A STUDY OF CORRELATION BETWEEN HIGH NORMAL HBA1C AS RISK FACTOR FOR CORONARY HEART DISEASE WITH FRAMINGHAM RISK SCORE IN NON-DIABETIC PATIENTS"

BY

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"A STUDY OF CORRELATION BETWEEN HIGH NORMAL HBA1C AS RISK FACTOR FOR CORONARY HEART DISEASE WITH FRAMINGHAM RISK SCORE IN NON-DIABETIC PATIENTS"

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LIST OF ABBREVIATIONS

CHD	**Coronary Heart Disease**
CAD	**Coronary Artery Disease**
CVD	**Coronary Vascular Disease**
FRS	**Framingham Risk Score**
FHS	**Framingham Heart Study**
HF	**Heart Failure**
IHD	**Ischemic Heart Disease**
CHF	**Congestive Heart Failure**
MI	**Myocardial Infarction**
AHA	**American Heart Association**
PAD	**Peripheral Arterial Disease**
eGFR	**Estimated Glomerular Filteration Rate**
HBA1C	**Glycosylated Hemoglobin**
LDL	**Low Density Lipoprotein**
HDL	**High Density Lipoprotein**
CRP	**C-Reactive Protein**
ECG	**Electrocardiography**
BMI	**Body Mass Index**
TC	**Total Cholesterol**
TG	**Triglycerides**
SBP	**Systolic Blood Pressure**
DBP	**Diastolic Blood Pressure**
FBS	**Fasting Blood Sugar**
PPBS	**Postprandial Blood Sugar**
DM	**Diabetes Mellitus**
T2DM	**Type 2 Diabetes Mellitus**
FDA	**The Food & Drug Administration**
GERD	**Gastro Esophageal Reflux Disease**
LVH	**Left Ventricular Hypertrophy**
CABG	**Coronary Artery Bypass Graft**
PCI	**Percutaneous Coronary Intervention**
STEMI	**ST Elevation Myocardial Infarction**
NSTEMI	**Non ST Elevation Myocardial Infarction**
ACS	**Acute Coronary Syndrome**

Title: A Study of Correlation between High Normal Hba1c as A Risk Factor For Coronary Heart Disease With Framingham Risk Score In Non-Diabetic Patients.

ABSTRACT:

INTRODUCTION:

For diagnosis of future risk, the Framingham Risk Score is conventionally used. The Framingham Risk Score takes many variables into account when predicting future Coronary Heart Disease (CHD) risks. In recent years, abnormal glucose metabolism has been identified as a major determinant of CHD. There is no threshold effect in the relationship between CHD and glycaemia, since it's a more precise and stable glucose homeostasis indicator. To determine the relationship between high normal HbA1c and Framingham Risk Score for CHD in non-diabetic patients was the goal of this study.

AIM OF THE STUDY:

A Study of Correlation between High Normal Hba1c as a Risk Factor For Coronary Heart Disease With Framingham Risk Score In Non-diabetic patients .

MATERIALS AND METHOD:

We cross-sectionally reviewed patients Age between 18 To 80 Years who underwent voluntary regular health check-ups at the Health Promotion Center of BLDE (To be deemed) University Shri B M Patil Medical College Hospital and Research Centre, Vijayapura from January 2021 to June 2022. Those patients were included in this study,

Who fulfill the inclusion criteria which are as follows: Sex: Both, Patient must give Written Consent to take part in the Study as well as the diagnosis of Coronary Heart Disease (CHD) or having any Anginal symptoms with either Diagnostic Electrocardiographic changes. Patients who were previously diagnosed with diabetes were excluded. Additionally exclusion criteria are as follows: Patients who refuse to take part in the study and Patient having Hba1c level $\geq$6.5. A total of 95 patients were included in the study after excluding ineligible subjects. Data were collected by reviewing medical questionnaires.

Written consent will be taken from the subjects before the collection of specimens. Blood samples will be taken at the time of admission. HbA1c, FBS, PPBS and Lipid profile will be determined by standard methods. For normally distributed continuous variables between two groups will be compared using Independent t-test. For not normally distributed variables Mann Whitney U test were used. Association of Categorical variables will be analyzed using Chi-square test. Relationship between variables will be found using Pearson's or Spearman's correlation. $p<0.05$ will be considered statistically significant. All statistical tests were performed two-tailed. All statistical analysis were performed using SPSS (software package used for statistical analysis) package.

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INTRODUCTION

CHD is a state which occurs when there is an imbalance between the supply and demand of oxygen in the myocardium, resulting in a portion of the myocardium receiving inadequate blood and oxygen. The most typical cause is plaque buildup, which results in the coronary artery narrowing and inadequate oxygen delivery to the heart muscles.

In a healthy state, the heart's muscle regulate the flow of blood rich in oxygen at any given amount of oxygen demand in order to avoid myocytes from receiving insufficient oxygen, which could lead to ischemia and infarction.

Framingham Risk Score

The 10-year cardiovascular risk of an individual is calculated using the Framingham Risk Score, a gender-specific classification. The 10-year risk of getting coronary heart disease was initially estimated using the Framingham Risk Score using information from the Framingham Heart Study. In order to quantify the 10-year risk of cardiovascular disease, cerebrovascular events, peripheral artery disease, and heart failure were subsequently added as illness outcomes for the 2008 Framingham Risk Score.

The Framingham Risk Score can be used to determine a person's 10-year percent risk of developing coronary heart disease (CHD).

- Those with LOW RISK have a 10-year CHD risk of 10% or less.
- CHD risk ranges from 10 to 20% for those with INTERMEDIATE RISK.
- People at HIGH RISK have a 20% or higher CHD risk.

Age	Points	Age	Points	Age	Points	
20-34	-7	50-54	6	65-69	12	
35-39	-3	55-59	8	70-74	14	
40-44	0	60-64	10	75-79	16	
45-49	3					Points ___

Total cholesterol (mg per dL)	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79	
<160	0	0	0	0	0	
160-199	4	3	2	1	1	
200-239	8	6	4	2	1	
240-279	11	8	5	3	2	
≥280	13	10	7	4	2	Points ___

Smoking	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79	
Nonsmoker	0	0	0	0	0	
Smoker	9	7	4	2	1	Points ___

HDL (mg per dL)	Points	
≥60	-1	
50-59	0	
40-49	1	
<40	2	Points ___

Systolic BP (mm Hg)	If untreated	If treated	
<120	0	0	
120-129	1	3	
130-139	2	4	
140-159	3	5	
≥160	4	6	Points ___
			Total points ___

Point total	10-year risk (%)	Point total	10-year risk (%)	Point total	10-year risk (%)
<9	<1	14	2	20	11
9	1	15	3	21	14
10	1	16	4	22	17
11	1	17	5	23	22
12	1	18	6	24	27
13	2	19	8	≥25	≥30
					10-year risk ___%

FRAMINGHAM RISK SCORE

HbA1c and CHD

The use of glycosylated haemoglobin (HbA1c), a measure of average blood sugar readings during a 12-week period, in clinical practise has likewise been suggested since it has advantages over fasting blood glucose, such as reduced intra-individual variability. Epidemiological studies also demonstrated that HbA1c was more accurately predictive of CHD outcome than fasting blood glucose, with a stronger association between HbA1c and the dangers of CHD and overall mortality.

The goal of their current investigation is to determine whether the seriousness of coronary heart disease (CHD) in people without diabetes diagnoses will be correlated with the HbA1c level. If any, we think the clinical implications of our study will add important knowledge to the discussion of whether the HbA1c level may be used to predict the risk of CHD in the non-diabetic population.

The foundation of glycemic control and therapy in diabetic patients is glycated haemoglobin (HbA1c), which has recently been recognised as a critical indicator for diagnosing diabetes and identifying those at risk of further development [1]. When compared to fasting or post-load blood glucose measurements, HbA1c has a higher dependability rate [2]. HbA1c is a suggested method for the diagnosis and screening of diabetes, and it can also accurately reflect blood glucose control obtained in the previous two to three months[3,4].

The Disease Coronary Atherosclerotic Heart Disease (CHD) has multiple underlying causes. Age, gender, cholesterol, hypertension, smoking, and diabetes are among the risk factors for coronary heart disease identified by the original Framingham Heart Study done in the US [5]. Chronic abnormalities in glucose metabolism are known to raise the risk of CHD. However, Conflicting results have been found in a series of studies that have looked at the relationship between HbA1c and the outcome of cardiovascular disease event. HbA1c was found to be a significant predictor of CHD and its severity in numerous studies. However, studies have

shown that while HbA1c level was not an independent predictor of cardiovascular risk in the population including women with diabetes, it was connected with future cardiovascular risk in women without diabetes[6]. There is conflicting information regarding the impact of HbA1c levels below the current recommendations (7.0%) on cardiovascular events and death from numerous observational studies and randomised trials. We conducted a secondary analysis based on a retrospective cohort study to observe the correlation between HbA1c and the development of coronary artery calcium scores (CACS) in individuals undergoing physical examinations at the Health Promotion Center. This was done due to the differences in the study population, study design, measurement of coronary artery stiffness, adjustment for covariates, and some methodological limitations.

The Framingham Heart Program enrolled its first participant in 1948, and is currently following the study's third generation of participants. [7,8] This was the first investigation on the risk factors for cardiovascular disease. Cohort studies have since kept track of the effects of various risk factors on cardiovascular disease. a continuing population-based observational research project, known FINRISK, was first conducted in Finland in 1972. [9] Cohort studies including At Uppsala University in Sweden, the ULSAM, PIVUS, POEM, EpiHealth, and SCAPIS were completed. Another research project finished in New Zealand was the PREDICT Cardiovascular Disease Cohort study[10]. These studies divide risk factors for CAD into two major categories: those that cannot be changed and those that can. Risk factors for CAD include age, gender, ethnicity, and family history; none of these factors can be modified. High blood pressure, high cholesterol, diabetes, obesity, smoking, an unhealthful diet, a sedentary lifestyle, and stress are risk factors that can be altered.[7,11]

To lessen the financial and health-related burden caused by CAD's enormous healthcare burden, There were both controllable and immutable risk factors identified. Over the past 40 years, CAD death rates in western nations have significantly decreased as a result of risk

factor identification and technological advancements in medicine. One public health study that examined mortality data from 1969 to 2014 found that by 2020, there would be a reduction in heart disease deaths of 21.3% for men and 13.4% for women.[12]

Poor glucose management is one possible risk factor linked to unfavourable outcomes. Glycosylated haemoglobin (HbA1C), which is used as a measure of mean glycemia and as a therapy goal in diabetic patients, reflects the ambient blood glucose over the previous two to three months. Elevated HbA1C has been linked to an increased risk of negative cardiovascular events in those without HF, including an increased risk of incident HF. Despite these facts, there have been few studies looking at the relationship between HbA1C and outcomes in diabetic patients with established HF, and those that have been done have produced mixed results. [13,14].

Recently, Currie et al. [15] reported that either very high or very low HbA1c increased the risk of all-cause mortality in a large cohort of patients routinely treated in UK primary care. Their main study employed the mean of all HbA1c readings obtained after the index date rather than taking into account variations in HbA1c over time. Even though yearly mean HbA1c was used for further time-dependent analyses, missing data were handled using the last observation carried forward method, which may introduce bias. This is a potentially important limitation, as Currie et al. [15] did not report on the completeness of HbA1c records and these may not have been routinely recorded during the period they examined (1986 to 2008).

AIMS AND OBJECTIVES

1. Study Relation between High Normal HbA1c Level and Coronary Heart Disease

2. Calculation of Framingham Risk Score for Developing Coronary Heart Disease And Its Correlation with HbA1c

REVIEW OF LITERATURE

Etiology

The fundamental causes of coronary artery disease are several. There are essentially two sorts of etiologic factors: modifiable and non-modifiable. Examples of immutable factors include gender, age, family history, and genetics. Risk factors that can be changed include smoking, being overweight, having high cholesterol levels, and psychological problems. The prevalence of ischemic heart illnesses has increased in the Western world as a result of people eating more fast food and unhealthy meals. The US has seen an increase in incidence in later life due to better primary care in the middle and upper socioeconomic groups. The greatest contributor to cardiovascular illnesses is still smoking. Adult smokers in the United States accounted for 15.5% of the population in 2016. [16]

Men are more susceptible than women in comparison. Still a significant modifiable risk factor for CAD, hypercholesterolemia is a risk factor. While elevated low-density lipoproteins (LDL) increase the risk for CAD, raised high-density lipoproteins (HDL) decrease the incidence of the disease. The American Heart Association portal provides an online version of the ASCVD equation that can be used to determine a person's 10-year risk of atherosclerotic cardiovascular disease. Additionally significant risk factors for coronary artery disease are indicators of inflammation. High sensitivity CRP (hsCRP) is thought to be the best indicator of coronary artery disease in some research, while its practical implications remain controversial[17].

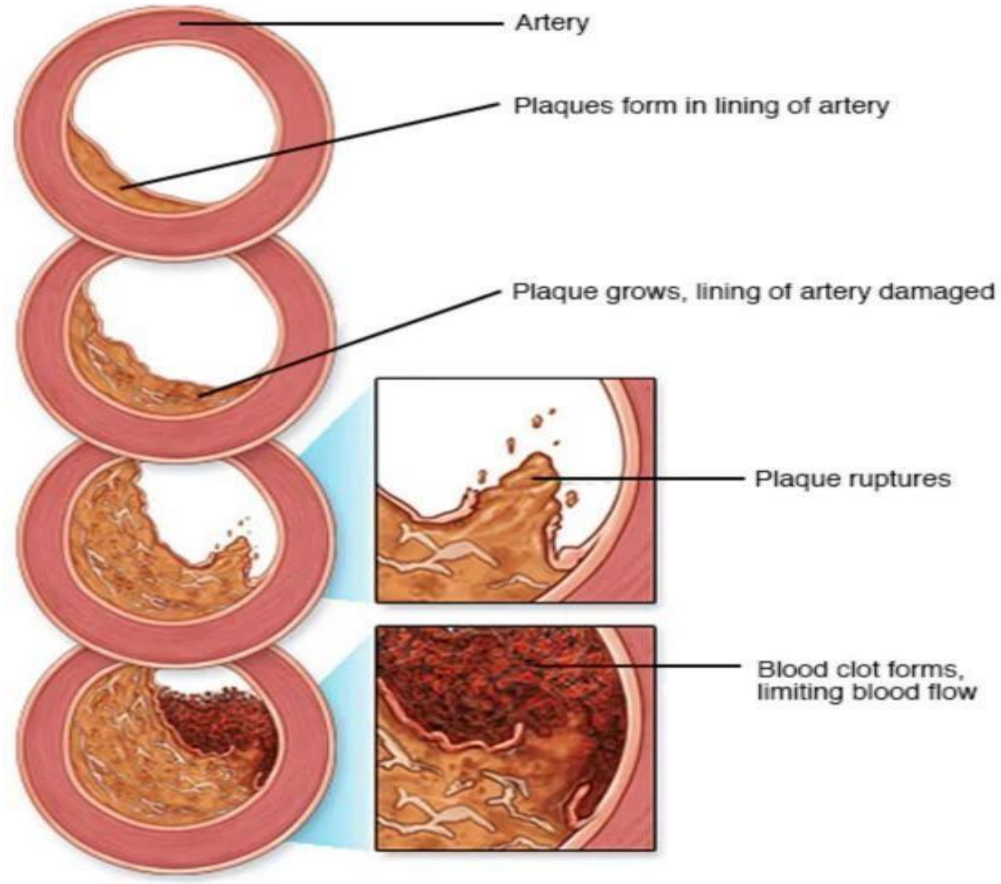


Figure 1 - Coronary Artery Atherosclerosis

Epidemiology

Coronary artery disease is a significant public health issue in both developed and developing nations. One study found that 2.2% of the global illness burden and 32.7% of cardiovascular diseases were caused by CAD. The annual cost of the healthcare system in the United States is roughly $200 billion. According to projections from the American Heart Association's annual health survey, 5.0% of women and 7.6% of men in the US were expected to have coronary artery disease between 2009 and 2012. (AHA). This amounts to 15.5 million Americans at the time who were afflicted by the sickness. [18,19]

Age has been demonstrated to raise the risk of CAD, regardless of gender. The incidence of CAD was nearly 1% in the 45–65 age range and roughly 4% in the 75–84 age range in the French ONACI registry. [20]

Pathophysiology

One distinguishing characteristic of the pathophysiology of CAD is the development of atherosclerotic plaque. The vessel lumen becomes clogged and restricts blood flow due to a buildup of fatty compounds termed plaque. The technique begins with the formation of a "fatty streak." Fatty streak develops as a result of foam cell-like macrophages, which are rich in lipids, depositing subendothelally. The intima layer ruptures as a result of a vascular injury, allowing monocytes to enter the subendothelial area and eventually develop into macrophages. Foam cells are created when these macrophages take up oxidised low-density lipoprotein (LDL) particles. Simply by generating cytokines, T cell activation aids the pathogenic process. Growth factors are created, and they activate smooth muscles. As oxidised LDL particles and collagen are sucked up by smooth muscles and deposited with activated macrophages, the number of foam cells increases. Subendothelial plaque is the result of this procedure. This plaque may eventually stabilise or enlarge if the endothelium is not further harmed. If it stabilises, a fibrous cap will develop, and the lesion will eventually turn calcific. The lesion may eventually become hemodynamically substantial enough for angina symptoms to manifest if sufficient blood flow does not reach the heart tissue during times of heightened demand. However, as the oxygen need dropped while at rest, symptoms would go away. A lesion must be at least 90% stenosed in order to elicit angina while at rest. There is a chance that some plaques could burst, producing thrombosis and tissue factor exposure. Depending on the severity of the insult, this thrombosis may cause a partial or complete obstruction of the lumen and the start of acute coronary syndrome (ACS), which can manifest as unstable angina, NSTEMI, or STEMI. [21]

Classification of coronary artery disease is typically done as under:

1. Stable ischemic heart disease (SIHD)
2. Acute coronary syndrome (ACS)
   - ST-elevation MI (STEMI)
   - Non-ST elevation MI (NSTEMI)
   - Unstable angina

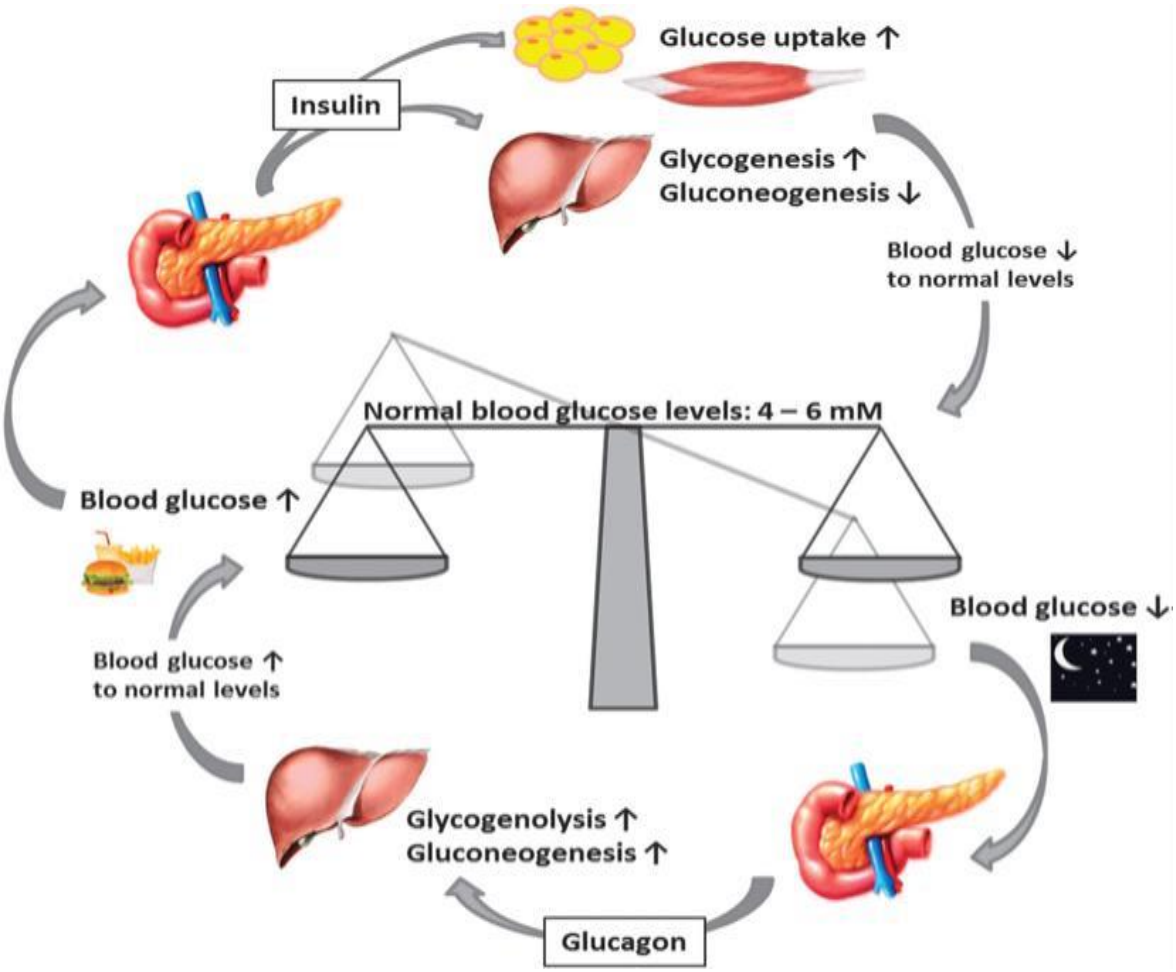


Figure-2 Maintenance of blood glucose levels by glucagon and insulin. When blood glucose levels are low, the pancreas secretes glucagon, which increases endogenous blood glucose levels through glycogenolysis. After a meal, when exogenous blood glucose levels are high, insulin is released to trigger glucose uptake into insulin-dependent muscle and adipose tissues as well as to promote glycogenesis.

History and Physical

A complete history and physical examination must be performed before continuing with additional workup. Two possible signs of coronary artery disease include the acute coronary syndrome and stable ischemic heart disease (SIHD) (ACS). It could get worse and develop into congestive heart failure if it is not treated (CHF). Patients should be questioned about their chest pain, its relationship to exercise, and whether it radiates to their jaw, neck, left arm, or back. Dyspnea needs to be assessed both at rest and during activity. Inquiries about syncope, palpitations, tachypnea, lower extremity edoema, orthopnea, and the patient's ability to exercise should also be made. Along with dietary, smoking, and lifestyle factors, a family history of ischemic heart disease should be gathered.

Inspection, palpation, and auscultation should all be part of the physical examination. Acute distress, jugular venous distention, and peripheral edoema should all be looked for. When palpating, it is important to feel for fluid thrill and heave. If peripheral edoema is evident, its severity should be assessed. It is important to gauge the jugular vein's distension. All four sites of the heart should be auscultated during auscultation, and the lower zones of the lungs should be given particular attention.

Evaluation

ECG, ECHO, CXR, Stress tests, cardiac catheterization, and blood tests are the principal techniques used to screen for coronary artery disease. Details about the many diagnostic methods we can use to evaluate coronary artery disease are provided below. These tests are conducted based on the environment the patients are :

Electrocardiogram (ECG)

To identify coronary artery disease, a relatively simple yet incredibly valuable ECG test is used. Ten leads that are affixed to the skin in certain places are used to measure electrical activity in the cardiac conduction system. It offers details on the physiology and anatomy of the heart. The paper that is produced after the test normally has 12 leads, each of which connects to a particular spot on the heart. The heart's axis, rhythm, and beat should be visible on an ECG. It is then possible to learn more about the subtleties of both short-term and long-term pathogenic processes. T wave and ST segment abnormalities are evident in acute coronary syndrome. Additionally, you can examine whether an ACS has turned into cardiac arrhythmia. The ECG can reveal information about axis deviation, bundle branch blockages, and ventricular hypertrophy in chronic illnesses. ECG is a test that is affordable, easy to use, and user-independent.

