DISSERTATION SUBMITTED FOR THE MASTER'S DEGREE

IN MEDICAL BIOCHEMISTRY

TITLE

ASSESSMENT OF CARDIOMETABOLIC RISK FACTORS IN DIAGNOSED PATIENTS OF HYPOTHYROIDISM AND CONTROL SUBJECTS

SUBMITTED

BY

MOHAMMAD SALMAN

2023

DEPARTMENT OF BIOCHEMISTRY

INTEGRAL INSTITUTE OF MEDICAL SCIENCES AND RESEARCH

FACULTY OF HEALTH & MEDICAL SCIENCES

INTEGRAL UNIVERSITY

LUCKNOW-226026, U.P

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A
DISSERTATION

SUBMITTED

In partial fulfillment of the requirement for the award of degree of

Master of Science

In

Medical Biochemistry

By

MOHAMMAD SALAMAN

Enrolment No: 2000101923

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Integral Institute of Medical Sciences & Research
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CERTIFICATE

This is to certify that **Mr.Mohammad Salaman** student of **M.Sc. Medical Biochemistry**, Integral University has completed his dissertation titled **"Assessment of Cardiometabolic Risk Factors in Diagnosed Patients of Hypothyroidism and Control Subjects"** successfully. He has completed this work in the department of Biochemistry, Integral institute of Medical Sciences and Research, Integral University under my supervision. The dissertation was a compulsory part of his M.Sc. degree.

I wish him good luck and a bright future

Guide

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Dr. Roshan Alam

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Declaration by the candidate

I hereby declare that Integral Institute of Medical Sciences & Research, Integral University, Lucknow shall have the right to preserve, use and disseminate this dissertation in print/electronic format for academic/research purposes.

I will publish the research paper related to my dissertation only with the consent of my guide.

Date:

Place: Lucknow **Mohammad Salaman**

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Date:

Place: *Lucknow* ***Mohammad Salaman***

CONTENTS

LIST OF ABBREVIATIONS

MetS	Metabolic syndrome
T3	Triiodothyronine
T4	Thyroxine
TSH	Thyroid Stimulating Hormone
WC	Waist Circumference
REE	Resting Energy Expenditure
CVDs	Cardiovascular Diseases
ASCVDs	Atherosclerotic Cardiovascular Diseases
TC	Total cholesterol
LDL	Low Density Lipoprotein
HDL	High Density Lipoprotein
TG	Triglycerides
BMI	Body Mass Index
FBS	Fasting Blood Sugar

SYMBOLS

mg	Milligram
dl	Deciliter
cm	Centimeter
kg	Kilogram
nmol/l	Nanomoles per liter
kg/m^2	Kilogram per meter square
%	Percentage
Lt	Liter
≥	Greater than or Equal
µIU/ l	Micro unit/ litre

INTRODUCTION

Endocrine glands included the thyroid gland. It is situated in the inferior, and frontal neck and is in responsible of iodine homeostasis in the body, as well as the production and release of thyroid hormones. The thyroid gland generates 90 percent of the inert thyroid hormone T4 (thyroxine) and 10 percent of the functional thyroid hormone T3 (triiodothyronine)**(Armstrong et al., 2019).**

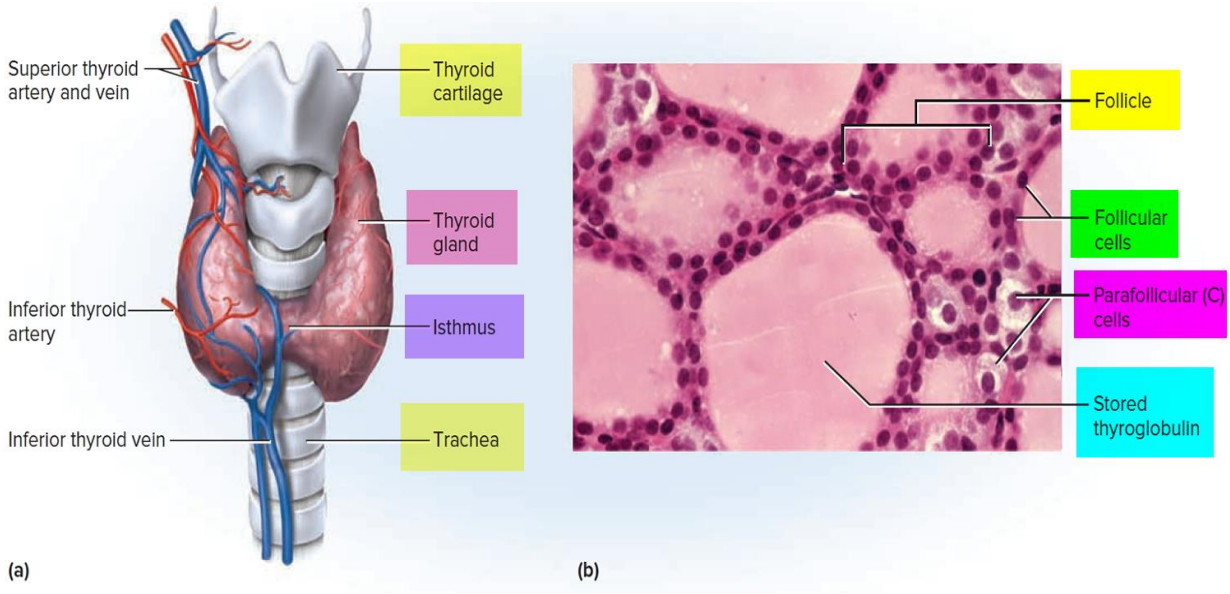

Figure1: Anatomy of Thyroid Gland (Health Jade)

A persistent problem associated with hypothyroidism is the deficiency of T4 and T3 **(Malaty W., 2017).**Untreated or insufficiently managed hypothyroidism can cause infertility, cardiovascular disease (CVD), nerve disease, and muscular discomfort.**(Chaker L. et al., 2018).** In the developed countries, hypothyroidism affects 4 to 5% of people **(Hollowell J. et al., 2002).**

There are 42 million peoples in India suffers from thyroid, according to information presented to participants of a national symposium on advanced thyroid diseases care on June 5, 2014, in Chennai, India. One in ten adults in India suffers from hypothyroidism, the most prevalent thyroid condition **(Bagcchi S., 2014).**

In India, 11% of people have hypothyroidism, compared to 2% in the United Kingdom and 4.6% in the United States of America. Interior cities like Hyderabad, Delhi, Bangalore, Ahmadabad and Kolkata have a greater incidence (11.7% versus 9.5%) than beaches cities like Goa, Mumbai and Chennai. **(Bagcchi S., 2014).**

Thyrotropin-releasing hormone, also called TRH, stimulates the anterior pituitary gland to secrete TSH.Thyroid hormones suppress TSH and TRH production. To obtain the precise levels of thyroid hormone, different people have drastically distinct TSH demands. Clinical effects of abnormal thyroid function are known to persist even when they are within the specified reference limits, according to various studies. It is being discussed to reevaluate the reference ranges for TSH and FT4 **(Bano A., 2018).**

The risk of hypertension, SBP(systolic blood pressure), DBP(diastolic blood pressure), CRP, WC (waist circumference), fat percentage of body, and a family history of cardiac disease were all associated with having a BMI (body mass index) of 45 or higher **(Bano et al., 2018).**

A sensitive TSH test should be used to screen for thyroid disease, according to recent American College of Physicians recommendations for primary care settings. The condition of the thyroid is not very prevalent. Therefore, according to these recommendations, monitoring of men and women under the age of 50 is not necessary **(Kutluturk et al., 2013).**

Triglyceride levels were consistently associated beneficially with TSH in FT3 at any percentile. To measure through a canopy and obtain a reading on REE, we used an indirect calorimeter **(Austin, 2018).**

The determination of cardiometabolic risk variables was done simultaneously with the measurement of TSH levels. More long-term studies may be required to determine

whether or not these cardio-mechanical risk factors are connected to suboptimal cardiometric outcomes. Despite these limitations, the reference ranges provided and the link between cardiometabolic risk factors and the highest quantile of TSH levels make this research an important resource for practitioners **(Spadafranca et al., 2015).**

A positive relationship was found between the recently identified adipose-myokineirisin and thyroid stimulating hormone (TSH), anti-triglyceride (anti-TG), lipid and inflammatory biomarkers, leptin, and risk factors of cardiovascular disease. Serum irisin and other biomarkers were examined in 16 people with subclinical hypothyroidism (SH) six months after L-T4 therapy in these patients. In this study, it was determined whether patients with subclinical hypothyroidism (SH) had any associations between circulating irisin and cardiometabolic risk factors **(Alsamhan et al., 2010).**

Fasting blood samples were tested for total T3, total T4, TSH, lipid profile, and blood glucose levels together with a comprehensive medical history and other relevant tests **(Ayub et al., 2021).**

Obesity, often known as excess body fat, is on the rise and poses serious risks to the general public's health. Thyroid hormone has an adverse effect on the majority of lipid metabolic processes, which explains why dyslipidemia is so common in persons having thyroid dysfunction. Raises the risk of cardiovascular disease when it occurs along with other metabolic disease. High blood pressure, insulin resistance, and oxidative stress are some of these disorders. To understand the importance of dyslipidemia or other metabolic abnormalities to CVD mortality &morbidity and death in clinical illness so, in subclinical thyroid illness, more research is necessary, particularly prospective studies. Along with quantitative alterations, qualitative changes in lipids, such as atherogenic and oxidized LDL-C and HDL-C particles, have also been seen **(Erem et al., 2015).**

Thyroid markers TSH, T4, antithyroid peroxidase antibody, and antithyroglobulin antibody were used to divide participants into groups according to their metabolic syndrome status, the amount of metaboilic syndrome components they had age-related and gender-specific reference values (TgAb). Metabolic syndrome and thyroid dysfunction are related in both directions. As part of a whole strategy for treating metabolic syndrome, we hope that this study may encourage further research on the therapeutic efficacy of restoring thyroid function.

Male individuals in thehighest TSH decile also had higher rates of high TG, WC, HDL-C, and DBP than did female participants **(Peppam et al., 2011).**

There should be cautious due to the complex and unproven link between thyroid autoimmunity and cardiovascular risks. The aim of this study was to explore the possibility that a sizable population with normal thyroid-stimulating hormone (TSH) also carried a higher risk of developing cardiometabolic disease. AITDs had a unique relationship with higher risks in women for abdominal obesity, higher lipid, and metabolic syndrome (MetS). In line with expectations, it was also connected to being overweight or obese in both sexes **(Y. Chen *et al.*, 2018).**

REVIEW

OF

LITERATURE

The thyroid's inability to create enough amounts of thyroid hormone is the most common cause of hypothyroidism; thyroid dysfunction can also be caused by the pituitary and hypothalamic glands.

Causes of hypothyroidism

Primary hypothyroidism

1. Goitrous hypothyroidism, which results in increasing impairment of hormone biosynthesis and growth of the thyroid gland.
2. Temporary hypothyroidism
3. Thyroid hormone resistance (generalized pituitary dominance).
4. Atrophic hypothyroidism, which is characterized by irreversible thyroid tissue atrophy or loss **(Salomon Melmed et al., 2016).**

Hypothalamic-pituitary axis dysfunction is the root cause of secondary and tertiary hypothyroidism, commonly referred to as central hypothyroidism. The following are some of its causes:-

- Pituitary tumors
- Hypothalamus compressing tumors
- Sheehan syndrome
- Resistance of Thyroid releasing hormone (TRH)
- Deficiency of TRH
- Lymphocytic hypophysitis
- Radiation therapy of the brain

Symptoms may include:- Tiredness, cold sensitivity, weight gain, skin dryness, constipation and rough hair & skin.

Adults with apparent and hidden hypothyroidism range in prevalence from 0.2%-5.3%. The 2.5th percentile of the corresponding distributions in a population that seems to be healthy is the TSH (or FT4) criteria for normalcy **(Bano A., 2018).**

Researchers studied the changes in body composition, calorimetric, and metabolic features of 15 female DTC patients using a case series methodology. TSH suppressive LT4 therapy enhanced total REE as well as, pulse, REE/LBM and DBP **(Izkhakov et al., 2019).**

According to GEE analysis, the TT3/fT4 ratio has a negative longitudinal connection with SBP, FBS, BMI, distribution of fat in the abdomen and visceral mesentery, the trunk and arms, REE, and REE/LBM. In females with DTC who had a lower TT3/fT4 ratio, there were relatively enhanced rates of energy expenditure (REE), relative excess lean body mass (REE/LBM), abdominal fat distribution (AFD), SBP, and FBS **(Izkhakov et al., 2019).**

The findings emphasize the significance of carefully evaluating the benefits and drawbacks of TSH suppression, with the latter resulting in a decrease in TSH-related metabolic changes.

In 40.0% of those who were highly overweight, the Framingham Risk Score (FRS) was a function of the level of obesity. Except for dyslipidemia, no significant changes were observed in the BMI categories for diabetes, lifestyle, lipid indicators, or the Functional Rating Scale. The findings shed new information on the connection between extreme obesity and cardiometabolic risks, which is a crucial advancement in the field of study **(Bano A., 2018).**

One hundred and five diabetics were recruited at random from the Jinnah Hospital in Lahore's diabetic clinic. For diabetics, thyroid dysfunction manifests early in life. People

with hypothyroidism have higher levels of a number of indicators of risk for atherosclerotic coronary artery disease, including high cholesterol levels and elevated blood pressure.**(Biondi et al., 2019).**

The study discovered that 16.7% of people with metabolic syndrome had thyroid abnormalities. None of the study participants had symptoms of hyperthyroidism. Subclinical hypothyroidism was present in 11.7% of people with thyroid problems. The risk for acquiring coronary artery disease is greater in both men and women with this condition than it would be in the general population **(Ayub et al., 2021).**

The levels of MDA, hyperglycemia, and TG were significantly greater in those with these two disorders. These people may have enhanced lipid peroxidation, which may be a major factor in the pathogenesis of atherosclerosis, based on the elevated MDA levels. There is a connection between IMA and hyperthyroidism, however further prospective study is needed to clarify this association. In conclusion, there were noticeable differences in the lipid profile and OS parameters between patients with SHyper and OHyper and healthy controls. People with SHyper and OHyper may experience less oxidative stress after receiving treatment with ATD **(Demirbas et al., 2021).**

Women made up 67.9% and males made up 32.1% of the 817 survey participants. The average BMI for individuals ranged from 29.90 to 6.6 kg/m2. The body fat percentage as determined by the BIA increased along with the subject's BMI (P 0.001). The body fat percentage & Body mass index were linked with the LAP index **(Stratigos et al., 2018).**

During the third National Health and Nutrition Examination Survey (1988-1994), 1,322 adolescents between the ages of 12 and 18 had their thyroid task and metabolic disorder elements examined. Being overweight or obese, having a big waist circumference,

having high BP, having high triglycerides, and having low HDL-C values are all conditions that might cause metabolic syndrome. According to research, abnormal thyroid hormone levels may set off a series of metabolic abnormalities, implying a link between the two **(Peppam et al., 2011).**

In order to determine whether thyroid-stimulating hormone (TSH) levels were related to cardiometabolic risk factors, 15.4 million American adolescents ranged in age from 12 to 18 participated in the study.

Thyroid hormones have an impact on several physiological processes, including development, metabolism, thermogenesis, and cardiovascular health. In this group of young people (51.3% of whom were male), the average incidence of SH was 2.0% (95% CI 1.2-3.1%) and 31.2%,of them were overweight or obese. The goal of the study was to analyze the link between TSH and cardiovascular & cardiometabolic risk factors. Obesity and insulin resistance have both been linked to thyroid-stimulating hormone (TSH). If the two are causally connected, though, remains unknown. Few population-based cohort studies exist **(Spade et al., 2015).**

Research was done on 30 patients who had clinical hypothyroidism symptoms. LDL oxidation, inflammation, and endothelial damage were all measured in all individuals. OxLDL concentration and LDL-C, apo B, triglyceride, and triglyceride levels all showed favorable correlations **(Chen X et al., 2021).**

The relationship between metabolic syndrome (MetS) and subclinical hypothyroidism (SCH) has attracted a lot of research. When those with SCH were compared to those without, the pooled OR for MetS were 1.28 (95% CI: 1.19 to 1.39, $p = 0.04$, $I2 = 40\%$). Age, ethnicity, and the diagnostic criteria for MetS appeared to have an impact on the probability of acquiring MetS among SCH participants.

There was a link found between SCH and an elevated risk of being overweight, developing hypertension, having high triglyceride levels, and having low levels ofhigh density lipoprotein (HDL-C). These findings require confirmation by more lengthy, extensive prospective cohort studies **(Warsaw et al., 2016).**

Patients with overt hypothyroidism showed elevated blood lipids, folic acid, and vitamin B12 levels both before and after L-thyroxin (LT4) medication. Fasting blood samples from patients were examined for TSH, free thyroxine (FT4), homocysteine, total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and other chemical markers**(Kutluturk et al., 2013)**.

Positive correlations were found between serum lipid concentrations and homocysteine concentrations. After thyroid functions were restored by LT4 replacement, there was a intenserelation between GFR and lipids that no longer existed. The improvement of these parameters following LT4 replacement may be correlated with a lower risk of cardiovascular disease caused by atherosclerosis in hypothyroid patients. Additionally, total, LDL, and TG lipid levels showed a significant adverse relationship with GFR (**Ding X et al., 2021).**

AIM

&

OBJECTIVES

Aim

It is aimed to determine the cardio metabolic risk factors in diagnosed cases of hypothyroidism and control subjects.

Objectives

1. To determine the biochemical parameters; blood sugar and lipid profile in diagnosed cases of hypothyroidism and control subjects.
2. To determine demographic parameters; BMI, waist circumference and blood pressure in diagnosed cases of hypothyroidism and control subjects.
3. To find the correlation between demographic parameters and biochemical parameters in diagnosed cases of hypothyroidism and control subjects, if any.

MATERIALS

&

METHODS

Research Question

Is there any significant association between biochemical parameters and demographic parameters of diagnosed cases of hypothyroidism?

Hypothesis: -

Null Hypothesis (H_0): There is no significant association between biochemical parameters and demographic parameters of diagnosed cases of hypothyroidism.

Alternate Hypothesis (H_1): There is a significant association between biochemical parameters and demographic parameters of diagnosed cases of hypothyroidism.

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METHODOLOGY

Types of Study:-Case-control study.

Sampling Method: Purposive sampling

Duration of Study: Six months (January-2023 to June-2023)

Study Design:-Prospective

PLACE OF STUDY:

Department of Biochemistry, Integral Institute of Medical Science and Research (IIMSR), Lucknow (U.P).

COLLABORATING DEPARTMENT –

Department of General Medicine, OPD at IIMS&R, Integral University, Lucknow.

SUBJECTS SELECTION

In this case-control study, a total of 60 subjects (30 diagnosed patients of hypothyroidism and 30 age-matched healthy controls) were enrolled from Out Patients' Department of Medicine, IIMSR, integral University, Lucknow (U.P.). Subjects were aged between 30 to 65 years. A detailed demographical, family and medical history has been taken from each subject. Written consent was taken from each subject. This study has been approved by the Institutional Ethical Committee, Integral University, Lucknow (U.P.) (IEC/IIMSR/2023/69).

Selection for Controls

1. Apparently healthy individuals.
2. Subjects between the ages of 30 to 65 years.
3. Individuals who have agreed to sign the consent form.

Selection for Cases

Inclusion criteria

1. Diagnosed cases of hypothyroidism **(Sharma et al., 2014).**
2. Subjects between the ages of 30 to 65 years.
3. Patients who have agreed to sign the consent form.

Exclusion criteria

1. History of any chronic diseases or infectious diseases.
2. Pregnant and lactating females

COLLECTION OF SAMPLES

Under an aseptic condition, 2 ml of venous blood was collected in the plain vial from the subjects. The blood sample was allowed to clot at room temperature for 15 minutes. The sample was then centrifuged at 1000 rpm for 10 minutes to separate the serum. About 1 ml serum was used for the determination of lipid profile (total cholesterol, triglyceride, high-density lipoprotein-cholesterol) in diagnosed cases of hypothyroidism.

Fasting blood sugar test was done by finger prick method via Glucometer.

Low-density lipoprotein-cholesterol and very low-density lipoprotein-cholesterol were calculated by Friedewald Formula)

LDL-Cholesterol was calculated by using formula-

- **LDL-C (mg/dl) = TC (mg/dl) − HDL-C (mg/dl) − TG (mg/dl)/5**

VLDL-Cholesterol was calculated by using formula-

- **VLDL-C(mg/dl) = TG (mg/dl)/5**

Storage of samples:-The serum samples for the estimation of total cholesterol, triglyceride, high density lipoprotein (HDL), & low density lipoprotein (LDL) was stored at -20°C until testing in Central Clinical Laboratory, Department of Biochemistry, IIMS&R, Lucknow (U.P).

Sample size

The sample size is calculated using the formula **(Allen Jr, J. C. 2011).**

$$n = \frac{2\,(Z_{\alpha/2} + Z_{1-\beta})^2}{\left(\frac{\mu_1 - \mu_2}{\sigma}\right)^2} = \frac{2(1.96 + 0.84)^2}{\left(\frac{\Delta}{\sigma}\right)^2}$$

Sigma = standard deviation (taken from previous studies) $Z_{1-\beta}$ = represent the desired power

$Z_{\alpha/2}$ = represent the desired level of statistical significance

Effect size (Δ) = 0.75 **(Kutluturk et al., 2013)**

Then,

For 80% power, $Z_{1-\beta}$ = (0.84)

For 0.05 significance level, $Z_{\alpha/2}$=1.96

Put the value in formula

Then n = 28.4 ≈ 30

Reference: Kutluturk F, Yuce S, Tasliyurt T, Yelken BM, Aytan P, Ozturk B, Yılmaz A. Changes in metabolic and cardiovascular risk factors before and after treatment in overt hypothyroidism. Medicinski Glasnik. 2013 Aug 1;10 (2).

LABORATORY INVESTIGATION:

a) Determination of serum total cholesterol by using Erba chem-7 Biochemistry Analyzer.

Methodology: -Modified Roeschlau's Method.

PRINCIPLE

The estimation of cholesterol involves the following enzyme catalyzed reactions.

- Cholesterol ester $\xrightarrow{\text{Cholesterol esterase}}$ cholesterol + fatty acid
- Cholesterol + O_2 $\xrightarrow{\text{CHOD}}$ cholest-4-en-3-one + H_2O_2(CHOD-Cholesterol Oxidase)
- $2H_2O_2$ + 4- aminoantipyrine $\xrightarrow{\text{POD}}$ $4H_2O$ + Quinoneimine (POD- Peroxidase)

NORMAL REFERENCE VALUES: - Desirable= <200 mg/dl

Borderline= 200-239 mg/dl

High level= >239 mg/dl

Assay Procedure for Total Cholesterol

Pipette into tubes marked	Blank (B)	Standard (S)	Test (T)
Working Reagents	1000µl	1000µl	1000µl
Distilled Water	20µl	–	–
Standard	–	20µl	–
Test	–	–	20µl

Mix well and incubate at 37^0C for 10 minutes. Aspirate Blank followed by Standard and Tests. Read the absorbance of standard and each test tube against blank at 505 nm or 505/670 nm on bichromatic analyzer **(Roeschlau et al., 1974).**

b) Determination of serum triglycerides by using Erba chem-7 Biochemistry Analyzer.

Methodology: - this reagent is based on the method of Wako and the modifications by McGowan et al and Fossati et al., 1984.

Principal

- Triglyceride + H_2O —LPL→ Glycerol + Free fatty acids
- Glycerol + ATP —Glycerol Kinase→ Glycerol-3-phosphate + ADP
- Glycerol-3-phosphate + O_2 —GPO→ DAP + H_2O_2
    - (Glycerol phosphate Oxidase)
- H_2O_2 + 4-aminoantipyrine + 3, 5-DHBS* —Peroxidase→ Quinoneimine Dye + $2H_2O$

*DHBS- 3, 5-Dichloro-2-hydroxybenzene sulfonate

The intensity of quinoneimine formed is proportional to the triglycerides concentration in the sample when measured at 505 nm.

NORMAL REFERENCE VALUES: Normal= <161 mg/dl

High= 161-199 mg/dl

Very High= >200

Assay Procedure for Triglycerides

Pipette into tubes marked	Blank (B)	Standard (S)	Test (T)
Working Reagents	1000µL	1000µL	1000µL
Distilled Water	10µL	–	–
Standard	–	10µL	–
Test	–	–	10µL

Mix and incubate for 10 min at 37^0C. Read the absorbance of standard and each test at 505 nm (500- 540 nm) or 505-670 nm on bichromatic analyzers against reagent blank.

c) Determination of serum HDL-Cholesterol by using Erba chem-7 Biochemistry Analyzer.

Principle

The assay is based on a modified polyvinyl sulfonic acid (PVS) and polyethylene glycol-methyl ether (PEGME) coupled classic precipitation method with the improvements in using optimized quantities of PVS/PEGME and selected detergents. LDL, VLDL and chylomicron (CM) react with PVS and PEGME and the reaction results in inaccessibility of LDL, VLDL and CM by cholesterol oxidase (CHOD) and cholesterol esterase (CHER). The enzymes selectively react with HDL to produce H2O2 which is detected through a tinder reaction.

HDL+ LDL VLDL + CM $\xrightarrow{\text{PVS, PEGME}}$ HDL+(LDL+VLDL+CM)*PVS/PEGME

HDL $\xrightarrow{\text{CHOD, CHER}}$ Fatty Acid + H_2O_2

$2H_2O_2$ + 4- aminoantipyrine $\xrightarrow{\text{Peroxidase}}$ Quinone + $5H_2O$

NORMAL REFERENCE VALUES: Male: 35.5-79.5 mg/dl

Female: 42-88 mg/dl

Assay Procedure for HDL-Cholesterol

Pipette into tubes marked	**Reagent Blank (B)**	**Sample / Calibrator**
Reagent 1	375µL	375µL
Distilled Water	5 µL	–
Sample / Calibrator	–	5 µL
Mix and incubate at 37°C for 5 min**.**		
Add Reagent 2	125 µL	125 µL
Mix and incubate at 37°C for 5 min		

Read final absorbances at the specified wavelength against reagent blank.

d) Determination of serum LDL-Cholesterol by using Erba chem-7 Biochemistry Analyzer.

Principle

The assay is based on a modified polyvinyl sulfonic acid (PVS) and polyethylene glycol methyl ether (PEGME) coupled classic precipitation method with the improvements in using optimized quantities of PVS/PEGME and selected detergents. LDL, VLDL, and chylomicron (CM) react with PVS and PEGME and the reaction results in inaccessibility of LDL, VLDL and CM by cholesterol oxidase (CHOD) and cholesterol esterase (CHER), whereas HDL reacts with the enzymes. Addition of R2 containing a specific detergent releases LDL from the PVS/PEGME complex. The released LDL reacts with the enzymes to produce H2 O2 which is quantified by the trinder reaction.

(LDL + VLDL + CM) • PVS/PEGME $\xrightarrow{\text{Detergent}}$ (LDL+VLDL+CM)*PVS/PEGME

LDL $\xrightarrow{\text{CHOD, CHER}}$ Fatty Acid + H_2O_2

$2H_2O_2$ + 4-Aminoantipyrine + TODB $\xrightarrow{\text{Peroxidase}}$ Quinone + $4H_2O$

NORMAL REFERENCE VALUES: - Normal= 100-130 mg/dl

Borderline= 130-159 mg/dl

High= >160 mg/dl

d. Estimation of fasting serum glucose:-

PRINCIPLE

Glucose in the sample is oxidized to yield gluconic acid and hydrogen peroxidized in the presence of glucose oxidase. The enzyme peroxidase catalyzes the oxidative coupling of 4-aminoantipyrine with phenol to yield a colored quinoneimine complex, with absorbance proportional to the concentration of glucose in samples.

