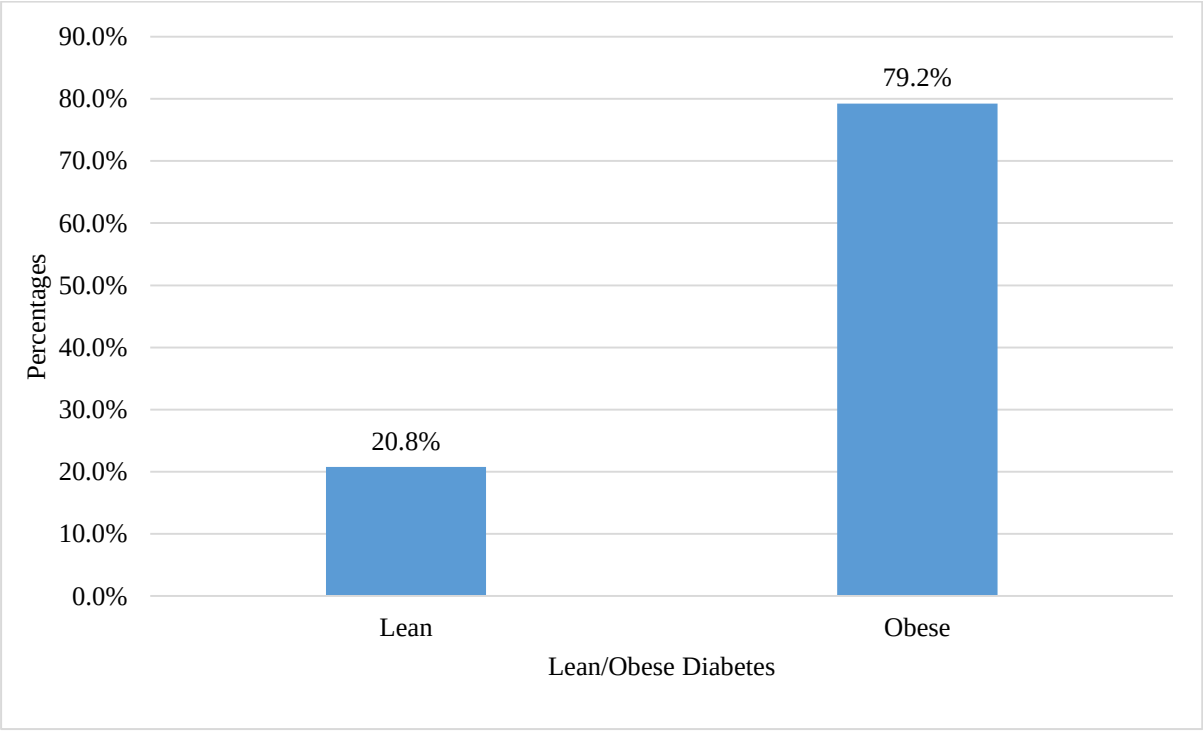

Table 5: Descriptive analysis of parameters in the study population (N=106)

Parameter	Mean ± SD	Median	Minimum	Maximum	95% C.I	
					Lower	Upper
GHB (mmol/mol)	9.25 ± 2.96	8.40	4.80	18.80	8.68	9.82
FBS (mmol/L)	8.58 ± 2.22	8.30	3.90	14.40	8.15	9.01
Fasting Insulin (mIU/L)	7.34 ± 7.26	5.05	1.00	33.10	5.95	8.74
C-Peptide	1.87 ± 2.15	1.22	0.05	14.40	1.46	2.28
Homa- Ir	2.56 ± 2.09	1.87	0.27	7.56	2.15	2.96

The mean GHB was 9.25 ± 2.96 (mmol/mol) in the study population, ranged between 4.80 to 18.80 (95% CI 8.68 to 9.82). The mean FBS was 8.58 ± 2.22mmol/L in the study population, ranged between 3.90 to 14.40 (95% CI 8.15 to 9.01). The mean fasting insulin was 7.34 ± 7.26 (mIU/L) in the study population, ranged between 1 to 33.10 (95% CI 5.95 to 8.74). The mean c-peptide was 1.87 ± 2.15in the study population, ranged between 0.05 to 14.40 (95% CI 1.46 to 2.28).The mean homa-IR was 2.56 ± 2.09in the study population, ranged between 0.27 to 7.56 (95% CI 2.15 to 2.96). (Table 5)

Table 6: Descriptive analysis of insulin resistant in the study population (N=106)

Insulin Resistant	Frequency	Percentages
Yes	44	41.5%
No	62	58.5%

Among the study population, 44 (41.5%) participants were taken insulin resistant. (Table 6 & Figure 3)

Figure 3: Pie chart of insulin resistant in the study population (N=106)

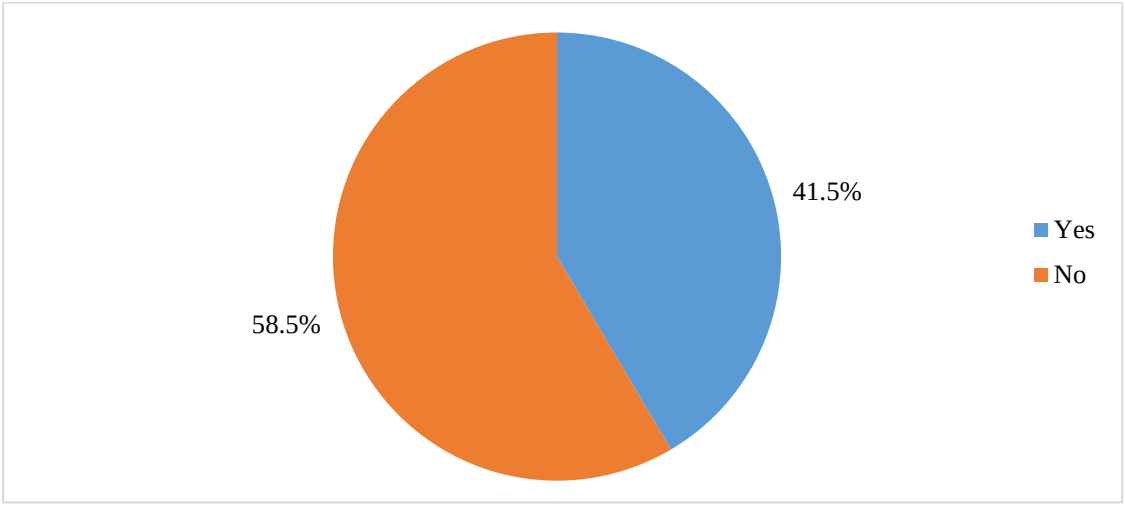

Table 7: Comparison of age group between lean/obese diabetes (N=106)