Echocardiography

In echocardiography, ultrasonography is used to visualise the heart. It is a valuable, non-invasive testing technique utilised in both inpatient and outpatient settings, for both acute and chronic diseases. In urgent situations, it can reveal details about chamber sizes, wall motion, valve stenosis and regurgitation, viral or autoimmune illnesses, and more. In the diagnosis of severe pulmonary diseases like pulmonary embolism, it is also helpful. In addition, the pericardial cavity is examined. It is possible to see both the facts listed above and a therapeutic response in chronic disorders. As part of stress testing, it is also utilised in an outpatient setting. It contributes to therapies in addition to diagnostics. For instance, an echocardiography could be used as the needle guide during pericardiocentesis. When compared to an ECG, this test is more individualised and potentially more expensive.[22]

Stress Test

The stress test is a reasonably non-invasive method to look for coronary artery disease. When properly interpreted, it can help confirm or rule out heart pathology in cases of suspected angina or angina-like symptoms. The patient's heart is artificially stressed throughout the procedure, and if they exhibit any unusual ECG changes in ST segments or angina symptoms, the test is terminated and coronary artery disease is determined. ECGs are taken before, during, and after the procedure, and the patient is continually monitored for any symptoms. The two most common types of stress evaluations are pharmacologic and exercise stress tests. During an exercise stress test, the patient must run on a treadmill until his heart rate hits 85% of what is expected for his age. When a patient exhibits ventricular or supraventricular arrhythmias, ST-segment elevations or depression, exertional hypotension, hypertension (>200/110 mmHg), or any of these conditions. [23]

Chest X-ray

The initial assessment of heart illness often includes a chest X-ray. The standing posteroanterior (PA) and left lateral decubitus imaging images are the norm. Anteroposterior (AP) projection may occasionally be achieved with the patient lying down, particularly in inpatient settings. However, this interpretation of AP films is severely constrained. An accurate examination of the PA and AP images can yield valuable and affordable knowledge regarding the heart, lungs, and vasculature.

Blood Work

Blood tests support diagnosis and assessment of a treatment's effectiveness. In acute conditions, B-type natriuretic peptides, metabolic panels, complete blood counts, and cardiac enzymes are frequently performed. BNP offers data on volume overload with a cardiogenic origin, however it has several drawbacks. It might be abnormally high with

kidney issues or improperly low with obesity. Cardiovascular enzymes CK and troponin offer insight into an acute ischemia event. Lipid panels offer crucial prognostic data in chronic diseases. Erythrocyte sedimentation rate (ESR) and C-reactive protein are biomarkers that can be used to detect diseases like acute pericarditis (CRP). An infiltrative disorder like hemochromatosis, which may have an influence on the liver and heart at the same time, can be evaluated using liver function tests (LFT). Additionally, liver examinations are carried out, especially in chronic circumstances, to assess high right heart pressures.

Cardiac Catheterization

The most reliable and precise method for assessing ischemic coronary heart disease is cardiac catheterization. But there are risks involved because it is an intrusive operation. The procedure is not appropriate for everyone. In non-ACS situations, patients with an intermediate pretest risk for CAD are often the best candidates. A subgroup of NSTEMI patients and all STEMI patients in the ACS scenario get an immediate cardiac catheterization. The patient is moderately sedated as this skill-required procedure is performed in a cardiac catheterization lab. Exposure to contrast during the process has the potential to cause serious allergic reactions and renal damage.

Treatment / Management

One or both of two probable symptoms of coronary artery disease, acute coronary syndrome or stable ischemic heart disease (SIHD), may occur (ACS). The former are more prominent right now, whilst the latter are more persistent over time. The specific disease kind determines the course of treatment. The management of each subtype will be covered separately:

Stable Ischemic Heart Disease

A sign of stable ischemic heart disease is stable angina. Stable angina frequently presents as two-month-long substernal chest pain or pressure that gets worse with activity or emotional stress and is relieved by rest or nitroglycerin. It's important to be aware that the traditional anginal symptoms may not occur in some populations, including as women, the elderly, and people with diabetes, and may instead express differently with atypical symptoms and exertional dyspnea. SIHD is treated with both pharmacological and non-pharmacologic therapy. Examples of lifestyle improvements include giving up smoking, exercising frequently, decreasing weight, maintaining good management of diabetes and hypertension, and maintaining a wholesome diet. Examples of pharmacologic therapies include angiotensin-blocking medications and cardioprotective medications.

Each patient has to get guideline-directed medical therapy (GDMT), which includes moderate to high-intensity statins, as-needed nitroglycerin, low-dose aspirin, and beta-blockers. If symptoms are not controlled byobeta-blocker therapy, it should be raised up to heart rates of 55 to 60. It may also be considered to add calcium channel blockers and long-acting nitrates. Ranolazine may also be used to alleviate lingering anginal symptoms. Depending on the patient profile, percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) should be selected after cardiac catheterization to assess the coronary anatomy if maximal GDMT has not been able to treat angina. [24]

Acute Coronary Syndrome

Sudden onset substernal chest pressure or pain that frequently radiates to the left arm and neck are symptoms of acute coronary syndrome. Other symptoms like dyspnea, palpitations, confusion, syncope, cardiac arrest, or newly established congestive heart failure could also be present. A pre-hospital emergency medical care crew typically performs an urgent ECG

on every patient with ACS to assess for STEMI. A STEMI is recognised by a 1 mm ST elevation in adjacent limb leads or precordial leads, with the exception of V2 and V3. Men must have elevations of 2 mm, whilst women must have elevations of 1.5 mm, for a STEMI diagnosis in V2 and V3. The STEMI analogue is thought to be a left bundle branch block (LBBB) with novel onset. If STEMI is present, immediate PCI is required in a PCI-capable institution, or within two hours if there is no PCI facility nearby. After ensuring there are no contraindications, intravenous thrombolytic treatment is advised if the distance to the closest PCI-capable facility is greater than 2 hours.

It's critical to distinguish between a true STEMI and other illnesses such acute pericarditis, Brugada syndrome, early repolarization abnormalities, and LVH-related changes that mimic STEMI on the ECG. All patients should be given a full dosage of aspirin sublingual at the time of presentation (325 mg). Nitrates should be given for pain relief after ensuring that there are no nitrate contraindications, such as hypotension, RV failure, roconsumption of PDE inhibitors during the previous 24-48 hours. Begin taking high-dose statins and beta-blockers as away as well. Based on the patient profile, P2Y12 inhibitors (prasugrel, ticagrelor, prasugrel) should be begun. Anticoagulation is necessary for patients with NSTE ACS; heparin or enoxaparin are frequently administered. Patients are advised to start early invasive therapy for NSTEMI within 24 hours if their TIMI values are moderate to high (>2).

The secret to effective long-term care of coronary artery disease is regular checkups with cardiologists and family doctors. Both medicine compliance and way of life changes are crucial.

Differential Diagnosis

Due to the proximity of the heart to other nearby organs such as the lungs, stomach, large vessels, and musculoskeletal organs, coronary artery disease has a wide variety of

differential diagnoses. Acute anginal chest pain can resemble other conditions such GERD, peptic ulcer illness, esophageal motility issues, costochondritis, Acute bronchitis, pneumonia, pleuritis, acute pericarditis, myocarditis, Prinzmetal angina, pericardial effusion, and pleural effusion. Stable ischemic heart disease can mimic GERD, peptic ulcer disease, costochondritis, and pleuritis. To whittle down the differential diagnosis and arrive at an appropriate diagnosis, meticulous consideration should be given to the history, physical examination, and diagnostic investigations.

Toxicity and Side Effect Management

There are disadvantages and dangers to both medical and surgical treatments for ischemic heart disease. Careful selection, professional medical care, and patient education could lessen these negative effects. The use of aspirin is linked to bruising, unpredictable, and adverse medication reactions. Myalgias, diarrhoea, and arthralgias are a few of the side effects of statin medication.[25]

The usage of beta-blockers may result in bradycardia and hypotension. ACEIs may cause angioedema, angiotension, hypotension, dizziness, elevated creatinine, cough, and other allergic responses. PCI may result in chronic in-stent restenosis, acute stent thrombosis, and perforation of the coronary arteries. The dangers associated with CABG include arrhythmias, cardiac tamponade, post-operative haemorrhage, infection, renal dysfunction, and phrenic nerve injury, to name a few.

Prognosis

The prognosis of the disease depends on multiple factors some of which could be modified while others are non-modifiable. Some of the determinants include the patient's age, gender, family history, genetics, ethnicity, eating and smoking habits, compliance with medicine, access to healthcare, financial situation, and the number of affected arteries. The total result is also influenced by comorbid disorders such chronic renal disease, hypertension,

dyslipidemia, and diabetes mellitus.

Complications

CAD's primary side effects include arrhythmias, acute coronary syndrome, congestive heart failure, mitral regurgitation, ventricular free wall rupture, pericarditis, aneurysm formation, and mural thrombi.

Issues of Concern

Modifiable and non-modifiable risk factors for coronary artery disease are two categories of risk factors.

According to a 2019 paper, modifiable risk factors made up only a small portion of predictive performance, with age, sex, and race accounting for 63% to 80%. However, controlling modifiable risk variables resulted in significant drops in CAD occurrences. First, we talk about risk factors that cannot be changed:

- Age: Both in men and in women, after age 35, CAD becomes more common. Men and women, respectively, have a lifetime chance of developing coronary artery disease of 49% and 32% after the age of 40. (CAD).
- Gender: Men are more at risk than women.
- Ethnicity: Southeast Asians, Hispanics, Latinos, and Blacks are ethnic groups that have higher rates of CAD morbidity and mortality.

- Family history: a significant risk factor as well. A higher risk of CAD mortality exists in patients under 50 years old who have a history of early heart disease in their family. According to a different source, Another risk factor includes having a father or brother diagnosed with the disease before the age of 55 and having aomother or sister diagnosed with CAD before the age of 65.

Modifiable risk elements play a less significant but nonetheless important role. Only two-thirds of patients, however, receive the best possible pharmacological interventions. A significant decrease in CAD occurrences would occur if this were to be accomplished. According to one study, people with the best risk factor profiles experienced significantly decreased rates of cardiovascular death.[26]

- Hypertension:

Hypertension affects one in three people. In a 2009 research evaluating twelve modifiable risk variables, hypertension and smoking were found to be the major contributors to the greatest number of fatalities. [27] Only 54% of these people, however, manage their blood pressure adequately.[28]

Due to the oxidative and mechanical stress that hypertension causes on the artery wall, it has long been recognised as a significant risk factor for heart disease.

According to a 1996 article, the Framingham cohort's systolic and diastolic blood pressure increased from age 30 to 65.

- Hyperlipidemia:

The second most frequent risk factor for ischemic heart disease is hyperlipidemia.

The World Health Organization estimates that elevated cholesterol contributed to 2.6 million fatalities.

A recent cross-sectional investigation using the coronary calcium score revealed that high cholesterol, combination hyperlipidaemia, and low HDL-c were all more prevalent, with respective prevalences of 55%, 41%, and 20%.

Coronary artery disease has also been associated with elevated triglycerides, but the connection is more nuanced since it weakens when other risk factors including central obesity, insulin resistance, and a poor diet are taken into account. Therefore, it is difficult to identify the role of triglycerides in coronary artery disease.[29]

- Diabetes mellitus:

More than one in three adult patients in the United States, according to the Centers for Disease Control (CDC), have prediabetes, this elevates the danger of type 2 diabetes, cardiovascular disease, and stroke.

Adult patients with diabetes had a 2.5 times higher male prevalence of cardiac disease than adult patients without diabetes, and a 2.4 times higher female prevalence.

A 2017 meta-analysis found that patients with diabetes who had an A1C > 7.0 had an 85% higher risk of dying from cardiovascular causes than those who had an A1C 7.0% (hazard ratio 1.85, 95% CI 1.14-2.55). Additionally, it revealed that cardiovascular mortality was greater in non-diabetic patients with an A1C > 6.0% compared to those with an A1C of 5.0% (hazard ratio, 1.50; 95% CI, 1.01-2.21). Additionally, a sizable level of study heterogeneity was found by researchers.

The primary cause of morbidity and mortality among diabetics is cardiovascular disease.

- Obesity:

In the US, 69% of adults are overweight or obese. Adult obesity rates are 35%.

Obesity raises the likelihood of acquiring other CAD risk factors such hypertension, hyperlipidemia, and diabetes mellitus in addition to being an independent risk factor for CAD.

Even after correcting for demographics, smoking, physical activity, and alcohol use, a recent study found that obese individuals had a hazard ratio of 2.00 (95% CI: 1.67-2.40) that was double that of non-obese patients for coronary heart disease.[30]

Obesity has been associated with coronary artery lesions that are more complicated, raised, and high-grade, according to a 1998 research study and a 2016 review article.

There have also been reports of the "obesity paradox." Despite the fact that there is evidence linking obesity to an increased risk of cardiovascular morbidity, some writers claim that

patients who are overweight or obese have better results. In light of these conflicting data, there is an ongoing discussion.[31]

- Smoking:

The Food & Drug Administration (FDA) estimates that cardiovascular disease causes 800,000 fatalities overall and 400,000 premature deaths per year. About one-third and one-half of these, respectively, are brought on by smoking.

According to a 2015 meta-analysis (21 studies, RR 1.51, 95% CI 1.41.1-62) smoking increased the incidence of coronary heart disease by 51% in adults with diabetes.

A other meta-analysis from 2015 found that smoking increased the risk of cardiovascular disease in people over 60 by 37% and by twice as much among former smokers.[32]

Nonsmokers who are frequently exposed to secondhand smoke have a 25%–30% higher risk of coronary heart disease than nonsmokers.

- Poor diet:

Saturated fat and coronary heart disease have just recently been connected. More recent analyses have put doubt on what was earlier thought to be a crucial causal role in the development of coronary heart disease and highlighted the return of refined carbohydrates as the main risk factor, raising more questions about this connection.

Trans-fat intake increases the risk of cardiovascular disease through affecting lipid metabolism, endothelial function, insulin sensitivity, and inflammation, according to increasingly conclusive research. The risk of getting coronary artery disease increased by 23% for every 2% of trans fat calories consumed (RR 1.23, 95% CI 1.11-1.37).

A thorough analysis from 2016 found a 22% increased risk of myocardial infarction among consumers of soft drinks and sweetened beverages. [33]

Compared to people who consumed less than 10% of their calories from added sugar, those who consumed 10% to 24.9% and 25% more added sugar, respectively, had a 30% and

175% higher risk of dying from cardiovascular disease (adjusted hazard ratio 1.30, 95% confidence interval 1.09-1.55) and less than 10% of their calories (adjusted hazard ratio 2.75, 95% confidence interval 1.40-5.42). According to reports, high fructose corn syrup, sucrose, and table sugar are important risk factors for coronary artery disease. [34]

On intake of red and processed meat, recent studies and systematic reviews have concentrated. Consuming red meat and processed meat increases the risk of coronary heart disease and cardiovascular events by 15% to 29% and 23% to 42%, respectively. These studies have shown this consistently. In most research, 50–100 grammes were consumed each day. One of these review articles included four studies with a risk ratio of 1.00 per 100 g of daily consumption, 95% CI 0.92-1.46, P=0.25. However, consumption of both red and processed meats was linked to a 23% higher risk of overall mortality (HR 1.23, 95% ci 1.11-1.36), according to a study. One study reported no statistically significant relationship between consumption of processed meat and overall mortality[35].

- Sedentary lifestyle:

Exercise helps prevent CAD by delaying its onset. A case-control research from 2004 that included 15,152 cases and 14,820 controls and was conducted in 52 countries covering all of the world's continents found that physical inactivity had a population attributable risk of myocardial infarction of 12.2%. [36]

Numerous observational studies have shown that those who consistently exercise have lower rates of morbidity and mortality. Some of the mechanisms underpinning this include improved vasculogenesis, greater endothelium nitrous oxide production, and more efficient reactive oxygen species deactivation.

Novel risk factors have also been studied in addition to these conventional cardiovascular risk factors. The following are a few of them:

Included in them are:

- Non-alcoholic Fatty Liver Disease (NAFLD)

NAFLD and heart disease are connected. It is also the most prevalent form of chronic liver disease in developed countries.

Patients with NAFLD had a 77% greater risk of cardiovascular events (RR 1.77, 95% CI 1.26 -2.48) and a risk of coronary artery disease that was more than double (RR 2.26, 95% CI 1.04-4.92), according to a 2017 meta-analysis.

A more recent prospective trial discovered that patients with NAFLD had a more than two-fold increased risk of cardiovascular events. Patients with liver fibrosis experienced a four-fold increase.

- Chronic Kidney Disease (CKD)

As a different risk factor, coronary artery disease has been associated to CKD. The endothelial dysfunction caused by decreased nitric oxide production, oxidative stress, and pro-inflammatory mediators are a few potential causes. Silent myocardial infarctions are more likely in CKD patients because diabetic and uremic neuropathy are more prevalent.[37] The American Heart Association's Guideline for the Primary Prevention of Cardiovascular Disease lists CKD as a risk factor, with a GFR of 15–59.

- Systemic Lupus Erythematosus (SLE):

The major cause of death in people with SLE is heart disease.

Additionally, these patients have a higher prevalence of atherosclerotic cardiovascular

disease. A pro-inflammatory impact on coronary microcirculation is most likely the mechanism.

Pericarditis is frequently one of SLE's symptoms. Pericarditis is the most typical cardiac symptom of SLE, according to one case report.

- RA (Rheumatoid Arthritis)

Estimates show that the risk of coronary artery disease is 1.5–2.0 times higher in RA patients. Body mass and lipoprotein levels, two conventional risk variables, also shown less predictable patterns in their capacity to predict risk. This related risk's underlying mechanism most likely has a pro-inflammatory effect. [38]

The American Heart Association's Guidelines for the Primary Prevention of Cardiovascular Disease identify rheumatoid arthritis as a risk factor.

- Inflammatory Bowel Disease (IBD):

IBD, or inflammatory bowel disease

A 2017 meta-analysis found a connection between IBD and an increased risk of coronary artery disease. Despite the variations in the investigations, the results were carefully analysed. Although the exact mechanism of the risk was unknown, a chronic inflammatory condition was once more believed to be to blame.

- HIV: Human Immunodeficiency Virus

The risk of cardiovascular disease and its side effects are known to rise with HIV. [39]

According to American College of Cardiology expert report published in 2018, people with HIV have a 1.5 to 2 times increased chance of developing coronary artery disease. Once more, an inflammatory condition served as the foundation for the mechanism.

- Thyroid disease:

The thyroid gland and heart health are tightly related. Although more research is needed in this area, some of the hypothesised causes include the effect of thyroid hormone on dyslipidemia, cardiac function, atherosclerosis, vascular compliance, and cardiac arrhythmias. The recommendations for screening for thyroid illness, hypothyroidism, and subclinical hypothyroidism vary depending on the standards.

- Testosterone:

Owing to a potential increase in heart attack and stroke risk connected with the use of low testosterone due to ageing, the FDA mandated a labelling update for low testosterone products in 2014. In further studies or assessments, this association has not kept up. According to some research, utilising testosterone supplements to treat low testosterone might potentially have healthful cardiovascular consequences. Additional research is required to provide more light on this particular subject.

- Vitamin D

The past ten years have seen an increase in the amount of study and conversation surrounding vitamin D. Vitamin D insufficiency is linked to an increased risk of coronary heart disease. Additional studies, however, have not confirmed a beneficial effect of vitamin D supplementation. More research is needed to understand whether vitamin D supplementation truly helps to prevent coronary artery disease.

- **Status Socioeconomic**

Socioeconomic status has a considerable impact on cardiovascular disease. Upstream determinants are important factors to consider because they are not currently taken into account by cardiovascular disease risk equations. Examples of upstream determinants include financial stress, lack of access to affordable, nutrient-dense food, being exposed to domestic violence, and substandard housing.

- **Women and Coronary Artery Disease**

Even while coronary artery disease continues to be the top cause of mortality in women, males are still more prone than women to develop it. In 2009, only 54% of women knew this. In women, cardiovascular disease was a factor in nearly one-third of fatalities. Contrary to men who more frequently had obstructive CAD, women were found to have non-obstructive CAD in 57% of cases. Changes in endothelial tone, structural alterations, and altered responses to vasodilator stimuli are a few of the hypothesised causes of this. Coronary microvascular dysfunction is the term for this (CMD). Estrogen is hypothesised to have protective effects on coronary vasoreactivity and anti-inflammatory effects on atherosclerosis, which help to stabilise plaque. [40]

Disparities in health outcomes have been attributed to a lack of knowledge on women's coronary artery disease. Obstructive CAD has received more attention from men than from women. According to a 2012 article, men of all ages experienced a decline in CAD mortality, despite young women's CAD mortality rising (under 55 years old).

- **Clinical Significance**

Coronary artery disease remains the main cause of deathoin the US. Given the prevalence of CAD and associated risk actors, interprofessional, team-based therapy may significantly improve patient outcomes. Clinicians must understand screening guidelines

and how lowering risk factors may improve the outcomes of CAD. Nurses are essential in routine screening and education. The pharmaceutical treatment of risk factors that can be altered, such as quitting smoking, diabetes, hypertension, and hyperlipidemia, depends heavily on clinical pharmacists. Nutritionists contribute by teaching people about nutrition. To decrease the complex but considerable influence that socioeconomic status can have on CAD risk and outcomes, all team members should participate in community outreach.

- **Hypertension**

The United States Preventive Services Task Force (USPSTF) advises grade I (current evidence insufficient) and grade A for screening children and adolescents (universal screening for hypertension in patients older than 18 years of age).

The absolute risk of developing CAD was significantly reduced when blood pressure in the systolic and diastolic chambers was decreased by more than 10 mmHg and 5 mmHg, respectively (NNT 91).

Systolic blood pressure was dropped to a target of 130 mmHg, which reduced the incidence of CAD (NNT 27). According to a meta-analysis published in 2002, lowering blood pressure by 20 mmHg systolic and 10 mmHg diastolic reduces the risk of dying from coronary heart disease by nearly 50% between the ages of 40 and 49 and by about 1/3 between the ages of 80 and 89.

- **Hyperlipidemia**

Between the ages of 40 and 75, the USPSTF advises considering statin usage for the primary prevention of cardiovascular disease. The USPSTF recommends routine screening for lipid abnormalities in children and adolescents despite giving it a grade of I. (current evidence insufficient). [41]

In 2011, the National Heart, Lung, and Blood Institute (NHLBI) promoted routine

examinations between the ages of 9 and 11 and once more between the ages of 17 and 21. Later, the American Academy of Pediatrics concurred. The practises around paediatric lipid screening have not changed despite the publication of these guidelines. According to an early 1994 assessment, a 10% decrease in blood cholesterol reduces the chance of developing coronary artery disease by 50%, 40%, 30%, and 20%, respectively, at ages 20, 50, 60, and 70.

The JUPITER study offered support for the use of statins as a preventative measure by demonstrating how they reduce the risk of major cardiovascular events. An absolute 2.7% decrease in the chance of developing CAD was seen when taking a moderate-intensity statin. (NNT 37). In absolute terms, a high-intensity statin therapy decreased the risk by 4.1%. (NNT 24).

- **Diabetes**

Patients who are overweight or obese and between the ages of 40 and 70 are advised to be screened for abnormal glucose levels, according to the USPSTF. Patients who are at higher risk may want to consider getting tested for diabetes sooner. This risk category includes patients who have a history of gestational diabetes, polycystic ovarian syndrome, or who belong to particular racial or cultural groups (oBlacks, American Indians, Alaskan natives, Asian Americans, Hispanics or Latinos, native Hawaiians or Pacific Islanders). [42]

A reasonable screening interval, according to the American Diabetes Association, is every three years.

The risk of major cardiovascular events decreased by 20% (95% CI 4-33%) with a 0.5% decrease in A1C, according to a 2019 meta-analysis of 12 cardiovascular outcomes trials. This analysis included patients onopeptidase-4 inhibitors,oGLP-1oagonists, and SGLT-2 inhibitors.[43]

- **Diet**

The diets with the strongest evidence for preventing cardiovascular disease include the DASH, Mediterranean, and vegetarian ones. [44]

The DASH diet can reduce systolic blood pressure in persons with hypertension by up to 11.5 mmHg. The DASH diet decreased the risk of coronary artery disease by 21%, according to a 2013 meta-analysis and in-depth review (RR 0.79, 95% CI 0.71–0.88). [45]

According to a 2017 meta-analysis and systematic review, eating 200 grammes of fruits and vegetables per day reduced the incidence of coronary artery disease by 8% (15 studies; RR 0.92; 95% CI 0.90-0.95). This influence was noticeable at doses as high as 800 grammes per day. According to a 2016 meta-analysis and systematic review, eating 28 grammes of nuts daily decreased the risk of coronary artery disease by 29% (RR 0.71, 95% CI 0.63-0.80; 29 studies).

According to a 2017 narrative review, eating a Mediterranean-style diet lowers the risk of cardiovascular disease by 20% to 25%. Additionally, advantages were seen in endothelin function, arterial stiffness, and heart function.

