DISSERTATION SUBMITTED FOR THE MASTER'S DEGREE IN MEDICAL BIOCHEMISTRY

TITLE

ESTIMATION OF NON-HDL-CHOLESTEROL IN DIAGNOSED PATIENTS OF HYPOTHYROIDISM AND CONTROL SUBJECTS

SUBMITTED

BY

MO KASHIF

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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SUBMITTED

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

Master of Science

In

Medical Biochemistry

By

MO KASHIF

Enrolment No: 2000101531

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Integral Institute of Medical Sciences
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Dashauli Kursi Road, Lucknow-226026

CERTIFICATE

This is to certify that **Mr. Mo Kashif**, student of **M.Sc. Medical Biochemistry**. Integral University has completed his dissertation titled **"Estimation of Non-HDL-Cholesterol 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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I wish him good luck and a bright future.

Dr. Roshan Alam

Professor and Head
Department of Biochemistry
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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 **Mo. Kashif**

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Date:

Place: *Lucknow* ***Mo. Kashif***

CONTENTS

LIST OF ABBREVIATIONS

TSH	Thyroid Stimulating Hormones
T3	Triiodothyronine
BP	Blood pressure
LDL	Low Density Lipoprotein
HDL	High Density Lipoprotein
TG	Triglycerides
VLDL	Very Low Density Lipoprotein
T. CHOL	Total cholesterol
T4	Thyroxine
WC	Waist Circumference
MS	Metabolic Syndrome
BMI	Body Mass Index

SYMBOLS

Mg	Milligram
Dl	Deciliter
Cm	Centimeter
Kg	Kilogram
mmol/l	Millimoles per liter
kg/m^2	Kilogram per meter square
%	Percentage
Lt	Liter
≥	Greater than or Equal

INTRODUCTION

Along the midline of the neck, the thyroid gland is located neck. These hormones are involved in regulating various bodily functions, including metabolism, growth, and the levels of electrolytes like calcium in the bloodstream.

The thyroid gland is split into two lobes that are joined by the isthmus, creating a connection across the central line of the upper trachea, specifically at the second and third tracheal rings. Positioned anatomically, the thyroid gland is situated behind the sternothyroid and sternohyoid muscles, encircling the cricoid cartilage and tracheal rings.

It is located in the neck region and is the site for the synthesis of thyroid hormones responsible for homeostatic activity in the body **(Armstrong et al., 2019).**

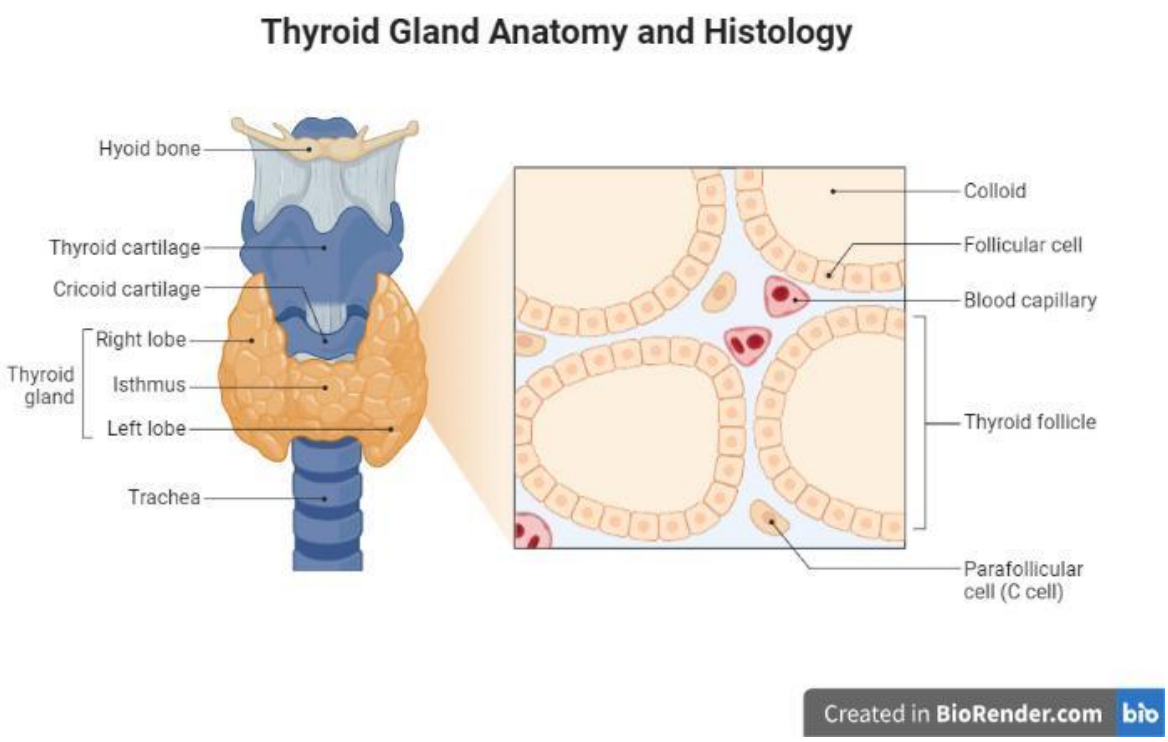

Figure 1: Thyroid Gland Histology and Anatomy

Thyroid gland produces the 2 thyroid hormones; Thyroxine T4, and Triiodothyronine T3, each playing crucial roles in the body **(Armstrong et al., 2019).**

As a result of anatomical and functional problems that limit thyroid hormone synthesis, hypothyroidism is characterized as a decrease in thyroid hormone production. **(Shlomon Melmed et al., 2016).**

Hypothyroidisms symptoms are first encountered by the clinician side effects of hypothyroidism include hypertension and dyslipidemia. It may also lead to infertility and impaired cognitive skills. A recent survey from the National Health and Nutrition Examination indicates that the prevalence of hypothyroidism is 1:300 persons in the US alone. This prevalence increases with as people age and has been found to be common in females than males. This condition can arise from primary gland failure, or an in efficiency in the mechanism that lead to formation of thyroid hormones. According to research, the main factor contributing to the rise in hypothyroidism instances in the United States is autoimmune thyroid disease. This condition is referred to as Hashimoto's disease **(Singer PA et al., 1991).**

Other subtle cause of hypothyroidism are post surgery complications of the thyroid gland, radioactive therapy and neck irradiation (Devdhar M et al ., 2007). Drugs therapy has also been found to induce Hypothyroidism. These drugs are generally tyrosine kinase inhibitors **(Barbesino G et al., 2010).**

Hypothyroidism is a common condition with multiple reasons resulting in the efficiency of thyroid gland to make enough thyroid hormone however, following autoimmune disease (Hashimoto's) and thyroid failure treatment with radioactive iodine (131I) or surgical treatment,except in regions where iodine shortage is widespread, therapy of thyrotoxicosis accounts for over 90% of causes. Women get hypothyroidism six times as often as men do. **(College et al., 2010).**

A prevalent condition, hypothyroidism affects 1% of the general population and 5% of people over 60. **(Banday et al., 2014).**

The prevalence of hypothyroidism was highest in Kolkata, India (21.67%), while rates in other cities ranged from 8.88% (Hyderabad) to 11.07% (Delhi). Delhi, Ahmedabad, Kolkata, Bangalore, and Hyderabad—cities in India's interior—reported a much greater frequency of hypothyroidism (11.73%) than did Mumbai, Chennai, and Goa acities in the nation's coastal regions.**(Unnikrishnan et al., 2013).**

In individuals experiencing hypothyroidism, there is an elevation in serum levels of total cholesterol, (LDL-C), apolipoprotein B, lipoprotein(a), and potentially TG. Certain indications propose that patients with hypothyroidism may exhibit heightened levels of total cholesterol, LDL cholesterol, and potentially triglycerides, HDL-C and Lp(a) appear to remain unaltered.**(Pearce E. N., 2004).**

Diastolic arterial pressure, non-HDL cholesterol, triglycerides, and waist circumference were positively linked with TSH levels. Subclinical hyperthyroidism has been shown to strongly correlate with LDL-C and non-HDL cholesterol, which may serve as predictive risk factors **(Wang et al., 2012).**

It has been observed that the overall lipid profile of patients is affected as increasing TSH levels are recorded **(Asvoid et al., 2007).**

Thyroid hormones are involved in the process of cholesterol biosynthesis by inducing the first step enzyme, HMG-CoA reductase. Moreover, T3stimulates LDL receptors actively controlling their gene activation mechanism. This happens when T3 directly binds to particular thyroid hormone-responsive elements situated on the DNA within cells.**(Bakker et al., 1998).**

Thyroid hormones have been known to increase cholesteryl ester transfer protein (CETP) activity affecting HDL metabolism (**Lagrost L., 1994).**

Furthermore, thyroid hormones trigger hepatic lipase (HL) activation, leading to the conversion of HDL2 into HDL3, facilitating the transformation of IDL into LDL, influencing these elements, and lipoprotein lipase (LPL) activation, which facilitates the breakdown of

triglyceride-rich lipoproteins. Despite the progress, all the nations we examined have room to enhance the lipid profiles of their populations. **(Santamarina-fojo et al., 2004).**

T3 is also involved in the up-regulation of apolipoprotein AV (ApoAV).This ApoAV has been involved in the active regulation of Triglicerydes **(Prieur et al., 2005).**

Non−HDL = total cholesterol – HDL cholesterol

REVIEW

OF

LITERATURE

Thyroid hormones are actively involved in the transcription of numerous genes from their mRNA. The result is many significant functions in the body which include, increase cellular metabolism activity and increase number and activity of mitochondria. Thyroid hormone also affects growth especially in growing children. Increase active transport of ions through cell membranes, cardiovascular activity and synthesize large numbers of proteins (structural proteins and transport proteins etc) **(Hall et al., 2012).**

Causes of hypothyroidism

Primary hypothyroidism

1. Enlarged thyroid gland caused by gradual decline in hormone production, resulting in hypothyroidism.

2. Transient hypothyroidism

3. Resistance to thyroid hormone (generalized pituitary dominant.)

4. Permanent atrophy or loss of thyroid tissue is known as atrophic hypothyroidism.

Hypothyroidism of secondary origin or central hypothyroidism (arising from disorders in the hypothalamus or pituitary gland, leading to insufficient activation of a normally functioning gland).**(Salomon Melmed et al., 2016).**

Hypothyroidism can affect every bodily system, including the integumentary system (skin and its appendages), heart, lungs, digestive system, peripheral and central nervous systems, musculoskeletal system (calcium and phosphorus balance), urinary system (water and electrolyte regulation), pituitary gland, and energy metabolism. **(ShlomonMelmed et al., 2016).**

Overt hypothyroidism was associated with increases in all three cardiovascular risk markers (UACR, LDL-cholesterol, and non-HDL-cholesterol) compared to euthyroid subjects **(Khan S et al., 2018).**

Adiposity, dyslipidemia, and insulin resistance are hallmarks of SCH in children and adolescents.

Cases of sub-chorionic hematoma are characterized by adiposity, as seen by elevated BMI, waist circumference (WC), and WHR. Imaging studies reveal that people with SCH had elevated

triglyceride (TG) levels, reduced HDL-C levels, high non-HDL cholesterol levels, and a high TG to HDL cholesterol ratio. The therapeutic relevance of these results and the need for therapy cannot be determined without further study **(Yadav Y et al., 2017).**

Elevated CETP activity has been linked to the development of metabolic syndrome and type two diabetes, two conditions that are characterized by an altered lipoprotein profile. This investigation focused on finding easy biochemical predictors of increased CETP activity. The levels of glucose, insulin, triglycerides, and non-HDL-C were all greater in MS patients, but HDL-C levels were lower **(Mukherjee et al., 2018).**

Nearly 80% of those with T2DM have a high or very high risk of cardiovascular complications. Currently, only around one-sixth of patients have optimal LDL or reduced lipoprotein and non-HDL-C (**Pattman S.J et al., 2013).**

There were no appreciable differences in the average blood levels of lipid profile. The prevalence of dyslipidemia in any of the subsets of the lipid profile did not vary considerably between the two groups, however. Subclinical hypothyroidism was a TSH range of **(5-10μIU/L)** with standard free T4 (FT4) (SH) **(Bentham J et al., 2019).**

As of now, it is still being determined if this ratio is a better or equal predictor of MetS and IR sensitivity in Koreans. No clear relationship between lipid ratios and cardiovascular outcomes could be established, nor could the influence of MetS components be disentangled from that of lipid interactions.

Although the non-HDLipid-C/HDL-C ratio was less accurate than the apoB/apoA1 ratio in identifying IR, MetS, and the individual components of MetS, it was still substantially more predictive. Using a longitudinal methodology, we assess the correlation between lipids and CVD and diabetes **(Kim et al., 2013).**

The risk of cardiovascular illness in patients with type-II diabetes is two to four times greater than in those without diabetes. Increased levels of LDL and Triglycerides and lower HDLC characterize diabetic dyslipidemia. Diabetes affects around 33 million individuals in India.

So, when Compared to controls, LDL-C and Non-HDL cholesterol levels were significantly higher **(Kondru S & Thakur A., 2015).**

Symptoms:-

1. Joint pain
2. Sensitivity to cold
3. Bowel irregularity
4. Mood disorders
5. Trouble focusing
6. Excessive menstrual bleeding
7. Muscle pains
8. Lack of strength
9. Increased body mass
10. Skin dryness
11. Tiredness
12. Reduced hair thickness/hair shedding
13. Cognitive decline

Clinical manifestations of hypothyroidism include:

1. Slow heart rate (Bradycardia)
2. Coarse facial features (Coarse facies)
3. Impaired cognitive function (Cognitive impairment)
4. Prolonged relaxation phase of deep tendon reflexes
5. Diastolic dysfunction of the blood vessels (Diastolic vascular disease)
6. Swelling and fluid accumulation (Edema)
7. Enlarged thyroid gland (Goiter)
8. Decreased body temperature (Hypothermia)
9. Increased levels of prolactin in the blood (Hyperprolactinemia)

10. Thinning of the outer part of the eyebrows (Lateral eyebrow thinning)

11. Abnormal low-voltage electrocardiogram (Low-voltage ECG)

12. Enlarged tongue (Macroglossia)

13. Swelling around the eyes (Periorbital edema)

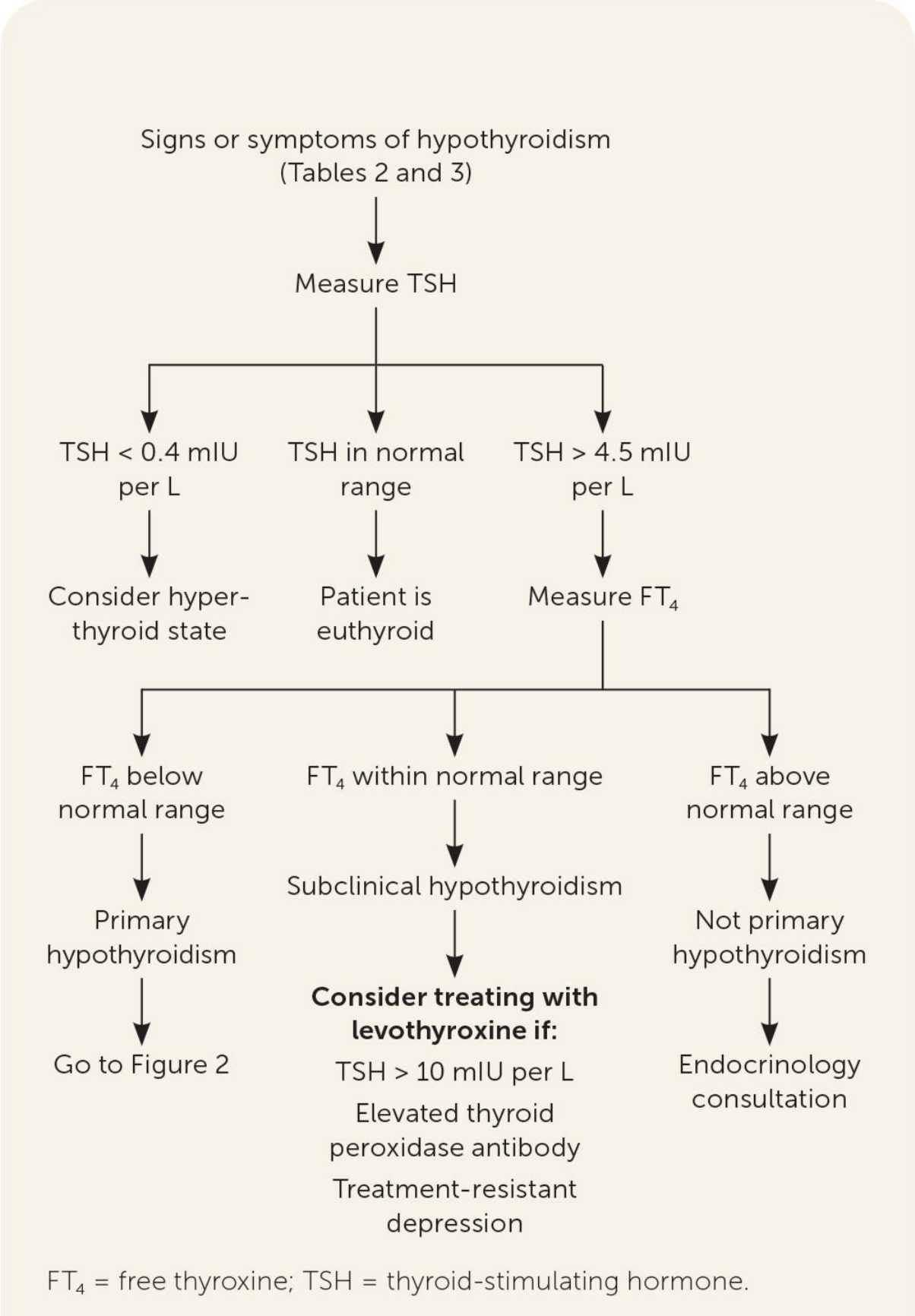

Figure 2: Illustration of TSH levels and diagnosis of thyroid disorders (Islam et al., 2017).