Age Group	Lean/Obese Diabetes		Chi square	P value
	Lean (N=22)	Obese (N=84)		
Up To 40	4 (18.18%)	8 (9.52%)	3.513	0.319
41 To 50	4 (18.18%)	25 (29.76%)		
51 To 60	6 (27.27%)	31 (36.9%)		
>60	8 (36.36%)	20 (23.81%)		

The difference in lean/obese across the age groups is found to be insignificant with a P- value of 0.319. (Table 7 & Figure 4)

Figure 4: Cluster bar chart of comparison of age group between lean/obese diabetes (N=106)

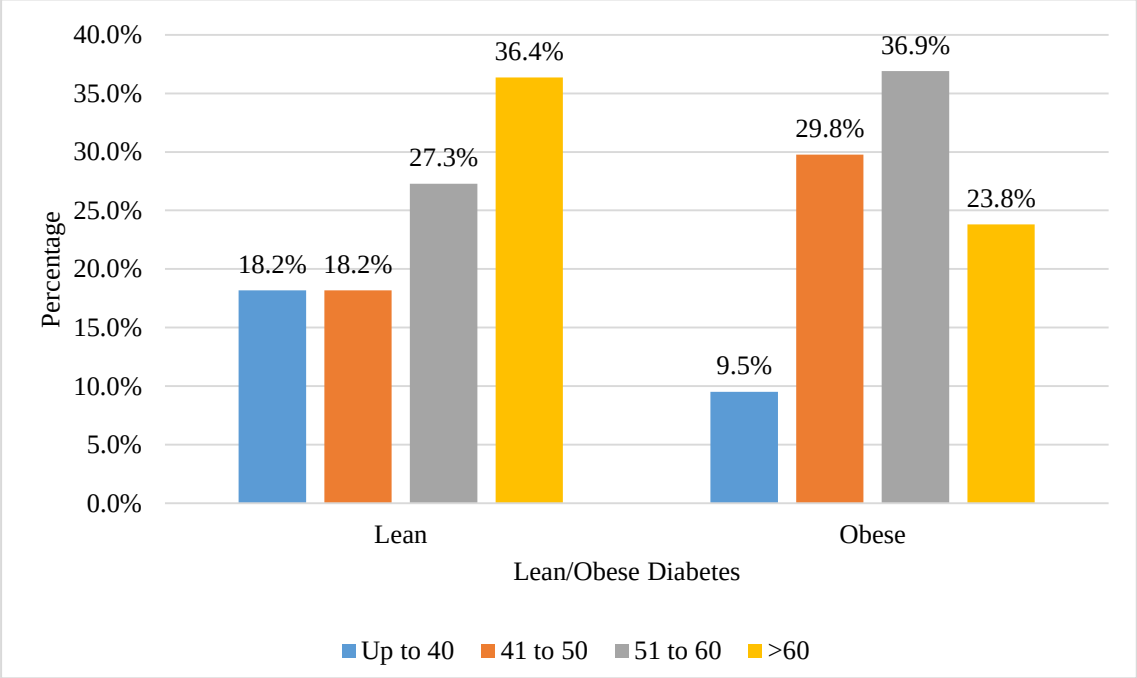

Table 8: Comparison of gender between lean/obese diabetes (N=106)

Gender	Lean/Obese Diabetes		Chi square	P value
	Lean (N=22)	Obese (N=84)		
Male	13 (59.09%)	52 (61.9%)	0.058	0.809
Female	9 (40.91%)	32 (38.1%)		

The difference in lean/obese between gender is found to be insignificant, with a P-value of 0.809. (Table 8 & Figure 5)

Figure 5: Stacked bar chart of comparison of gender between lean/obese diabetes (N=106)

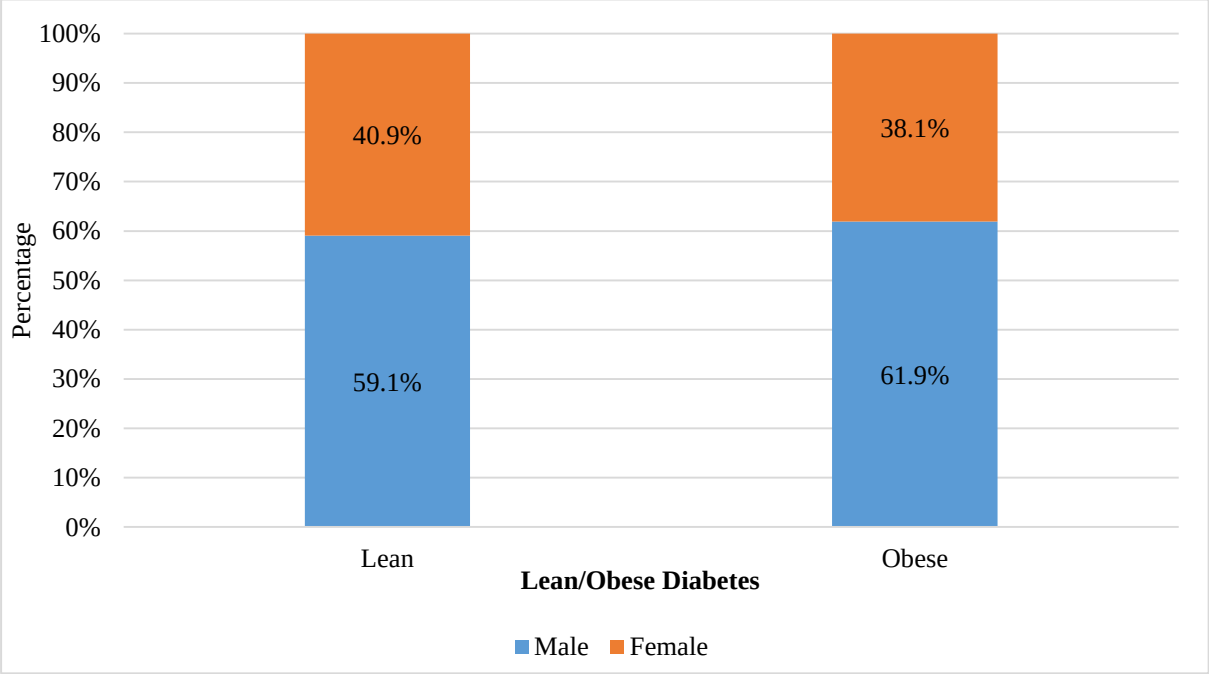

Table 9: Comparison of insulin resistant between lean/obese diabetes (N=106)