The American Heart Association advises substituting polyunsaturated and monounsaturated fats for saturated fat. A 10% decreased incidence of CAD is linked to a 5% substitution of polyunsaturated fat for saturated fat (RR 0.90, 95% CI 0.83-0.97). In contrast to other nutrients, the established link between saturated fat and a higher risk of coronary artery disease (CAD), as was previously reported, has been called into question according to a 2018 review. A different review concluded that the lack of a meaningful link between saturated fat and cardiovascular disease was the result of research using highly refined carbohydrates in place of saturated fat. Polyunsaturated fats could replace saturated fats and reduce the risk of coronary heart disease. There has been a lot of research on nutrition and coronary artery disease in the past, despite the fact that it can be difficult. A diet high in fish,

vegetables, fruits, legumes, nuts, and whole grains is advised by the AHA/ACC guidelines. Trans fats should be completely avoided, whereas processed meats, refined carbs, and sweetened beverages should all be consumed in moderation. Polyunsaturated and monounsaturated fats should take the place of saturated fats. [46]

In order to encourage a healthy diet and regular exercise, the USPSTF advises giving or referring people who are obese/overweight and have one additional cardiovascular risk factor to intensive behavioural therapy (Grade B). The USPSTF also advises suggesting or referring those without obesity or other cardiovascular risk factors for behavioural therapy.

- **Smoking**

The USPSTF recommends doing a tobacco use screening on every patient during a clinician encounter in addition to offering behavioural and pharmaceutical smoking cessation treatments. In order to prevent children and teenagers from starting to smoke, the USPSTF also advises educating them about the risks associated with smoking.

To increase quit rates, the American Heart Association suggests combining a behavioural and pharmaceutical strategy.

Within four years of quitting smoking, according to theoFDA, and within ten years, according to the CDC, the risk of coronary artery disease lowers to that of lifetime nonsmokers.

Motivational interviewing is one type of behavioural intervention (Ask, Advise, Assess, Assist, Arrange for follow-up).

Drug therapies include varenicline, bupropion, and nicotine replacement therapy lessen cravings and withdrawal symptoms. Using nicotine replacement therapies like nicotine gum and patches increased the likelihood of quitting smoking by 49% (55 trials, RR 1.49, 95% CI 1.40-1.60) and 64% o(43 trials, RR 1.64, 95% CI 1.52-1.78) respectively,

according to a 2014 Cochrane research. The oral nicotine tablets/lozenges (6 trials, RR 1.95, 95% CI 1.61-2.36), inhaler (4 trials, RR 1.90, 95% CI 1.36-2.67), and nasal sprays (4 trials, RR 2.02, 95% CI 1.49-2.73) all roughly doubled the chances of success. The likelihood of success increased by 24% when bupropion and nicotine replacement therapy were combined (4 trials, RR 1.24, 95% CI 1.06-1.45). [47]

The likelihood of stopping smoking increased by a factor of two withovarenicline. There have been a few rare reports of neuropsychiatric adverse effects from varenicline. The FDA withdrew this black box warning in 2016 after it was discovered that the risk was less than anticipated.

Bupropion enhances the likelihood of quitting smoking by 62%, according to a 2014 Cochrane review (44 studies, N=13,728, RR 1.62, 95% CI 1.48-2.78).

A 2016oCochrane study found that there was a greater chance of success when behavioural assistance and medication were used together. [48]

- **Obesity**

A patient's body mass index (BMI) must be determined at each visit to the doctor. According to the USPSTF, doctors should refer obese individuals to a multi-component behavioural interventionist.

Numerous studies have shown that in obese or overweight individuals, even a small 5% body weight reduction might result in clinically significant health benefits.

- **Exercise**

Patients who are overweight, obese, or who have CAD risk factors are advised by the USPSTF to get comprehensive behavioural counselling for measures that will encourage

physical activity in an effort to avoid CAD.

Accordingoto the National Health Interview Survey, only 20.9% of people met the 2008 government physical activity guidelines for aerobic and strengthening activities.

Cardiovascular disease is reduced by moderate aerobic activity, such as 150 minutes per week. Moderate-intensity aerobic exercise is defined as heart rates between 50 and 70 percentoof the patient's maximum heart rate, or 220 beats per minute less the patient's age. It has been established that physical activity helps to reduce CAD risk in any way. For the most active people, the risk of coronary artery disease is lowered by 35 to 40%. In order to improve physical function and exercise capacity, resistance strength training is also encouraged by the AHA/ACC guidelines to be incorporated into regular physical activity.

- **Aspirin in the First Line of Defense**

Aspirin has been used for a very long time to prevent cardiovascular diseases brought on by atherosclerosis. Although it is still well-established for secondary prevention, a less favourable risk-benefit ratio has recently raised questions about its usefulness in primary prevention. Recent research suggest aspirin use should be more carefully individualised. [49]

Patients between the ages of 50 and 59 with a 10-year atherosclerotic cardiovascular disease risk and no bleeding risk factors are advised to take aspirin. For people 60 to 69 years old, aspirin might be studied, but it might provide less overall benefit and raise the risk of bleeding. [50]

- **New CAD Screening Tests**

- **Coronary Artery Calcium (CAC) Score**

the widely accepted coronary artery calcium score (CAC) test, which is noninvasive.

A non-contrast cardiac CT is used to measure the amount of calcium in the coronary arteries, which is a factor in atherosclerosis.

An important prospective cohort study discovered that CAC could assist clinicians better match the right individuals for statin therapy by identifying those who were at an increased risk of having a coronary event.

For those with intermediate risk (10-year >/=7.5% to 20%) or borderline risk (10-year ASCVD risk 5-7.5%), the 2019 AHA/ACC primary preventive guideline suggests CAC. Before beginning treatment, patients who want more information may find the CAC score to be helpful. Unless the patient smokes, has diabetes, has a family history of early-onset clinical ASCVD, or has diabetes mellitus, a statin is not necessary if the CAC score is 0. In patients 55 years of age and older, a statin is preferred if the CAC ranges from 1 to 99. Treatment with statins is indicated if the CAC is 100 or in the 75th percentile or higher.

Shared decision-making is advised by the 2017 SCCT (Society of Cardiovascular Computed Tomography) recommendation for those with a 5% to 20% 10-year ASCVD risk or a 5% 10-year ASCVD risk but another strong justification, such as those with a family history of early CAD.[51]

- **Carotid Intimal Medial Thickness (CIMT)**

CIMT is a different recommended method for non-invasive risk stratification for CAD. The primary diagnostic method for this evaluation is ultrasound, though MRI may also be employed. Contradictory findings about this modality have been found in a number of large research, most likely as a result of irregular image acquisition and analysis as well as differences in study design.

A meta-analysis conducted in 2012 that combined CIMT with the Framingham Risk Score (FRS) did not significantly enhance risk prediction.

The AHA/ACC advised against it in a 2013 update, reversing a 2010 class IIa recommendation for its use in people at moderate risk.

An observational multi-ethnic study of atherosclerosis (MESA) carried out in 2017 found that the prediction of cardiovascular risk was improved when the CIMT and a positive CAC were combined.[52]

- **Flow-Mediated Dilation (FMD) and Endothelin Function**

Another suggested test that may be able to predict cardiovascular risk is FMD, which evaluates the state of blood vessel endothelial function. Stress from physiologicoand pharmacological sources, such asohypertension, smoking, or particular medications, might alterothis. [53]

There are several methods for measuring FMD. Using cardiac catheterization protocols that contain vasoactive medications will provide a more precise method of measuring coronary flow reserve or coronary artery endothelial function (CFR). [54]

- **Novel biomarkers**

In a 2017 article, novel potential biomarkers for CAD were examined, including fibrinogen, hs-CRP, lipoprotein-associated PA2, lipoprotein A, hs-troponin, NT-proBNP, and cystatin C. None met all the criteria to be considered an excellent biomarker. [55]

FRAMINGHAM RISK SCORE

A sex-specific method called the Framingham Risk Score is used to calculate a person's 10-year cardiovascular risk. The Framingham Risk Score was initially created to calculate the 10-year risk of getting coronary heart disease using information from the Framingham Heart Study. In order to quantify the 10-year cardiovascular disease risk, cerebrovascular events, peripheral artery disease, and heart failure were subsequently added as disease outcomes for the 2008 Framingham Risk Score.[56]

Cardiovascular Risk Scoring systems

One of the scoring methods used to estimate a person's risk of acquiring cardiovascular disease is the Framingham Risk Score. These grading systems can all be found online. Cardiovascular risk score systems predict a person's likelihood of developing cardiovascular disease within a given time frame, often 10 to 30 years. They also show who is most likely to benefit from prevention because they indicate the risk of acquiring cardiovascular disease. In order to decide who should be prescribed preventive medications like those to decrease blood pressure and cholesterol, cardiovascular risk scores are utilised. [Reference needed] For instance, high blood pressure (>130/85) was solely responsible for roughly 30% of coronary heart disease (CHD) occurrences in both men and women, demonstrating the importance of managing and monitoring blood pressure for cardiovascular health and outcome prediction.[57]

Usefulness

Risk scores, like the Framingham Risk Score, are helpful for both Whether lifestyle changes, preventive medical care, and patient education are suitable will depend on the particular patient and the practitioner. They accomplish this by identifying both men and women who are more likely to experience future cardiovascular events and indicating the potential advantages of preventive. [6]

The Framingham Risk Score can be used to quantify the percentage risk of coronary heart disease (CHD) at 10 years. A person's 10-year CHD risk is 10% or less for low-risk individuals, 10% to 20% for intermediate-risk individuals, and 20% or more for high-risk individuals. However, it is important to keep in mind that these classifications are subjective. To take treatment effects into account would be a more helpful statistic. If there is ao20% ten-year risk of cardiovascular disease in a group of 100 people, in other words, we should expect that in the next ten years, 20 of them will have cardiovascular disease (coronary heart disease or stroke) and 80 of them won't.

It follows that If they were to receive a combination of treatments, 10 of these 100 individuals should be expected to have cardiovascular disease in the following ten years, whereas 90 of them should not be expected to develop cardiovascular disease (for example, drugs to lower cholesterol levels along with drugs to lower blood pressure). If such were the case, 10 of these people would have been able to avoid cardiovascular disease by receiving treatment for 10 years; 10 would still develop the disease regardless of receiving treatment; and 80 would not have developed cardiovascular disease regardless of receiving treatment.

Randomized studies evaluating the impact of employing cardiovascular disease risk factors have found little difference in patient outcomes, despite their widespread use. Although there is strong evidence that focusing on people who have a high overall CVD risk is the

most effective method to lower CVD-related morbidity and death, studies to date evaluating the value of risk scores in assisting clinicians in focusing on high-risk patients have found little benefit.

It's critical to understand thatoage is the most accurate predictor of cardiovascular risk in any risk calculation.

Cardiovascular disease is common in the general population, affecting the majority of adults. It contains.:

1. Myocardial infarction (MI), angina pectoris, heart failure (HF), and coronary death are examples of coronary heart disease (CHD).
2. Transient ischemic attack, stroke, and cerebral vascular disease (TIA).
3. Significant limb ischemia, intermittent claudication, and peripheral arterial disease.
4. There are three types of aortic disease: abdominal, thoracic, and atherosclerotic.

By altering one's lifestyle and receiving preventative medical care, a person's risk for future cardiovascular events can be reduced. Stopping smoking, eating well, exercising frequently, and other lifestyle improvements are examples. A statin, low-dose aspirin, treatment for high blood pressure, and other preventive medical procedures are examples. To decide when to start making lifestyle changes and receiving preventative medical care, it is critical to be able to forecast the risk of a specific patient. Numerous risk models have been created to forecast each patient's cardiovascular risk. The Framingham Risk Score is one important risk model.

The results of the Framingham Heart Study serve as the foundation for the Framingham Risk Score

CORONARY HEART DISEASE WITH FRAMINGHAM RISK SCORE

Guidelines for the illness's prevention suggest the use of risk scores to identify people who are more likely to develop coronary heart disease (CHD) and for whom preventive therapy, such as medication to decrease cholesterol, has bigger absolute benefits. The Framingham risk score (FRS) is the most common of the scoring systems that are available to help clinicians determine the 10-year CHD risk. US recommendations for the administration of lipid-lowering pharmaceutical therapy and aspirin for primary prevention are based on the risk estimations provided by the FRS.

Most risk ratings were developed in white middle-aged groups. It is therefore uncertain if risk forecasts based on these ratings can be made for seniors as a whole.For instance, the FRS was created by middle-aged white people who ranged in age from 30 to 74. Participants had a mean age of 49. Some classical risk factors exhibit weaker correlations with CHD risk in the elderly than they do in middle-aged individuals, therefore actual risk prediction with FRS may perform worse in this age range. Middle-aged people have higher levels of total and LDL cholesterol cardiovascular risk factors than older people do. [58]

We sought to compare the predictive capabilities of 1) the FRS, directly and 2) following recalibration. Due to the fact that it is still unknown whether and how CHD risk prediction could be improved in the ageing population to support primary preventive activities, the Health ABC Study, a cohort of older white and black men and women, was used as the third source of data. 4) Another objective of our study was to determine the value of including readily available lifestyle and basic laboratory data, such as creatinine, glucose, and lifestyle variables, which have been found to predict CHD in older people but are not included in the FRS (alcohol consumption, physical activity).

The scenario is different for younger people under the age of 30. Clinical cardiovascular disease (CVD) events do not manifest until later in life, despite the fact that the atherosclerotic process starts at a young age in accordance with the amount of classical risk factors including smoking, high blood pressure, and high cholesterol. The apparent disparity between atherosclerotic load and incident rates in younger persons raises a major concern: can the FRS, one of the risk estimation methods now in use, effectively distinguish risk when applied to those under 30? The research that are currently accessible have not yet addressed this topic. Since the release of ATP III, numerous large-scale clinical trials of statin medication have been published, changing the focus of risk estimate to hard clinical results. The performance of risk estimates in younger people with high risk factor burden is important for both clinical practise and public health recommendations, despite the fact that one could contend that the therapeutic importance of the limitations of risk estimations in different populations is minimal. Risk assessment offers clinicians the chance for an interactive conversation in which patients decide to start medical treatment and/or way of life adjustments to lower their risk factor profile while taking into account their disease. If the risk assessment techniques currently in use are unable to discriminate between young adults who are actually low risk and those who may someday be at high risk, this vital doctor-patient conversation will be hindered. Effective risk communication to the greater population is necessary for public health to successfully raise awareness and change behavioural patterns. [59,60].

Although earlier research has successfully developed risk prediction tools for subclinical disease in young adults[61,62], The ability of the ATP III online risk estimator and/or the Framingham risk score to identify clinical CHD risk in younger populations has not been verified (age 30 years). Our aim was to assess the ability of the FRS and online ATP III risk estimator to predict the 10-year and longer-term risk of CHD death in these young men.

"HBA1C AS A RISK FACTOR FOR CORONARY HEART DISEASE WITH FRAMINGHAM RISK SCORE"

When it comes to detrimental effects on mortality and life expectancy globally, cardiovascular diseases (CVDs) are the main culprits [63]. Based on epidemiological studies from the 20th century, the idea of risk factors (RFs) is widely accepted. According to this concept, lifestyle variables and related RFs are to blame for the frequent occurrence of circulatory system problems. Traditional and non-traditional risk factors for circulatory system diseases and myocardial infarction (MI) include smoking, arterial hypertension, dyslipidemia, diabetes mellitus, and abdominal obesity (stress, anxiety and depression, an income level, marital status, and family conflicts). According to the results of the international INTERHEART study, unusual RFs, like hypertension and abdominal obesity, are important indicators of MI risk (conducted in 52 countries)[64]. Finding the demographic groups most vulnerable to CVDs is a crucial and pertinent issue for the healthcare system. Genetic and behavioural variables work together to establish an individual's risk for a poor cardiovascular prognosis. When compared to individuals with low genetic risk, patients with high genetic risk had a relative risk of new coronary events that is 91% greater (hazard ratio (HR) = 1.91; 95% confidence interval (CI); 1.75-2.09) [65]. It has been demonstrated that DNA structural alterations have a distinct impact on the total mortality brought on by MI and cardiovascular events. An allele or genotype's presence determines the likelihood of a negative outcome.

Cardiovascular risk is the probability of experiencing one or more negative cardiovascular events over time (including death from CVD or its consequences). The total risk of cardiovascular pathology is evaluated using a number of methods in clinical and research settings (Framingham, the Prospective Cardiovascular Munster Study (PROCAM), and the Systematic Coronary Risk Evaluation (SCORE).

Scale of Framingham Risk was developed in response to the findings of the largest prospective study ever carried out in the United States (the 5209-person Framingham Heart Study, 1949–1984). The 10-year risk of fatal and nonfatal cardiovascular problems can be evaluated using this technique, and the risk is divided into four categories: low (risk of complications less than 10%), medium (risk more than 10% but less than 20%), high (risk > 20%), and extremely high (risk > 30%). There are five characteristics considered in total, including two that cannot be changed (gender and age) (smoking, total cholesterol, and systolic blood pressure). This risk calculator has demonstrated strong predictive ability in several cohorts that are comparable to those for which it was intended, However, it is well recognised to overstate the risk in populations of European ancestry and other ethnic groups where coronary heart disease is less common (CHD)[66,67].

The SCORE (Systematic Coronary Risk Evaluation) scale was developed in Europe in 2003 using data from 205,178 participants from 12 cohort studies[68]. It makes predictions about the likelihood of a negative CVD result based on factors like sex, age, systolic blood pressure, total cholesterol, and smoking history. This tool makes it feasible to estimate the risk of dying from all CVDs, accounts for the complex nature of illness aetiology, allows physicians from different countries to assess the risk, and unequivocally shows that the risk rises with age (by 69 years old). It has a few restrictions: Low-density lipoprotein cholesterol levels (LDL-C), blood sugar, excess weight, and abdominal obesity are not taken into account in this risk calculator, which is designed for individuals between the ages of 40 and 65..

The outcomes of a prospective research called PROCAM (Munster, Germany), which started in 1979, were used to create the PROCAM (Prospective Cardiovascular Munster Study) scale. 21,306 participants (14,799 men between the ages of 40 and 65 and 6507 postmenopausal women) participated in the study. This model is based on three fixed RFs

(age, history of MI, and hereditary history of associated illnesses) and six adjustable RFs (smoking status, systolic blood pressure, LDL-C, high-density lipoprotein cholesterol, triglycerides, and the presence of diabetes mellitus). Risks of 20% or less are considered low, and risks of 20% or more are considered high[69,70].

For determining cardiovascular risk, a family history of pertinent disorders is crucial. There are currently being developed risk calculators that take hereditary factors into account. Their intricacy results from a combination of genetic factors, climatic and social living situations, and population-specific CVD prevalence.

This article discusses the stages of development, calculation methods, and implementation of a genetic risk score (GRS) for coronary heart disease (CHD) in different populations.

Liu Y et al [71](2011) showed that Hemoglobin A1c's (HbA1c) predictive significance in coronary artery disease (CAD) is still debatable. According to the pooled analysis, a higher HbA1c level was substantially linked to a higher risk of both short- and long-term mortality (OR 2.32, 95% CI, 1.61 to 3.35) According to subgroup analysis, persons without diabetes who had elevated HbA1c levels had a greater mortality risk (OR 1.84, 95% CI, 1.51 to 2.24). In contrast, elevated HbA1c levels in diabetic patients were not linked to an increased risk of death (OR 0.95, 95% CI, 0.70 to 1.28). In a risk-adjusted sensitivity analysis, increased HbA1c was linked to a borderline effect in patients with diabetes (adjusted OR 1.05, 95% CI, 1.00 to 1.11) but was significantly linked to a high risk of adjusted mortality in patients without diabetes (adjusted OR 1.49, 95% CI, 1.24 to 1.79).

Patil VC et al [72](2011) observed that the prevalence of diastolic dysfunction in diabetic people and how it relates to factors including age, the length of diabetes mellitus (DM), HbA1c levels, obesity indices, and diabetic microangiopathies. Diastolic dysfunction was present in 69 (54.33%) of the 127 total subjects from the case group, and in 11% of the 100 participants in the control group (P 0.001). Diastolic dysfunction was more common in

patients with DM who had had it for 11 to 15 years or longer (P = 0.02). With "P" = 0.001 and "P" = 0.02, respectively, subjects with high waist circumference and high waist to hip ratio showed statistically significant diastolic dysfunction. Diastolic dysfunction was more common in persons with HbA1c > 7.5% than in subjects with HbA1c 7.5% (P = 0.02). The majority of the participants who had retinopathy and autonomic neuropathy had diastolic dysfunction. They arrive to the conclusion that early diagnosis and treatment will improve outcomes, lower morbidity, and avoid future heart failure.

Su G et al [73](2011) examined that to evaluate the association between Continuous glucose monitoring (CGM) system assessment of glycemic variability and existence and severity of coronary artery disease (CAD) in type 2 diabetes mellitus patients (T2DM). Patients with CAD had significantly higher levels of serum high-sensitive C-reactive protein (hs-CRP) (10.7 12.4 mg/L vs. 5.8 6.7 mg/L, p 0.001), creatinine (Cr) (87 23 mmol/L vs. 77 14 mmol/L, p 0.001), mean amplitude of glycemic excursions (MAGE) (3.7 Age, MAGE, PPGE, haemoglobin A1c (HbA1c), hs-CRP, and total cholesterol have strong relationships with the Gensini score (TC). Age (p 0.001), MAGE (p 0.001), serum HbA1c levels (p = 0.022), and hs-CRP (p = 0.005) were found to be independent predictors of Gensini score according to multivariate analysis. The results of a logistic regression study showed that MAGE 3.4 mmol/L was a reliable indicator of CAD. MAGE's area under the receiver-operating characteristic curve (0.618, p = 0.001) outperformed HbA1c's (0.554, p = 0.19) by a significant margin.

Pischon T et al [75](2011) examined that when matching variables, parental myocardial infarction history, hormone replacement therapy, alcohol use, physical activity, body mass index, hypertension, and levels of low-density lipoprotein cholesterol were taken into account, the relative risk in the highest versus lowest quintile for total adiponectin, HMW adiponectin, and HMW/total adiponectin was 0.50 (95%-CI 0.33-0.75; p trend = 0.001),

0.53 These correlations were diminished and no longer significant after accounting for diabetes, HDL cholesterol, HbA1c, and CRP (RRs, 0.84; 95%-CI 0.53-1.33; p trend = 0.62; 0.95; 95%-CI 0.60-1.52; p trend = 0.98; 0.97; 95%-CI 0.64-1.47; p trend=0.80). Even after adjustmentoin the Cox proportional hazard model, HUA remained an independent risk factor for coronary heart disease. Diabetes-related micro- and macroangiopathies are linked to HUA. For people with type 2 diabetes, HUA is a predictor of coronary heart disease and renal failure. HUA is thought to have a rather small impact.

Agarwal AK et al [76](2012) observed that Peripheral artery disease is one of type 2 diabetes mellitus's macrovascular side effects (PAD). The researchers looked at 146 individuals (79 men and 67 women; average age, 59.4 7.2 years; average time since diagnosis, 8.8 3.8 years). The frequency of PAD was 14.4%, and women were somewhat more likely to have it (14.9%) than men (13.9%) (p=0.864). 28% of patients had CAD. Significant risk factors for PAD were age, the duration of diabetes, smoking, systolic and diastolic blood pressures, and a HbA1c >7%. They failed to discover a link between obesity-related metrics and PAD. Older age (p=0.01), higher HbA1C levels (p=0.02), microalbuminuria (p=0.03), and an abnormal lipid profile (total cholesterol, HDL, and triglycerides) were revealed to be significant predictors of CAD using binary logistic regression. The ankle brachial index allowed us to detect PAD in 14.3% of type 2 diabetes. Risk factors that were closely related to PAD included older age, longer duration of diabetes, higher systolic and diastolic blood pressure, smoking, higher HbA1C levels, and CAD. Patients with PAD were more likely to have CAD (52.38% compared to 24% in those without PAD; p=0.007). A high likelihood of underlying CAD should therefore be indicated to the clinician by the existence of PAD.

An X et al [78](2012) observed that coronary atherosclerotic plaque progression. The greater insulin lower insulin resistance groups' index and follow-up Gensini scores (9.09 14.33 vs. 9.44 12.88, p = 0.813, and 17.21 18.46 vs. 14.09 14.18, p =0.358) were comparable.

However, the greater insulin resistance group had a substantially higher Gensini score measuring the advancement of coronary lesions between visits (8.13 11.83 versus 4.65 7.58, p = 0.019). Insulin resistance (HOMA-IR > 3.4583) was identified as an independent predictor of coronary artery plaque progression (OR = 4.969, p = 0.011) by multivariate logistic binomial regression analysis. Additionally, they split up each participant into two groups: diabetics (n = 136) and non-diabetics (n = 230) and HOMA-IR continued to be a reliable indicator of the development of atherosclerotic plaque. In both diabetic and non-diabetic patients with coronary heart disease, insulin resistance is a standalone predictor of atherosclerotic plaque progression.