Age and gender can affect how hypothyroidism manifests in symptoms. Lack of energy and failure to thrive may be more common in infants and young children. Infertility and irregular periods are two symptoms of hypothyroidism in females. Deterioration of cognitive function may be the only symptom in elderly patients. Goitre, an extended relaxation stage of deep reflexes of the tendon, thin or weak hair, cracked skin, and swelling in the peripheral region are only a few of the test results linked to hypothyroidism. Common ECG findings for patients with hypothyroidism include bradycardia and flattened T waves. Hypothyroidism cases also present symptoms of pericardial and pleural effusion. Severe cases present an enlarged colon, hemodynamic instability, and in worse cases, this leads to a unconsciousness (**Ladenson PW et al ., 2000).**

Treatment

The majority of patients with hypothyroidism will need ongoing thyroid hormone therapy. Despite the fact that T4 is created in higher quantities, T3 is the physiologically active version. Deiodinase enzymes convert T4 in the periphery to produce around 80% of the T3 in the body none the less, due to the predominant utilization of short-acting synthetic thyroxine formulations (T3 preparations) for the management of hypothyroidism. Similar to endogenous thyroxine, artificial thyroxine is converted into the more physiologically active T3 after being digested. Both brand-name and generic versions of synthetic thyroxine are offered.

In 2004, the conclusion that the absence of TSH indicators to establish biological equivalents in combination with potentially deficient pharmacokinetic parameters methods could result in significant under- and inaccurate estimations of generic equivalents relative to brand-name levothyroxine stuff. As a result, they advise against switching back and forth between brand-name and generic levothyroxine compositions for patients who are starting and maintaining their treatment. To maintain optimal levels within the normal range, individuals who alter their medication regimen should undertake additional testing for TSH and free T4 over a period of six weeks. Levothyroxine should be administered at a beginning dose of 1.6 g/kg/day in individuals who are young and healthy for full replacement. Levothyroxine should not be taken within 4 hours

of ca+ and Fe supplements since these substances may reduce the absorption of thyroid hormones. The most frequent reason for persistently increased TSH in patients receiving appropriate dosages of thyroid hormone is poor adherence to levothyroxine medication. For newborns and kids, the dosage of levothyroxine is weight-based and age-specific **(Roos A et al., 2005).**

According to patient response and test results, medication should be modified. A great substitute for patients who struggle with morning levothyroxine dosage is nighttime medication. Levothyroxine night dose led to lower TSH and greater free T4 levels in a designed effectively research carried out in the Netherlands, but there was no difference in quality of life **(Bolk N et al., 2010).**

On the flip side, individuals who struggle with maintaining a once-daily routine of levothyroxine can confidently opt for a Levothyroxine substitute that has received approval from the DA (regulatory authority). They presented at the pharmacy with a full week's worth of levothyroxine supply. **(Grebe SK et al., 1997).**

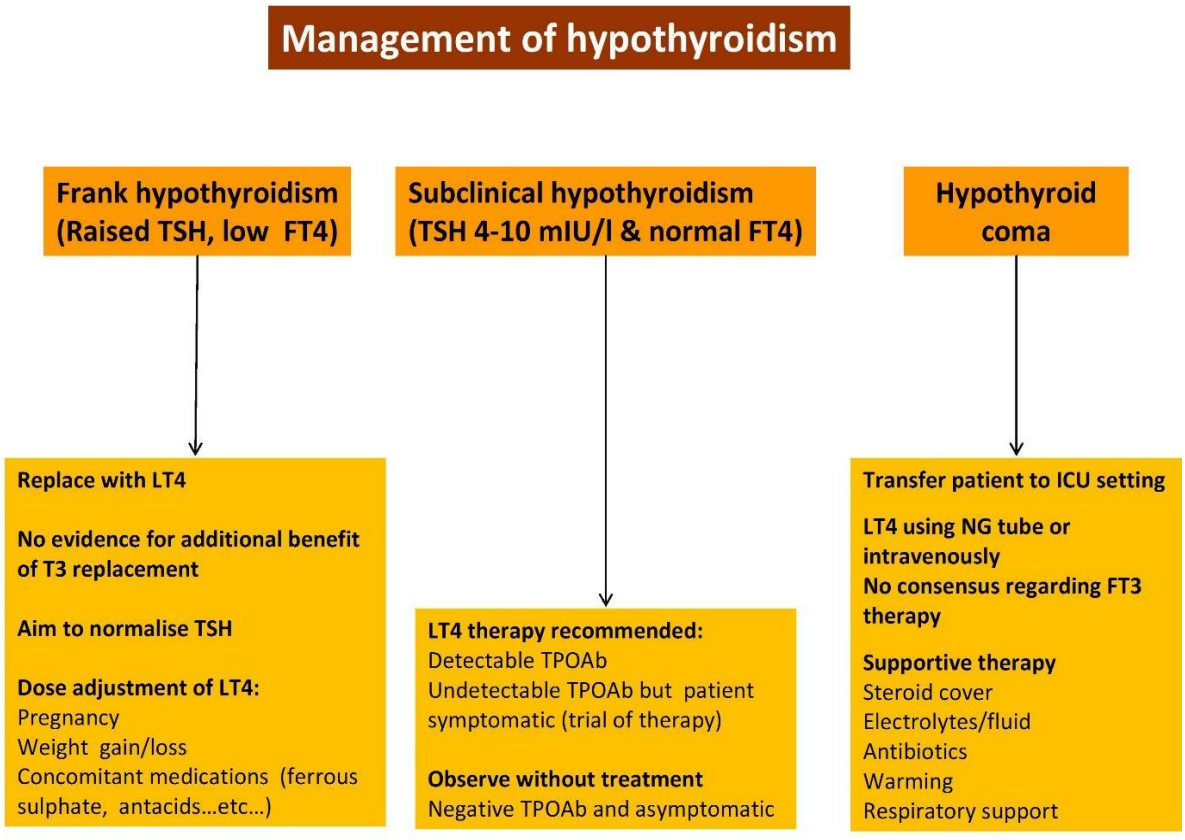

Figure 3: Management of hypothyroidism (King et al., 2012)

AIM

&

OBJECTIVES

AIM

To find the association of non-HDL-C and cardiometabolic risk factors in patients with hypothyroidism.

OBJECTIVES

1. To estimate serum FBS and lipid profile in patients of hypothyroid patients and apparently healthy controls.

2. To estimate the BMI, waist circumference and blood pressure in patients of hypothyroid patients and apparently healthy controls.

3. To find the correlation between non-HDL-C and cardiometabolic risk factors in patients of hypothyroid patients and apparently healthy controls, if any.

MATERIAL

&

METHODS

Research Question:-

Is there any significant association between non-HDL-C and cardiometabolic risk factors in patients with hypothyroidism?

Null Hypothesis H_0: There is no significant association between non-HDL-C and cardiometabolic risk factors in patients with hypothyroidism.

Alternate Hypothesis H_1: There is a significant association between non-HDL-C and cardiometabolic risk factors in patients with hypothyroidism.

METHODOLOGY

Study Design: - A case-control Study.

Place of Study: -Department of Biochemistry, Integral Institute of Medical Science and Research, Lucknow (IIMSR), Uttar Pradesh (U.P.)

Sampling Method: - Non-probability, Purposive sampling.

Duration of Study: January 2023 to June 2023

Collaborating Department: - Department of Medicine, OPD at IIMS&R, Lucknow

SUBJECT SELECTION

In this case-control study, a total of 60 subjects (30 subjects of diagnosed hypothyroidism patients and 30 subjects of age-matched healthy controls) were enrolled from the OPD, Department of Medicine, Integral Institute of Medical Sciences & Research (IIMSR) based on inclusion and exclusion criteria. A detailed demographic, medical and family history was taken from each subject. Written informed consent was taken from each subject.

INCLUSION CRITERIA FOR CASES

1. Diagnosed cases of hypothyroidism (TSH ≥5μIU/mL) (Sheehan et al.,2016).
2. Subjects between the ages of 30 to 65 years.
3. Patients who have agreed to sign the consent form.

EXCLUSION CRITERIA FOR CASES

1. History of any chronic disease or infectious disease.

2. Pregnant and lactating females.

Selection of 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.

SAMPLE SIZE

$$n = \left(\frac{r+1}{r}\right)\frac{\sigma^2(Z_\beta + Z_{\alpha/2})^2}{(d\text{ifference})^2}$$

Sample size calculation formula

Charan J, Biswas T. How to calculate sample size for different study designs in medical research?. Indian journal of psychological medicine. 2013 Apr; 35(2):121-6.

n = sample size in the case group. ***r***

= ratio of controls to cases.

σ = standard deviation of the outcome variables.

Difference = effect size (the difference in means of cases and controls)

Zβ = Represent the derived power (typically .84% for 80% power)

$Z\alpha_{/2}$ = Represents the derived level of statistical

For 95% CI $Z_{\alpha/2}$ = 1.96, for 80% power ***Z***β = 0.84.

Expected mean difference between cases and controls (d) = 3.6**(Chandrika et al., 2021).**

Standard Deviation is = 7

n1 (Cases) = 30

n2 (Control) = 30

Reference: Chandrika N, Devaki RN, Reshma S. Non High Density Lipoprotein Cholesterol, a Simple and Reliable Marker to Assess Cardiovascular Disease Risk in Hypothyroid Patients.

Sample Collection:-

Under the 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 samples were then centrifuged at 1000 rpm for 10 minutes to separate the serum **(Henry J.B., 1979).** 1 ml serum was used for the determination of lipid profile (total cholesterol, triglyceride, high density lipoprotein, & low density lipoprotein) in diagnosed cases of hypothyroidism.

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, and Lucknow (U.P)

LABORATORY INVESTIGATION:

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

Methodology:-Modified Roeschlau'sMethod.

PRINCIPLE

The estimation of cholesterol involves the following enzyme catalysed reactions.

1. Cholesterol ester $\xrightarrow{\text{Cholesterol esterase}}$ cholesterol + fatty acid

2. Cholesterol + O_2 $\xrightarrow{\text{CHOD}}$ cholest-4-en-3-one + H_2O_2 (CHOD-Cholesterol Oxidase)

3. $2H_2O_2$ + 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	1000 µl
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 Analyser.

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

Principal

1. Triglyceride + H_2O —LPL→ Glycerol + Free fatty acids
2. Glycerol + ATP —Glycerol Kinase→ Glycerol-3-phosphate + ADP
3. Glycerol-3-phosphate + O_2 —GPO→ DAP + H_2O_2

(Glycerol phosphate Oxidase)

4. 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	1000 µl
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 analysers against reagent blank **(McGowan et al., 1984).**

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

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 **(Pisani et al., 1995).**

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

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

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: < 94 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 **(France).**

ETHICS REVIEW

Permission from the Institutional Ethics Committee was taken (IEC/IIMS&R/2023/63).

STATISTICAL ANALYSIS

Statistical analysis was performed using IBM-SPSS software (version 16), Graph Pad (Prism 6.0) and Microsoft – Excel (version 2013). All the data were 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-value<0.05 was considered statistically significant.

OBSERVATIONS

AND

RESULTS

Results:

Mean of BMI, WC, FBS, TSH, TC, TG, non-HDL-C, LDL-C, VLDL-C, SBP, and DBP were significantly elevated in cases compared to controls ($p < 0.001$). However, mean of T3, T4, and HDL-C

Table 1 Baseline characteristics of cases and controls

Groups	Cases (n=30)	Controls (n=30)	p-value
Age (years)	39.46 ± 7.87	42.46 ± 8.80	0.1693
BMI (kg/m^2)	26.40 ± 3.94	22.41 ± 2.15	0.0001
WC (cm)	90.66 ± 6.06	83.67 ± 4.73	0.0001
FBS (mg/dL)	99.93 ± 19.60	91.73 ± 14.41	0.0700
T3 (nmol/L)	1.56±0.41	2.05 ± 0.88	0.0076
T4 (nmol/L)	86.87 ± 15.91	127.25 ± 55.42	0.0003
TSH (µIU/mL)	7.78 ± 4.45	2.17 ± 0.91	0.0001
TC (mg/dL)	195.01 ± 41.28	124.54 ± 20.87	0.0001
TG (mg/dL)	150.96 ± 64.77	123.17 ± 35.94	0.0444
HDL-C (mg/dL)	42.15±7.07	49.01 ± 6.43	0.0002
NON-HDL-C (mg/dL)	144.03 ± 44.58	75.86 ± 24.83	0.0001
LDL-C (mg/dL)	119.55 ± 40.16	50.89 ± 19.90	0.0001
VLDL-C (mg/dL)	31.19 ± 13.74	24.63 ± 7.18	0.0240
***SBP*(mmHg)**	146.53 ± 12.76	122.23 ± 5.65	0.0001
***DBP*(mmHg)**	93.63 ± 7.21	84.36 ± 5.48	0.0001

**p<0.05 was considered statistically significant.*

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 (39.46 ± 7.87) have been found.

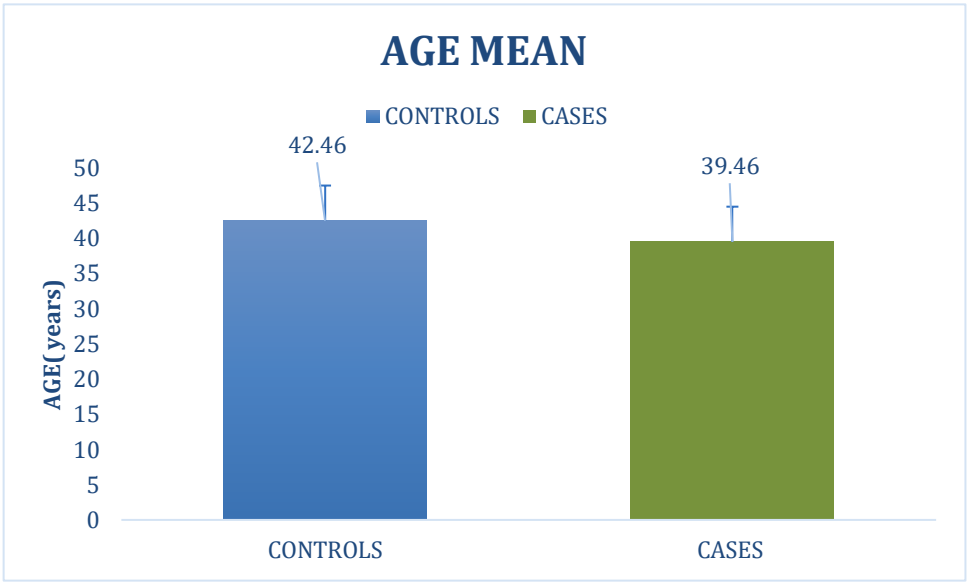

Figure.4. Comparison of ages (years) in cases & controls

BODY MASS INDEX (BMI)

Anthropometric parameter BMI were significant in patients of hypothyroidism, comparing with control subjects, (p=0.0001) shown in table 1.

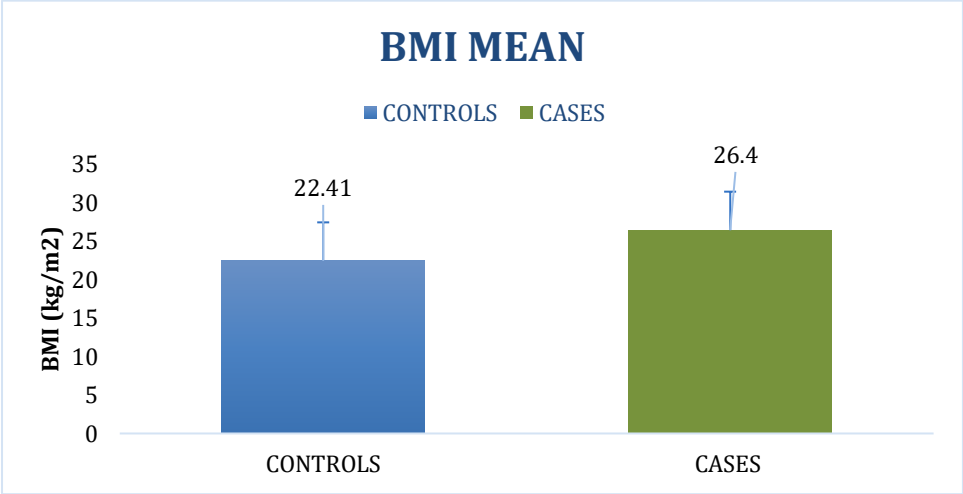

Figure 5. Comparison of BMI in cases and controls.

Total Cholesterol

Serum total cholesterol is significantly increased in patients of hypothyroidism, comparing with control subjects, (p= 0.0001) shown in table. 1.