NORMAL REFERENCE VALUES: - 70-110 mg/dl

Assay Procedure for serum glucose

Pipette into tubes marked	Blank (B)	Standard (S)	Test (T)
Working Reagents	1000µl	1000µl	1000µl
Distilled Water	10µl	--	--
Standard	--	10µl	--
Test	--	--	10µl

Mix well and incubate for 15 minutes at 37.C. Read the absorbance of Standard and each test tube against reagent blank at 505 nm (500 -540nm) or 505 /670 nm on bichromatic analyzer.

e. Measurement of Waist circumference:-

Methodology: - Waist circumference is measured by using the measuring tape.

Procedure-

1. Remove or raise clothing
2. Find the waist
3. Wrap the measuring tape around your waist.
4. Read the tape (inch/cm)
5. Double-check your measurement

NORMAL REFERENCE VALUES: **Male:** <90 cm

Female: <80 cm

f. Measurement of Blood Pressure:

Methodology: Blood Pressure is measured by using the fully automatic blood pressure monitor (Omron HEM 7120), based on Oscillometry principle.

PRINCIPLE

Oscillometry is based on the principle that the artery wall oscillates when blood flows through an artery during cuff deflation.

NORMAL REFERENCE VALUES: Systolic blood pressure= 120 mmHg.

Diastolic blood pressure = 80 mmHg.

Thyroid Hormone Estimation: T3, T4 and TSH were estimated by commercially available kit antigen-antibody Immuno assay based on the Enzyme-Linked Fluorescent Assay principle by Mini-VIDAS (BIOMERIEUX SA).

ETHICS REVIEW

Permission from the Integral University ethics committee was taken (**IEC/IIMS&R 2023/69**)

STATISTICAL ANALYSIS

Statistical analysis was performed using IBMSPSS software (version 16), Graph Pad software(version 6.0) and Microsoft – Excel(2007). All the data was expressed as mean ± standard deviation. An unpaired t-test was performed to compare the study parameters between cases and controls. Karl Pearson's correlation analysis was employed to determine the relationship between variables. A $p<0.05$ was considered statistically significant.

OBSERVATIONS

&

RESULTS

OBSERVATION& RESULTS:-

Results showed that mean of BMI, WC, TC, TG, LDL-C, VLDL-C, TSH, SBP, and DBP were found significantly elevated in cases compared to controls ($p<0.001$). However, mean of HDL-C, T3, and T4 were found significantly decreased in cases compared to controls ($p<0.001$), shown in **Table 1.**

Table 1 Baseline characteristics of cases and controls

Parameters	Case (n=30)	Control (n=30)	p-value
Age (years)	41.16 ± 9.50	42.46 ± 8.80	0.5845
BMI (kg/m^2)	26.30 ± 3.87	22.41 ± 2.15	0.0001
WC (cm)	90.66 ± 6.06	83.67 ± 4.73	0.0001
FBS (mg/dL)	102.73 ± 23.76	91.73 ± 14.41	0.0343
T3 (nmol/L)	1.60 ± 0.44	2.05 ± 0.88	0.0151
T4 (nmol/L)	86.87 ± 15.91	127.22 ± 55.97	0.0004
TSH (µIU/mL)	7.63 ± 3.34	2.17 ± 0.91	0.0001
TC (mg/dL)	203.19 ± 33.34	124.54 ± 20.87	0.0001
TG (mg/dL)	152.93 ± 65.46	123.17 ± 35.94	0.0331
HDL-C (mg/dL)	44.36± 9.41	49.01 ± 6.43	0.0293
LDL-C (mg/dL)	128.24± 35.48	50.89 ± 19.90	0.0001
VLDL-C (mg/dL)	30.58 ± 13.09	24.63 ± 7.18	0.0331
SBP (mmHg)	137.33 ± 13.22	123.66 ± 5.89	0.0001
DBP (mmHg)	94.66 ± 11.25	85.2 ± 5.59	0.0001

**p<0.05 was considered statistically significant.*
Data was represented as Mean ± SD (Standard deviation).
BMI: Body mass index, WC: Waist circumference, FBS: Fasting blood sugar, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid stimulating hormone, TC: Total cholesterol, TG: Triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, VLDL-C: Very Low-density lipoprotein-cholesterol, SBP: Systolic blood pressure, DBP: Diastolic blood pressure

AGE

In this study, 30 control Subjects aged between 30 to 65 with 30 patients of hypothyroidism were included. The mean age of control subjects (42.46 ± 8.80) and hypothyroidism patients (41.16 ± 9.50) have been found.

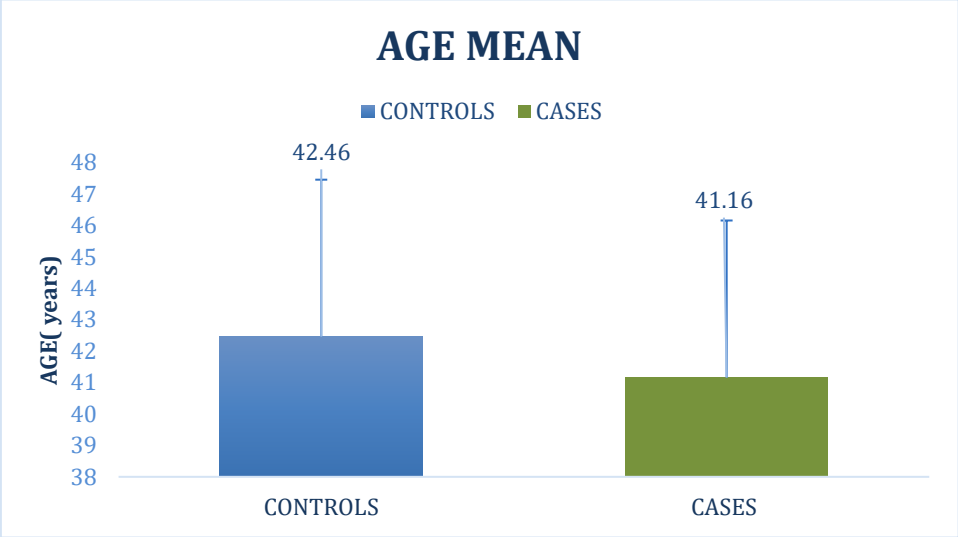

Figure.2. Comparison of ages (years) in cases & controls.

BODY MASS INDEX (BMI)

Anthrpometric parameter body mass index (BMI) were significant in patients of hypothyroidism, comparing patients to control subjects, p=0.0001 shown in table 3.

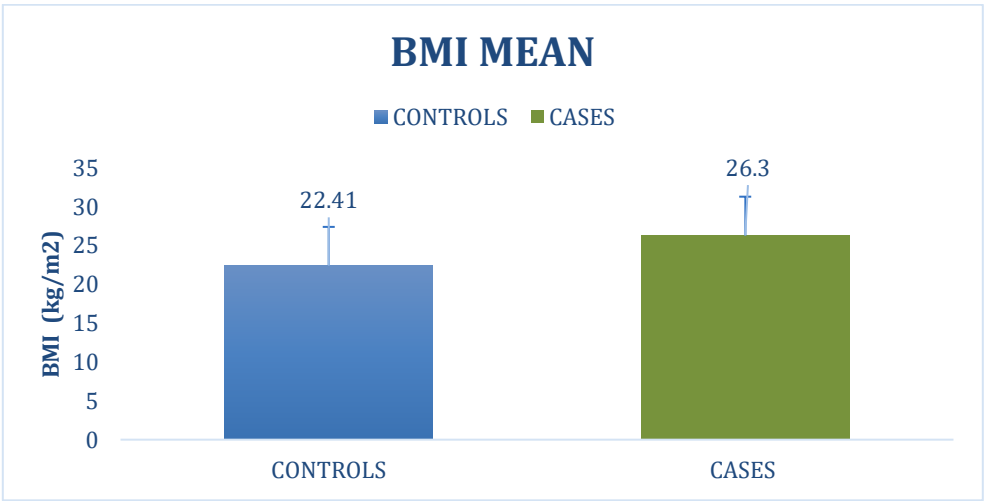

Figure 3. Comparison of BMI in cases and controls.

Total Cholesterol

Serum TC is significantly increased in patients of hypothyroidism, comparing patients to control subjects, p= 0.0001 shown in table. 3.

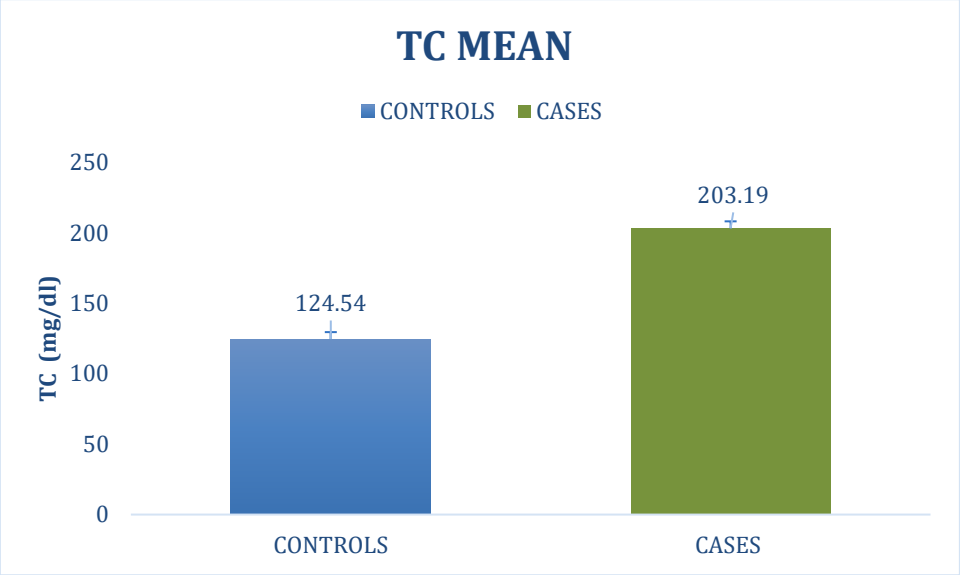

Figure 4. Comparison of TC in cases and controls.

Serum triglycerides

In patients of hypothyroidism compared to control subjects, TG are considerably higher (p= 0.0331) shown in table.3.

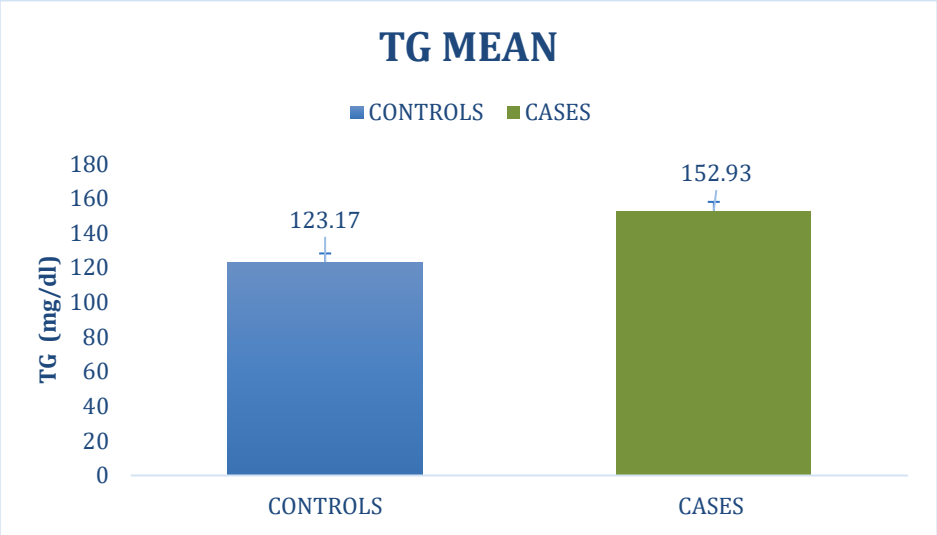

Figure 5. Comparison of TG in cases and controls.

Serum HDL-C

Compared to control persons, in patients of hypothyroidism serum HDL-C is considerably lower (p=0.0616) shown in table.3.

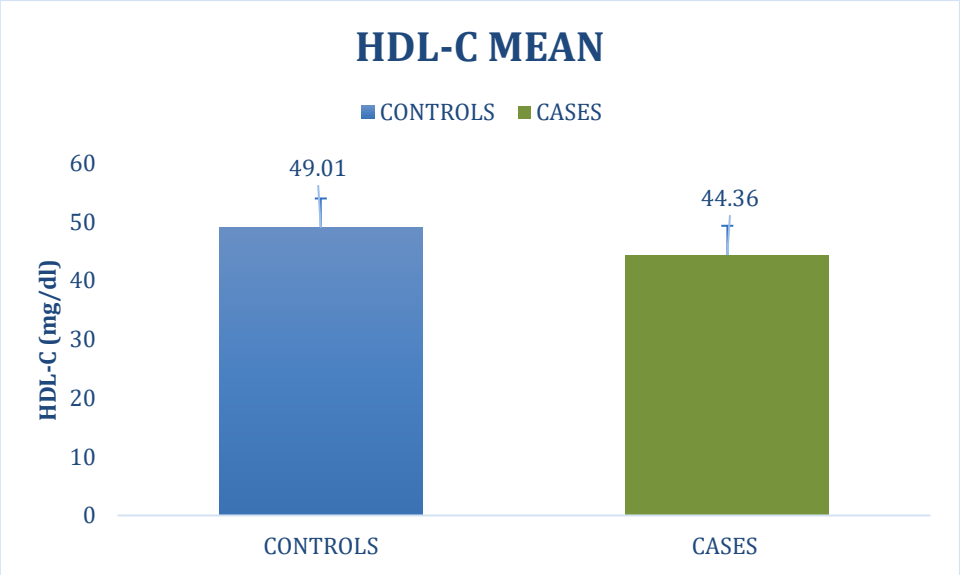

Figure 6. Comparisonof HDL-C in cases and controls.

Serum LDL-C

When compared to control persons, in patients of hypothyroidism serum LDL-C is considerably higher (p=0.0001) shown in table.4

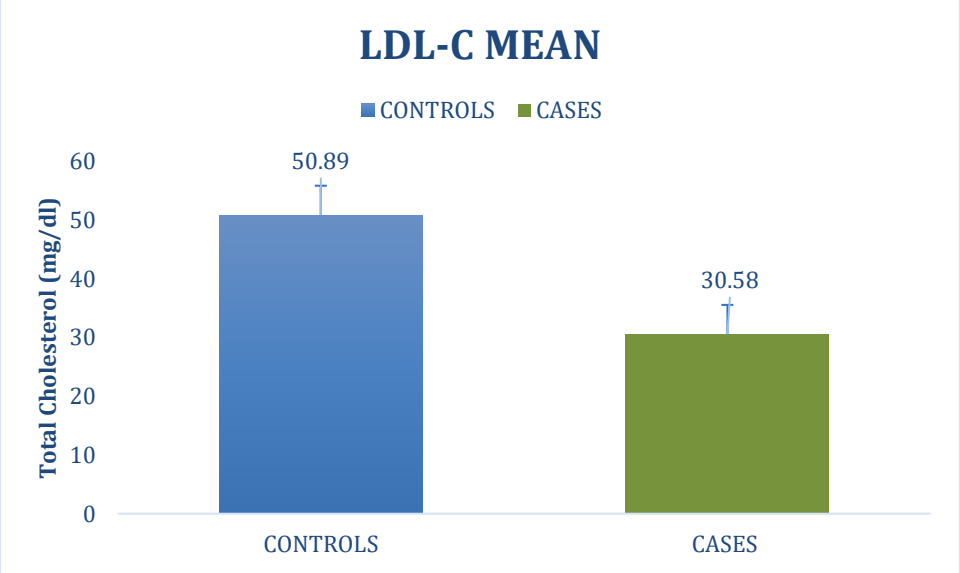

Figure 7. Comparison of LDL-C in cases and controls.

Serum VLDL-C

When compared to control persons, in patients of hypothyroidism serum VLDL-C is considerably higher (p=0.0001) shown in table.5

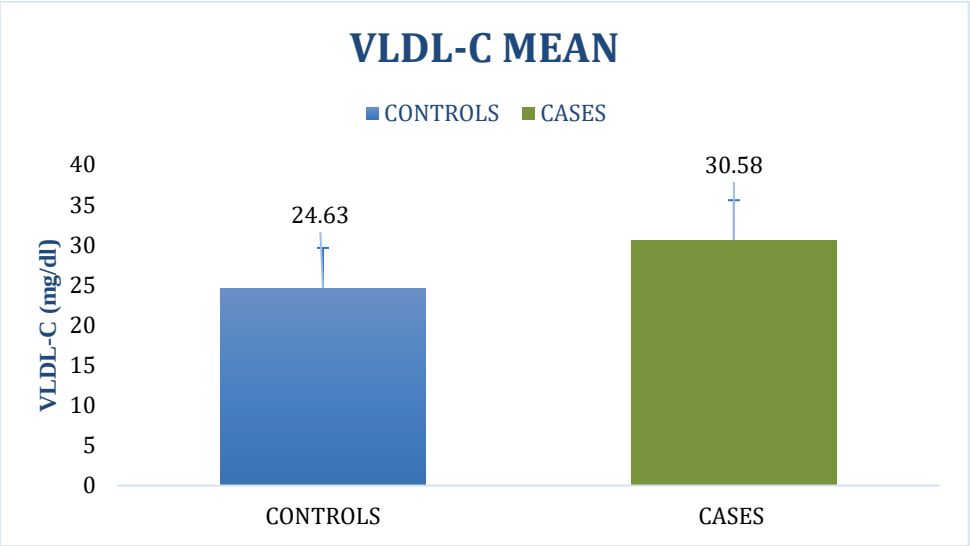

Figure 8. Comparison of VLDL-C in cases and controls.

Fasting blood sugar

In patients of hypothyroidism compared to control subjects, FBS are considerably higher (p=0.0343)

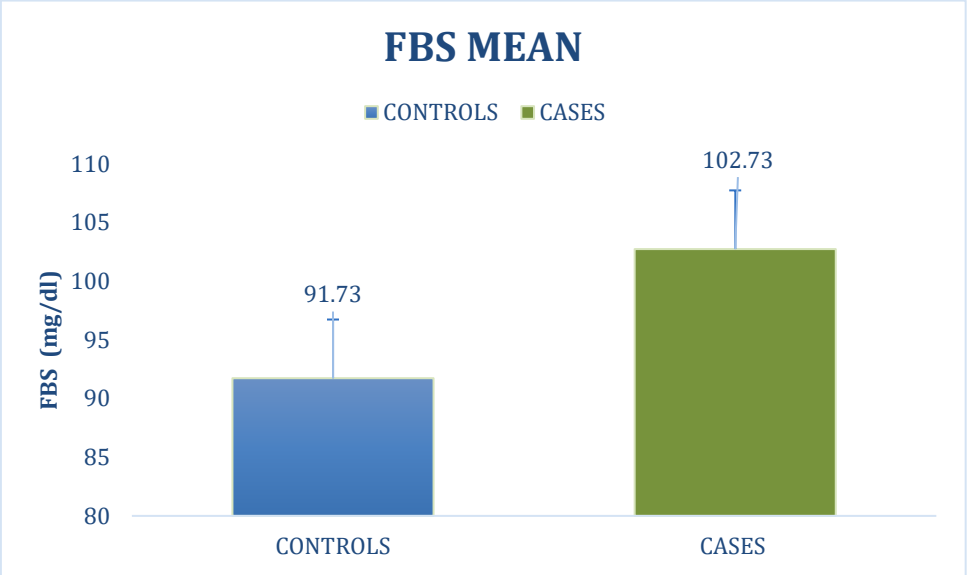

Figure 9. Comparison of FBS in cases and controls.

Waist Circumference

When compared to control persons, in patients of hypothyroidism, WC is considerably higher (p=0.0001).

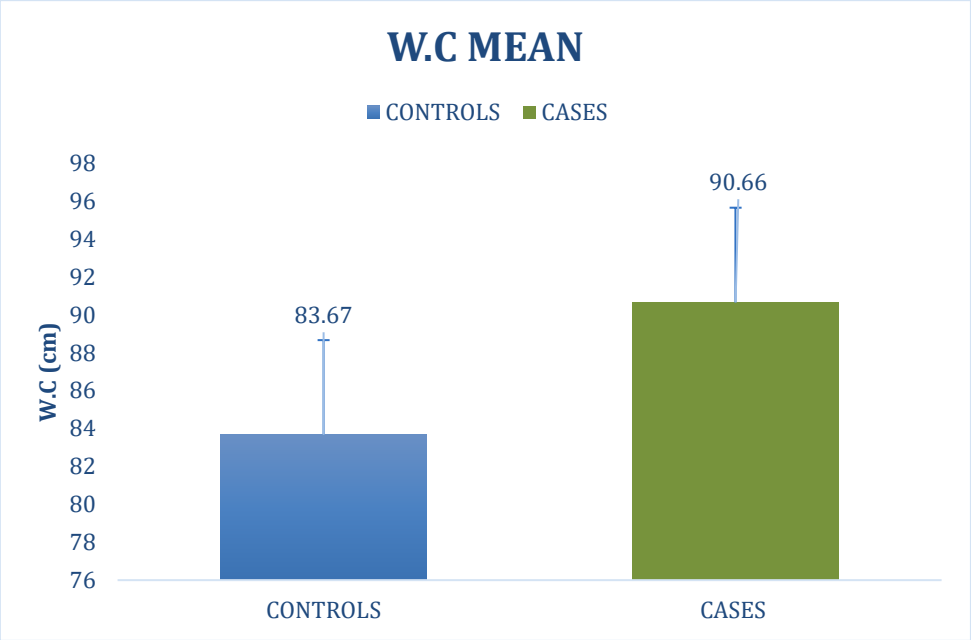

Figure 10. Comparison of W.C. in cases and controls.

Blood pressure (systolic)

When compared to control persons, in patients of hypothyroidism, SBP is considerably higher (p=0.0001).

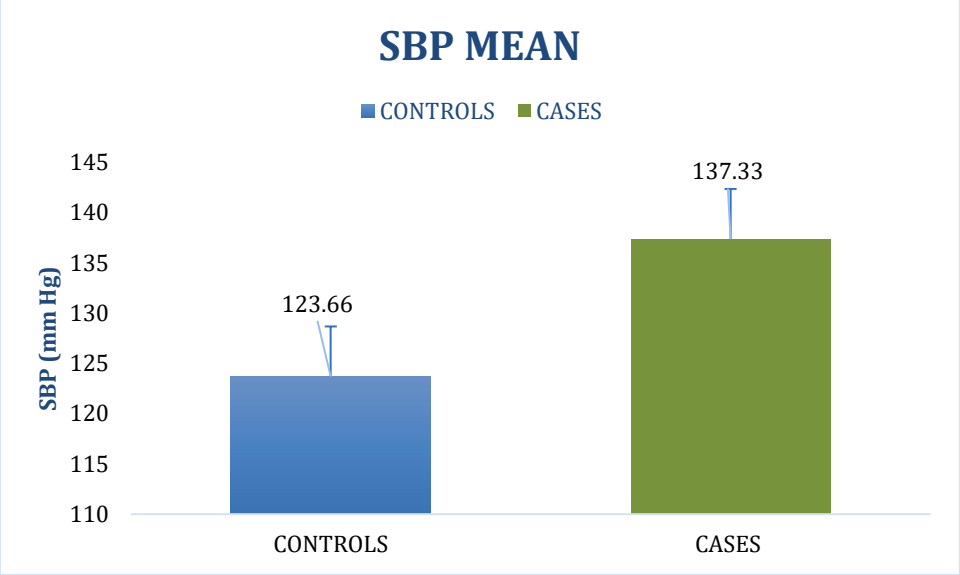

Figure 11. Comparison of SBP in cases and controls.

Blood pressure (diastolic)

When compared to control persons, in patients of hypothyroidism, DBP is considerably higher (p=0.0001).

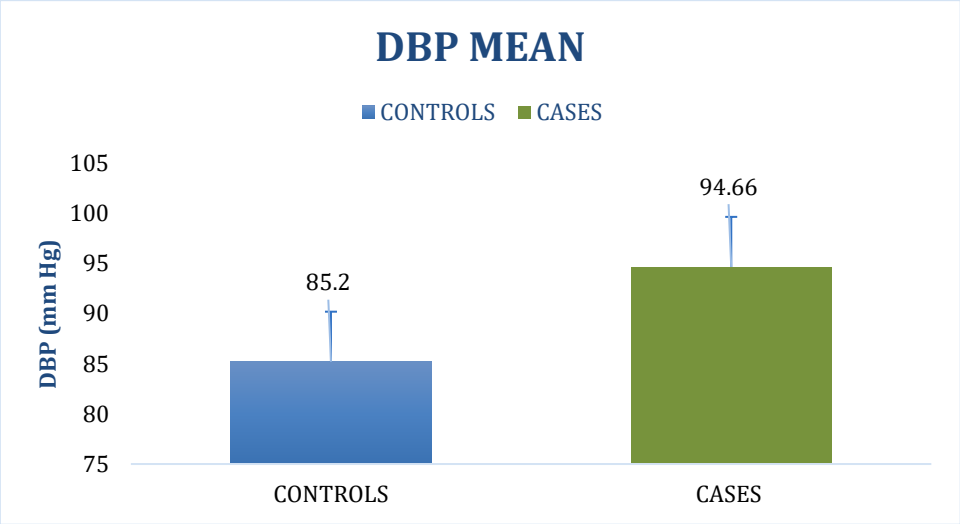

Figure 12. Comparison of DBP in cases and controls.

T3 LEVEL

When compared to control persons, in patients of hypothyroidism, T3 is considerably lower (p=0.0151).

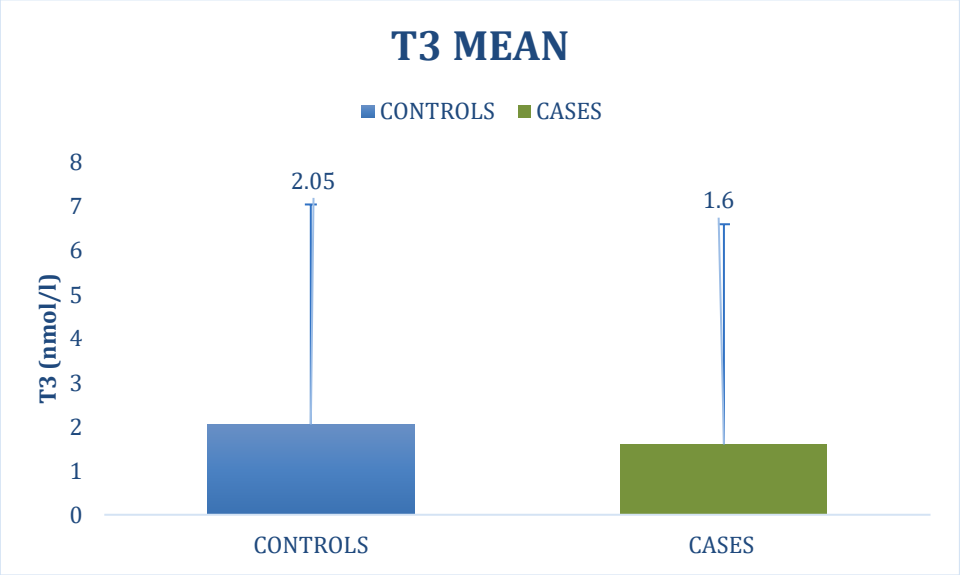

Figure 13. Comparison of T3in cases and controls.

T4 LEVEL

When compared to control persons, in patients of hypothyroidism, T4 is considerably lower (p=0.0004).