Insulin Resistant	Lean/Obese Diabetes		Chi square	P value
	Lean (N=22)	Obese (N=84)		
Yes	12 (54.55%)	32 (38.1%)	1.943	0.163
No	10 (45.45%)	52 (61.9%)		

The difference in lean/obese between insulin resistant is found to be insignificant, with a P- value of 0.163. (Table 9 & Figure 6)

Figure 6: Cluster bar chart of Comparison of insulin resistant between lean/obese diabetes (N=106)

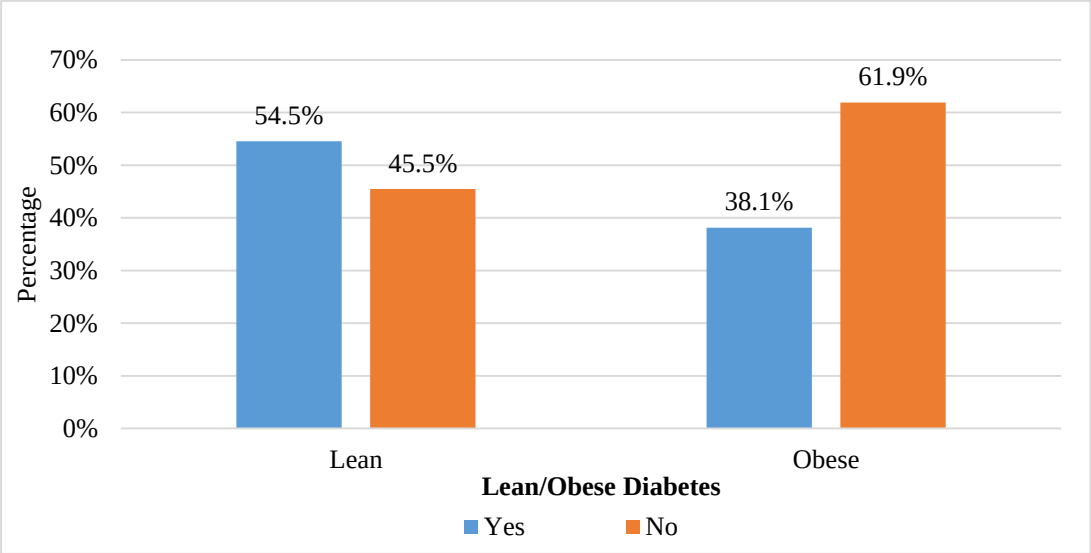

Table 10: Factors associated with insulin resistant in study population univariate logistic regression analysis

Factor	Un adjusted odds ratio	95 % CI of odds ratio		P value
		lower	upper	
Age group (Base line= >60)				
Up to 40	.600	.131	2.738	0.510
41 to 50	1.462	.504	4.240	0.484
51 to 60	1.705	.623	4.666	0.299
Lean (baseline= Obese)	1.950	.756	5.031	0.167
Male (baseline=female)	1.653	.736	3.712	0.223
GHB	1.036	.909	1.181	0.594
FBS	1.049	.881	1.249	0.592
Fasting Insulin	2.442	1.665	3.581	<0.001
C-peptide	1.446	1.123	1.861	0.004

During univariate logistic regression analysis, the factors which have shown statistically significant association were fasting insulin and C-peptide. (Table 10)

DISCUSSION

DISCUSSION

Diabetes is the most common and prevalent metabolic disorder worldwide. Obesity is one of the various factors which contributes considerably greater to the prevalence of diabetes mellitus. However, the population with lesser BMI or lean have also shown its association to diabetes due to genetic predisposition. Hence the present study was conducted to accesses the relationship between insulin resistance in lean and obese type 2 diabetes mellitus patients.

The current study involved 106 subjects with a mean age of 53.88 ± 9.21 years. The proportion of male subjects 65 (61.3%) were greater compared to female subjects 41 (38.7%). The study population had a greater proportion of obese subjects 84 (79.2%) compared to lean subjects 22 (20.8%). A similar study by Gonzalez-Cantero J et al[71], had study subjects 113 with a mean age of 45.1± 10.2 years with almost equal distribution of genders. In another study, the authors have studied insulin resistance in females in particular with polycystic ovarian disease among lean subjects only.[72]

The mean BMI was 29.27 ± 5.84 in the study population, ranged between 17.90 to 38 (95% CI 28.14 to 30.39). The mean GHB was 9.25 ± 2.96 in the study population, ranged between 4.80 to 18.80 (95% CI 8.68 to 9.82). The mean FBS was 8.58 ± 2.22 in the study population, ranged between 3.90 to 14.40 (95% CI 8.15 to 9.01). The mean fasting insulin was 7.34 ± 7.26 in the study population, ranged between 1 to 33.10 (95% CI 5.95 to 8.74).

The mean c-peptide was 1.87 ± 2.15 in the study population, ranged between 0.05 to 14.40 (95% CI 1.46 to 2.28). The mean HOMA-IR was 2.56 ± 2.09 in the study

population, ranged between 0.27 to 7.56 (95% CI 2.15 to 2.96). Among the study population, 44 (41.5%) participants were taken insulin resistant. The difference in lean/obese across the age groups is found to be insignificant with a P- value of 0.319. The difference in lean/obese between gender is found to be insignificant, with a P-value of 0.809. The difference in lean/obese between insulin resistant is found to be insignificant with a P- value of 0.163. During univariate logistic regression analysis, the factors which have shown statistically significant association were fasting insulin and C-peptide.

Over the years, high levels of C- peptide has been studied as a useful marker for metabolic syndrome, death due to insulin resistance and cardiovascular complications among various racial.[73, 74] A study by Anoop S et al[75], was the first study which correlated C-peptide and fasting Insulin in nonobese and non-lean type 2 diabetic patients among North Indians. They found high C-peptide levels in normal BMI patients with Type 2 diabetes among North Indian population. The present study has also found a significant association of fasting insulin and c-peptide but among both lean and obese type 2 diabetic patients. The c peptide levels and fasting insulin showed no statistical difference among the lean and obese group. Further from past literature, the non- obese diabetics can be characterized based on BMI. This found to be grouped as 2, which are lean with BMI<19kg/m2 and non- lean and non -obese with BMI >19Kg/m^2.[75] The pathophysiology of diabetes type 2 has known to be related with obesity, perhaps in lean and non-obese groups the pathophysiology might differ.