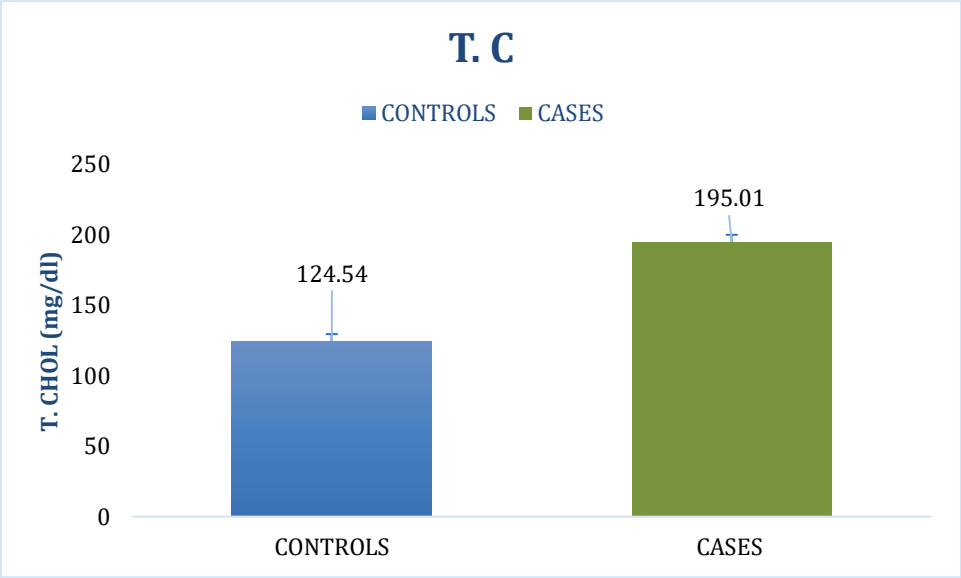

Figure 6. Comparison of total cholesterol in cases and controls.

Serum triglycerides

In patients of hypothyroidism compared to control subjects, serum triglycerides are considerably higher (p= 0.0444) shown in table.1.

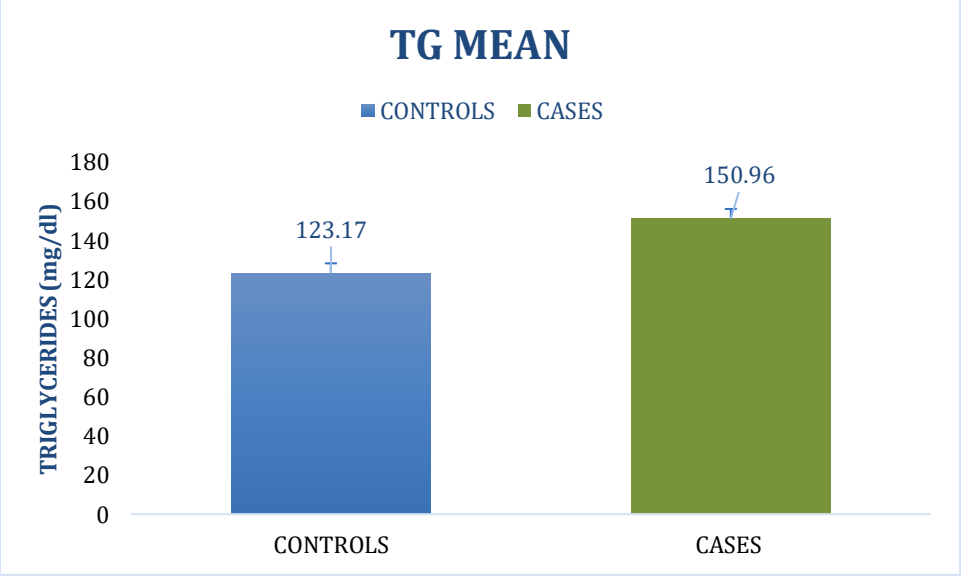

Figure 7. Comparison of triglycerides in cases and controls.

Serum Non-HDL

Compared to control subjects, in patients of hypothyroidism serum HDL-C is considerably lower (p=0.0001) shown in table.1.

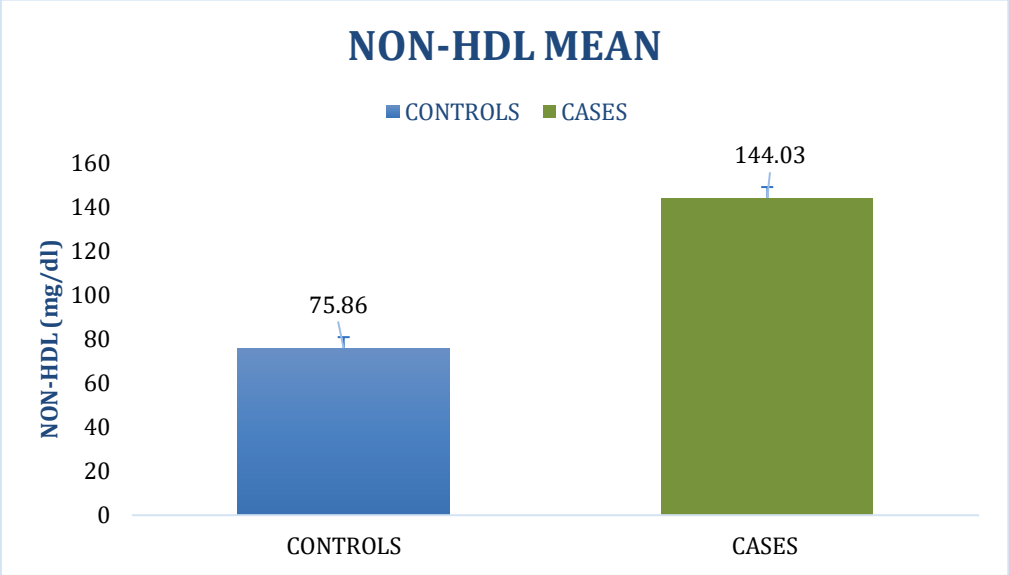

Figure 8. Comparisonof HDL-C in cases and controls.

Serum LDL

When compared to control subject, in patients of hypothyroidism serum LDL-C is considerably higher (p=0.0001) shown in table.1.

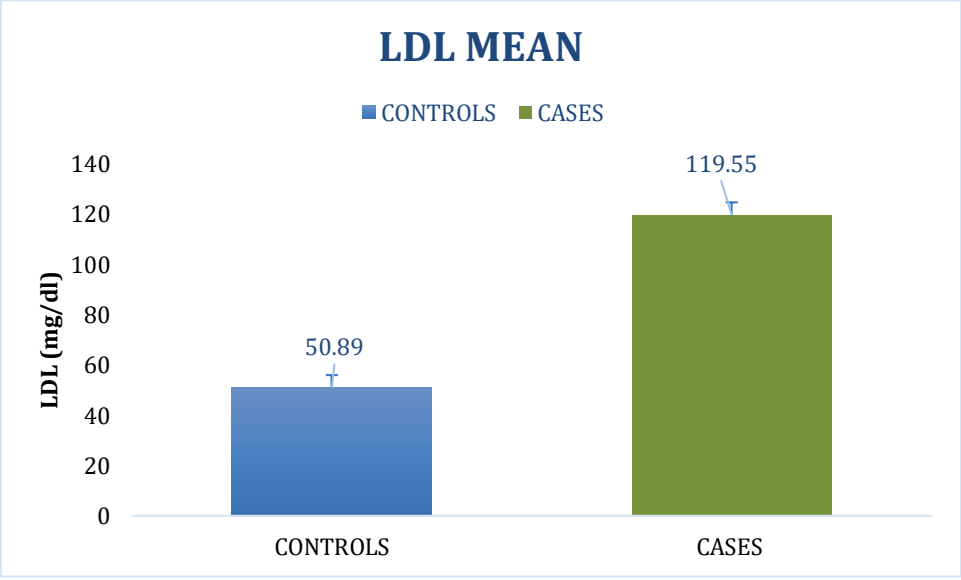

Figure 9. Comparison of LDL-C in cases and controls.

Fasting blood sugar

In patients of hypothyroidism compared to control subjects, fasting blood sugar are considerably higher (p=0.0700) shown in table.1.

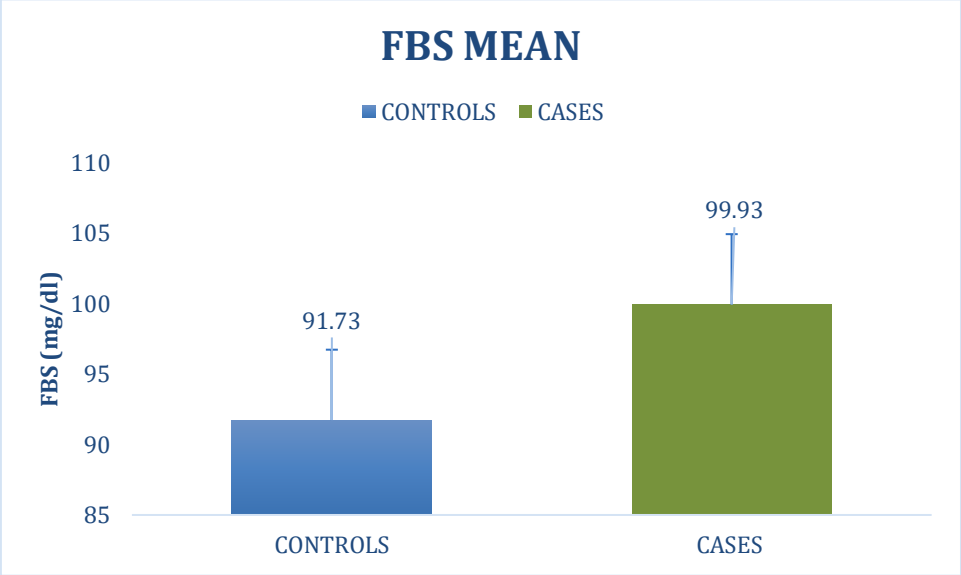

Figure 10. Comparison of FBS in cases and controls

Waist Circumference

When compared to control subjects, in patients of hypothyroidism, waist circumference is considerably higher (p=0.0001) shown in table.1.

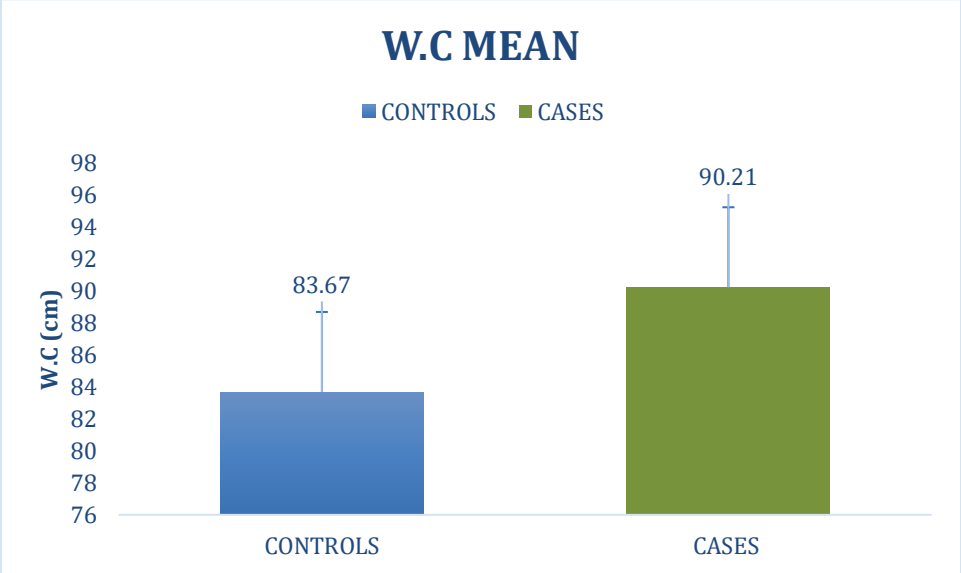

Figure 11. Comparison of W.C. in cases and controls

Blood pressure (systolic)

When compared to control subjects, in patients of hypothyroidism, systolic blood pressure is considerably higher (p=0.0001) shown in table.1.

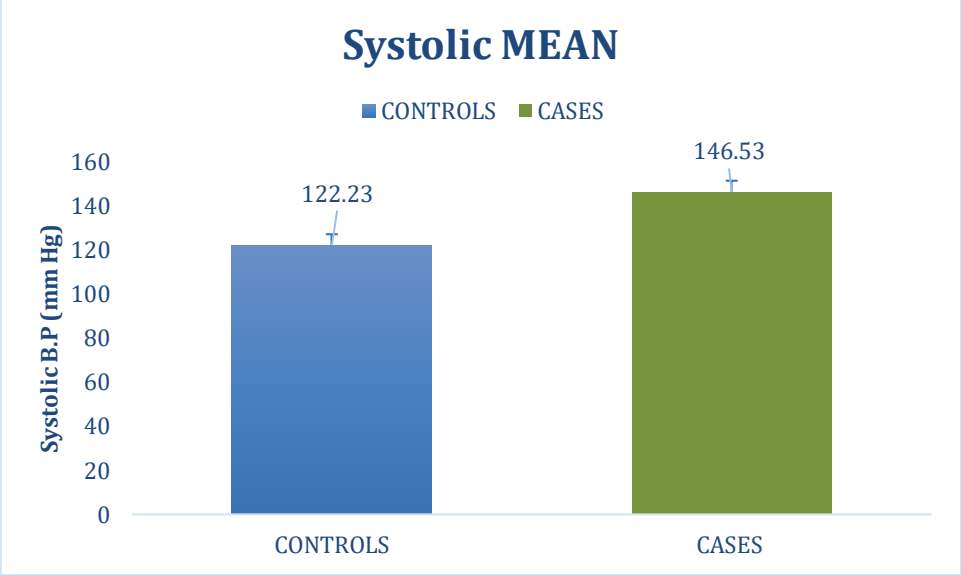

Figure 12. Comparison of Systolic BP in cases and controls

Blood pressure (diastolic)

When compared to control persons, in patients of hypothyroidism, diastolic blood pressure is considerably higher (p=0.0001) shown in table.1.

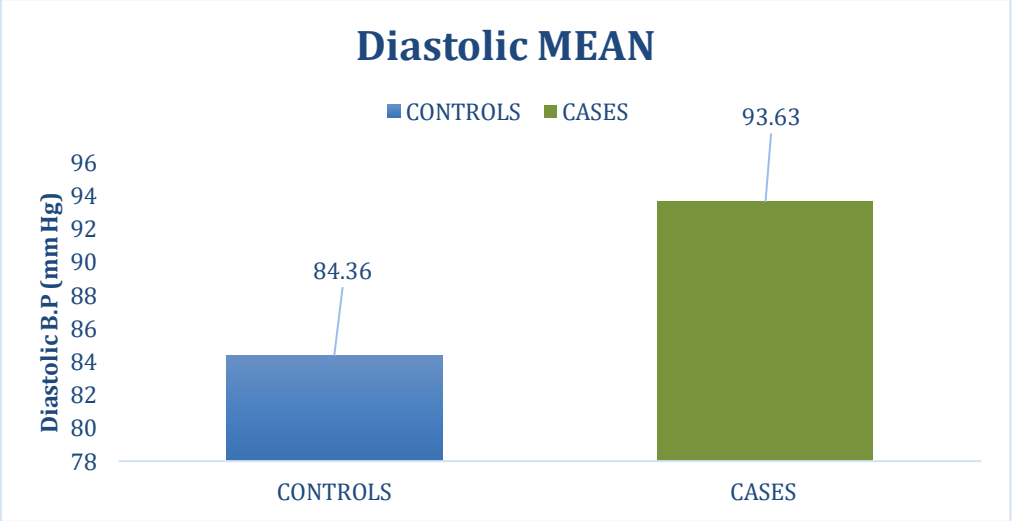

Figure 13. Comparison of Diastolic BP in cases and controls.

KARL PEARSON'S CORRELATION

TC has shown a significant positive correlation with non-HDL-C ($r = 0.707$, $p<0.01$), and LDL-C ($r = 0.933$, $p<0.01$), TG has shown a significant positive correlation with VLDL-C ($r = 0.918$, $p<0.01$), and Age ($r = 0.0.421$, $p<0.05$), Non-HDL-C has shown a significant positive correlation with LDL-C ($r = 0.719$, $p<0.01$), and Age ($r = 0.375$, $p<0.05$), VLDL-C has shown a significant positive correlation with Age ($r = 0.450$, $p<0.05$), BMI has shown a significant positive correlation with WC ($r = 0.580$, $p<0.01$), and DBP ($r = 0.547$, $p<0.01$), WC has shown a significant positive correlation with DBP ($r = 0.538$, $p<0.01$), Age has shown a significant positive correlation with FBS ($r = 0.497$, $p<0.01$), and SBP has shown a significant positive correlation with DBP ($r = 0.386$, $p<0.05$).