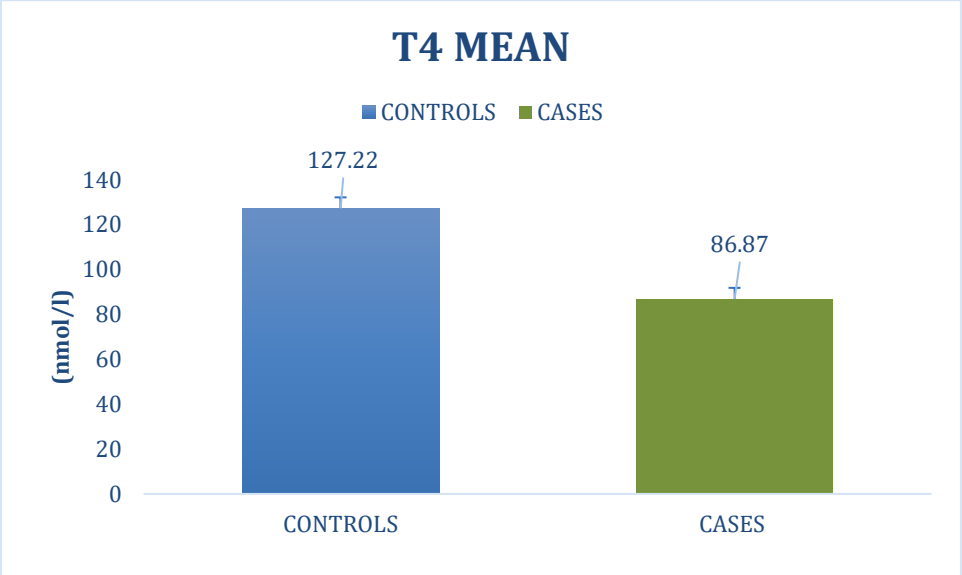

Figure 14. Comparison of T4 in cases and controls.

TSH LEVEL

When compared to control persons, in patients of hypothyroidism, TSH is considerably higher (p=0.0001).

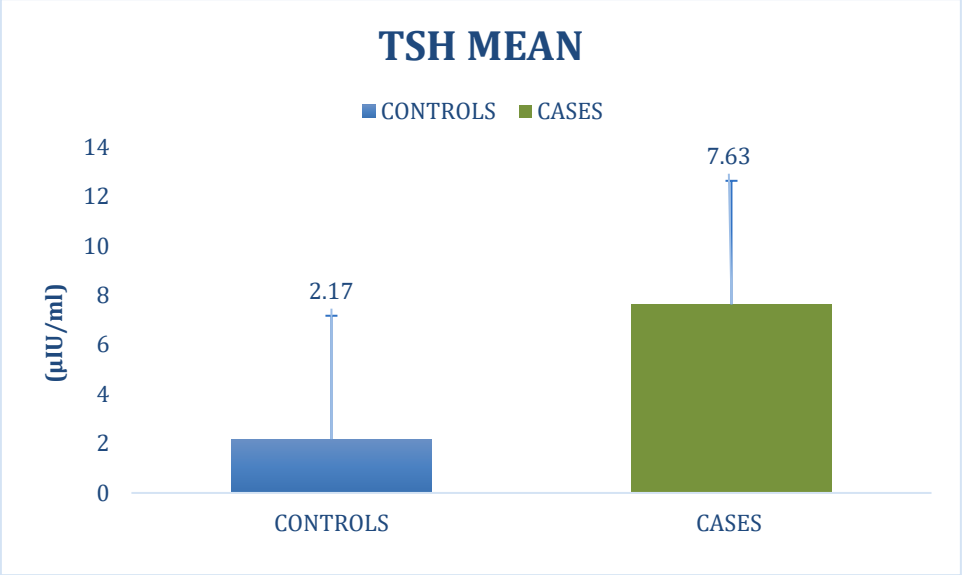

Figure 15. Comparison of TSH in cases and controls.

Age has shown a significant positive correlation with WC ($r = 0.400$, $p<0.05$), FBS ($r = 0.827$, $p<0.01$), TSH ($r = 0.553$, $p<0.01$), TC ($r = 0.598$, $p<0.01$), TG ($r = 0.534$, $p<0.01$), LDL-C ($r = 0.464$, $p<0.05$), VLDL-C ($r = 0.533$, $p<0.01$), SBP ($r = 0.812$, $p<0.01$) & DBP ($r = 0.831$, $p<0.01$) among cases.

BMI has shown a significant positive correlation with WC ($r = 0.833$, $p<0.01$), FBS ($r = 0.412$, $p<0.05$), T3 ($r = 0.389$, $p<0.05$), T4 ($r = 0.558$, $p<0.01$), TC ($r = 0.476$, $p<0.01$), LDL-C ($r = 0.386$, $p<0.05$), SBP ($r = 0.619$, $p<0.01$) & DBP ($r = 0.573$, $p<0.01$) among cases.

WC has shown a significant positive correlation with FBS ($r = 0.0.399$, $p<0.05$), T3 ($r = 0.575$, $p<0.01$), T4 ($r = 0.670$, $p<0.01$), TC ($r = 0.602$, $p<0.01$), HDL-C ($r = 0.551$, $p<0.01$), LDL-C ($r = 0.407$, $p<0.05$), SBP ($r = 0.780$, $p<0.01$) & DBP ($r = 0.744$, $p<0.01$) among cases.

FBS has shown a significant positive association with TSH ($r = 0.461$, $p<0.01$), TC ($r = 0.579$, $p<0.01$), TG ($r = 0.383$, $p<0.05$), LDL-C ($r = 0.487$, $p<0.01$), VLDL-C ($r = 0.383$, $p<0.05$), SBP ($r = 0.743$, $p<0.01$) & DBP ($r = 0.743$, $p<0.01$) among cases.

T3 has shown a significant positive correlation with T4 ($r = 0.422$, $p<0.05$), TC ($r = 0.445$, $p<0.05$), LDL-C ($r = 0.388$, $p<0.05$), SBP ($r = 0.376$, $p<0.05$) & DBP ($r = 0.363$, $p<0.05$) among cases.

T4 has shown a significant positive correlation with HDL-C ($r = 0.638$, $p<0.01$), SBP ($r = 0.442$, $p<0.05$) & DBP ($r = 0.381$, $p<0.05$) among cases.

TSH has shown a significant positive correlation with SBP ($r = 0.377$, $p<0.05$) & DBP ($r = 0.406$, $p<0.05$) among cases.

TC has shown a significant positive correlation with TG ($r = 0.432$, $p<0.05$), LDL-C ($r = 0.893$, $p<0.01$), VLDL-C ($r = 0.431$, $p<0.05$), SBP ($r = 0.766$, $p<0.01$) & DBP ($r = 0.767$, $p<0.01$) among cases.

TG has shown a significant positive correlation with VLDL-C ($r = 1.000$, $p<0.01$), SBP ($r = 0.463$, $p<0.01$) & DBP ($r = 0.476$, $p<0.01$) among cases.

LDL-C has shown a significant positive correlation with SBP ($r = 0.533$, $p<0.01$) & DBP ($r = 0.552$, $p<0.01$) among cases.

VLDL-C has shown a significant positive correlation with SBP ($r = 0.462$, $p<0.01$) & DBP ($r = 0.475$, $p<0.01$) among cases.

SBP has shown a significant positive correlation with DBP ($r = 0.978$, $p<0.01$) among cases.

Table 2: Correlation analysis between different variables among cases.

Variables	Age (Year)	BMI (kg/m2)	WC (cm)	FBS (mg/dl)	T3 (nmol/l)	T4 (nmol/l)	TSH (µIU/ml)	TC (mg/dl)	TG(mg/dl)	HDL-C(mg/dl)	LDL-C(mg/dl)	VLDL-C(mg/dl)	SBP (mm Hg)	DBP (mm Hg)
Age (Year)	1	0.348	**0.400***	**0.827****	0.028	0.189	**0.553****	**0.598****	**0.534****	-0.055	**0.464****	**0.533****	**0.812****	**0.831****
BMI (kg/m2)		1	**0.833****	**0.412***	**.389***	**0.558****	0.086	**0.476****	-0.042	0.334	**0.386***	-0.039	**0.619****	**0.573****
WC (cm)			1	**0.399***	**0.575****	**0.670****	0.164	**0.602****	0.079	**0.551****	**0.407***	0.078	**0.780****	**0.744****
FBS (mg/dl)				1	0.174	0.123	**0.461****	**0.579****	**0.383***	0-.031	**0.487****	**0.383***	**0.743****	**0.743****
T3 (nmol/l)					1	**0.422***	0.026	**0.445***	-0.069	0.314	**0.388***	-0.068	**0.376***	**0.363***
T4 (nmol/l)						1	0.048	0.304	0.071	**0.638****	0.067	0.072	**0.442***	**0.381***
TSH (µIU/ml)							1	0.346	0.310	-0.049	0.278	0.305	**0.377***	**0.406***
TC (mg/dl)								1	**0.432***	0.137	**0.893****	**0.431***	**0.766****	**0.767****
TG(mg/dl)									1	0.007	0.126	**1.000****	**0.463****	**0.476****
HDL-C(mg/dl)										1	-0.198	0.009	0.331	0.276
LDL-C(mg/dl)											1	0.125	**0.533****	**0.552****
VLDL-C(mg/dl)												1	**0.462****	**0.475****
SBP (mmHg)													1	**0.978****
DBP (mmHg)														1

**p<0.05 was considered statistically significant.*

Data was represented as Mean ± SD (Standard deviation).

BMI: Body mass index, WC: Waist circumference, FBS: Fasting blood sugar, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid stimulating hormone, TC: Total cholesterol, TG: Triglyceride, HDL-C: High-density lipoprotein-cholesterol, LDL-C: Low-density lipoprotein-cholesterol, VLDL-C: Very Low-density lipoprotein-cholesterol, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

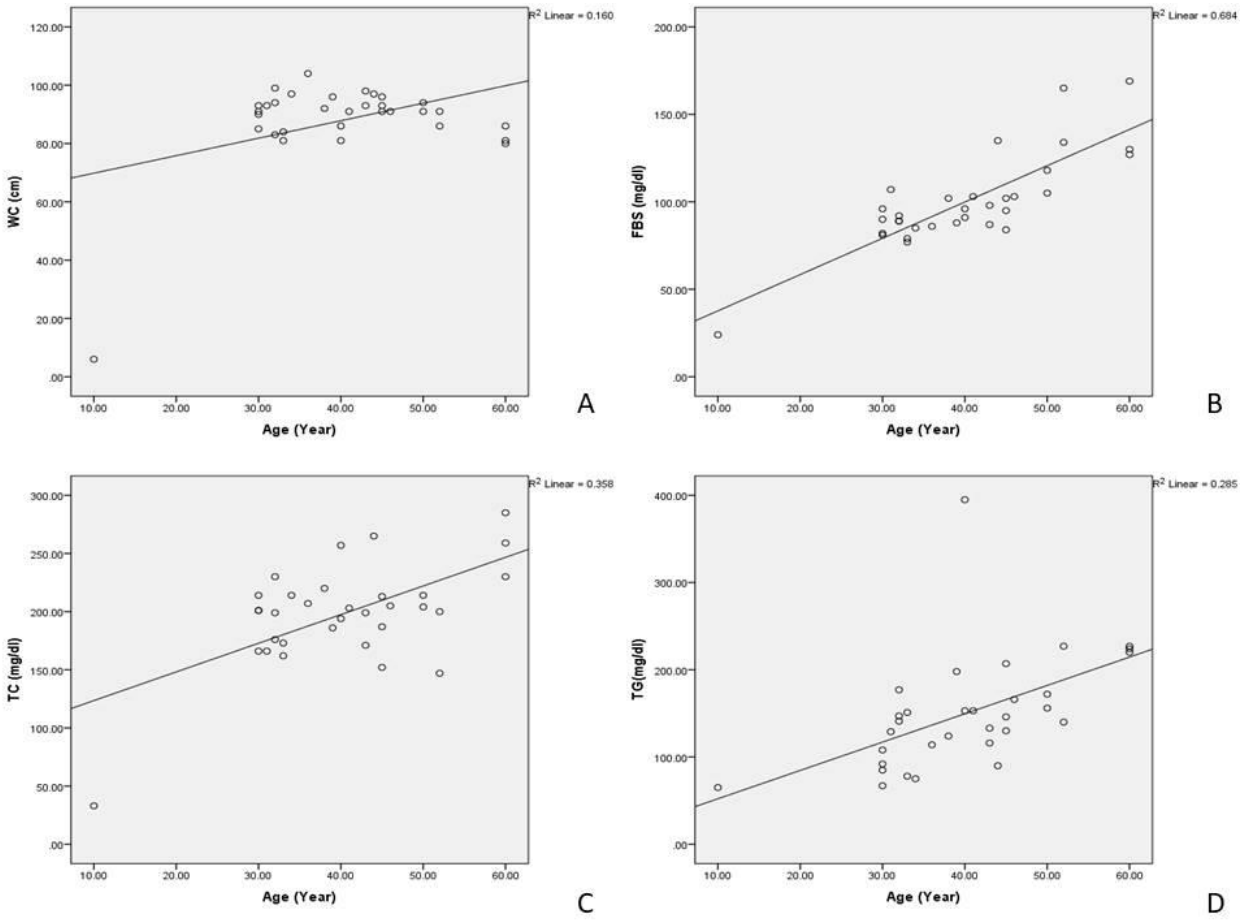

Figure.16.1: Correlation of Age, WC, FBS, TC &TG among cases.

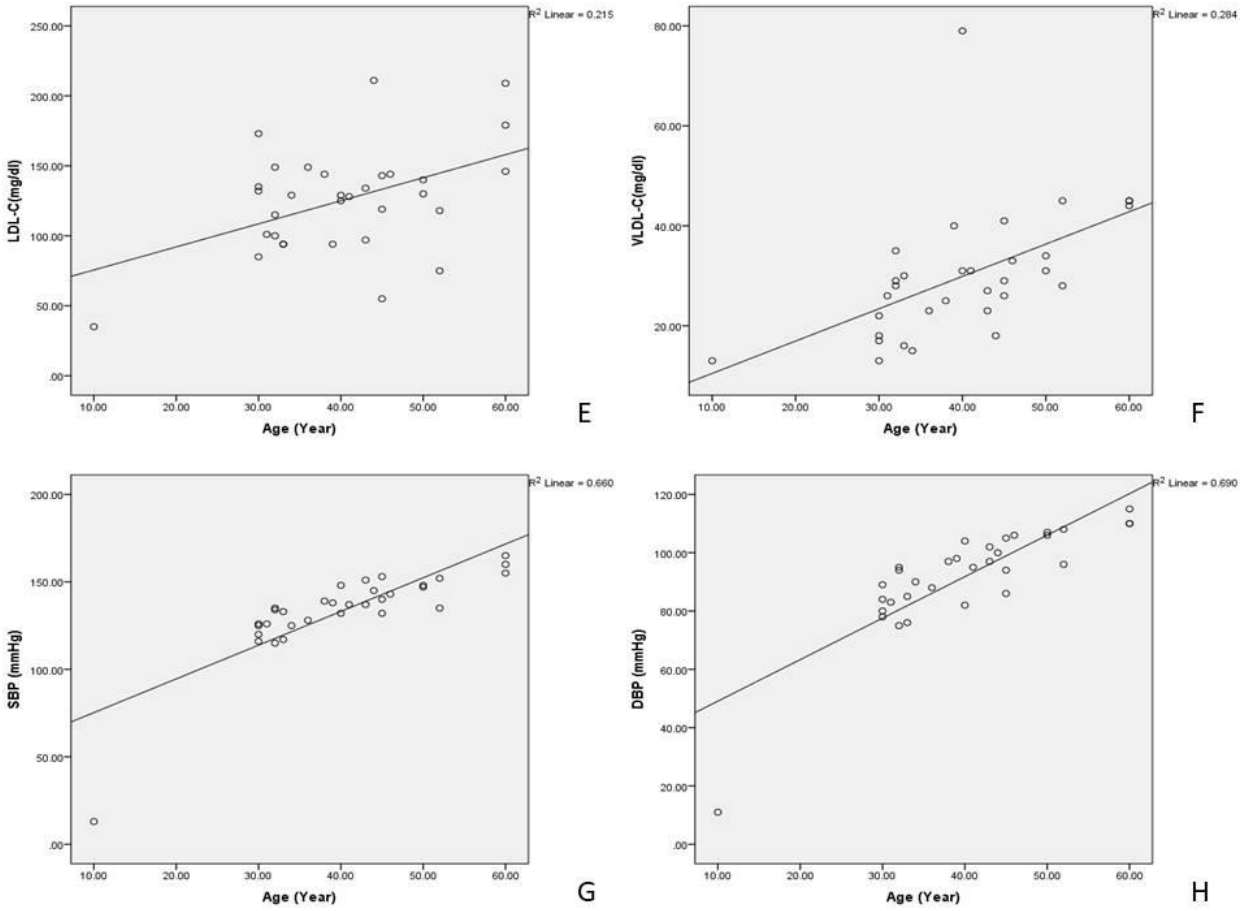

Figure.16.2: Correlation of Age, LDL-C, VLDL-C, SBP & DBP among cases.

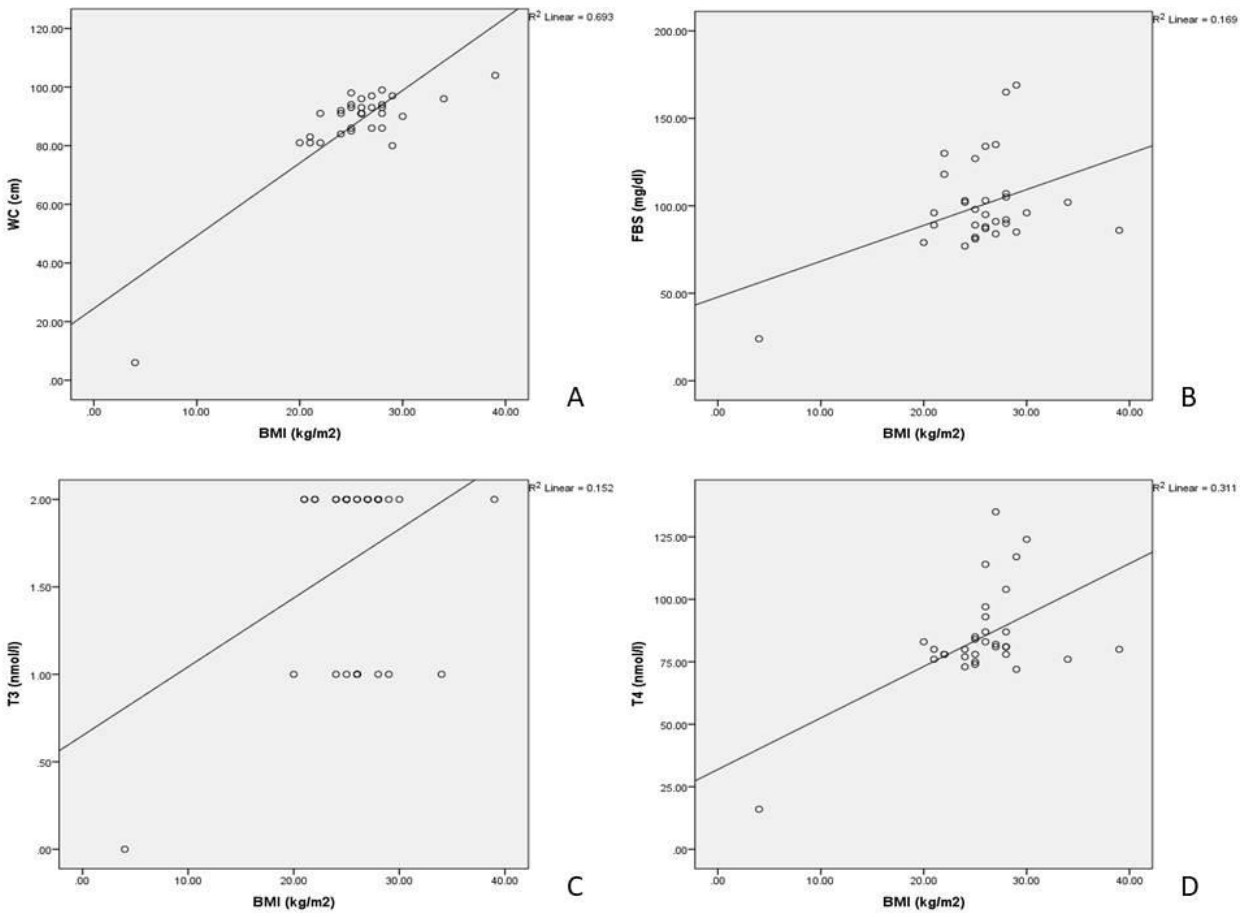

Figure.17.1: Correlation of BMI, WC, FBS, T3 & T4 among cases.

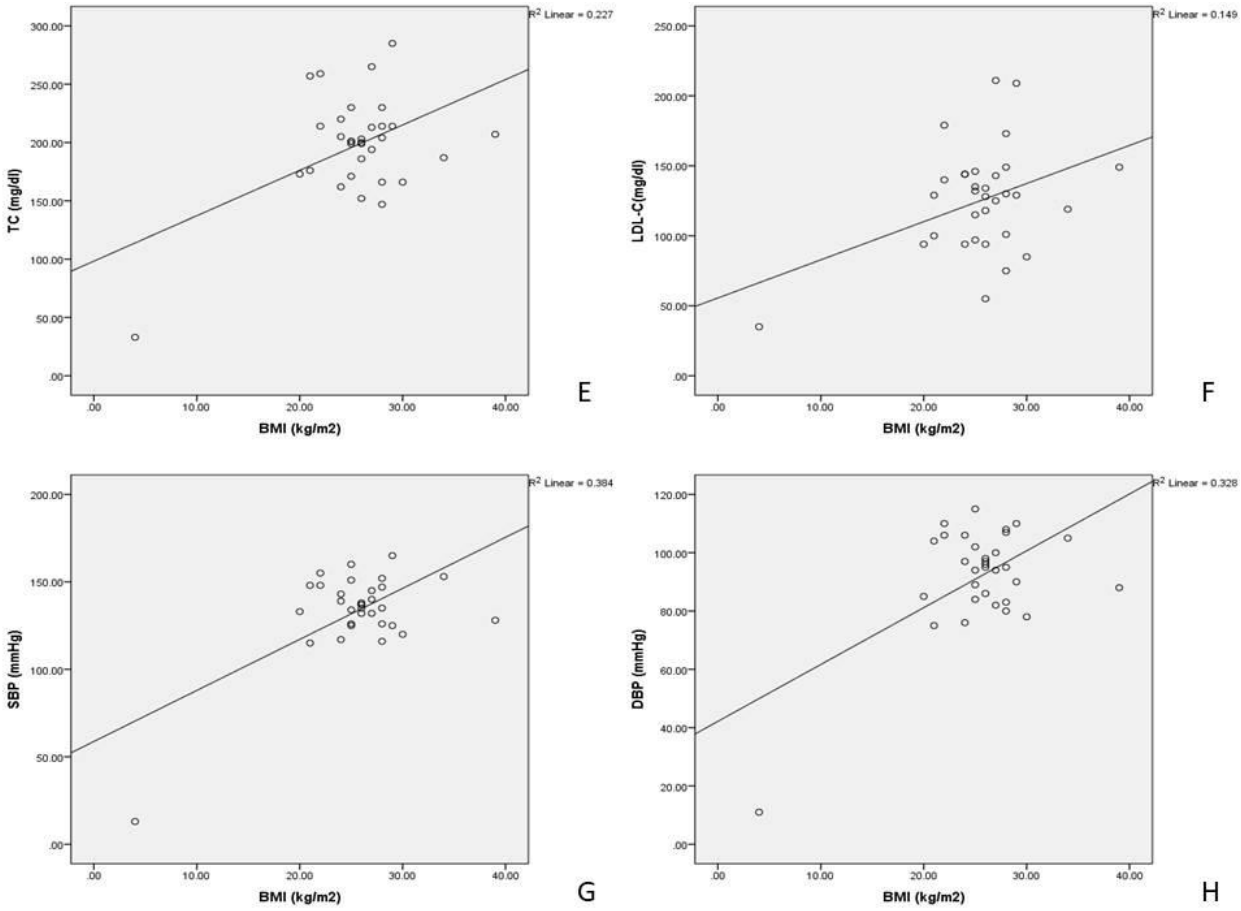

Figure.17.2: Correlation of BMI, TC, LDL-C, SBP & DBP among cases.

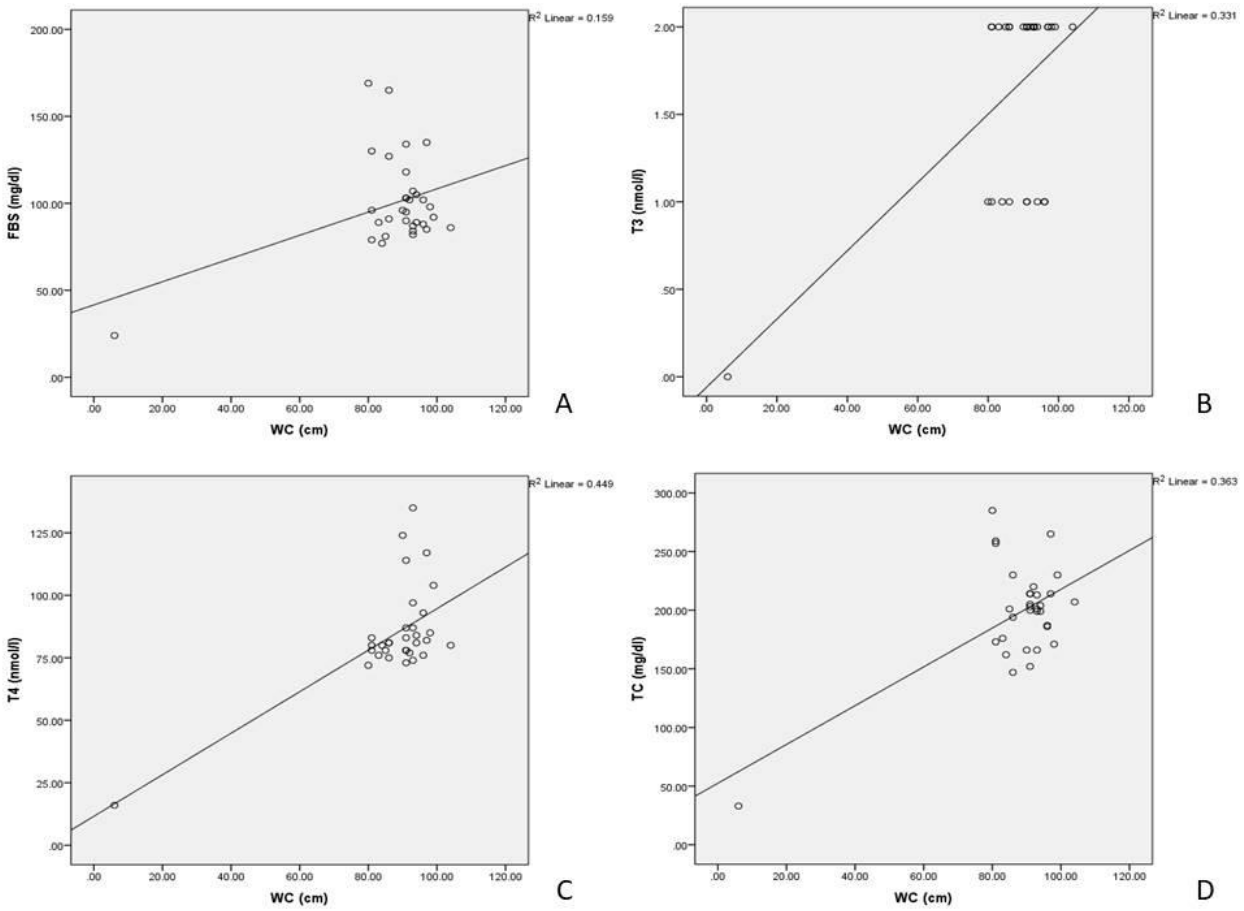

Figure.18.1: Correlation of WC, FBS, T3, T4 & TC among cases.