Several reasons for diabetes among the lean population could be due to LADA(late-onset of auto immune diabetes), MODY (maturity-onset diabetes in young), chronic calcific pancreatitis etc.[75] However, in the present study, these conditions in lean diabetic patients was not suitable. A previous study on South Asian Indians showed lean type 2 diabetic population had normal levels of C-peptide, less serum insulin and were negative for autoimmune markers.[76] Lean individuals with type 2 diabetes especially among Indians, have certain unique insulin kinetics, with a different profile and enzymatic behavior related to carbohydrate breakdown. Further, these patients had less susceptibility for macrovascular disease.[77] A study by Misra A et al[78], witnessed NAFLD, increased body fat and abdominal in non -lean and non-obese Diabetic Indians. Hence these results reflect the disturbed metabolic condition in Indian racial group with BMI levels of non -obese group.[79] Further, the evidence was strengthened by Petersen et al[80], were they examined healthy young non-obese adults of 5 racial, which included Asian Indians also. The authors found greater prevalence rate of insulin resistance among Indians compared to others. Other contributing factors such as triglycerides, proinflammatory markers were found higher among Asian Indians compared to the counterparts of the study.[80] While the other study conducted in Singapore, on a normal lean individual with BMI <23kg/m2 among 24 Indians, 14 Chinese and 21 Malays, witnessed Indians with greater waist circumference, body fat and were less insulin sensitive compared to other racial groups in spite of alike BMI.[81]

Further when we observe the results of Petersen et al[80], and Tan VM et al[81], it is clearly evident that Asian Indians had greater resistance to insulin and inflammation of subclinical in nature among non-obese Indians. Although, Asian Indians had BMI levels of the non-obese group, their body fat, waist circumference and triglycerides

were higher. Thus, this leads to an inclination to develop diabetes among Indians than the other racial. Other studies have shown greater volume of subcutaneous fat cells with insulin resistance and greater influx of free fatty acid among Indians with hyperactivity of genes related to inflammation.[82,83] The genetic association such as polymorphism in gene PNPLA 3 (palatin-like like phospholipase-3) and PPAR-g (peroxisome proliferator-activated receptor-gamma) have been found by few genetic studies.[84, 85]

An evidence by various studies have shown an increased susceptibility of Indians to IR even in individuals with BMI falling within the range of non-obese and obese diabetic and nondiabetics. Through these studies, it is noticed that Asian Indians of both lean and obese show increased IR aggravating the prevalence of type 2 diabetes in India. However, the present study results were inclusive due to inadequate sample size and small number of lean diabetics involved

CONCLUSION

CONCLUSION

The current cross-sectional study involved 106 subjects with a mean age of 53.88 ± 9.21 years. There was male preponderance 65 (61.3%) among the study population compared to females 41 (38.7%). The percentage of obese diabetic subjects 84 (79.2%) was greater compared to lean diabetics 22 (20.8%).The mean BMI was 29.27 ± 5.84 in the study population, ranged between 17.90 to 38 (95% CI 28.14 to 30.39). The mean GHB was 9.25 ± 2.96 in the study population, ranged between 4.80 to 18.80 (95% CI 8.68 to 9.82). The mean FBS was 8.58 ± 2.22 in the study population, ranged between 3.90 to 14.40 (95% CI 8.15 to 9.01). The mean fasting insulin was 7.34 ± 7.26 in the study population, ranged between 1 to 33.10 (95% CI 5.95 to 8.74). The mean c-peptide was 1.87 ± 2.15 in the study population, ranged between 0.05 to 14.40 (95% CI 1.46 to 2.28). The mean HOMA-IR was 2.56 ± 2.09 in the study population, ranged between 0.27 to 7.56 (95% CI 2.15 to 2.96). Among the study population, 44 (41.5%) participants were taken insulin resistant. The difference in lean/obese across the age groups is found to be insignificant with a P- value of 0.319. The difference in lean/obese between gender is found to be insignificant, with a P-value of 0.809. The difference in lean/obese between insulin resistant is found to be insignificant with a P- value of 0.163. During univariate logistic regression analysis, the factors which have shown statistically significant association were fasting insulin and C-peptide. Due to inadequate sample size of 2 groups, the statistical analysis showed inconclusive results. Hence further studies with adequate sampling technique with a control group are required to validate the results.

Limitations and Recommendation

Inadequate sample size of 2 groups with a smaller number of subjects among the lean group allowed statistical analysis with inconclusive results.

Other factors which define insulin resistance such as waist circumference, hepatic glycerides levels, NAFDL could have been include for the analysis.

Hence further studies with adequate sampling technique with a control group are required to validate the results

SUMMARY

SUMMARY

The metabolic disorder most prevalent across countries is diabetes mellitus. The insulin resistance is usually a precursor sign of type 2 DM. Insulin resistance is often related with factors such as increased weight, NAFDL (non-alcoholic fatty liver disease), metabolic syndrome and increased fat accumulation around the liver. There is accumulated evidence of insulin resistance among obese individuals compared to lean subjects. However, a review of the literature has also shown an increased susceptibility of lean individuals to insulin resistance. Hence the present study we aimed to study the correlation between insulin resistance (by HOMA-IR) in lean and obese type 2 diabetes mellitus patients.

The current cross-sectional study involved 106 subjects with a mean age of 53.88 ± 9.21 years. There was male preponderance 65 (61.3%) among the study population compared to females 41 (38.7%). The percentage of obese diabetic subjects 84 (79.2%) was greater compared to lean diabetics 22 (20.8%). The mean BMI was 29.27 ± 5.84 in the study population, ranged between 17.90 to 38 (95% CI 28.14 to 30.39). The mean GHB was 9.25 ± 2.96 in the study population, ranged between 4.80 to 18.80 (95% CI 8.68 to 9.82). The mean FBS was 8.58 ± 2.22 in the study population, ranged between 3.90 to 14.40 (95% CI 8.15 to 9.01). The mean fasting insulin was 7.34 ± 7.26 in the study population, ranged between 1 to 33.10 (95% CI 5.95 to 8.74).

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The difference in lean/obese between gender is found to be insignificant with a P-value of 0.809. The difference in lean/obese between insulin resistant is found to be insignificant with a P- value of 0.163. During univariate logistic regression analysis, the factors which have shown statistically significant association were fasting insulin and C-peptide.