Ashraf H et al [79](2013) examined that to ascertain the relationship between glycated haemoglobin (HbA1c) and coronary artery disease (CAD) in non-diabetics and the severity of the disease. Mean age was 58.8±10.4 year; 60.9% men. There was substantial CAD in 147 patients (50% stenosis in any major artery). The frequency of CAD and the number of affected vessels significantly increased with rising HbA1c levels. In multivariate analysis, HbA1c emerged as an independent predictor of significant CAD (OR: 2.8, 95% CI: 1.3–6.2, p = 0.009). Adjusted ORs for the occurrence of CAD were highest in subjects with both hsCRP and HbA1c in the upper 2 quartiles (OR: 4.183; 95% CI: 1.883–9.290, p < 0.0001). There was a significant association between Gensini score and increasing HbA1c tertiles (p = 0.038). HbA1c could be used to stratify CAD risk in non-diabetic people, independent of conventional cardiovascular risk factors, insulin resistance, and inflammatory markers.

Sakurai M et al [80](2013) showed that HbA1c and cardiovascular diseases (CVD) have been linked, primarily in Western nations. During the study, there were 1,104 deaths, including 304 from CVD, 61 from coronary heart disease, and 127 from stroke (78 from cerebral infarction, 25 from cerebral hemorrhage, and 24 from unclassified stroke). Participants' multivariate-adjusted HRs for CVD death were graded and continuous in relation to HbA1c

with all-cause mortality and CVD death Compared to those with HbA1c 5.0%, those with HbA1c 6.0-6.4% and 6.5% were 2.18 (95% CI 1.22-3.87) and 2.75 (1.43-5.28), respectively. It was shown that there was a correlation between HbA1c and mortality from myocardial infarction and coronary heart disease. High HbA1c levels were associated with an increased risk for all-cause mortality as well as death from CVD, coronary heart disease, and cerebral infarction in general East Asian communities as well as in Western populations.

Farkouh ME et al [81](2013) observed that researchers examined data from 3 federally funded trials that focused on the most effective medical treatment to determine whether formalised attempts at risk factor control within clinical trials are successful in achieving guideline-driven treatment goals for diabetic patients with coronary artery disease (CAD). In COURAGE, BARI 2D, and FREEDOM, the percentages of patients attaining the 1-year low-density lipoprotein cholesterol objectives relative to baseline increased from 55% to 77%, 59% to 75%, and 34% to 42%, respectively. At one year of follow-up, only 18% of the COURAGE diabetic subgroup, 23% of BARI 2D patients, and 8% of FREEDOM patients reached all 4 pre-specified treatment targets, despite similar better trends for systolic blood pressure, glycemic management, and quitting smoking. In clinical trials, a sizable fraction of patients with diabetic CAD fall short of the pre-set goals for 4 major modifiable cardiovascular risk variables. They come to the conclusion that in order to examine strategies for achieving the best secondary prevention therapy goals, fundamentally fresh thinking is required. Clinical Results Using Aggressive Drug Evaluation and Revascularization.

Shin JH et al [82](2013) observed that the middle tertile (8.44.0) and lower tertile (7.63.8) groups' mean FRSs were considerably lower than the upper tertile (9.63.8) group's. The IRD group also had the highest FRS (10.53.7). When controlling for confounding factors, multiple linear regression analysis showed that HbA1c levels significantly correlated

positively with FRS in all individuals (standard error [SE], 0.0180.002; R2, 0.131), women (SE, 0.0230.003; R2, 0.170), and men (SE, 0.0160.004; R2, 0.109). In older, seemingly healthy Korean adults without diabetes, HbA1c levels were strongly linked with FRS. They suggest that HbA1c levels could indicate CVD risk in people who are not diabetic.

Madhumitha H et al [85](2014) observed that Less is known about the function of T helper cytokines in the co-morbidity of type-2 diabetes mellitus (T2DM) and coronary artery disease, which is prevalent in chronic, low-grade inflammation (CAD). Multiplex cytokine assays were used to assess the serum cytokine profiles of 61 Control, 60 T2DM, 23 CAD, and 21 T2DM-CAD patients. The Th1-Th2 phenotype was mixed in T2DM individuals. While T2DM-CAD participants displayed an improved Th1 profile with substantial Th2 cytokine suppression, CAD subjects displayed a Th1 profile with mild Th2 suppression. FPG, HbA1c, hsCRP, IMT, and AGI all shown favourable correlations with both Th1 and Th2 cytokines. Logistic regression analysis revealed a significant association of IL-12 (OR = 9.3; 95% CI = 3.2-70.7; p = 0.016), IFN-γ (OR = 2.8; 95% CI = 2.7-2.9, p = 0.010), IL-4 (OR = 2.7; 95% CI 2.7-2.7, p = 0.010), IL-5 (OR = 1.1; 95% CI = 1.0-1.4; p = 0.003) and IL-13 (OR = 2; 95% CI = 1.7-2.6; p = 0.017) with T2DM-CAD. As a result of the current investigation, it appears that the change from T2DM or CAD to T2DM-CAD co-morbidity is accompanied with a significant upregulation of Th1 responses and a strong downregulation of Th2 cytokines.

Parry HM et al [87](2015) examined that Although type 2 diabetes mellitus is a known risk factor for developing heart failure, the connection between antecedent glycemia and incident heart failure has not been studied. According to specified HbA1c ranges, there is a computed risk of developing heart failure that takes into account heart failure comorbidities such blood pressure, body mass index, and coronary artery disease. This method is known as proportional hazard regression. During follow-up (mean 5.5 years, 2.8 years), 701 people

with type 2 diabetes mellitus (8%) experienced heart failure. A time-updated analysis using longitudinal HbA1c revealed that the risk of heart failure was independently correlated with HbA1c 6% (hazard ratio =1.60; 95% confidence interval, 1.38-1.86; P value 0.0001) and HbA1c >10% (hazard ratio =1.80; 95% confidence interval, 1.60-2.16; P-value 0.0001). Heart failure development in their sample was predicted by both high and low HbA1c, creating a U-shaped relationship.

Leon BM et al [88](2015) observed that Diabetes mellitus (DM) is one of the most common and expensive chronic diseases in the world and its incidence is still on the rise. Cardiovascular disease (CVD), the most common cause of morbidity and mortality in diabetic individuals, and DM are closely related. Patients with diabetes mellitus (DM) frequently have cardiovascular (CV) risk factors include obesity, hypertension, and dyslipidemia, which puts them at higher risk for cardiac events. Additionally, numerous investigations have shown molecular pathways linked to DM that, on their own, raise diabetic patients' risk of CVD. Targeting CV risk factors in DM patients is essential to reducing the disease's long-term CV consequences. This paper summarizes the relationship between diabetes and CVD, examines possible mechanisms of disease progression, discusses current treatment recommendations, and outlines future research directions.

Sherwani SI et al [89](2016) found that Glycated haemoglobin (HbA1c) has been suggested by the American Diabetes Association as a potential alternative to fasting blood glucose for the diagnosis of diabetes. The ability to reflect the cumulative glycemic history of the previous two to three months makes HbA1c an essential biomarker of long-term glycemic control. HbA1c not only offers a trustworthy indicator of chronic hyperglycemia but also has a strong correlation with the likelihood of long-term consequences from diabetes. Additionally, elevated HbA1c has been recognised as a stand-alone risk factor for both patients with and without diabetes developing coronary heart disease and stroke. A

single HbA1c test's valuable information has made it a trustworthy biomarker for the diagnosis and prognosis of diabetes.

Cavero-Redondo I et al [90](2016) observed that in clinical practise, the glycosylated haemoglobin level (HbA1c) is a practical and well-known biomarker that provides information on the average blood glucose levels during the previous two to three months. The systematic review or meta-included analysis's studies' risk of bias will be evaluated using the Quality in Prognosis Studies tool. As primary outcomes, 95% confidence intervals (CIs) for HRs for cardiovascular events and causes of death will be calculated. Based on the cardiovascular outcomes, the examined causes of death, and the study population type, subgroup analyses will be carried out. The evidence on the possible use of HbA1c level as a predictive marker for cardiovascular disease outcomes and/or death will be synthesised in this comprehensive review. The results will be disseminated by publication in a peer-reviewed journal. Ethics approval will not be needed because the data used for this systematic review will be obtained from published studies and there will be no concerns about privacy.

Scicali R et al [91](2016) examined that An HbA1c level between 5.7 and 6.4% was considered to be prediabetes. Consensus criteria were used to evaluate the coronary artery calcium (CAC) score, mean common carotid intima medium thickness (IMT), and the presence of plaque. When compared to non-prediabetic patients, the prediabetes group's CAC score was greater (131.7 295.6 vs. 62.4 178.8 AU, p 0.001). In contrast to non-exposed patients, prediabetic subjects showed greater mean IMT (0.77 0.14 vs. 0.61 0.15 mm, p 0.001). When compared to those who weren't exposed, the proportion of prediabetic patients with CAC = 0 was substantially lower (35% vs. 63%, p 0.01). In contrast, the percentage of patients in the prediabetes group (10% vs. 3%, p 0.05) who had a CAC >400 was significantly higher. Additionally, patients with prediabetes had considerably more

carotid plaques than did participants with normoglycemia (p 0.01). IMT and continuous HbA1c levels were connected in a multiple linear model (p 0.001). Additionally, logistic regression demonstrated an association between the presence of CAC and carotid plaques and higher HbA1c levels (p for trend for all 0.001).

Jiménez-Lucena et al [92](2018) observed that aimed was to Furthermore, those with prediabetes had significantly more carotid plaques than those with normoglycemia (p 0.01). A multiple linear model related IMT and continuous HbA1c readings (p 0.001). Additionally, logistic regression showed a connection between carotid plaques and CAC, as well as higher HbA1c levels (p for trend for all 0.001). The miRNA and HbA1c-based model did not improve when the FINDRISC was included (AUC = 0.8293). Cox regression analysesshowed that patients with low miR-103, miR-28-3p, miR-29a, and miR-9 and high miR-30a-5p and miR-150circulating levels have a higher risk of disease (HR = 11.27; 95% CI = 2.61–48.65). Their results suggest that circulating miRNAs could potentiallybe used as a new tool for predicting the development of type 2 diabetes in clinical practice.

Jin JL et al [93](2018) examined that A novel marker for metabolic problems, the triglyceride glucose (TyG) index has recently been linked to an increased risk of cardiovascular disease (CVD) in those who appear to be in good condition. 1,450 controls and 290 (7.7%) patients with CVEs were matched for age, gender, prior history of PCI or CABG, and length of follow-up. Fasting plasma glucose (mg/dL) divided by fasting triglycerides (mg/dL) was used to produce the TyG index. TyG index was found to be positively correlated with the probability of CVEs by multivariable Cox proportional hazards models (hazard ratio: 1.364, 95% confidence interval: 1.100-1.691, P=0.005). Patients in the top quartile of the TyG index had the lowest event-free survival, according to the Kaplan-Meier analysis (P=0.029). Furthermore, compared to other lipid or glycemic related markers, a 1-standard deviation (SD) rise in TyG index was linked with a 23.2% higher risk of CVEs [hazard ratio (HR):

1.232, 95% confidence interval (95% CI): 1.084-1.401].

Wei F et al [94](2019) examined that to explore the clinical effects of diabetes patients' changing levels of glycosylated haemoglobin on hypertension and coronary heart disease. However, patients in the observation group had significantly lower levels of high-density lipoprotein cholesterol (HDL-C) than those in the control group (P 0.05). Patients in the observation group had higher levels of high-sensitivity C-reactive protein (hs-CRP), HbA1c, fasting plasma glucose (FPG), fasting insulin (FINS), and systolic and diastolic blood pressure (P0.05) than those in the control group. Patients with hypertension had significantly greater HbA1c levels than those without hypertension (P 0.05). Individuals with coronary heart disease appeared to have greater levels of HbA1c than patients without coronary heart disease (P 0.05). The findings of the Pearson correlation analysis showed a positive link between the level of hs-CRP, SBP, and DBP in the diabetic group of patients and their HbA1c level (P0.05). Diabetes patients' HbA1c levels were positively correlated with their hs-CRP and blood pressure levels.

Xia J et al [95](2019) examined that For the treatment of diabetes, fasting blood glucose, postprandial blood glucose, and glycated haemoglobin are all essential markers. More and more research points to the fact that glucose fluctuation harms coronary arteries more severely than chronic persistent hyperglycemia. The most recent research on glucose variability and its potential connection to coronary artery disease is summarised in this overview. Variability in blood sugar levels may be a sign of accelerated coronary disease progression and plaque vulnerability. It might be a new therapeutic target with promise for secondary coronary artery disease prevention. Future studies will focus on the early detection and control of glucose variability to improve the clinical outcomes in patients with coronary artery disease.

Li S et al [96](2020) observed that to look into the relationship between cardiovascular events and microvascular problems in patients with newly diagnosed type 2 diabetes and visit-to-visit HbA1c variability. They made use of the previously published HbA1c variability score (HVS), which was determined by dividing the total number of HbA1c measurements taken from a person by the proportion of variations in HbA1c > 0.5% (5.5 mmol/mol). The use of Cox proportional hazards models was used to evaluate the relationship between HVS and 10 outcomes. In the analysis of each outcome, 13,111–19,883 patients were included. In comparison to the lowest quintile, patients with HVS >60% were linked to higher risks of all outcomes (for instance, HVS >80 to 100 vs. HVS 0 to 20, hazard ratio 2.38 [95% CI 1.61-3.53] for major adverse cardiovascular events, 2.4 [1.72-3.33] for all-cause mortality, etc.). 2.63 [1.81-3.84] for coronary artery disease, 2.04 [1.12-3.73] for ischemic stroke, 3.23 [1.76-5.93] for heart failure, 2.4 [1.13-5.11] for atherosclerotic cardiovascular death, 5.24 [2.61-10.49] for diabetic foot ulcer, 7.4 [3.84-14.27] for diabetic retinopathy, 3.07 [2.23-4.22] for diabetic peripheral neuropathy, and 3.49 [2.47-4.95] for newly developed chronic kidney disease). The robustness of the findings was validated by four sensitivity analyses, including the adjustment for time-weighted average HbA1c.

Bhatt K et al [97](2020) Theoaim of the current study was to investigate the relationship between high normal HbA1c and the 10-year Framingham risk score for coronary artery disease in non-diabetics. A greater HsCRP value was associated with a higher HbA1c level, according to the Chi square Test, which was significant (p=0.04). Since the correlation coefficient (r) was -0.02 between HbA1c and Framingham risk score, there was no linear relationship between the two. The average patient age and Framingham risk score in their study were 53.7 years and 9.72, respectively. A linear association between the patient's age and the Framingham 10-year risk score was found (r=0.60). It was common for patients with coronary artery disease to have high HsCRP levels. High HsCRP and glycosylated

haemoglobin indicated a significant correlation (p=0.004). They discover that the patient's age and sex have a linear connection with the Framingham 10-year risk score.

Van Dongen LH et al [98](2020) sought to determine whether greater levels of glycated haemoglobin in non-diabetics are associated with an increased risk of sudden cardiac arrest (SCA) (HbA1c). They studied 306 cases (56.4 6.8 years, 79.1% male) and 1722 controls (54.0 6.8 years, 64.8% male). Cases had higher HbA1c readings than controls (5.8 0.3% vs. 5.4 0.3%, P 0.001) When compared to controls, which had a HbA1c of 19.3%, cases had a 63.1% higher percentage (5.7%). (P 0.001). Multivariate regression models revealed that elevated HbA1c was associated with a > six-fold increased risk of VF [adjusted odds ratio (ORadj) 6.74 (5.00-9.09)]. demonstrating that a 0.1% increase in HbA1c level was associated with a 1.4-fold increase in VF risk, regardless of other cardiovascular risk factors present. Although the link between HbA1c and VF was the same in non-MI patients [OR 1.32 (1.21-1.44)] and MI patients [OR 1.47 (1.37-1.58)], acute myocardial infarction (MI) as the cause of VF is related with increased VF risk at increasing HbA1c [OR 1.14 (1.04-1.24)].

Kayali Y et al [99](2021) examined that aimed to research the importance of HbA1c, or glycosylated haemoglobin, in predicting coronary artery disease 120 individuals in the study group had no stenosis in any coronary artery, 56 had stenosis in one coronary artery greater than 50%, and 71 had stenosis in more than one coronary artery. According to the degree of stenosis, there was a statistically significant difference between the HbA1c values (P =.001 and P .01, respectively). HbA1c had an odd ratio of 6.260 (95% CI: 3,160-12,401). The cutoff point for HbA1c was discovered to be 5.6 and higher based on the stenosis positive. HbA1c served as an independent risk factor for CAD in the regression analysis. Stenosis risk can increase up to 12.4 times (95% CI: 5,990-25,767) for every unit higher HbA1c level.. According to the study, HbA1c can be used in primary care to predict coronary artery disease and can be used independently to assess the likelihood and severity of the condition in non-

diabetics.

Khan FR et al [100](2021) showed that to determine a relationship exists between coronary artery disease and high levels of glycated haemoglobin (HbA1c) (CAD). To compare the categorical variables between the two classes, the fisher's exact test was used. 89 (58.9%) of the 151 patients were male, with the remaining patients being female. It was 55.4 11.2 years on average. Diabetes and hypertension were the two most prevalent risk factors, and ST-segment elevation myocardial infarction (STEMI) was the most typical presentation. HbA1c > 7.5% in 107 patients, or 70.86%, had poor glycemic control. TVD was detected during coronary angiographies in 77 (50.9%) patients. Six (14%) of these TVD patients had good glycemic control, compared to 71 (66%) of them, which is significantly different (P .001). None of the patients had NCAs who had poor glycemic control. According to this study, there is a connection between high HbA1c levels and the severity of coronary artery disease (CAD) in diabetic patients. The findings of their investigation showed that severe CAD and high HbA1c were associated. Additional research using a sizable sample size would be necessary to assess the more significant effect of HBA1c on coronary arteries.

MATERIALS AND METHODS

MATERIALS AND METHOD

STUDY DESIGN: It is a cross-sectional study.

STUDY PERIOD : It is a One and half year study from January 2021 to June 2022.

SOURCE OF DATA:

1. The material of the present study will be collected from the patients who are admitted in BLDE (To be deemed) University Shri B M Patil Medical College Hospital and ResearchCentre, Bijapur who h a v e s y mp t o ms o f Coronary Heart Disease without Diabetes Mellitus will be included in the study.

2. Patients will be informed about the study, and written consent will be obtained.

Method of collection of Data (including sampling procedures if any):

SAMPLE COLLECTION

Written consent will be taken from the subjects before the collection of specimens.Blood samples will be taken at the time of admission.

HbA1c, FBS, PPBS, and Lipid profile will be determined by standard methods.

INCLUSION CRITERIA:

- Age between 18 To 80 Years.
- Sex: Both.
- Patient must give Written Consent to take part in the Study.
- Diagnosis of Coronary Artery Disease or a ny Anginal symptoms with either Diagnostic Electrocardiographic Changes.

EXCLUSION CRITERIA:

- Known case of Diabetes Mellitus.
- Patients who refuse to take part in the study.
- Patients having Hba1c level ≥6.5

SAMPLE SIZE:

With the anticipated Proportion of HbA1c in Coronary Artery Disease 78% [4], the study would require a sample size of **95 patients** with a 98**%** level of confidence and 10% absolute precision**.**

Formula usedn = $\frac{z^2 p*q}{d^2}$

Where

Z= Z statistic at α level of significance

d^2= Absolute error

P= Proportion rate

q = 100-p

STATISTICAL ANALYSIS

For statistical analysis data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t-tests were a form of blocking and had greater power than unpaired tests. One-way analysis of variance (one-way ANOVA) was a technique used to compare means of three or more samples for numerical data (using the F distribution). A chi-squared test ($\chi 2$ test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a chi-squared distribution when the null hypothesis is true. Without other qualification, 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate .

The Mann–Whitney U test is a non-parametric test of the null hypothesis that it is equally likely that a randomly selected value from one sample is less than or greater than a randomly selected value from a second sample. This test can be used todetermine whether two independent samples were selected from populations having the same distribution; a similar non-parametric test used on dependent samples is the Wilcoxon signed-rank test .

Z-test (Standard Normal Deviate) was used to test the significant difference of proportions. Correlation was calculated by Pearson correlation analysis. The Pearson product-moment correlation coefficient was a measure of the linear dependence between two variables X and Y. Multivariate analysis was performed by logistic regression method for calculation of risk factors. The Kaplan–Meier estimator (Kaplan-Meier survival analysis) was a non-parametric statistic used to estimate the survival function from time data .

Explicit expressions that can be used to carry out various *t*-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a *t*-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carryout either a one-tailed test or a two-tailed test .

Once a *t* value is determined, a *p*-value can be found using a table of values from Student's t-distribution .If the calculated *p*-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favor of the alternative hypothesis .

P-value ≤ 0.05 wasconsidered for statistically significant .

RESULT & ANALYSIS

Table 1: Association between AGE CATEGORY: HBA1C Category

	HBA1C CATEGORY		
Age Category	**<5.5**	**≥5.5**	**TOTAL**
20-34	12	4	16
Row %	75.0	25.0	100.0
Col %	32.4	6.9	16.8
35-39	2	4	6
Row %	33.3	66.7	100.0
Col %	5.4	6.9	6.3
40-44	4	6	10
Row %	40.0	60.0	100.0
Col %	10.8	10.3	10.5
45-49	4	8	12
Row %	33.3	66.7	100.0
Col %	10.8	13.8	12.6
50-54	1	5	6
Row %	16.7	83.3	100.0
Col %	2.7	8.6	6.3
55-59	4	2	6
Row %	66.7	33.3	100.0
Col %	10.8	3.4	6.3
60-64	3	11	14
Row %	21.4	78.6	100.0
Col %	8.1	19.0	14.7
65-69	2	7	9
Row %	22.2	77.8	100.0
Col %	5.4	12.1	9.5
70-74	3	9	12
Row %	25.0	75.0	100.0
Col %	8.1	15.5	12.6
75-79	2	2	4
Row %	50.0	50.0	100.0
Col %	5.4	3.4	4.2
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 16.2337; **p-value:** 0.0622

In <5.5, 12 (32.4%) patients were 20-34 years of age, 4 (10.8%) patients were 40-44 years of age, 4 (10.8%) patients were 55-59years of age and 3 (8.1%) patients were 70-74 years of age.

In ≥5.5, 8 (13.8%) patients were 45-49 years of age, 11 (19.0%) patients were 60-64 years of age and 9 (15.5%) patients were 70-74 years of age.

Association of Age Category with HBA1C Category was not statistically significant (p=0.0622).

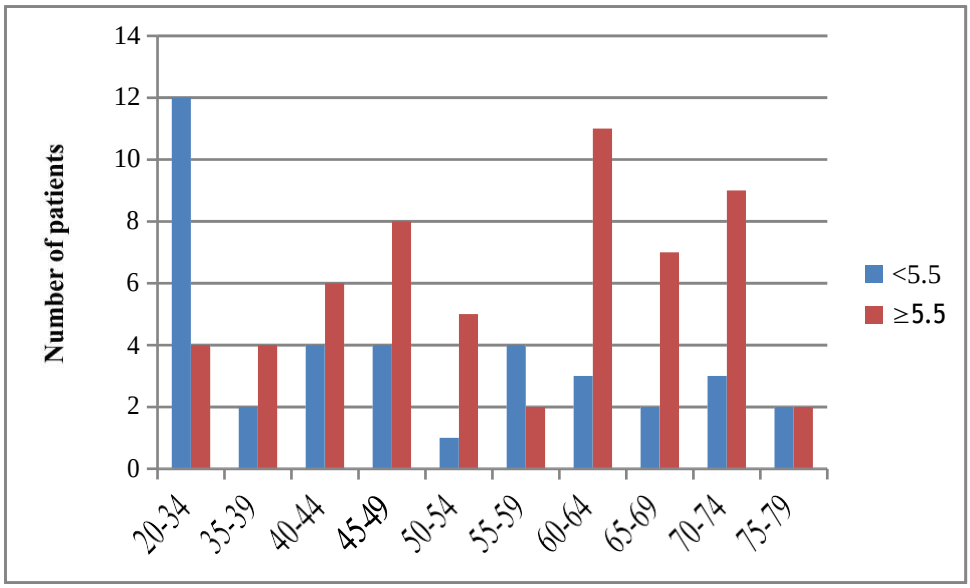


Figure 3

Table 2: Association between GENDER: HBA1C CATEGORY

	HBA1C CATEGORY		
GENDER	**<5.5**	**≥5.5**	**TOTAL**
Female	22	22	44
Row %	50.0	50.0	100.0
Col %	59.5	37.9	46.3
Male	15	36	51
Row %	29.4	70.6	100.0
Col %	40.5	62.1	53.7
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 5.2865; **p-value:** 0.0711

Odds Ratio: 2.4000 (1.0321, 5.5806)

In <5.5, 22 (59.5%) patients were Female and 15 (40.5%) patients were Male. In ≥5.5, . 22 (59.5%) patients were Female and 36 (62.1%) patients were Male.