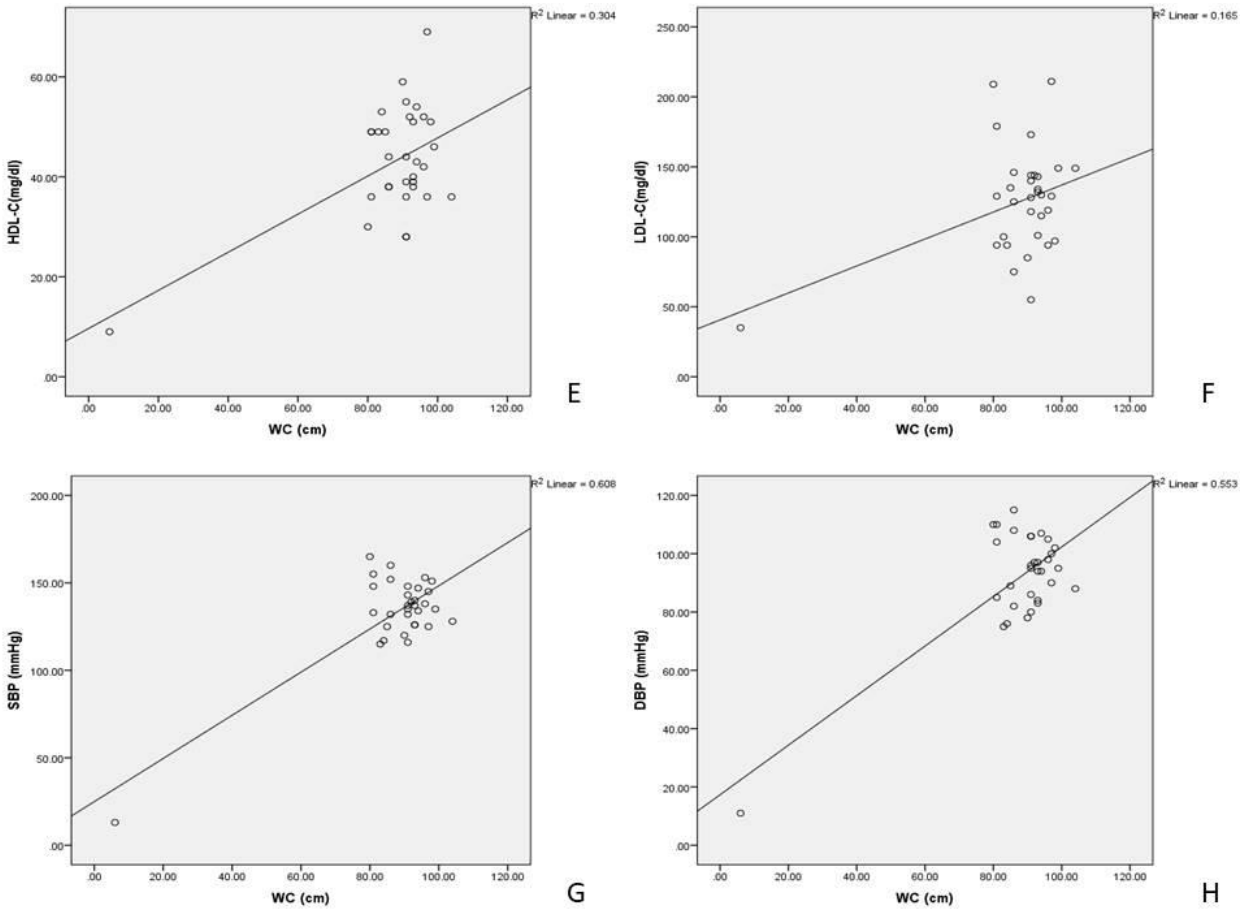

Figure.18.2: Correlation of WC, HDL-C, LDL-C, SBP & DBPamong cases.

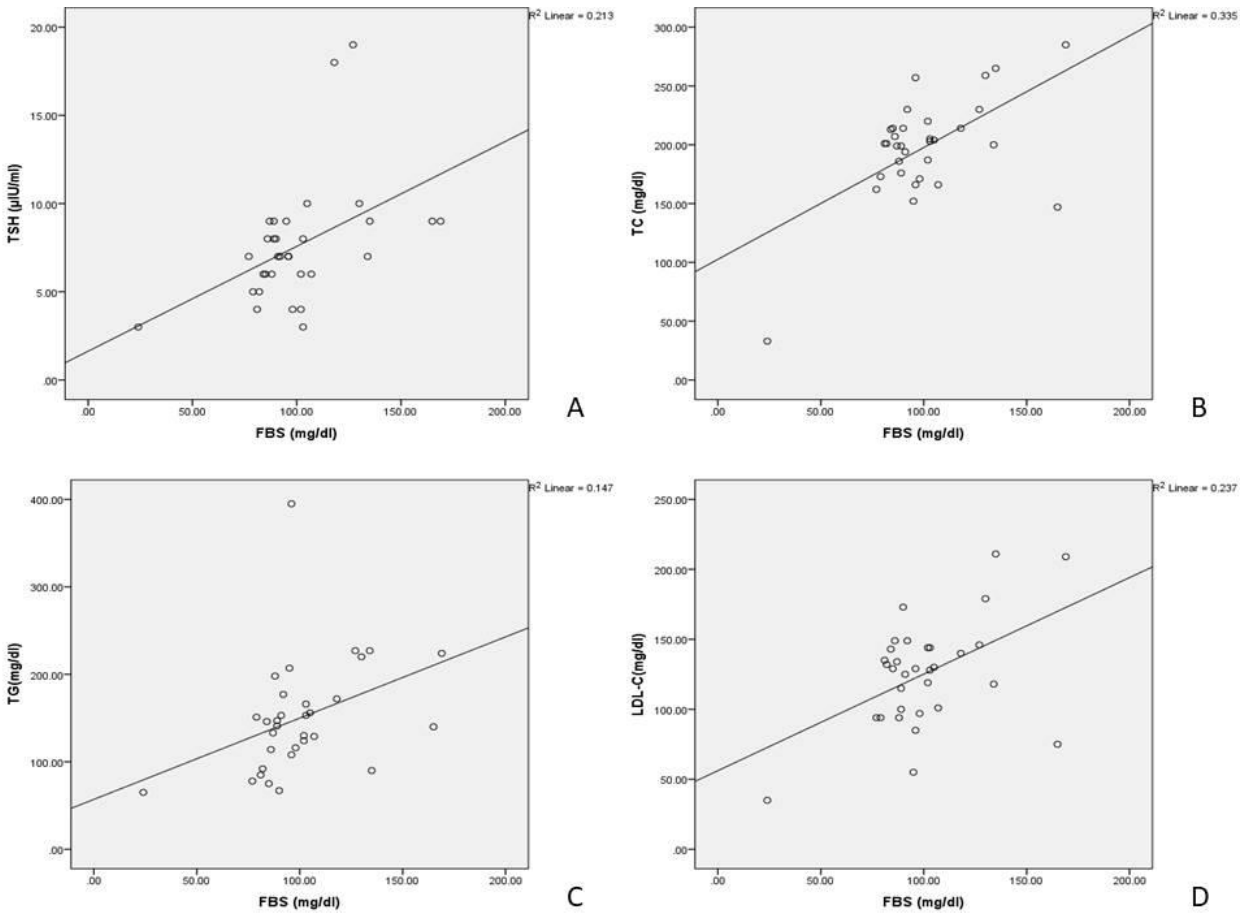

Figure.19.1: Correlation of FBS, TSH, TC, TG & LDL-C among cases.

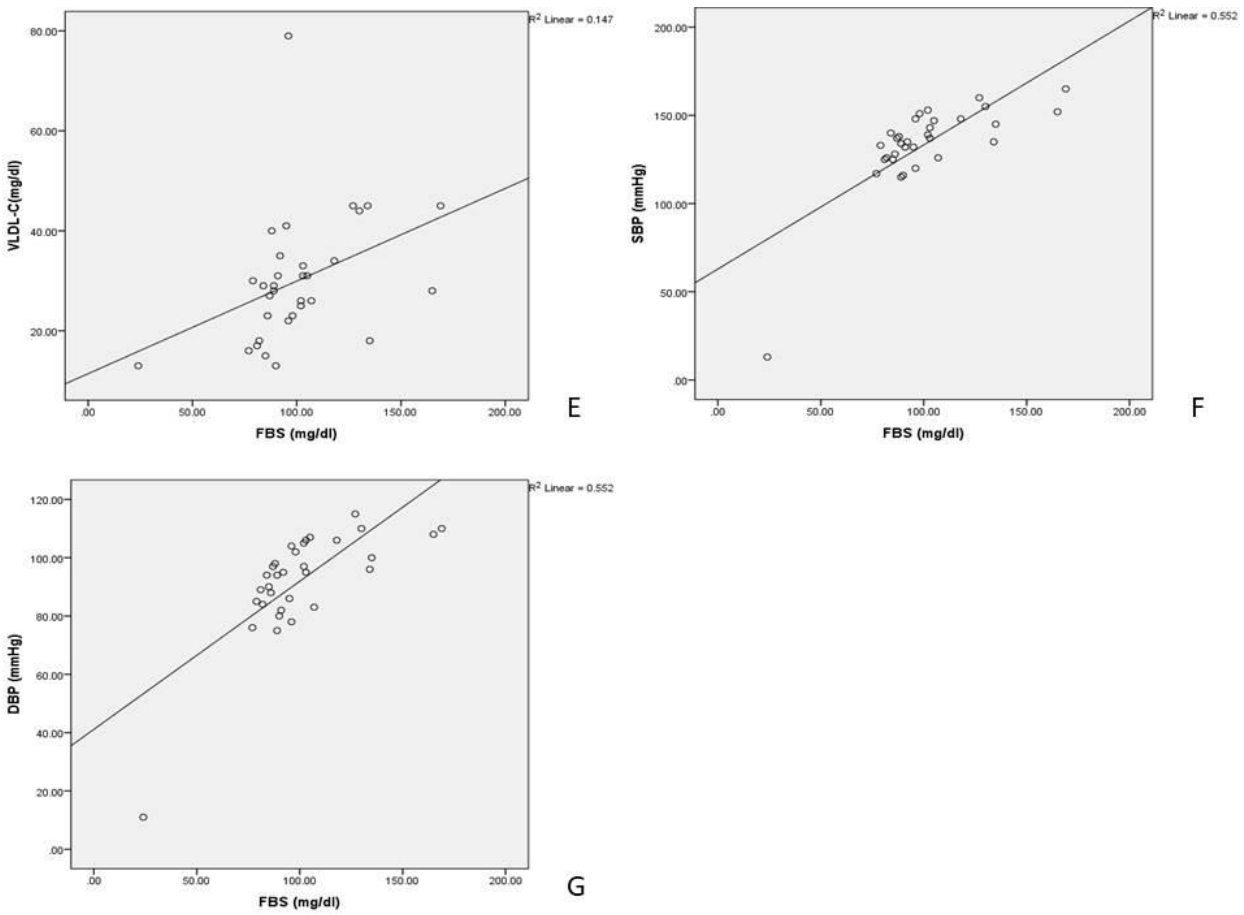

Figure.19.2: Correlation of FBS, VLDL-C, SBP & DBP among cases.

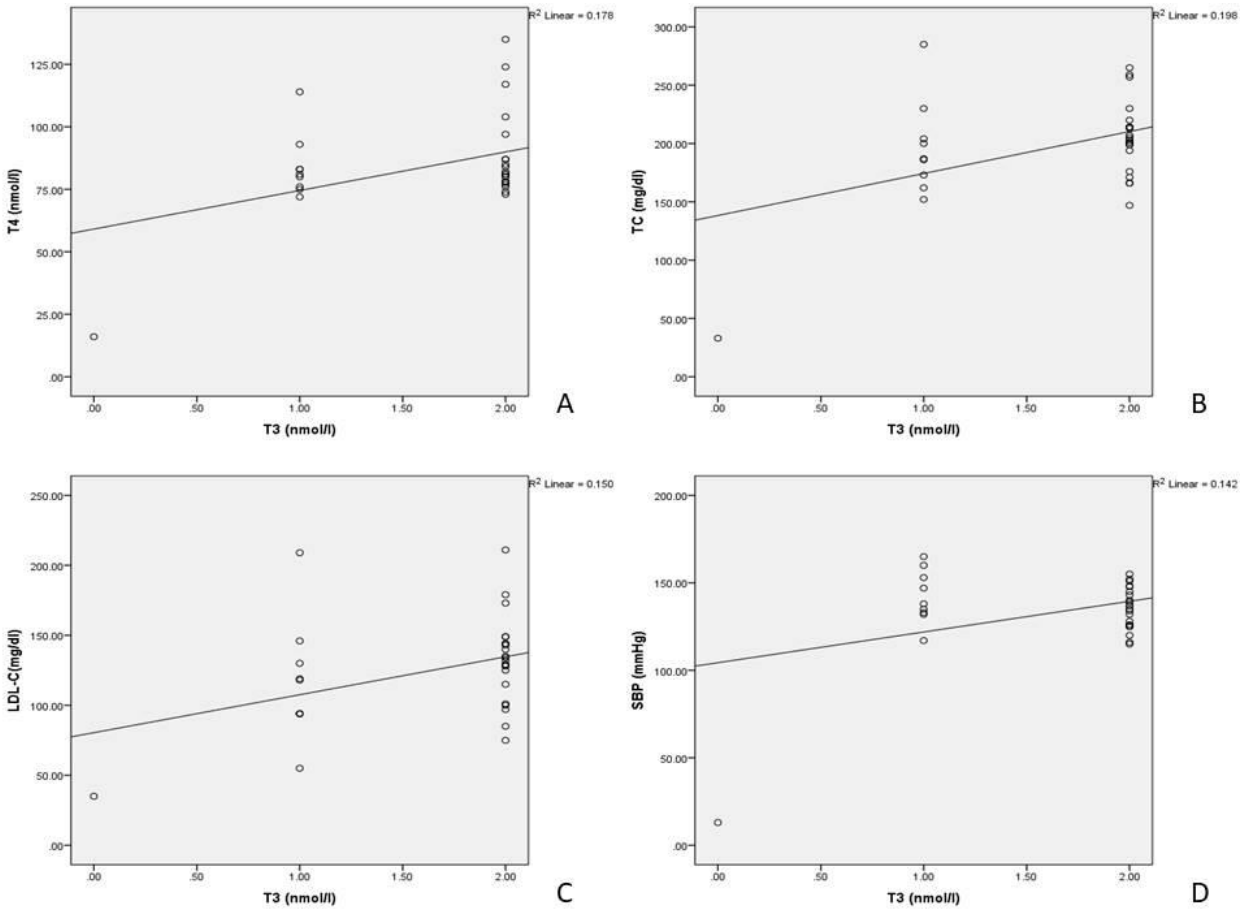

Figure.20: Correlation of T3, T4, TC, LDL-C & SBP among cases.

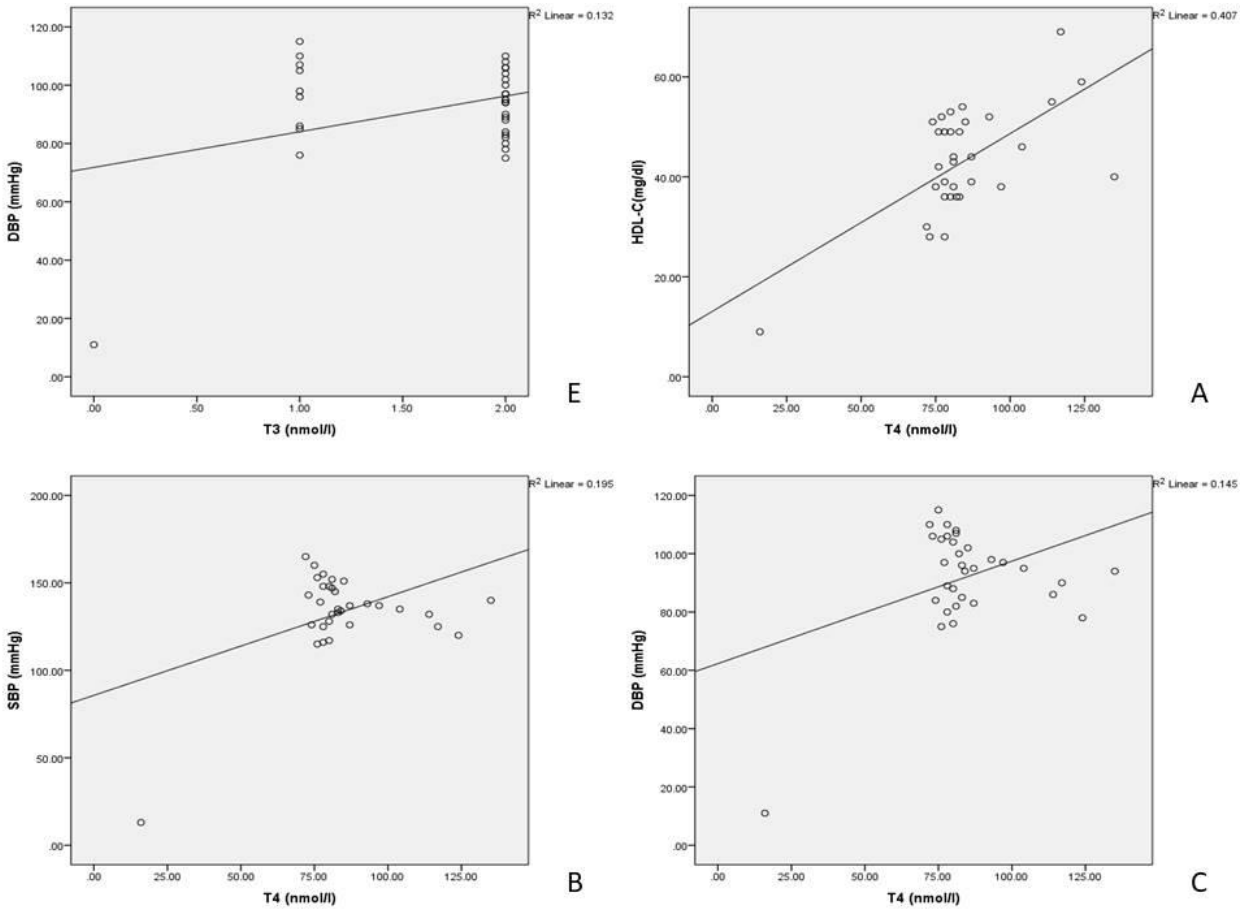

Figure.21: Correlation of T3 with T4 and correlation of T4, HDL-C, SBP & DBP among cases.

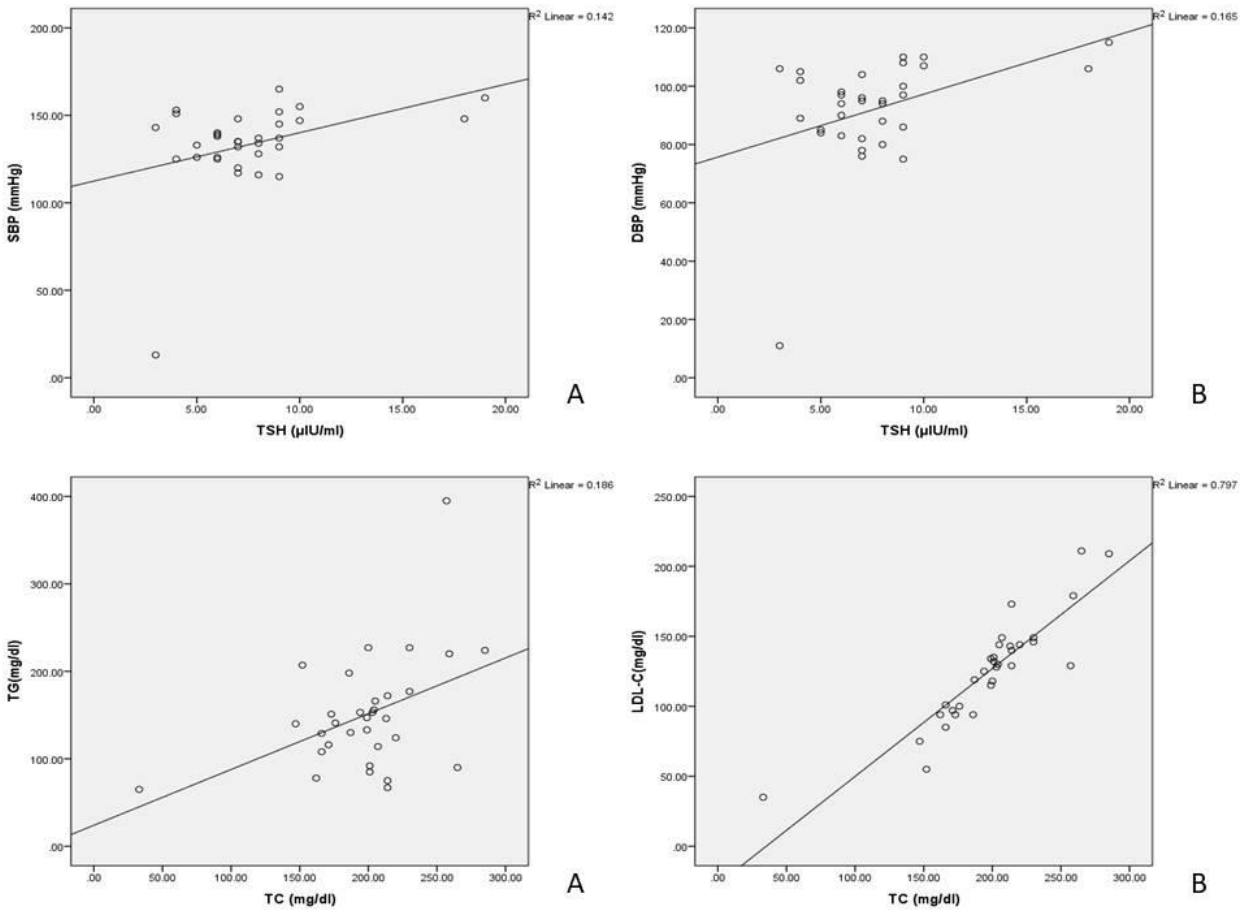

Figure.22: Correlation of TSH, SBP & DBP and correlation of TC, TG & LDL-C among cases.

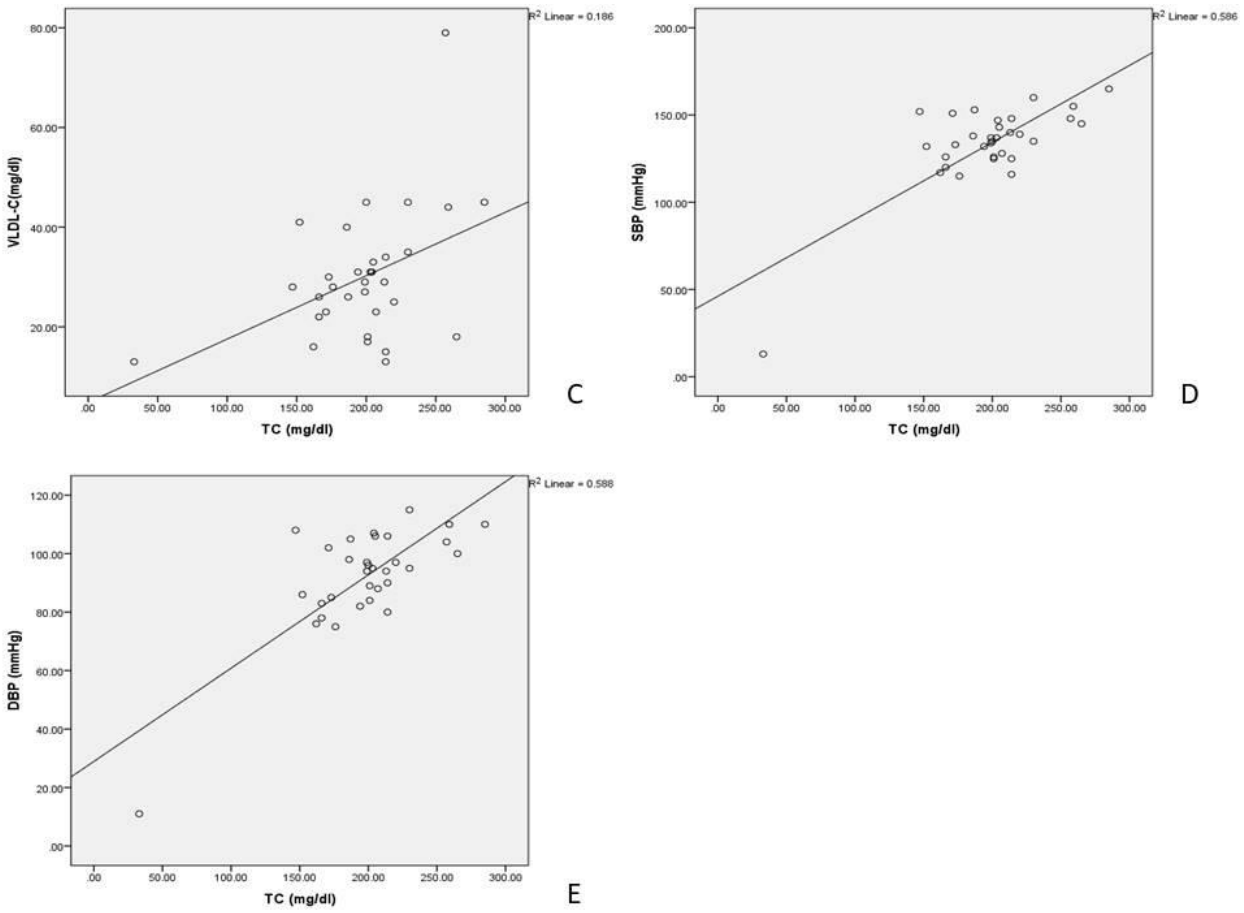

Figure.23: Correlation of TC, VLDL-C, SBP & DBP among cases.