Table 2: Correlation analysis of different parameters among cases

Parameters	TC	TG	NON. HDL	LDL	VLDL	T3	T4	TSH	BMI	WC	AGE	FBS	SBP	DBP
TC	1	0.315	**0.707****	**0.933****	0.282	-0.084	-0.064	0.249	0.022	-0.141	0.183	0.311	0.061	0.099
TG		1	.212	0.035	**0.918****	0.124	-0.077	0.245	-0.330	-0.281	**0.421***	0.331	-0.286	-0.273
NON.HDL			1	**0.719****	0.202	-0.047	-0.017	0.271	-0.104	-0.014	**0.375***	-0.026	-0.188	-0.126
LDL				1	0.032	-0.110	-0.128	0.234	0.129	-0.062	0.159	0.302	0.096	0.159
VLDL					1	0.040	-0.125	0.173	-0.157	-0.195	**0.450***	0.320	-0.314	-0.243
T3						1	-0.191	-0.052	-0.187	-0.128	-0.045	0.027	-0.125	-0.068
T4							1	-0.142	0.160	0.292	-0.069	-0.285	0.092	0.129
TSH								1	-0.135	-0.210	0.327	0.318	-0.310	-0.181
BMI									1	**0.580****	-0.131	0.097	0.009	**0.547****
WC										1	0.012	-0.073	0.251	**0.538****
AGE											1	**0.497****	-0.042	-0.218
FBS												1	0.161	0.160
SBP													1	**0.386***
DBP														1

**p<0.05 was considered statistically significant.*

***p<0.01 was considered statistically significant.*

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

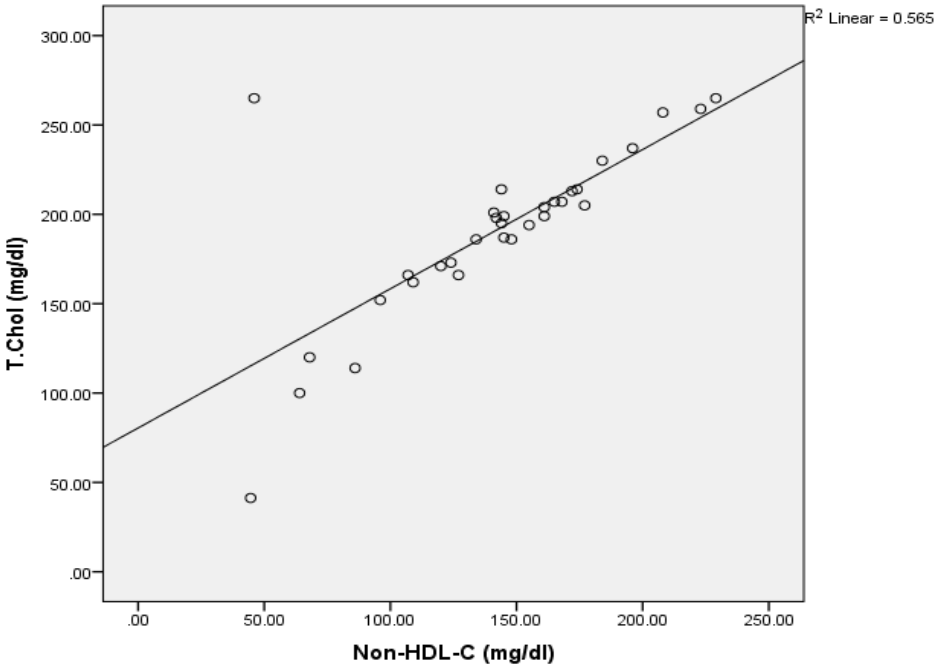

Figure.14: Correlation of Non-HDL-C and T.Chol among cases.

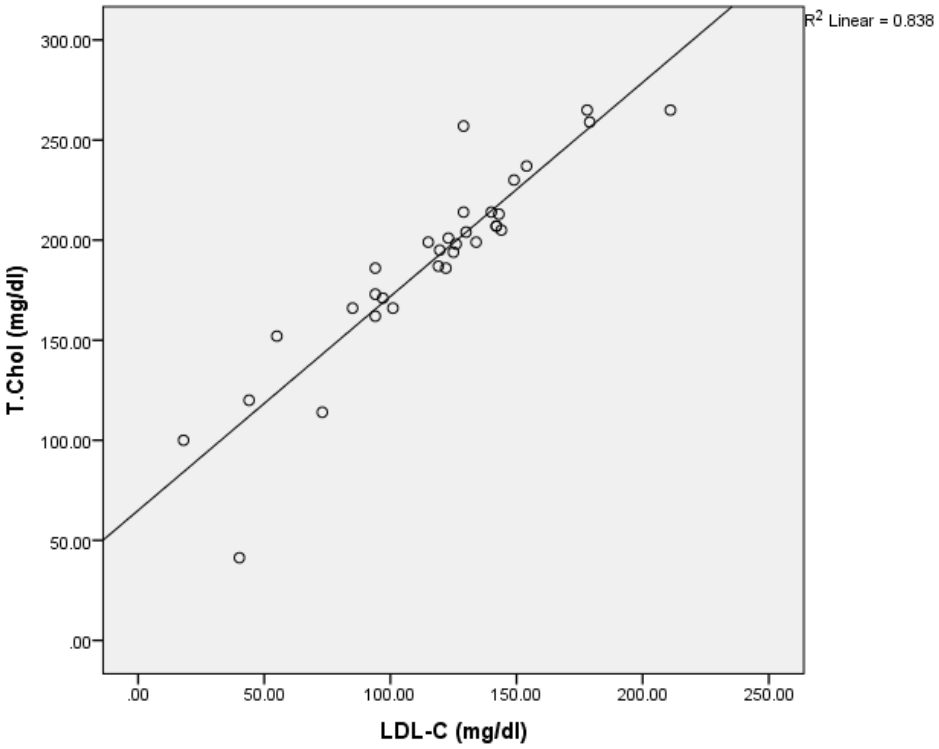

Figure.15: Correlation of LDL-C and T.Chol among cases.

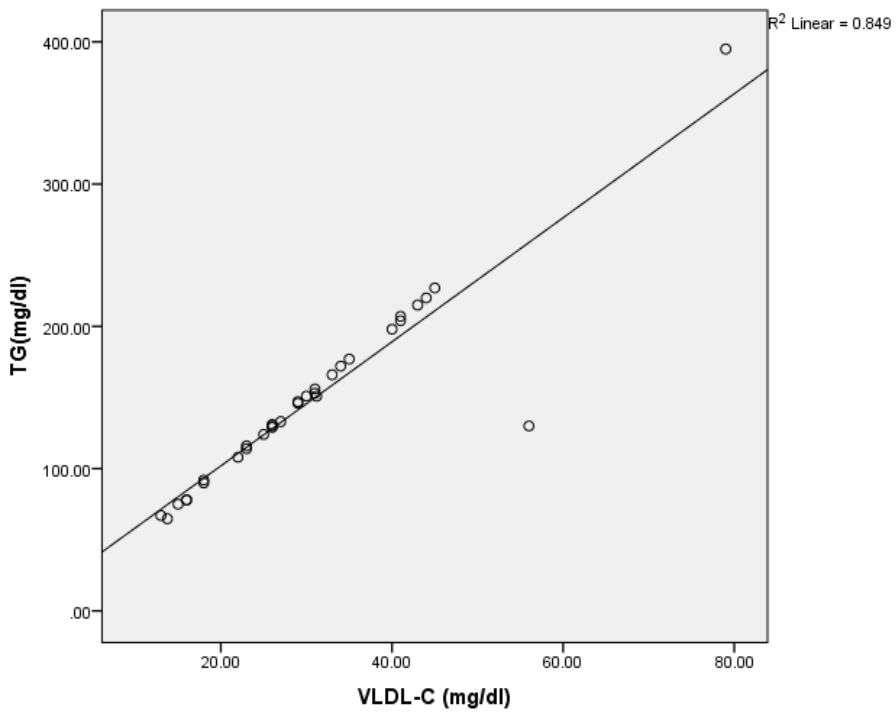

Figure.16: Correlation of VLDL-C and TG among cases.

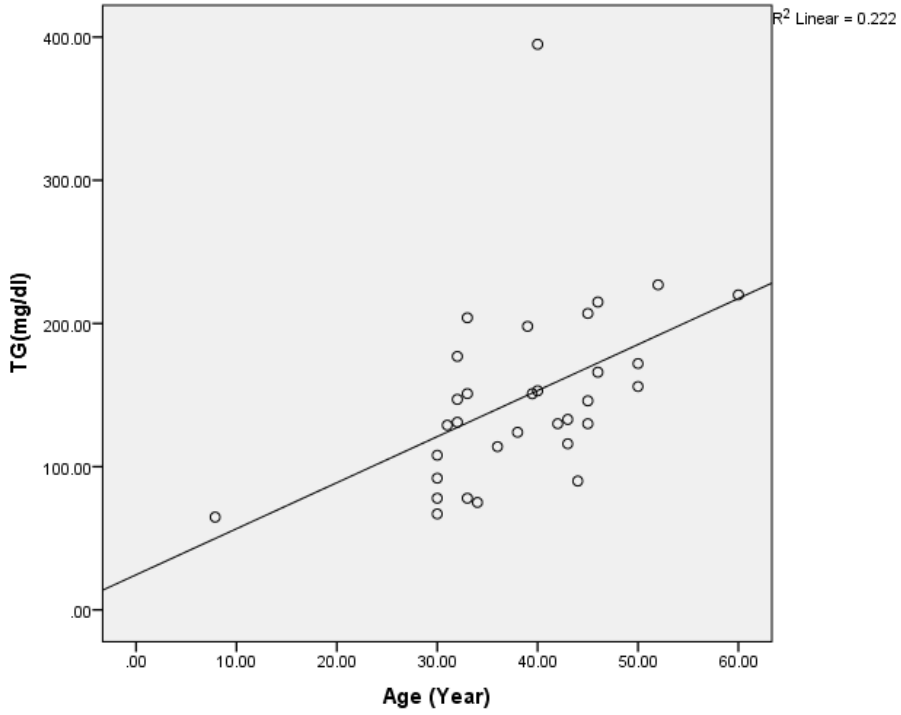

Figure.17: Correlation of Age and TG among cases.

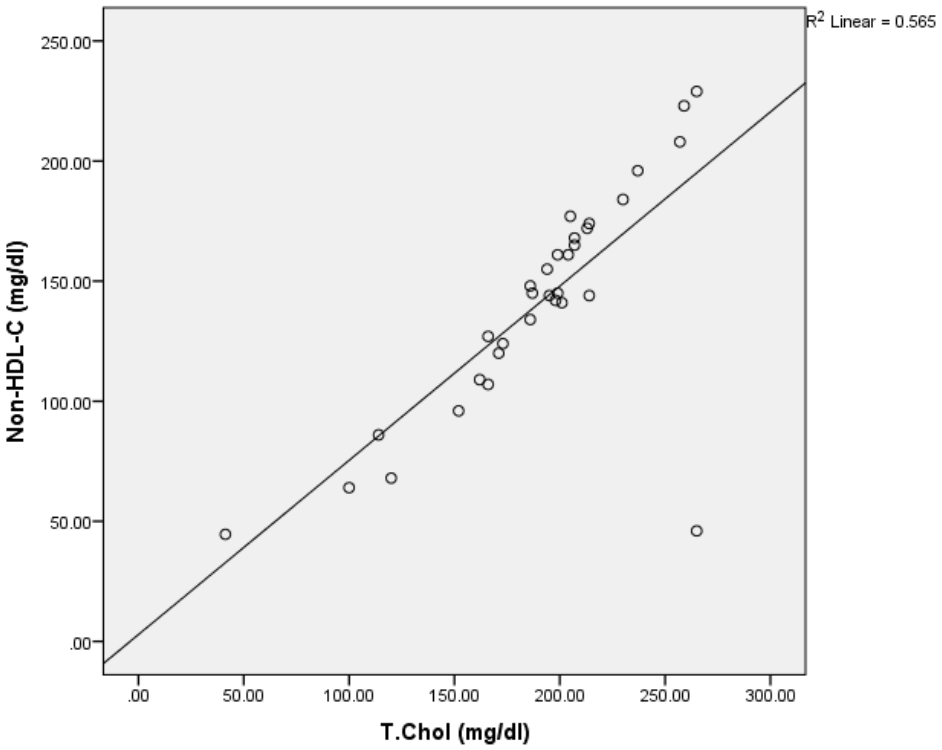

Figure.18: Correlation of T.Chol and Non-HDL-C among cases.

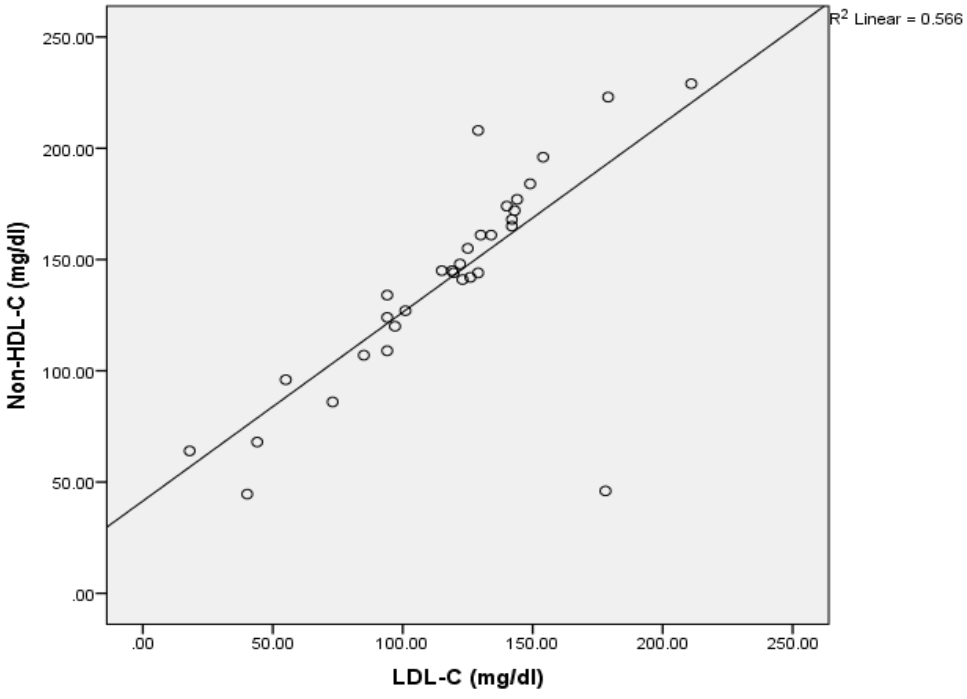

Figure.19: Correlation of LDL-C and Non-HDL-C among cases.

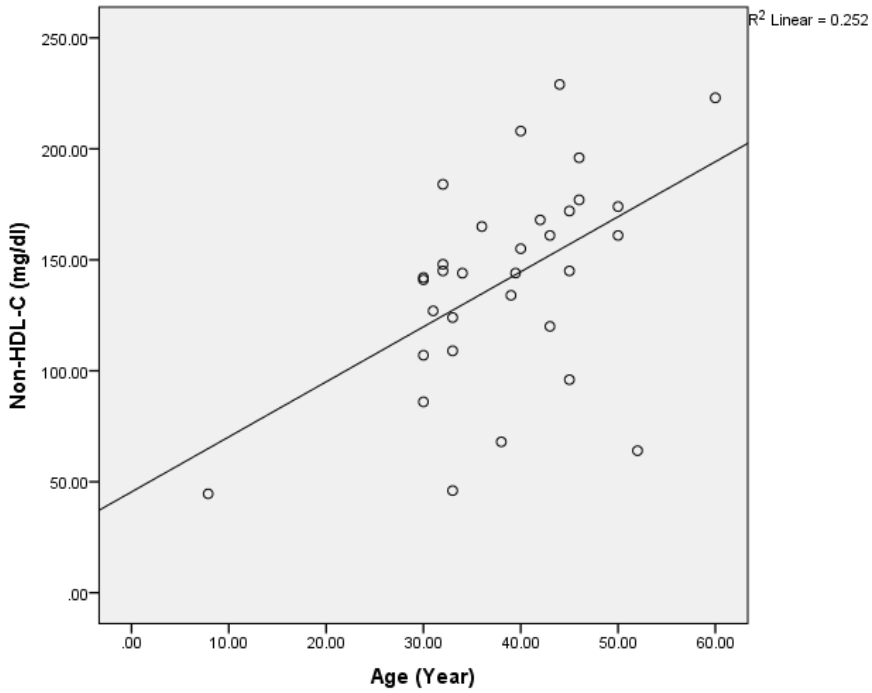

Figure.20: Correlation of Age and Non-HDL-C among cases.

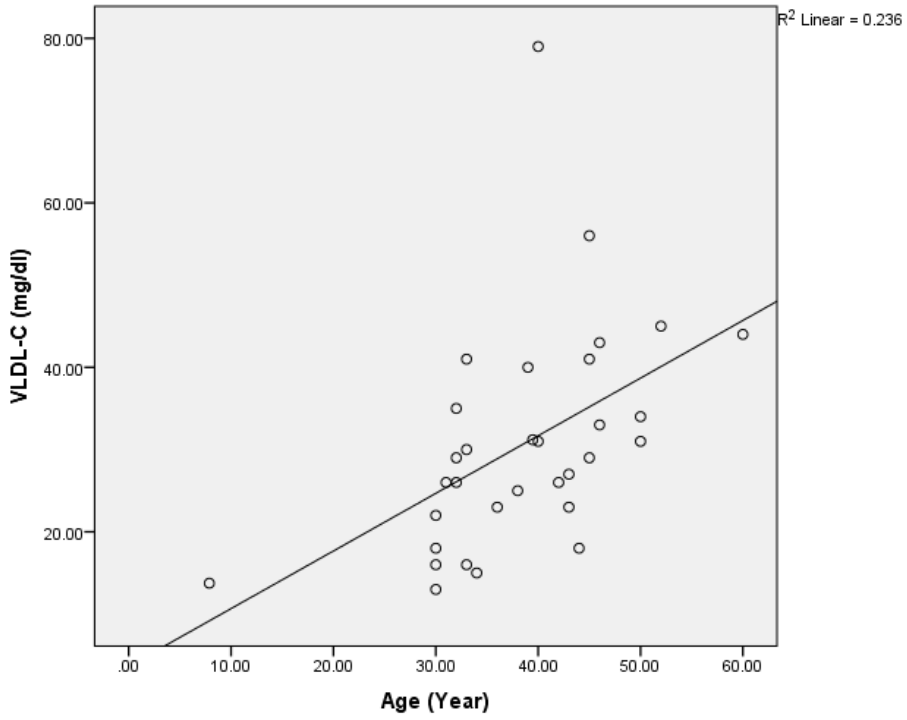

Figure.21: Correlation of Age and VLDL-C among cases.