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ANNEXURES

ANNEXURES

PROFORMA

Name: Date:

Age / Sex:

Residential Address:

Mobile No:

Email ID:

Case History:

Other known Illness:

Family & Personal History:

BP: Pulse rate:

CVS-
RS-
P/A-
CNS-
Outcome Measures:

BMI	
Fasting Insulin levels	
Fasting Glucose levels	
C-Peptide levels	
HOMA-IR level	

Signature

PATIENT INFORMATION SHEET

Study Title: **Correlation of insulin resistance in lean and obese patients with type 2 diabetes mellitus.**

Study site: R.L Jalappa hospital, Tamaka, Kolar.

Aim: To Correlate insulin resistance in lean and obese patients with type 2 diabetes mellitus.

Type 2 diabetes mellitus associated with obesity and insulin resistance which are important in the causation of the type 2 diabetes mellitus. Patients with diabetes who are lean have younger age of onset, high prevalence in male population, poor glycemic control and higher mortality rates. We aim to study the importance of insulin resistance in lean as well as obese type 2 diabetes persons which is an important therapeutic target for oral antidiabetic drugs.

5 ml of venous blood will be taken from the median cubital vein and sent for Fasting Glucose, Fasting insulin and C- peptide levels. This information is intended to give you the general background of the study. Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in the study we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for dissertation and publication.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For any further clarification you can contact the study investigator:

Dr. S. Deepa

Mobile no: 9591955300

E-mail id: Sandinti.reddy@gmail.com

CONSENT FORM

I ---------- participant, hereby give consent to participate in the study entitled "**Correlation of insulin resistance in lean and obese patients with type 2 diabetes mellitus.**"

I have been explained that;

1. I would have to provide a blood sample for the study purpose.
2. I have to answer the questionnaires related to project.
3. I do not have to incur any additional expenditure on my inclusion into the study.
4. The data generated from my clinical examination and laboratory tests and other reports will be used in the study (which may be subsequently published) without revealing my identity in any manner.

I affirm that I have been given full information about the purpose of the study and the procedures involved and have been given ample opportunity to clarify my doubts in my mother tongue. In giving my consent, I have not faced any coercion. I have been informed that, notwithstanding this consent given, I can withdraw from the study at any stage.

For any further clarification you can contact the study investigator:

Dr. S. Deepa

Mobile no: 9591955300

E-mail id: Sandinti.reddy@gmail.com

Signature & Name of the participant: Place:

Signature & Name of the witness: Date:

Signature of the Investigator:

ತಿಳಿವಳಿಕೆಯ ಸಮ್ಮತಿ ನಮೂನೆ

ರೋಗಿಯ ಮಾಹಿತಿನಮೂನೆ

ಯೋಜನೆಯ ಹೆಸರು	ಟೈಪ್ 2 ಮಧುಮೇಹತೆಳುವಾದ ಮತ್ತು ಬೊಜ್ಜು ರೋಗಿಗಳಲ್ಲಿ ಇನ್ಸುಲಿನ್ ಪ್ರತಿರೋಧದ ಪರಸ್ಪರ ಸಂಬಂಧ.
ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ ಹೆಸರು	ಡಾ. ಎಸ್.ದೀಪಾ
ಸಂಸ್ಥೆಯ ಹೆಸರು	ಶ್ರೀ ದೇವರಾಜ್ ಉರ್ಸ್ ವೈದ್ಯಕೀಯ ಕಾಲೇಜು ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ, ತಮಕ, ಕೋಲಾರ

ಪಾಲ್ಗೊಳ್ಳುವವರ ಹೆಸರು: ವಯಸ್ಸು: ಸಂಖ್ಯೆ:

ಅಧ್ಯಯನದ ಉದ್ದೇಶ:ಟೈಪ್ 2 ಮಧುಮೇಹಸ್ಥೂಲಕಾಯತೆ ಮತ್ತು ಇನ್ಸುಲಿನ್ ನಿರೋಧಕತೆಯೊಂದಿಗೆ ಸಂಬಂಧಿಸಿದೆ, ಇದುಟೈಪ್ 2 ಮಧುಮೇಹದ ಕಾರಣವಾಗಿದೆ. ಮಧುಮೇಹ ಹೊಂದಿರುವ ತೆಳುವಾದ ರೋಗಿಗಳು ಆಕ್ರಮಣಕ್ಕೆ ಕಿರಿಯ ವಯಸ್ಸಿನವರು, ಪುರುಷ ಜನಸಂಖ್ಯೆಯಲ್ಲಿ ಹೆಚ್ಚಿನ ಪ್ರಮಾಣದಲ್ಲಿದ್ದಾರೆ, ಕಳಪೆ ಗ್ಲೈಸೆಮಿಕ್ ನಿಯಂತ್ರಣ ಮತ್ತು ಹೆಚ್ಚಿನ ಮರಣ ಪ್ರಮಾಣಗಳು. ಬಾಯಿಯಲ್ಲಿರುವ ಇನ್ಸುಲಿನ್ ಪ್ರತಿರೋಧದ ಪ್ರಾಮುಖ್ಯತೆ ಮತ್ತು ಬೊಜ್ಜು ಟೈಪ್ 2 ಡಯಾಬಿಟಿಸ್ ವ್ಯಕ್ತಿಗಳನ್ನು ಮೌಖಿಕ ಪ್ರತಿಜೀವಕ ಔಷಧಿಗಳ ಪ್ರಮುಖ ಚಿಕಿತ್ಸಕ ಗುರಿ ಎಂದು ನಾವು ಅಧ್ಯಯನ ನಡೆಸುತ್ತೇವೆ.

ಸ್ವಯಂಪ್ರೇರಿತ ಭಾಗವಹಿಸುವಿಕೆ:ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆ ಸಂಪೂರ್ಣವಾಗಿ ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿರುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಯಾವುದೇ ನಿರ್ಬಂಧವಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನೀವು ಭಾಗವಹಿಸಲು ಬಯಸದಿದ್ದರೆ ನೀವು ಯಾವುದೇ ರೀತಿಯಲ್ಲಿ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಕೊಳ್ಳುವುದಾದರೆ ಮಾತ್ರ ಹೆಬ್ಬೆರಳು ಅನಿಸಿಕೆಗೆ ನೀವು ಸಹಿ / ನೀಡಬೇಕಾಗಿದೆ. ಮತ್ತಷ್ಟು ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂಪಡೆಯಲು ಸ್ವತಂತ್ರರಾಗಿರುತ್ತಾರೆ. ನಿಮ್ಮ ಹಿಂತೆಗೆದುಕೊಳ್ಳುವಿಕೆಯು ನಿಮ್ಮ ಚಿಕಿತ್ಸೆಯನ್ನು ಯಾವುದೇ ರೀತಿಯಲ್ಲಿ ಯಾವುದೇ ವೈದ್ಯರ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ ಎಂದು ನಾವು ನಿಮಗೆ ಭರವಸೆ ನೀಡುತ್ತೇವೆ.