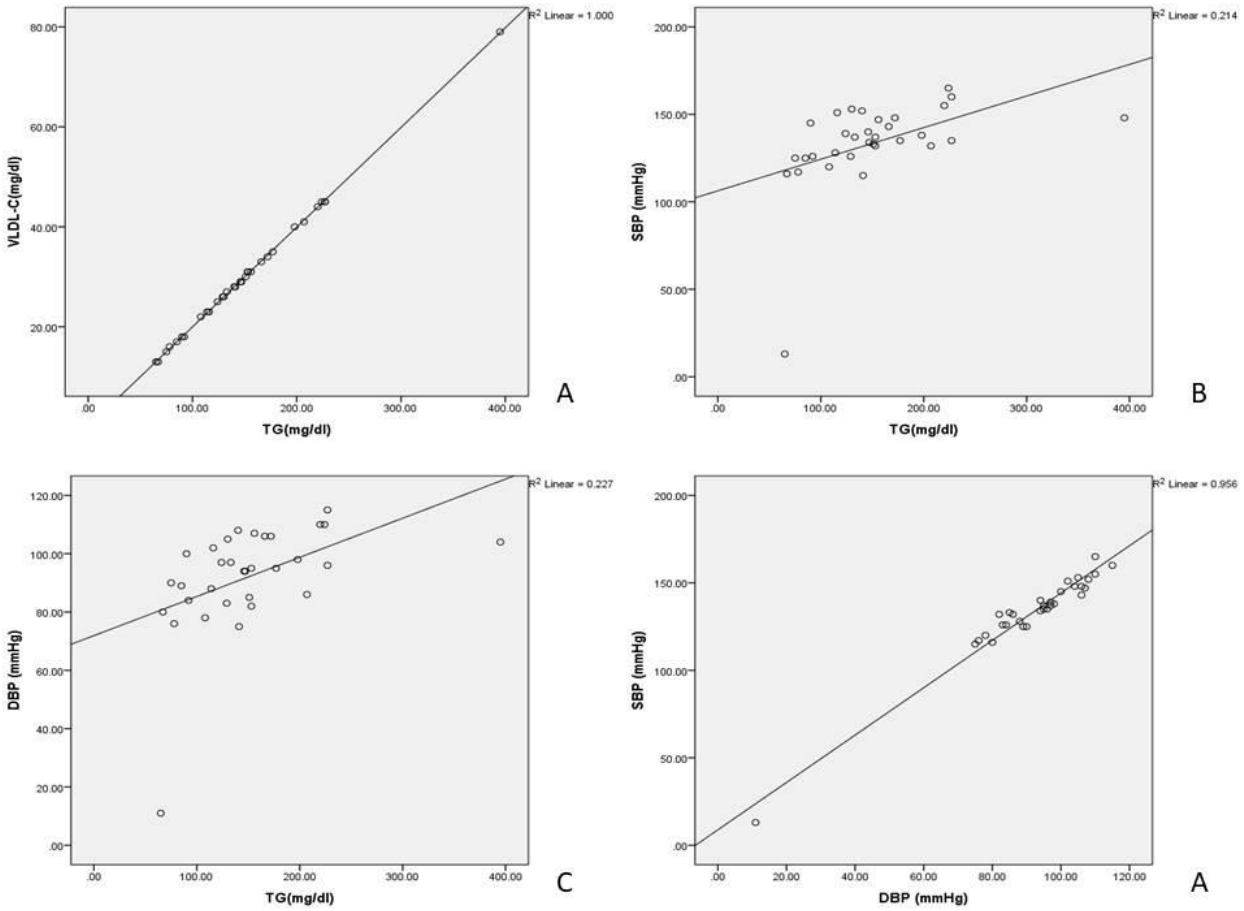

Figure.24: Correlation of TG, VLDL-C, SBP & DBP and between SBP & DBP among cases.

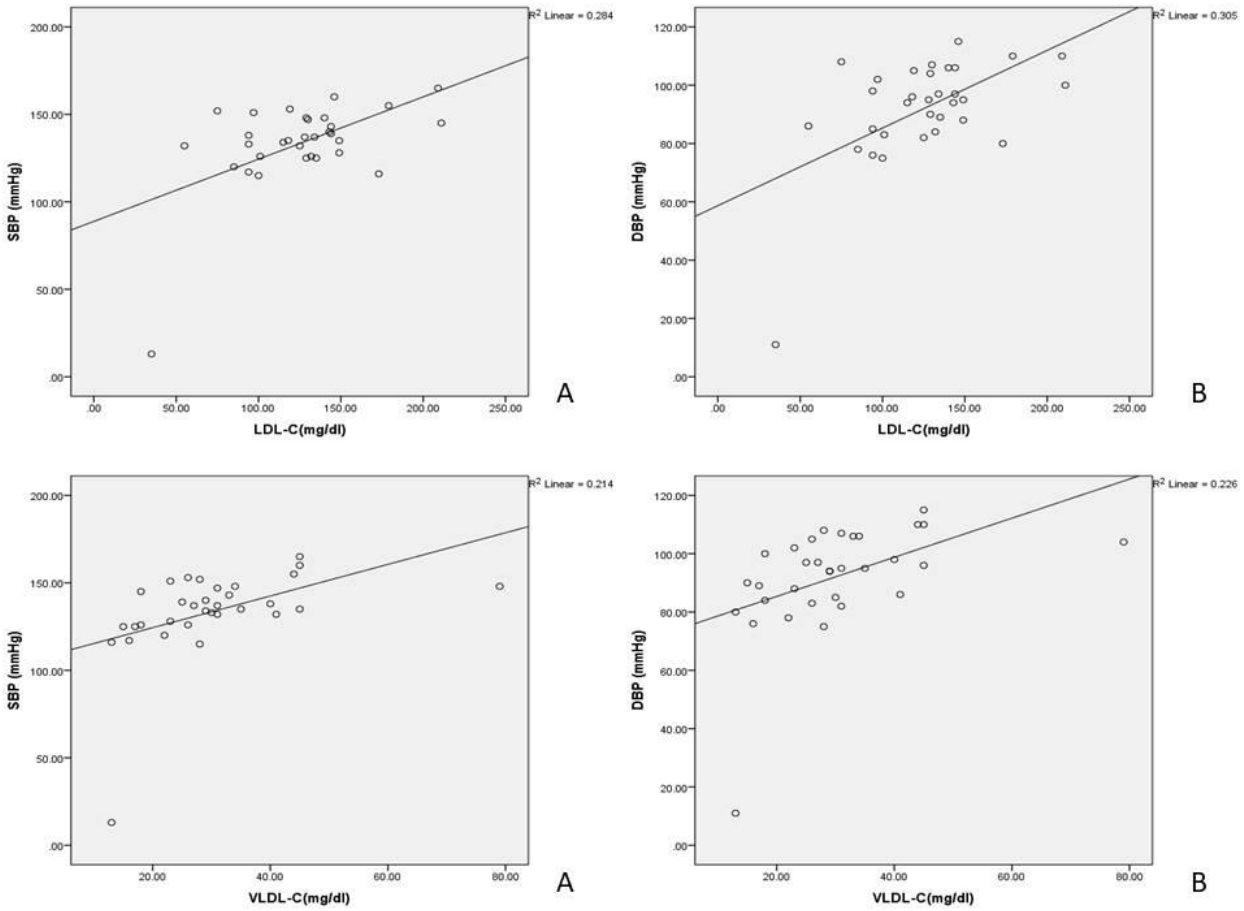

Figure.25: Correlation of LDL-C, SBP & DBP and correlation of VLDL-C, SBP & DBP among cases.

DISCUSSION

DISCUSSION

Result showed that mean of BMI, WC, FBS, TSH, TC, TG, LDL-C, VLDL-C, SBP, and DBP were significantly elevated in cases than controls. However, mean of T3, T4, and HDL-C was found significantly low in cases than controls. Correlation analysis has shown that lipid abnormalities were significantly associated with obesity and hypertension in patients with hypothyroidism.

Gutch et al reported that levels of serum LDL-C, VLDL-C, TG, TC, and TSH were found significantly elevated in cases than controls. However, levels of HDL-C, T3, and T4 were found significantly low in cases than controls. It was further suggested that thyroid functions and obesity are interlinked because thyroid hormones regulate the metabolic pathways and energy expenditure **(Gutch et al 2017).**

A study reported that 96.1% of hypothyroid patients have dyslipidemia and mostly have low HDL-C and high TG. It was further suggested that hypothyroidism with obesity is a significant risk factors for dyslipidemia **(Alarcón-González et al 2021).**

It was reviewed that lipid abnormalities and elevated TSH has strongly associated. The degree of lipid abnormality is directly proportional to the degree of elevation of TSH. It was further suggested that age, gender, and BMI may influence the pattern of the lipid abnormalities. TSH mainly elevated with increase of LDL-C in patients with hypothyroidism. This indicated that lipid abnormalities are associated with cardiometabolic risk factors in patients with hypothyroidism. It was further recommended that clinical management of thyroid hormones and lipid profile are important factors to reduce/reverse hypothyroidism-associated cardiometabolic risk factors **(Jonklaas 2023).**

Cappola et al reviewed that thyroid hormone T3 induces cholesterol biosynthesis initiation enzyme HMG-CoA reductase and up-regulates LDL-C receptor that slow down the clearance of LDL-C in patients with hypothyroidism. Thyroid hormones also affect activity of cholesterol degradation first step enzyme 7α-hydroxylase that regulates the rates of excretion of bile acid and fecal cholesterol. It was indicated that hypothyroidism is linked with elevated LDL-C and adverse effects in number, size, and oxidation of LDL-C **(Cappola et al 2019).**

Deficiency of T3 & T4 can increase TG levels by inhibiting the activity of enzyme lipoprotein lipase (Sinha et al 2018). A study reported that hypothyroidism patients who

have serum TSH (>10 mIU/L) also have high levels of small and dense LDL-C that has more atherogenic characteristics **(Saric et al 2017).**

In addition, a meta-analysis study indicated that hypothyroidism was linked with chronic heart disease (CHD) risk factors. This study further reported that patients with hypothyroidism who have serum TSH levels (≥10 mIU/L) were associated with CHD risk factors and who have serum TSH levels (≥7 mIU/L) were more prone to CHD-associated mortality **(Rodondi et al 2010).**

The incident of heart failure (biventricular) were found high in patients with untreated hypothyroidism who have serum TSH levels (≥10 mIU/L) because of abnormal hemodynamic functions. This study further suggested that thyroid hormone supplementation and restoration therapy may reverse the physiological abnormalities and maintain the hemodynamic functions of the heart **(Gencer et al 2012).**

A US population-based cohort study reported that elevated serum TSH were associated with increased cardiometabolic risk and all-cause mortality (Inoue et al 2020). It was suggested that development of atherosclerotic cardiovascular disease (CVD) in hypothyroidism patients is mediated by hyperlipidemia. Because hyperlipidemia is strongly influenced by changes in serum T3, T4, and TSH levels **(Su et al 2022).**

Present study showed that SBP and DBP have shown a significant positive correlation with BMI and WC. An epidemiological study conducted on the West-Bengal, India urban adult academic professions reported that sedentary lifestyle increases the risk factors for hypertension, diabetes, hypothyroid in obese individuals **(Ghosh et al 2023).**

In addition, hypothyroid patients have shown reduction in vascular resistance. Abnormalities in thyroid hormones and blood pressure may be leading cause mechanisms in renal functions alternations in hypothyroid patients **(Allam et al 2023).**

Limitations of the study

The study duration was only 06 months and sample size was only 60 (30 diagnosed hypothyroidism patients and 30 age-matched healthy controls). Further study are required to strengthen the hypothesis that hypothyroidism is strongly associated with cardiometabolic risk factors.

SUMMARY

AND

CONCLUSIONS

SUMMARY

Introduction: Hypothyroid can be defined as elevated levels of TSH and reduced levels of T3 and T4. Hypothyroid may affect the metabolic activities and energy expenditure. Abnormal metabolic activities may cause obesity, dyslipidemia, hypertension, and hyperglycemia. These all are the risk factors for metabolic syndrome and cardiovascular disease. Several studies reported that hypothyroidism was associated with cardiometabolic risk, but results were inconsistent. **Aim:** It is aimed to determine the cardio metabolic risk factors in diagnosed cases of hypothyroidism and control subjects.

Objectives:

1. To determine the biochemical parameters; blood sugar and lipid profile in diagnosed cases of hypothyroidism and control subjects.
2. To determine demographic parameters; BMI, waist circumference and blood pressure in diagnosed cases of hypothyroidism and control subjects.
3. To find the correlation between demographic parameters and biochemical parameters in diagnosed cases of hypothyroidism and control subjects, if any.

Materials and Methods: In this case-control study, a total of 60 subjects (30 diagnosed cases of hypothyroidism and 30 age-matched healthy controls) were enrolled, aged between 30 to 65 years. A detailed medical, family and demographical history has been taken from each subject. Written consent has been taken from each subject. Subjects were enrolled as per the inclusion and exclusion criteria. Biochemical parameters such as FBS, Lipid profile, and Thyroid hormones were estimated by commercially available kit. Anthropometric parameters such as BMI, WC, SBP, and DBP were measured and recorded.

Results: Results showed that mean of BMI, WC, TC, TG, LDL-C, VLDL-C, TSH, SBP, and DBP were found significantly elevated in cases compared to controls ($p<0.001$). However, mean of HDL-C, T3, and T4 were found significantly decreased in cases compared to controls ($p<0.001$). Correlation analysis has shown that lipid abnormalities were significantly associated with obesity and hypertension in patients with hypothyroidism.

Conclusion: Result showed that mean of BMI, WC, FBS, TSH, TC, TG, LDL-C, VLDL-C, SBP, and DBP were significantly elevated in cases than controls. However, mean of T3, T4, and HDL-C was found significantly low in cases than controls. Correlation analysis has shown that lipid abnormalities were significantly associated with obesity and hypertension in patients with hypothyroidism that increase the cardiometabolic risk.

FLOW CHART OF RESEARCH PROJECT

Aim: It was aimed to determine the cardio metabolic risk factors in diagnosed cases of hypothyroidism and control subjects.

Material and Methods: In this case-control study, a total of 60 subjects (30 diagnosed cases of hypothyroidism and 30 age-matched healthy controls), aged between 30 to 65 years.

Biochemical parameters: FBS, Lipid profile, and Thyroid hormones.

Anthropometric parameters: BMI, WC, SBP, and DBP.

Results: Case

- Mean of FBS, TC, TG, LDL-C, VLDL-C, BMI, WC, SBP, and DBP were significantly elevated ($p<0.001$).
- Correlation analysis shown that lipid abnormalities were significantly associated with obesity and hypertension in patients with hypothyroidism that increase the cardiometabolic risk.

Results: Controls

- Mean of FBS, TC, TG, LDL-C, VLDL-C, BMI, WC, SBP, and DBP were significantly reduced ($p<0.001$).
- Control subjects were Non-obese, Normal blood sugar levels, normal blood pressure, and normal lipid profile and were at low cardiometabolic risk.

Conclusion: Hypothyroid patients were at greater risk to develop cardiometabolic diseases. Regular monitoring of hypothyroid patients is required to reduce the disease complications.

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ANNEXURE

Unique Identification No:

INTEGRAL INSTITUTE OF MEDICAL SCIENCES AND RESEARCH LUCKNOW -226026

INCLUSION AND EXCLUSION CRITERIA -CASES

Inclusion Criteria

S. N.	Criteria	YES	NO
1.	Diagnosed cases of hypothyroidism.		
2.	Subjects between the ages of 30 to 65 years.		
3.	Patients who will agree to sign the consent form.		

Exclusion Criteria

S.N.	Criteria	YES	NO
1.	History of any chronic diseases		
2.	Pregnant and lactating females		

Subject is eligible for the study, if all **INCLUSION** criteria are **YES** and all **EXCLUSION** Criteria are No.

INVESTIGATOR

STATEMENT

I have verified the data entered in the case report form and have determined that it is complete, accurate and compatible with the source documents

Investigator's name Investigator's signature Date

Unique Identification No

IDENTIFIERS- CASES

Registration No:

Contact No:

Name:

Father's Name /Husband's Name:

Address:

DEMOGRAPHICS- CASES

Age:

Sex: Male Female

Place of Residence: Urban Rural

Social / Economical Status: a) Upper b) Upper Middle c) Lower Middle

d) Upper Lower e) Lower

Education: a) Illiterate b) Primary c) Middle d) High School e) Intermediate

f) Graduation g) Post-graduation & above

ANTHROPOMETRIC PARAMETERS- CASES

Height (mts)

Weight (kgs)

Waist circumference (cm):

Body Mass Index (kg/ m^2):

Physical activity (Sedentary/Moderate/Active):

Unique Identification No:

INTEGRAL INSTITUTE OF MEDICAL SCIENCES AND RESEARCH LUCKNOW -226026

INCLUSION AND EXCLUSION CRITERIA -CONTROLS

Inclusion Criteria

S. N.	Criteria	YES	NO
1.	Apparently healthy individuals		
2.	Subjects within the age of 30 to 65 years		

Subject is eligible for the study, if all **INCLUSION** criteria are **YES** and all **EXCLUSION** Criteria are **No.**

INVESTIGATOR

STATEMENT

I have verified the data entered in the control report form and have determined that it is complete, accurate and compatible with the source documents

Investigator's name Investigator's signature Date

Unique Identification No:

IDENTIFIERS-CONTROL

Registration No:

Contact No:

Name:

Father's Name /Husband's Name:

Address:

DEMOGRAPHICS- CONTROL

Age:

Sex: Male Female

Place of Residence: Urban Rural

Social / Economical Status:

Education: a) Illiterate b) Primary c) Middle d) High School e) Intermediate

f) Graduation g) Post-graduation & above

ANTHROPOMETRIC PARAMETERS- CONTROL

Height (mts)

Weight (kgs)

Body Mass Index (kg/ m^2)

ANNEXURE I

CONSENT FORM

I……aged.....D/O/S/O.....R/O..... .....……here with state that I have been duly informed about the study titled **"ASSESSMENT OF CARDIOMETABOLIC RISK FACTORS IN DIAGNOSED PATIENTS OF HYPOTHYROIDISM AND CONTROL SUBJECTS",** its prospects and consequences. I hereby give informed and written consent for the collection of my blood sample for the above said study only.

INFORMED CONSENT FORM

- I, Mohammad Salman Research Scholar Medical Biochemistry IIMS&R Lucknow.
- I'm not associated with your treating doctor panel.
- You are not suffering from any critical illness or infectious disease and you are not undergoing any such treatment.
- For this study, I will take your 02 ml blood sample for the determination of blood sugar and lipid profile.
- The blood is only subjected for determination of blood sugar and lipid profile test, not else for the study.
- There will be no charges /fees/any consideration will be given or taken for the study.
- Your identity will be confidential and information and the result of your blood test will not be revealed to any other except you if you desire.
- The study is not going to hamper you if you refuse to participate.
- The study will not be beneficial for you but may improve the knowledge and understanding of the disease process and that knowledge may or not be helpful in future.
- After knowing all the above details, would you like to participate in our study? Yes/No

Signature/thumb impression of the Volunteer/Guardian: Signature of the Research Scholar:

अनुलग्नक ।

सहमति पत्र

मैं.....उम्र.....डी/ओ/एस/ओ.....आर/ओ.....
.....यहां यह बताते हुए कि मुझे "हाइपोथायरायडिज्म और नियंत्रण विषयों के निदान किए गए रोगियों में कार्डियोमेटाबोलिक जोखिम कारकों का आकलन", इसकी संभावनाओं और परिणामों के बारे में विधिवत जानकारी दी गई है। मैं इसके द्वारा केवल उपरोक्त अध्ययन के लिए अपने रक्त के नमूने के संग्रह के लिए सूचित और लिखित सहमति देता हूं।
सूचित सहमति प्रपत्र

- मैं, मोहम्मद सलमान रिसर्च स्कॉलर मेडिकल बायोकेमिस्ट्री ।IMS&R लखनऊ।
- मैं आपके उपचार करने वाले डॉक्टर पैनल से संबद्ध नहीं हूं।
- आप किसी गंभीर बीमारी या संक्रामक रोग से पीड़ित नहीं हैं और आपका ऐसा कोई इलाज नहीं चल रहा है।
- इस अध्ययन के लिए, मैं रक्त शर्करा और लिपिड प्रोफाइल के निर्धारण के लिए आपका 02 मिलीलीटर रक्त का नमूना लूंगा।
- रक्त का परीक्षण केवल रक्त शर्करा और लिपिड प्रोफ़ाइल परीक्षण के निर्धारण के लिए किया जाता है, अन्य अध्ययन के लिए नहीं।
- अध्ययन के लिए कोई शुल्क/फीस नहीं दी जाएगी या कोई विचार नहीं किया जाएगा।
- आपकी पहचान गोपनीय रहेगी और यदि आप चाहें तो जानकारी और आपके रक्त परीक्षण का परिणाम आपके अलावा किसी अन्य को नहीं बताया जाएगा।
- यदि आप भाग लेने से इनकार करते हैं तो अध्ययन में कोई बाधा नहीं आएगी।
- अध्ययन आपके लिए फायदेमंद नहीं होगा लेकिन रोग प्रक्रिया के ज्ञान और समझ में सुधार कर सकता है और वह ज्ञान भविष्य में सहायक हो भी सकता है और नहीं भी।
- उपरोक्त सभी विवरण जानने के बाद, क्या आप हमारे अध्ययन में भाग लेना चाहेंगे?हां नहीं

स्वयंसेवक/अभिभावक के हस्ताक्षर/अंगूठे का निशान: शोधार्थी के हस्ताक्षर:

INSTITUTIONAL ETHICS COMMITTEE (IEC)

IIMS&R INTEGRAL UNIVERSITY, LUCKNOW

IEC/IIMS&R/2023/62

CERTIFICATE

This is to certify that research work entitled "**Assessment of Cardiometabolic Risk Factors in Diagnosed Patients of Hypothyroidism and Control Subjects**" submitted by **Mohammad Salaman, Dr. Mohd. Mustufa Khan** for ethical approval before the Institutional Ethics Committee IIMS&R. The above mentioned research work has been approved by Institutional Ethics Committee, IIMS&R with consensus in the meeting held on **30th December 2022**.

Dr.Q.S.Ahmed
(Member Secretary)
IRC/IEC
IIMS &R

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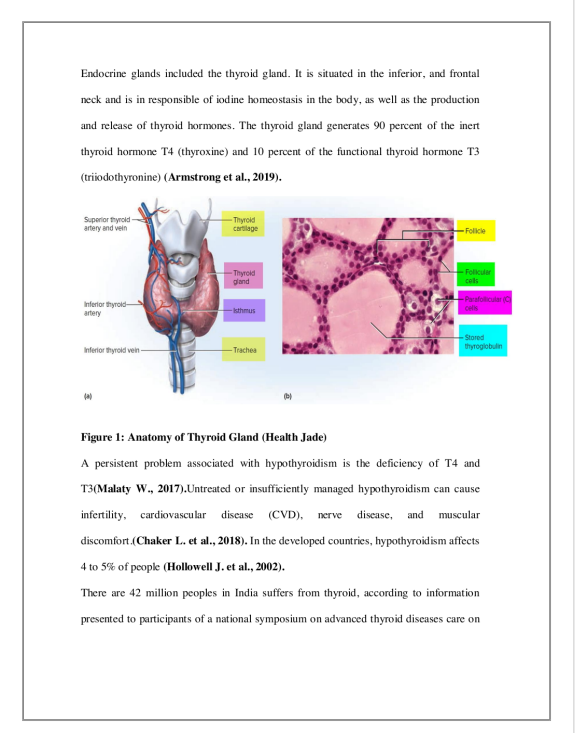

Endocrine glands included the thyroid gland. It is situated in the inferior, and frontal neck and is in responsible of iodine homeostasis in the body, as well as the production and release of thyroid hormones. The thyroid gland generates 90 percent of the inert thyroid hormone T4 (thyroxine) and 10 percent of the functional thyroid hormone T3 (triiodothyronine) **(Armstrong et al., 2019).**

Figure 1: Anatomy of Thyroid Gland (Health Jade)

A persistent problem associated with hypothyroidism is the deficiency of T4 and T3**(Malaty W., 2017).**Untreated or insufficiently managed hypothyroidism can cause infertility, cardiovascular disease (CVD), nerve disease, and muscular discomfort.**(Chaker L. et al., 2018).** In the developed countries, hypothyroidism affects 4 to 5% of people **(Hollowell J. et al., 2002).**

There are 42 million peoples in India suffers from thyroid, according to information presented to participants of a national symposium on advanced thyroid diseases care on

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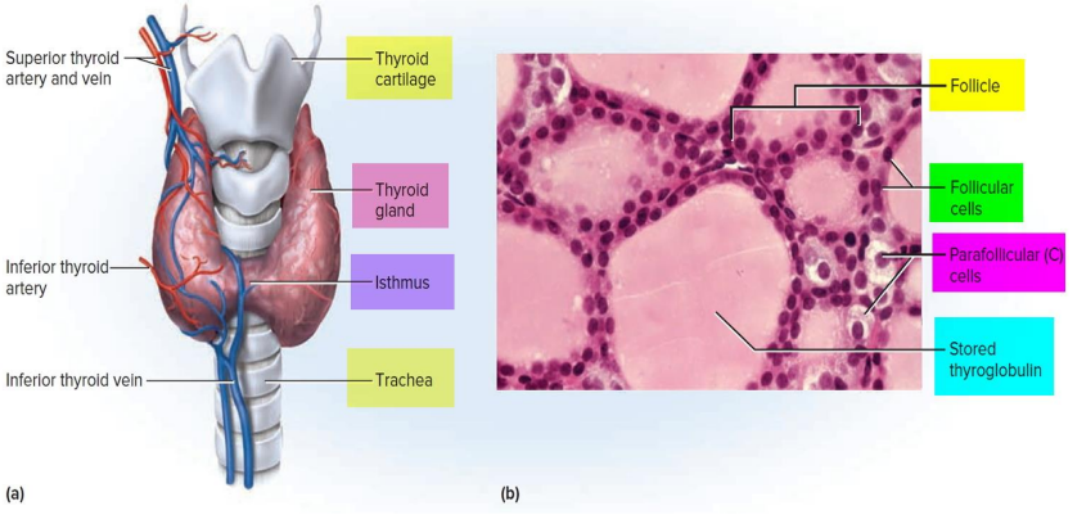

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There are 42 million peoples in India suffers from thyroid, according to information presented to participants of a national symposium on advanced thyroid diseases care on

June 5, 2014, in Chennai, India. One in ten adults in India suffers from hypothyroidism, the most prevalent thyroid condition **(Bagcchi S., 2014).**

In India, 11% of people have hypothyroidism, compared to 2% in the United Kingdom and 4.6% in the United States of America. Interior cities like Hyderabad, Delhi, Bangalore,Ahmadabad and Kolkata have a greater incidence (11.7% versus 9.5%) than beaches cities like Goa, Mumbai and Chennai. **(Bagcchi S., 2014).**

Thyrotropin-releasing hormone, also called TRH, stimulates the anterior pituitary gland to secrete TSH.Thyroid hormones suppress TSH and TRH production. To obtain the precise levels of thyroid hormone, different people have drastically distinct TSH demands. Clinical effects of abnormal thyroid function are known to persist even when they are within the specified reference limits, according to various studies. It is being discussed to reevaluate the reference ranges for TSH and FT4 **(Bano A., 2018).**

The risk of hypertension, SBP(systolic blood pressure), DBP(diastolic blood pressure), CRP, WC (waist circumference), fat percentage of body, and a family history of cardiac disease were all associated with having a BMI (body mass index) of 45 or higher **(Bano et al., 2018).**

A sensitive TSH test should be used to screen for thyroid disease, according to recent American College of Physicians recommendations for primary care settings. The condition of the thyroid is not very prevalent. Therefore, according to these recommendations, monitoring of men and women under the age of 50 is not necessary **(Kutluturk et al., 2013).**

Triglyceride levels were consistently associated beneficially with TSH in FT3 at any percentile. To measure through a canopy and obtain a reading on REE, we used an indirect calorimeter **(Austin, 2018).**

The determination of cardiometabolic risk variables was done simultaneously with the measurement of TSH levels. More long-term studies may be required to determine whether or not these cardio-mechanical risk factors are connected to suboptimal cardiometric outcomes. Despite these limitations, the reference ranges provided and the link between cardiometabolic risk factors and the highest quantile of TSH levels make this research an important resource for practitioners **(Spadafranca et al., 2015).**

A positive relationship was found between the recently identified adipose-myokineirisin and thyroid stimulating hormone (TSH), anti-triglyceride (anti-TG), lipid and inflammatory biomarkers, leptin, and risk factors of cardiovascular disease. Serum irisin and other biomarkers were examined in 16 people with subclinical hypothyroidism (SH) six months after L-T4 therapy in these patients. In this study, it was determined whether patients with subclinical hypothyroidism (SH) had any associations between circulating irisin and cardiometabolic risk factors **(Alsamhan et al., 2010).**

Fasting blood samples were tested for total T3, total T4, TSH, lipid profile, and blood glucose levels together with a comprehensive medical history and other relevant tests **(Ayub et al., 2021).**

Obesity, often known as excess body fat, is on the rise and poses serious risks to the general public's health. Thyroid hormone has an adverse effect on the majority of lipid metabolic processes, which explains why dyslipidemia is so common in persons having thyroid dysfunction. Raises the risk of cardiovascular disease when it occurs along with

other metabolic disease. High blood pressure, insulin resistance, and oxidative stress are some of these disorders. To understand the importance of dyslipidemia or other metabolic abnormalities to CVD mortality &morbidity and death in clinical illness so, in subclinical thyroid illness, more research is necessary, particularly prospective studies. Along with quantitative alterations, qualitative changes in lipids, such as atherogenic and oxidized LDL-C and HDL-C particles, have also been seen **(Erem et al., 2015).**

Thyroid markers TSH, T4, antithyroid peroxidase antibody, and antithyroglobulin antibody were used to divide participants into groups according to their metabolic syndrome status, the amount of metaboilic syndrome components they had age-related and gender-specific reference values (TgAb). Metabolic syndrome and thyroid dysfunction are related in both directions. As part of a whole strategy for treating metabolic syndrome, we hope that this study may encourage further research on the therapeutic efficacy of restoring thyroid function.

