PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE DIAGNOSIS OF METABOLIC SYNDROME, CASE-CONTROL STUDY ATA TERTIARY CARE CENTRE, TAMAKA, KOLAR

By

DR. KASARANENI RUPA

DISSERTATION SUBMITTED TO

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH CENTRE, KOLAR

In partial fulfilment of the requirements for the degree of

DOCTOR OF MEDICINE
IN
GENERAL MEDICINE

GUIDE:

DR. VIDYASAGAR C. R **M.B.B.S, MD (MEDICINE)**

PROFESSOR & HOD

DEPARTMENT OF GENERAL MEDICINE

SDUMC, KOLAR

DEPARTMENT OF GENERAL MEDICINE

SRI DEVARAJ URS MEDICAL COLLEGE,

TAMAKA, KOLAR-563101

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

DECLARATION BY THE CANDIDATE

I HEREBY DECLARE THAT THIS DISSERTATION ENTITLED **"PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE DIAGNOSIS OF METABOLIC SYNDROME, CASE-CONTROL STUDY ATA TERTIARY CARE CENTRE, TAMAKA, KOLAR"** IS A BONAFIDE AND GENUINE RESEARCH WORK CARRIED OUT BY ME UNDER THE DIRECT GUIDANCE OF **DR. VIDYASAGAR C.R.** **M.B.B.S, MD (MEDICINE)** PROFESSOR, DEPARTMENT OF **GENERAL MEDICINE**, SRI DEVARAJ URS MEDICAL COLLEGE, KOLAR

DATE:

PLACE: KOLAR

SIGNATURE OF THE CANDIDATE

DR. KASARANENI RUPA

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

CERTIFICATE BY THE GUIDE

THIS IS TO CERTIFYTHAT THE DISSERTATION ENTITLED **"PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE DIAGNOSIS OF METABOLIC SYNDROME, CASE-CONTROL STUDY ATA TERTIARY CARE CENTRE, TAMAKA, KOLAR"** AT R.L. JALAPPA HOSPITAL AND RESEARCH CENTRE, KOLAR IS A BONAFIDE RESEARCH WORK DONE BY **DR. KASARANENI RUPA** IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF DOCTOR OF MEDICINE (M.D) IN GENERAL MEDICINE.

DATE:

PLACE: KOLAR

SIGNATURE OF THE GUIDE

DR. VIDYASAGAR. C.R
PROFESSOR & HOD
DEPARTMENT OF GENERAL MEDICINE, SDUMC, KOLAR

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

ENDORSEMENT BY THE HOD, PRINCIPAL / HEAD OF THE INSTITUTION

THIS IS TO CERTIFY THAT THE DISSERTATION ENTITLED "**PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE DIAGNOSIS OF METABOLIC SYNDROME, CASE-CONTROL STUDY ATA TERTIARY CARE CENTRE, TAMAKA, KOLAR"** IS A BONAFIDE RESEARCH WORK DONE BY **DR. KASARANENI RUPA** IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF DOCTOR OF MEDICINE (M.D) IN GENERAL MEDICINE.

Dr. VIDYASAGAR C R
PROFESSOR & HOD
DEPARTMENT OF MEDICINE
SDUMC, KOLAR

Dr. K PRABHAKAR
PROFESSOR & PRINCIPAL
DEPARTMENT OF MEDICINE
SDUMC, KOLAR

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

COPYRIGHT

DECLARATION BY THE CANDIDATE

I HEREBY DECLARE THAT **SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA** SHALL HAVE THE RIGHTS TO PRESERVE, USE AND DISSEMINATE THIS DISSERTATION, IN PRINT OR ELECTRONIC FORMAT, FOR ACADEMIC / RESEARCH PURPOSE.

DATE SIGNATURE OF THE CANDIDATE PLACE:

KOLAR **Dr. KASARANENI RUPA**

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH

SRI DEVARAJ URS MEDICAL COLLEGE

Tamaka, Kolar

INSTITUTIONAL ETHICS COMMITTEE

Members

1. **Dr. D.E.Gangadhar Rao, (Chairman)** Prof. & HOD of Zoology, Govt. Women's College, Kolar
2. **Dr. Sujatha.M.P, (Member Secretary),** Prof. Dept. of Anesthesia, SDUMC
3. Mr. Gopinath Paper Reporter, Samyukth Karnataka
4. Mr. G. K. Varada Reddy Advocate, Kolar
5. Dr. Hariprasad S, Assoc. Prof Dept. of Orthopedics, SDUMC
6. Dr. Abhinandana R Asst. Prof. Dept. of Forensic Medicine, SDUMC
7. Dr. Ruth Sneha Chandrakumar Asst. Prof. Dept. of Psychiatry, SDUMC
8. Dr. Usha G Shenoy Asst. Prof., Dept. of Allied Health & Basic Sciences SDUAHER
9. Dr. Munilakshmi U Asst. Prof. Dept. of Biochemistry, SDUMC
10. Dr.D.Srinivasan, Assoc. Prof. Dept. of Surgery, SDUMC
11. Dr. Waseem Anjum, Asst. Prof. Dept. of Community Medicine, SDUMC
12. Dr. Shilpa M D Asst. Prof. Dept. of Pathology, SDUMC

No. SDUMC/KLR/IEC/244/2022-23 Date: 20-07-2022

PRIOR PERMISSION TO START OF STUDY

The Institutional Ethics Committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has examined and unanimously approved the synopsis entitled **"Procalcitonin as an additional marker for the diagnosis of metaboloic syndrome, case - control study at a teritiary care center, Tamaka, Kolar"** being investigated by **Dr.Kasaraneni Rupa** & Dr.B.N.Raghavendra Prasad in the Department of General Medicine at Sri Devaraj Urs Medical College, Tamaka, Kolar. **Permission is granted by the Ethics Committee to start the study.**

Member Secretary

Member Secretary
Institutional Ethics Committee
Sri Devaraj Urs Medical College
Tamaka, Kolar

Chairman

CHAIRMAN
Institutional Ethics Committee
Sri Devaraj Urs Medical College
Tamaka, Kolar

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH

Tamaka, Kolar 563103

Certificate of Plagiarism Check

Title of the Thesis/Dissertation	PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE DIAGNOSIS OF METABOLIC SYNDROME , CASE-CONTROL STUDY AT A TERTIARY CARE CENTRE, TAMAKA, KOLAR
Name of the Student	DR. KASARANENI RUPA
Registration Number	21GM1010
Name of the Supervisor / Guide	DR VIDYASAGAR C.R.
Department	GENERAL MEDICINE
Acceptable Maximum Limit (%) of Similarity (PG Dissertation)	10%
Similarity	6%
Software used	Turnitin
Paper ID	2411155290
Submission Date	01/07/2024

Signature of Student

Signature of Guide/Supervisor

Professor of Medicine
SDUMC, Tamaka, Kolar

HOD Signature

Prof & HOD of Medicine
SDUMC, Tamaka, Kolar

University Librarian

Senior Librarian
ULLRC, SDUAHER
Tamaka, KOLAR-563103

PG Coordinator

PG Coordinator
Sri Devaraj Urs Medical College
Tamaka, Kolar-563103

turnitin

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	Dr. Kasaraneni Rupa
Assignment title:	PG Dissertation - 2024
Submission title:	PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE DIAG...
File name:	TROL_STUDY_AT_A_TERTIARY_CARE_CENTRE,_TAMAKA,_KOLA...
File size:	562.39K
Page count:	85
Word count:	15,935
Character count:	102,305
Submission date:	01-Jul-2024 03:36PM (UTC+0530)
Submission ID:	2411155290

PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE DIAGNOSIS OF METABOLIC SYNDROME : CASE CONTROL STUDY AT A TERTIARY CARE CENTRE, TAMAKA, KOLAR

ABSTRACT

Prof & HOD of Medicine
SDUMC, Tamaka, Kolar

Librarian
ULLRC, SDUAHER
Tamaka KOLAR-563103

Document Viewer

Turnitin Originality Report

Processed on: 01-Jul-2024 15:37 IST
ID: 2411155290
Word Count: 15935
Submitted: 1

PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE... By Dr. Kasaraneni Rupa

Similarity Index	Similarity by Source	
6%	Internet Sources:	4%
	Publications:	4%
	Student Papers:	1%

include quoted | include bibliography | excluding matches < 10 words | mode:
quickview (classic) report | print | refresh | download

1% match (Internet from 15-Sep-2023)
https://www.isakos.com/Assets/Meetings/2023Congress/Manuscripts/Ramakanth-Manuscript.pdf

<1% match (A.H., Harish. "Study of Clinical and Biochemical Profile of Metabolic Syndrome in Acute Myocardial Infarction", Rajiv Gandhi University of Health Sciences (India), 2023)
A.H., Harish. "Study of Clinical and Biochemical Profile of Metabolic Syndrome in Acute Myocardial Infarction", Rajiv Gandhi University of Health Sciences (India), 2023

<1% match (Internet from 03-Jan-2024)
https://cajmns.centralasianstudies.org/index.php/CAJMNS/article/download/217/2213/

<1% match (Internet from 18-Jan-2019)
http://www.japi.org

<1% match ()
El Kassas, Ghada M., Shehata, Manal A. et al. "Role of Procalcitonin As an Inflammatory Marker in a Sample of Egyptian Children with Simple Obesity", Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia, 2018

<1% match (Internet from 30-Jul-2020)
https://worldwidescience.org/topicpages/m/metabolic+risk+insulin.html

<1% match (Internet from 03-Jan-2024)
https://worldwidescience.org/topicpages/p/practical+step-by-step+approach.html

<1% match (Internet from 02-Jul-2018)
https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-015-2409-7

Prof & HOD of Medicine
SDUMC, Tamaka, Kolar

Senior Librarian
ULLRC, SDUAHER
Tamaka, KOLAR-563103

ACKNOWLEDGEMENT

No academic work is single handedly accomplished. This work is no exception. Words fail me in expressing my heartfelt and humble gratitude to thank the almighty for showering his blessings on me. I sincerely thank my guide **Dr.VIDYASAGAR C.R.** who have the substance of genius and for their step-by-step guidance and constant extended support with the timely advices which helped me for this study. Their encouragement, sense of punctuality, research oriented approach, the painstaking effort to weed out errors and their affection during the entire course of study leaves me permanently indebted to them.

I express my deep sense of gratitude and humble thanks to my Professors, **DR.PRABHAKAR K, DR. RAVEESHA A, DR. SRINIVASA S V, DR. ANITHA A** for their advice and encouragement throughout the study.

I am extremely indebted to and I thank **DR. B.N.RAGHAVENDRA PRASAD[Retd], DR. PRAVEEN P, DR MANJUNATH N, DR CHETHAN REDDY, DR. LOKESH, DR APARNA, DR. SRIVATSAV** Department of General Medicine for their constant support and encouragement throughout with patience and care. They have been my well wisher and a source of inspiration throughout my study.

My heartfelt thanks to all my teachers throughout my life for having made me what I am today for their practical tips, invaluable advice and constant encouragement.

I extend my sincere thanks to my seniors **DR. SANMITHA RAM, DR. DHEERAJ KUMAR REDDY, DR. HEMANTH KUMAR REDDY, DR. RAKESH KUMAR, DR. PAVAN TUNGALA**, **DR MANOHAR GOWDA.B.G, DR.AMULYA, DR.MANASA DIXIT, DR. INBA PRAVEEN, DR. KAVYA B.K, DR. SUJITHA, DR. POONGULALI** whose knowledge has guided and inculcated in me a sense of confidence. I am thankful for their valuable guidance and helping me with my dissertation.

I express my sincere thanks to dearest friends **DR. SANJANA**

MARAM, DR. KRUTHI PALLU, DR. KATTA DINESH for becoming a home away from home, for their love, support and encouragement throughout the course. Without whom, it would have been a tough road.

I thank all my colleagues **DR. MANIMOHAN REDDY, DR. BILAL, DR. BALAKRISHNA, DR. GAGAN, DR. LAKWAN SAKTHI, and my** Juniors DR. PREM CHANDAR REDDY, DR. AMULYA REDDY, DR. LAKSHMISHA, DR. MADHURIMA, DR. SUNAYANA REDDY, DR. NEHA PALLA, DR. HARSHITHA, DR. VINEELA, DR.HULESH, DR.PRATEEK VARMA, DR. MAANSI, DR. ARAVIND VENKAT, DR DILIP, DR JAYRAJ for their love and support towards me.

I thank my beloved interns DR.ANAND KATARI, DR.KRISHNA NAG, DR.KALYANI, DR. ARSHITA BISLA for their constant love, support and encouragement towards me.

I would express my deepest gratitude to my my beloved grandparents **N.VENKATESWARA RAO**, **N.KRISHNA KUMARI**, beloved parents **K.SATYANARAYANA, K. SREELAKSHMI ,** my uncles **N.RAVI KUMAR**, **N.RAMESH BABU,** my brother **K. DHANA SREE RAM,** my sister in law **DR.MEGHANA RAO** whose love, blessings and sacrifices made me the person I am today. Without them I would have never reached to this level.

I thank all my nurses of ICU, MICU and General ward for their help and assistance.

Last, but not the least, I thank my patients for providing me the opportunity to carry out my study.

Place: Kolar **Dr. KASARANENI RUPA**

LIST OF ABBREVIATIONS USED

American Association of Clinical Endocrinologists -AACE

Atherosclerotic cardiovascular disease -ASCVD

Cardiovascular disease -CVD

European Group for the study of Insulin Resistance -EGIR

Interleukin 1,6 - IL-1, IL-6,

International Diabetes Federation -IDF

Metabolic syndrome- MetS

Monocyte chemoattractant protein-1 -MCP-1,

National Cholesterol Education Program Adult Treatment Panel -NCEP/ATP

Plasminogen activator inhibitor-1 -PAI-1,

Procalcitonin -PCT

Tumour necrosis factor -TNF

Type 2 diabetes mellitus -T2DM

World Health Organization -WHO

LIST OF TABLES

LIST OF FIGURES

TABLE OF CONTENTS

ABSTRACT

Background: Metabolic syndrome (MS) is a clustering of metabolic risk factors namely abdominal obesity, hypertension, hyperglycemia, high serum triglyceride levels and low serum HDL. Procalcitonin is a polypeptide precursor of hormone calcitonin that is released in response to systemic inflammation not only by neuroendocrine cells of the lungs, intestine, and thyroid (C cells), but also by adipose tissue. Therefore, plasma procalcitonin can serve as a potential biomarker for detection of obesity related low-grade inflammation even in the very early stages, thereby increasing the sensitivity and specificity.

Methodology: Patients admitted with diagnosis of metabolic syndrome at RL Jalappa Hospital and Research Centre, Kolar will be selected and results of waist circumference, SBP, DBP, TG, cholesterol, HDL, LDL, VLDL, FBS, Plasma procalcitonin will be correlated in two different groups separately.

Results: Mean Procalcitonin level in the case group was seen to be 1.806±1.236 ng/dl and among the controls was seen to be 0.163±0.1613 ng/dl. This difference in the Procalcitonin level was statistically significant ($p < .001$). We also found that the Procalcitonin levels had significant association with Waist circumference, Triglycrides, HDL & FBS values with a p value < .001. Area under the ROC for Procalcitonin as a diagnostic test was found to be 0.942 which indicates that it has an excellent prediction value ($p< .001$). At 0.013 cut off value, we found that Procalcitonin has a sensitivity of 97% and a specificity of 87.9%.

Conclusion: Metabolic Syndrome, reflecting the underlying inflammatory state associated with the condition. While current evidence suggests a positive correlation between elevated PCT levels and MetS, integrating PCT into the diagnostic framework for MetS could improve early detection, risk stratification, and monitoring of treatment efficacy, ultimately enhancing

patient outcomes. However, practical challenges related to specificity, standardization, cost, and clinical integration must be addressed to realize its full potential.

Keywords: Metabolic Syndrome, Procalcitonin, Hyperglycaemia

INTRODUCTION

INTRODUCTION

A group of metabolic diseases known as the Metabolic Syndrome increase the risk of cardiovascular disease events and promote the development of atherosclerosis.[1] Other names for metabolic syndrome include the deadly quartet, syndrome X and insulin resistance syndrome.Metabolic syndrome is linked to numerous other systemic illnesses, including fatty liver disease and chronic lung disease, in addition to type 2 DM and cardiovascular disease.[2]

Globally, The metabolic syndrome was not always prevalent but is becoming more common and it is turning into a serious public health issue[3]. Numerous research investigations have demonstrated that the frequency of Metabolic Syndrome rises with age, necessitating its diagnosis because of a 2.5-fold rise in cardiovascular mortality and a 5-fold increased risk of acquiring diabetes[4].In a research by Kuk JL[5], 55.0% of the subjects who were elderly (over 65) had metabolic syndrome. According to WHO and NCEP [6], In an elderly population, the prevalence of metabolic syndrome varied from 11% to 43% (median 21%) and from 23% to 55% (median 31%), respectively.

Adipocytes that are viscerally obese emit proinflammatory cytokines, which results in a continuous low-grade inflammatory state. The biology of metastatic stress syndrome (MetS) is complex and yet poorly understood.[7,8] Proinflammatory adipokines include resistin; tumour necrosis factor (TNF); interleukin (IL)-1; IL-6; lipocalin-2; monocyte chemoattractant protein-1 (MCP-1); and plasminogen activator inhibitor-1 (PAI-1). These adipokines work together to mediate effects that include promoting insulin resistance, which raises glucose and free fatty acid levels.[9] In the context of MetS, an imbalance between pro- and anti-inflammatory adipokines increases inflammation, endothelial dysfunction and oxidative stress.[10]

In healthy people, the thyroid and adipose tissue create procalcitonin (PCT), a 116-amino acid peptide that is a precursor to calcitonin. It is broken down to create calcitonin,

which is then regulated in storage and secretion to lower serum calcium levels and preserve calcium homeostasis.[11] Less than 0.1 ng/mL is the typical PCT serum result. In critical illness, procalcitonin may have a negative effect on the host's response to inflammation. Assicot et al. were the first to report finding it in higher concentrations in patients suffering from systemic illnesses.[11]

It has been demonstrated that procalcitonin increases the inflammatory response and promotes the expression of CD14 on lymphocytes and CD16 on human neutrophils' surfaces [12,13]. Procalcitonin exposure has been shown in experiments to affect hepatocyte function and the function of the endothelium barrier [14,15.] Additionally, procalcitonin is shown in experimental models of sepsis to exacerbate the severity and course of the illness [16.]

Although studies on the correlation between procalcitonin and metabolic syndrome are still in progress, procalcitonin levels may be higher in those who have the condition (Ormsbee et al., 2014). Because of the continuous low-grade inflammation linked to metabolic syndrome, high levels of procalcitonin may be a sign of infection or inflammation, both of which are frequently seen in patients with the illness. According to this association, procalcitonin may be used as a potential biomarker for metabolic syndrome monitoring and diagnosis, as well as for identifying those who are more likely to develop type 2 diabetes and cardiovascular disease (Eisenman, 2006).

AIMS & OBJECTIVES

AIMS AND OBJECTIVES

AIM

To determine procalcitonin as an additional marker for the diagnosis of metabolic syndrome.

OBJECTIVES

1. Determine procalcitonin levels in patients with metabolic syndrome.
2. Determine procalcitonin levels in normal.
3. Compare procalcitonin levels in two groups

REVIEW OF LITERATURE

REVIEW OF LITERATURE

METABOLIC SYNDROME - AN OVERVIEW:

Urbanization, increased calorie intake, rising obesity rates, and sedentary lifestyles are the main causes of the metabolic syndrome (MetS), which is a major and expanding global public health and clinical concern. MetS raises the risk of cardiovascular disease (CVD) by two times and type 2 diabetes mellitus (T2DM) by five times over the next five to ten years[16]. Furthermore, patients with the MetS had a 2- to 4-fold increased risk of stroke, a 3- to 4-fold increased risk of myocardial infarction (MI), and a 2-fold increased likelihood of dying from such an event compared to those without the syndrome 17. For a version of MetS with the WHO International Classification of Disease (ICD-9) code (277.7), reimbursement for medical services is permitted. This demonstrates how the phrase "metabolic syndrome" has become established and included in medical jargon. MetS is regarded as a primary risk factor for problems related to atherothrombosis. For this reason, its existence or lack should be regarded as a long-term risk indication.

HISTORY OF METABOLIC SYNDROME:

Originally, MetS was not a diagnosis, but rather a concept [18]. The Swedish physician Kylin established the link between hypertension, hyperglycemia, and gout in 1920, which is when the metabolic syndrome first emerged [19.] After Reaven20's 1988 Banting Lecture, the field made considerable progress. The phrase "Syndrome X" was created by him to describe "a cluster of risk factors for diabetes and cardiovascular disease." His introduction of the idea of insulin resistance was his principal contribution. Surprisingly, he neglected to include visceral obesity in the definition, which was subsequently added as a critical anomaly. Kaplan [21] coined the term "The Deadly Quartet" in 1989 to describe the syndrome including

upper body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. But in 1992, the name was changed to "The Insulin Resistance Syndrome" [22]. A number of organizations have made an effort to create diagnostic standards for the MetS [23.] In 1998, a World Health Organization (WHO) diabetic group made an initial attempt to define the MetS [24]. In response, the European Group for the Research of Insulin Resistance (EGIR) revised the WHO criteria in 1999. The National Cholesterol Education Program Adult Treatment Panel (NCEP/ATP) released definition [26] in 2001. The definition of the syndrome was then discussed and comments were expressed by the American Association of Clinical Endocrinologists (AACE) in 2003 [27]. A single, unified definition was deemed desirable due to the abundance of definitions [28.] In an effort to do this, the International Diabetes Federation (IDF) suggested a revised definition of the MetS in April 2005.. [29]

Definition

The metabolic syndrome (MetS) is a group of interconnected physiological, biochemical, clinical, and metabolic factors that directly increase the risk of T2DM, atherosclerotic cardiovascular disease (ASCVD) and all-cause mortality.[30, 31.] This group of aberrant lab test results and unhealthy body measures includes glucose intolerance, hypertension, and atherogenic dyslipidemia.