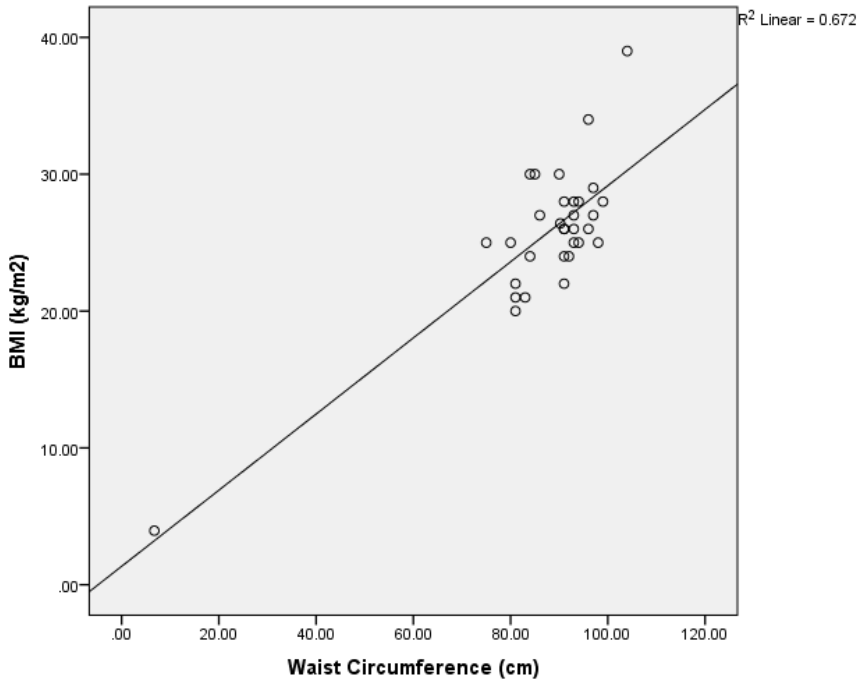

Figure.22: Correlation of Waist Circumference and BMI among cases.

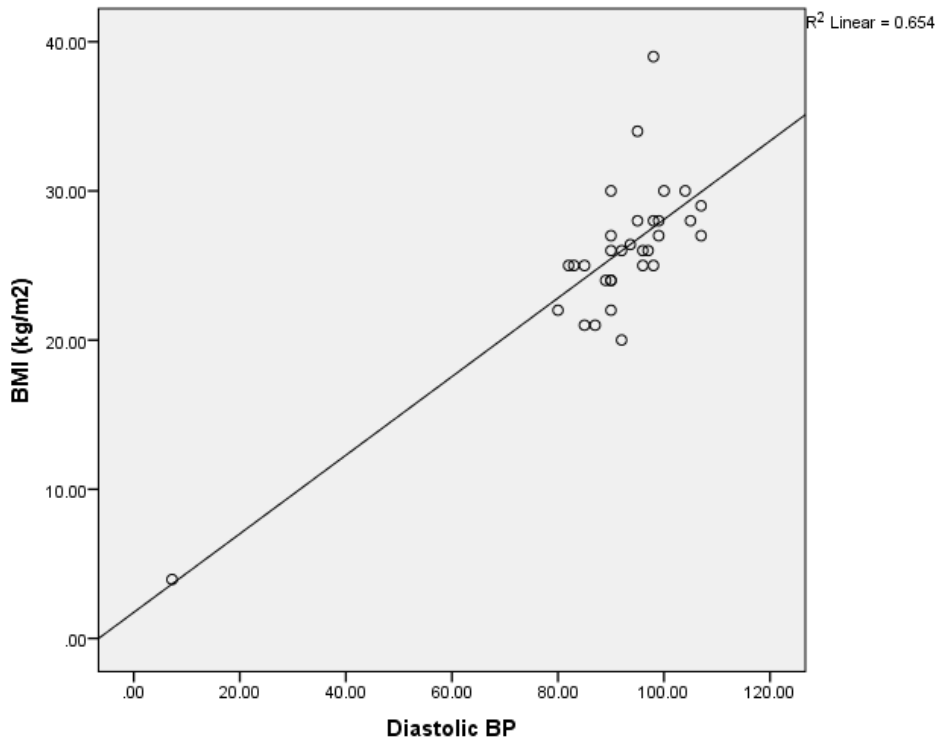

Figure.23: Correlation of Diastolic BP and BMI among cases.

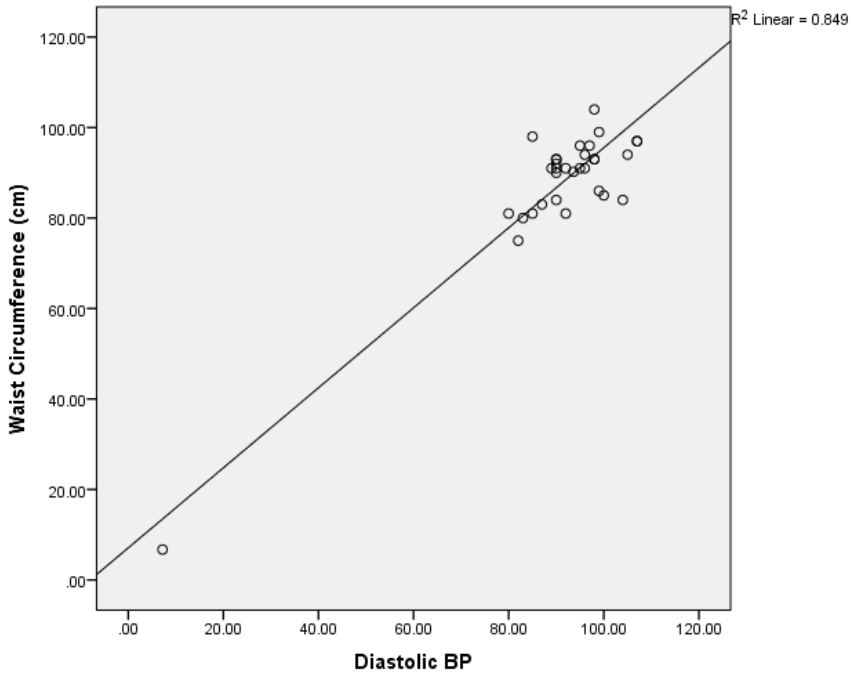

Figure.24: Correlation of Diastolic BP and Waist Circumference among cases.

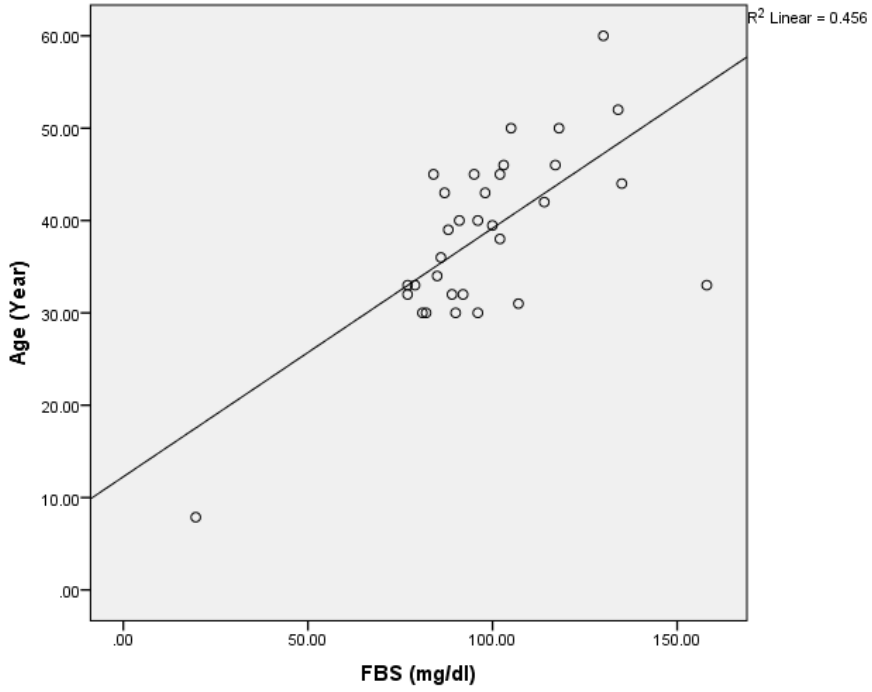

Figure.25: Correlation of FBS and Age among cases.

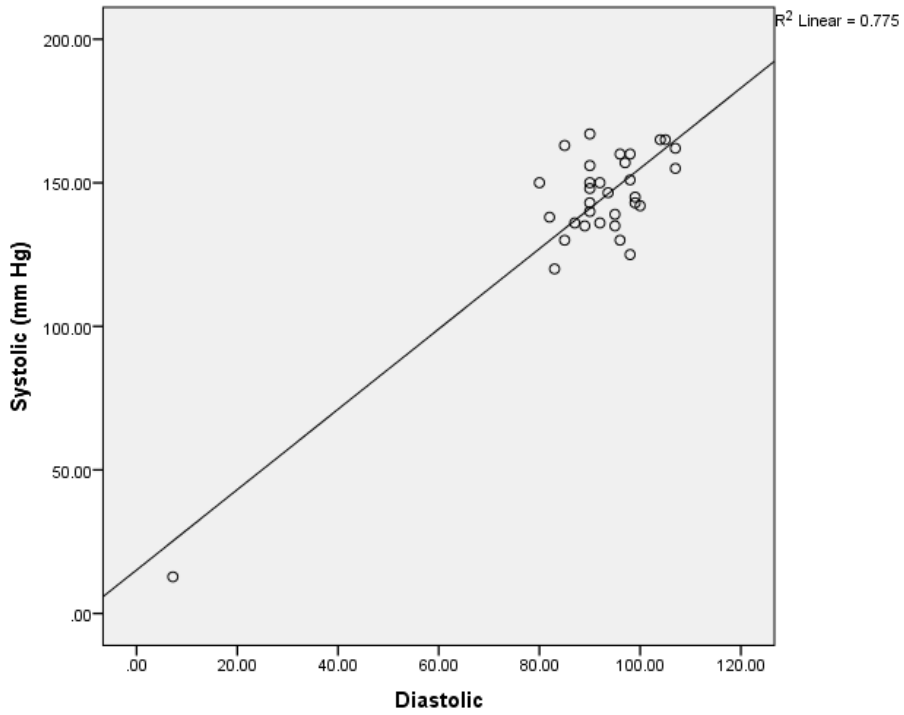

Figure.26: Correlation of Diastolic BP and Systolic BP among cases.

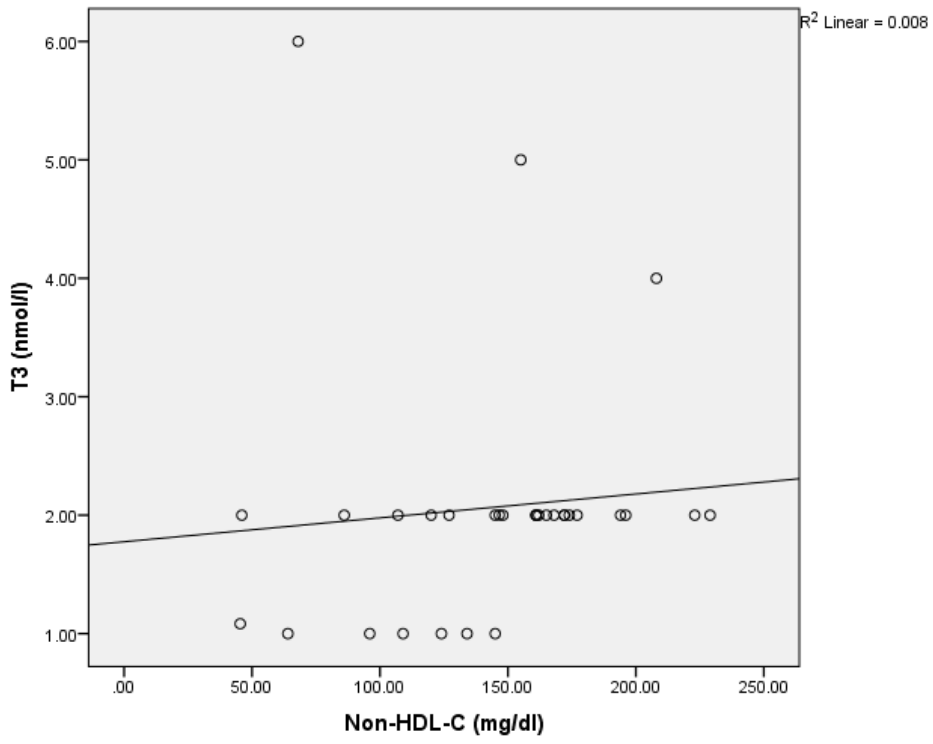

Figure.27: Correlation of Non-HDL-C and T3 among cases.

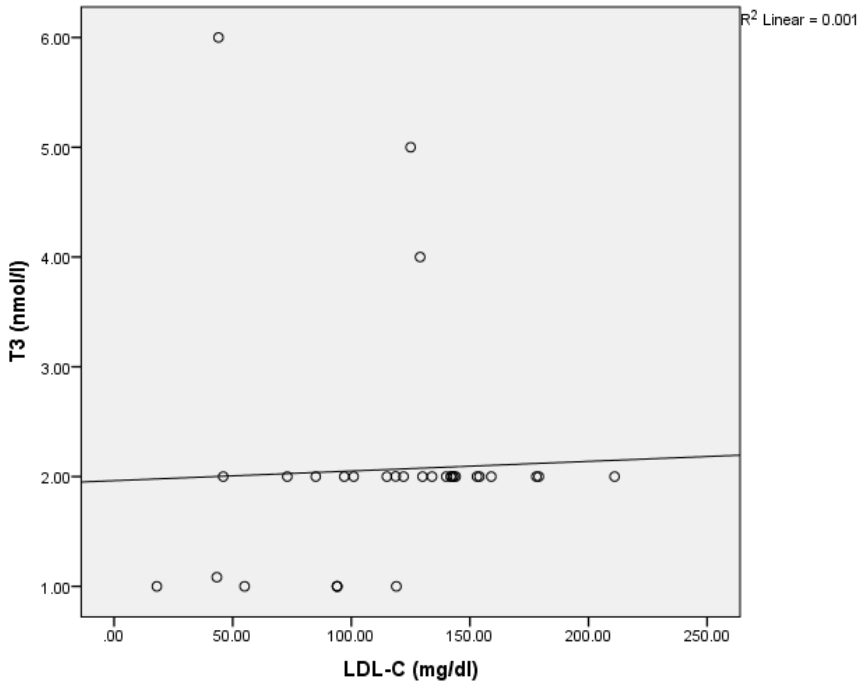

Figure.28: Correlation LDL-C and T3 among cases.

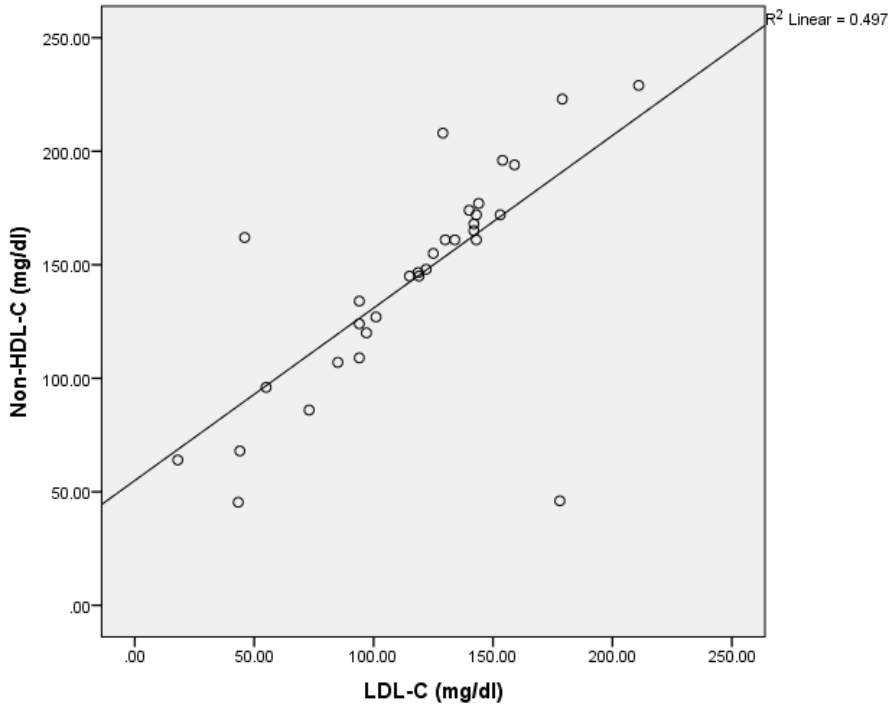

Figure.29: Correlation LDL-C and Non-HDL-C among cases.

DISCUSSION

Result showed that mean of BMI, WC, FBS, TSH, TC, TG, non-HDL-C, LDL-C, VLDL-C, SBP, and DBP were significantly elevated in cases compared to controls. However, mean of T3, T4, and HDL-C was found significantly low in cases compared to 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 the development of 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 associated with high

levels of 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 high levels of 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 patients with hypothyroidism 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 non-HDL-C has a significant positive correlation with age and TC in patients with hypothyroidism. Non-HDL-C may act as a novel marker for prognosis of insulin resistance and atherogenic CVD and coronary artery disease (CAD) (Mao et al 2023).