Male individuals in thehighest TSH decile also had higher rates of high TG, WC, HDL-C, and DBP than did female participants **(Peppam et al., 2011).**

There should be cautious due to the complex and unproven link between thyroid autoimmunity and cardiovascular risks. The aim of this study was to explore the possibility that a sizable population with normal thyroid-stimulating hormone (TSH) also carried a higher risk of developing cardiometabolic disease. AITDs had a unique relationship with higher risks in women for abdominal obesity, higher lipid, and metabolic syndrome (MetS). In line with expectations, it was also connected to being overweight or obese in both sexes**(Y. Chen *et al.*, 2018).**

LITERATURE

The thyroid's inability to create enough amounts of thyroid hormone is the most common cause of hypothyroidism; thyroid dysfunction can also be caused by the pituitary and hypothalamic glands.

Causes of hypothyroidism

Primary hypothyroidism

1. Goitrous hypothyroidism, which results in increasing impairment of hormone biosynthesis and growth of the thyroid gland.
2. Temporary hypothyroidism
3. Thyroid hormone resistance (generalized pituitary dominance).
4. Atrophic hypothyroidism, which is characterized by irreversible thyroid tissue atrophy or loss **(Salomon Melmed et al., 2016).**

Hypothalamic-pituitary axis dysfunction is the root cause of secondary and tertiary hypothyroidism, commonly referred to as central hypothyroidism. The following are some of its causes:-

- Pituitary tumors
- Hypothalamus compressing tumors
- Sheehan syndrome
- Resistance of Thyroid releasing hormone (TRH)
- Deficiency of TRH
- Lymphocytic hypophysitis
- Radiation therapy of the brain

Symptoms may include:-Tiredness, cold sensitivity, weight gain, skin dryness, constipation and rough hair & skin.

Adults with apparent and hidden hypothyroidism range in prevalence from 0.2%-5.3%. The 2.5th percentile of the corresponding distributions in a population that seems to be healthy is the TSH (or FT4) criteria for normalcy **(Bano A., 2018).**

Researchers studied the changes in body composition, calorimetric, and metabolic features of 15 female DTC patients using a case series methodology. TSH suppressive LT4 therapy enhanced total REE as well as, pulse, REE/LBM and DBP **(Izkhakov et al., 2019).**

According to GEE analysis, the TT3/fT4 ratio has a negative longitudinal connection with SBP, FBS, BMI, distribution of fat in the abdomen and visceral mesentery, the trunk and arms, REE, and REE/LBM. In females with DTC who had a lower TT3/fT4 ratio, there were relatively enhanced rates of energy expenditure (REE), relative excess lean body mass (REE/LBM), abdominal fat distribution (AFD), SBP, and FBS **(Izkhakov et al., 2019).**

The findings emphasize the significance of carefully evaluating the benefits and drawbacks of TSH suppression, with the latter resulting in a decrease in TSH-related metabolic changes.

In 40.0% of those who were highly overweight, the Framingham Risk Score (FRS) was a function of the level of obesity. Except for dyslipidemia, no significant changes were observed in the BMI categories for diabetes, lifestyle, lipid indicators, or the Functional Rating Scale. The findings shed new information on the connection between extreme

obesity and cardiometabolic risks, which is a crucial advancement in the field of study **(Bano A., 2018).**

One hundred and five diabetics were recruited at random from the Jinnah Hospital in Lahore's diabetic clinic. For diabetics, thyroid dysfunction manifests early in life. People with hypothyroidism have higher levels of a number of indicators of risk for atherosclerotic coronary artery disease, including high cholesterol levels and elevated blood pressure.**(Biondi et al., 2019).**

The study discovered that 16.7% of people with metabolic syndrome had thyroid abnormalities. None of the study participants had symptoms of hyperthyroidism. Subclinical hypothyroidism was present in 11.7% of people with thyroid problems. The risk for acquiring coronary artery disease is greater in both men and women with this condition than it would be in the general population **(Ayub et al., 2021).**

The levels of MDA, hyperglycemia, and TG were significantly greater in those with these two disorders. These people may have enhanced lipid peroxidation, which may be a major factor in the pathogenesis of atherosclerosis, based on the elevated MDA levels. There is a connection between IMA and hyperthyroidism, however further prospective study is needed to clarify this association. In conclusion, there were noticeable differences in the lipid profile and OS parameters between patients with SHyper and OHyper and healthy controls. People with SHyper and OHyper may experience less oxidative stress after receiving treatment with ATD **(Demirbas et al., 2021).**

Women made up 67.9% and males made up 32.1% of the 817 survey participants. The average BMI for individuals ranged from 29.90 to 6.6 kg/m2. The body fat percentage as determined by the BIA increased along with the subject's BMI (P 0.001). The body

fat percentage &Body mass index were linked with the LAP index **(Stratigos et al., 2018).**

During the third National Health and Nutrition Examination Survey (1988-1994), 1,322 adolescents between the ages of 12 and 18 had their thyroid task and metabolic disorder elements examined. Being overweight or obese, having a big waist circumference, having high BP, having high triglycerides, and having low HDL-C values are all conditions that might cause metabolic syndrome. According to research, abnormal thyroid hormone levels may set off a series of metabolic abnormalities, implying a link between the two **(Peppam et al., 2011).**

In order to determine whether thyroid-stimulating hormone (TSH) levels were related to cardiometabolic risk factors, 15.4 million American adolescents ranged in age from 12 to 18 participated in the study.

Thyroid hormones have an impact on several physiological processes, including development, metabolism, thermogenesis, and cardiovascular health. In this group of young people (51.3% of whom were male), the average incidence of SH was 2.0% (95% CI 1.2-3.1%) and 31.2%,of them were overweight or obese. The goal of the study was to analyze the link between TSH and cardiovascular & cardiometabolic risk factors. Obesity and insulin resistance have both been linked to thyroid-stimulating hormone (TSH). If the two are causally connected, though, remains unknown. Few population-based cohort studies exist **(Spade et al., 2015).**

Research was done on 30 patients who had clinical hypothyroidism symptoms. LDL oxidation, inflammation, and endothelial damage were all measured in all individuals.

OxLDL concentration and LDL-C, apo B, triglyceride, and triglyceride levels all showed favorable correlations **(Chen X et al., 2021).**

The relationship between metabolic syndrome (MetS) and subclinical hypothyroidism (SCH) has attracted a lot of research. When those with SCH were compared to those without, the pooled OR for MetS were 1.28 (95% CI: 1.19 to 1.39, p = 0.04, I2 = 40%). Age, ethnicity, and the diagnostic criteria for MetS appeared to have an impact on the probability of acquiring MetS among SCH participants.

There was a link found between SCH and an elevated risk of being overweight, developing hypertension, having high triglyceride levels, and having low levels of high density lipoprotein (HDL-C). These findings require confirmation by more lengthy, extensive prospective cohort studies **(Warsaw et al., 2016).**

Patients with overt hypothyroidism showed elevated blood lipids, folic acid, and vitamin B12 levels both before and after L-thyroxin (LT4) medication. Fasting blood samples from patients were examined for TSH, free thyroxine (FT4), homocysteine, total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and other chemical markers(**Kutluturk et al., 2013**).

Positive correlations were found between serum lipid concentrations and homocysteine concentrations. After thyroid functions were restored by LT4 replacement, there was a intenserelation between GFR and lipids that no longer existed. The improvement of these parameters following LT4 replacement may be correlated with a lower risk of cardiovascular disease caused by atherosclerosis in hypothyroid patients. Additionally, total, LDL, and TG lipid levels showed a significant adverse relationship with GFR (**Ding X et al., 2021).**

Aim

It is aimed to determine the cardio metabolic risk factors in diagnosed cases of hypothyroidism and control subjects.

Objectives

1. To determine the biochemical parameters; blood sugar and lipid profile in diagnosed cases of hypothyroidism and control subjects.
2. To determine demographic parameters; BMI, waist circumference and blood pressure in diagnosed cases of hypothyroidism and control subjects.
3. To find the correlation between demographic parameters and biochemical parameters in diagnosed cases of hypothyroidism and control subjects, if any.

OBSERVATION& RESULTS:-

Results showed that mean of BMI, WC, TC, TG, LDL-C, VLDL-C, TSH, SBP, and DBP were found significantly high in cases compared to controls ($p<0.001$). However, mean of HDL-C, T3, and T4 were found significantly low in cases compared to controls ($p<0.001$), shown in **Table 1.**

Table 1 Baseline characteristics of cases and controls

Parameters	Case (n=30)	Control (n=30)	p-value
Age (years)	41.16 ± 9.50	42.46 ± 8.80	0.5845
BMI (kg/m^2)	26.30 ± 3.87	22.41 ± 2.15	0.0001
WC (cm)	90.66 ± 6.06	83.67 ± 4.73	0.0001
FBS (mg/dL)	102.73 ± 23.76	91.73 ± 14.41	0.0343
T3 (nmol/L)	1.60 ± 0.44	2.05 ± 0.88	0.0151
T4 (nmol/L)	86.87 ± 15.91	127.22 ± 55.97	0.0004
TSH (μIU/mL)	7.63 ± 3.34	2.17 ± 0.91	0.0001
TC (mg/dL)	203.19 ± 33.34	124.54 ± 20.87	0.0001
TG (mg/dL)	152.93 ± 65.46	123.17 ± 35.94	0.0331
HDL-C (mg/dL)	44.36± 9.41	49.01 ± 6.43	0.0293
LDL-C (mg/dL)	128.24± 35.48	50.89 ± 19.90	0.0001
VLDL-C (mg/dL)	30.58 ± 13.09	24.63 ± 7.18	0.0331
SBP (mmHg)	137.33 ± 13.22	123.66 ± 5.89	0.0001
DBP (mmHg)	94.66 ± 11.25	85.2 ± 5.59	0.0001

AGE

In this study, 30 control Subjects aged between 30 to 65with 30 patients of hypothyroidism were included. The mean age of control subjects (42.46 ± 8.80) and hypothyroidism patients (41.16 ± 9.50) have been found.

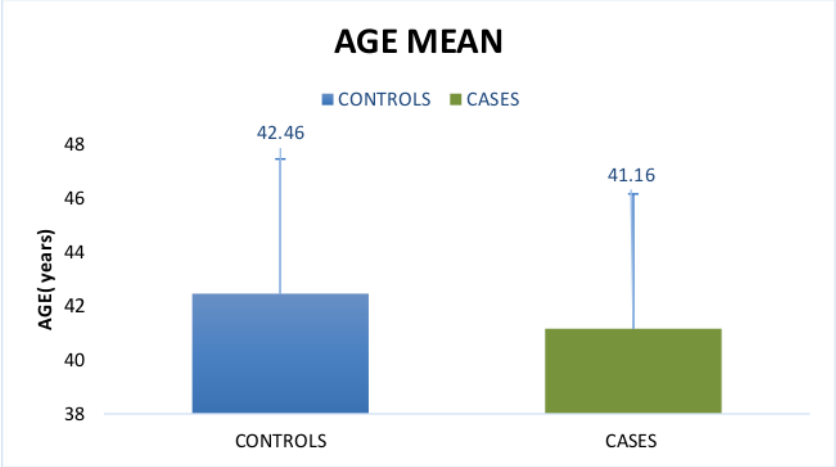

Figure.2. Comparison of ages (years)in cases & controls.

BODY MASS INDEX (BMI)

Anthrpometric parameter body mass index (BMI)were significant in patients of hypothyroidism, comparing patients to control subjects, p=0.0001shown in table 3.

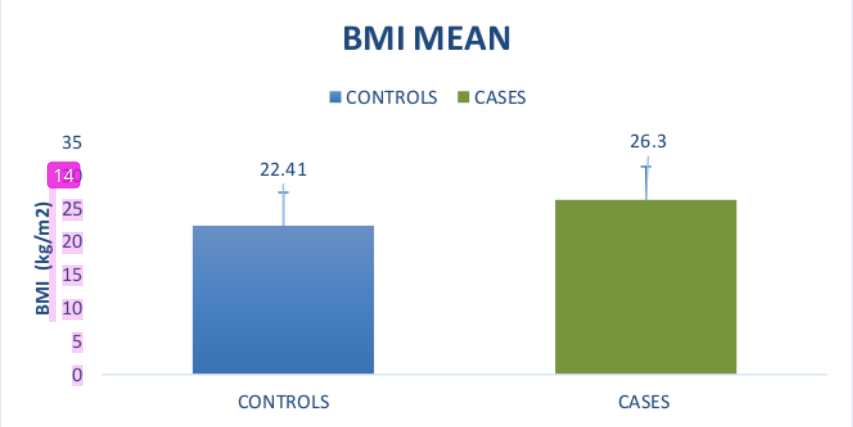

Figure 3. Comparison of BMI in cases and controls.

Total Cholesterol

Serum TC is significantly increasedin patients of hypothyroidism, comparing patients to control subjects, p= 0.0001 shown in table. 3.

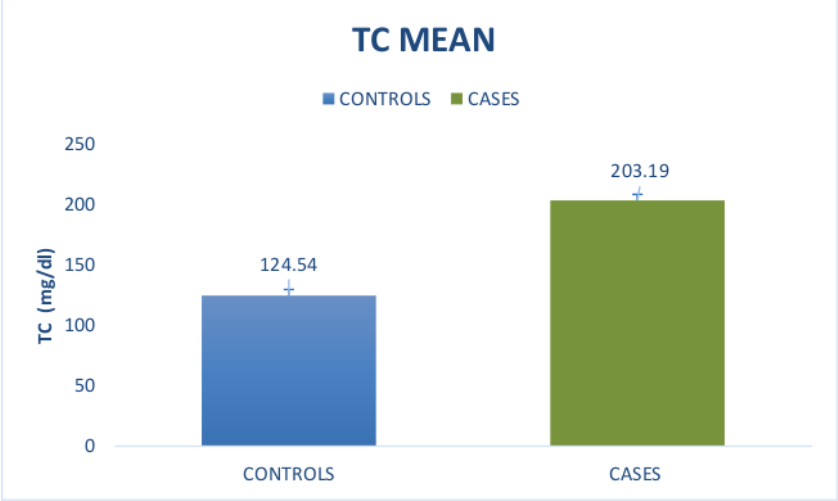

Figure 4. Comparison of TC in cases and controls.

Serum triglycerides

Inpatients of hypothyroidismcompared to control subjects, TG are considerably higher (p= 0.0331) shown in table.3.

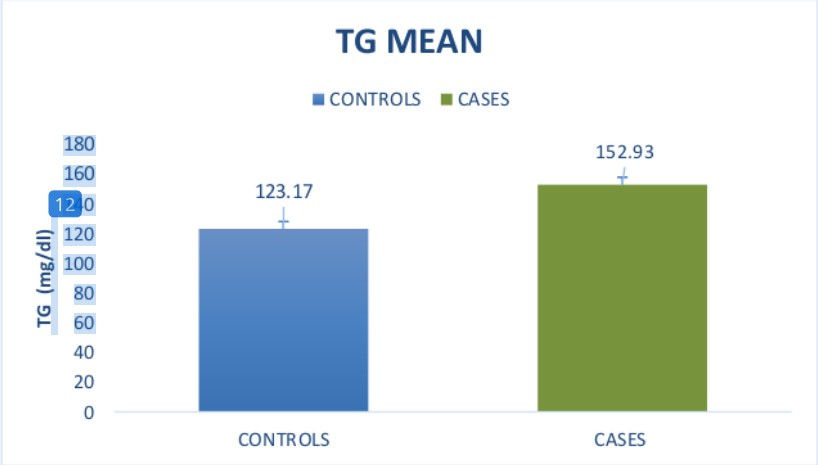

Figure 5. Comparison of TG in cases and controls.

Serum HDL-C

Compared to control persons, inpatients of hypothyroidism serum HDL-C is considerably lower (p=0.0616) shown in table.3.

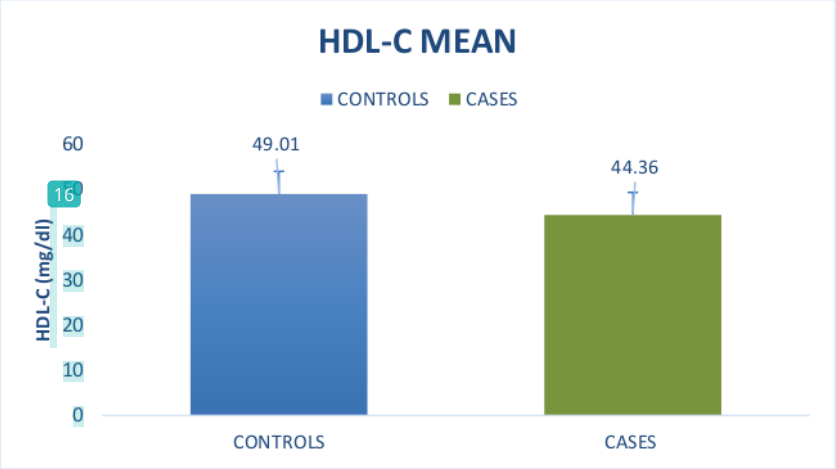

Figure 6. Comparisonof HDL-C in cases and controls.

Serum LDL-C

When compared to control persons, in patients of hypothyroidismserum LDL-C is considerably higher (p=0.0001) shown in table.4

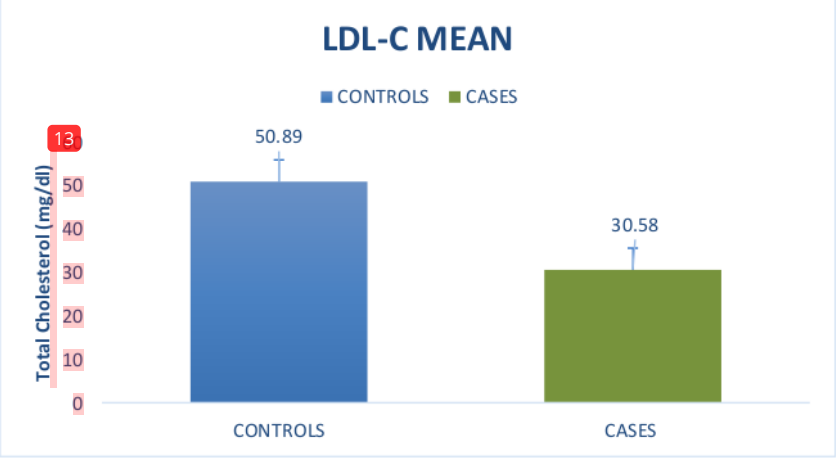

Figure 7. Comparison of LDL-C in cases and controls.

Serum VLDL-C

When compared to control persons, inpatients of hypothyroidismserum VLDL-C is considerably higher (p=0.0001) shown in table.5

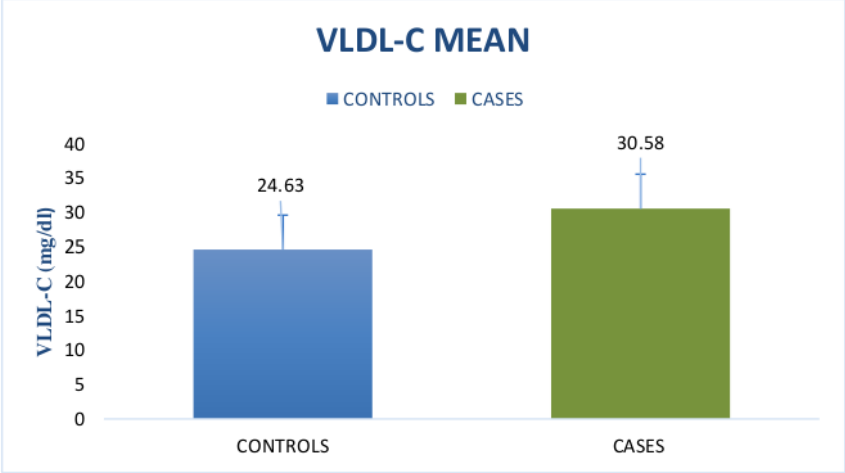

Figure 8. Comparison of VLDL-C in cases and controls.

Fasting blood sugar

In patients of hypothyroidism compared to control subjects, FBS are considerably higher (p=0.0343)

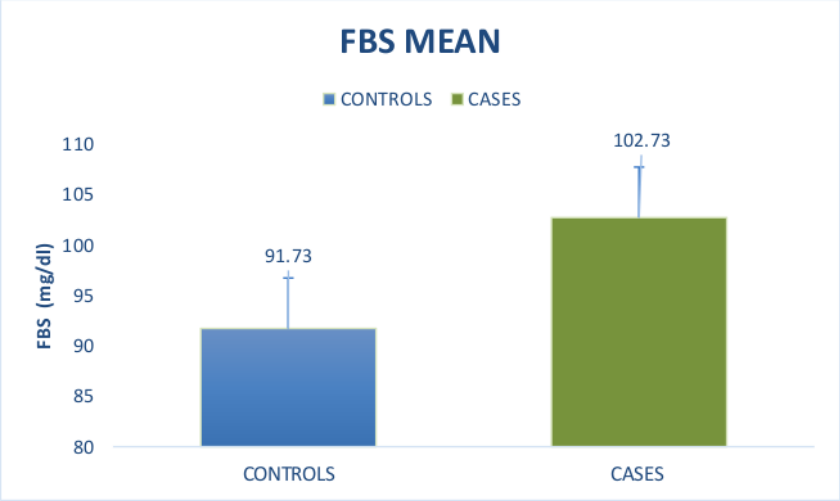

Figure 9. Comparison of FBS in cases and controls.

Waist Circumference

When compared to control persons, inpatients of hypothyroidism, WC is considerably higher (p=0.0001).

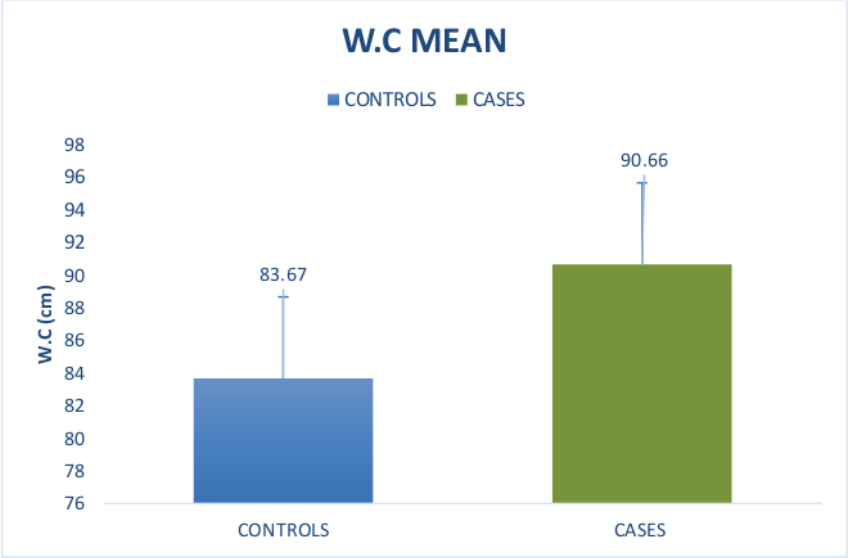

Figure 10. Comparison of W.C. in cases and controls.

Blood pressure (systolic)

When compared to control persons, inpatients of hypothyroidism, SBP is considerably higher (p=0.0001).

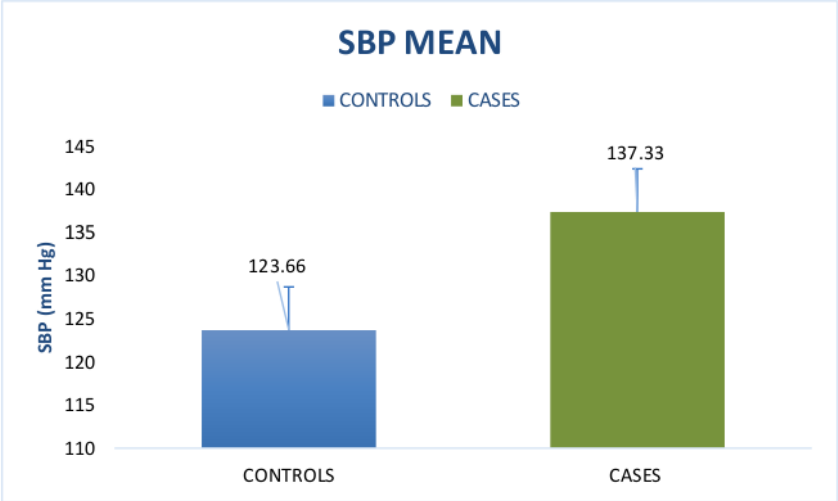

Figure 11. Comparison of SBP in cases and controls.

Blood pressure (diastolic)

When compared to control persons, in patients of hypothyroidism, DBP is considerably higher (p=0.0001).

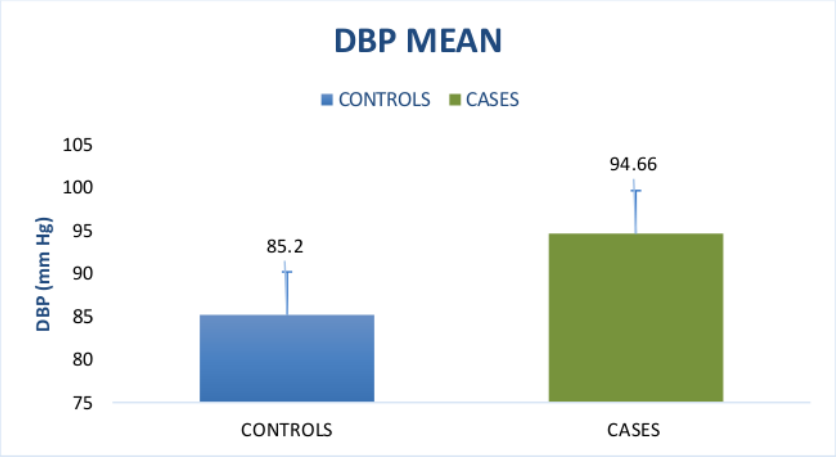

Figure 12. Comparison of DBP in cases and controls.

T3 LEVEL

When compared to control persons, inpatients of hypothyroidism, T3 is considerably lower (p=0.7305).