Association of Gender with HBA1C Category was not statistically significant (p=0.0711).

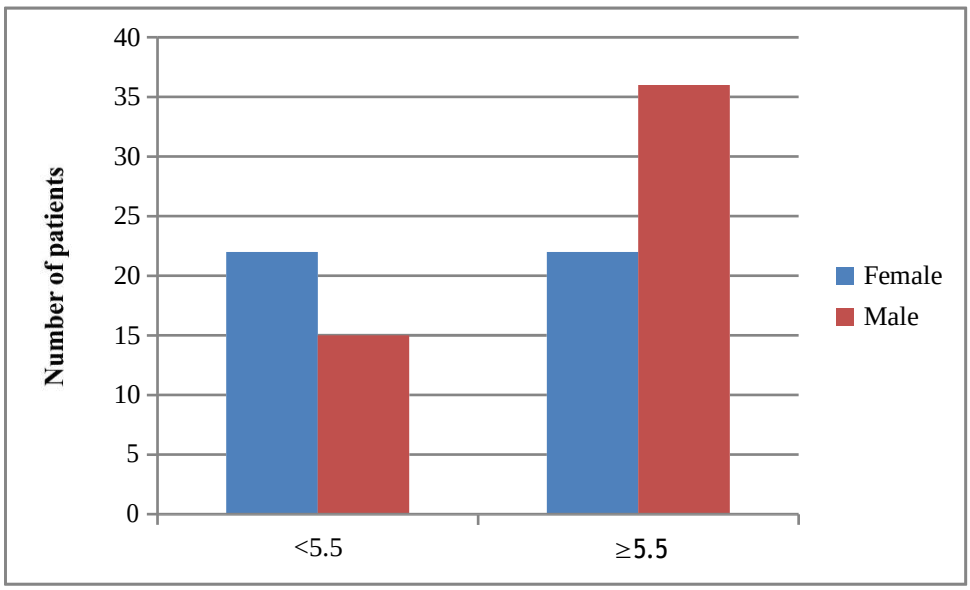


Figure 4

Table 3: Association between PAST HISTORY: HBA1C CATEGORY

	HBA1C CATEGORY		
Past History	**<5.5**	**≥5.5**	**TOTAL**
K/C/O ASTHMA	0	3	3
Row %Col %	0.0	100.0	100.0
	0.0	5.2	3.2
K/C/O COPD	2	1	3
Row %Col %	66.7	33.3	100.0
	5.4	1.7	3.2
K/C/O HTN	16	36	52
Row %	30.8	69.2	100.0
Col %	43.2	62.1	54.7
K/C/O TB	0	1	1
Row %	0.0	100.0	100.0
Col %	0.0	1.7	1.1
NO	19	17	36
Row %	52.8	47.2	100.0
Col %	51.4	29.3	37.9
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 7.8797; **p-value:** 0.0961

In <5.5, 16 (43.2%) patients had K/C/O HTN.In ≥5.5, 36 (62.1%) patients had K/C/O HTN. Association of Past History with HBA1C Category was not statistically significant (p=0.0961).

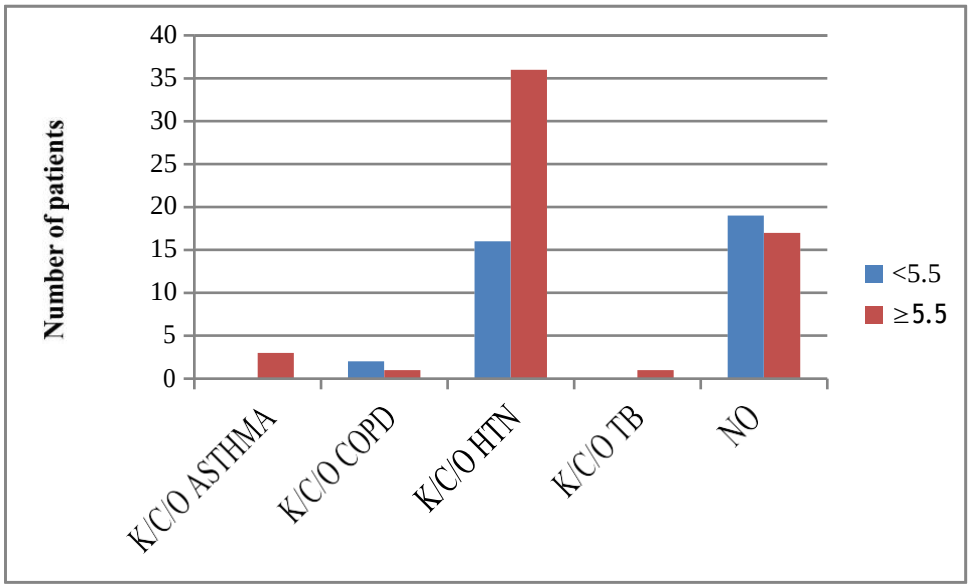


Figure 5

Table 4: Association between SBP Category: HBA1C Category

	HBA1C CATEGORY		
SBP Category	**<5.5**	**≥5.5**	**TOTAL**
<120	9	6	15
Row %	60.0	40.0	100.0
Col %	24.3	10.3	15.8
120-129	5	3	8
Row %	62.5	37.5	100.0
Col %	13.5	5.2	8.4
130-139	5	10	15
Row %	33.3	66.7	100.0
Col %	13.5	17.2	15.8
140-159	12	22	34
Row %	35.3	64.7	100.0
Col %	32.4	37.9	35.8
≥160	6	17	23
Row %	26.1	73.9	100.0
Col %	16.2	29.3	24.2
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 6.6516; **p-value:** 0.1555

In <5.5, 9 (24.3%) patients had SBP<120 and 12 (32.4%) patients had SBP (140-159).

In ≥5.5, 10 (17.2%) patients had SBP130-139, 22 (37.9%) patients had SBP140-159 and 17 (29.3%) patients had SBP≥160.

Association of SBP Category with HBA1C Category was not statistically significant (p=0.1555).

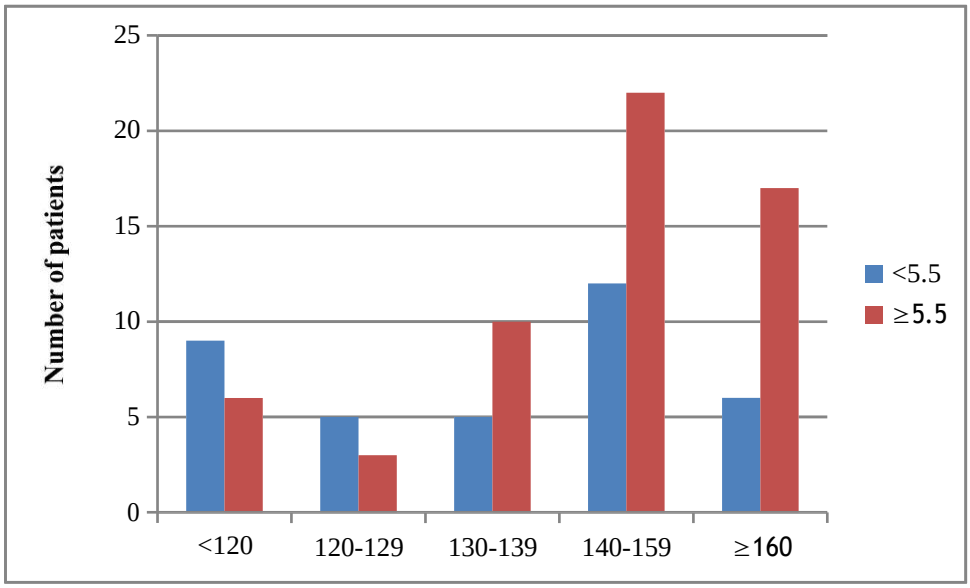


Figure 6

Table 5: Association between TC Category: HBA1C Category

	HBA1C CATEGORY		
TC Category	**<5.5**	**≥5.5**	**TOTAL**
<160	24	22	46
Row %	52.2	47.8	100.0
Col %	64.9	37.9	48.4
160-199	2	12	14
Row %	14.3	85.7	100.0
Col %	5.4	20.7	14.7
200-239	3	4	7
Row %	42.9	57.1	100.0
Col %	8.1	6.9	7.4
240-279	5	10	15
Row %	33.3	66.7	100.0
Col %	13.5	17.2	15.8
≥280	3	10	13
Row %	23.1	76.9	100.0
Col %	8.1	17.2	13.7
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 8.5860; **p-value:** 0.0723

In <5.5, 24 (64.9%) patients had TC <160

In ≥5.5, 22 (37.9%) patients had TC <160.

Association of TC Category with HBA1C Category was not statistically significant (p=0.0723).

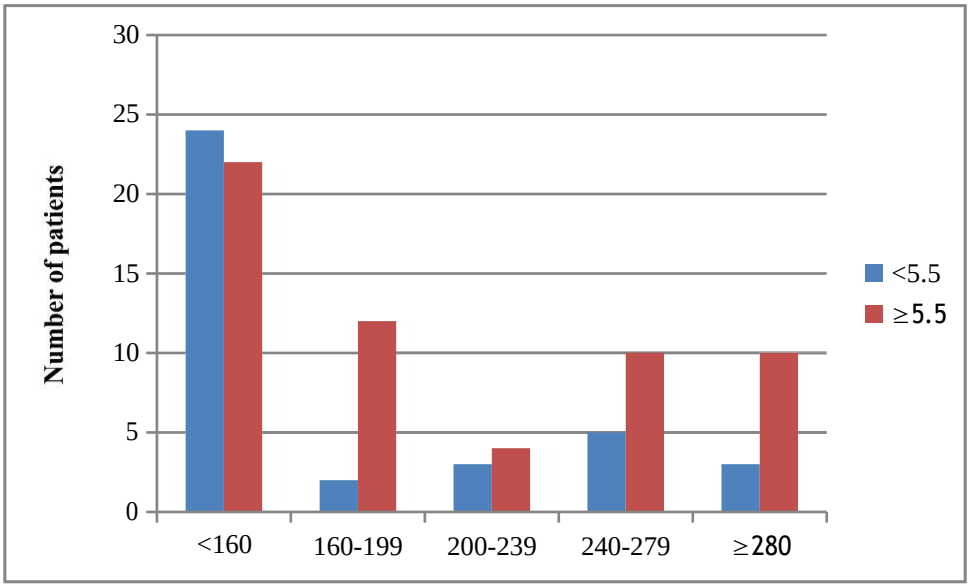


Figure 7

Table 6: Association between HDL Category: HBA1C Category

	HBA1C CATEGORY		
HDL Category	**<5.5**	**≥5.5**	**TOTAL**
<40	20	44	64
Row %	31.3	68.8	100.0
Col %	54.1	75.9	67.4
40-49	5	4	9
Row %	55.6	44.4	100.0
Col %	13.5	6.9	9.5
50-59	8	6	14
Row %	57.1	42.9	100.0
Col %	21.6	10.3	14.7
≥60	4	4	8
Row %	50.0	50.0	100.0
Col %	10.8	6.9	8.4
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 4.9990; **p-value:** 0.1719

In <5.5, 20 (54.1%) patients had HDL Category <40

In ≥5.5, 44 (75.9%) patients had HDL Category <40.

Association of HDL Category with HBA1C Category was not statistically significant (p=0.1719).

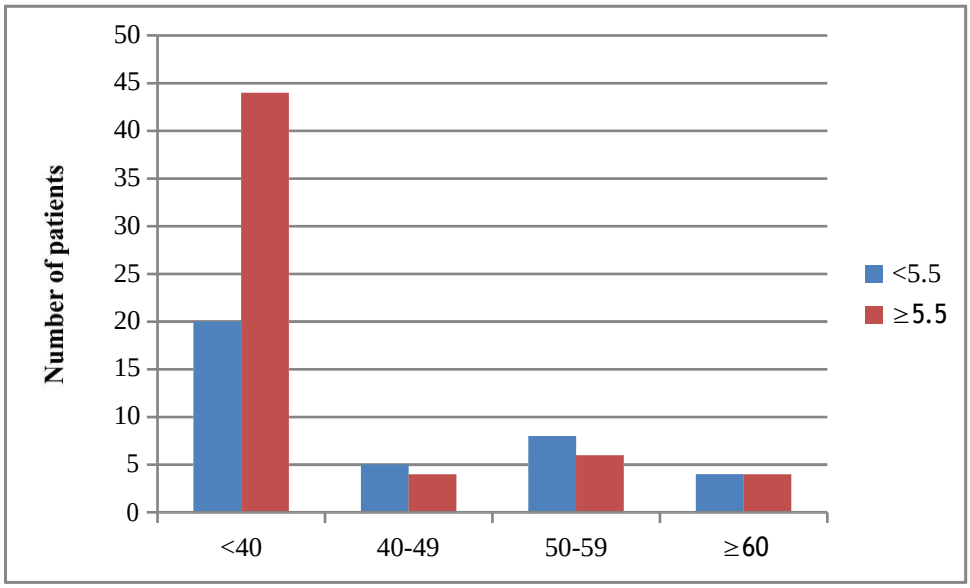


Figure 8

Table 7: Association between CRP CATEGORY: HBA1C CATEGORY

	HBA1C CATEGORY		
CRP Category	**<5.5**	**≥5.5**	**TOTAL**
High	12	53	65
Row %	18.5	81.5	100.0
Col %	32.4	91.4	68.4
Normal	25	5	30
Row %	83.3	16.7	100.0
Col %	67.6	8.6	31.6
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 36.3279; **p-value:** <0.0001

Odds ratio: 0.0453 (0.0144, 0.1425)

In <5.5, 12 (32.4%) patient's had High and 25(67.6%) patient's had Normal in CRP Category.

In ≥5.5, 53 (91.4%) patient's had High and 5(8.6%) patient's had Normal in CRP Category..

Association of CRP Category with HBA1C Category was statistically significant(p<0.0001).

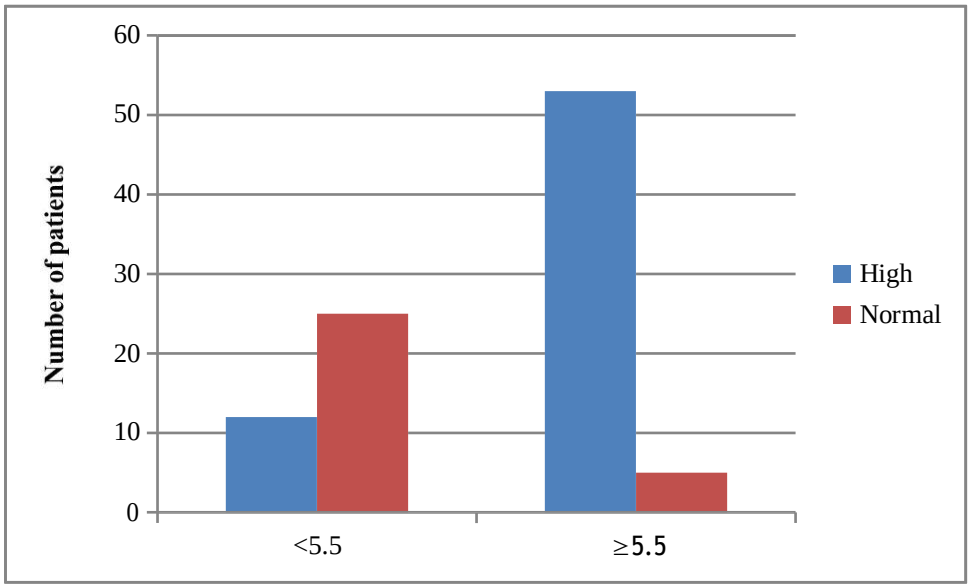


Figure 9

Table 8: Association between Current Smoker: HBA1C CATEGORY

	HBA1C CATEGORY		
Current Smoker	**<5.5**	**≥5.5**	**TOTAL**
NO	25	27	52
Row %	48.1	51.9	100.0
Col %	67.6	46.6	54.7
YES	12	31	43
Row %	27.9	72.1	100.0
Col %	32.4	53.4	45.3
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 4.0269; **p-value:** 0.0447

Odds ratio: 2.3920 (1.0120, 5.6539)

In <5.5, 12 (32.4%) patients were smoker In ≥5.5, 31 (53.4%) patients were smoker. Association of Current Smoker with HBA1C Category was statistically significant (p=0.0447).

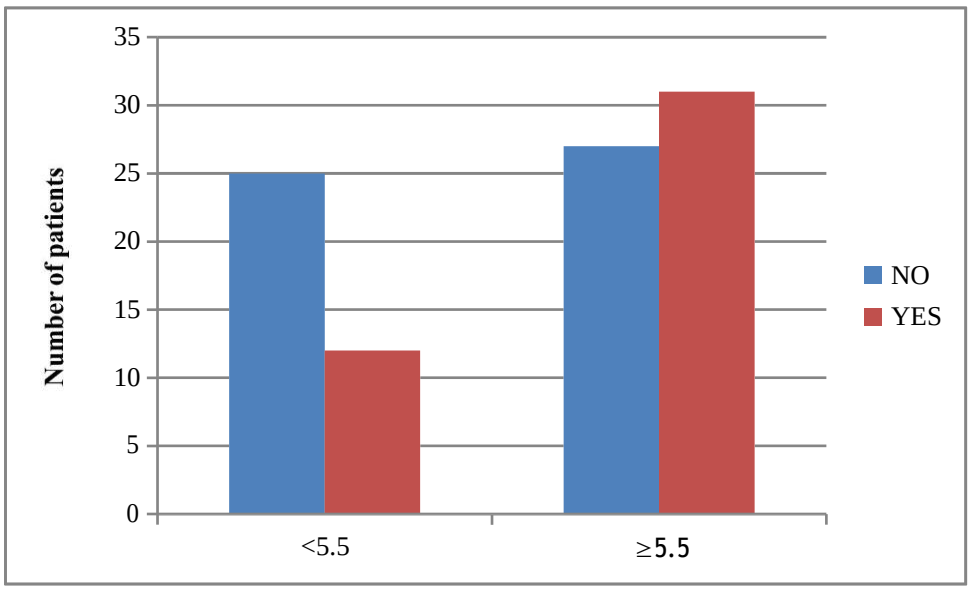


Figure 10

Table 9: Association between FRS CATEGORY: HBA1C CATEGORY

	HBA1C CATEGORY		
FRS Category	**<5.5**	**≥5.5**	**TOTAL**
High	5	20	25
Row %	20.0	80.0	100.0
Col %	13.5	34.5	26.3
Intermittent	20	30	50
Row %	40.0	60.0	100.0
Col %	54.1	51.7	52.6
Low	12	8	20
Row %	60.0	40.0	100.0
Col %	32.4	13.8	21.1
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 7.5256; **p-value:** 0.0232

In <5.5, 5 (13.5%) patients had High, 20 (54.1%) patients had Intermittent and 12 (32.4%) patients had Low in FRS Category.

In ≥5.5, 20 (34.5%) patients had High, 30 (51.7%) patients had Intermittent and 8 (13.8%) patients had Low in FRS Category .

Association of FRS Category with HBA1C Category was statistically significant(p=0.0232).

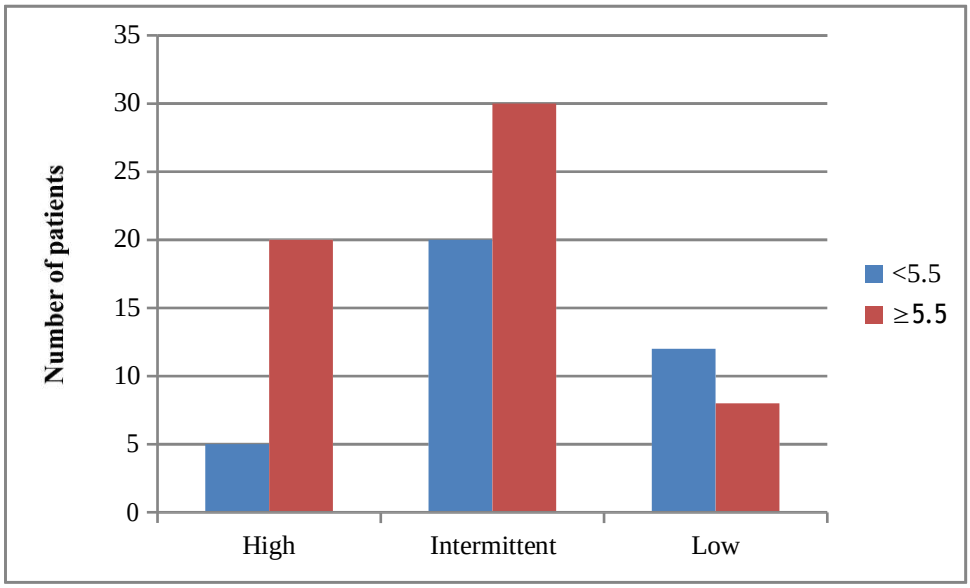


Figure 11

Table 10: Association between 10 Year CVD Risk gr: HBA1C Category

	HBA1C CATEGORY		
10 Year CVD Risk % gr	**<5.5**	**≥5.5**	**TOTAL**
<1	11	7	18
Row %	61.1	38.9	100.0
Col %	29.7	12.1	18.9
1-5	19	19	38
Row %	50.0	50.0	100.0
Col %	51.4	32.8	40.0
6-10	2	9	11
Row %	18.2	81.8	100.0
Col %	5.4	15.5	11.6
11-20	2	10	12
Row %	16.7	83.3	100.0
Col %	5.4	17.2	12.6
21-30	1	9	10
Row %	10.0	90.0	100.0
Col %	2.7	15.5	10.5
≥30	2	4	6
Row %	33.3	66.7	100.0
Col %	5.4	6.9	6.3
TOTAL	37	58	95
Row %	38.9	61.1	100.0
Col %	100.0	100.0	100.0

Chi-square value: 13.7744; **p-value:** 0.0171

Association of 10 Year CVD Risk % gr with HBA1C Category was statisticallysignificant (p=0.0171).

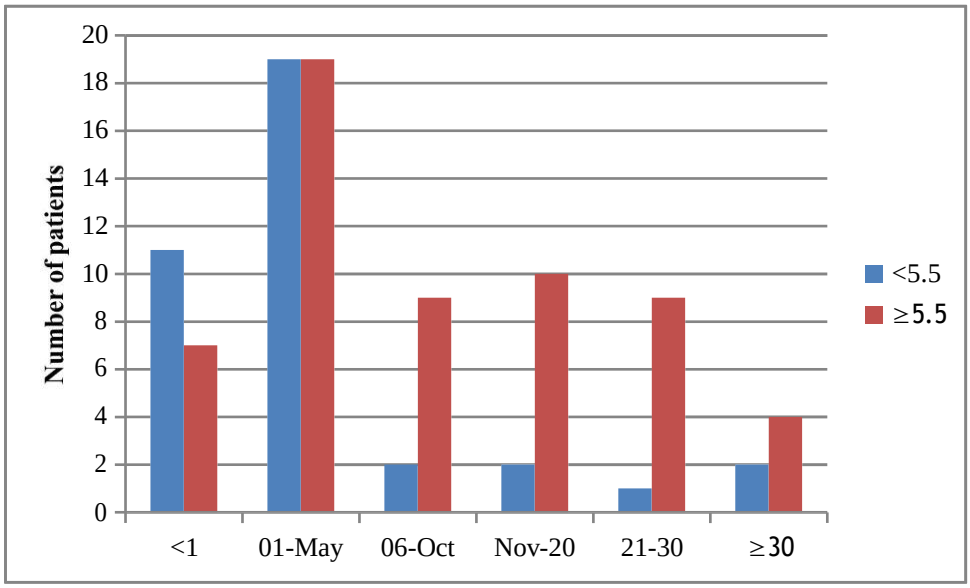


Figure 12

Table 11: Distribution of mean AGE: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
AGE	<5.5	37	45.4865	17.8195	20.0000	78.0000	45.0000	0.0050
	≥5.5	58	54.7759	13.5996	25.0000	75.0000	59.0000	

In <5.5, the mean Age (mean± s.d.) of patientswas45.4865±17.8195.In ≥5.5, the mean Age (mean± s.d.) of patientswas 54.7759±13.5996.

Distribution of mean Age with HBA1C Category was statistically significant(p=0.0050).