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 confirm our findings and strengthen the hypothesis that hypothyroidism is strongly associated with cardiometabolic risk factors.

SUMMARY

AND

CONCLUSION

Introduction: Hypothyroid can be defined as high amount of TSH and decreased amount 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

To find the association of non-HDL-C and cardiometabolic risk factors in patients with hypothyroidism.

OBJECTIVES

1. To estimate serum FBS and lipid profile in patients of hypothyroid patients and apparently healthy controls.
2. To estimate the BMI, waist circumference and blood pressure in patients of hypothyroid patients and apparently healthy controls.
3. To find the correlation between non-HDL-C and cardiometabolic risk factors in patients of hypothyroidism patients 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, total chol, tg, LDL-C, VLDL-C, TSH, SBP, & DBP was found significantly elevated in cases compared to control subjects ($p < 0.001$). However, mean of Non-HDL-C, T3, and T4 were found reduced in cases compared to control subjects ($p < 0.001$). 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, non-HDL-C, LDL-C, VLDL-C, SBP, and DBP were significantly elevated in cases compared to controls. However, mean of T3, T4, and HDL-C was found significantly low in cases compared to controls. Correlation analysis has shown that lipid abnormalities were significantly associated with obesity and hypertension in patients with hypothyroidism that increase the cardiometabolic risk. Non-HDL-C may act as a novel marker for prognosis of insulin resistance and atherogenic CVD and coronary artery disease (CAD).

FLOW CHART OF RESEARCH PROJECT

Aim: It was aimed to find the association of non-HDL-C and cardiometabolic risk factors in patients with hypothyroidism.

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 cardiovascular risk. Non-HDL-C may act as an independent predictive marker for cardiovascular risk in patients with hypothyroidism.

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 cardiovascular risk.

Conclusion: Non-HDL-C may act as an independent predictive marker for cardiovascular risk in patients with hypothyroidism.

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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 **"ESTIMATION OF NON-HDL CHOLESTEROL 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, Mohd Kashif 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 2 ml blood sample for the estimation of lipid profile.
- The blood is only subjected for estimation of 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 research scholar:

अनुलग्नक I

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 गैर एचडीएल कोलेस्ट्रॉल का आकलन" शीर्षक वाले अध्ययन, 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 काशिफ़ रिसर्च स्कॉलर मेडिकल बायोकैमिस्ट्री IIMS&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 लिपिड प्रोफाइल के आकलन के लिए आपका 2 मिलीलीटर रक्त का नमूना लूंगा।
- रक्त का परीक्षण केवल लिपिड प्रोफाइल परीक्षण के आकलन के लिए किया जाता है, अन्य अध्ययन के लिए नहीं।
- अध्ययन के लिए कोई शुल्क / शुल्क नहीं दिया जाएगा / कोई विचार नहीं किया जाएगा।
- आपकी पहचान गोपनीय रहेगी और यदि आप चाहें तो जानकारी और आपके रक्त परीक्षण का परिणाम आपके अलावा किसी और 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: शोध छात्र के हस्ताक्षर:

INSTITUTIONAL ETHICS COMMITTEE (IEC)

IIMS&R INTEGRAL UNIVERSITY, LUCKNOW

IEC/IIMS&R/2023/63

CERTIFICATE

This is to certify that research work entitled "**Estimation of Non-HDL-Cholesterol in Diagnosed Patients of Hypothyroidism and Control Subjects**" submitted by **Md. Kashif, 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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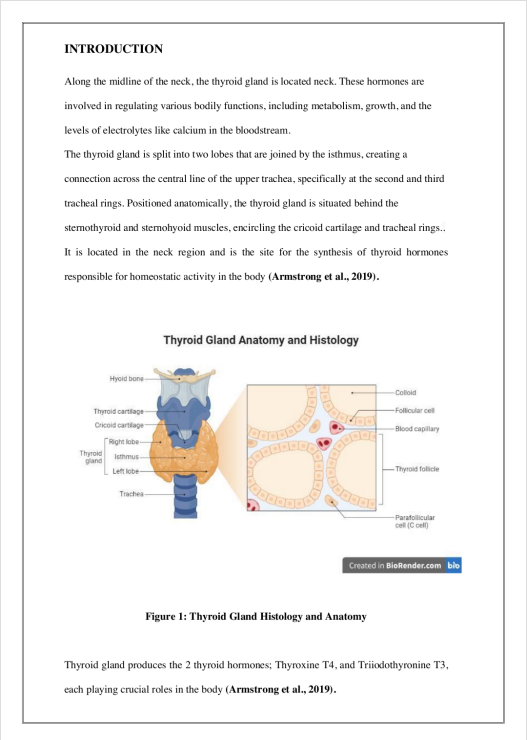

INTRODUCTION

Along the midline of the neck, the thyroid gland is located neck. These hormones are involved in regulating various bodily functions, including metabolism, growth, and the levels of electrolytes like calcium in the bloodstream.

The thyroid gland is split into two lobes that are joined by the isthmus, creating a connection across the central line of the upper trachea, specifically at the second and third tracheal rings. Positioned anatomically, the thyroid gland is situated behind the sternothyroid and sternohyoid muscles, encircling the cricoid cartilage and tracheal rings.. It is located in the neck region and is the site for the synthesis of thyroid hormones responsible for homeostatic activity in the body **(Armstrong et al., 2019).**

Thyroid Gland Anatomy and Histology

Figure 1: Thyroid Gland Histology and Anatomy

Thyroid gland produces the 2 thyroid hormones; Thyroxine T4, and Triiodothyronine T3, each playing crucial roles in the body **(Armstrong et al., 2019).**

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INTRODUCTION

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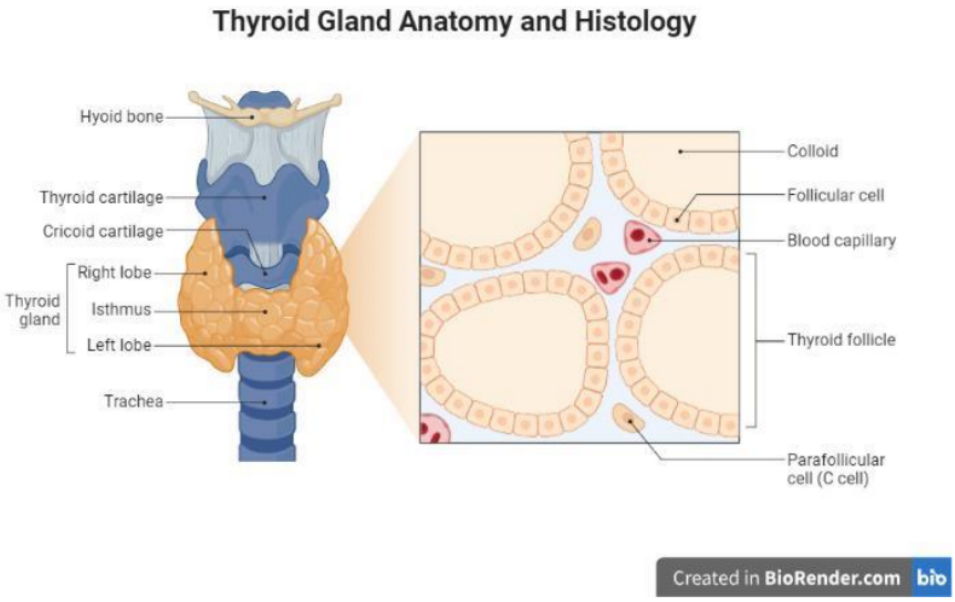


Figure 1: Thyroid Gland Histology and Anatomy

Thyroid gland produces the 2 thyroid hormones; Thyroxine T4, and Triiodothyronine T3, each playing crucial roles in the body **(Armstrong et al., 2019).**

As a result of anatomical and functional problems that limit thyroid hormone synthesis, hypothyroidism is characterized as a decrease in thyroid hormone production. **(Shlomon Melmed et al., 2016).**

Hypothyroidisms symptoms are first encountered by the clinician side effects of hypothyroidism include hypertension and dyslipidemia. It may also lead to infertility and impaired cognitive skills. A recent survey from the National Health and Nutrition Examination indicates that the prevalence of hypothyroidism is 1:300 persons in the US alone. This prevalence increases with as people age and has been found to be common in females than males. This condition can arise from primary gland failure, or an in efficiency in the mechanism that lead to formation of thyroid hormones. According to research, the main factor contributing to the rise in hypothyroidism instances in the United States is autoimmune thyroid disease. This condition is referred to as Hashimoto's disease **(Singer PA et al., 1991).**

Other subtle cause of hypothyroidism are post surgery complications of the thyroid gland, radioactive therapy and neck irradiation (Devdhar M et al ., 2007). Drugs therapy has also been found to induce Hypothyroidism. These drugs are generally tyrosine kinase inhibitors **(Barbesino G et al., 2010).**

Hypothyroidism is a common condition with multiple reasons resulting in the efficiency of thyroid gland to make enough thyroid hormone however, following autoimmune disease (Hashimoto's) and thyroid failure treatment with radioactive iodine (131I) or surgical treatment,except in regions where iodine shortage is widespread, therapy of thyrotoxicosis accounts for over 90% of causes. Women get hypothyroidism six times as often as men do. **(College et al., 2010).**

A prevalent condition, hypothyroidism affects 1% of the general population and 5% of people over 60. **(Banday et al., 2014).**

The prevalence of hypothyroidism was highest in Kolkata, India (21.67%), while rates in other cities ranged from 8.88% (Hyderabad) to 11.07% (Delhi). Delhi, Ahmedabad, Kolkata,

Bangalore, and Hyderabad—cities in India's interior—reported a much greater frequency of hypothyroidism (11.73%) than did Mumbai, Chennai, and Goa—cities in the nation's coastal regions.**(Unnikrishnan et al., 2013).**

In individuals experiencing hypothyroidism, there is an elevation in serum levels of total cholesterol, (LDL-C), apolipoprotein B, lipoprotein(a), and potentially TG. Certain indications propose that patients with hypothyroidism may exhibit heightened levels of total cholesterol, LDL cholesterol, and potentially triglycerides, HDL-C and Lp(a) appear to remain unaltered.**(Pearce E. N., 2004).**

Diastolic arterial pressure, non-HDL cholesterol, triglycerides, and waist circumference were positively linked with TSH levels. Subclinical hyperthyroidism has been shown to strongly correlate with LDL-C and non-HDL cholesterol, which may serve as predictive risk factors **(Wang et al., 2012).**

It has been observed that the overall lipid profile of patients is affected as increasing TSH levels are recorded **(Asvoid et al., 2007).**

Thyroid hormones are involved in the process of cholesterol biosynthesis by inducing the first step enzyme, HMG-CoA reductase. Moreover, T3stimulates LDL receptors actively controlling their gene activation mechanism. This happens when T3 directly binds to particular thyroid hormone-responsive elements situated on the DNA within cells.**(Bakker et al., 1998).**

Thyroid hormones have been known to increase cholesteryl ester transfer protein (CETP) activity affecting HDL metabolism (**Lagrost L., 1994).**

Furthermore, thyroid hormones trigger hepatic lipase (HL) activation, leading to the conversion of HDL2 into HDL3, facilitating the transformation of IDL into LDL, influencing these elements, and lipoprotein lipase (LPL) activation, which facilitates the breakdown of triglyceride-rich lipoproteins. Despite the progress, all the nations we examined have room to enhance the lipid profiles of their populations. **(Santamarina-fojo et al., 2004).**

T3 is also involved in the up-regulation of apolipoprotein AV (ApoAV).This ApoAV has been involved in the active regulation of Triglicerydes **(Prieur et al., 2005).**

Non−HDL = total cholesterol – HDL cholesterol

REVIEW OF LITERATURE

Thyroid hormones are actively involved in the transcription of numerous genes from their mRNA. The result is many significant functions in the body which include, increase cellular metabolism activity and increase number and activity of mitochondria. Thyroid hormone also affects growth especially in growing children. Increase active transport of ions through cell membranes, cardiovascular activity and synthesize large numbers of proteins (structural proteins and transport proteins etc) **(Hall et al., 2012).**

Causes of hypothyroidism

Primary hypothyroidism

1. Enlarged thyroid gland caused by gradual decline in hormone production, resulting in hypothyroidism.

2. Transient hypothyroidism

3. Resistance to thyroid hormone (generalized pituitary dominant.)

4. Permanent atrophy or loss of thyroid tissue is known as atrophic hypothyroidism.

Hypothyroidism of secondary origin or central hypothyroidism (arising from disorders in the hypothalamus or pituitary gland, leading to insufficient activation of a normally functioning gland).**(Salomon Melmed et al., 2016).**

Hypothyroidism can affect every bodily system, including the integumentary system (skin and its appendages), heart, lungs, digestive system, peripheral and central nervous systems, musculoskeletal system (calcium and phosphorus balance), urinary system (water and electrolyte regulation), pituitary gland, and energy metabolism. **(ShlomonMelmed et al., 2016).**

Overt hypothyroidism was associated with increases in all three cardiovascular risk markers (UACR, LDL-cholesterol, and non-HDL-cholesterol) compared to euthyroid subjects **(Khan S et al., 2018).**

Adiposity, dyslipidemia, and insulin resistance are hallmarks of SCH in children and adolescents.

Cases of sub-chorionic hematoma are characterized by adiposity, as seen by elevated BMI, waist circumference (WC), and WHR. Imaging studies reveal that people with SCH had elevated triglyceride (TG) levels, reduced HDL-C levels, high non-HDL cholesterol levels, and a high TG to HDL cholesterol ratio. The therapeutic relevance of these results and the need for therapy cannot be determined without further study **(Yadav Y et al., 2017).**

Elevated CETP activity has been linked to the development of metabolic syndrome and type two diabetes, two conditions that are characterized by an altered lipoprotein profile. This investigation focused on finding easy biochemical predictors of increased CETP activity. The levels of glucose, insulin, triglycerides, and non-HDL-C were all greater in MS patients, but HDL-C levels were lower **(Mukherjee et al., 2018).**

Nearly 80% of those with T2DM have a high or very high risk of cardiovascular complications. Currently, only around one-sixth of patients have optimal LDL or reduced lipoprotein and non-HDL-C (**Pattman S.J et al., 2013).**

There were no appreciable differences in the average blood levels of lipid profile. The prevalence of dyslipidemia in any of the subsets of the lipid profile did not vary considerably between the two groups, however. Subclinical hypothyroidism was a TSH range of **(5-10μIU/L)** with standard free T4 (FT4) (SH) **(Bentham J et al., 2019).**

As of now, it is still being determined if this ratio is a better or equal predictor of MetS and IR sensitivity in Koreans. No clear relationship between lipid ratios and cardiovascular outcomes could be established, nor could the influence of MetS components be disentangled from that of lipid interactions.

Although the non-HDLipid-C/HDL-C ratio was less accurate than the apoB/apoA1 ratio in identifying IR, MetS, and the individual components of MetS, it was still substantially more predictive. Using a longitudinal methodology, we assess the correlation between lipids and CVD and diabetes **(Kim et al., 2013).**

The risk of cardiovascular illness in patients with type-II diabetes is two to four times greater than in those without diabetes. Increased levels of LDL and Triglycerides and lower HDLC characterize diabetic dyslipidemia. Diabetes affects around 33 million individuals in India.