World Health Organization (WHO) diabetes team made the initial attempt to define the metabolic syndrome in 1998 [32]. According to the World Health Organization's criteria, individuals must either have type 2 diabetes, be insulin resistant as defined by the euglycemic clamp technique, or have impaired glucose tolerance (IGT), as assessed by an oral glucose tolerance test. The WHO definition's applicability is limited by the practical difficulties of fulfilling the insulin criterion. In addition to insulin resistance, there are two more prerequisites that must be met. These included obesity (characterized as an elevated waist-hip

ratio or body mass index [BMI]), hypertension, dyslipidemia (high triglycerides or low HDL-C), and microalbuminuria. Microalbuminuria has been questioned for being a major component, primarily since it is uncommon in people who are not diabetic.

WHO criteria

Diabetes, inadequate glucose absorption in the lowest 25% of blood, hyperinsulinemia, euglycemic readings, or impaired fasting glycaemic or insulin resistance plus two or more of the subsequent

- Obesity: BMI > 30 kg/m^2 or waist-to-hip ratio >0.9 (male) or >0.85 (female)
- Microalbuminuria: albumin excretion >20 mg/min
- Dyslipidaemia:Triglycerides≥150mg/dL or HDL cholesterol: < 35 mg/dL (male) or < 39mg/dL (female)
- Hypertension: Blood pressure ≥140/90 mmHg and/or medication

A revision to the WHO definition was made in 1999 by the European Group for the study of Insulin Resistance (EGIR) in response. The EGIR offered their own definition, which relies on fasting insulin instead of the euglycemic clamp to measure insulin resistance [33,] and the WHO definition was changed for good practical approach.Therefore, as serum fasting insulin may not be a useful indicator of insulin resistance in diabetics, those with type 2 diabetes mellitus were not included. Waist circumference was used to simplify the obesity criterion. Moreover, the metabolic syndrome was redefined without including micro-albuminuria.

Group for the Study of Insulin Resistance in Europe, 1999

Insulin resistance:

Hyperinsulinemia: Over 25% of fasting insulin tolerance from Non-diabetic population adittion 2 or more of the following:-

- Central obesity: means, waist circumference ≥ 94 cm (male), ≥ 80 cm (female)
- Fasting plasma glucose : > 110 mg/dL
- Dyslipidaemia: triglycerides ≥ 150mg/dL or HDL cholesterol < 39mg/dL (male, female)
- Hypertension: blood pressure ≥ 140/90 mm Hg and/or medication

The definition or criterion was provided by the National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP III) in 200134.The NCEP criteria sought to identify individuals who would benefit from clinical lifestyle intervention to reduce their long-term risk of cardiovascular diseases. Although metabolic risk factors were shown to be clustered, pathogenesis-related results were not revealed. NCEP adopted a less glucose-centric strategy by giving equal weight to each element of the metabolic syndrome. The waist circumference cut off points were significantly higher than those found in the EGIR criteria because they were derived from the 1998 National Institutes of Health obesity clinical recommendations (1998), which identified the upper quartile of the US population. An modified NCEP-ATP III criteria was announced in 2005 by the American Heart Association (AHA) and the National Heart Lung and Blood Institute (NHLBI). [30.] The majority of the NCEP ATP III criteria were maintained in this definition, while a lower threshold for higher fasting glucose was suggested (the 2001 definition classified fasting plasma glucose as elevated if it was greater than 110 mg/dL (6.1 mmol/L). According to the most recent definition of impaired fasting glucose (IFG) published by the American Diabetes Association in 2004, this was changed to >100 mg/dL (5.6 mmol/L). Because it is useful and simple to use, the NCEP definition is

among the most widely used MS definitions. However, as it excludes the measurement of insulin while fasting, accounting for insulin resistance may not be successful.

ATP III, 2001

Three or more of the following

- Central obesity: means, waist circumference: ≥ 102 cm (male), ≥ 88 cm (female)
- Fasting plasma glucose: > 110 mg/dL.
- Hypertriglyceridemia: triglycerides ≥ 150mg/dL
- Hypertension: Blood pressure ≥ 135/85 mm Hg or on medication
- Low HDL cholesterol: < 40mg/dL (male), < 50 mg/dL (female)

The American Association of Clinical Endocrinologists (AACE) then provided comments on the description of the metabolic syndrome in 2003. A single, unified definition was suggested to be desirable by the abundance of definitions. The International Diabetes Federation (IDF) revised the definition of the metabolic syndrome in April 2005 with the hopes of accomplishing this. [34, 35]

IDF Criteria:

Abdominal Circumference + 2 criteria

- Abdominal circumference: > 80cm
- Triglycerides: ≥ 150mg/dl
- HDL- Cholesterol: < 50mg/dl (male, female)
- Blood pressure

  SBP: ≥130mmHg

  DBP: ≥85mmHg

- Use of antihypertensive medication
- Fasting Blood Glucose: ≥100mg/dl or use of hypoglycaemic drug Risk Factors

TABLE 1: Criteria for Metabolic Syndrome

Clinical measure	WHO (1998)	EGIR	ATP III (2005)	AACE (2003)	IDF (2005)
Insulin resistance	IGT,IFG,T2 DM or lowered insulin sensitivity plus any 2 of the following	Hyperinsulinemia top 25% of fasting insulin tolerance from non-diabetic population Plus 2 or more of the following	3 or more of the Following	IGT, IFG plus any of the following	NONE
Body weight	BMI >30 kg/m2 or W:H>0·9 (male) or > 0·85 (female)	WC >94 cm (male) >8ocm (female)	Waist circumference > 80cm in females, > 90cm males.	WC >102cm (male) >88 cm (female)	AC > 80cm
Lipids	TG ≥150mg/dL or HDL-C: < 35mg/dL (male) or <39mg/dL (female)	TG≥150mg/dL or HDL-C: <39mg/dL (male, female)	TG >150mg/dl or specific medication HDL<50mg/dl for women and <40mg/dl for men or specific medication	TG1≥50mg/dL or HDL-C: <40mg/dL (male) <50mg/dL (female)	TG >150mg/dl HDL- C <50mg/dl
Blood pressure	≥140/90 mm Hg and/or medication	≥140/90 mm Hg and/or medication	systolic blood pressure >130mmhg or diastolic >85mmhg or specific medication	≥135/85 mm Hg or medication	SBP>130m mHg DBP>85m mHg Use of antihyperte nsive medication
Glucose	IGT,IFG,T2 DM	IGT,IFG	Fasting plasma glucose level >100mg/dl or specific medication or previously diagnosed type 2 diabetes.	IGT,IFG but not diabetes	FBS>100m g/dl or use of hypoglycae mic drug Risk Factors
Others	Microalbum inuria				

EPIDEMIOLOGY:

Depending on the definition and population under study, there are variations in the prevalence of MetS by age, ethnicity, and sex. Factors such as an individual's diet, level of physical activity, genetic makeup, and extent of malnutrition all influence the frequency of the disorder and its constituent parts. Because so many confounding factors may have an impact, generalizations about the prevalence of sex differences may be deceptive. To make matters more complicated, a diagnosis of the syndrome can be made at any time if three out of five symptoms are met. Therefore, any of the 16 risk factor combinations may be used to make a diagnosis, and prevalence data do not differentiate between these subtypes, which may also differ by sex and population. However, a recent analysis of the Third National Health and Nutrition Survey (NHANES III, 1998–1994, NCEP criteria) in the US found that abdominal obesity was the most common MetS feature in women, but men's risk factor combinations were more variable [35,36] This national representative survey was conducted.

The most common cluster among younger women (16.7%) included elevated WC, low HDL cholesterol, and elevated triglycerides (TG). For younger boys (18.0%), increased TG, low HDL cholesterol, and hypertension were the most often occurring combinations. It's interesting to note that in this cohort of older individuals (65 years and above), the gender difference in subtype distribution was nearly abolished, meaning that older men and women equally shared the most prevalent subtype—having all five traits. These results demonstrate that the condition varies with age, sex, and subtype. The information at hand makes it difficult to determine which criteria—the simple existence or absence of the syndrome, the entirety of risk factors, or a specific mix of risk factors—better captures the essence of cardiac metabolic risk. Further investigation[37] not with standing the continuous growth in obesity rates, recent data from the NHANES 1999–2006 indicate that 68 million US

individuals (overall prevalence 34.2%) currently suffer from the illness. Both men and women are equally likely to be obese (age-adjusted prevalence: 34.9% and 33.3%, respectively) [38.]

The estimates of prevalence differ according to the standards applied in defining MetS. According to the IDF definition, the prevalence of MetS was 37.4%, the ATP III criterion was [34] 7%, and the ATP III/AHA/NHLBI criteria was 41.6%, according to a national survey conducted in Iran in 2007. In Tunisia, a different Middle Eastern nation, the frequency was 24.3% according to ATP III standards and 45.5% according to IDF criteria. However, the frequency was significantly higher in women than in men in all of the Middle Eastern countries. [39]

In India, the prevalence of the metabolic syndrome as determined by the Adult Treatment Panel III (NCEP, ATP III), the National Cholesterol Education Programme, and other criteria varies from 11 to 41%. Although studies indicate that Asian Indians residing in India have a high frequency of the metabolic syndrome, there are no genuinely representative data available from all regions of India [40.]

Based on the modified ATP III, International Diabetes Federation, and Japanese criteria, middle-aged and senior males did not differ in the three criteria, however the prevalence of MetS was almost three times higher in old women than in middle-aged women. The International Diabetes Federation and modified ATP III criteria showed a significantly higher prevalence of MetS in women than did the Japanese criteria. Among the risk factors, as people aged, the prevalence of high fasting glucose and high blood pressure increased in both genders, whereas the prevalence of central obesity and dyslipidemia increased exclusively in women. There was greater risk clustering in older subjects compared to middle-aged subjects among the MetS participants who met the modified ATP III criteria,

particularly in women. In both sexes, blood pressure went up, triglycerides went down, and in older males, non-high-density lipoprotein cholesterol went down. In older men, the prevalence of dyslipidemia declined [41].

Numerous investigations have demonstrated that insulin resistance has a significant hereditary component. Obesity is one of the main causes of insulin resistance. Asian Indians are rarely extremely obese, yet even when they are, they still have insulin resistance. Asian Indians need higher insulin dosages to keep their normoglycemic levels stable. Asian Indians are more likely to develop hyperinsulinemia, upper body adiposity, and a high body fat percentage as early signs of insulin resistance. Compared to other ethnic groups, Indians had larger waist-to-hip ratios (W: H) for every BMI. [42], despite the fact that body mass index (BMI), a measure of obesity, is lower among Indians.

RISK FACTORS:

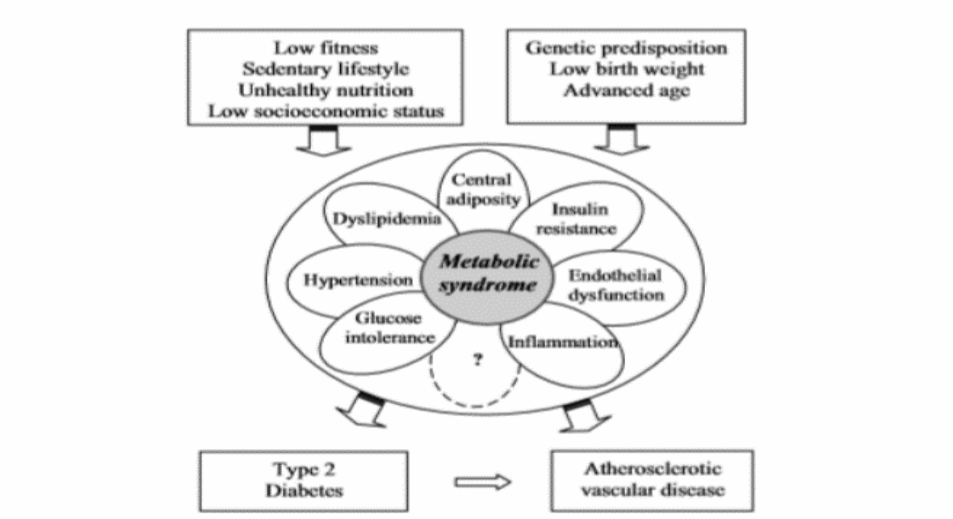
Risk factors for the development of MetS:

- Positive family history
- Smoking
- Low socioeconomic status
- Increasing age
- Obesity
- Low cardiorespiratory fitness
- Physical inactivity
- Excessive alcohol consumption
- Use of antiretroviral drugs in human immunodeficiency virus (HIV) infection
- Excessive television-watching
- Western dietary patterns
- Atypical antipsychotic drug use (e.g., clozapine etc)
- Genetic factors [43].

AETIOLOGY:

The aetiology of metabolic syndrome involves interactions between sedentary lifestyle, poor food, genes, and numerous other risk factors (Figure 1). Over the past few decades, the obesity and metabolic syndrome epidemic has been fueled by an abundance of food, pre-packaged fast food with high calorie density, and everyday gadgets that limit physical activity. Obesity and the metabolic syndrome are on the rise, which is problematic because they increase the risk of type 2 diabetes, cardiovascular disease (CVD), coronary heart disease (CHD), and premature death. Diabetes affects over 200 million people globally, and by 2030, the prevalence is expected to quadruple. [44]

Fig 1: Predictors, Components and Consequences of MetS.



Sedentary Lifestyle

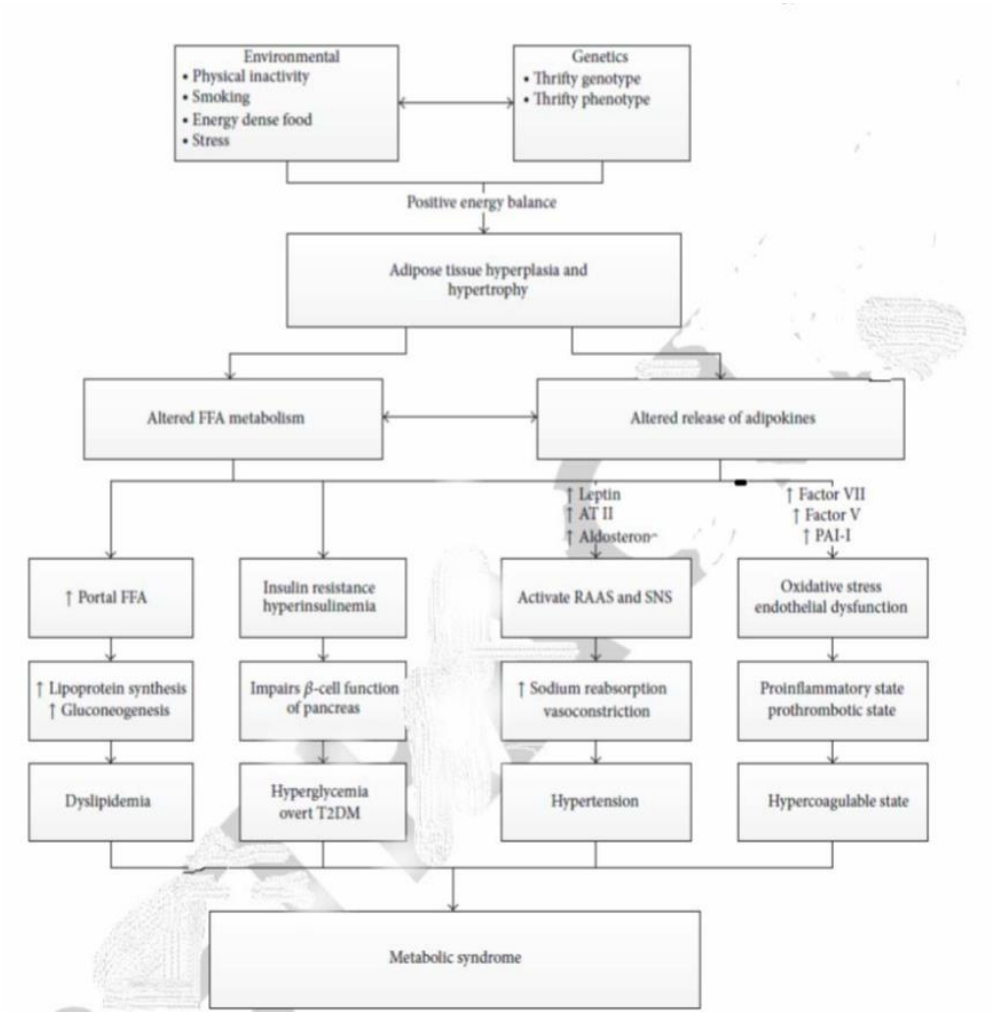
Physical inactivity is the most important predictor of cardiovascular events and the death that is linked to them. Sedentary lifestyles are linked to many metabolic syndrome components, such as reduced HDL cholesterol, increased subcutaneous adipose tissue (primarily central), and a tendency toward elevated triglycerides, hypertension, and elevated blood glucose in genetically susceptible individuals. More than four hours a day spent in these activities

doubles the risk of having metabolic syndrome [45] as compared to less than an hour a day spent watching TV, watching videos, or using a computer.

PATHOPHYSIOLOGY:

MetS is a long-term, low-grade inflammatory state brought on by a complicated interaction between environmental and genetic variables. The syndrome is characterized by a number of variables, including hereditary predisposition, high blood pressure, hypercoagulable condition, visceral obesity, insulin resistance, atherogenic dyslipidemia, endothelial dysfunction, and chronic stress. (Fig 2)

Fig 2 Diagrammatic representation of MetS.



Abdominal Obesity: The "obesity epidemic" is mostly brought on by a rise in the intake of low-cost, high-calorie meals and a decline in physical activity. Through adipocyte hypertrophy and hyperplasia, adipose tissue can respond quickly and dynamically to changes in dietary excess[43]. It is a heterogeneous collection of immune cells, endothelium, stromal preadipocytes, and adipocytes. Obesity-related reduced blood supply to adipocytes and increased adipocyte growth can lead to hypoxia[46.] A theory suggests that hypoxia triggers necrosis and macrophage infiltration into adipose tissue, which in turn causes an excess of physiologically active metabolites called adipocytokines, such as glycerol, Free fatty acids (FFA), plasminogen activator inhibitor-1 (PAI-1), C-reactive protein (CRP), proinflammatory mediators (interleukin-6 (IL-6) and tumor necrosis factor alpha (TNFα)[47.] This causes a localized inflammation in the adipose tissue, which spreads to the entire system and is linked to the emergence of comorbidities connected to obesity [48..] It is believed that a number of mechanisms, including insulin sensitivity, oxidant stress, energy metabolism, blood coagulation, and inflammatory response, accelerate atherosclerosis, plaque rupture, and atherothrombosis. To mediate these activities, adipocytokines integrate autocrine, paracrine, and endocrine signals. This indicates that adipose tissue is a distinct endocrine organ that is specialized in the storage and mobilization of lipids and also produces a broad range of cytokines.[48,49,50]

FFA: Subcutaneous adipocytes in the upper body create the majority of circulating free fatty acids (FFA). The amount of fat within the abdomen has been positively correlated with splanchnic FFA levels, which may play a role in the liver fat deposition that is commonly seen in abdominal obesity [51.] Furthermore, a chronic exposure to elevated FFA in the pancreas affects pancreatic β cell function, whereas an acute exposure to elevated FFA in skeletal muscle inhibits insulin-mediated glucose uptake and causes insulin resistance [52.] Fibrinogen and PAI-1 production are elevated by FFAs [53.]

TNF α: It functions as a paracrine mediator in adipocytes and seems to have a local effect on adipocytes' insulin sensitivity [47.] Research indicates that TNF-α inhibits the insulin receptor substrate 1 signaling pathway [55,] which in turn enhances insulin resistance by inducing apoptosis in adipocytes [(54, 55).] An atherogenic dyslipidemia would be caused by the paracrine effect, which would further tend to increase the FFA release [56.] Body weight, white cholesterol, and triglycerides (TGs) are all favorably correlated with plasma TNF-α. On the other hand, HDL-C (high density lipoprotein) and plasma TNF-α are negatively correlated.

CRP: Elevated CRP levels are associated with increased WC, insulin resistance, BMI, and hyperglycemia[58], and they rise in direct proportion to the number of components of the MetS. It is more likely to be elevated in obese insulin-resistant individuals than in obese insulin-sensitive persons[60]. Additionally, it has been demonstrated that CRP levels, regardless of the degree or existence of MetS in an individual, independently predicted the occurrence of future CVD events[61]. Since the MetS has been linked to an elevated risk of future CVD events, levels of CRP may be a substantial independent predictor of adverse outcomes in the MetS.[62.]