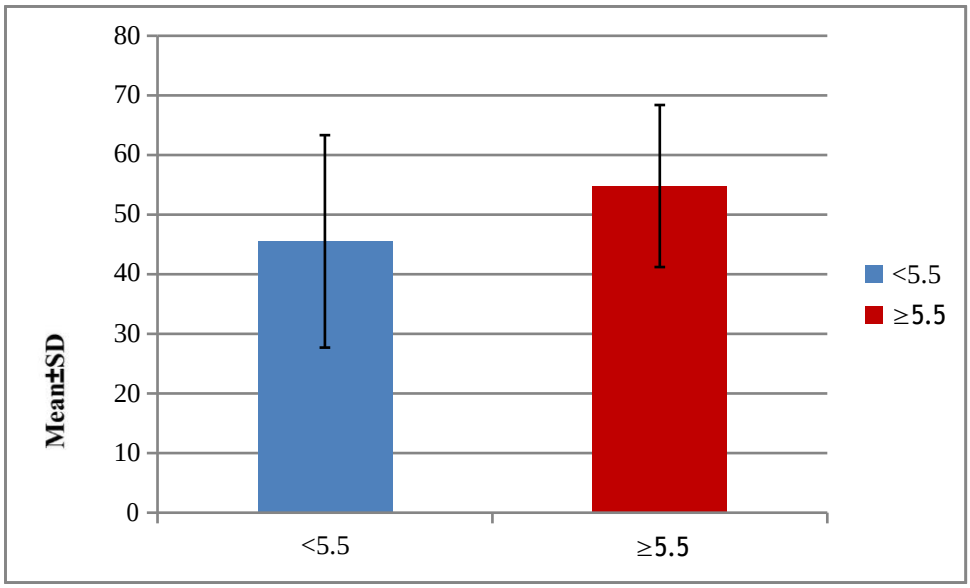


Figure 13

Table 12: Distribution of mean BMI kg/m2: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
BMI kg/m2	<5.5	37	24.6081	5.1724	16.9000	39.3000	24.2000	0.0184
	≥5.5	58	27.0293	4.5381	20.1000	38.1000	26.4000	

In <5.5, the mean BMI kg/m2 (mean± s.d.) of patientswas24.6081±5.1724.In ≥5.5, the mean BMI kg/m2 (mean± s.d.) of patientswas 27.0293±4.5381.

Distribution of mean BMI kg/m2 with HBA1C Category was statistically significant (p=0.0184).

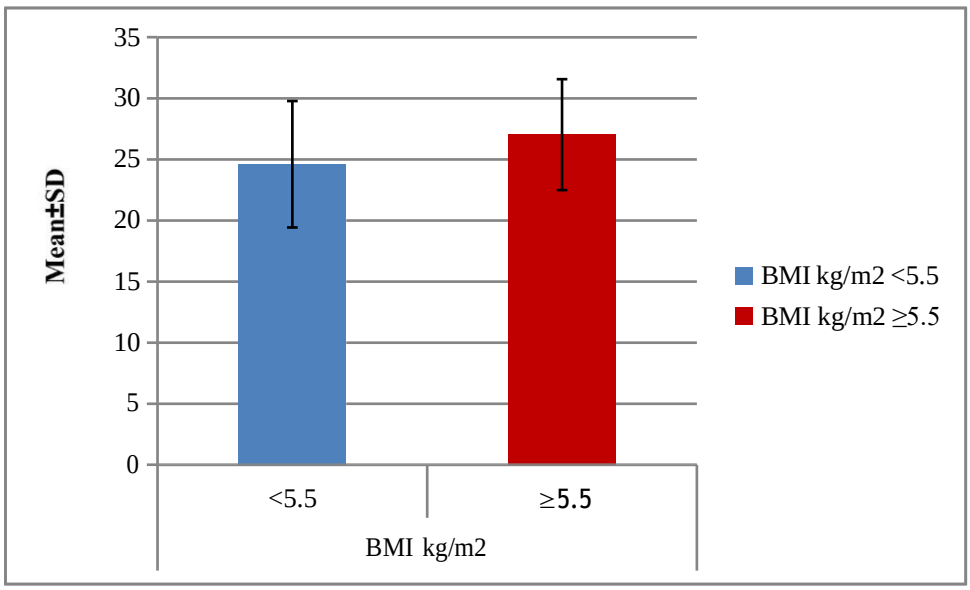


Figure 14

Table 13: Distribution of mean FBS mg/dL: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
FBS mg/dL	<5.5	37	118.7568	43.7070	57.0000	281.0000	106.0000	0.5049
	≥5.5	58	124.6207	40.2705	37.0000	278.0000	121.5000	

In <5.5, the mean FBS mg/dL (mean± s.d.) of patientswas 118.7568±43.7070.In ≥5.5, the mean FBS mg/dL (mean± s.d.) of patientswas 124.6207±40.2705.

Distribution of mean FBS mg/dL with HBA1C Category was not statistically significant (p=0.5049).

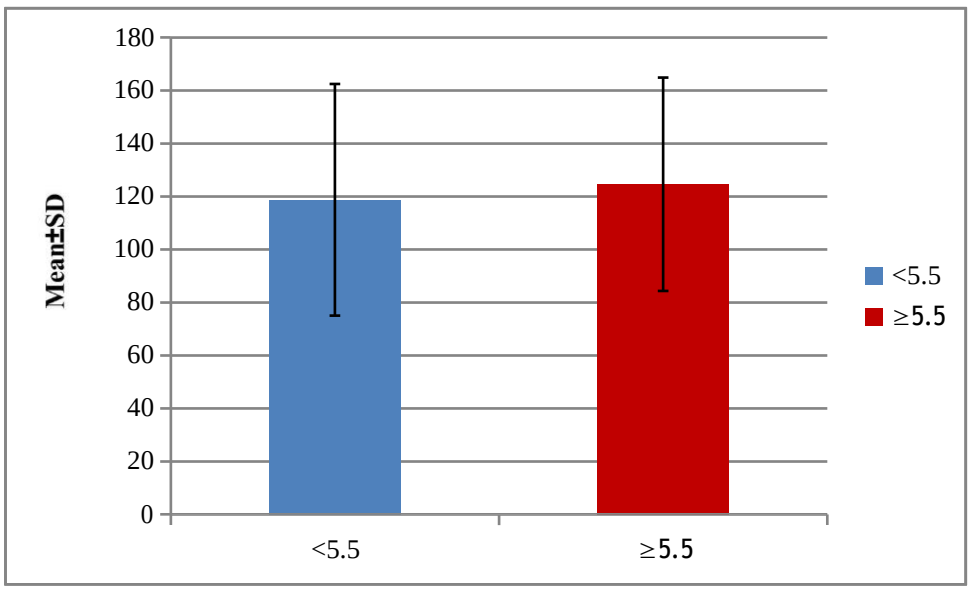


Figure 15

Table 14: Distribution of mean PPBS mg/dL: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
PPBS mg/dL	<5.5	37	165.4865	54.7300	91.0000	373.0000	148.0000	0.3561
	≥5.5	58	176.4828	57.3568	43.0000	296.0000	160.5000	

In <5.5, the mean PPBS mg/dL (mean± s.d.) of patientswas 165.4865±54.7300.In ≥5.5, the mean PPBS mg/dL (mean± s.d.) of patientswas 176.4828±57.3568.

Distribution of mean PPBS mg/dL with HBA1C Category was not statistically significant (p=0.3561).

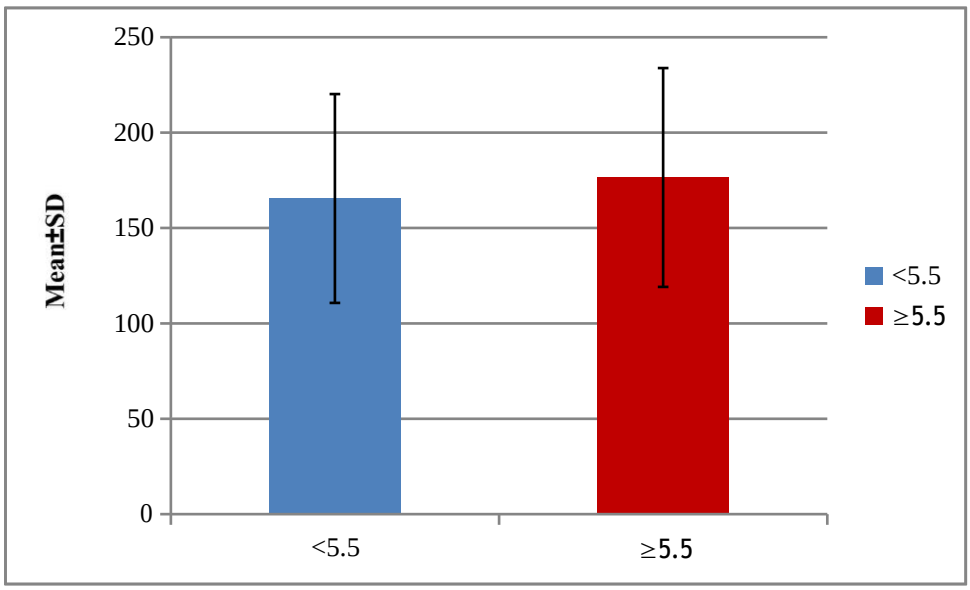


Figure 16

Table 15: Distribution of mean SBP mm/Hg: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
SBP mm/Hg	<5.5	37	138.8108	21.6048	110.0000	192.0000	138.0000	0.0768
	≥5.5	58	147.1379	22.4378	92.0000	188.0000	152.0000	

In <5.5, the mean SBP mm/Hg (mean± s.d.) of patientswas 138.8108±21.6048.In ≥5.5, the mean SBP mm/Hg (mean± s.d.) of patientswas 147.1379±22.4378.

Distribution of mean SBP mm/Hg with HBA1C Category was not statistically significant (p=0.0768).

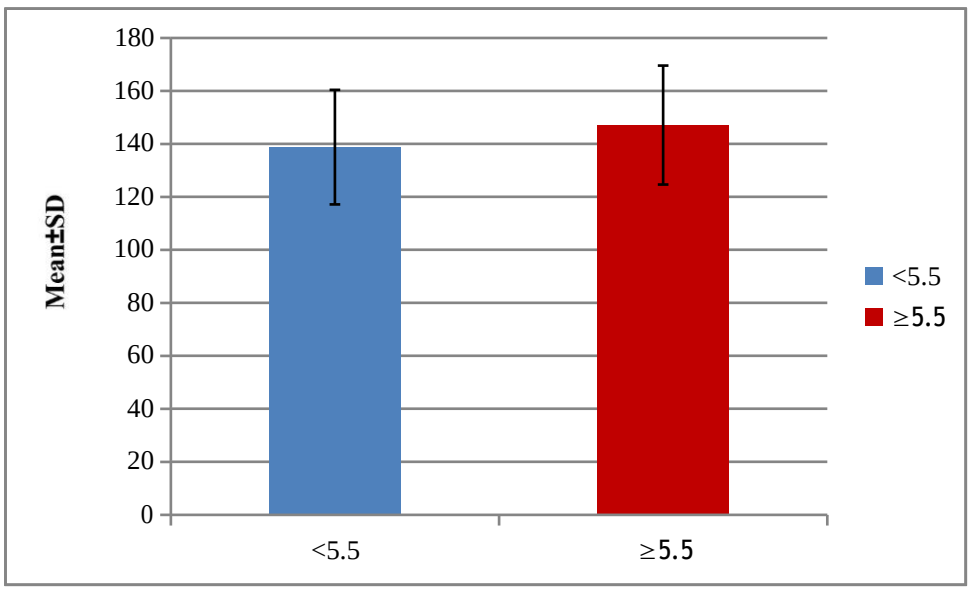


Figure 17

Table 16: Distribution of mean DBP mm/Hg: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
DBP mm/Hg	<5.5	37	85.4054	10.8409	66.0000	106.0000	86.0000	0.2822
	≥5.5	58	87.7931	10.2645	60.0000	112.0000	89.0000	

In <5.5, the mean DBP mm/Hg (mean± s.d.) of patientswas 85.4054±10.8409.In ≥5.5, the mean DBP mm/Hg (mean± s.d.) of patients was 87.7931±10.2645.

Distribution of mean DBP mm/Hg with HBA1C Category was not statistically significant (p=0.2822).

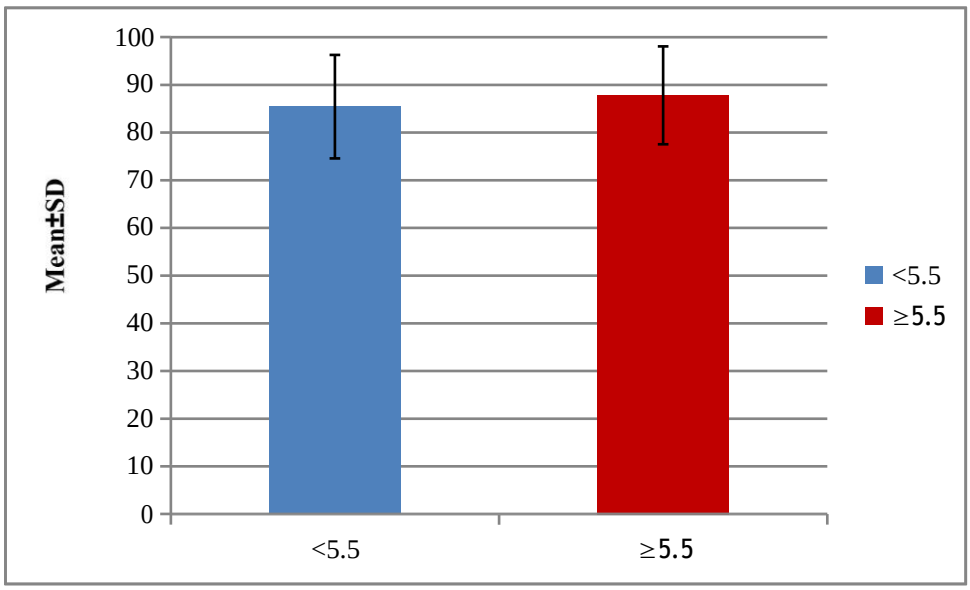


Figure 18

Table 17: Distribution of mean TC- mg/dL: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
TC- mg/dL	<5.5	37	169.0000	63.8074	69.0000	302.0000	148.0000	0.0665
	≥5.5	58	194.8103	67.4434	82.0000	305.0000	184.5000	

In <5.5, the mean TC-mg/dL (mean± s.d.) of patientswas169.0000±63.8074.In ≥5.5, the mean TC-mg/dL (mean± s.d.) of patients was 194.8103±67.4434.

Distribution of mean TC-mg/dL with HBA1C Category was not statistically significant (p=0.0665).

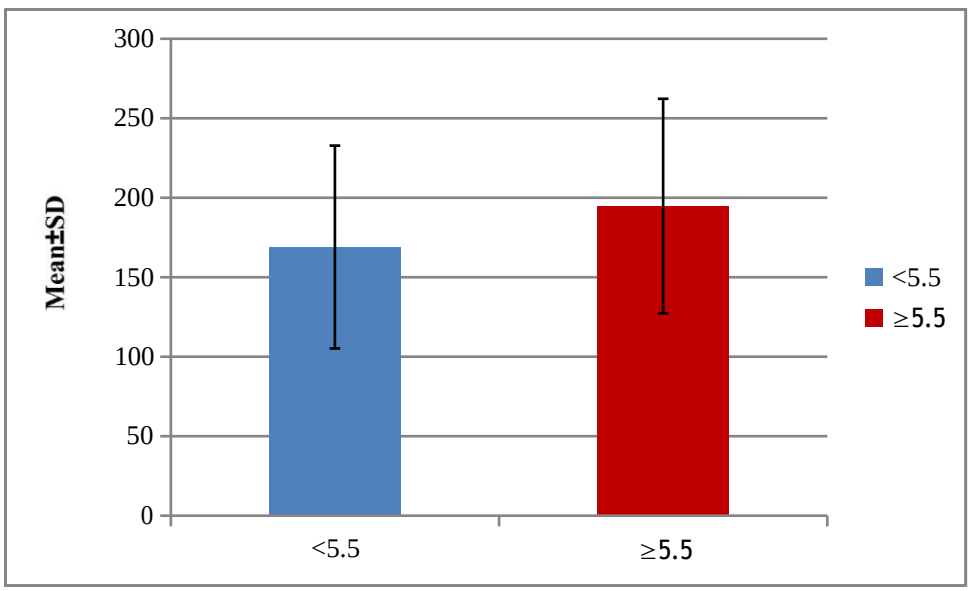


Figure 19

Table 18: Distribution of mean TG-mg/dL: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
TG- mg/dL	<5.5	37	117.8649	50.2859	45.0000	234.0000	105.0000	0.0004
	≥5.5	58	171.9655	79.2367	52.0000	387.0000	175.0000	

In <5.5, the mean TG-mg/dL (mean± s.d.) of patientswas117.8649±50.2859.In ≥5.5, the mean TG-mg/dL (mean± s.d.) of patients was 171.9655±79.2367.

Distribution of mean TG-mg/dL with HBA1C Category was statistically significant (p=0.0004).

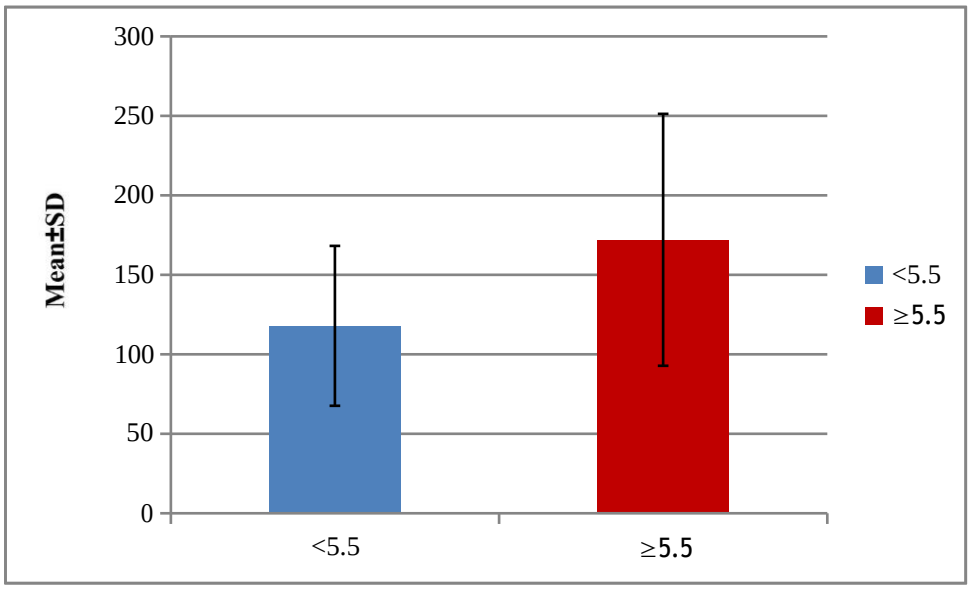


Figure 20

Table 19: Distribution of mean LDL-mg/dL: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
LDL -mg/DL	<5.5	37	69.3514	53.1111	10.0000	213.0000	53.0000	0.0160
	≥5.5	58	96.2241	51.3680	12.0000	203.0000	87.0000	

In <5.5, the mean LDL-mg/dL (mean± s.d.) of patientswas69.3514±53.1111.In ≥5.5, the mean LDL-mg/dL (mean± s.d.) of patientswas96.2241±51.3680.

Distribution of mean LDL-mg/dL with HBA1C Category was statistically significant (p=0.0160).

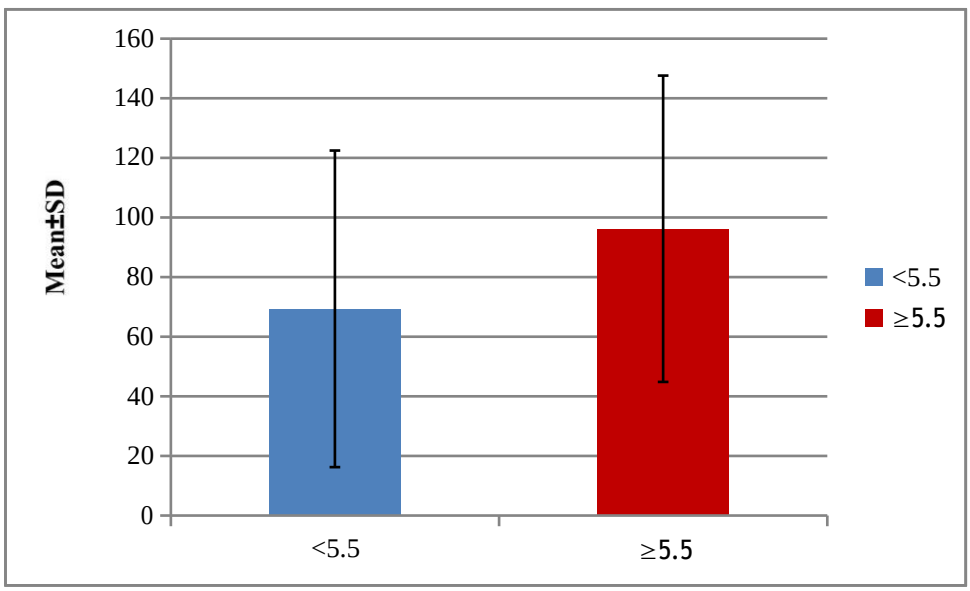


Figure 21

Table 20: Distribution of mean HDL- mg/dL: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
HDL -mg/dL	<5.5	37	38.4595	17.2508	8.0000	85.0000	31.0000	0.3433
	≥5.5	58	35.4310	13.5894	13.0000	66.0000	33.0000	

In <5.5, the mean HDL-mg/dL (mean± s.d.) of patientswas 38.4595±17.2508.In ≥5.5, the mean HDL-mg/dL (mean± s.d.) of patientswas 35.4310±13.5894.

Distribution of mean HDL-mg/dL with HBA1C Category was not statistically significant (p=0.3433).

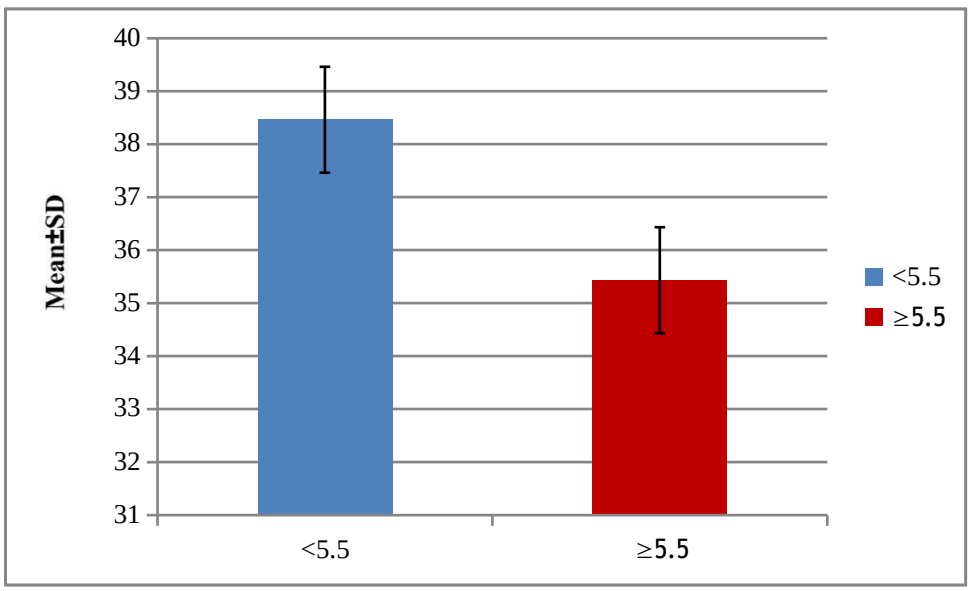


Figure 22

Tableo 21: Distribution of mean HBA1C %: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
HBA1C %	<5.5	37	.0497	.0039	0.0400	0.0540	0.0510	<0.0001
	≥5.5	58	.0604	.0029	0.0550	0.0640	0.0610	

In <5.5, the mean HBA1C % (mean± s.d.) of patientswas.0497±.0039.

In ≥5.5, the mean HBA1C % (mean± s.d.) of patientswas.0604±.0029.

Distribution of meanoHBA1C % with HBA1C Category was statistically significant (p<0.0001).