So, when Compared to controls, LDL-C and Non-HDL cholesterol levels were significantly higher **(Kondru S & Thakur A., 2015).**

Symptoms:-

1. Joint pain
2. Sensitivity to cold
3. Bowel irregularity
4. Mood disorders
5. Trouble focusing
6. Excessive menstrual bleeding
7. Muscle pains
8. Lack of strength
9. Increased body mass
10. Skin dryness
11. Tiredness
12. Reduced hair thickness/hair shedding
13. Cognitive decline

Clinical manifestations of hypothyroidism include:

1. Slow heart rate (Bradycardia)
2. Coarse facial features (Coarse facies)

3. Impaired cognitive function (Cognitive impairment)

4. Prolonged relaxation phase of deep tendon reflexes

5. Diastolic dysfunction of the blood vessels (Diastolic vascular disease)

6. Swelling and fluid accumulation (Edema)

7. Enlarged thyroid gland (Goiter)

8. Decreased body temperature (Hypothermia)

9. Increased levels of prolactin in the blood (Hyperprolactinemia)

10. Thinning of the outer part of the eyebrows (Lateral eyebrow thinning)

11. Abnormal low-voltage electrocardiogram (Low-voltage ECG)

12. Enlarged tongue (Macroglossia)

13. Swelling around the eyes (Periorbital edema)

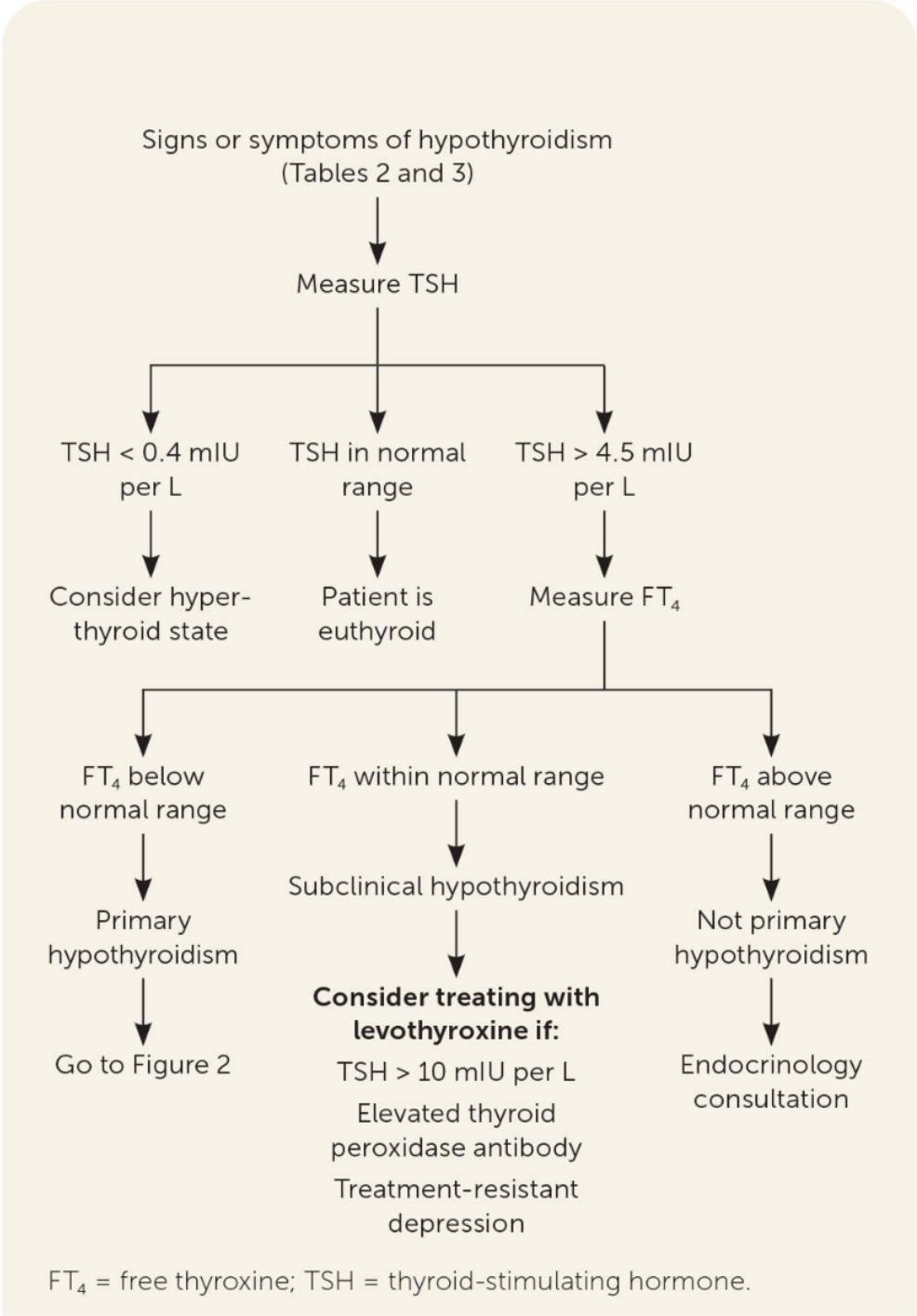


Figure 2: Illustration of TSH levels and diagnosis of thyroid disorders (Islam et al., 2017).

Age and gender can affect how hypothyroidism manifests in symptoms. Lack of energy and failure to thrive may be more common in infants and young children. Infertility and irregular periods are two symptoms of hypothyroidism in females. Deterioration of cognitive function may be the only symptom in elderly patients. Goitre, an extended relaxation stage of deep reflexes of the tendon, thin or weak hair, cracked skin, and swelling in the peripheral region are only a few of the test results linked to hypothyroidism. Common ECG findings for patients with hypothyroidism include bradycardia and flattened T waves. Hypothyroidism cases also present symptoms of pericardial and pleural effusion. Severe cases present an enlarged colon, hemodynamic instability, and in worse cases, this leads to a unconsciousness (**Ladenson PW et al ., 2000).**

Treatment

The majority of patients with hypothyroidism will need ongoing thyroid hormone therapy. Despite the fact that T4 is created in higher quantities, T3 is the physiologically active version. Deiodinase enzymes convert T4 in the periphery to produce around 80% of the T3 in the body none the less, due to the predominant utilization of short-acting synthetic thyroxine formulations (T3 preparations) for the management of hypothyroidism. Similar to endogenous thyroxine, artificial thyroxine is converted into the more physiologically active T3 after being digested. Both brand-name and generic versions of synthetic thyroxine are offered.

In 2004, the conclusion that the absence of TSH indicators to establish biological equivalents in combination with potentially deficient pharmacokinetic parameters methods could result in significant under- and inaccurate estimations of generic equivalents relative to brand-name levothyroxine stuff. As a result, they advise against switching back and forth between brand-name and generic levothyroxine compositions for patients who are starting and maintaining their treatment. To maintain optimal levels within the normal range, individuals who alter their medication regimen should undertake additional testing for TSH and free T4 over a period of six weeks. Levothyroxine should be administered at a beginning dose of 1.6

g/kg/day in individuals who are young and healthy for full replacement. Levothyroxine should not be taken within 4 hours of ca+ and Fe supplements since these substances may reduce the absorption of thyroid hormones. The most frequent reason for persistently increased TSH in patients receiving appropriate dosages of thyroid hormone is poor adherence to levothyroxine medication. For newborns and kids, the dosage of levothyroxine is weight-based and age-specific **(Roos A et al., 2005).**

According to patient response and test results, medication should be modified. A great substitute for patients who struggle with morning levothyroxine dosage is nighttime medication. Levothyroxine night dose led to lower TSH and greater free T4 levels in a designed effectively research carried out in the Netherlands, but there was no difference in quality of life **(Bolk N et al., 2010).**

On the flip side, individuals who struggle with maintaining a once-daily routine of levothyroxine can confidently opt for a Levothyroxine substitute that has received approval from the DA (regulatory authority). They presented at the pharmacy with a full week's worth of levothyroxine supply. **(Grebe SK et al., 1997).**

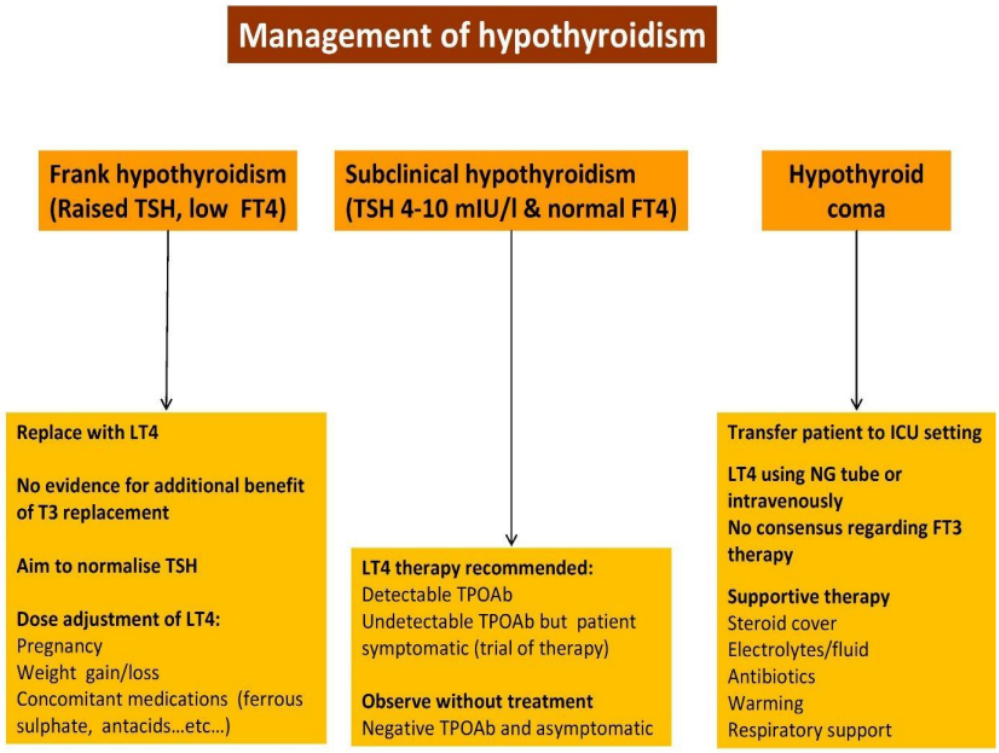


Figure 3: Management of hypothyroidism (King et al., 2012)

Results:

Table 1 Baseline characteristics of cases and controls

Groups	Cases (n=30)	Controls (n=30)	p-value
Age (years)	39.46 ± 7.87	42.46 ± 8.80	0.1693
BMI (kg/m²)	26.40 ± 3.94	22.41 ± 2.15	0.0001
WC (cm)	90.66 ± 6.06	83.67 ± 4.73	0.0001
FBS (mg/dL)	99.93 ± 19.60	91.73 ± 14.41	0.0700
T3 (nmol/L)	1.56±0.41	2.05 ± 0.88	0.0076
T4 (nmol/L)	86.87 ± 15.91	127.25 ± 55.42	0.0003
TSH (μIU/mL)	7.78 ± 4.45	2.17 ± 0.91	0.0001
TC (mg/dL)	195.01 ± 41.28	124.54 ± 20.87	0.0001
TG (mg/dL)	150.96 ± 64.77	123.17 ± 35.94	0.0444
HDL-C (mg/dL)	42.15±7.07	49.01 ± 6.43	0.0002
NON-HDL-C (mg/dL)	144.03 ± 44.58	75.86 ± 24.83	0.0001
LDL-C (mg/dL)	119.55 ± 40.16	50.89 ± 19.90	0.0001
VLDL-C (mg/dL)	31.19 ± 13.74	24.63 ± 7.18	0.0240
***SBP*(mmHg)**	146.53 ± 12.76	122.23 ± 5.65	0.0001
***DBP*(mmHg)**	93.63 ± 7.21	84.36 ± 5.48	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 (39.46 ± 7.87) have been found.

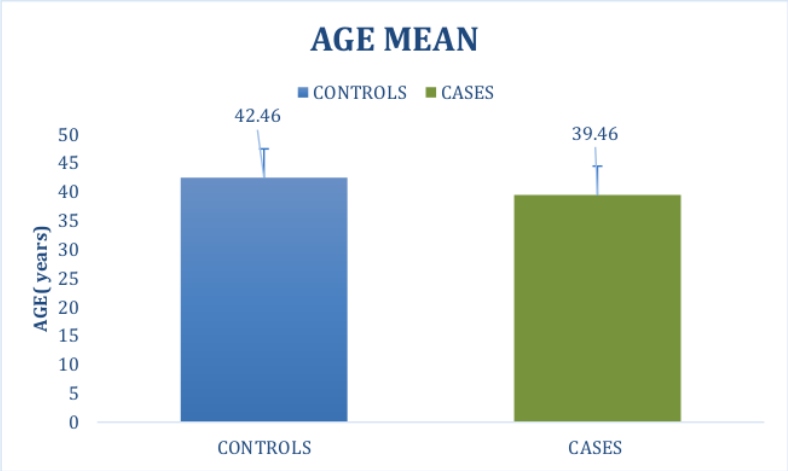


Figure.2. Comparison of ages (years) in cases & controls

BODY MASS INDEX (BMI)

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

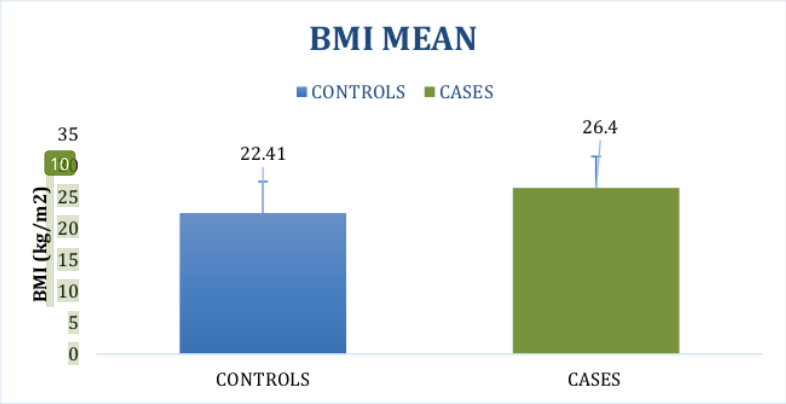


Figure 3. Comparison of BMI in cases and controls

Total Cholesterol

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

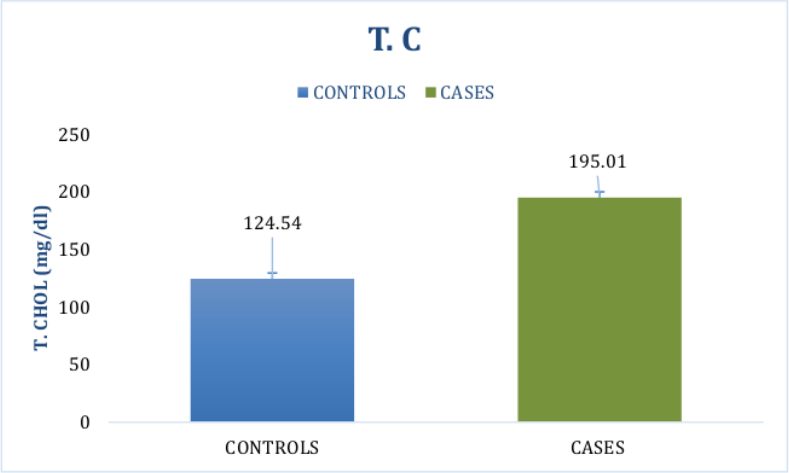


Figure 4. Comparison of total cholesterol in cases and controls

Serum triglycerides

Inpatients of hypothyroidism compared to control subjects, serum triglycerides are considerably higher (p= 0.0444) shown in table.3.

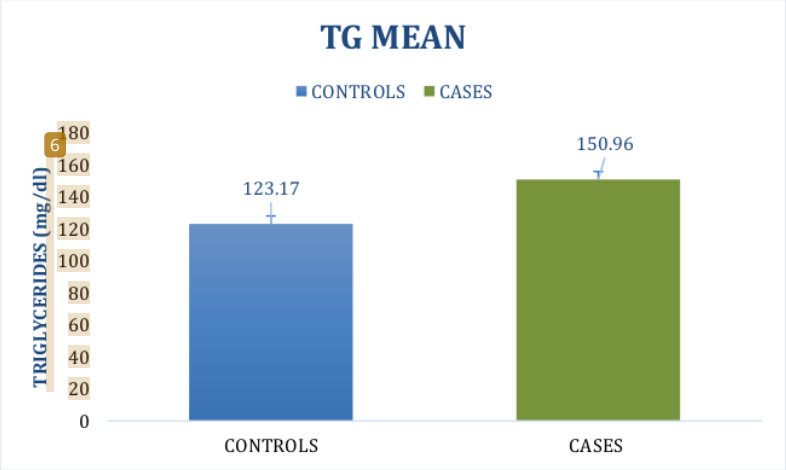


Figure 5. Comparison of triglycerides in cases and controls

Serum Non-HDL

Compared to control persons, inpatients of hypothyroidism serum HDL-C is considerably lower (p=0.0001) shown in table.3.