IL-6: In humans, adipose tissue and skeletal muscle both release it [63.]It works as an anti-inflammatory as well as an inflammatory marker. Additionally expressed in the brain's many areas, including the hypothalamus, where it regulates energy intake and appetite, is the IL-6 receptor [64.] It is a systemic adipokine that affects insulin sensitivity and plays a significant role in determining the amount of CRP [65] produced by the liver. It is possible for IL-6 to inhibit lipoprotein lipase function. It has been demonstrated to have a negative correlation with HDL-C [67] and a favorable relationship between fasting insulin, BMI, and the onset of T2DM [66.]

PAI-1: This serine protease inhibitor is produced by vascular endothelium[47], platelets, and intra-abdominal adipocytes. Because it inhibits the tissue plasminogen activator (tPA) [68], atherothrombosis and decreased fibrinolysis are believed to be its indicators. Plasma PAI-1 levels are higher in inflammatory conditions[68] and people with abdominal obesity [69], which increases the risk of intravascular thrombus and adverse cardiovascular outcomes. [70.]

Adiponectin: It controls body weight and food intake, improves insulin sensitivity, controls lipid and glucose metabolism, and guards against long-term inflammation [71.] It suppresses the pace at which the liver produces glucose on its own and hepatic gluconeogenic enzymes. It improves fatty acid oxidation and muscle glucose transport [23.] Its complex anti-atherogenic properties include suppression of endothelial activation, decreased macrophage to foam cell conversion, and suppression of smooth muscle proliferation and arterial remodelling, which are hallmarks of the mature atherosclerotic plaque development [72] .Adiponectin has an inverse correlation with low density lipoprotein cholesterol (LDL-C), TGs and blood pressure, among other CVD risk factors. [73]. Furthermore, adiponectin has been demonstrated by Pischon et al. to be a potent inverse independent risk factor for CVD [74.] Moreover, Fumeron et al. came to the conclusion that, regardless of fat content, hypoadiponectinemia is linked to insulin resistance, hyperinsulinemia, and the potential to develop type 2 diabetes [75.] An anti-inflammatory molecule called adiponectin is negatively correlated with blood pressure, body weight, WC, TGs, insulin resistance (HOMA-Homeostasis Model Assessment), fasting insulin, and BMI. Adiponectin and HDL-C54, on the other hand, correlate favorably. TNF α [76] lowers its expressions and secretions, potentially by stimulating the synthesis of IL-6, which also prevents the secretion of adiponectin [77]. Adiponectin is perceived as "protective" due to its antagonistic action against TNF α as well as its inverse correlation with MetS [78] characteristics action [79.]

Leptin: It is an adipokine that controls appetite and energy intake [62.] When obesity develops, leptin levels in the plasma rise, and when weight is lost, they fall. The brain stem and the hypothalamus contain the majority of leptin receptors. Signals from these receptors regulate neuroendocrine function, energy expenditure, and satiety. Leptin resistance, or high levels of leptin that do not control hunger, is present in the majority of overweight and obese people. One basic pathophysiology in obesity is likely to be leptin resistance [80.] Leptin affects hunger and metabolism in addition to raising blood pressure in the hypothalamus via stimulating the sympathetic nervous system (SNS) [81]. A significant portion of the elevation in renal sympathetic tone seen in obese human participants is said to be explained by high levels of leptin in the blood [82.] Leptin [83] causes an increase in blood pressure and renal sympathetic activity, which is mediated by the ventromedial and dorsomedial hypothalamus. Leptin is a nitric oxide (NO) dependent vasodilator that also increases peripheral vascular resistance and sympathetic nerve activity [84]. Plasma leptin levels and obesity are correlated, and hyperleptinemia is actually considered a different risk factor for cardiovascular disease. [85.]

Insulin Resistance (IR): Normal body weight, absence of visceral or abdominal obesity, moderate physical activity, and low-saturated-fat diet are characteristics of the insulin-sensitive phenotype[86]. Insulin-resistant individuals exhibit impaired glucose metabolism or tolerance, as evidenced by abnormal responses to glucose challenges, elevated fasting glucose levels and/or overt hyperglycemia, or decreased insulin action following intravenous insulin administration (euglycemic clamp technique) with decreased insulin-mediated glucose clearance and/or reductions in the suppression of endogenous glucose production. It's characterized as a pathophysiological state wherein normal insulin concentrations are insufficient to trigger a typical insulin response in peripheral target tissues like the liver, muscle and adipose. In order to combat hyperglycemia in insulin-resistant people, pancreatic beta cells release extra insulin in this situation (hyperinsulinemia). While hyperinsulinemia

may make up for insulin resistance to certain of the physiological effects of insulin, such as the preservation of normoglycemia, it can also cause an excess of insulin activity in certain normally sensitive tissues. An concentration on some of insulin's effects combined with resistance to other actions of the hormone results in the clinical symptoms of MetS [87].

Hyperglycemia and overt T2DM[88] are caused by the pancreatic beta cells' gradual incapacity to generate enough insulin to reverse the tissue insulin resistance that is getting worse. Physiological insulin signaling occurs after ligand-activated tyrosine kinase-mediated binding of insulin to the insulin receptor. Insulin binding results in the tyrosine phosphorylation of downstream substrates and the activation of two parallel pathways: the phosphoinositide 3-kinase (PI3K) pathway and the mitogen-activated protein (MAP) kinase pathway. The MAP kinase pathway is unaffected by insulin resistance, whereas the PI3K-Akt pathway is disturbed. This throws off the balance between these two parallel pathways. Endothelial dysfunction results from a decrease in endothelial NO production brought on by inhibition of the PI3K-Akt pathway. Furthermore, there is a decrease in GLUT4 translocation, which lowers the quantity of glucose absorbed by skeletal muscle and fat. On the other hand, since the MAP kinase pathway remains intact, endothelin-1 (ET-1) synthesis, the expression of vascular cell adhesion molecules, and the stimulation of mitosis in vascular smooth muscle cells all persist. These are some of the ways that vascular anomalies that increase the risk of atherosclerosis are caused by insulin resistance. Insulin-resistant people often have an aberrant fat distribution with a predominance of upper body fat, even though they do not necessarily need to be clinically obese. Regardless of the proportional contributions of visceral fat and abdominal subcutaneous fat to insulin resistance, a pattern of trunk (upper body) obesity correlates more strongly with insulin resistance and the MetS than does lower body obesity [89].

Dyslipidaemia: The range of qualitative lipid abnormalities that define this dyslipidemia is indicative of disruptions in the biochemical activity, metabolism, and structure of both antiatherogenic HDL-C and atherogenic lipoproteins[90]. These abnormalities include low levels of HDL-C, elevated TGs, elevated levels of small particles of LDL, and elevated lipoproteins containing apolipoprotein B (apoB). An atherogenic dyslipidemia is caused by insulin resistance in multiple ways. First, because insulin generally inhibits lipolysis in adipocytes, a disruption in insulin signaling causes lipolysis to rise, which raises FFA levels. FFAs serve as a substrate for the liver's production of TGs. When apoB is generated, more very low density lipoprotein (VLDL) particles are created, the primary lipoprotein of VLDL particles, is stabilized by FFAs. Second, insulin resistance directly raises the synthesis of VLDL since insulin typically destroys apoB through PI3K-dependent pathways. Third, lipoprotein lipase, a key modulator of VLDL clearance and the rate-limiting enzyme, is regulated by insulin. Thus, both an increase in VLDL synthesis and a decrease in VLDL clearance lead to hypertriglyceridemia in insulin resistance. Remaining lipoproteins and tiny dense LDL are produced during the metabolism of VLDL, and both can encourage the development of atheromas. To create particles of TG-enriched HDL and cholesteryl ester-enriched VLDL, the cholesterol ester transport protein (CETP) transports the TGs from VLDL to HDL in exchange for cholesteryl esters. Furthermore, TG-enriched HDL is rapidly eliminated from the circulation due to its superior substrate status for hepatic lipase, which means that fewer HDL particles are available to participate in the vasculature's reverse cholesterol transport. As a result, insulin-resistant patients' livers have high FFA flow, increased TG synthesis and storage, and excess TG secreted as VLDL [90.] The prevailing belief is that elevated liver VLDL secretion is the primary cause of the dyslipidemia linked to insulin resistance [91]. These abnormalities strengthen the proinflammatory character of

macrovascular atherosclerotic disease by being intimately linked to elevated oxidative stress and endothelial dysfunction.

Hypertension: Obesity, glucose intolerance, and dyslipidemia are the three metabolic disorders most commonly linked to essential hypertension [92, 53]. Studies show that via upregulating the expression of AT II, AT1 receptor, and angiotensinogen, hyperglycemia and hyperinsulinemia activate the Renin-Angiotensin System (RAS). Individuals with insulin resistance may develop hypertension as a result of these combined variables [93]. Furthermore, evidence exists that insulin resistance and hyperinsulinemia activate the sympathetic nervous system, which subsequently prompts the heart to elevate cardiac output, the kidneys to improve sodium reabsorption, and the arteries to constrict in response, resulting in hypertension [94]. More recently, it has been discovered that adipocytes also produce aldosterone in response to ATII [95]. In this way, the adipocyte can be compared to a miniature renin-angiotensin-aldosterone system.

Genetics: Significant differences in beginning age and susceptibility amongst people with comparable risk profiles indicate a significant interaction between hereditary and environmental factors [96]. It is acknowledged that some individuals with high levels of metabolic risk factors and insulin resistance can be found in people who do not meet typical definitions of obesity. Examples include people with one parent and a first- or second-degree relative who also has diabetes [97]; many people of South Asian heritage also have this condition [98]. In obese/insulin-resistant people, there are significant individual differences as well as ethnic variations in the clinical pattern of metabolic risk factors [99]. Each metabolic risk factor most certainly has some genetic control over how it expresses itself, which affects how it reacts to various environmental stimuli. For instance, a number of polymorphisms in genes influencing lipoprotein metabolism are linked to the deterioration of dyslipidemia in

obese individuals100. In a similar vein, insulin resistance plus a hereditary propensity for impaired insulin production can cause abnormally high plasma glucose levels [101] . Neel's[102] thrifty genotype theory from 1962 states that if an organism could optimize its capacity to store excess energy, it would increase its chances of surviving in a hostile environment with erratic food supplies. Thus, under such conditions, genetic selection would favor the genotypes that conserve energy. But when nutrition improved, the specific genetic differences that had been advantageous during starvation would no longer be so. According to this theory, MetS is predisposed by common genetic variations of thrifty genes. Hales and Barker presented a second frugal phenotypic theory in 1992 [103.] This theory suggests that infants who suffered from intrauterine starvation may have become "thrifty" by lowering their energy consumption in response to inadequate nutrition. When people receive inadequate nutrition as children or adults, these metabolic adaptations help them; but, when people consume more food, these adaptations lose their benefits and raise the chance of developing Metabolic Syndrome (MetS) in the future. The reported links between low birth weight and the development of insulin resistance and type 2 diabetes in a number of populations [104] provide evidence in favor of this theory.

Endothelium Purpose: It is typified by decreased arterial compliance, accelerated atherosclerosis, and poor endothelium-dependent vasodilatation [105]. Adipokines, oxidative stress, advanced glycation products, FFAs, inflammatory cytokines, and hyperglycemia are just a few of the factors that hinder the endothelium's ability to perform its normal defensive and physiological roles. According to Hansson, immune cells are involved in every stage of the atherosclerotic process[106]; additionally, endothelial dysfunction and a proatherogenic vascular bed[107] are caused by an increase in reactive oxygen species and a decrease in NO, a crucial regulator of endothelial homeostasis.

Hypercoagulable State: Proinflammatory states are indicated by circulating cytokines and acute-phase reactants (e.g., CRP). Furthermore, endothelial dysfunction, platelet abrasions, and a rise in fibrinogen, factor VII, factor VIII, and the antifibrinolytic factor (PAI-1) are all signs of a prothrombotic state. A fibrinogen, an acute-phase reactant protein similar to CRP, has been demonstrated by Grundy SM[108] to increase in response to a high-cytokine condition. This suggests that there may be a metabolic connection between the prothrombotic and proinflammatory states.

Diet: According to a study by Aljada et al.[109,] a high dietary fat intake is linked to oxidative stress and the activation of nuclear factor kappa-beta (NFκB), a transcription factor that promotes inflammation. On the other hand, even when a diet high in fat contains the same number of calories, one high in fruits and fiber cannot cause inflammation [110.]

Long-Term Stress and the Action of Glucocorticoids (GC): Individuals who are genetically predisposed to persistently oversecrete stress mediators such as cortisol may experience favorable environmental conditions leading to inadequate growth hormone synthesis, hypogonadism, and visceral fat storage[111]. GCs promote preadipocyte differentiation into adipocytes, which may lead to an increase in body fat mass, block adipocytes' uptake of amino acids stimulated by insulin, increase lipolysis or lipid oxidation, which causes peripheral insulin resistance[113], and stimulate the hepatic gluconeogenic pathway. They also increase lipoprotein secretion and the activities of enzymes involved in fatty acid synthesis[112]. The frequency of MetS features, total urine GC metabolites, and plasma cortisol levels were found to be strongly correlated in these patients. A positive connection was noted in these patients between the [114], as well as the secretion rate and peripheral clearance of cortisol.These hormonal changes may cause sarcopenia, increased

visceral adiposity, and reactive insulin hypersecretion, which can result in dyslipidemia, hypertension, and T2DM [115].

Controlling Metabolic Syndrome:

Life style changes:

The underlying cause of the Metabolic syndrome is obesity. Therefore, the main strategy for treating the illness is weight loss. Controlling obesity by non-pharmacologic lifestyle management is crucial.

Numerous studies show that cutting back on calories to < 500–1000 kcal below daily requirements will help obese patients lose up to 0.5 kilograms/week. Exercise has numerous long-term advantages, even if it only slightly improves the success of calorie intake programs when combined with exercise. The majority of the component risk factors and the metabolic syndrome will be reduced with reaching the target weight loss by lifestyle modifications to lower BMI to less than 23 (for Asians) or 25 (for Caucasians).

Weight control and diet modifications:

Based on the information now available, patients with metabolic syndrome should begin their treatment with targeted weight reduction and increased physical activity.

According to current dietary guidelines, a balanced meal should contain 45–60% of calories from carbs, 20 to 35% from lipids, and 10–35% from protein [116]. Low consumption of cholesterol, trans fats, and saturated fats, along with low-glycaemic index meals, are the usual dietary guidelines. Animal protein may not be as useful as soy protein.

Physical activity:

Engaging in physical activity is linked to effective weight loss, and these therapeutic lifestyle modifications can cut the risk of early-onset diabetes in people with metabolic syndrome in half. It lowers the risk of cardiovascular disease overall. Recommendations for physical activity should include realistic, consistent, and moderate exercise programs that last at least 30 to 60 minutes each day. Exercise increases the benefits. Frequent exercise also enhances vascular health and endothelial function.[117]

Thus, it is evident that controlling the IR situation that characterizes the metabolic syndrome requires a comprehensive strategy that includes weight loss, consistent exercise, and yoga.[117]

Table 2: Treatment goals and clinical recommendations for the management of metabolic syndrome[117]

Target	Goal	Recommendations
Abdominal obesity:	10% weight reduction in first yearand continued weight reduction there after.	Healthy Diet and improved regular physical activity.
Physical inactivity	Daily physical activity.	30-60 minutes of exercise daily.
Atherogenic food	Limit intake to saturated fats, trans fats.	Total lipids 25-35% of total calories, Saturated fats less than 7% of calories.
Smoking	Complete stop	Complete stop
High LDL cholesterol	LDL cholesterol <100mg/dl (moderate) and <70mg /dl inhigh-risk patients.	Lifestyle modifications and cholesterollowering drugs to achieve targets.
Low HDL cholesterol	Inadequate data.	Lifestyle changes and HDL-raising drugs.
High blood pressure	In diabetes and CKD <130/80mmHg.	Lifestyle therapy and antihypertensive medications.
Elevated glucose	Control and maintenance of Fasting glucose less than 90mg/dl.HBA1C<7.0% for diabetics.	Lifestyle therapy and hypoglycemicdrugs if required.

PHARMACOTHERAPY:

Adjuvant pharmaceutical therapy, in conjunction with lifestyle adjustments, is an essential part of managing patients with metabolic syndrome, particularly those with a BMI more than 30 kg/m2 or a BMI more than 27 kg/m2 who also have obesity-related disorders and do not meet therapeutic goals [116.] The drugs that are used are

1. Centrally working anorexiants (appetite suppressants) – Sibutramine

2. Endocannabinoids - Rimonabant

3. Peripherally acting drugs – Orlistat

Sibutramine and Orlistat:

By modifying these neurotransmitters in the central nervous system(CNS), sibutramine, a selective serotonin and norepinephrine reuptake inhibitor, reduces appetite and promotes fullness without making people feel deprived. According to Krejs, weight loss and weight maintenance produced by sibutramine result in clinically significant decreases in risk variables linked to the metabolic syndrome [118.] Glycosylated hemoglobin (Hb A1c), uric acid concentrations, visceral fat and lipid levels all decrease during medication treatment.

Orlistat substantially inhibits the function of pancreatic, stomach, and carboxyl ester lipases, which are necessary for the breakdown of dietary fat into fatty acids and monoacylglycerols. When taken at a dose of 120 mg tid, orlistat slows the digestion and absorption of about 30% of dietary fat.It was determined that orlistat might successfully control co-morbidities associated with obesity, including IR and atherosclerosis risk. But the main issue with these anti-obesity medications that are now on the market is that they have a high rate of side effects that make it difficult to build tolerance and adhere to a long-term regimen.[117]

Antagonists of the cannabinoid-1 receptor (CB1):

A novel class of medications known as cannabinoid type 1 receptor (CB1) antagonists includes rimonabant. CB1 receptors are widely distributed throughout the brain [116.] It has been shown that high-risk patients with atherogenic dyslipidemia who are overweight or obese may benefit from this new class of medications.

Reduction in body weight in the overweight group combined with a commensurate decrease in waist circumference and improvement in metabolic profile as evidenced by a decrease in fasting insulin, glucose, and CRP [119] and an increase in plasma adiponectin levels. Depression, anxiety, and nausea were the most frequent side effects that resulted in the medicine being discontinued.

Surgical approach of obesity:

Patients with a BMI >40 kg/m2 or those whose BMI >35 kg/m2 is linked to a major medical condition may be candidates for surgery. Many industrialized nations treat severe obesity with liposuction or bariatric surgery. Despite a considerable reduction in weight, a randomized trial on liposuction revealed no effect on the lipid profile or other metabolic syndrome indicators.[116]

Among patients with diabetes mellitus and hypertension, it causes a 25–30% reduction in weight and a quick return to normalcy in blood pressure and glucose handling [23, 120.] However, there are no long-term data available, and new reports of significant procedure-related mortality and morbidity, particularly in the elderly, have brought up serious safety concerns.

Individual risk factor modification:

The American Heart Association (AHA) and the National Heart, Lung, and Blood Institute[30] have released a new scientific statement that highlights the importance of treating each individual risk factor in metabolic syndrome and suggests a multimodal therapeutic approach.

LIPID control:

Atherogenic dyslipidemia[121] is the term used to characterize the lipid abnormalities associated with the metabolic syndrome. Even in cases of metabolic syndrome, the ATP-III guidelines stress that the main goal of lipid therapy is LDL reduction, with low HDL and TGs acting as secondary targets [26.] It is well known that statins are effective at lowering LDL cholesterol levels. According to studies, statins seem tocontrol the LDL sub-fraction profile, either by reducing small dense LDL or by reducing all LDL subclasses while shifting the distribution of LDL particles.The objective is less than 100 mg/dl for persons at moderate risk and less than 70 mg/dl for subjects at high risk. Patients with the metabolic syndrome typically require medication therapy[121] in order to reach the appropriate LDL values, which are difficult to attain with diet or exercise therapy alone. Medications for dyslipidemia include

1. Cholesterol absorption inhibitors – Ezetimibe
2. HMG-CoA reductase inhibitors
3. Fibrates and Nicotinic acid (Niacin)
4. Bile acid sequestrants (Resins)
5. Omega 3 Fatty acids (Fish oils)
6. For dyslipidaemias, combination therapy has been recommended to reach goal levels of LDL and other lipids. Studies have shown that ezetimibeis a new cholesterol-lowering drug that works just as well either taken alone or in

combination with any statin at a dose of 10 mg per day. For instance, ezetimibe + 10 mg of atorvastatin was equally efficacious as atorvastatin plus 80 mg. Additionally, this combination increased HDL cholesterol and reduced TGs and apolipoprotein B (ApoB) more effectively than statins alone. Statins can also be used to safely increase target levels of HDL cholesterol, TGs, and non-HDL cholesterol when paired with a fibrate, particularly fenofibrate, and niacin.[26]

Fibrates:

Fibrates are helpful in treating metabolic syndrome dyslipidemia and atherogenic dyslipidemia. They work especially well when combined with statins to lower TGs and LDL cholesterol. However, combined therapy carries a slight but elevated risk of myopathy and rhabdomyolysis. It is necessary to monitor and provide counseling to patients who are being treated with these two drugs. The ATP-III has recommended using a statin in addition to fenofibrate because of the incredibly low risk of myopathy.[117,26]

The hypolipidemic activity is mediated by fibric acid, synthetic ligand of the nuclear receptor PPARγ that stimulates fatty acid oxidation. PPARγ enhances endothelial function and directly inhibits atherogenic processes on the vessel wall.