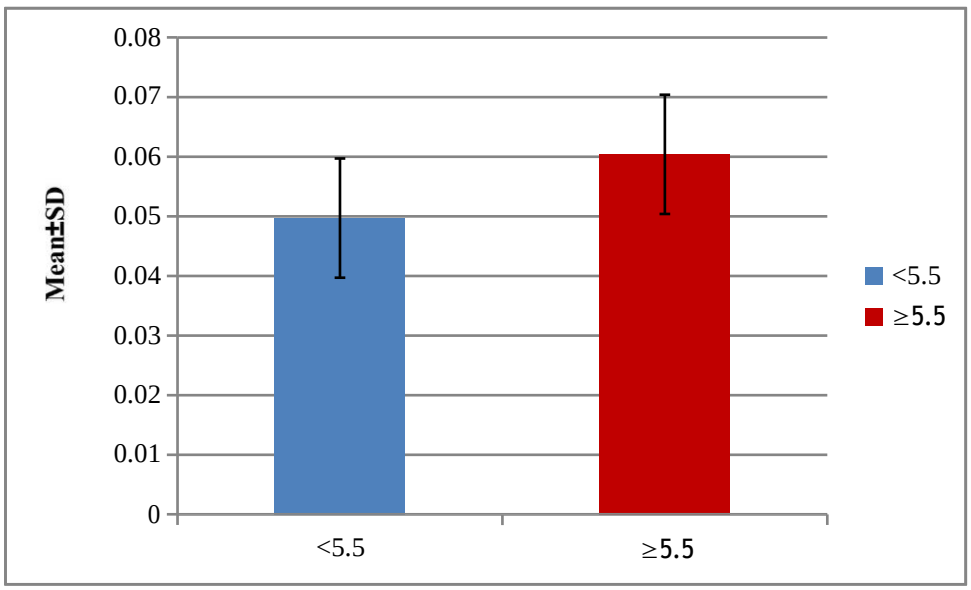


Figure 23

Table 22: Distribution of mean CRP mg/L: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
CRP mg/L	<5.5	37	18.4303	21.6220	5.5000	88.4000	8.2000	0.0020
	≥5.5	58	33.7985	19.7337	0.7360	86.7000	30.4000	

In <5.5, the mean CRP mg/L (mean± s.d.) of patientswas18.4303±21.6220.In ≥5.5, the mean CRP mg/L (mean± s.d.) of patientswas 33.7985±19.7337.

Distribution of mean CRP mg/L with HBA1C Category was statistically significant (p=0.0020).

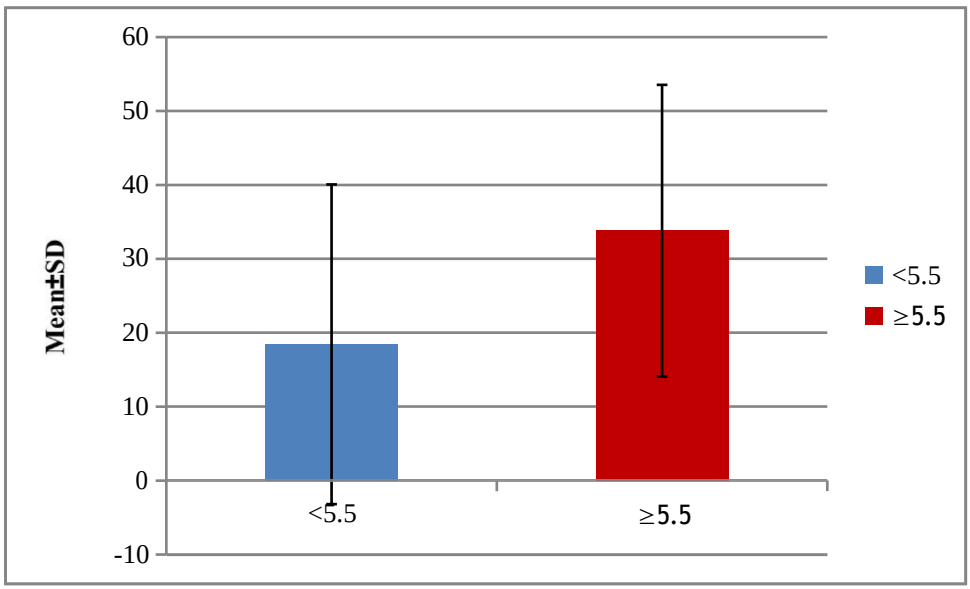


Figure 24

Table 23: Distribution of mean FRS: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
FRS	<5.5	37	10.7838	9.8577	-6.0000	27.0000	13.0000	0.0007
	≥5.5	58	16.8793	7.0414	-3.0000	28.0000	18.0000	

In <5.5, the mean FRS (mean± s.d.) of patientswas10.7838±9.8577.In ≥5.5, the mean FRS (mean± s.d.) of patientswas 16.8793±7.0414.

Distribution of mean FRS with HBA1C Category was statistically significant (p=0.0007).

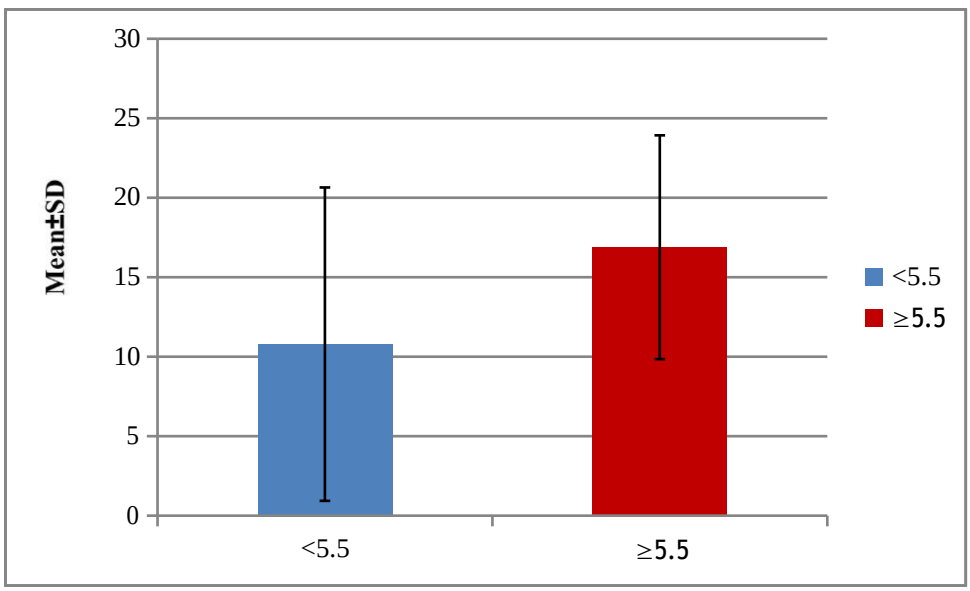


Figure 25

Table 24: Distribution of mean 10 YEAR CVD RISK %: HBA1C CATEGORY

		Number	Mean	SD	Minimum	Maximum	Median	p-value
10 YEAR CVD RISK %	<5.5	24	5.0417	5.3445	1.0000	22.0000	4.0000	0.0083
	≥5.5	47	10.3191	8.7006	1.0000	27.0000	8.0000	

In <5.5, the mean 10 YEAR CVD RISK % (mean± s.d.) of patients was 5.0417 ±5.3445 .

In ≥5.5, the mean 10 YEAR CVD RISK % (mean± s.d.) of patients was 10.3191 ±8.7006.

Distribution of mean 10 YEAR CVD RISK % with HBA1C Category was statistically significant (p=0.0083).

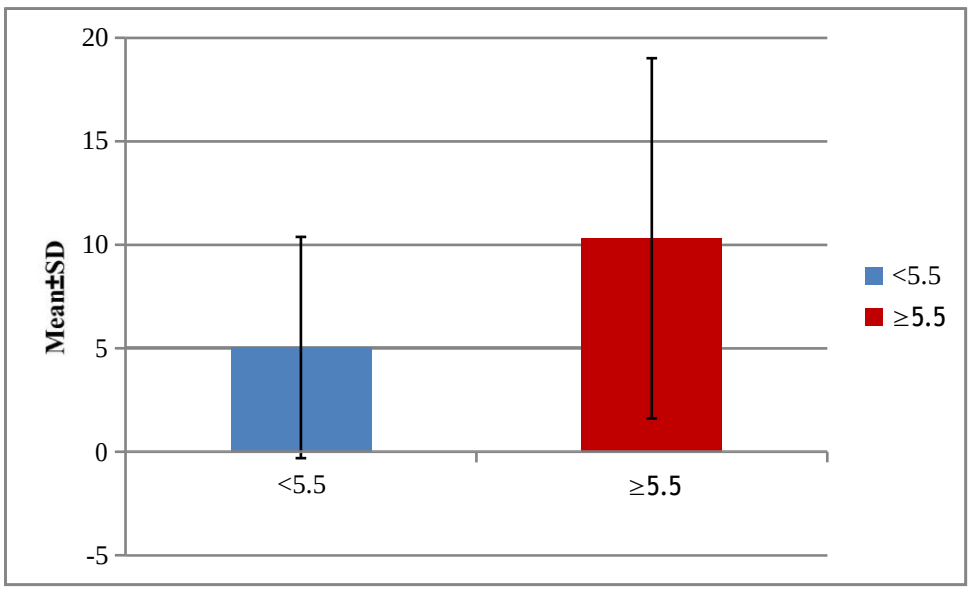


Figure 26

Table 25: Correlation of HBA1C % in all parameters

		HBA1C %	Remarks
AGE	Pearson Correlation Coefficient (r)	.337**	Positive correlation
	p-value	.001	Significant
	Number	95	
BMI kg/m2	Pearson Correlation Coefficient (r)	.273**	Positive correlation
	p-value	.007	Significant
	Number	95	
FBS mg/dL	Pearson Correlation Coefficient (r)	.166	Positive correlation
	p-value	.107	Not Significant
	Number	95	
PPBS mg/dL	Pearson Correlation Coefficient (r)	.129	Positive correlation
	p-value	.212	Not Significant
	Number	95	
SBP mm/Hg	Pearson Correlation Coefficient (r)	.338**	Positive correlation
	p-value	.001	Significant
	Number	95	

DBP mm/Hg	Pearson Correlation Coefficient (r)	.247*	Positive correlation
	p-value	.016	Significant
	Number	95	
TC-mg/dL	Pearson Correlation Coefficient (r)	.180	Positive correlation
	p-value	.081	Not Significant
	Number	95	
TG-mg/dL	Pearson Correlation Coefficient (r)	.321**	Positive correlation
	p-value	.002	Significant
	Number	95	
LDL-mg/DL	Pearson Correlation Coefficient (r)	.278**	Positive correlation
	p-value	.006	Significant
	Number	95	
HDL-mg/dL	Pearson Correlation Coefficient (r)	-.074	Negative correlation
	p-value	.478	Not Significant
	Number	95	
FRS	Pearson Correlation Coefficient (r)	.426**	Positive correlation
	p-value	.000	Significant
	Number	95	