ವಿಧಾನ:ನಿಮ್ಮ ತೋಳಿನಿಂದ ನಾವು ಸ್ವಲ್ಪ ಪ್ರಮಾಣದ ರಕ್ತವನ್ನು (6 ಮಿಲಿ) ಸಂಗ್ರಹಿಸುತ್ತೇವೆ. ಮಾದರಿ ರೋಗ ಮತ್ತು ಜೈವಿಕ ಪರೀಕ್ಷೆಗಾಗಿ ಬಳಸಲಾಗುತ್ತದೆ.

ಅವಧಿ:ಸಂಶೋಧನೆಯು 1 ವರ್ಷ ಅವಧಿಯವರೆಗೆ ನಡೆಯುತ್ತದೆ.

ಅಪಾಯಗಳು:ನಿಮ್ಮ ಮೇಲೆ ಯಾವುದೇ ಔಷಧಿ ಪರೀಕ್ಷಿಸಲಾಗುವುದಿಲ್ಲ. ರಕ್ತವನ್ನು ಒಂದು ಬರಡಾದ ಮತ್ತು ಬಿಸಾಡಬಹುದಾದ ಸೂಜಿ ಮತ್ತು ಸಿರಿಂಜ್ ಬಳಸಿ ಸಂಗ್ರಹಿಸಲಾಗುತ್ತದೆ.

ಗೋಪ್ಯತೆ:ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಿದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿರಿಸಲಾಗುವುದು ಮತ್ತು ಕಾನೂನಿನ ಅಗತ್ಯವಿದ್ದರೆ ಹೊರತುಪಡಿಸಿ ಯಾರಿಗಾದರೂ ಅದನ್ನು ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಯೋಜನೆಯ ಶೋಧಕರು ಮಾತ್ರ ಗುರುತಿನ ವಿವರಗಳಿಗೆ ಪ್ರವೇಶವನ್ನು ಹೊಂದಿರುತ್ತಾರೆ.

ಫಲಿತಾಂಶಗಳನ್ನು ಹಂಚಿಕೆ:ಈ ಅಧ್ಯಯನದಿಂದ ಪಡೆದ ಫಲಿತಾಂಶಗಳನ್ನು ವೈಜ್ಞಾನಿಕ ಅಥವಾ ವೈದ್ಯಕೀಯ ನಿಯತಕಾಲಿಕಗಳಲ್ಲಿ ಅಥವಾ ವೈದ್ಯಕೀಯ ಸಮಾವೇಶಗಳಲ್ಲಿ ಪ್ರಕಟಿಸಲಾಗುತ್ತದೆ.

ಈ ಪ್ರಕ್ರಿಯೆಯಲ್ಲಿ ನಾವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ನಿಮ್ಮನ್ನು ಒತ್ತಾಯಿಸುವುದಿಲ್ಲ; ಸಹ, ನಾವು ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಸಹಕಾರವನ್ನು ಬಹಳವಾಗಿ ಶ್ಲಾಘಿಸುತ್ತೇವೆ. ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನಿಮ್ಮ ಒಪ್ಪಿಗೆಯನ್ನು ಪಡೆಯಲು ನಾವು ಬಯಸುತ್ತೇವೆ.

ಯಾವುದೇ ಮಾಹಿತಿಗಾಗಿ ನೀವು ತನಿಖೆದಾರನನ್ನು ಸಂಪರ್ಕಿಸಲು ಮುಕ್ತವಾಗಿರುತ್ತೀರಿ. ಈ ಅಧ್ಯಯನವನ್ನು ಸಾಂಸ್ಥಿಕ ನೀತಿಶಾಸ್ತ್ರ ಸಮಿತಿಯಿಂದ ಪರಿಶೀಲಿಸಲಾಗಿದೆ ಮತ್ತು ಅನುಮೋದಿಸಲಾಗಿದೆ ಮತ್ತು ಅವರ ಔಪಚಾರಿಕ ಅನುಮೋದನೆಯ ನಂತರ ಮಾತ್ರ ಪ್ರಾರಂಭಿಸಲಾಗಿದೆ. ಈ ಡಾಕ್ಯುಮೆಂಟ್ ಅನ್ನು ಮೆಡಿಸಿನ್ ಇಲಾಖೆಯ ಸುರಕ್ಷಿತ ಲಾಕರ್ನಲ್ಲಿ ಮತ್ತು ನಿಮ್ಮ ಮಾಹಿತಿಗಾಗಿ ನಿಮಗೆ ನೀಡಿದ ಪ್ರತಿಯನ್ನು ಸಂಗ್ರಹಿಸಲಾಗುತ್ತದೆ.

ಮತ್ತಷ್ಟು ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ನೀವು ಅಧ್ಯಯನ ಶೋಧಕವನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು:
ಡಾ. ಎಸ್.ದೀಪಾ (ಸ್ನಾತಕೋತ್ತರ ಪದವಿ)
ಜನರಲ್ ಮೆಡಿಸಿನ್ ಇಲಾಖೆ
SDUMC, ಕೋಲಾರ್
ಸಂಪರ್ಕ ಸಂಖ್ಯೆ: 9591955300

ಪರಿಶೀಲನೆ ಪ್ರಮಾಣೀಕರಣ

ಪಾಲ್ಗೊಳ್ಳುವವರ ಘೋಷಣೆ:

ಈ ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನನಗೆ ಆಹ್ವಾನಿಸಲಾಗಿದೆ. ನಾನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವಂತೆ ಕೇಳಿದೆ ಏಕೆಂದರೆ ನಾನು ಅರ್ಹತಾ ಮಾನದಂಡಗಳನ್ನು ಪೂರೈಸುತ್ತೇನೆ.

ನಾನು ಓದಿದ್ದೇನೆ ಅಥವಾ ನನಗೆ ಓದುತ್ತಿದ್ದೇನೆ ಮತ್ತು ಅಧ್ಯಯನದ ಉದ್ದೇಶ, ಬಳಸಲಾಗುವ ಕಾರ್ಯವಿಧಾನ, ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ನನ್ನ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಗೆ ಸಂಬಂಧಿಸಿರುವ ಲಾಭ ಮತ್ತು ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಸಂಗ್ರಹಿಸಿದ ಮತ್ತು ಬಹಿರಂಗಪಡಿಸುವ ಮಾಹಿತಿಯ ಸ್ವರೂಪವನ್ನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಪರೀಕ್ಷೆ, ಕಾರ್ಯವಿಧಾನ, ಸಂಬಂಧಿತ ಅಪಾಯ, ಪರ್ಯಾಯಗಳು ಮತ್ತು ಮಿತಿಗಳನ್ನು ನಾನು ಹೊಂದಿರಬಹುದಾದ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶವಿದೆ ಮತ್ತು ಯೋಗ್ಯ ಆರೋಗ್ಯ ವೃತ್ತಿಪರರಿಂದ ನನ್ನ ತೃಪ್ತಿಗೆ ನಾನು ಕೇಳಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರ ನೀಡಲಾಗಿದೆ.