Niacin:

Niacin decreases non-HDL cholesterol while increasing HDL cholesterol. Individuals taking nicotinic acid for diabetes, poor glucose tolerance, or impaired fasting glucose levels should be closely watched for signs of worsening hyperglycemia. Niacin dosage reductions lessen this danger. For patients with metabolic syndrome, the combination of a statin and a low dose of niacin is a very appealing option.[122]

Adverse effects related to dermatology, such as flushing, pruritus, and rash, are frequent. Research has indicated that niacin at low doses can be beneficial in treating both metabolic syndrome and mixed dyslipidemia.[117]

Omega-3 fatty acids:

Following myocardial infarction, studies have demonstrated that taking fish oils (decohexaenoic acid and eicosapentaenoic acid) in levels of 3–4 gm daily can prevent cardiovascular events. Patients with diabetes mellitus and metabolic syndrome who require further triglyceride lowering have been treated with fish oils. Three grams of fish oil has been demonstrated to significantly lower small dense LDL, postprandial lipemia, and TGs by 20% in these patients.[30, 117]

HDL cholesterol modulation:

Several methods of raising HDL cholesterol are being studied. These comprise acetyl coenzyme A-cholesterol acyltransferase inhibitors, raising ApoA1, and cholesterol ester transfer protein (CETP) inhibitors (Torcetrapib).[123]

Hypertension:

Modifying one's lifestyle is crucial to lowering high blood pressure. The objective is to lower it as much as possible, ideally to less than 130/85 mm Hg or even less than 120/80 mm Hg. Similar to the Dietary Management to Stop Hypertension (DASH) diet, lifestyle therapies include things like weight loss, higher consumption of fresh fruits and vegetables, enhanced physical activity, reduced alcohol intake, and sodium limitation. [124.] Antihypertensive medication therapy are typically required to prevent long-term harmful effects if lifestyle interventions are insufficient in controlling hypertension.

Both beta-blockers and thiazide diuretics have been clearly shown to have a diabetogenic effect, and as of right now, these medications may not be the first choice for patients with metabolic syndrome[117]. Patients with metabolic syndrome are better off using ARBs and ACE inhibitors as antihypertensives.

ACE inhibitors:

More and more experts support ACE inhibitors as the initial line of treatment for the metabolic syndrome, especially when type 2 diabetes or renal impairment are present. By blocking the renin-angiotensin system, ACE inhibitors and angiotensin receptor blockers (ARBs) has been shown in large-scale randomized clinical trials to lower the risk of diabetes. ACE inhibitors and ARBs reduced the incidence of diabetes by 14% and 25%, respectively.

A good control in glucose tolerance and insulin sensitivity could be a possible cause. Insulin sensitivity is increased when angiotensin II blocks the post-receptor insulin signaling pathway. These medications also lessen inflammation. These medications also lessen oxidative stress and boost endothelial function, which would increase skeletal muscle's consumption of glucose because of enhanced flow and higher delivery. When ACE inhibitors are poorly tolerated, ARBs can be administered; they also have similar positive benefits on preventing diabetes.[117]

IGT, or impaired glucose tolerance, and insulin resistance:

Many of the problems linked to insulin resistance can be corrected by lowering elevated insulin levels through medication and lifestyle modifications. The risk of IGT turning into type 2 diabetes can be decreased by pharmacological interventions including medications such as metformin or thiazolidinediones.

Agonists for PPAR-α and PPAR-γ:

Insulin sensitivity is increased by thiazolidinedione medications such as pioglitazone, rosiglitazone, and troglitazone. Pioglitazone has been demonstrated to lower blood pressure, blood glucose, TGs, urine albumin/creatinine ratio, and other metabolic syndrome-related parameters.[126]

Proinflammatory and thrombotic state:

The only long-term strategy for primary prophylaxis that combats the thrombotic condition is low dose aspirin, i.e. 75–150 mg taken daily, or other anti-platelet medications. For people with existing cardiovascular disease, aspirin is generally advised. Aspirin at a dose of 75–150 mg per day is an appealing therapeutic option to reduce vascular events in individuals with metabolic syndrome who are at high risk of cardiovascular events in the future. Not to be overlooked is the fact that suppression of the renin-angiotensin system also lowers levels of PAI-1 and inflammatory cytokines, which may lower the risk of elevated thrombotic events in patients with metabolic syndrome.[23, 126, and 127.]

CRP readings more than 3 mg/dl are indicative of a need for lifestyle modifications. Numerous drugs used to address other metabolic risk factors in the metabolic syndrome have been shown to reduce CRP levels These medications include fibrates, ACE inhibitors or ARBs, thiazolidinediones, statins, and nicotinic acid; however, isolated, routine use of these medications to lower inflammatory markers has not yet been shown to enhance clinical results.[117]

Polypill Therapy method:

A polypharmacy approach has been proposed by Wald and Law to avoid cardiovascular disease [127.] Based on available clinical data, a combination "polypill"

containing low dosages of folic acid, statin, aspirin, and There are three antihypertensives that have been suggested: ACE inhibitors, beta-blockers, and thiazides.

This combination emphasizes the clinical significance of the metabolic syndrome and the necessity for multiple therapies in the prevention of CVD. The polypill idea is appealing and appears to hold a lot of promise for managing metabolic syndrome and lowering the burden of CVD, particularly in secondary and high-risk primary prevention.

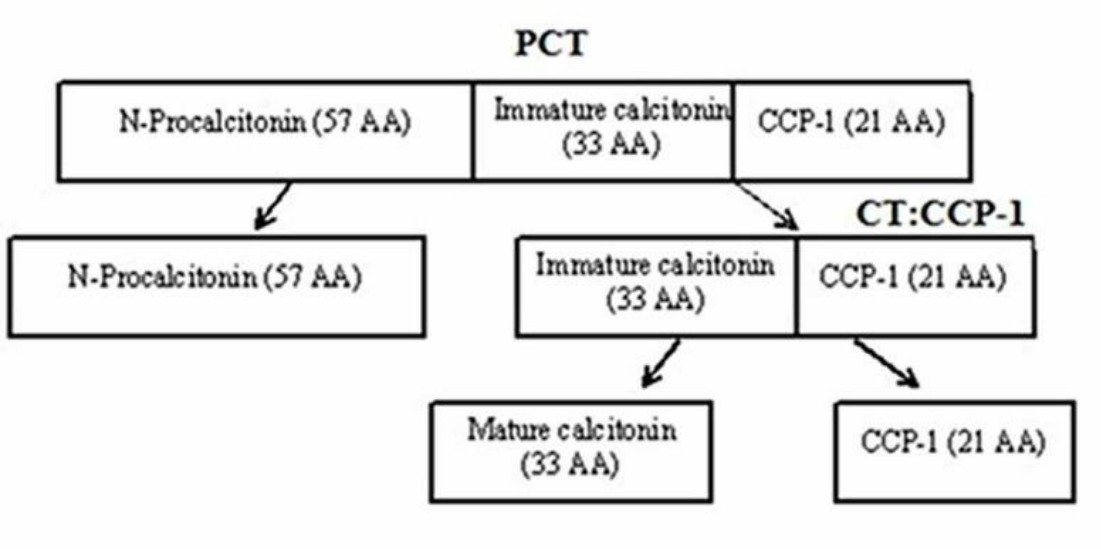
These drug combinations—two, three, and four—are currently accessible in India; nevertheless, adequately constructed multivariate randomized clinical trials are necessary to address concerns over long-term safety and benefits [117.] It shouldn't cause a doctor to lose focus on how crucial risk factor level management.

PROCALCITONIN

PCT is a peptide having a molecular weight of 14.5 kDa and 116 amino acids. It is composed of three parts: the amino terminus (57 amino acids), the carboxyl-terminus peptide 1 (CCP-1), also known as katacalcin, which comprises 21 amino acids, and immature calcitonin (33 amino acids) (Figure 1).128Its production is regulated by the calcitonin 1 gene (CALC-1) on chromosome 11. Proteases cleave the product of this gene, prePCT, which is then converted into the mature calcitonin molecule. The thyroid C-cell and, to a lesser extent, other neuroendocrine cells are the only cells generally capable of translating and transcribed the CALC-1 gene. However, in response to bacterial infection, production is stimulated in all parenchymal tissues through the action of the cytokines interleukin-6 (IL-6), interleukin-1β (IL-β), and tumour necrosis factor-α (TNF-α).[128] There is an accumulation of PCT in these other tissues because they are unable to split PCT into its mature form, calcitonin.[129] On the other hand, interferon-γ, which is mainly released in reaction to viral infection, reduces the

generation of PCT.[130] Because of this feature, PCT is a more accurate indicator of bacterial infection.

Figure 3. Schematic representation of the PCT molecule and the peptide that makes it up. [131]



When individuals with extra-thyroid disorders had high levels of calcitonin-like immunoreactivity in their blood in 1993, PCT was 1st identified as a sign of bacterial infection.[132] Scientists assessed the serum levels of procalcitonin in 79 children with bacterial and viral illnesses using a monoclonal immunoradiometric test for calcitonin precursors. Furthermore, they noted that, irrespective of PCT levels, all participants' calcitonin levels were normal and that PCT levels dropped quickly following antibiotic therapy. Patients with severe invasive bacterial infections had serum PCT levels between 6 and 53 ng/mL, which was significantly higher than those with mild local bacterial infections or viral infections (0.1 to 1.5 ng/mL). They came to the conclusion that serum concentrations are connected with the degree of microbial invasion and that PCT levels are elevated in bacterially septic situations.

PCT'S CLINICAL USEFULNESS IN CONTAMINOUS DISEASES:

The clinical assessment of PCT levels is still ongoing. PCT levels are currently used for four common purposes. Initially, the FDA approved the current immunoassay [133] to determine the probability of death in critically unwell septic patients. Second, PCT levels have been utilized to direct empirical antibiotic therapy in patients [134,135] who have acute exacerbations of sepsis, CAP, and chronic bronchitis. Third, PCT levels can help assess the efficacy of the patient's empirical antibiotic therapy in conjunction with standard clinical markers [134] Ultimately, the most practical usage is to use successive PCT values to assess when antibacterial medication is no longer necessary [136,137.]

Relationship between the severity of sepsis and PCT:

In the diagnosis of sepsis, PCT has been shown to be more clinically relevant and superior to other laboratory tests and often obtained clinical factors. It is also connected with the degree and severity of microbial invasion [138]. Animal studies provide compelling evidence that PCT is pathophysiologically involved in the formation of severe sepsis and related mortality, in contrast to other diagnostic biomarkers such as CRP. The course of PCT predicts the probability of mortality in critically ill patients with infections and in patients with ventilator-associated pneumonia, and it correlates with the breadth and severity of infection. These findings have prognostic implications. Moreover, the generation of PCT appears to be unaffected by nonsteroidal and steroidal anti-inflammatory medications, unlike other indicators such as CRP [139,140].

PCT to direct antibiotic treatment for upper respiratory tract infections

PCT levels can be utilized as a surrogate biomarker to direct antibiotic therapy in individual individuals because they rise during bacterial infection and fall after recovery [141,142.] For the purpose of accurately diagnosing both CAP and non-CAP lower respiratory tract infections (RTIs), highly sensitive PCT assays are required [143]. A lower number of patients were started

on empirical antibacterials as a result of two low PCT readings during the first four to six hours after hospital admission. An excellent negative predictive value for bacterial infection is found in low PCT levels during the first four hours of inpatient care.[143]

PCT for guidance on antibiotics in other infections:

According to certain proposals, PCT is a potentially useful marker for accurately differentiating bacterial infections from other infections, such as suspected bloodstream infections, arthritis, surgical fever, fungal infections, and neutropenic fever [144]. Crucially, all published studies were observational, Apart from respiratory tract infections, meningitis, and sepsis in the critical care unit, it remains uncertain if PCT may be utilized safely for antibiotic recommendations in other contexts. [145.] PCT might not be sensitive enough for everyday clinical use in certain infections. PCT levels may stay low in people with subacute endocarditis and cannot be utilized to distinguish between infected and uninfected individuals. Similar to this, PCT levels may stay low in individuals infected with viruses or Mycoplasma, but PCT clearly increases when infected with other uncommon bacteria like Legionella pneumophila. On the other hand, significant initial PCT levels were discovered in individuals who experienced hypothermia following cardiac arrest, regardless of any underlying infection. The diagnostic potential for early antibiotic stewardship in these high-risk individuals was limited due to the nonspecific increase in PCT, which appeared more like an inflammatory reaction than a genuine infection [143].

LIMITATIONS OF PCT

The use of PCT as a sepsis and infection marker has several drawbacks. In cases of extreme stress, such as following major surgery or trauma, or in patients experiencing cardiac shock, nonspecific increases in PCT levels may occur in the absence of a bacterial infection [134,136.] This explains why medical patients benefit more from PCT's ability to distinguish between sterile inflammation and sepsis than surgical patients do. There are several known causes of

nonbacterial systemic inflammation, such as heat shock, acute graft-versus-host disease, and stress during neonatal birth, granulocyte transfusions, antilymphocyte globulin or anti-CD3 antibody injection, cytokine or related antibody therapy (IL-2 or TNF-α) 135, and other immunotherapy modalities. Additionally, a number of autoimmune diseases, such as Kawasaki disease, various types of vasculitis, and paraneoplastic syndromes, have been connected to elevated PCT levels.[141].

The Metabolic Syndome and Procalcitonin has been linked to several metabolic syndrome components. Procalcitonin levels have been shown to be correlated with obesity, insulin resistance, and every aspect of the metabolic syndrome [146,147.] Procalcitonin has also been connected to cardiovascular events, atherosclerosis, and inflammation—all of which are strongly associated with metabolic syndrome [148,149.] Studies have demonstrated a correlation between obesity, insulin resistance, and metabolic syndrome [150] and procalcitonin expression in adipose tissue. In the general population, elevated plasma procalcitonin levels within the normal range have been linked to metabolic syndrome, obesity, and insulin resistance [147.]

Procalcitonin may also be a risk factor for cardiovascular events because it has been shown to be a marker for inflammation linked to atherosclerosis and metabolic syndrome [148.] Moreover, it has been linked to metabolic problems [150] and has been found to be a marker for low-grade inflammation associated with obesity. Procalcitonin's correlation with a number of clinical characteristics and biomarkers suggestive of metabolic dysfunction [151,152] lends credence to the relationship between the protein and metabolic syndrome.

All of these studies' data point to a strong correlation between procalcitonin and metabolic syndrome. Procalcitonin levels have been repeatedly linked to cardiovascular events, inflammation, atherosclerosis, obesity, insulin resistance, and other major elements or outcomes of metabolic syndrome. One fascinating area of investigation is the relationship between procalcitonin and metabolic syndrome. A precursor hormone called procalcitonin is

raised in response to sepsis, bacterial infections, and systemic inflammation. On the other hand, heart disease, stroke, and type 2 diabetes are more common among those with the metabolic syndrome, a collection of conditions that includes obesity, hypertension, hyperglycemia, and abnormal cholesterol levels.

Studies have shown a possible connection between procalcitonin levels, inflammation, and elements of the metabolic syndrome, even though a direct causal linkage between procalcitonin and the syndrome has not been proven. Procalcitonin is a sign of inflammation, and chronic low-grade inflammation is thought to play a major role in the development of metabolic syndrome.According to certain research, people with metabolic syndrome—especially those who also have other inflammatory diseases like obesity or type 2 diabetes—had higher procalcitonin levels. Nevertheless, further research is needed to determine the precise nature of this connection and its therapeutic significance.

It is noteworthy that procalcitonin is principally employed in clinical settings as a marker of sepsis and bacterial infection. Further research is necessary to properly understand the relationship and any potential consequences it may have for the diagnosis, prognosis, and treatment of metabolic syndrome and related disorders, even though its association with the syndrome is an intriguing topic of inquiry.

MATERIALS & METHODS

MATERIALS AND METHODS

Data source: Out patients and In patients of RL JALAPPA HOSPITAL, KOLAR.

Study design: A Prospective - Case Control Study.

Study period: September 2022 – December 2023

Method of collection of data: Patients admitted with diagnosis of metabolic syndrome at RL Jalappa Hospital and Research Centre, Kolar will be selected in a randomized manner.

Inclusion Criteria:

- Patients aged > 18 years with Metabolic Syndrome enrolled as cases after voluntary informed consent.
- Increased waist circumference (South Asian cut off > 90 cm for men and ≥ 80 cm for women) plus any two of the following, per NCEP guidelines: Systolic/diastolic blood pressure > 130 or 85 mm Hg; diabetes therapy or fasting plasma glucose ≥100 mg/dl; HDL cholesterol < 40 mg/dl in men and < 50 mg/dl in women or treatment for HDL; hypertension treatment or systolic/diastolic blood pressure > 150 mg/dl;[13].

Exclusion Criteria:

- Patients who are on lipid lowering drugs.
- S. Creatinine more than 1.2 mg/dl.
- Patients with any evidence of infections.

Methodology:

- Patients will be selected as per the inclusion and exclusion criteria.
- They will be explained about the procedure and their consent will be taken and they will be subjected to blood investigations.

- Clinical, laboratory and sociodemographic data will be elicited and collected in a predefined proforma

1. Socio demographic details

- Age
- Sex

2.Clinical data

- Height
- Weight
- Waist circumference
- Clinical examination

3. Investigations

- Plasma procalcitonin
- Complete lipid profile,
- fasting blood glucose
- Parameters like age and gender were matched.
- Results of waist circumference, Systolic BP, DBP, TG, cholesterol, HDL, LDL, VLDL, FBS, Plasma procalcitonin will be correlated in two different groups separately.

Individuals who meet the metabolic syndrome criteria are placed in the cases group; those who do not meet the criteria are placed in the control group. The fully automated PCT sensitive KRYPTOR Random Access Analyzer14 (BRAHMS PCT sensitive LIA; Hennigsdorf, Germany) was used to assess plasma procalcitonin (PCT).The required volume of blood sample was 50 µl, which was obtained in EDTA aliquots and incubated for 19 minutes. It has a measurement range of 0.02 to 5000 ng/ml.With a 95% probability, the functional assay sensitivity was 0.06 ng/ml, which is the lowest analyte concentration

that can be measured with an inter-assay CV <20. With a 95% probability, its analytical sensitivity, or the detection limit determined by utilizing the imprecision profile, is 0.019 ng/mlOver the complete PCT concentration range, the intra-assay and inter-assay coefficients of variation (CV) are 2-3The antibodies used in this experiment do not react with human calcitonin (up to 2.5 ng/ml), human katacalcin (up to 10 ng/ml), or human α- and ß-CGRP (up to 4 µg/ml).. This test method has already been explained.

Statistical analysis :

- For categorical variables: Descriptive statistics presented as frequency and percentage, and for continuous variables, as mean and SD.
- The relationship between different MS components and plasma PCTvalues.
- Compare plasma PCT levels in patients versus controls, the Mann-Whitney test was used
- "p value" ≤0.05 from two-sided tests was taken as statistically significant.

A Microsoft Excel data sheet will be used to record the data, and SPSS version 22 software will be used for analysis. Frequencies and proportions were used to depict categorical data.

Statistical software: MS Excel**,** SPSS version 26.0 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Sample size:

Sample size was estimated by using the difference in Mean procalcitonin between cases and controls repair from the study Divya bajpai et. al. as 0.55 ± 0.60 ng/ml and 0.00 ±0.00 ng/ml .

Using the formula below and the Med Calc sample size program, a sample size of 14 was obtained in each group using these values at the 95% Confidence Limit and 90% Power. With 10% nonresponse sample size of 14+ 1.4 ≈ 16 minimum subjects will be included in each group.

Sample size estimation formula:

$$N = \frac{2\,SD^2(Z_{\alpha/2} + Z_{\beta})^2}{d^2}$$

- Where $Z_{\alpha/2}$ is the critical point of the Normal distribution at $_{\alpha/2}$ (e.g. for a confidence level of 95%, **α** is 0.05 and the critical value is 1.96).
- Z_{β} is the critical value of the Normal distribution at β (e.g. for a power of 90%, ß is 0.1 and the critical value is 1.28),
- SD is the standard deviation from previous study population variance, and
- d is the difference between two mean

N = 33 in each group

RESULTS

RESULTS

TABLE 3: AGE DISTRIBUTION AMONG STUDY SUBJECTS

AGE (YEARS)		Mean	SD
GROUP	CASES	54.76	12.510
	CONTROLS	48.27	14.719
P VALUE		0.058	

The mean age of our study participants was 54.76±12.51 years and 48.27±14.72 years in the case & control group respectively. The small difference in the mean ages between the two groups was not statistically significant and hence they were comparable (p = .058).