FIGURE 27

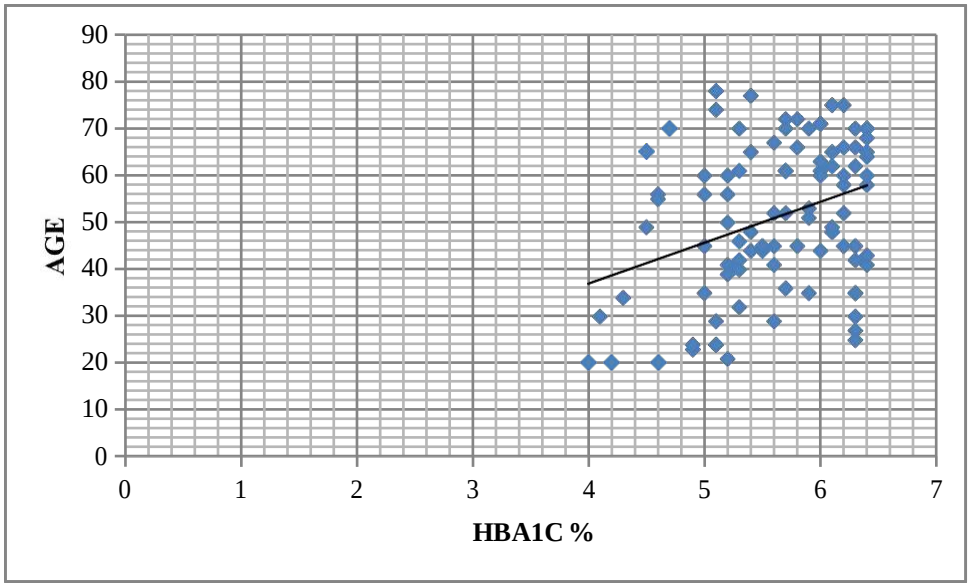


FIGURE 28

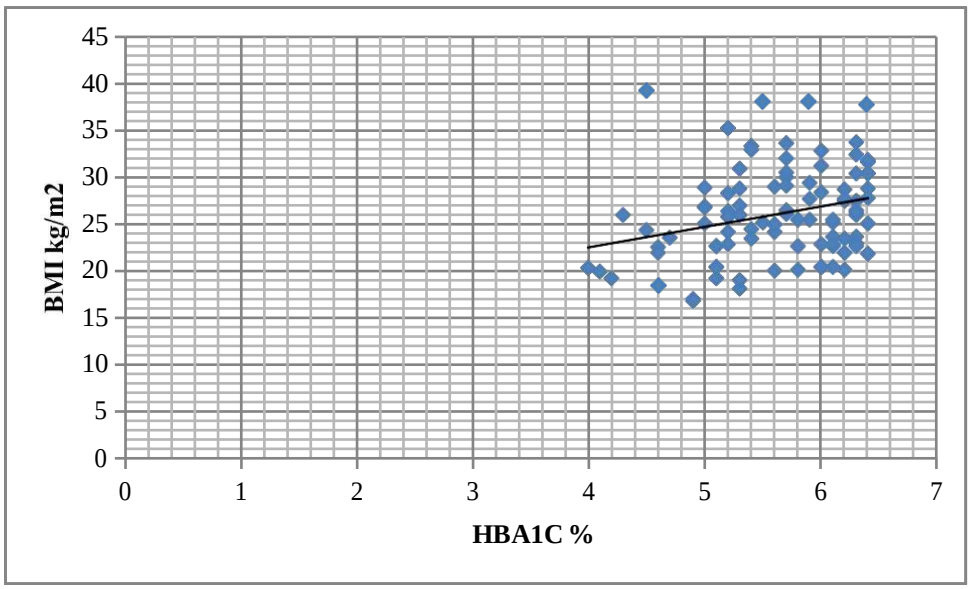


FIGURE 29

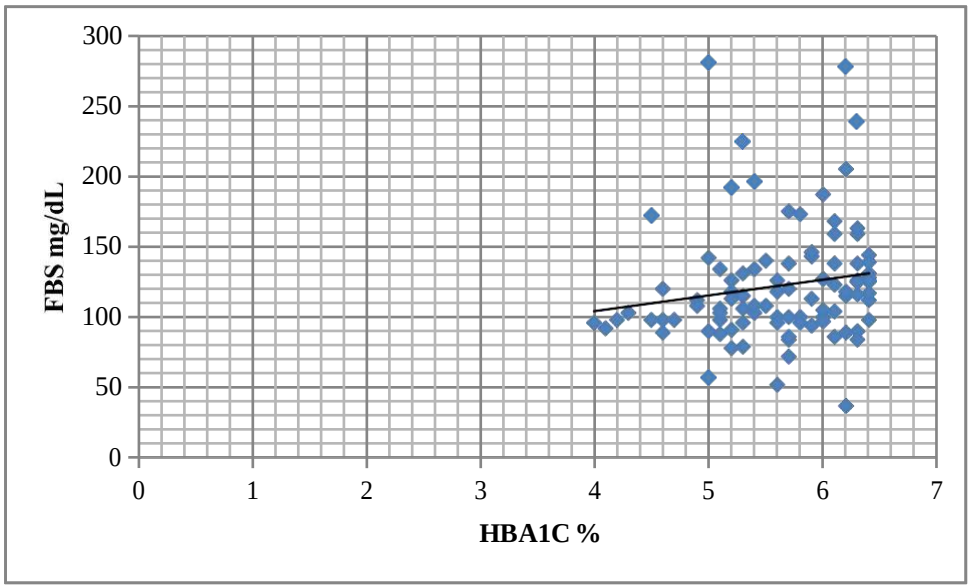


FIGURE 30

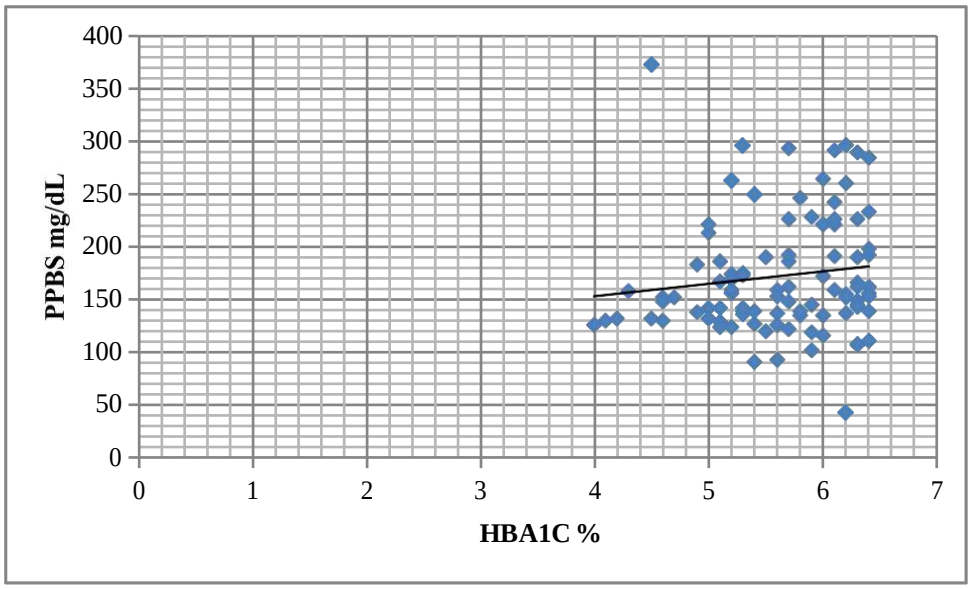


FIGURE 31

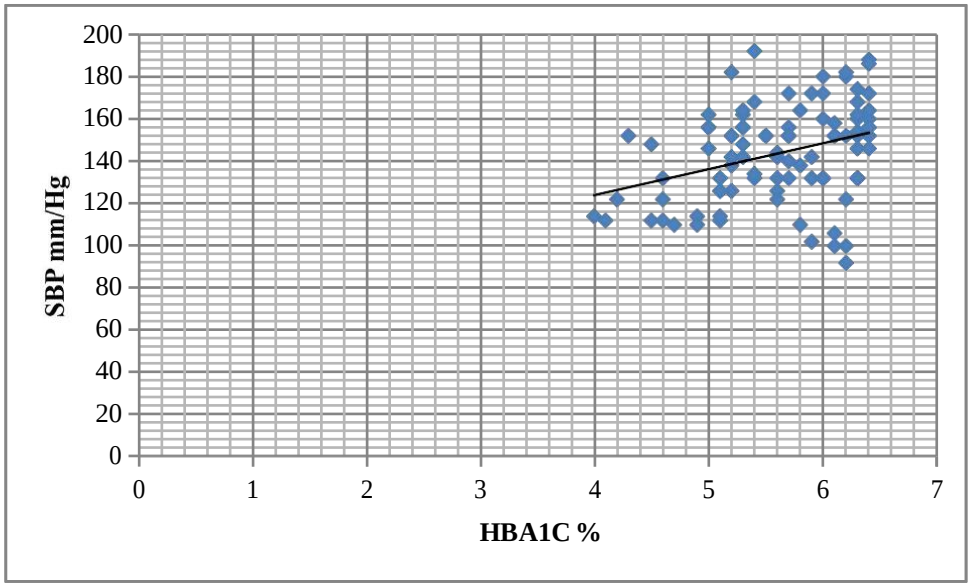


FIGURE 32

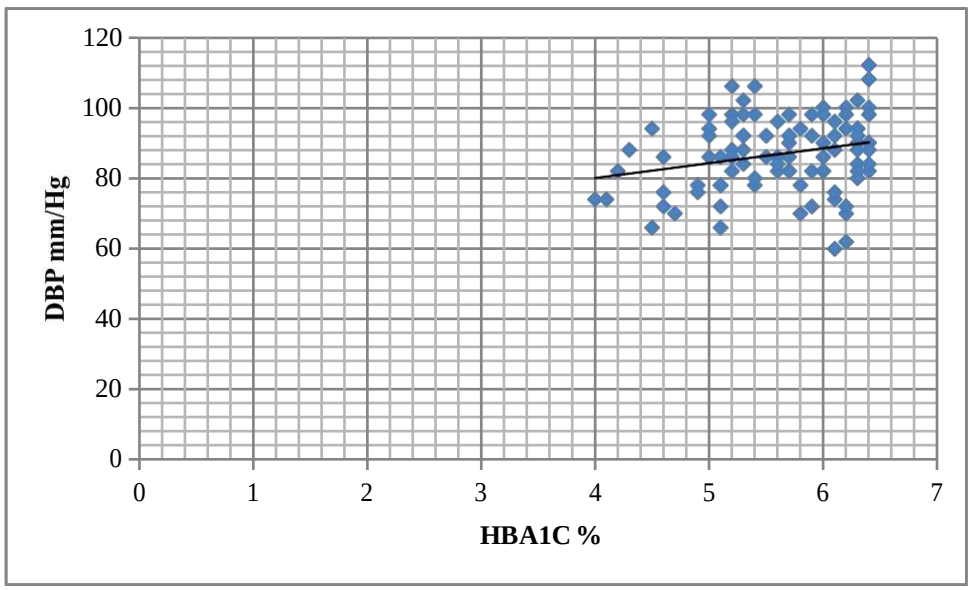


FIGURE 33

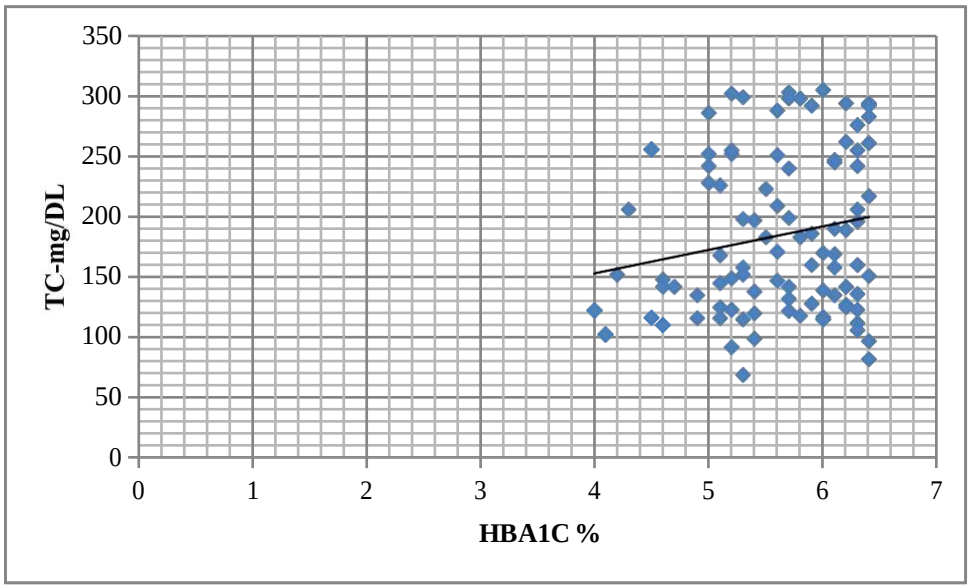


FIGURE 34

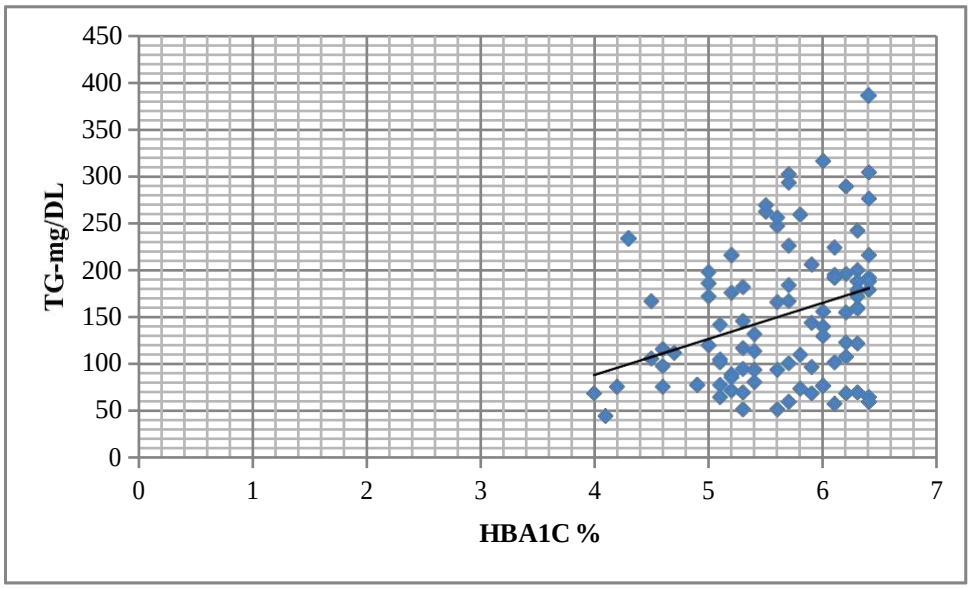


FIGURE 35

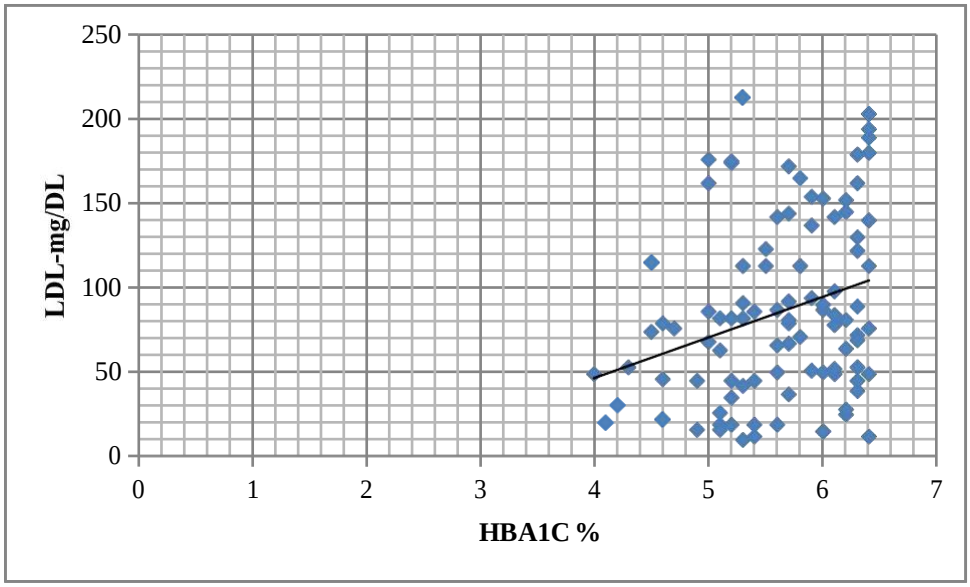


FIGURE 36

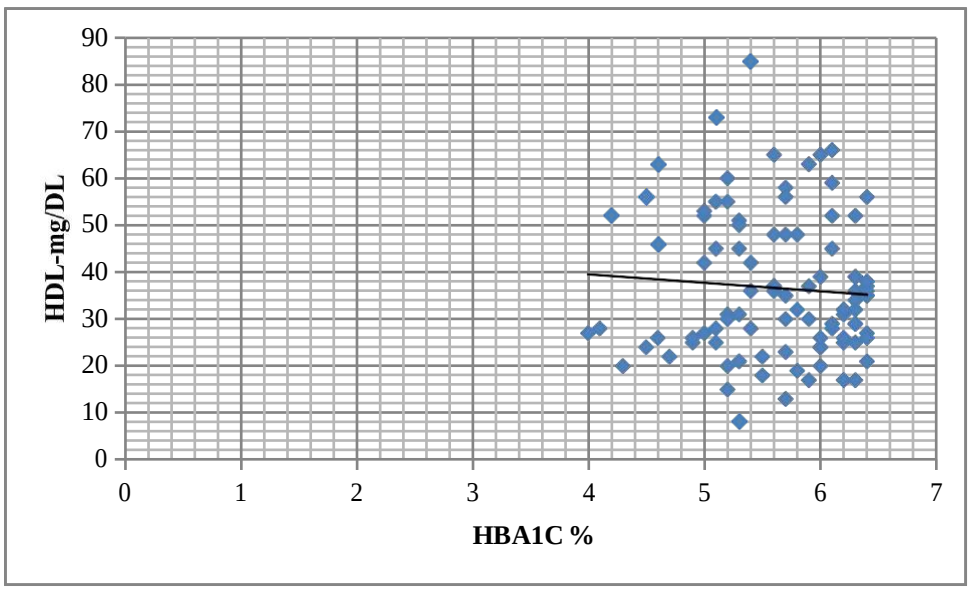
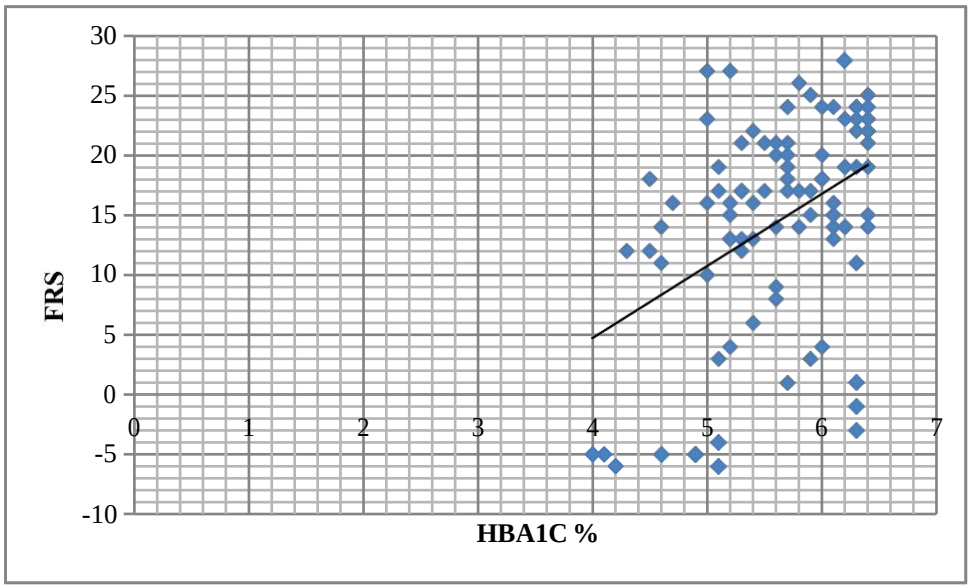


FIGURE 37



DISCUSSION

The present study was a cross-sectional study. This Study was conducted at BLDE University Shri B M Patil Medical College Hospital and Research Centre, Bijapur from January 2021 to June 2022. Total 95 patients were included in this study.

In our study, out of 95 patients, most of the patients were [16 (16.8%)] 20-34 years of age. Age Category was not statistically significant with HBA1C Category (p=0.0622). Distribution of mean Age with HBA1C Category was statistically significant (p=0.0050).

We found that, male population [51 (53.7%)] was higher than the female population [44(46.3%)] but this was not statistically significant (p=0.0711).

Liu Y et al [71](2011) showed that Hemoglobin A1c's (HbA1c) predictive significance in coronary artery disease (CAD) is still debatable. Here, they carried out a systematic review to measure the relationship between high HbA1colevels and all-cause mortality in CAD patients who were hospitalised. For papers published between 1970 and May 2011, a thorough search of electronic databases (PubMed, EMBASE, OVID, Web of Science, and The Cochrane Library) was conducted. Included were cohort, case-control, and randomised controlled trials that looked at how HbA1c affected all-cause death. Final inclusion criteria were met by 20 studies (a total of 13, 224). According to the pooled analysis, a higher HbA1c level was substantially linked to a higher risk of both short- and long-term mortality (OR 2.32, 95% CI, 1.61 to 3.35). According to subgroup analysis, persons without diabetes who had elevated HbA1c levels had a greater mortality risk (OR 1.84, 95% CI, 1.51 to 2.24). In contrast, elevated HbA1c levels in diabetic patients were not linked to an increased risk of death (OR 0.95, 95% CI, 0.70 to 1.28).

Ito H et al [74](2011) observed that to investigate the connection between type 2 diabetes mellitus in Japanese patients and hyperuricemia (HUA) clinical backgrounds. Following a cross-sectional study evaluating the association of HUA with the clinical characteristics in 1,213 patients with type 2 diabetes mellitus, an investigation into the estimated glomerular filtration rate (eGFR) and the prevalence of diabetic macroangiopathies was carried out in a prospective observational study involving 1,073 patients over a time period of 3.5 years. 299 subjects (or 25%) were found to have HUA during the cross-sectional examination. Even after controlling for sex, drinking habits, diabetes treatment, body mass index, hypertension, diuretic use, hyperlipidemia, HbA1c, and/or the eGFR, the HUA was still associated with a number of diabetic issues on its own. During the first year of observation, the eGFR of HUA patients was significantly lower than that of normourecemia patients. HUA continued to be an important factor even after the Cox proportional hazard model was, HUA remained an independent risk factor for CAD. It was found that, most of the patients had [36 (62.1%)] K/C/O HTN in ≥5.5 group compared to <5.5 group [16 (43.2%)] but this was not statistically significant (p=0.0961) and we also found that, most of the patients had [22 (37.9%)] SBP 140-159 in ≥5.5 group compared to <5.5 group [12 (32.4%)] it was not statistically significant (p=0.1555).

Our study showed that, more number of patients had [24 (64.9%)] TC <160 in <5.5 group compared to ≥5.5 group [22 (37.9%)] but this was not statistically significant (p=0.0723). Higher number of patients had [44 (75.9%)] HDL Category <40 in ≥5.5 group compared to <5.5 group [20 (54.1%)] it was not statistically significant (p=0.1719). Most of the patients had [53 (91.4%)] High CRP Category in ≥5.5 group compared to <5.5 group [25(67.6%)] which was statistically significant (p<0.0001).

Masuda D et al [77](2012) examined that the postprandial buildup of chylomicrons and chylomicron remnants is one aspect of postprandial hyperlipidemia (CM-R). By using multiple logistic regression analysis, they attempted to ascertain which metabolic factors were associated with the prevalence of CAD and whether or not the concomitant presence of high apo B-48 and other coronary risk factors (high triglyceride, low HDL-C, high HbA1c, or low adiponectin levels increased the prevalence of CAD. Fasting serum apo B-48 levels demonstrated the strongest connection with the presence of CAD (3.9 2.4 vs. 6.9 2.6 g/mL, P 0.0001) and were substantially higher in CAD patients than in non-CAD subjects. In comparison to single high fasting apo B-48 levels, clustering of high fasting apo B-48 levels (> 4.34 g/mL, the cut-off value) and other coronary risk factors was found to be related with a higher risk of CAD.

We showed that, majority number of patients were smoker [31 (53.4%)] in ≥5.5 group compared to <5.5 group [12 (32.4%)] though it was statistically significant (p=0.0447).More number of patients had [30 (51.7%)] Intermittent in ≥5.5 group compared to <5.5 group [20 (54.1%)] which was statistically significant (p=0.0232). Association of 10 Year CVD Risk % gr with HBA1C Category was statistically significant (p=0.0171).

We observed that, the mean BMI kg/m2 was more [27.0293±4.5381] in ≥5.5 group compared to <5.5 group [24.6081±5.1724] it was statistically significant (p=0.0184). The mean FBS mg/dL was more [124.6207±40.2705] in ≥5.5 group compared to <5.5 group [118.7568±43.7070] but this was not statistically significant (p=0.5049).

Ashraf H et al [79](2013) examined that to determine the relationship between glycated haemoglobin (HbA1c) and the severity of non-diabetic people's coronary artery disease (CAD) as determined by angiograms. The participants with both hsCRP and HbA1c in the higher 2 quartiles had the highest adjusted ORs for the development of CAD (OR: 4.183; 95% CI: 1.883-9.290, p 0.0001). Gensini score and rising HbA1c tertiles were significantly

correlated (p = 0.038). HbA1c 5.6% 38 mmol/mol) (sensitivity: 60.5%, specificity: 52%) was the optimum cut-off value for predicting the development of CAD. HbA1c could be used to stratify CAD risk in non-diabetic people, independent of conventional cardiovascular risk factors, insulin resistance, and inflammatory markers.

In our study, the mean PPBS mg/dL was higher [176.4828±57.3568] in ≥5.5 group compared to <5.5 group [165.4865±54.7300] it was not statistically significant (p=0.3561). The mean SBP and DBP mm/Hg was more [147.1379±22.4378], [87.7931±10.2645] in ≥5.5 group compared to <5.5 group [138.8108±21.6048], [85.4054±10.8409] it was not statistically significant (p=0.2822). Distribution of mean TC-mg/dL with HBA1C Category was not statistically significant (p=0.0665).

Sakurai M et al [80](2013) showed that associations between Cardiovascular diseases (CVD) and HbA1c have primarily been reported in Western nations. 1,104 people passed away throughout the trial, including 304 from cardiovascular disease (CVD), 61 from coronary heart disease, and 127 from stroke (78 from cerebral infarction, 25 from cerebral hemorrhage, and 24 from unclassified stroke). In contrast to those with HbA1c 5.0%, the multivariate-adjusted HRs for CVD death were 2.18 (95% CI 1.22-3.87) and 2.75 (1.43-5.28) in the participants with HbA1c 6.0-6.4% and 6.5%, respectively. Relations to HbA1c with all-cause mortality and CVD death were graded and continuous. Similar associations were observed between HbA1c and death from coronary heart disease and death from cerebral infarction.

We found that, the mean TG-mg/dL was higher [171.9655±79.2367] in ≥5.5 group compared to <5.5 group [117.8649±50.2859] which was statistically significant (p=0.0004), the mean LDL-mg/dL was more [96.2241±51.3680] in ≥5.5 group compared to <5.5 group [69.3514±53.1111] which was statistically significant (p=0.0160) and the mean HDL-

mg/dL was lower [35.4310±13.5894] in ≥5.5 group compared to <5.5 group [38.4595±17.2508] but this was not statistically significant (p=0.3433). Distribution of mean HBA1C % with HBA1C Category was statistically significant (p<0.0001).

Our study showed that, the mean CRP mg/L was more [33.7985±19.7337] in ≥5.5 group compared to <5.5 group [18.4303±21.6220] it was statistically significant (p=0.0020). The mean FRS was higher [16.8793±7.0414] in ≥5.5 group compared to <5.5 group [10.7838±9.8577] it was statistically significant (p=0.0007). Distributionof mean 10 YEAR CVD RISK % with HBA1C Category was statistically significant (p=0.0083).

Zhao W et al [84](2014) found that clinical trials to date have not provided definitive evidence regarding the effects of glucose lowering with coronary heart disease (CHD) risk among diabetic patients. They prospectively looked into the relationship between baseline and follow-up HbA1c levels and the risk of CHD among 12,592 white and 17,510 African American patients with type 2 diabetes. 7,258 incident CHD cases over a 60-year follow-up on average were found. The multivariable-adjusted hazard ratios of CHD wereo1.00, 1.07 (95% CI 0.97-1.18), 1.16 (1.04-1.31), 1.15 (1.01-1.32), 1.26 (1.09-1.45), 1.27 (1.09-1.48), and 1.24 (1.10-1.40) (P trend = 0.002) for African Americans and 1.00, 1.04 (0.94 -1.14), 1.15 (1.03-1.28), Both African American and white diabetes individuals showed a graded connection between follow-up HbA1c and CHD risk (all P trends 0.001).

It was found that, the positive correlation was found between HBA1C % vs AGE [.337] and the result was statistically significant (p.001). The positive correlation was found between HBA1C % vs BMI kg/m2, the result was statistically significant (p.007). The positive correlation was found between HBA1C **%** vs FBS mg/dL [.166].The P-Value was (p.107). The result was not statistically significant.

We showed that, the positive correlation was found between HBA1C **%** vs PPBS mg/dL

[.129]. The P-Value was (p.212). The result was not statistically significant. The positive correlation was found between HBA1C **%** vs SBP mm/Hg [.338]. The P- Value was (p.001). The result was statistically significant. The positive correlation was found between HBA1C **%** vs DBP mm/Hg [.247]. The P-Value was (p.016). The result was statistically significant.

We observed that, the positive correlation was found between HBA1C **%** vs TC- mg/dL [.180]. The P-Value was (p.081). The result was not statistically significant. The positive correlation was found between HBA1C **%** vs TG-mg/dL [.321]. The P- Value was (p.002). The result was statistically significant. The positive correlation

was found between HBA1C **%** vs LDL-mg/dL [.278]. The P-Value was (p.006). The result was statistically significant.

Yousefzadeh G et al [86](2015) observed that in order to lower the risk of diabetes-related adverse events, as well as the burden and cost it places on patients, the objective of diabetes control should be achievable. The current study's objective was to evaluate the state of glycemic control in male and female Kerman, Iran, T2DM patients. The Kerman Coronary Artery Disease Risk Study (KERCADRS), a population-based study from 2009 to 2011, was used to select 500 T2DM (300 women and 200 men) for the current study. Patients required to be over the age of 18, had Fasting Blood Sugar (FBS) levels greater than 126 mg/dl,oand had undergone therapy for the identified illness. Analyses of Glycosylated Hemoglobin (HbA1c) were performed on each subject. Good glycemic management was defined as HbA1c less than 7%. Other metabolic indicators based on target recommendations from the American Diabetes Association (ADA) were taken into consideration. Among all participants, the mean HbA1c level was 8.56 4.72%, with only 31.66% of males and 26.00% of women having a controlled level.

In our study, the Negative correlation was found between HBA1C **%** vs HDL-mg/dL [-.074]. The P-Value was (p.478). The result was not statistically significant. The positive correlation was found between HBA1C **%** vs FRS [.426]. The P-Value was <0.0001. The result was statistically significant.

SUMMARY AND CONCLUSION

- In our study, out of 95 patients, most of the patients were 20-34 years of age.

Age Category was not statistically significant with HBA1C Category.Distribution of mean Age with HBA1C Category was statistically significant.

- We found that, male population was higher than the female population andmale: female ratio was 1.15:1 but this was not statistically significant.
- It was found that, most of the patients had K/C/O HTN in ≥5.5 group compared to <5.5 group but this was not statistically significant and we also found that, most of the patients had SBP 140-159 in ≥5.5 group compared to <5.5 group it was not statistically significant.
- Our study showed that, more number of patients had TC <160 in <5.5 group compared to ≥5.5 group but this was not statistically significant. Higher number of patients had HDL Category <40 in ≥5.5 group compared to <5.5 group it was not statistically significant. Most of the patients had High CRP Category in ≥5.5 group compared to <5.5 group which was statistically significant.
- We showed that, majority numbers of patients were smoker in ≥5.5 group compared to <5.5 group though it was statistically significant. More number of patients had Intermittent in ≥5.5 group compared to <5.5 group which was statistically significant. Association of 10 Year CVD Risk % gr with HBA1C Category was statistically significant).
- We observed that, the mean BMI kg/m2 was more in ≥5.5 group compared to <5.5 group it was statistically significant. The mean FBS mg/dL was more in ≥5.5 group compared to <5.5 group but this was not statistically significant.

- In our study, the mean PPBS mg/dL was higher in ≥5.5 group compared to <5.5 group it was not statistically significant. The mean SBP and DBP mm/Hgwas more in ≥5.5 group compared to <5.5 group it was not statistically significant. Distribution of mean TC-mg/dL with HBA1C Category was not statistically significant.

- We found that, the mean TG-mg/dL was higher in ≥5.5 group compared to <5.5 group which was statistically significant, the mean LDL-mg/dL was more in ≥5.5 group compared to <5.5 group which was statistically significant and the mean HDL-mg/dL was lower in ≥5.5 group compared to <5.5 group but this was not statistically significant. Distribution of mean HBA1C % with HBA1C Category was statistically significant.
- Our study showed that, the mean CRP mg/L was more in ≥5.5 group compared to <5.5 group it was statistically significant. The mean FRS was higher in ≥5.5 group compared to <5.5 group it was statistically significant. Distribution of mean 10 YEAR CVD RISK %with HBA1C Category was statistically significant.
- It was found that, the positive correlation was found between HBA1C % vs AGE and the result was statistically significant. The positive correlation was found between HBA1C % vs BMI kg/m2, the result was statistically significant. The positive correlation was found between HBA1C **%** vs FBS mg/dL. The result was not statistically significant.

- We showed that, the positive correlation was found between HBA1C **%** vs PPBS mg/dL. The result was not statistically significant. The positive correlation was found between HBA1C **%** vs SBP mm/Hg. The result was statistically significant. The positive correlation was found between HBA1C **%** vs DBP mm/Hg. The result was statistically significant.

- We observed that, the positive correlation was found between HBA1C **%** vs TC-mg/dL. The result was not statistically significant. The positive correlation was found between HBA1C **%** vs TG-mg/dL. The result was statistically significant. The positive correlation was found between HBA1C **%** vs LDL- mg/dL. The result was statistically significant.
- In our study, the Negative correlation was found between HBA1C **%** vs HDL-mg/dL. The result was not statistically significant. The positive correlation was found between HBA1C **%** vs FRS. The result was statistically significant.

LIMITATIONS OF THE STUDY

In spite of every sincere effort my study has lacunae.The notable short comings of this study are:

- The sample size was small. Only 95 cases are not sufficient for this kind ofstudy.
- The study has been done in a single center.
- The study was carried out in a tertiary care hospital, so hospital bias cannot be ruled out.

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ANNEXURE – I

ETHICAL CLEARANCE CERTIFICATE

IEC/NO-09/2021
Date- 22/01/2021

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A study of correlation between high normal glycosylated hemoglobin as a risk factor for coronary heart disease with Framingham 10 year risk factor in non-diabetic patients.

Name of PG student: Dr Bhushan Patil, Department of Medicine

Name of Guide/Co-investigator: Dr M.S.Biradar Professor of Medicine

DR .S.V.PATIL
CHAIRMAN
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

3

ANNEXURE – II

INFORMED CONSENT FORM

TITLE OF RESEARCH: A STUDY OF CORRELATION BETWEEN HIGH NORMAL HBA1C AS A RISK FACTOR FOR CORONARY HEART DISEASE WITH FRAMINGHAM RISK SCORE IN NON-DIABETIC PATIENTS.

GUIDE : DR PRAKASH.G.MANTUR M. D

P.G.STUDENT : DR BHUSHAN VIJAY PATIL - CONTACT (9307200480)

All aspects of this consent form are explained to the patient in the language understood by him or her.

PURPOSE OF STUDY:

I have been informed that the purpose of this study is to study correlation between high normal HbA1c as a risk factor for coronary heart disease with framingham risk score in non-diabetic patients.

.

PROCEDURE:

I understand that I will undergo detailed history and clinical examination and investigations

BENEFITS:

I understand that my participation in this study will have no direct benefit to me other than the potential benefit of treatment which is planned to prevent further morbidity and mortality in me.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulation of hospital. If the data is used for publication the identity will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may ask for more information about the study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw from study at any time.

(Signature ofpatient) (Signature of Guardian)

STUDY SUBJECT CONSENT FORM:

I confirm that **Dr.BHUSHAN VIJAY PATIL** has explained to me the purpose ofthis research, the study procedure that I will undergo and the possible discomforts and benefits that I may experience, in my own language.

I have been explained all above in detail in my own language and I understand the same. I agree to give my consent to participate as a subject in this research project.

DATE: DATE:

SIGNATURE OF PARTICIPANT : SIGNATURE OF WITNESS:

ANNEXURE – III

PROFORMA

SCHEME OF CASE TAKING

Name: CASE NO:

Age: OP/IP NO:

Sex:

Religion: DOA:

Occupation: DOD:

Address:

Presenting complaints with duration:

History of presenting complaints:

Past History:

Family History:

Personal History:

Treatment History:

General Physical

Examination Pallor: present/absent
Icterus: present/absent
Cyanosis: present/absent
Clubbing: present/absent
Generalized lymphadenopathy: present/absent
Odema: present/absent

Weight:
Height:
BMI:

VITALS: PR:
BP: Systolic/Diastolic (mm hg)RR:

Temp:

SYSTEMIC EXAMINATION:

Cardiovascular system

- Respiratory system
- Per abdomen
- Central nervous system

INVESTIGATIONS PATHOLOGY:

1.) LIPID PROFILE	
T.CHOLESTEROL	mg/dl
TRIGLYCERIDES	mg/dl
LDL	mg/dl
HDL	mg/dl
2.) CRP	mg/L
3.) HbA1c	%
4.) FRAMINGHAM RISK SCORE	POINTS
5.) FBS	mg/dl
6.) PPBS	mg/dl

7.) CVD RISK	%
8.) FRS CATEGORY	LOW
	INTERMEDIATE
	HIGH

9.) CURRENT SMOKER	YES
	NO

TROPONIN I

2D ECHO

ELECTROCARDIOGRAPHY:

Other relevant investigations will be done when required.

CONCLUSION:

SIGNATURE
DATE:

ANNEXURE – IV : MASTERCHART