ನಾನು ಯಾವ ಸಮಯದಲ್ಲಾದರೂ ಈ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆಗೆದುಕೊಳ್ಳಲು ಮುಕ್ತವಾಗಿರುತ್ತೇನೆ ಮತ್ತು ಇದು ನನ್ನ ಮುಂದಿನ ಕಾಳಜಿಯನ್ನು ಬದಲಿಸುವುದಿಲ್ಲ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ನಾನು, ಈ ಗೌಪ್ಯತೆ ನಿರ್ವಹಿಸಲ್ಪಡುವವರೆಗೆ ವೈದ್ಯಕೀಯ ಸಂಶೋಧನೆ, ಪರೀಕ್ಷೆ ಮೌಲ್ಯಮಾಪನ ಅಥವಾ ಶಿಕ್ಷಣಕ್ಕಾಗಿ ನನ್ನ ವೈಯಕ್ತಿಕ ಮಾಹಿತಿಯ ಸಂಗ್ರಹ ಮತ್ತು ಪ್ರಕಟಣೆಯನ್ನು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಕೊಳ್ಳುತ್ತೇನೆ ಮತ್ತು ಒಪ್ಪುತ್ತೇನೆ.

ರೋಗಿಯ ಹೆಸರು:
(ಪಾಲಕರು / ಪೋಷಕರ ಹೆಸರು):
ದಿನಾಂಕ:
ಸಹಿ / ಹೆಬ್ಬೆರಳು ಗುರುತು:

MASTER SHEET

Sl No	Age	Gender	IP No	BMI	Lean/Obese diabetes	GHb	FBS	Fasting Insulin	C-peptide	HOMA-IR	Insulin resistant
1	45	Male	689500	31.00	Obese	18.80	3.90	25.30	2.70	4.40	Yes
2	40	Male	202036	33.00	Obese	7.60	13.90	2.58	3.01	1.50	No
3	55	Female	675271	18.30	Lean	12.10	13.90	1.21	0.51	0.75	No
4	54	Male	689639	31.00	Obese	7.90	10.00	12.30	14.40	5.47	Yes
5	52	Male	670510	30.50	Obese	7.60	8.90	8.01	1.83	3.17	Yes
6	55	Female	689401	18.90	Lean	6.30	7.80	14.70	1.60	5.10	Yes
7	55	Male	688861	32.00	Obese	8.70	10.50	2.48	0.81	1.16	No
8	65	Male	684455	31.00	Obese	13.60	7.80	1.00	0.77	0.35	No
9	47	Male	156254	30.60	Obese	10.70	8.90	3.99	0.67	1.58	No
10	40	Female	685172	18.60	Lean	6.70	5.00	33.10	4.64	7.36	Yes
11	48	Female	688584	37.00	Obese	13.20	6.10	1.07	0.44	0.29	No
12	60	Female	686323	33.00	Obese	8.20	7.80	1.95	1.06	0.68	No
13	53	Female	164333	31.00	Obese	6.80	10.50	6.06	5.52	2.83	Yes
14	63	Male	688591	17.90	Lean	7.70	8.30	8.09	1.83	2.98	Yes
15	65	Female	680603	30.40	Obese	6.30	6.10	9.57	2.14	2.59	No
16	45	Female	688472	30.50	Obese	8.10	4.70	11.60	2.14	2.42	No
17	38	Male	688359	33.00	Obese	13.70	6.10	6.16	7.60	1.67	No
18	50	Male	688460	37.00	Obese	9.90	5.60	13.70	4.46	3.41	Yes
19	48	Female	688118	32.00	Obese	6.80	4.70	5.31	7.78	1.11	No
20	59	Male	688752	31.00	Obese	11.90	6.10	11.00	2.14	2.98	Yes
21	62	Male	515087	31.00	Obese	8.90	14.00	5.10	0.95	3.17	Yes
22	48	Female	668638	30.40	Obese	13.30	11.00	4.10	1.35	2.00	No
23	60	Male	688036	30.50	Obese	7.70	8.30	8.00	1.35	2.95	Yes
24	55	Male	687838	30.60	Obese	9.00	8.90	1.85	0.18	0.73	No
25	63	Male	687709	37.00	Obese	8.40	9.40	5.33	1.60	2.23	No
26	60	Male	686994	32.00	Obese	13.60	12.00	5.50	2.60	2.93	Yes
27	46	Female	687280	18.00	Lean	8.80	6.10	21.00	0.09	5.69	Yes
28	40	Male	576391	33.00	Obese	5.40	7.20	1.00	0.12	0.32	No
29	55	Male	687542	34.00	Obese	8.90	5.00	28.90	4.54	6.42	Yes
30	32	Male	684704	33.80	Obese	10.10	10.00	1.93	0.58	0.86	No
31	60	Female	687478	30.30	Obese	10.60	12.20	3.03	1.41	1.64	No
32	48	Male	686442	31.00	Obese	5.90	6.70	5.38	0.99	1.60	No
33	60	Female	684133	31.00	Obese	9.40	10.00	6.58	1.03	2.92	Yes