FIGURE 4: AGE DISTRIBUTION AMONG STUDY SUBJECTS

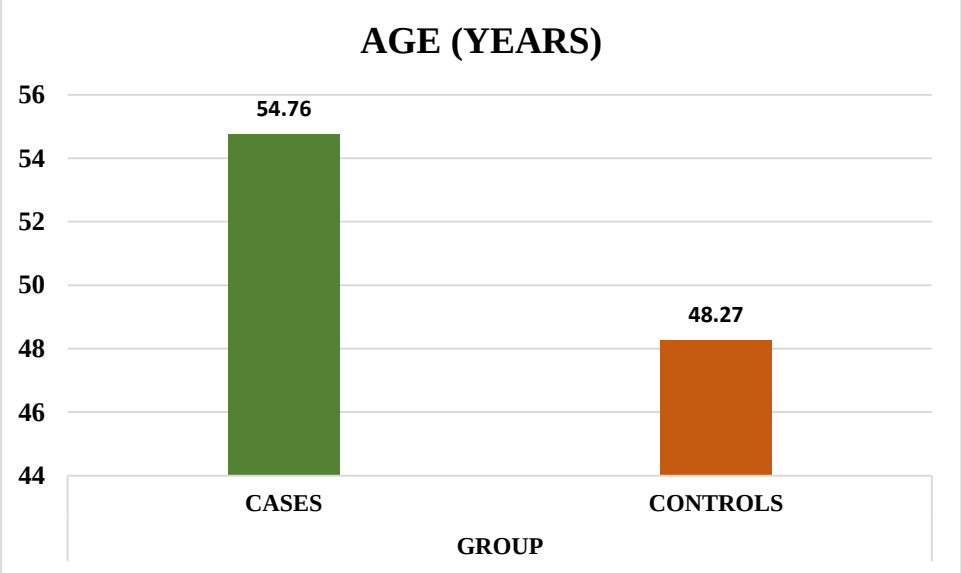


TABLE 4: GENDER DISTRIBUTION AMONG STUDY SUBJECTS

GENDER		GROUP		Total	P VALUE
		CASES	CONTROLS		
MALE	N	15	20	35	0.218
	%	45.5%	60.6%	53.0%	
FEMALE	N	18	13	31	
	%	54.5%	39.4%	47.0%	
Total	N	33	33	66	
	%	100.0%	100.0%	100.0%	

The case group had 45.5% males and 54.5% females while the control group had 60.6% males and 39.4% females. The two groups were still comparable as the difference in gender distribution between the two groups was not statistically significant (p = .218).

FIGURE 5: GENDER DISTRIBUTION AMONG STUDY SUBJECTS

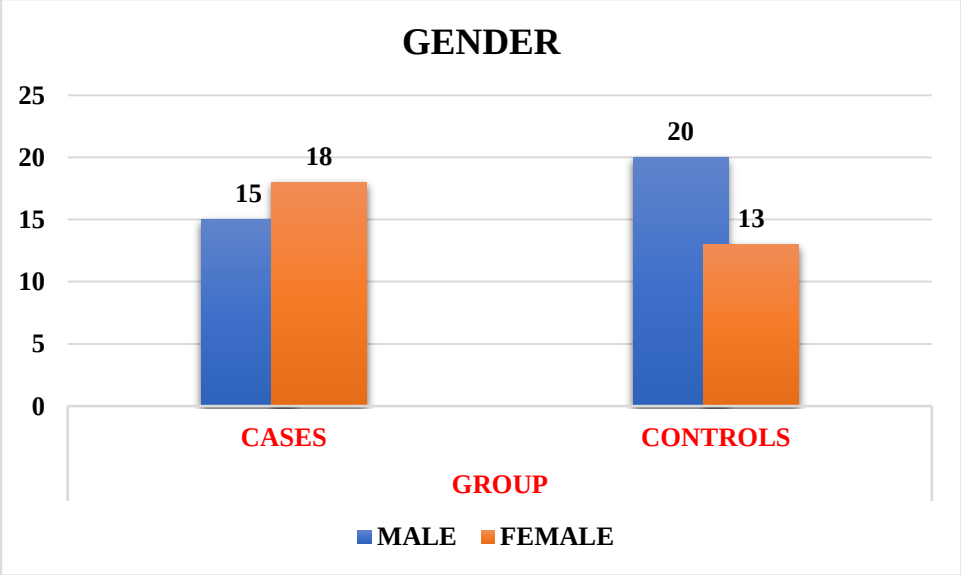


TABLE 6: WAIST CIRCUMFERENCE AMONG STUDY SUBJECTS

WAIST CIRCUMFERENCE (cm)		Mean	SD
GROUP	CASES	98.88	8.728
	CONTROLS	75.24	5.374
P VALUE		<0.001	

The mean waist circumference was seen to be 98.88±8.728 cm among the cases while the same was seen to be 75.24±5.374 cm among the controls. The difference in waist circumference noted between the two groups was seen to be statistically significant (p < .001).

FIGURE 7: WAIST CIRCUMFERENCE AMONG STUDY SUBJECTS

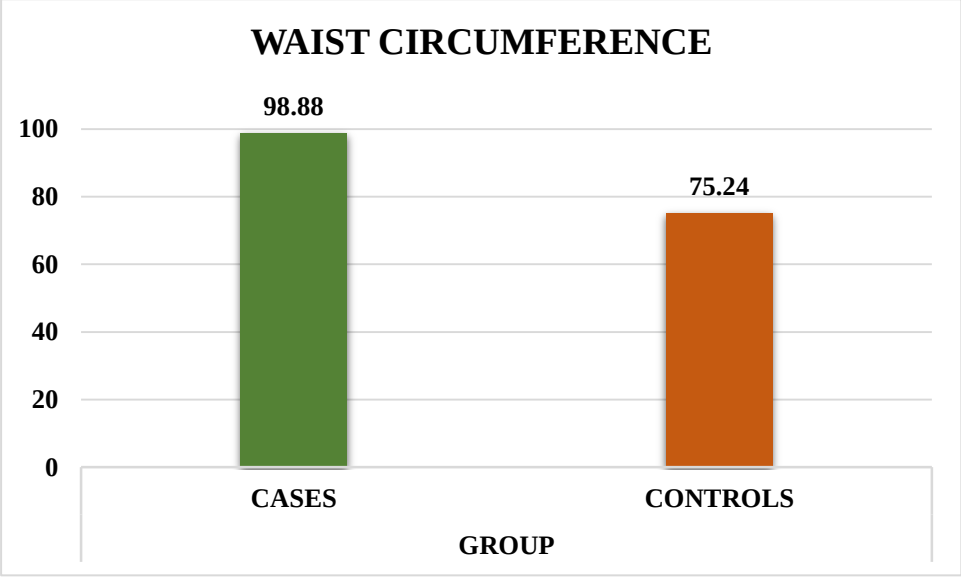


TABLE 7: Lipid Profile AMONG STUDY SUBJECTS

Lipid Profile		Mean	SD	P VALUE
TRIGLYCERIDES [mg/dl]	**CASES**	160.18	19.651	**<0.001**
	CONTROLS	137.70	7.122	
HDL [mg/dl]	**CASES**	38.33	6.213	**<0.001**
	CONTROLS	48.91	6.535	

In our study result, we found statistically significant differences in the lipid profile of cases & controls ($p < .001$). The mean Triglyceride value & the mean HDL value was seen to be 160.18±19.651 mg/dl and 38.33±6.213 mg/dl respectively. The mean Triglyceride value & the mean HDL value was seen to be 137.7±7.122 mg/dl and 48.91±6.535 mg/dl respectively.

FIGURE 8: Lipid Profile AMONG STUDY SUBJECTS

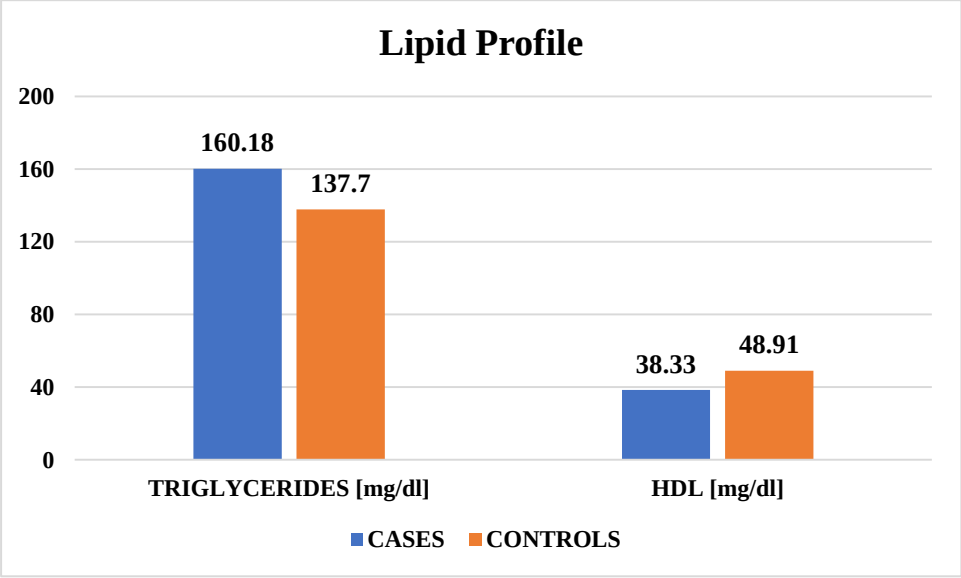


TABLE 8: FBS AMONG STUDY SUBJECTS

FBS [mg/dl]		Mean	SD
GROUP	CASES	129.55	17.090
	CONTROLS	83.09	8.095
P VALUE		<0.001	

The mean FBS value among the cases was 129.55±17.09 mg/dl and the same among controls was 83.09±8.095 mg/dl. The difference seen between the groups with respect to FBS values was found to be statistically significant ($p < .001$).

FIGURE 9: FBS AMONG STUDY SUBJECTS

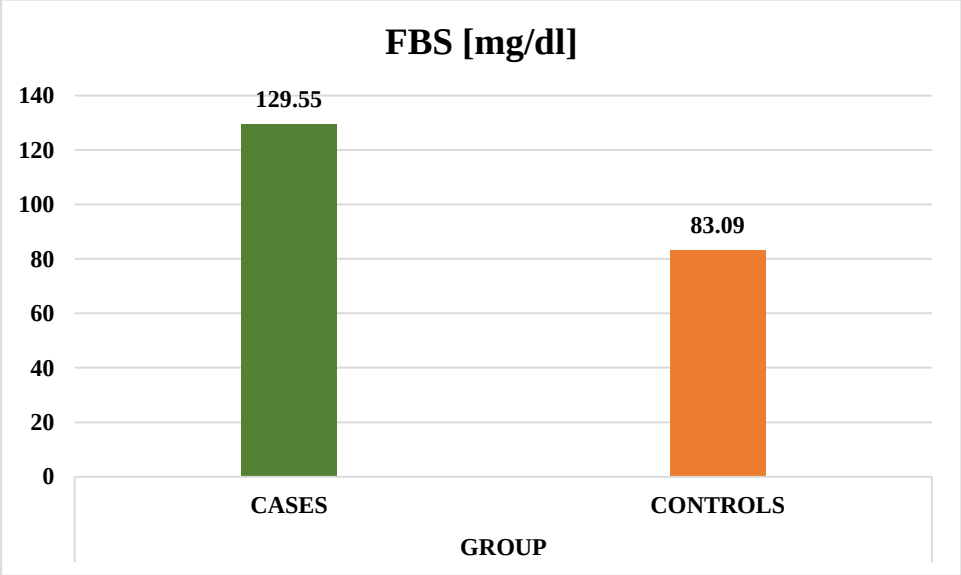


TABLE 9: PROCALCITONIN AMONG STUDY SUBJECTS

PROCALCITONIN [ng/dl]		Mean	SD
GROUP	CASES	1.806	1.236
	CONTROLS	0.163	0.163
P VALUE		<0.001	

The mean Procalcitonin level in the case group was seen to be 1.806±1.236 ng/dl and among the controls was seen to be 0.163±0.1613 ng/dl. This difference in the Procalcitonin level was statistically significant ($p < .001$).

FIGURE 10: PROCALCITONIN AMONG STUDY SUBJECTS

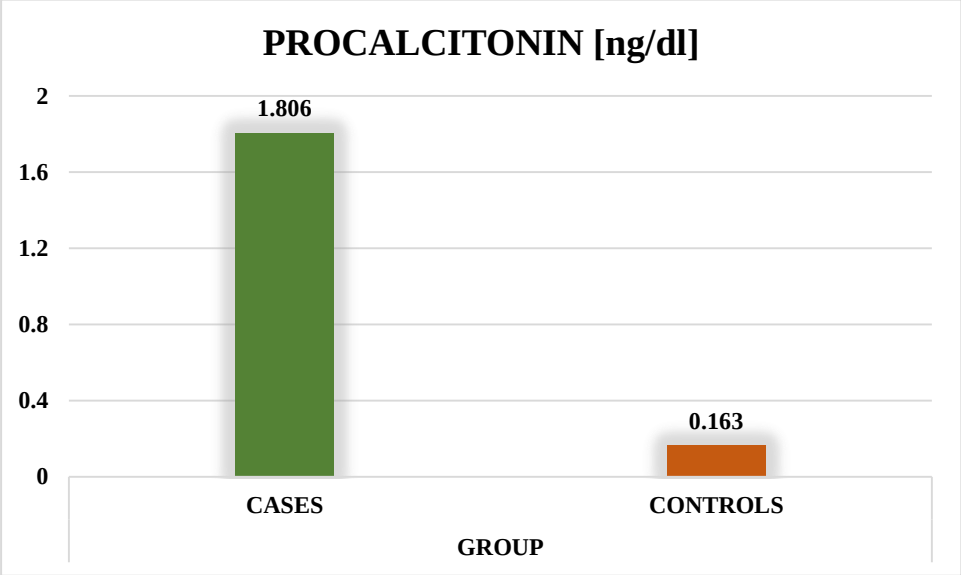
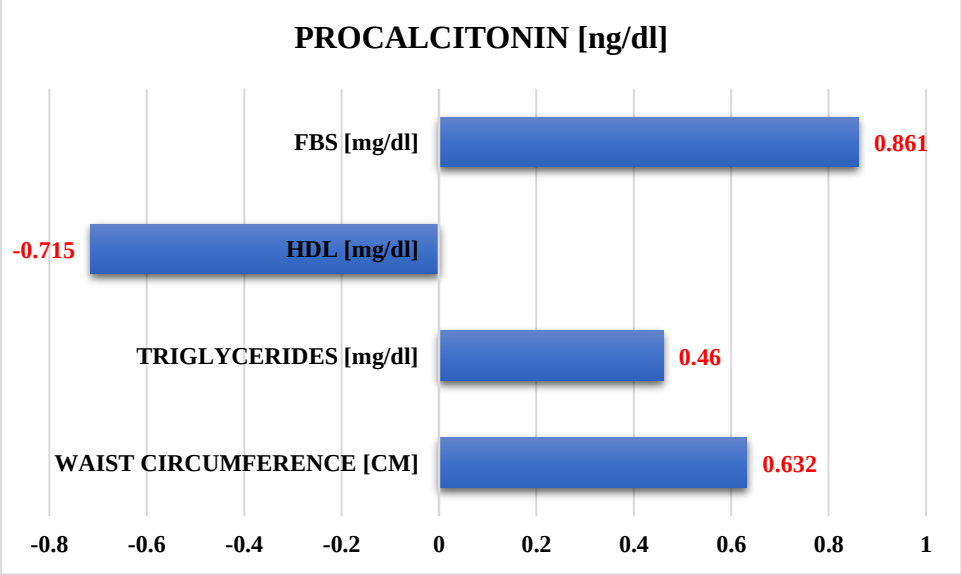


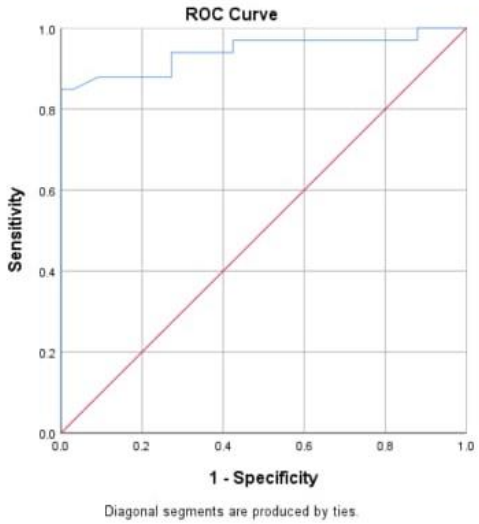
TABLE 10: ASSOCIATION OF PROCALCITONIN WITH LABORATORY PARAMETERS

		PROCALCITONIN [ng/dl]
WAIST CIRCUMFERENCE [CM]	Pearson Correlation	0.632
	P VALUE	**<0.001**
TRIGLYCERIDES [mg/dl]	Pearson Correlation	0.460
	P VALUE	**<0.001**
HDL [mg/dl]	Pearson Correlation	-0.715
	P VALUE	**<0.001**
FBS [mg/dl]	Pearson Correlation	0.861
	P VALUE	**<0.001**

This result shows that the Procalcitonin levels have significant association with Waist circumference, Triglycrides, HDL & FBS values in our study with a p value < .001.

FIGURE 11: ASSOCIATION OF PROCALCITONIN WITH LABORATORY PARAMETERS





Area Under the Curve - PROCALCITONIN [ng/ml]				
Area	**Std. Error**	**P Value**	**Asymptotic 95% CI**	
			Lower Bound	**Upper Bound**
0.942	0.032	**<0.001**	0.880	1.000

Cut-off	Sensitivity	Specificity
0.013	97%	87.9%
0.018	97%	84.8%
0.027	97%	75.8%
0.037	97%	72.7%
0.043	97%	66.7%
0.048	97%	63.6%
0.06	97%	60.6%

Area under the ROC for Procalcitonin as a diagnostic test was found to be 0.942 which indicates that it has an excellent prediction value ($p < .001$). At 0.013 cut off value, we found that Procalcitonin has a sensitivity of 97% and a specificity of 87.9%.

DISCUSSION

DISCUSSION

The thyroid gland produces procalcitonin (PCT), a precursor of the hormone calcitonin, which is involved in maintaining calcium homeostasis. Normal physiological conditions result in extremely low blood PCT levels. However, in response to a systemic bacterial infection or inflammatory stimuli, PCT levels can rise significantly. This characteristic has made PCT a valuable biomarker in diagnosing bacterial infections and sepsis.

Chronic low-grade inflammation is a common complication of Metabolic Syndrome (MetS). Insulin resistance and other metabolic disorders are facilitated by the secretion of inflammatory cytokines by adipose tissue, especially visceral fat, which include TNF-α, IL-6, and CRP (C-reactive protein). Procalcitonin, being an inflammatory marker, reflects this underlying inflammation. Elevated PCT levels have been observed in patients with conditions characterized by systemic inflammation, such as infections and sepsis, but also in non-infectious inflammatory states like MetS.

In this study we tried to determine if Procalcitonin can act as an additional marker for the diagnosis for Metabolic Syndrome. Our study population was divided into two groups: cases of MetS & controls. The two groups were comparable with respect to their age and gender distribution. The mean age of our study participants was 54.76±12.51 years and 48.27±14.72 years in the case & control group respectively. The case group had 45.5% males and 54.5% females while the control group had 60.6% males and 39.4% females.

The mean waist circumference was seen to be 98.88±8.728 cm among the cases while the same was seen to be 75.24±5.374 cm among the controls. Hence, the waist circumference, on an average, was significantly higher among patients with MetS ($p < .001$).

In our study result, we found statistically significant differences in the lipid profile of cases & controls ($p < .001$). The mean Triglyceride value & the mean HDL value was seen to be 160.18±19.651 mg/dl and 38.33±6.213 mg/dl respectively. The mean Triglyceride value & the mean HDL value was seen to be 137.7±7.122 mg/dl and 48.91±6.535 mg/dl respectively. Thus, we found higher Triglyceride values & lower HDL values in patients of MetS.

Patients with MetS were seen to have significantly higher FBS values when compared to controls ($p < .001$). The mean FBS value among the cases was 129.55±17.09 mg/dl and the same among controls was 83.09±8.095 mg/dl.

In our study, the mean Procalcitonin level in the case group was seen to be 1.806±1.236 ng/dl and among the controls was seen to be 0.163±0.1613 ng/dl. This difference in the Procalcitonin level was statistically significant ($p < .001$). We also found that the Procalcitonin levels had significant association with Waist circumference, Triglycrides, HDL & FBS values with a p value < .001.

Area under the ROC for Procalcitonin as a diagnostic test was found to be 0.942 which indicates that it has an excellent prediction value ($p< .001$). At 0.013 cut off value, we found that Procalcitonin has a sensitivity of 97% and a specificity of 87.9%.

Abbasi et al. found in one of the earliest investigations on this subject that the metabolic syndrome, insulin resistance, and obesity are associated with plasma procalcitonin (2010) [146]. 631 (19.7%) and 616 (16.9%) of the 3197 men and 3638 women in their study, respectively, had metabolic syndrome. Participants with elevated procalcitonin levels were seen to be older, more obese, and more likely to meet metabolic syndrome criteria. They also had reduced insulin sensitivity, decreased creatinine clearance, greater urine albumin excretion, and elevated hs-CRP. Procalcitonin levels were seen to progressively rise as waist

circumference and BMI values increased. Insulin resistance (HOMA-IR and fasting insulin) and components of the metabolic syndrome (waist circumference, systolic and diastolic blood pressure, triglycerides, HDL cholesterol, glucose) were found to be substantially linked with procalcitonin levels.

They came to the conclusion that higher-than-normal plasma procalcitonin levels are linked to higher obesity metrics, elements of the metabolic syndrome, and an increased chance of developing insulin resistance and the metabolic syndrome. Plasma procalcitonin may be a novel marker for persistent low-grade inflammation, adipocyte dysfunction, or both, as relationships are not entirely dependent on BMI.