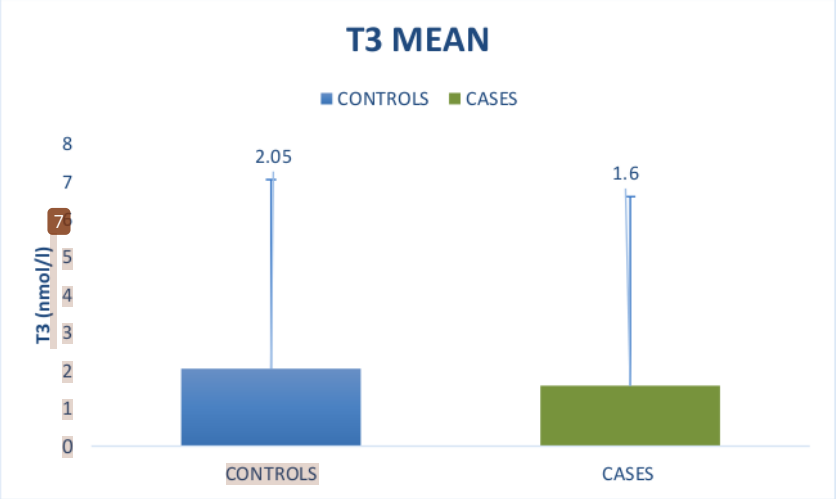

Figure 13. Comparison of T3in cases and controls.

T4 LEVEL

When compared to control persons, inpatients of hypothyroidism, T4 is considerably lower (p=0.0004).

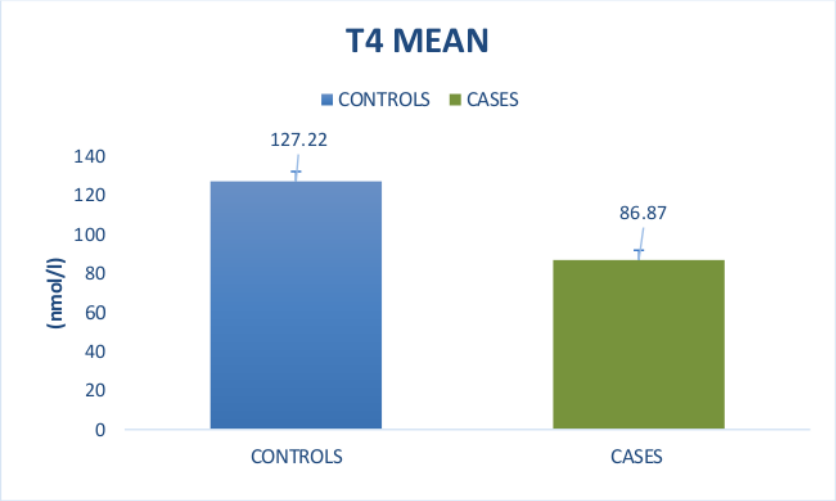

Figure 14. Comparison of T4 in cases and controls.

TSH LEVEL

When compared to control persons, in patients of hypothyroidism, TSH is considerably higher (p=0.0001).

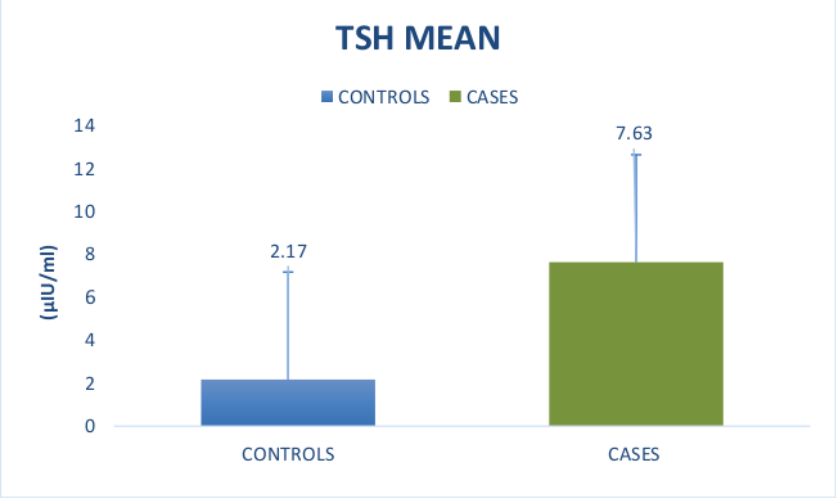

Figure 15. Comparison of TSH in cases and controls.

Age has shown a significant positive correlation with WC ($r = 0.400$, $p<0.05$), FBS ($r = 0.827$, $p<0.01$), TSH ($r = 0.553$, $p<0.01$), TC ($r = 0.598$, $p<0.01$), TG ($r = 0.534$, $p<0.01$), LDL-C ($r = 0.464$, $p<0.05$), VLDL-C ($r = 0.533$, $p<0.01$), SBP ($r = 0.812$, $p<0.01$) & DBP ($r = 0.831$, $p<0.01$) among cases.

BMI has shown a significant positive correlation with WC ($r = 0.833$, $p<0.01$), FBS ($r = 0.412$, $p<0.05$), T3 ($r = 0.389$, $p<0.05$), T4 ($r = 0.558$, $p<0.01$), TC ($r = 0.476$, $p<0.01$), LDL-C ($r = 0.386$, $p<0.05$), SBP ($r = 0.619$, $p<0.01$) & DBP ($r = 0.573$, $p<0.01$) among cases.

WC has shown a significant positive correlation with FBS ($r = 0.0.399$, $p<0.05$), T3 ($r = 0.575$, $p<0.01$), T4 ($r = 0.670$, $p<0.01$), TC ($r = 0.602$, $p<0.01$), HDL-C ($r = 0.551$, $p<0.01$), LDL-C ($r = 0.407$, $p<0.05$), SBP ($r = 0.780$, $p<0.01$) & DBP ($r = 0.744$, $p<0.01$) among cases.

FBS has shown a significant positive association with TSH ($r = 0.461$, $p<0.01$), TC ($r = 0.579$, $p<0.01$), TG ($r = 0.383$, $p<0.05$), LDL-C ($r = 0.487$, $p<0.01$), VLDL-C ($r = 0.383$, $p<0.05$), SBP ($r = 0.743$, $p<0.01$) & DBP ($r = 0.743$, $p<0.01$) among cases.

T3 has shown a significant positive correlation with T4 ($r = 0.422$, $p<0.05$), TC ($r = 0.445$, $p<0.05$), LDL-C ($r = 0.388$, $p<0.05$), SBP ($r = 0.376$, $p<0.05$) & DBP ($r = 0.363$, $p<0.05$) among cases.

T4 has shown a significant positive correlation with HDL-C ($r = 0.638$, $p<0.01$), SBP ($r = 0.442$, $p<0.05$) & DBP ($r = 0.381$, $p<0.05$) among cases.

TSH has shown a significant positive correlation with SBP ($r = 0.377$, $p<0.05$) & DBP ($r = 0.406$, $p<0.05$) among cases.

TC has shown a significant positive correlation with TG ($r = 0.432$, $p<0.05$), LDL-C ($r = 0.893$, $p<0.01$), VLDL-C ($r = 0.431$, $p<0.05$), SBP ($r = 0.766$, $p<0.01$) & DBP ($r = 0.767$, $p<0.01$) among cases.

TG has shown a significant positive correlation with VLDL-C ($r = 1.000$, $p<0.01$), SBP ($r = 0.463$, $p<0.01$) & DBP ($r = 0.476$, $p<0.01$) among cases.

LDL-C has shown a significant positive correlation with SBP ($r = 0.533$, $p<0.01$) & DBP ($r = 0.552$, $p<0.01$) among cases.

VLDL-C has shown a significant positive correlation with SBP ($r = 0.462$, $p<0.01$) & DBP ($r = 0.475$, $p<0.01$) among cases.

SBP has shown a significant positive correlation with DBP ($r = 0.978$, $p<0.01$) among cases.

Table 2: Correlation analysis between different variables among cases.

Variables	Age (Year)	BMI (kg/m2)	WC (cm)	FBS (mg/dl)	T3 (nmol/l)	T4 (nmol/l)	TSH (μIU/ml)	TC (mg/dl)	TG(mg/dl)	HDL-C(mg/dl)	LDL-C(mg/dl)	VLDL-C(mg/dl)	SBP (mmHg)	DBP (mmHg)
Age (Year)	1	0.348	**0.400***	**0.827****	0.028	0.189	**0.553***	**0.598****	**0.534****	-0.055	**0.464***	**0.533***	**0.812****	**0.831****
BMI (kg/m2)		1	**0.833****	**0.412***	**.389***	**0.558****	0.086	**0.476****	-0.042	0.334	**0.386***	-0.039	**0.619****	**0.573****
WC (cm)			1	**0.399***	**0.575****	**0.670****	0.164	**0.602****	0.079	**0.551***	**0.407***	0.078	**0.780****	**0.744****
FBS (mg/dl)				1	0.174	0.123	**0.461***	**0.579****	**0.383***	0-.031	**0.487***	**0.383***	**0.743****	**0.743****
T3 (nmol/l)					1	**0.422***	0.026	**0.445***	-0.069	0.314	**0.388***	-0.068	**0.376***	**0.363***
T4 (nmol/l)						1	0.048	0.304	0.071	**0.638***	0.067	0.072	**0.442***	**0.381***
TSH (μIU/ml)							1	0.346	0.310	-0.049	0.278	0.305	**0.377***	**0.406***
TC (mg/dl)								1	**0.432***	0.137	**0.893***	**0.431***	**0.766****	**0.767****
TG(mg/dl)									1	0.007	0.126	**1.000***	**0.463****	**0.476****
HDL-C(mg/dl)										1	-0.198	0.009	0.331	0.276
LDL-C(mg/dl)											1	0.125	**0.533****	**0.552****
VLDL-C(mg/dl)												1	**0.462****	**0.475****
SBP (mmHg)													1	**0.978****
DBP (mmHg)														1

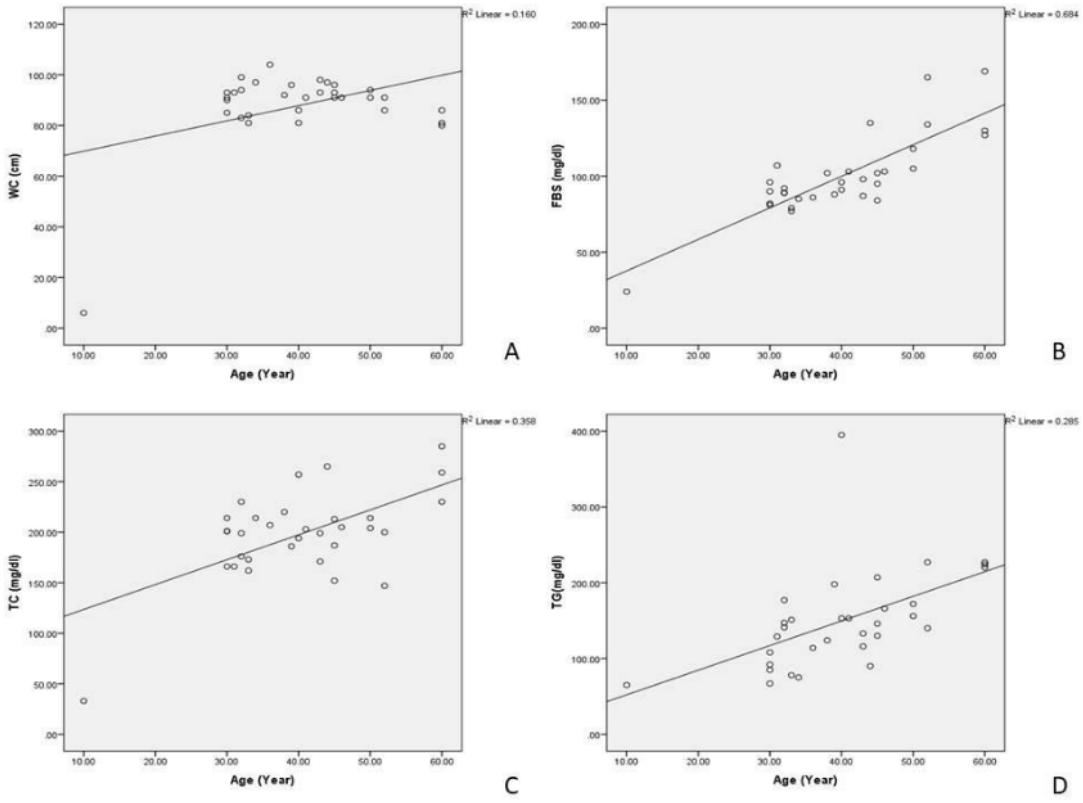

Figure.16.1: Correlation of Age, WC, FBS, TC &TG among cases.

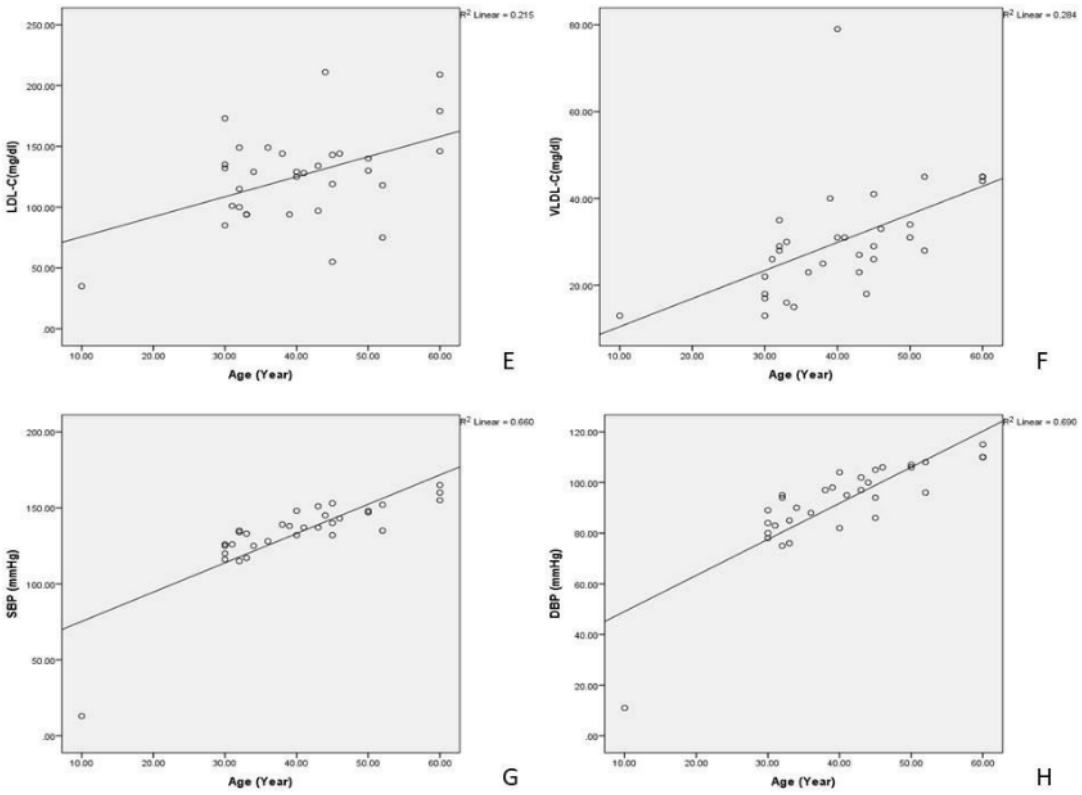

Figure.16.2: Correlation of Age, LDL-C, VLDL-C, SBP & DBP among cases.

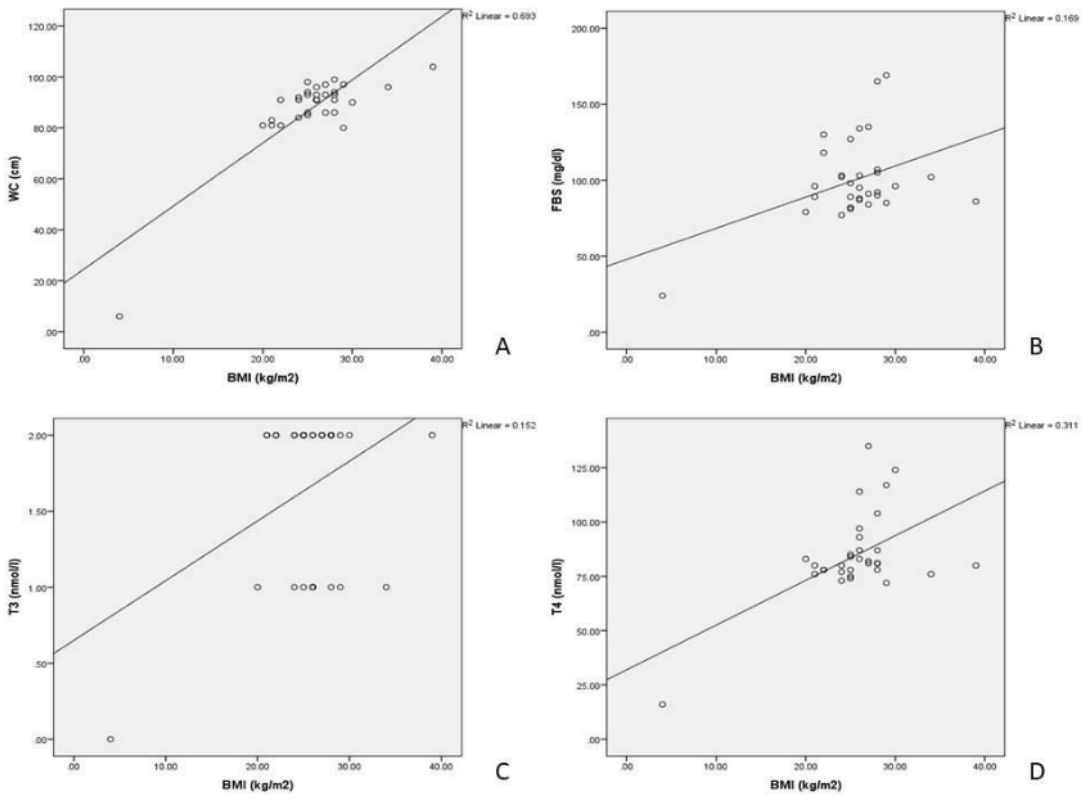

Figure.17.1: Correlation of BMI, WC, FBS, T3 &T4 among cases.

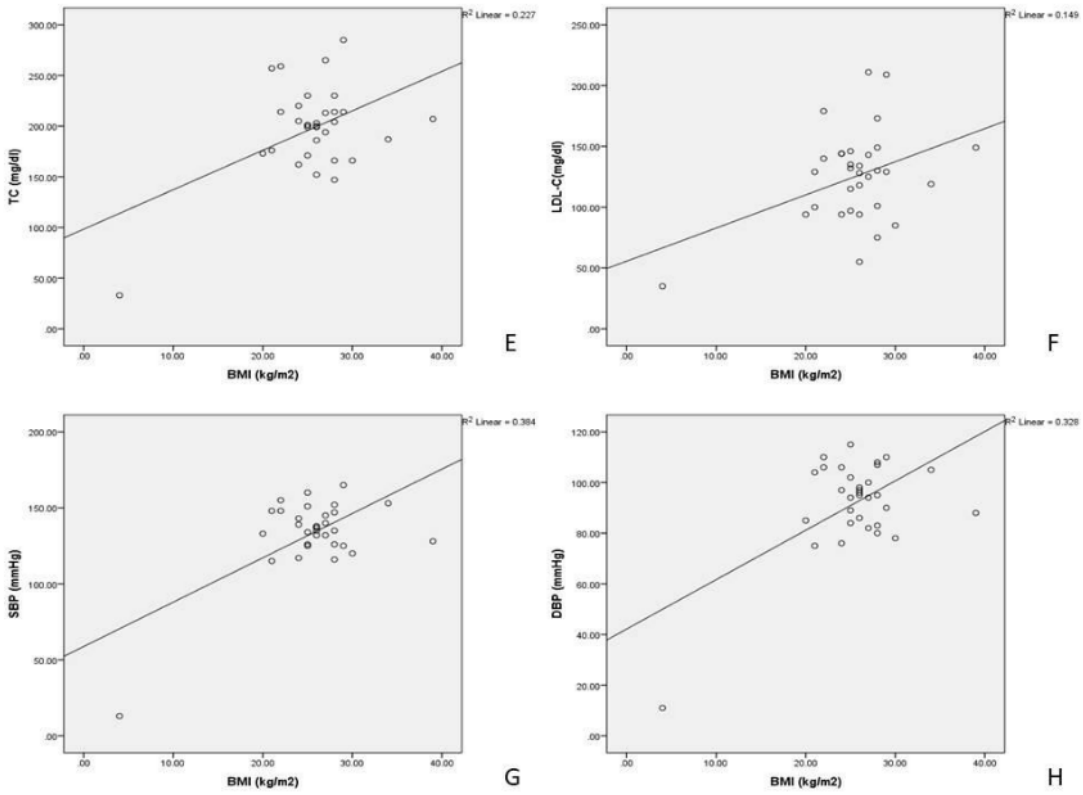

Figure.17.2: Correlation of BMI, TC, LDL-C, SBP & DBP among cases.

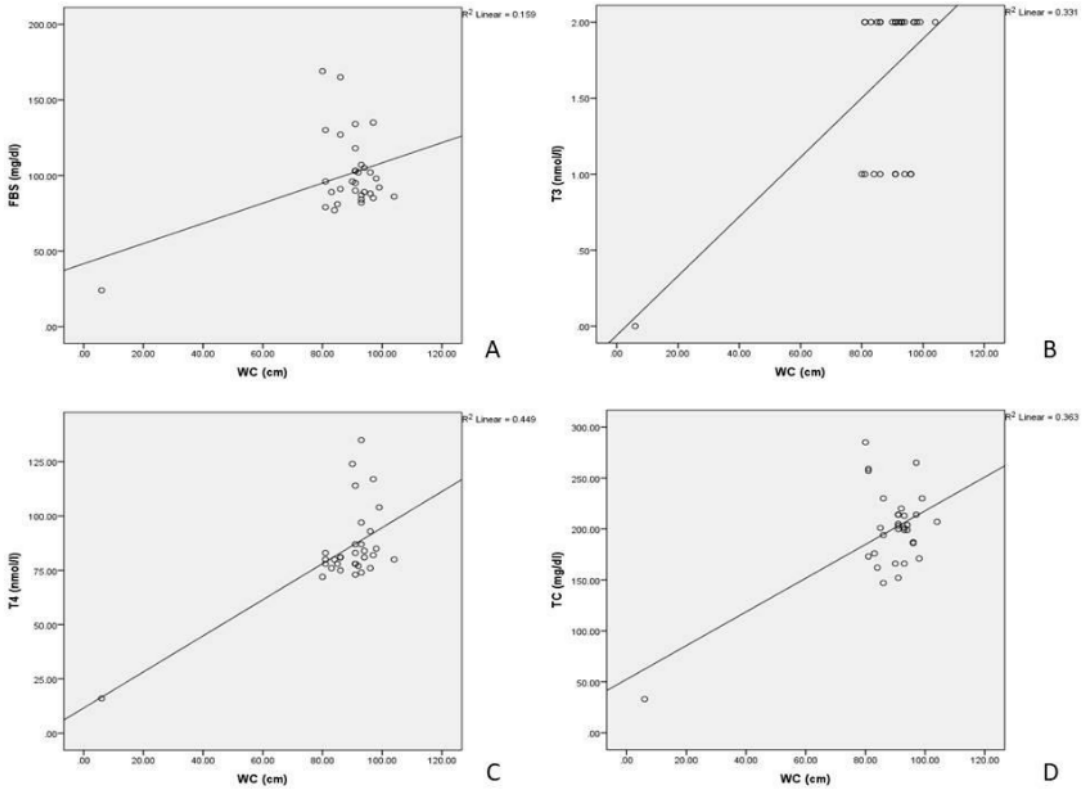

Figure.18.1: Correlation of WC,FBS, T3, T4 & TC among cases.

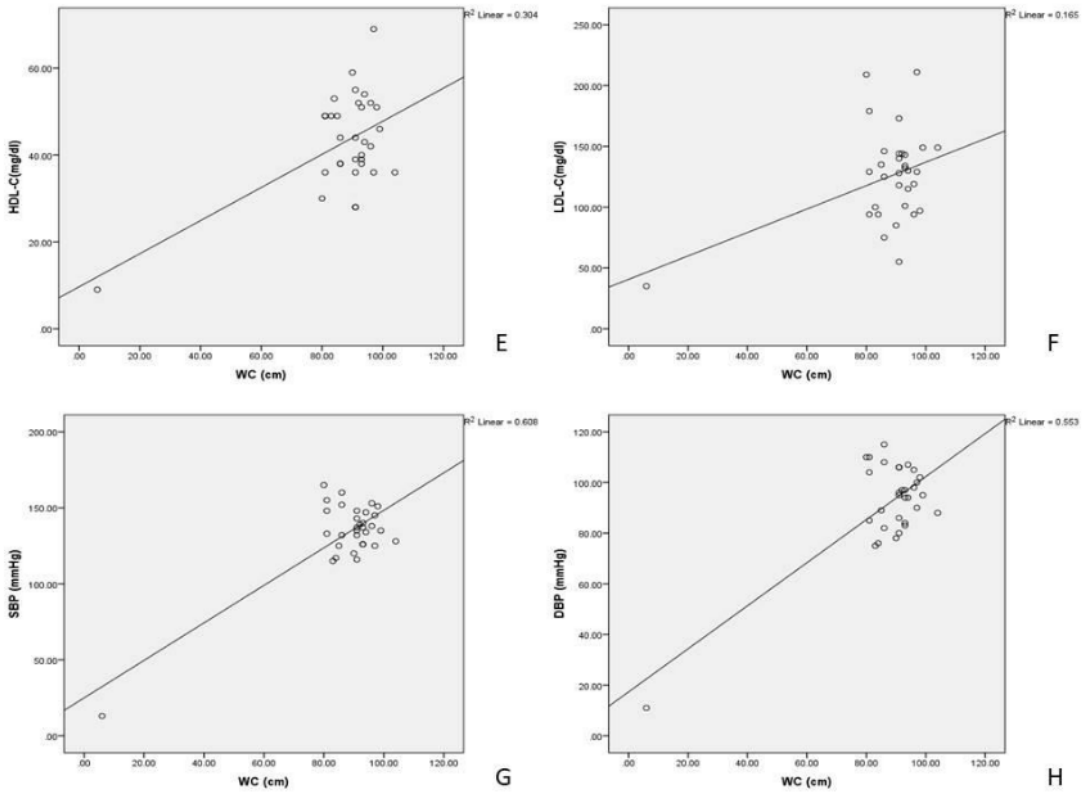

Figure.18.2: Correlation of WC, HDL-C, LDL-C, SBP & DBP among cases.