34	66	Male	686883	30.30	Obese	8.50	8.90	2.58	0.60	1.02	No
35	50	Male	687143	31.00	Obese	7.50	8.90	7.59	1.79	3.00	Yes
36	54	Male	361525	30.70	Obese	6.50	7.80	5.00	0.97	1.73	No
37	47	Male	588645	34.00	Obese	6.40	6.70	23.80	2.24	7.09	Yes
38	46	Male	667289	31.00	Obese	6.50	10.00	4.14	7.60	1.84	No
39	40	Female	687364	32.00	Obese	10.60	8.30	4.60	3.23	1.70	No
40	49	Male	378419	31.00	Obese	8.40	8.30	19.50	4.60	7.19	Yes
41	55	Male	686875	30.80	Obese	6.00	8.30	10.20	3.67	3.76	Yes
42	62	Male	686582	31.00	Obese	8.70	9.00	7.31	1.43	2.92	Yes
43	45	Male	686522	31.00	Obese	6.20	6.70	10.10	0.76	3.01	Yes
44	60	Male	686456	18.00	Lean	10.10	11.70	5.75	1.43	2.99	Yes
45	63	Male	686915	37.00	Obese	7.80	8.30	2.77	1.01	1.02	No
46	46	Male	687026	31.00	Obese	7.40	10.00	13.80	3.15	6.13	Yes
47	62	Male	686914	31.00	Obese	5.80	6.30	6.38	1.32	1.79	No
48	51	Male	686840	34.00	Obese	11.30	11.10	8.79	2.25	4.34	Yes
49	54	Male	686332	18.90	Lean	12.00	6.70	21.50	2.71	6.40	Yes
50	65	Female	686424	31.00	Obese	5.80	6.70	4.04	1.94	1.20	No
51	55	Female	665899	34.00	Obese	13.10	6.10	1.00	0.12	0.27	No
52	38	Male	645176	18.90	Lean	16.80	11.70	8.43	2.59	4.38	Yes
53	48	Male	645179	18.00	Lean	6.40	7.80	1.00	0.49	0.35	No
54	55	Male	645554	34.00	Obese	9.60	6.70	1.00	0.05	0.30	No
55	70	Female	645521	32.00	Obese	7.90	8.30	1.00	1.76	0.37	No
56	60	Female	533841	33.00	Obese	5.60	8.60	14.60	3.40	5.58	Yes
57	60	Male	654741	34.00	Obese	13.10	12.20	3.69	0.17	2.00	No
58	42	Male	654847	18.40	Lean	10.30	10.00	11.00	2.84	4.89	Yes
59	60	Male	656956	18.20	Lean	11.10	7.80	1.00	0.93	0.35	No
60	50	Male	657010	34.00	Obese	5.70	8.90	1.00	0.05	0.40	No
61	70	Female	662479	30.40	Obese	7.50	7.80	21.80	3.53	7.56	Yes
62	60	Male	662434	30.50	Obese	6.20	6.70	16.20	0.29	4.82	Yes
63	51	Male	662895	30.50	Obese	8.10	7.80	2.18	3.53	0.76	No
64	70	Male	662953	31.00	Obese	6.40	7.80	5.95	0.60	2.06	No
65	50	Male	663468	31.00	Obese	9.60	6.10	1.03	0.08	0.28	No
66	62	Female	664374	32.00	Obese	9.70	7.20	13.40	6.56	4.29	Yes
67	65	Female	664261	32.00	Obese	10.40	9.40	3.21	0.06	1.34	No
68	49	Male	667351	30.70	Obese	8.00	9.10	4.69	1.11	1.90	No
69	70	Male	664510	33.00	Obese	7.40	7.20	1.00	1.82	0.32	No
70	40	Male	666879	18.00	Lean	5.50	7.80	3.69	2.14	1.28	No

71	45	Male	668056	35.00	Obese	15.10	14.40	10.00	0.66	6.40	Yes
72	45	Female	642523	18.40	Lean	13.70	8.90	1.00	0.12	0.40	No
73	63	Male	641835	18.20	Lean	4.80	12.20	5.71	0.90	3.10	Yes
74	58	Female	642155	18.70	Lean	5.40	6.70	1.00	0.11	0.30	No
75	65	Female	642772	18.70	Lean	7.10	8.30	3.42	0.05	1.26	No
76	70	Female	639533	35.40	Obese	11.10	10.00	12.20	0.74	5.42	Yes
77	42	Female	643742	31.20	Obese	12.10	11.70	2.00	2.47	1.04	No
78	52	Male	644164	31.20	Obese	16.10	7.20	22.50	0.06	7.20	Yes
79	47	Female	635523	33.60	Obese	10.10	9.00	1.04	0.69	0.42	No
80	62	Male	635536	31.30	Obese	6.90	8.00	2.96	0.19	1.05	No
81	48	Female	631191	30.40	Obese	13.10	10.00	12.90	3.14	5.73	Yes
82	58	Male	642784	30.30	Obese	17.10	8.30	2.18	0.73	0.80	No
83	68	Male	644135	30.50	Obese	11.80	6.70	1.82	0.65	0.54	No
84	55	Female	644143	32.00	Obese	10.10	11.00	4.60	2.10	2.25	No
85	50	Female	641424	38.00	Obese	7.30	14.00	4.87	0.62	3.03	Yes
86	54	Female	679927	33.00	Obese	8.00	9.40	5.95	0.60	2.49	No
87	64	Male	439086	18.40	Lean	6.60	8.90	1.00	0.19	0.40	No
88	42	Female	684242	31.00	Obese	8.20	9.40	3.06	0.05	1.28	No
89	43	Female	683707	30.60	Obese	11.00	10.00	7.67	0.79	3.41	Yes
90	60	Male	667977	30.30	Obese	10.30	7.80	5.20	0.30	1.80	No
91	52	Male	670510	30.50	Obese	7.60	8.90	8.01	1.83	3.17	Yes
92	40	Female	687364	32.00	Obese	10.60	8.30	4.60	3.23	1.70	No
93	64	Male	439086	18.40	Lean	6.60	8.90	1.00	0.19	0.40	No
94	55	Female	665899	34.00	Obese	13.10	6.10	1.00	0.12	0.27	No
95	63	Male	688591	17.90	Lean	7.70	8.30	8.09	1.83	2.98	Yes
96	55	Female	665899	34.00	Obese	13.10	6.10	1.00	0.12	0.27	No
97	40	Male	202036	33.00	Obese	7.60	13.90	2.58	3.01	1.50	No
98	62	Female	664374	32.00	Obese	9.70	7.20	13.40	6.56	4.29	Yes
99	52	Male	644164	31.20	Obese	16.10	7.20	22.50	0.06	7.20	Yes
100	47	Female	635523	33.60	Obese	10.10	9.00	1.04	0.69	0.42	No
101	32	Male	684704	33.80	Obese	10.10	10.00	1.93	0.58	0.86	No
102	40	Female	685172	18.60	Lean	6.70	5.00	33.10	4.64	7.36	Yes
103	54	Male	361525	30.70	Obese	6.50	7.80	5.00	0.97	1.73	No
104	70	Female	645521	32.00	Obese	7.90	8.30	1.00	1.76	0.37	No
105	63	Male	688591	17.90	Lean	7.70	8.30	8.09	1.83	2.98	Yes
106	65	Female	642772	18.70	Lean	7.10	8.30	3.42	0.05	1.26	No