In contrast to healthy controls, Bajpai et al. (2018) assessed the relationship between insulin resistance and plasma Procalcitonin (PCT) and the metabolic syndrome's four main components—abdominal obesity, dyslipidemia, hypertension, and hyperglycemia [153.] Plasma procalcitonin levels in 53 metabolic syndrome patients (n = 53) were significantly higher (mean 0.55 ± 0.60 nano gram/ml, median 0.156 ng/ml) than in 26 healthy controls ($p < 0.001$). PCT showed a significant inverse relationship with S.HDL ($p<0.05$), and a strong positive correlation with the levels of Insulin Resistance ($p<0.01$), Waist Circumference, S. Triglycerides, and S. VLDL ($p<0.05$). PCT was significantly higher in patients with microalbuminuria (n=18/53, z = - 7.265) and cardiovascular difficulties (n=16/53, z = -7.137) compared to cases without problems. This study indicated that elevated levels of plasma procalcitonin within the normal range are linked to insulin resistance and elements of the metabolic syndrome, including hypertriglyceridemia, abdominal obesity, low HDL, high VLDL, and hyperglycemia. As such, it may be a useful biomarker.

In order to test procalcitonin's promise as an inflammatory biomarker for the identification of low-grade inflammation associated with obesity [154,] Kassas et al. published a study in 2018

that examined the protein's role as an inflammatory marker in a group of Egyptian children with simple obesity. This case-control study comprised fifty obese and thirty-five normal weight children and adolescents, ages five to fifteen. Obese patients had higher serum PCT levels, total cholesterol level, triglycerides, LDL-c, hyperglycemia, and Hs-CRP (high sensitivity-CRP) than did the control group. According to correlation analysis, procalcitonin significantly positively correlated with insulin (P = 0.00), insulin resistance (HOMA-IR) (P = 0.006), triglycerides (P = 0.00), total cholesterol (P = 0.04), Hs-CRP (P = 0.02), and BMI z-score (P = 0.02) in the obese group. They came to the conclusion that measurements of adiposity, Hs-CRP, and insulin resistance were strongly correlated with elevated serum procalcitonin concentrations. This suggests that PCT may be a useful biomarker for chronic low-grade inflammation in children and adolescents that is linked to obesity.

A study on the correlation between Plasma Procalcitonin and Insulin Resistance [155] and Various Components of Metabolic Syndrome (abdominal obesity, dyslipidemia, hypertension, and hyperglycemia) was published in 2022 by Vyas et al. Thirty healthy controls and thirty cases of metabolic syndrome participated in this hospital-based observational study. They found that patients' mean plasma procalcitonin levels (0.11) were significantly higher than controls' levels (0.002 ng/ml). The case group had greater waist and neck circumference values (102.87±5.19 and 42.03±3.08) than the control group (79.67 ±7.98 and 37.10±1.35). The following indicators showed a significant ($p<.05$) connection with plasma procalcitonin in the case group: waist circumference, neck circumference, fasting blood glucose, fasting insulin level, S. triglycerides, and S. VLDL. They came to the conclusion that higher-than-normal plasma procalcitonin levels are linked to higher obesity metrics, elements of the metabolic syndrome, and an increased chance of developing insulin resistance and the metabolic syndrome.

All these study findings are in line with our study findings. They align with observational and experimental findings suggesting that, even in the absence of sepsis or systemic infection symptoms, plasma procalcitonin may function as an inflammatory biomarker. [156-159]

A recent paper discovered a correlation between the distribution of central body fat and plasma procalcitonin in women diagnosed with polycystic ovary syndrome. We found a strong independent connection between procalcitonin and waist circumference, which is consistent with this.

LIMITATIONS

The limitations of our study include a small sample size, done in a single hospital setting. PCT only acts as an additional marker for the diagnosis of metabolic syndrome, as relying only on PCT per se is not validated as it is difficult to rule out other ongoing inflammatory process in body and its cost effectiveness. A larger study with a higher sample size is required to prove it's efficacy as a diagnostic marker.

CONCLUSION

CONCLUSIONS

Procalcitonin holds promise as an additional marker for diagnosing Metabolic Syndrome, reflecting the underlying inflammatory state associated with the condition. While current evidence says a positive correlation between elevated PCT levels and MetS, further detailed research is needed to fully understand its role and establish standardized guidelines for its use. Integrating PCT into the diagnostic framework for MetS could improve early detection, risk stratification, and monitoring of treatment efficacy, ultimately enhancing patient outcomes. However, practical challenges related to specificity, standardization, cost, and clinical integration must be addressed to realize its full potential.

SUMMARY

SUMMARY

The metabolic syndrome (MetS) is a collection of conditions that increases the risk of heart disease, stroke, and type 2 diabetes. It includes excessive blood sugar, high blood pressure, unusually high triglyceride or cholesterol levels, and excess body fat around the waist. Early detection of MetS is essential to avoid its serious consequences. Traditionally, diagnostic indicators such as blood pressure, waist circumference, triglycerides, HDL cholesterol, and fasting glucose are employed. Recently, procalcitonin (PCT) has emerged as a potential additional marker for MetS diagnosis, offering insights into the inflammatory and metabolic disturbances underlying the syndrome.

Several clinical studies, including ours, have investigated the relationship between PCT levels and MetS and a consistent finding across these studies is that PCT levels tend to be higher in individuals with MetS compared to those without it. These findings suggest that PCT could serve as a useful additional marker for MetS, complementing traditional diagnostic criteria. Elevated PCT levels in individuals meeting the criteria for MetS might indicate a more pronounced inflammatory state, highlighting the need for more aggressive management of cardiovascular risk factors. Adding PCT to the diagnostic panel for MetS could enhance early detection and risk stratification. Patients with elevated PCT levels might be at higher risk for cardiovascular events and diabetes, warranting more intensive lifestyle and pharmacological interventions. PCT could also be used to monitor the efficacy of interventions aimed at reducing inflammation and metabolic risk.

Despite the potential benefits, several challenges need to be addressed before PCT can be widely adopted as a marker for MetS: PCT is a marker of systemic inflammation, not specific to MetS. Elevated PCT levels can occur in various conditions, including infections and other inflammatory diseases. Thus, it should be interpreted in the context of other clinical findings and markers. There is a need for standardized cut-off values for PCT levels in the context of

MetS. Establishing these thresholds will require large-scale studies across diverse populations. Measuring PCT levels involves additional costs and laboratory resources. The cost-effectiveness of adding PCT to routine MetS screening needs to be evaluated. Also, the role of PCT in conjunction with other established markers of MetS needs to be clearly defined. This includes understanding how PCT adds value beyond traditional markers and its impact on clinical decision-making.

BIBLIOGRAPHY

BIBLIOGRAPHY

1. Grundy SM. Hypertriglyceridemia, insulin resistance, and the metabolic syndrome. Am J Cardiol. 1999;83(9B):25F-29F. doi:10.1016/s0002-9149(99)00211-8.
2. Kim SK, Hur KY, Choi YH, Kim SW, Chung JH, Kim HK, et al. The relationship between lung function and metabolic syndrome in obese and non-obese korean adult males. Korean Diabetes J. 2010;34(4):253.
3. Pan W-H, Yeh W-T, Weng L-C. Epidemiology of metabolic syndrome in Asia. Asia Pac J Clin Nutr. 2008;17 Suppl 1:37–42.
4. Bonomini F, Rodella LF, Rezzani R. Metabolic syndrome, aging and involvement of oxidative stress. Aging Dis. 2015 Mar 10;6(2):109–20.
5. Kuk JL, Ardern CI. Age and sex differences in the clustering of metabolic syndrome factors: association with mortality risk. Diabetes Care. 2010 Nov 1;33(11):2457–61.
6. Denys K, Cankurtaran M, Janssens W, Petrovic M. Metabolic syndrome in the elderly: an overview of the evidence. Acta Clinica Belgica. 2009 Feb;64(1):23–34.
7. Lumeng CN, Saltiel AR. Inflammatory links between obesity and metabolic disease. J Clin Invest 2011;121:2111–7. https://doi.org/10.1172/JCI57132.
8. Abella V, Scotece M, Conde J, López V, Lazzaro V, Pino J, et al. Adipokines, metabolic syndrome and rheumatic diseases. J Immunol Res 2014;2014:343746. https://doi.org/10.1155/2014/343746.
9. Medina G, Vera-Lastra O, Peralta-Amaro AL, Jiménez-Arellano MP, Saavedra MA, Cruz-Domínguez MP, et al. Metabolic syndrome, autoimmunity and rheumatic diseases. Pharmacol Res 2018;133:277–88. https://doi.org/10.1016/j.phrs.2018.01.009.
10. Mok CC. Metabolic syndrome and systemic lupus erythematosus: the connection. Expert Rev Clin Immunol 2019;15:765 https://d

11. oi.org/10.1080/1744666X.2019. 1620601.
12. Jin M, Khan AI. Procalcitonin: Uses in the Clinical Laboratory for the Diagnosis of Sepsis. Lab Med 2010;41:173–7. https://doi.org/10.1309/LMQ2GRR4QLFKHCH9.
13. Whang KT, Vath SD, Becker KL, Snider RH, Nylen ES, Muller B, et al. Procalcitonin and proinflammatory cytokine interactions in sepsis. Shock 2000;14:73–8. https://doi.org/10.1097/00024382-200014010-00013.
14. Wei JX, Verity A, Garle M, Mahajan R, Wilson V. Examination of the effect of procalcitonin on human leucocytes and the porcine isolated coronary artery. Br J Anaesth 2008;100:612–21. https://doi.org/10.1093/bja/aen073.
15. Wagner N-M, Van Aken C, Butschkau A, Bierhansl L, Kellner P, Schleusener V, et al. Procalcitonin Impairs Endothelial Cell Function and Viability. Anesth Analg 2017;124:836–45. https://doi.org/10.1213/ANE.0000000000001574.
16. Sauer M, Doß S, Ehler J, Mencke T, Wagner N-M. Procalcitonin Impairs Liver Cell Viability and Function In Vitro: A Potential New Mechanism of Liver Dysfunction and Failure during Sepsis? Biomed Res Int 2017;2017:6130725. https://doi.org/10.1155/2017/6130725.
17. Tavares E, Miñano FJ. Immunoneutralization of the aminoprocalcitonin peptide of procalcitonin protects rats from lethal endotoxaemia: neuroendocrine and systemic studies. Clin Sci (Lond) 2010;119:519–34. https://doi.org/10.1042/CS20100007.
18. Alberti KGMM, Zimmet P, Shaw J, IDF Epidemiology Task Force Consensus Group. The metabolic syndrome--a new worldwide definition. Lancet. 2005 Sep 24;366(9491):1059–62
19. Shaw JE, Chisholm DJ. 1: Epidemiology and prevention of type 2 diabetes and the metabolic syndrome. Med J Aust [Internet]. 2003 Oct 6 [cited 2020 Oct 2];179(7).

Available from:https://www.mja.com.au/journal/2003/179/7/1-epidemiology-and-prevention-type-2-diabetes-and-metabolic-syndrome

20. Kylin E. Studienueber das Hypertonie-Hyperglyca \"mie-Hyperurika\" miesyndrom. ZentralblattfuerInnereMedizin. 1923; 44: 105–127.
21. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes. 1988 Dec;37(12):1595–607.
22. Kaplan NM. The deadly quartet. Upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. JAMA Internal Medicine. 1989 Jan 1;149(7):1514–20.
23. S. M. Haffner, R. A. Valdez, H. P. Hazuda, B. D. Mitchell, P. A. Morales, and M. P.Stern, "Prospective analysis of the insulin resistance syndrome (Syndrome X),"Diabetes, vol. 41, no. 6, pp. 715–722, 1992
24. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet. 2005 Apr 16;365(9468):1415–28.
25. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998 Jul;15(7):539–53
26. Balkau B, Charles MA. Comment on the provisional report from the who consultation. European group for the study of insulin resistance(Egir). Diabet Med. 1999 May;16(5):442–3.
27. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the third report of the national cholesterol education program (Ncep) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults(Adult treatment panel iii). JAMA. 2001 May 16;285(19):2486–97.

28. Einhorn D, Reaven GM, Cobin RH, Ford E, Ganda OP, Handelsman Y et al. American College of Endocrinology position statement on the insulin resistance syndrome. Endocrine practice : official journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists. 2003;9(3):237-252.
29. Ford ES. Prevalence of the metabolic syndrome in US populations. Endocrinology and Metabolism Clinics of North America. 2004 Jun 1;33(2):333–50.
30. Shaw JE, Zimmet PZ, Alberti KGMM. Point: Impaired fasting glucose: The case for the new American Diabetes Association criterion. Diabetes Care. 2006 Jan 1;29(5):1170-1172. https://doi.org/10.2337/dc06-0013
31. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an american heart association/national heart, lung, and blood institute scientific statement. Circulation. 2005 Oct 25;112(17):2735–52.
32. Wilson PWF, D'Agostino RB, Parise H, Sullivan L, Meigs JB. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation. 2005 Nov 15;112(20):3066–72.
33. Yamauchi T, Kadowaki T. Adiponectin receptor as a key player in healthy longevity and obesity-related diseases. Cell Metab. 2013 Feb 5;17(2):185–96.
34. Löfgren P, Andersson I, Adolfsson B, Leijonhufvud B-M, Hertel K, Hoffstedt J, et al. Long-term prospective and controlled studies demonstrate adipose tissue hypercellularity and relative leptin deficiency in the postobese state. J Clin Endocrinol Metab. 2005 Nov;90(11):6207–13.

35. Ferrannini E, Buzzigoli G, Bonadonna R, Giorico MA, Oleggini M, Graziadei L, et al. Insulin resistance in essential hypertension. N Engl J Med. 1987 Aug 6;317(6):350–7.

36. Yamauchi T, Kamon J, Waki H, Terauchi Y, Kubota N, Hara K, et al. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. Nat Med. 2001 Aug;7(8):941–6.

37. Kuk JL, Ardern CI. Age and sex differences in the clustering of metabolic syndrome factors: association with mortality risk. Diabetes Care. 2010 Nov;33(11):2457–61.

38. Després J-P, Lemieux I, Bergeron J, Pibarot P, Mathieu P, Larose E, et al. Abdominal obesity and the metabolic syndrome: contribution to global cardiometabolic risk. Arterioscler Thromb Vasc Biol. 2008 Jun;28(6):1039–49.

39. Mozumdar A, Liguori G. Persistent increase of prevalence of metabolic syndrome among U.S. adults: NHANES III to NHANES 1999-2006. Diabetes Care. 2011 Jan;34(1):216–9.

40. Firmann M, Mayor V, Vidal PM, Bochud M, Pécoud A, Hayoz D, et al. The CoLaus study: a population-based study to investigate the epidemiology and genetic determinants of cardiovascular risk factors and metabolic syndrome. BMC Cardiovasc Disord. 2008 Dec;8(1):6. doi: 10.1186/1471-2261-8-6

41. Venugopal V, Dongre AR, Saravanan S. Prevalence and determinants of metabolic syndrome among the rural adult population of Puducherry. Indian Journal of Community Medicine. 2019 Jan 1;44(1):21.

42. Arai H, Yamamoto A, Matsuzawa Y, Saito Y, Yamada N, Oikawa S, et al. Prevalence of the metabolic syndrome in elderly and middle-aged Japanese. Journal of Clinical Gerontology and Geriatrics. 2010 Dec;1(2):42–7.

43. Deepa R, Shanthirani CS, Premalatha G, Sastry NG, Mohan V. Prevalence of insulin resistance syndrome in a selected south Indian population--the Chennai urban population study-7 [CUPS-7]. Indian J Med Res. 2002 Mar;115:118–27

44. Halberg N, Wernstedt-Asterholm I, Scherer PE. The adipocyte as an endocrine cell. Endocrinol Metab Clin North Am. 2008 Sep;37(3):753–68, x–xi.

45. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004 May;27(5):1047–53.

46. Bankoski A, Harris TB, McClain JJ, Brychta RJ, Caserotti P, Chen KY, et al. Sedentary activity associated with metabolic syndrome independent of physical activity. Diabetes Care. 2011 Feb;34(2):497–503.

47. Cinti S, Mitchell G, Barbatelli G, Murano I, Ceresi E, Faloia E, et al. Adipocyte death defines macrophage localization and function in adipose tissue of obese mice and humans. J Lipid Res. 2005 Nov;46(11):2347–55.

48. Lau DCW, Dhillon B, Yan H, Szmitko PE, Verma S. Adipokines: molecular links between obesity and atheroslcerosis. Am J Physiol Heart Circ Physiol. 2005 May;288(5):H2031-2041.

49. Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. Br J Nutr. 2004 Sep;92(3):347–55.

50. Tsimikas S, Willeit J, Knoflach M, Mayr M, Egger G, Notdurfter M, et al. Lipoprotein-associated phospholipase A2 activity, ferritin levels, metabolic syndrome, and 10-year cardiovascular and non-cardiovascular mortality: results from the Bruneck study. Eur Heart J. 2009 Jan;30(1):107–15.

51. Jacobs M, van Greevenbroek MMJ, van der Kallen CJH, Ferreira I, Blaak EE, Feskens EJM, et al. Low-grade inflammation can partly explain the association

between the metabolic syndrome and either coronary artery disease or severity of peripheral arterial disease: the CODAM study. Eur J Clin Invest. 2009 Jun;39(6):437–44.

52. Miles JM, Jensen MD. Counterpoint: Visceral adiposity is not causally related to insulin resistance. Diabetes Care. 2005 Sep;28(9):2326–8.

53. Boden G, Lebed B, Schatz M, Homko C, Lemieux S. Effects of acute changes of plasma free fatty acids on intramyocellular fat content and insulin resistance in healthy subjects. Diabetes. 2001 Jul;50(7):1612–7.

54. Kahn SE, Prigeon RL, Schwartz RS, Fujimoto WY, Knopp RH, Brunzell JD, et al. Obesity, body fat distribution, insulin sensitivity and islet β-cell function as explanations for metabolic diversity. The Journal of Nutrition. 2001 Feb 1;131(2):354S-360S.

55. Xydakis AM, Case CC, Jones PH, Hoogeveen RC, Liu M-Y, Smith EO, et al. Adiponectin, inflammation, and the expression of the metabolic syndrome in obese individuals: the impact of rapid weight loss through caloric restriction. J Clin Endocrinol Metab. 2004 Jun;89(6):2697–703.

56. Hotamisligil GS, Peraldi P, Budavari A, Ellis R, White MF, Spiegelman BM. IRS-1-mediated inhibition of insulin receptor tyrosine kinase activity in TNF-alpha- and obesity-induced insulin resistance. Science. 1996 Feb 2;271(5249):665–8.

57. Krauss RM. Lipids and lipoproteins in patients with type 2 diabetes. Diabetes Care. 2004 Jun;27(6):1496–504.

58. González AS, Guerrero DB, Soto MB, Díaz SP, Martinez-Olmos M, Vidal O. Metabolic syndrome, insulin resistance and the inflammation markers C-reactive protein and ferritin. Eur J Clin Nutr. 2006 Jun;60(6):802–9.

59. Deepa R, Velmurugan K, Arvind K, Sivaram P, Sientay C, Uday S, et al. Serum levels of interleukin 6, C-reactive protein, vascular cell adhesion molecule 1, and monocyte chemotactic protein 1 in relation to insulin resistance and glucose intolerance--the Chennai Urban Rural Epidemiology Study (Cures). Metabolism. 2006 Sep;55(9):1232–8

60. Guldiken S, Demir M, Arikan E, Turgut B, Azcan S, Gerenli M, et al. The levels of circulating markers of atherosclerosis and inflammation in subjects with different degrees of body mass index: Soluble CD40 ligand and high-sensitivity C-reactive protein. Thromb Res. 2007;119(1):79–84.

61. McLaughlin T, Abbasi F, Lamendola C, Liang L, Reaven G, Schaaf P, et al. Differentiation between obesity and insulin resistance in the association with c-reactive protein. Circulation. 2002 Dec 3;106(23):2908–12.

62. Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14 719 initially healthy American women. Circulation. 2003 Jan 28;107(3):391–7.

63. Clearfield MB. C-reactive protein: a new risk assessment tool for cardiovascular disease. Journal of the American Osteopathic Association.2005; 105(9):409–16.

64. Pedersen BK, Steensberg A, Fischer C, Keller C, Keller P, Plomgaard P, et al. Searching for the exercise factor: is IL-6 a candidate? J Muscle Res Cell Motil. 2003 Apr 1;24(2):113.

65. Stenlöf K, Wernstedt I, Fjällman T, Wallenius V, Wallenius K, Jansson J-O. Interleukin-6 levels in the central nervous system are negatively correlated with fat mass in overweight/obese subjects. J Clin Endocrinol Metab. 2003 Sep;88(9):4379–83

66. Diamant M, Lamb HJ, van de Ree MA, Endert EL, Groeneveld Y, Bots ML, et al. The association between abdominal visceral fat and carotid stiffness is mediated by circulating inflammatory markers in uncomplicated type 2 diabetes. The Journal of Clinical Endocrinology & Metabolism. 2005 Mar 1;90(3):1495–501.

67. Pradhan AD, Manson JE, Rifai N, Buring JE, Ridker PM. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. JAMA. 2001 Jul 18;286(3):327–34.

68. Zuliani G, Volpato S, Blè A, Bandinelli S, Corsi AM, Lauretani F, et al. High interleukin-6 plasma levels are associated with low HDL-C levels in community-dwelling older adults: The InChianti study. Atherosclerosis. 2007 Jun;192(2):384–90.