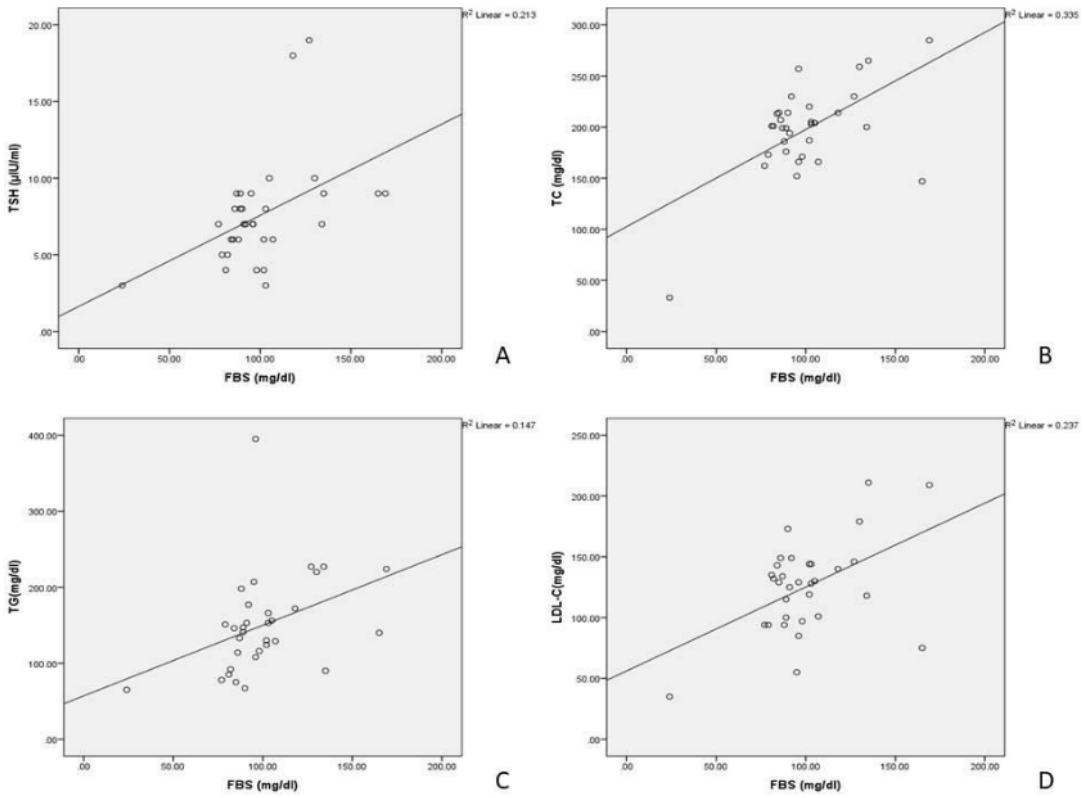

Figure.19.1: Correlation of FBS, TSH, TC, TG & LDL-C among cases.

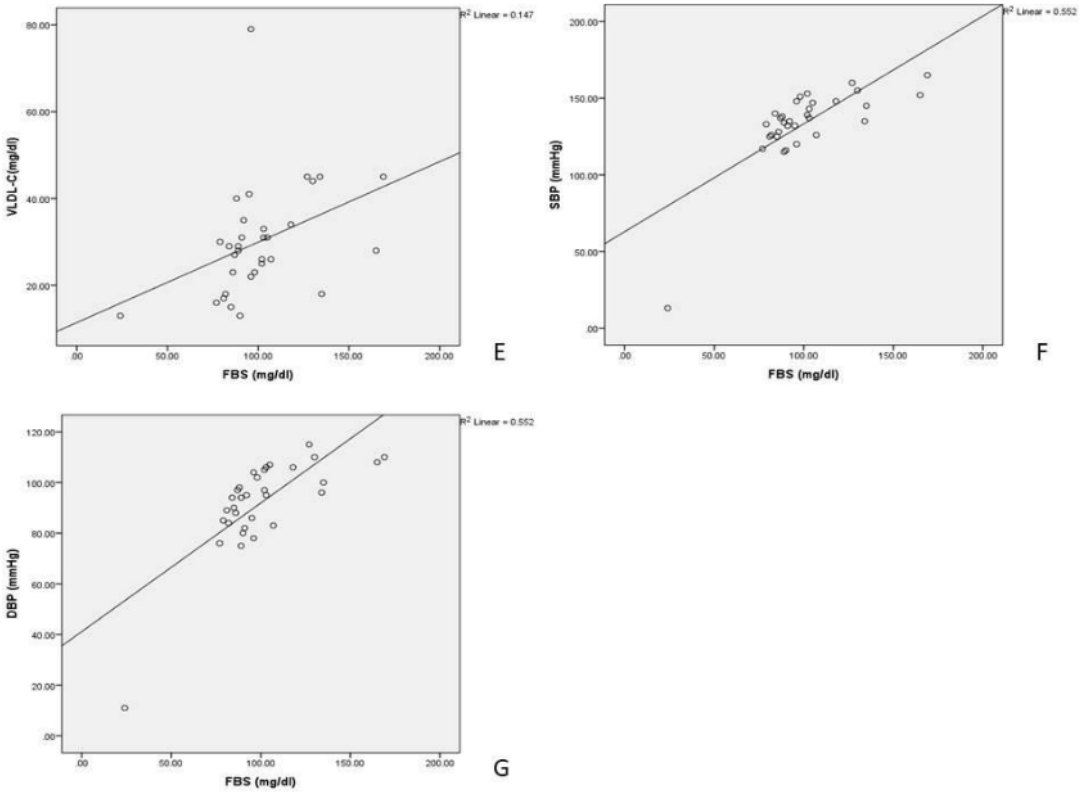

Figure.19.2: Correlation of FBS, VLDL-C, SBP & DBP among cases.

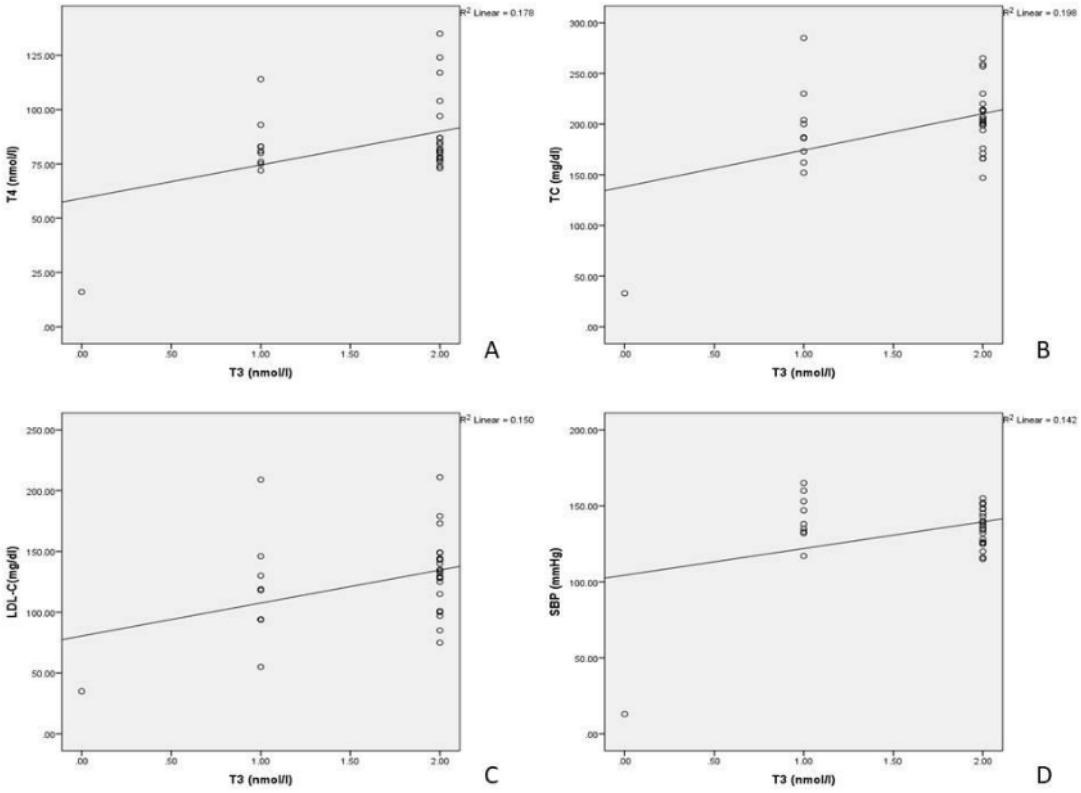

Figure.20: Correlation of T3, T4, TC, LDL-C & SBP among cases.

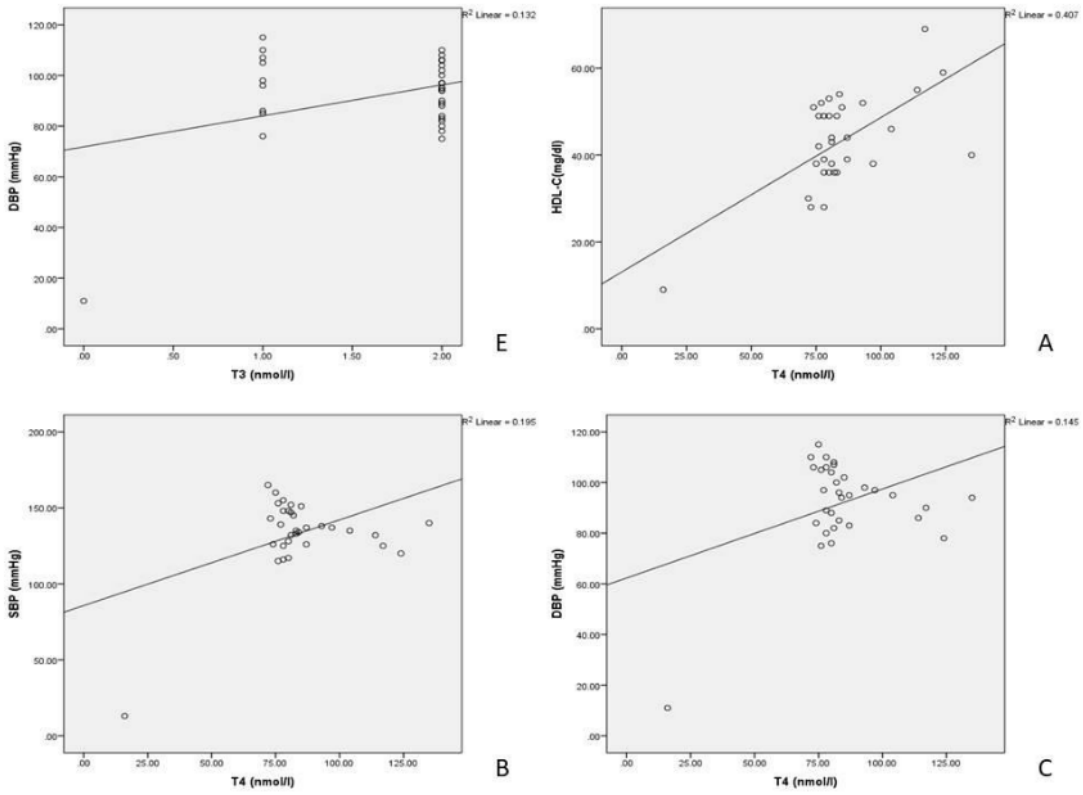

Figure.21: Correlation of T3 with T4 and correlation of T4, HDL-C, SBP & DBP among cases.

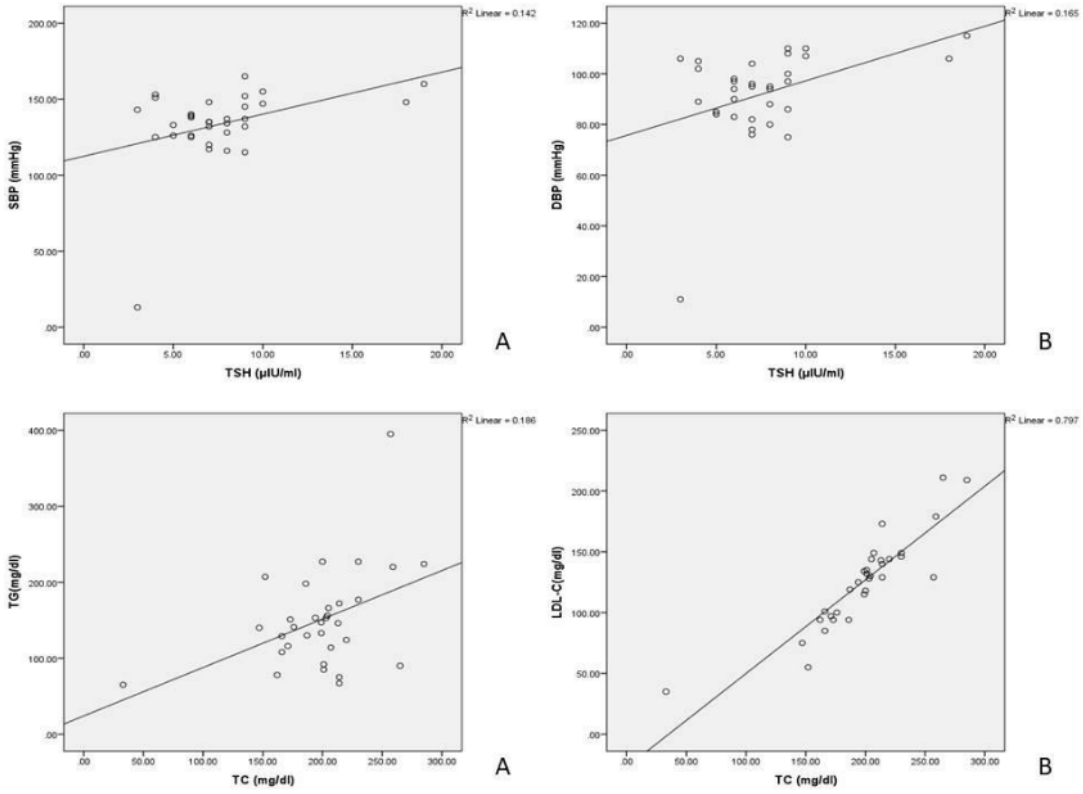

Figure.22: Correlation of TSH, SBP & DBP and correlation of TC, TG & LDL-C among cases.

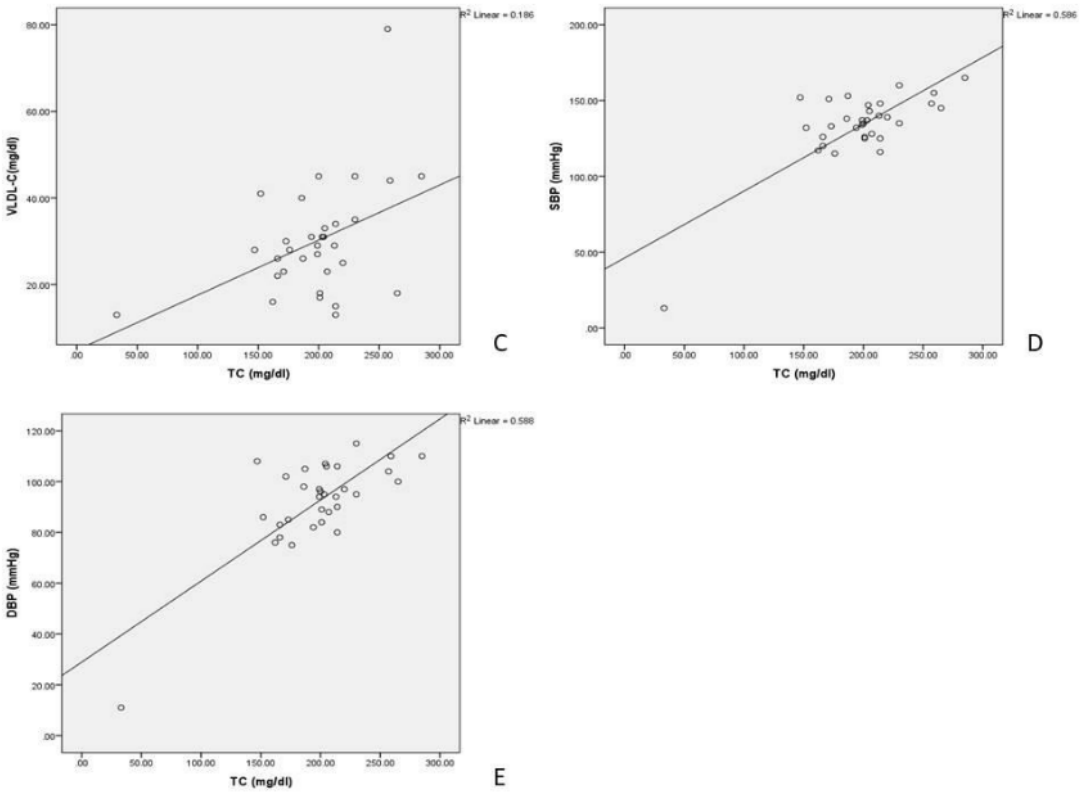

Figure.23: Correlation of TC, VLDL-C, SBP & DBP among cases.

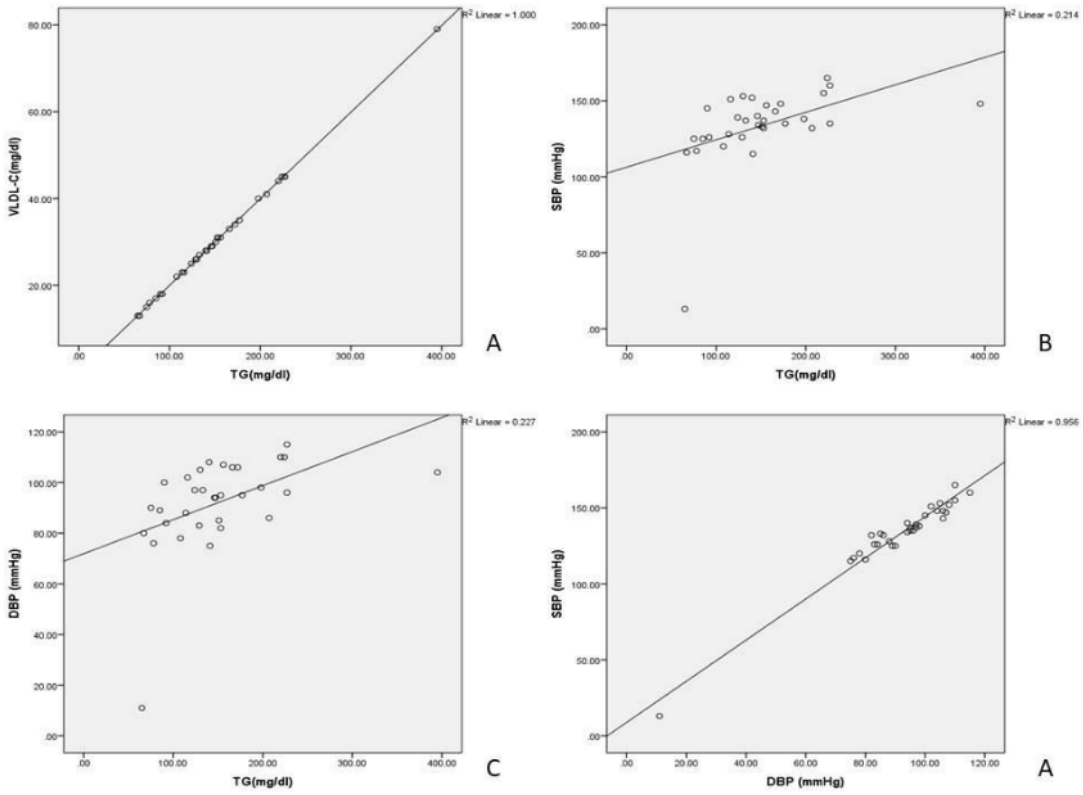

Figure.24: Correlation of TG, VLDL-C, SBP & DBP and between SBP & DBP among cases.

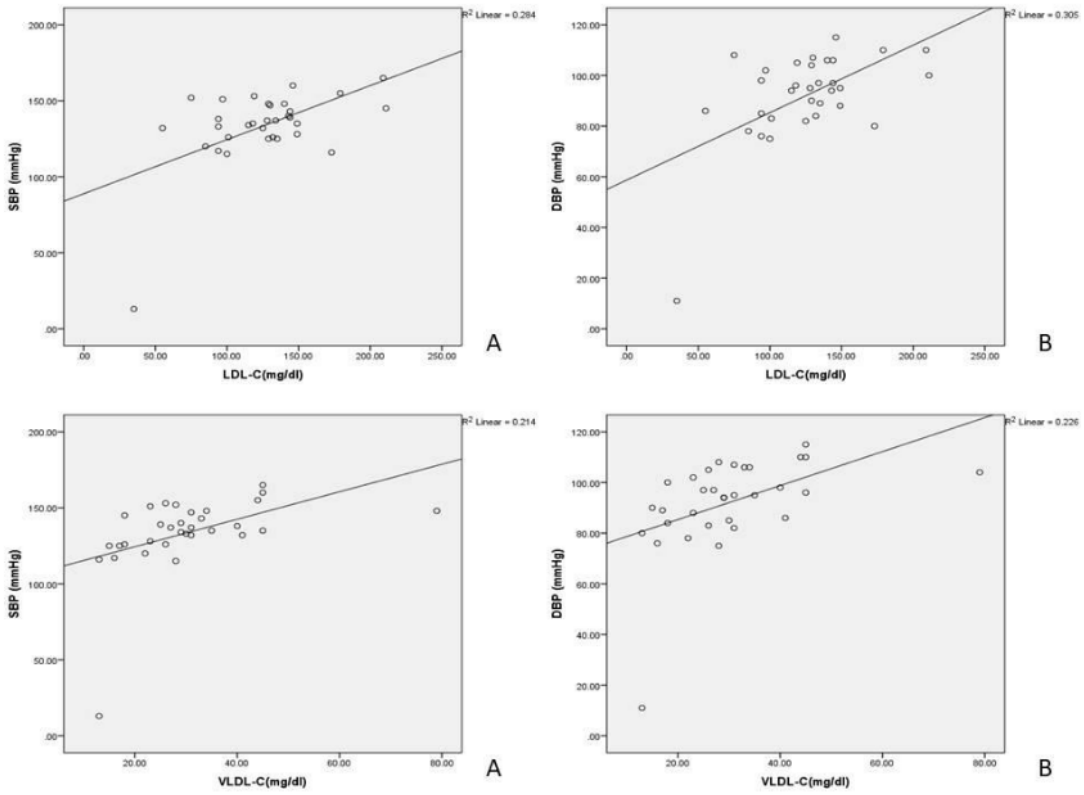

Figure.25: Correlation of LDL-C, SBP & DBP and correlation of VLDL-C, SBP & DBP among cases.

DISCUSSION

Result showed that mean of BMI, WC, FBS, TSH, TC, TG, LDL-C, VLDL-C, SBP, and DBP were significantly elevated in cases than controls. However, mean of T3, T4, and HDL-C was found significantly low in cases than controls. Correlation analysis has shown that lipid abnormalities were significantly associated with obesity and hypertension in patients with hypothyroidism.

Gutch et al reported that levels of serum LDL-C, VLDL-C, TG, TC, and TSH were found significantly elevated in cases than controls. However, levels of HDL-C, T3, and T4 were found significantly low in cases than controls. It was further suggested that thyroid functions and obesity are interlinked because thyroid hormones regulate the metabolic pathways and energy expenditure **(Gutch et al 2017).**

A study reported that 96.1% of hypothyroid patients have dyslipidemia and mostly have low HDL-C and high TG. It was further suggested that hypothyroidism with obesity is a significant risk factors for dyslipidemia **(Alarcón-González et al 2021).**

It was reviewed that lipid abnormalities and elevated TSH has strongly associated. The degree of lipid abnormality is directly proportional to the degree of elevation of TSH. It was further suggested that age, gender, and BMI may influence the pattern of the lipid abnormalities. TSH mainly elevated with increase of LDL-C in patients with hypothyroidism. This indicated that lipid abnormalities are associated with cardiometabolic risk factors in patients with hypothyroidism. It was further recommended that clinical management of thyroid hormones and lipid profile are important factors to reduce/reverse hypothyroidism-associated cardiometabolic risk factors **(Jonklaas 2023).**

Cappola et al reviewed that thyroid hormone T3 induces cholesterol biosynthesis initiation enzyme HMG-CoA reductase and up-regulates LDL-C receptor that slow down the clearance of LDL-C in patients with hypothyroidism. Thyroid hormones also affect activity of cholesterol degradation first step enzyme 7α-hydroxylase that regulates the rates of excretion of bile acid and fecal cholesterol. It was indicated that hypothyroidism is linked with elevated LDL-C and adverse effects in number, size, and oxidation of LDL-C **(Cappola et al 2019).**

Deficiency of T3 & T4 can increase TG levels by inhibiting the activity of enzyme lipoprotein lipase (Sinha et al 2018). A study reported that hypothyroidism patients who have serum TSH

(>10 mIU/L) also have high levels of small and dense LDL-C that has more atherogenic characteristics **(Saric et al 2017).**

In addition, a meta-analysis study indicated that hypothyroidism was linked with chronic heart disease (CHD) risk factors. This study further reported that patients with hypothyroidism who have serum TSH levels (≥10 mIU/L) were associated with CHD risk factors and who have serum TSH levels (≥7 mIU/L) were more prone to CHD-associated mortality **(Rodondi et al 2010).**

The incident of heart failure (biventricular) were found high in patients with untreated hypothyroidism who have serum TSH levels (≥10 mIU/L) because of abnormal hemodynamic functions. This study further suggested that thyroid hormone supplementation and restoration therapy may reverse the physiological abnormalities and maintain the hemodynamic functions of the heart **(Gencer et al 2012).**

A US population-based cohort study reported that elevated serum TSH were associated with increased cardiometabolic risk and all-cause mortality (Inoue et al 2020). It was suggested that development of atherosclerotic cardiovascular disease (CVD) in hypothyroidism patients is mediated by hyperlipidemia. Because hyperlipidemia is strongly influenced by changes in serum T3, T4, and TSH levels **(Su et al 2022).**

Present study showed that SBP and DBP have shown a significant positive correlation with BMI and WC. An epidemiological study conducted on the West-Bengal, India urban adult academic professions reported that sedentary lifestyle increases the risk factors for hypertension, diabetes, hypothyroid in obese individuals **(Ghosh et al 2023).**

In addition, hypothyroid patients have shown reduction in vascular resistance. Abnormalities in thyroid hormones and blood pressure may be leading cause mechanisms in renal functions alternations in hypothyroid patients **(Allam et al 2023).**

Limitations of the study

The study duration was only 06 months and sample size was only 60 (30 diagnosed hypothyroidism patients and 30 age-matched healthy controls). Further study are required to strengthen the hypothesis that hypothyroidism is strongly associated with cardiometabolic risk factors.

SUMMARY

Introduction: Hypothyroid can be defined as elevated levels of TSH and reduced levels of T3 and T4. Hypothyroid may affect the metabolic activities and energy expenditure. Abnormal metabolic activities may cause obesity, dyslipidemia, hypertension, and hyperglycemia. These all are the risk factors for metabolic syndrome and cardiovascular disease. Several studies reported that hypothyroidism was associated with cardiometabolic risk, but results were inconsistent. **Aim:** It is aimed to determine the cardio metabolic risk factors in diagnosed cases of hypothyroidism and control subjects.

Objectives:

1. To determine the biochemical parameters; blood sugar and lipid profile in diagnosed cases of hypothyroidism and control subjects.
2. To determine demographic parameters; BMI, waist circumference and blood pressure in diagnosed cases of hypothyroidism and control subjects.
3. To find the correlation between demographic parameters and biochemical parameters in diagnosed cases of hypothyroidism and control subjects, if any.

Materials and Methods: In this case-control study, a total of 60 subjects (30 diagnosed cases of hypothyroidism and 30 age-matched healthy controls) were enrolled, aged between 30 to 65 years. A detailed medical, family and demographical history has been taken from each subject. Written consent has been taken from each subject. Subjects were enrolled as per the inclusion and exclusion criteria. Biochemical parameters such as FBS, Lipid profile, and Thyroid hormones were estimated by commercially available kit. Anthropometric parameters such as BMI, WC, SBP, and DBP were measured and recorded.

Results: Results showed that mean of BMI, WC, TC, TG, LDL-C, VLDL-C, TSH, SBP, and DBP were found significantly elevated in cases compared to controls ($p<0.001$). However, mean of HDL-C, T3, and T4 were found significantly decreased in cases compared to controls ($p<0.001$). Correlation analysis has shown that lipid abnormalities were significantly associated with obesity and hypertension in patients with hypothyroidism.

Conclusion: Result showed that mean of BMI, WC, FBS, TSH, TC, TG, LDL-C, VLDL-C, SBP, and DBP were significantly elevated in cases than controls. However, mean of T3, T4, and HDL-C was found significantly low in cases than controls. Correlation analysis has shown that lipid abnormalities were significantly associated with obesity and hypertension in patients with hypothyroidism that increase the cardiometabolic risk.

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