69. Alessi M-C, Juhan-Vague I. PAI-1 and the metabolic syndrome: links, causes, and consequences. Arterioscler Thromb Vasc Biol. 2006 Oct;26(10):2200–7.

70. Cigolini M, Targher G, Andreis IAB, Tonoli M, Agostino G, De Sandre G. Visceral fat accumulation and its relation to plasma hemostatic factors in healthy men. Arteriosclerosis, Thrombosis, and Vascular Biology. 1996 Mar 1;16(3):368–74.

71. Kohler HP, Grant PJ. Plasminogen-activator inhibitor type 1 and coronary artery disease. N Engl J Med. 2000 Jun 15;342(24):1792–801.

72. Liu M, Liu F. Transcriptional and post-translational regulation of adiponectin. Biochemical Journal. 2010 Jan 1;425(1):41–52.

73. Matsuzawa Y, Funahashi T, Kihara S, Shimomura I. Adiponectin and metabolic syndrome. Arteriosclerosis, Thrombosis, and Vascular Biology. 2004 Jan 1;24(1):29–33.

74. Kazumi T, Kawaguchi A, Sakai K, Hirano T, Yoshino G. Young men with high-normal blood pressure have lower serum adiponectin, smaller LDL size, and higher

elevated heart rate than those with optimal blood pressure. Diabetes Care. 2002 Jun;25(6):971–6.

75. Pischon T, Girman CJ, Hotamisligil GS, Rifai N, Hu FB, Rimm EB. Plasma adiponectin levels and risk of myocardial infarction in men. JAMA. 2004 Apr 14;291(14):1730–7.

76. Fumeron F, Aubert R, Siddiq A, Betoulle D, Péan F, Hadjadj S, et al. Adiponectin gene polymorphisms and adiponectin levels are independently associated with the development of hyperglycemia during a 3-year period: the epidemiologic data on the insulin resistance syndrome prospective study. Diabetes. 2004 Apr;53(4):1150–7

77. Maeda N, Takahashi M, Funahashi T, Kihara S, Nishizawa H, Kishida K, et al. PPARgamma ligands increase expression and plasma concentrations of adiponectin, an adipose-derived protein. Diabetes. 2001 Sep;50(9):2094–9.

78. Fasshauer M, Kralisch S, Klier M, Lossner U, Bluher M, Klein J, et al. Adiponectin gene expression and secretion is inhibited by interleukin-6 in 3T3-L1 adipocytes. Biochem Biophys Res Commun. 2003 Feb 21;301(4):1045–50.

79. Engeli S, Feldpausch M, Gorzelniak K, Hartwig F, Heintze U, Janke J, et al. Association between adiponectin and mediators of inflammation in obese women. Diabetes. 2003 Apr 1;52(4):942–7.

80. Ouchi N, Kihara S, Arita Y, Okamoto Y, Maeda K, Kuriyama H, et al. Adiponectin, an adipocyte-derived plasma protein, inhibits endothelial NF-kappaB signaling through a cAMP-dependent pathway. Circulation. 2000 Sep 12;102(11):1296–301.

81. Hutley L, Prins JB. Fat as an endocrine organ: relationship to the metabolic syndrome. Am J Med Sci. 2005 Dec;330(6):280–9.

82. Carlyle M, Jones OB, Kuo JJ, Hall JE. Chronic cardiovascular and renal actions of leptin: role of adrenergic activity. Hypertension. 2002 Feb;39(2 Pt 2):496–501.

83. Eikelis N, Schlaich M, Aggarwal A, Kaye D, Esler M. Interactions between leptin and the human sympathetic nervous system. Hypertension. 2003 May;41(5):1072–9.

84. Marsh AJ, Fontes MAP, Killinger S, Pawlak DB, Polson JW, Dampney RAL. Cardiovascular responses evoked by leptin acting on neurons in the ventromedial and dorsomedial hypothalamus. Hypertension. 2003 Oct 1;42(4):488–93.

85. Shirasaka T, Takasaki M, Kannan H. Cardiovascular effects of leptin and orexins. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2003 Mar 1;284(3):R639–51.

86. Considine RV, Sinha MK, Heiman ML, Kriauciunas A, Stephens TW, Nyce MR, et al. Serum immunoreactive-leptin concentrations in normal-weight and obese humans. New England Journal of Medicine. 1996 Feb 1;334(5):292–5.

87. Mayer-Davis EJ, D'Agostino R, Karter AJ, Haffner SM, Rewers MJ, Saad M, et al. Intensity and amount of physical activity in relation to insulin sensitivity: the Insulin Resistance Atherosclerosis Study. JAMA. 1998 Mar 4;279(9):669–74.

88. Gill H, Mugo M, Whaley-Connell A, Stump C, Sowers JR. The key role of insulin resistance in the cardiometabolic syndrome. Am J Med Sci. 2005 Dec;330(6):290–4.

89. Petersen KF, Shulman GI. Etiology of insulin resistance. Am J Med. 2006 May;119(5 Suppl 1):S10-16.

90. Jensen MD, Haymond MW, Rizza RA, Cryer PE, Miles JM. Influence of body fat distribution on free fatty acid metabolism in obesity. J Clin Invest. 1989 Apr;83(4):1168–73.

91. Lewis GF, Steiner G. Acute effects of insulin in the control of VLDL production in humans. Implications for the insulin-resistant state. Diabetes Care. 1996 Apr;19(4):390–3.

92. Ginsberg HN, Zhang Y-L, Hernandez-Ono A. Regulation of plasma triglycerides in insulin resistance and diabetes. Arch Med Res. 2005 Jun;36(3):232–40.

93. Ferrannini E, Natali A. Essential hypertension, metabolic disorders, and insulin resistance. Am Heart J. 1991 Apr;121(4 Pt 2):1274–82.

94. Malhotra A, Kang BP, Cheung S, Opawumi D, Meggs LG. Angiotensin II promotes glucose-induced activation of cardiac protein kinase C isozymes and phosphorylation of troponin I. Diabetes. 2001 Aug;50(8):1918–26.

95. Morse SA, Zhang R, Thakur V, Reisin E. Hypertension and the metabolic syndrome. Am J Med Sci. 2005 Dec;330(6):303–10.

96. Briones AM, Nguyen Dinh Cat A, Callera GE, Yogi A, Burger D, He Y, et al. Adipocytes produce aldosterone through calcineurin-dependent signaling pathways: implications in diabetes mellitus-associated obesity and vascular dysfunction. Hypertension. 2012 May;59(5):1069–78.

97. Ordovas JM. Genetic links between diabetes mellitus and coronary atherosclerosis. Curr Atheroscler Rep. 2007 May 1;9(3):204–10.

98. Perseghin G, Ghosh S, Gerow K, Shulman GI. Metabolic defects in lean nondiabetic offspring of NIDDM parents: a cross-sectional study. Diabetes. 1997 Jun;46(6):1001–9.

99. Abate N, Chandalia M, Snell PG, Grundy SM. Adipose tissue metabolites and insulin resistance in nondiabetic Asian Indian men. J Clin Endocrinol Metab. 2004 Jun;89(6):2750–5.

100. Martin LJ, North KE, Dyer T, Blangero J, Comuzzie AG, Williams J. Phenotypic, genetic, and genome-wide structure in the metabolic syndrome. BMC Genetics. 2003 Dec 31;4(1):S95.

101. Laakso M. Gene variants, insulin resistance, and dyslipidaemia. Curr Opin Lipidol. 2004 Apr;15(2):115–20

102. Poulsen P, Levin K, Petersen I, Christensen K, Beck-Nielsen H, Vaag A. Heritability of insulin secretion, peripheral and hepatic insulin action, and intracellular glucose partitioning in young and old danish twins. Diabetes. 2005 Jan 1;54(1):275–83.

103. Neel JV. Diabetes mellitus: a "thrifty" genotype rendered detrimental by "progress"? Am J Hum Genet. 1962 Dec;14(4):353–62.

104. Hales CN, Barker DJ. Type 2 (Non-insulin-dependent) diabetes mellitus: the thrifty phenotype hypothesis. Diabetologia. 1992 Jul;35(7):595–601.

105. Hales CN, Desai M, Ozanne SE. The thrifty phenotype hypothesis: how does it look after 5 years? Diabetic Medicine. 1997;14(3):189–95.

106. Kraemer-Aguiar LG, Laflor CM, Bouskela E. Skin microcirculatory dysfunction is already present in normoglycemic subjects with metabolic syndrome. Metabolism. 2008 Dec;57(12):1740–6

107. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med. 2005 Apr 21;352(16):1685–95.

108. Harrison DG. Cellular and molecular mechanisms of endothelial cell dysfunction. J Clin Invest. 1997 Nov 1;100(9):2153–7.

109. Grundy SM. Obesity, metabolic syndrome, and cardiovascular disease. J Clin Endocrinol Metab. 2004 Jun;89(6):2595–600.

110. Aljada A, Mohanty P, Ghanim H, Abdo T, Tripathy D, Chaudhuri A, et al. Increase in intranuclear nuclear factor kappaB and decrease in inhibitor kappaB in mononuclear cells after a mixed meal: evidence for a proinflammatory effect. Am J Clin Nutr. 2004 Apr;79(4):682–90.

111. Dandona P, Aljada A, Chaudhuri A, Mohanty P, Garg R. Metabolic syndrome: a comprehensive perspective based on interactions between obesity, diabetes, and inflammation. Circulation. 2005 Mar 22;111(11):1448–54.
112. Charmandari E, Tsigos C, Chrousos G. Endocrinology of the stress response. Annu Rev Physiol. 2005;67:259–84.
113. Wang C-N, McLeod RS, Yao Z, Brindley DN. Effects of dexamethasone on the synthesis, degradation, and secretion of apolipoprotein b in cultured rat hepatocytes. Arteriosclerosis, Thrombosis, and Vascular Biology. 1995 Sep 1;15(9):1481–91.
114. Guillaume-Gentil C, Assimacopoulos-Jeannet F, Jeanrenaud B. Involvement of non-esterified fatty acid oxidation in glucocorticoid-induced peripheral insulin resistance in vivo in rats. Diabetologia. 1993 Oct;36(10):899–906.
115. Andrew R, Gale CR, Walker BR, Seckl JR, Martyn CN. Glucocorticoid metabolism and the Metabolic Syndrome: associations in an elderly cohort. Exp Clin Endocrinol Diabetes. 2002;110(6):284–90.
116. Chrousos GP. Stress and disorders of the stress system. Nat Rev Endocrinol. 2009 Jul;5(7):374–81.
117. Kushner RF. Evaluation and management of obesity. In: Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, editors. Harrison's Principles of Internal Medicine [Internet]. 20th ed. New York, NY: McGraw-Hill Education; 2018 [cited 2020 Jun 22]. Available from: https://accessmedicine.mhmedical.com/content.aspx?aid=1156520775
118. Deedwania PC, Gupta R. Management issues in the metabolic syndrome. J Assoc Physicians India. 2006 Oct;54:797–810.
119. Krejs GJ. Metabolic benefits associated with sibutramine therapy. Int J Obes Relat Metab Disord. 2002 Dec;26 Suppl 4:S34-37.

120. Pagotto U, Pasquali R. Fighting obesity and associated risk factors by antagonising cannabinoid type 1 receptors. Lancet. 2005 Apr 16;365(9468):1363–4.
121. Sjöström L, Lindroos A-K, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004 Dec 23;351(26):2683–93.
122. Rader DJ, Hobbs HH. Disorders of lipoprotein metabolism. In: Kasper D, Fauci A, Hauser S, Longo D, Jameson JL, Loscalzo J, editors. Harrison's Principles of Internal Medicine [Internet]. 19th ed. New York, NY: McGraw-Hill Education; 2014 [cited 2020 Jun 23]. Available from: https://accessmedicine.mhmedical.com/content.aspx?aid=1120816563
123. Sharma M, Sharma DR, Singh V, Panwar R, Hira H, Mohan B, et al. Evaluation of efficacy and safety of fixed dose lovastatin and niaciner combination in asian indian dyslipidemic patients: a multicentric study. Vasc Health Risk Manag. 2006 Mar;2(1):87–93.
124. Libby P. The forgotten majority: unfinished business in cardiovascular risk reduction. J Am Coll Cardiol. 2005 Oct 4;46(7):1225–8.
125. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, et al. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the jnc 7 report. JAMA. 2003 May 21;289(19):2560–72.
126. Patrono C, García Rodríguez LA, Landolfi R, Baigent C. Low-dose aspirin for the prevention of atherothrombosis. N Engl J Med. 2005 Dec 1;353(22):2373–83.
127. Deedwania PC, Fonseca VA. Diabetes, prediabetes, and cardiovascular risk: shifting the paradigm. Am J Med. 2005 Sep;118(9):939–47.

128. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. BMJ. 2003 Jun 28;326(7404):1419.

129. Becker KL, Snider R, Nylen ES. Procalcitonin in sepsis and systemic inflammation: a harmful biomarker and a therapeutic target. Br J Pharmacol 2010;159:253–64. https://doi.org/10.1111/j.1476-5381.2009.00433.x.

130. Linscheid P, Seboek D, Schaer DJ, Zulewski H, Keller U, Müller B. Expression and secretion of procalcitonin and calcitonin gene-related peptide by adherent monocytes and by macrophage-activated adipocytes. Crit Care Med 2004;32:1715–21. https://doi.org/10.1097/01.ccm.0000134404.63292.71.

131. Linscheid P, Seboek D, Nylen ES, Langer I, Schlatter M, Becker KL, et al. In vitro and in vivo calcitonin I gene expression in parenchymal cells: a novel product of human adipose tissue. Endocrinology 2003;144:5578–84. https://doi.org/10.1210/en.2003-0854.

132. Schneider H-G, Lam QT. Procalcitonin for the clinical laboratory: a review. Pathology 2007;39:383–90. https://doi.org/10.1080/00313020701444564.

133. Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, Bohuon C. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 1993;341:515–8. https://doi.org/10.1016/0140-6736(93)90277-n.

134. Müller B, Becker KL, Schächinger H, Rickenbacher PR, Huber PR, Zimmerli W, et al. Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit. Crit Care Med 2000;28:977–83. https://doi.org/10.1097/00003246-200004000-00011.

135. Schuetz P, Albrich W, Mueller B. Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future. BMC Med 2011;9:107. https://doi.org/10.1186/1741-7015-9-

136. Schuetz P, Albrich W, Christ-Crain M, Chastre J, Mueller B. Procalcitonin for guidance of antibiotic therapy. Expert Rev Anti Infect Ther 2010;8:575–87. https://doi.org/10.1586/eri.10.25.
137. Gilbert DN. Use of plasma procalcitonin levels as an adjunct to clinical microbiology. J Clin Microbiol 2010;48:2325–9. https://doi.org/10.1128/JCM.00655-10.
138. Agarwal R, Schwartz DN. Procalcitonin to guide duration of antimicrobial therapy in intensive care units: a systematic review. Clin Infect Dis 2011;53:379–87. https://doi.org/10.1093/cid/cir408.
139. Tang BMP, Eslick GD, Craig JC, McLean AS. Accuracy of procalcitonin for sepsis diagnosis in critically ill patients: systematic review and meta-analysis. Lancet Infect Dis 2007;7:210–7. https://doi.org/10.1016/S1473-3099(07)70052-X.
140. Uzzan B, Cohen R, Nicolas P, Cucherat M, Perret G-Y. Procalcitonin as a diagnostic test for sepsis in critically ill adults and after surgery or trauma: a systematic review and meta-analysis. Crit Care Med 2006;34:1996–2003. https://doi.org/10.1097/01.CCM.0000226413.54364.36.
141. Meisner M, Tschaikowsky K, Palmaers T, Schmidt J. Comparison of procalcitonin (PCT) and C-reactive protein (CRP) plasma concentrations at different SOFA scores during the course of sepsis and MODS. Crit Care 1999;3:45–50. https://doi.org/10.1186/cc306.
142. Reinhart K, Bauer M, Riedemann NC, Hartog CS. New approaches to sepsis: molecular diagnostics and biomarkers. Clin Microbiol Rev 2012;25:609–34. https://doi.org/10.1128/CMR.00016-12.
143. Li H, Luo Y-F, Blackwell TS, Xie C-M. Meta-analysis and systematic review of procalcitonin-guided therapy in respiratory tract infections. Antimicrob Agents Chemother 2011;55:5900–6. https://doi.org/10.1128/AAC.00335-11.

144. Sakr Y, Sponholz C, Tuche F, Brunkhorst F, Reinhart K. The role of procalcitonin in febrile neutropenic patients: review of the literature. Infection 2008;36:396–407. https://doi.org/10.1007/s15010-008-7374-y.

145. Jereb M, Muzlovic I, Hojker S, Strle F. Predictive value of serum and cerebrospinal fluid procalcitonin levels for the diagnosis of bacterial meningitis. Infection 2001;29:209–12. https://doi.org/10.1007/s15010-001-1165-z.

146. Becker KL, Snider R, Nylen ES. Procalcitonin assay in systemic inflammation, infection, and sepsis: clinical utility and limitations. Crit Care Med 2008;36:941–52. https://doi.org/10.1097/CCM.0B013E318165BABB.

147. Abbasi A, Corpeleijn E, Postmus D, Gansevoort RT, De Jong PE, Gans ROB, et al. Plasma Procalcitonin Is Associated with Obesity, Insulin Resistance, and the Metabolic Syndrome. Endocrinology 2010;151:3472–3472. https://doi.org/10.1210/endo.151.7.9997.

148. Abbasi A, Corpeleijn E, Postmus D, Gansevoort RT, De Jong PE, Gans ROB, et al. Plasma procalcitonin and risk of type 2 diabetes in the general population. Diabetologia 2011;54:2463–5. https://doi.org/10.1007/s00125-011-2216-3.

149. Danielewski M, Gomułkiewicz A, Kucharska A, Matuszewska A, Nowak B, Piórecki N, et al. Cornelian Cherry (Cornus mas L.) Iridoid and Anthocyanin-Rich Extract Reduces Various Oxidation, Inflammation, and Adhesion Markers in a Cholesterol-Rich Diet Rabbit Model. IJMS 2023;24:3890. https://doi.org/10.3390/ijms24043890.

150. Göde F, Yücesoy F, Sağlam A, Akarsu S, Örem A, Sharafkhanov K. Serum Procalcitonin and Proinflammatory markers in Polycystic Ovary Syndrome. Gynecol Obstet Reprod Med 2017;23:20–5. https://doi.org/10.21613/GORM.2016.619.

151. Mathiesen DS, Lund A, Vilsbøll T, Knop FK, Bagger JI. Amylin and Calcitonin: Potential Therapeutic Strategies to Reduce Body Weight and Liver Fat. Front Endocrinol 2021;11:617400. https://doi.org/10.3389/fendo.2020.617400.
152. Schiopu A, Hedblad B, Engström G, Struck J, Morgenthaler NG, Melander O. Plasma procalcitonin and the risk of cardiovascular events and death: a prospective population-based study. Journal of Internal Medicine 2012;272:484–91. https://doi.org/10.1111/j.1365-2796.2012.02548.x.
153. Singh N, Hooja N. TO ASSESS ROLE OF C-REACTIVE PROTEIN TO ALBUMIN RATIO AS A NEW BIOMARKER FOR POLYCYSTIC OVARY SYNDROME. Ijsr 2022:20–1. https://doi.org/10.36106/ijsr/6803464.
154. Bajpai D, Pednekar S, Pandey D, Moulick ND, Humane D, Bedmutha K. Association of Plasma Procalcitonin with Various Components of Metabolic Syndrome and Insulin Resistance in Urban Indian Population: A Novel Biomarker. J Assoc Physicians India 2018;66:35–8.
155. El Kassas GM, Shehata MA, El Wakeel MA, Amer AF, Elzaree FA, Darwish MK, et al. Role of Procalcitonin As an Inflammatory Marker in a Sample of Egyptian Children with Simple Obesity. Open Access Maced J Med Sci 2018;6:1349–53. https://doi.org/10.3889/oamjms.2018.323.
156. Vyas A, Keswani P, Sharma S, Khandelwal M, Pilaniya M, Sharma R. A Study of Association of Plasma Procalcitonin with Various Components of Metabolic Syndrome and Insulin Resistance. J Assoc Physicians India 2022;70:11–2.
157. Linscheid P, Seboek D, Nylen ES, Langer I, Schlatter M, Becker KL, et al. In Vitro and in Vivo Calcitonin I Gene Expression in Parenchymal Cells: A Novel Product of Human Adipose Tissue. Endocrinology 2003;144:5578–84. https://doi.org/10.1210/en.2003-0854.

158. Linscheid P, Seboek D, Zulewski H, Keller U, Müller B. Autocrine/paracrine role of inflammation-mediated calcitonin gene-related peptide and adrenomedullin expression in human adipose tissue. Endocrinology 2005;146:2699–708. https://doi.org/10.1210/en.2004-1424.

159. van Ree RM, de Vries APJ, Oterdoom LH, Seelen MA, Gansevoort RT, Schouten JP, et al. Plasma procalcitonin is an independent predictor of graft failure late after renal transplantation. Transplantation 2009;88:279–87. https://doi.org/10.1097/TP.0b013e3181ac9ea0.

160. Puder JJ, Varga S, Kraenzlin M, De Geyter C, Keller U, Müller B. Central fat excess in polycystic ovary syndrome: relation to low-grade inflammation and insulin resistance. J Clin Endocrinol Metab 2005;90:6014–21. https://doi.org/10.1210/jc.2005-1002.

****

ANNEXURE

PATIENT INFORMATION SHEET

STUDY TITLE: " ***PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE DIAGNOSIS OF METABOLIC SYNDROME, CASE-CONTROL STUDY AT A TERITIARY CARE CENTRE , TAMAKA , KOLAR*** **"**

STUDY SITE: R.L Jalappa Hospital and Research Centre, Tamaka, Kolar.

This is to inform you that, you require fasting blood glucose, complete lipid profile, plasma procalcitonin to determine metabolic syndrome and its association with procalcitonin. The above mentioned investigations are required for the making the early diagnosis of the disease and for planning of the treatment. Patients who satisfy the diagnostic criteria of metabolic syndrome referred to department of General Medicine at R.L Jalappa hospital and research Centre, Tamaka, Kolar to undergo above mentioned investigations and of those patients who meet the inclusion criteria will be taken for the study.

We are conducting this study for early diagnosis of metabolic syndrome.

If you are willing you will be enrolled in this study and we will do above mentioned investigations.

You will receive the standard care.

This will facilitate identifying use of plasma procalcitonin in early diagnosis of metabolic syndrome. It will also benefit other patients with similar condition in future. You are free to opt-out of the study at any time if you are not satisfied or apprehensive to be a part of the study. Your treatment and care will not be compromised if you refuse to be a part of the study. The study will not add any risk or financial burden to you if you are part of the study. All investigations cost will be beared by principal investigator. In case of any complications during procedures patient will be treated accordingly.

Your identity and clinical details will be confidential. You will not receive any financial benefit for being part of the study. You are free to contact Dr. Rupa Kasaraneni or any other member of the above research team for any doubt or clarification you have.

Dr. RUPA KASARANENI

Mobile no: 9505529767

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: '' ಮೆಟಾಬಾಲಿಕ್ ಸಿಂಡ್ರೋಮ್ ರೋಗನಿರ್ಣಯಕ್ಕೆ ಹೆಚ್ಚುವರಿ ಮಾರ್ಕರ್ ಆಗಿ ಪ್ರೊಕಾಲ್ಸಿಟೋನಿನ್, ಕೋಲಾರದ ತಮಕಾದ ಟೆರಿಟಿಯರಿ ಕೇರ್ ಸೆಂಟರ್‌ನಲ್ಲಿ ಕೇಸ್-ಕಂಟ್ರೋಲ್ ಸ್ಟಡಿ''

ಸ್ಟಡಿ ಸೈಟ್: ಆರ್.ಎಲ್ ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ, ಟಮಕ, ಕೋಲಾರ.

ಮೆಟಾಬಾಲಿಕ್ ಸಿಂಡ್ರೋಮ್ ಮತ್ತು ಪ್ರೊಕಾಲ್ಸಿಟೋನಿನ್ ಜೊತೆಗಿನ ಅದರ ಸಂಬಂಧವನ್ನು ನಿರ್ಧರಿಸಲು ನಿಮಗೆ ಉಪವಾಸದ ರಕ್ತದಲ್ಲಿನ ಗ್ಲೂಕೋಸ್, ಸಂಪೂರ್ಣ ಲಿಪಿಡ್ ಪ್ರೊಫೈಲ್, ಪ್ಲಾಸ್ಮಾ ಪ್ರೊಕಾಲ್ಸಿಟೋನಿನ್ ಅಗತ್ಯವಿದೆ ಎಂದು ನಿಮಗೆ ತಿಳಿಸಲು ಇದು. ರೋಗದ ಆರಂಭಿಕ ರೋಗನಿರ್ಣಯವನ್ನು ಮಾಡಲು ಮತ್ತು ಚಿಕಿತ್ಸೆಯನ್ನು ಯೋಜಿಸಲು ಮೇಲೆ ತಿಳಿಸಲಾದ ಅಧ್ಯಯನಗಳು ಅಗತ್ಯವಿದೆ. ಮೆಟಾಬಾಲಿಕ್ ಸಿಂಡ್ರೋಮ್‌ನ ರೋಗನಿರ್ಣಯದ ಮಾನದಂಡಗಳನ್ನು ಪೂರೈಸುವ ರೋಗಿಗಳನ್ನು ಆರ್.ಎಲ್ ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ ಮತ್ತು ಸಂಶೋಧನಾ ಕೇಂದ್ರ, ಟಮಕ, ಕೋಲಾರದಲ್ಲಿ ಜನರಲ್ ಮೆಡಿಸಿನ್ ವಿಭಾಗಕ್ಕೆ ಉಲ್ಲೇಖಿಸಲಾಗಿದೆ ಮತ್ತು ಮೇಲೆ ತಿಳಿಸಿದ ಪರೀಕ್ಷೆಗಳಿಗೆ ಒಳಗಾಗಲು ಮತ್ತು ಸೇರ್ಪಡೆ ಮಾನದಂಡಗಳನ್ನು ಪೂರೈಸುವ ರೋಗಿಗಳನ್ನು ಅಧ್ಯಯನಕ್ಕೆ ತೆಗೆದುಕೊಳ್ಳಲಾಗುತ್ತದೆ.

ಮೆಟಾಬಾಲಿಕ್ ಸಿಂಡ್ರೋಮ್ನ ಆರಂಭಿಕ ರೋಗನಿರ್ಣಯಕ್ಕಾಗಿ ನಾವು ಈ ಅಧ್ಯಯನವನ್ನು ನಡೆಸುತ್ತಿದ್ದೇವೆ.

ನೀವು ಸಿದ್ಧರಿದ್ದರೆ ನೀವು ಈ ಅಧ್ಯಯನಕ್ಕೆ ದಾಖಲಾಗುತ್ತೀರಿ ಮತ್ತು ನಾವು ಮೇಲೆ ತಿಳಿಸಿದ ತನಿಖೆಗಳನ್ನು ಮಾಡುತ್ತೇವೆ.

ನೀವು ಪ್ರಮಾಣಿತ ಆರೈಕೆಯನ್ನು ಸ್ವೀಕರಿಸುತ್ತೀರಿ.

ಮೆಟಬಾಲಿಕ್ ಸಿಂಡ್ರೋಮ್ನ ಆರಂಭಿಕ ರೋಗನಿರ್ಣಯದಲ್ಲಿ ಪ್ಲಾಸ್ಮಾ ಪ್ರೊಕಾಲ್ಸಿಟೋನಿನ್ ಬಳಕೆಯನ್ನು ಗುರುತಿಸಲು ಇದು ಅನುಕೂಲವಾಗುತ್ತದೆ. ಭವಿಷ್ಯದಲ್ಲಿ ಇದೇ ರೀತಿಯ ಸ್ಥಿತಿಯನ್ನು ಹೊಂದಿರುವ ಇತರ ರೋಗಿಗಳಿಗೆ ಇದು ಪ್ರಯೋಜನವನ್ನು ನೀಡುತ್ತದೆ. ಅಧ್ಯಯನದ ಭಾಗವಾಗಲು ನೀವು ತೃಪ್ತರಾಗದಿದ್ದರೆ ಅಥವಾ ಭಯಪಡದಿದ್ದರೆ ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹೊರಗುಳಿಯಲು ನೀವು ಸ್ವತಂತ್ರರಾಗಿದ್ದೀರಿ. ನೀವು ಅಧ್ಯಯನದ ಭಾಗವಾಗಲು ನಿರಾಕರಿಸಿದರೆ ನಿಮ್ಮ ಚಿಕಿತ್ಸೆ ಮತ್ತು ಕಾಳಜಿಗೆ ಧಕ್ಕೆಯಾಗುವುದಿಲ್ಲ. ನೀವು ಅಧ್ಯಯನದ ಭಾಗವಾಗಿದ್ದರೆ ಅಧ್ಯಯನವು ನಿಮಗೆ ಯಾವುದೇ ಅಪಾಯ ಅಥವಾ ಆರ್ಥಿಕ ಹೊರೆಯನ್ನು ಸೇರಿಸುವುದಿಲ್ಲ. ಎಲ್ಲಾ ತನಿಖೆಯ ವೆಚ್ಚವನ್ನು ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ ಭರಿಸುತ್ತಾರೆ. ಕಾರ್ಯವಿಧಾನದ ಸಮಯದಲ್ಲಿ ಯಾವುದೇ ತೊಡಕುಗಳ ಸಂದರ್ಭದಲ್ಲಿ ರೋಗಿಗೆ ಅನುಗುಣವಾಗಿ ಚಿಕಿತ್ಸೆ ನೀಡಲಾಗುತ್ತದೆ.

ನಿಮ್ಮ ಗುರುತು ಮತ್ತು ಕ್ಲಿನಿಕಲ್ ವಿವರಗಳು ಗೌಪ್ಯವಾಗಿರುತ್ತವೆ. ಅಧ್ಯಯನದ ಭಾಗವಾಗಿರುವುದರಿಂದ ನೀವು ಯಾವುದೇ ಹಣಕಾಸಿನ ಪ್ರಯೋಜನವನ್ನು ಪಡೆಯುವುದಿಲ್ಲ. ನಿಮ್ಮಲ್ಲಿರುವ ಯಾವುದೇ ಸಂದೇಹ ಅಥವಾ ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ಡಾ. ರೂಪಾ ಕಾಸರನೇನಿ ಅಥವಾ ಮೇಲಿನ ಸಂಶೋಧನಾ ತಂಡದ ಇತರ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಲು ನೀವು ಮುಕ್ತರಾಗಿದ್ದೀರಿ.

ಡಾ.ರೂಪಾ ಕಸರನೇನಿ

ಮೊಬೈಲ್ ಸಂಖ್ಯೆ: 9505529767

CONSENT FORM

Title: - **PROCALCITONIN AS AN ADDITIONAL MARKER IN DIAGNOSIS OF METABOLIC SYNDROME, STUDY HELD AT TERTIARY CARE CENTRE, TAMAKA, KOLAR**

Principal investigator: Dr.RUPA KASARANENI

I, Mr/Ms/Mrs. …….. Have been explained in my own understandable language, that I will be included in a study which is PROCALCITONIN AS AN ADDITIONAL MARKER IN DIAGNOSIS OF METABOLIC SYNDROME at RL Jalappa Hospital.

I have been explained that my clinical findings, investigations, findings will be assessed and documented for study purpose.

I have been explained my participation in this study is entirely voluntary and I can withdraw from the study any time and this will not affect my relation with my doctor or treatment for my ailment.

I have been explained about the risk/benefit of the study.

I understand that the medical information produced by this study will become part of institutional records and will be kept confidential by my said institute.

I agree not to restrict the use of any data or result that arise from this study provided such a use is only for scientific purpose(s).

I have principal investigator mobile number for enquiries.

I have been informed that standard of care will be maintained throughout the treatment period.

I, in my sound mind, give full consent to be added in the part of this study.

Investigator: Dr. RUPA KASARANENI

Phone number- 9505529767

Participant's signature/ thumb impression

Name:

Signature/thumb impression of the witness: Date:

Name:

Relation to patient

ಒಪ್ಪಿಗೆ ಪತ್ರ

ಶೀರ್ಷಿಕೆ: - ಮೆಟಾಬಾಲಿಕ್ ಸಿಂಡ್ರೋಮ್ ರೋಗನಿರ್ಣಯದಲ್ಲಿ ಹೆಚ್ಚುವರಿ ಮಾರ್ಕರ್ ಆಗಿ ಪ್ರೊಕಾಲ್ಸಿಟೋನಿನ್, ತಮಕ, ಕೋಲಾರದ ತೃತೀಯ ಆರೈಕೆ ಕೇಂದ್ರದಲ್ಲಿ ನಡೆದ ಅಧ್ಯಯನ

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ.ರೂಪಾ ಕಸರನೇನಿ

ನಾನು, ಶ್ರೀ/ಮತಿ/ಶ್ರೀಮತಿ. …….. ನನ್ನದೇ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ, **RL** ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆಯಲ್ಲಿ ಮೆಟಾಬಾಲಿಕ್ ಸಿಂಡ್ರೋಮ್ ರೋಗನಿರ್ಣಯದಲ್ಲಿ ಹೆಚ್ಚುವರಿ ಮಾರ್ಕರ್ ಆಗಿ ಪ್ರೊಕಾಲ್ಸಿಟೋನಿನ್ ಅನ್ನು ಅಧ್ಯಯನದಲ್ಲಿ ಸೇರಿಸಲಾಗುವುದು.

ನನ್ನ ಕ್ಲಿನಿಕಲ್ ಸಂಶೋಧನೆಗಳು, ತನಿಖೆಗಳು, ಸಂಶೋಧನೆಗಳನ್ನು ಮೌಲ್ಯಮಾಪನ ಮಾಡಲಾಗುತ್ತದೆ ಮತ್ತು ಅಧ್ಯಯನ ಉದ್ದೇಶಕ್ಕಾಗಿ ದಾಖಲಿಸಲಾಗುತ್ತದೆ ಎಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನನ್ನ ಭಾಗವಹಿಸುವಿಕೆಯು ಸಂಪೂರ್ಣವಾಗಿ ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ ಮತ್ತು ನಾನು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ಹಿಂದೆ ಸರಿಯಬಹುದು ಮತ್ತು ಇದು ನನ್ನ ವೈದ್ಯರೊಂದಿಗಿನ ನನ್ನ ಸಂಬಂಧ ಅಥವಾ ನನ್ನ ಕಾಯಿಲೆಯ ಚಿಕಿತ್ಸೆಯ ಮೇಲೆ ಪರಿಣಾಮ ಬೀರುವುದಿಲ್ಲ ಎಂದು ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.

ಅಧ್ಯಯನದ ಅಪಾಯ/ಪ್ರಯೋಜನದ ಬಗ್ಗೆ ನನಗೆ ವಿವರಿಸಲಾಗಿದೆ.

ಈ ಅಧ್ಯಯನದಿಂದ ಉತ್ಪತ್ತಿಯಾಗುವ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿಯು ಸಾಂಸ್ಥಿಕ ದಾಖಲೆಗಳ ಭಾಗವಾಗುತ್ತದೆ ಮತ್ತು ನಾನು ಹೇಳಿದ ಸಂಸ್ಥೆಯು ಗೌಪ್ಯವಾಗಿಡುತ್ತದೆ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಈ ಅಧ್ಯಯನದಿಂದ ಉಂಟಾಗುವ ಯಾವುದೇ ಡೇಟಾ ಅಥವಾ ಫಲಿತಾಂಶದ ಬಳಕೆಯನ್ನು ನಿರ್ಬಂಧಿಸದಿರಲು ನಾನು ಸಮ್ಮತಿಸುತ್ತೇನೆ, ಅಂತಹ ಬಳಕೆಯನ್ನು ಕೇವಲ ವೈಜ್ಞಾನಿಕ ಉದ್ದೇಶ(ಗಳಿಗೆ)

ವಿಚಾರಣೆಗಾಗಿ ನಾನು ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಮೊಬೈಲ್ ಸಂಖ್ಯೆಯನ್ನು ಹೊಂದಿದ್ದೇನೆ.

ಚಿಕಿತ್ಸೆಯ ಅವಧಿಯುದ್ದಕ್ಕೂ ಆರೈಕೆಯ ಗುಣಮಟ್ಟವನ್ನು ನಿರ್ವಹಿಸಲಾಗುವುದು ಎಂದು ನನಗೆ ತಿಳಿಸಲಾಗಿದೆ.

ನಾನು, ನನ್ನ ಉತ್ತಮ ಮನಸ್ಸಿನಲ್ಲಿ, ಈ ಅಧ್ಯಯನದ ಭಾಗದಲ್ಲಿ ಸೇರಿಸಲು ಸಂಪೂರ್ಣ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡುತ್ತೇನೆ.

ತನಿಖಾಧಿಕಾರಿ: ಡಾ.ರೂಪಾ ಕಸರನೇನಿ

ದೂರವಾಣಿ ಸಂಖ್ಯೆ- **9505529767**

ಭಾಗವಹಿಸುವವರ ಸಹಿ/ಹೆಬ್ಬೆರಳಿನ ಗುರುತು

ಹೆಸರು:

ಸಾಕ್ಷಿಯ ಸಹಿ/ಹೆಬ್ಬೆರಳಿನ ಗುರುತು: ದಿನಾಂಕ:

ಹೆಸರು:

ರೋಗಿಗೆ ಸಂಬಂಧ

PROFORMA

PROCALCITONIN AS AN ADDITIONAL MARKER FOR THE DIAGNOSIS OF METABOLIC SYNDROME, CASE-CONTROL STUDY AT A TERTIARY CARE CENTRE, TAMAKA, KOLAR

Name:

Age:

Sex:

Occupation:

UHID number:

Phone number:

Address:

Complaints with duration:

Previous history:

Family history:

Past history:

GENERAL PHYSICAL EXAMINATION:

Built and nourishment:

Pallor/Cyanosis/Icterus/Clubbing/edema/Generalized lymphadenopathy

VITAL DATA:

Pulse:

Temperature:

BP:

Respiration rate:

Systemic examination:

Per abdomen:

Respiratory system:

Cardio vascular system:

Central nervous system:

INVESTIGATIONS

COMPLETE LIPID PROFILE:
TRIGLYCERIDES -
HDL –
LDL -
VLDL –
TOTAL CHOLESTEROL -

FASTING BLOOD GLUCOSE -

SERUM PROCALCITONIN -

MASTER CHART

S.NO	AGE [YEARS]	GENDER	WAIST CIRCUMFERENCE [CM]	TRIGLYCERIDES [MG/DL]	HDL [MG/DL]	BP [MMHG]	FBS [MG/DL]	PROCALCITONIN [NG/ML]
1	55	F	97	248	32	100/70	156	3.5
2	80	M	127	202	43	170/80	107	0.26
3	39	F	110	129	19	150/90	156	4.4
4	40	F	92	168	29	110/70	136	2.081
5	52	M	105	170	34	140/70	140	2.11
6	46	M	95	154	35	120/70	130	3.46
7	52	F	98	140	41	130/80	124	0.14
8	62	F	110	151	43	120/80	121	1.6
9	70	M	97	155	36	120/80	162	4.24
10	54	F	85	150	45	100/70	120	0.01
11	35	F	85	152	40	110/70	115	0.5
12	41	F	91	155	40	110/70	112	0.96
13	55	M	99	171	35	140/80	130	2.27
14	61	M	100	156	32	110/80	140	2.14
15	65	F	86	150	45	140/90	115	1.02
16	44	F	110	162	40	120/90	117	1.56
17	56	M	102	166	37	140/90	121	2.01
18	77	M	96	152	33	150/70	142	3.06
19	55	F	101	160	42	130/90	134	1.56
20	60	F	90	152	45	135/90	120	1.14
21	56	M	96	154	35	130/80	142	2.78
22	60	M	100	162	36	130/80	166	4.12
23	45	F	106	157	44	140/80	100	0.65
24	72	M	102	155	40	120/90	120	0.6
25	67	F	95	152	42	130/80	110	1.26
26	40	F	92	160	46	120/80	105	0.96
27	50	M	110	153	38	110/80	125	1.64
28	71	M	106	158	30	110/70	144	2.95
29	56	F	102	154	47	110/80	120	0.26
30	73	F	90	151	48	100/70	116	1.64
31	35	M	92	162	41	140/90	153	1.42
32	39	F	100	151	32	130/80	144	2.76
33	44	M	96	174	40	150/80	132	0.55
34	45	F	76	143	42	120/80	98	0.04
35	55	M	82	140	48	110/80	99	0.5
36	61	M	85	138	51	120/80	86	0.16
37	50	F	70	150	40	130/80	90	0.24
38	32	M	72	136	50	110/80	84	0.08
39	29	M	78	141	68	100/80	86	0.54
40	60	F	76	139	40	130/80	74	0.02
41	45	M	80	130	49	120/90	73	0.02
42	62	M	77	140	47	120/80	96	0.04
43	36	F	64	126	62	110/90	70	0.001
44	54	M	80	137	50	100/70	84	0.12
45	61	M	86	128	55	120/80	95	0.36
46	77	F	70	143	49	100/80	83	0.004
47	82	M	65	144	45	120/90	90	0.002
48	36	M	74	138	46	110/70	88	0.016
49	55	F	79	150	44	120/70	78	0.18
50	34	M	71	140	51	100/70	80	0.34
51	50	M	77	141	51	120/80	77	0.05
52	37	F	70	143	47	110/80	74	0.134

S.NO	AGE [YEARS]	GENDER	WAIST CIRCUMFERENCE [CM]	TRIGLYCERIDES [MG/DL]	HDL [MG/DL]	BP [MMHG]	FBS [MG/DL]	PROCALCITONIN [NG/ML]
53	49	M	79	135	50	110/80	84	0.5
54	31	F	75	127	54	110/70	81	0.07
55	35	F	72	139	44	120/90	87	0.29
56	44	M	74	144	50	130/80	72	0.09
57	62	M	82	150	47	100/80	97	0.21
58	73	F	75	136	41	120/80	75	0.087
59	42	M	76	140	49	100/60	79	0.034
60	30	M	65	130	60	120/80	80	0.003
61	70	M	70	131	41	100/80	72	0.047
62	52	F	78	137	45	120/80	86	0.02
63	36	M	76	127	54	120/80	80	0.18
64	28	M	77	121	58	120/80	75	0.41
65	45	F	80	136	46	110/80	81	0.309
66	35	F	72	144	40	100/70	88	0.3