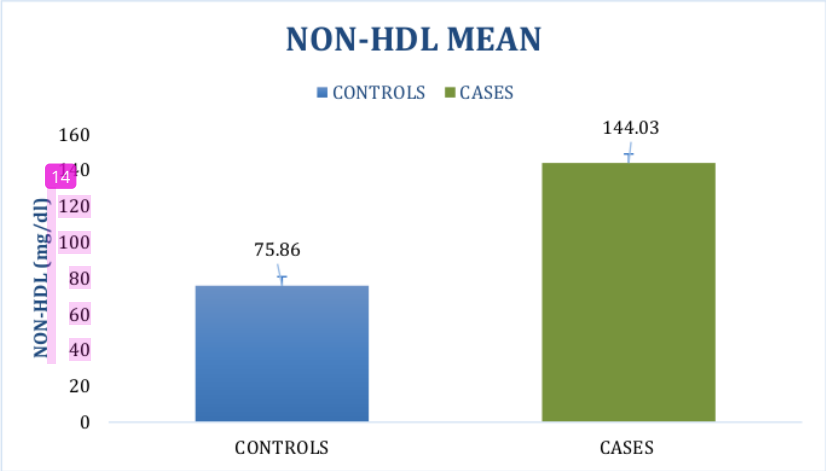


Figure 6. Comparisonof HDL-C in cases and controls

Serum LDL

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

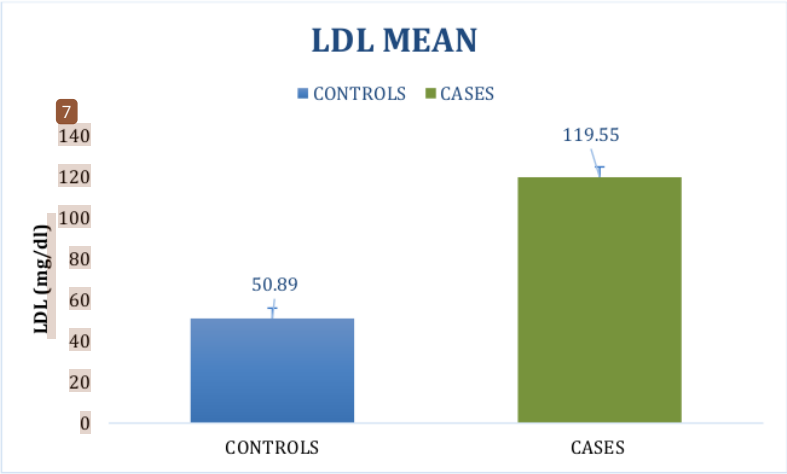


Figure 7. Comparison of LDL-C in cases and controls

Fasting blood sugar

In patients of hypothyroidism compared to control subjects, fasting blood sugar are considerably higher (p=0.0700)

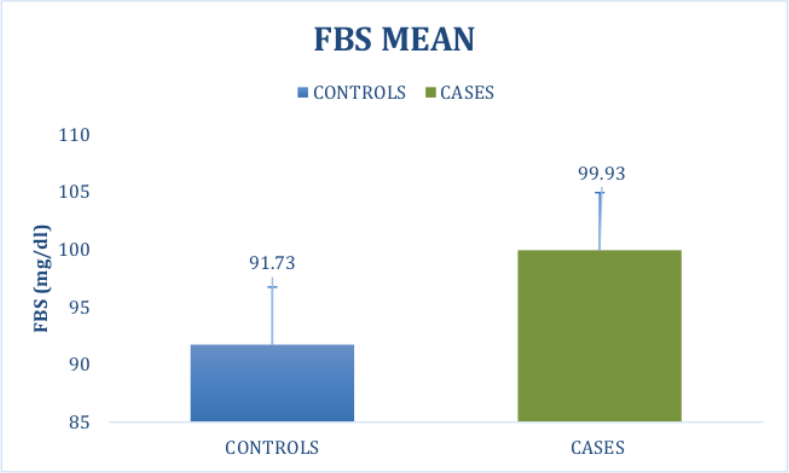


Figure 8. Comparison of FBS in cases and controls

Waist Circumference

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

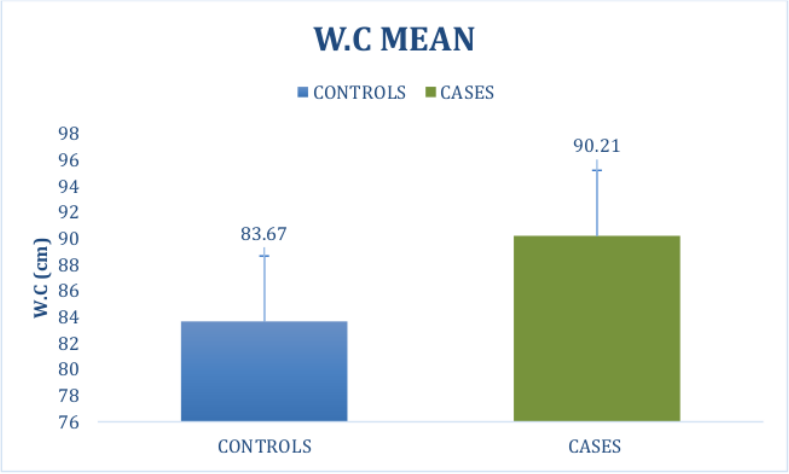
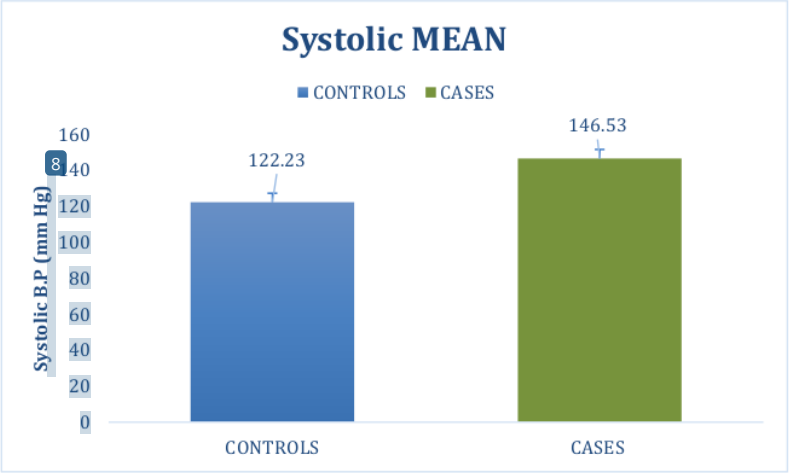


Figure 9. Comparison of W.C. in cases and controls

Blood pressure (systolic)

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



Blood pressure (diastolic)

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

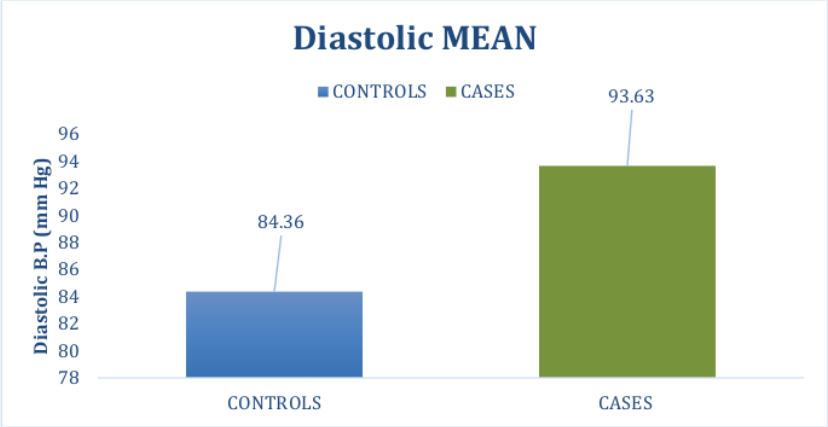
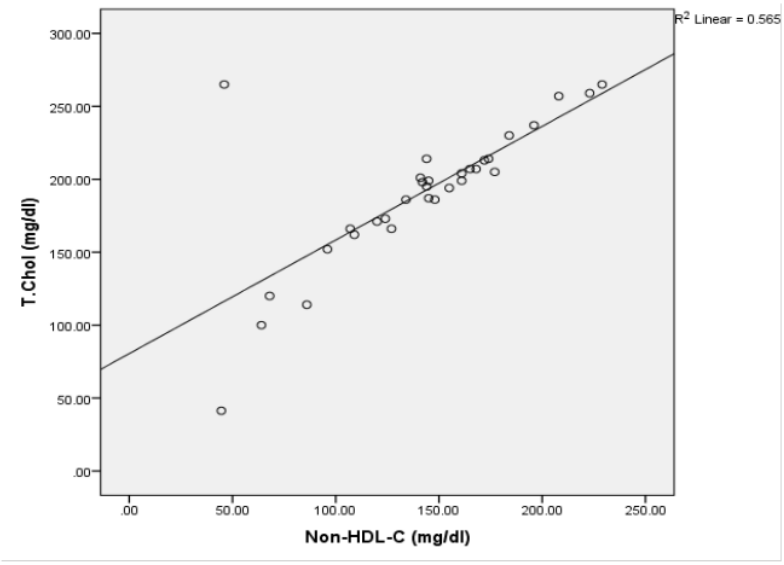
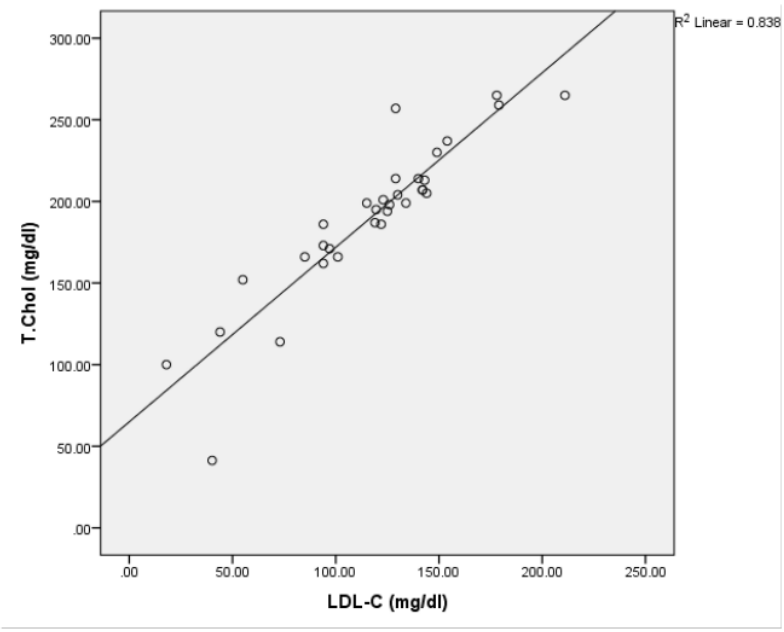
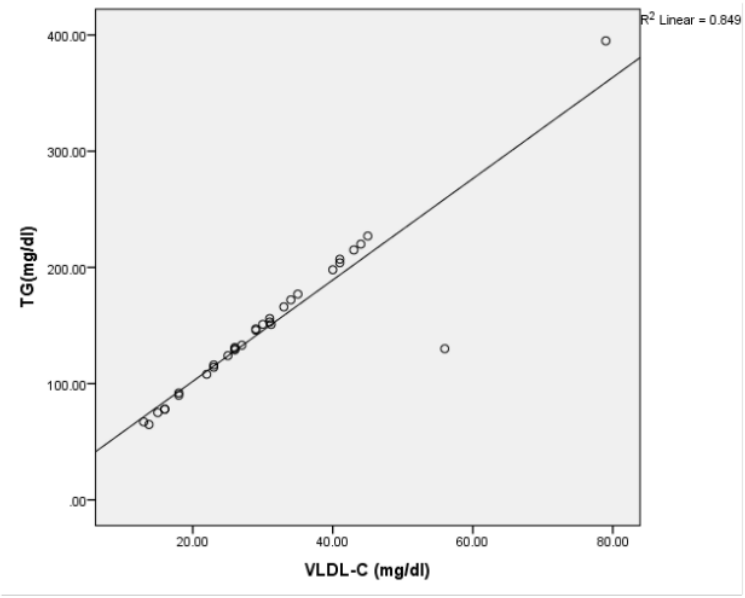


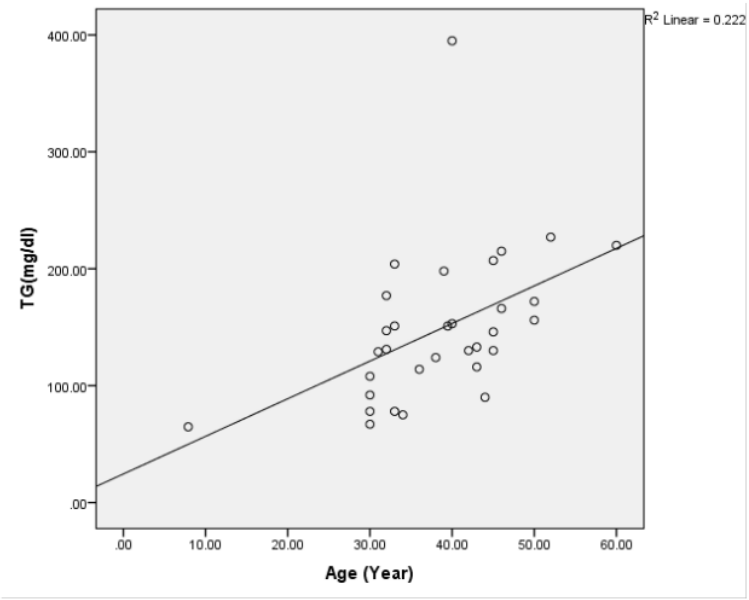
Table 4: Correlation analysis of different parameters among cases

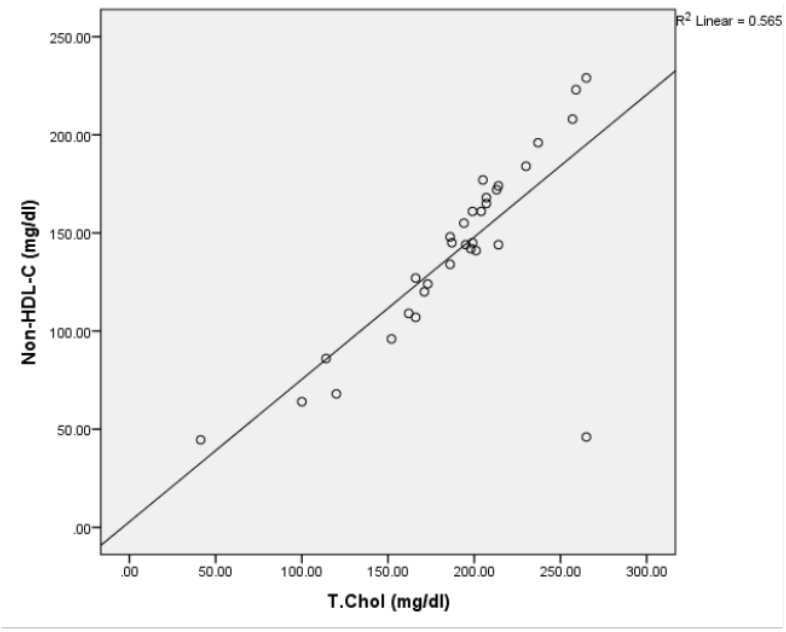
Parameters	TC	TG	NON.HDL	LDL	VLDL	T3	T4	TSH	BMI	WC	AGE	FBS	SBP	DBP
TC	1	0.315	**0.707****	**0.933****	0.282	-0.084	-0.064	0.249	0.022	-0.141	0.183	0.311	0.061	0.099
TG		1	.212	.035	**.918****	.124	-0.077	.245	-0.330	-0.281	**.421***	.331	-0.286	-0.273
NON.HDL			1	**.719****	.202	-0.047	-0.017	.271	-0.104	-0.014	**.375***	-0.026	-0.188	-0.126
LDL				1	.032	-0.110	-0.128	.234	.129	-0.062	.159	.302	.096	.159
VLDL					1	.040	-0.125	.173	-0.157	-0.195	**.450***	.320	-0.314	-0.243
T3						1	-0.191	-0.052	-0.187	-0.128	-0.045	.027	-0.125	-0.068
T4							1	-0.142	.160	.292	-0.069	-0.285	.092	.129
TSH								1	-0.135	-0.210	.327	.318	-0.310	-0.181
BMI									1	**.580****	-0.131	.097	.009	**.547****
WC										1	.012	-0.073	.251	**.538****
AGE											1	**.497***	-0.042	-0.218
FBS												1	.161	.160
SBP													1	**.386***
DBP														1

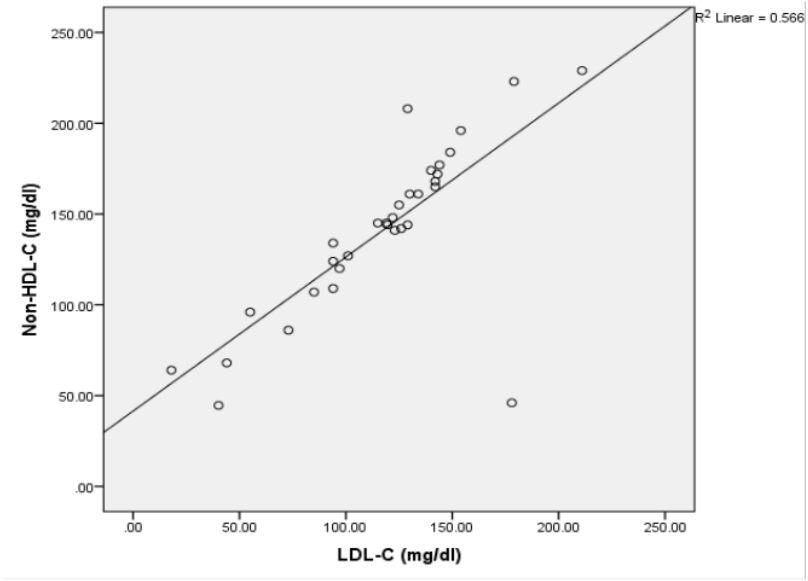

R² Linear = 0.565
T.Chol (mg/dl)
Non-HDL-C (mg/dl)
300.00
250.00
200.00
150.00
100.00
50.00
.00
.00
50.00
100.00
150.00
200.00
250.00

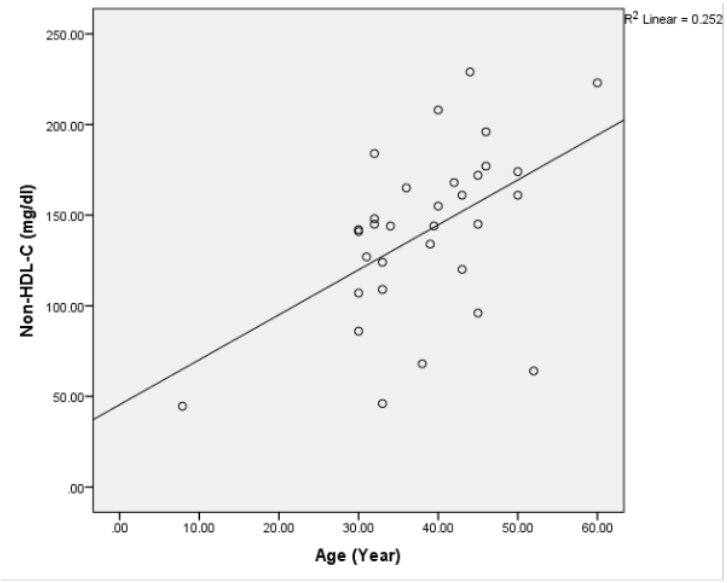

R² Linear = 0.838
T.Chol (mg/dl)
LDL-C (mg/dl)
300.00
250.00
200.00
150.00
100.00
50.00
.00
.00
50.00
100.00
150.00
200.00
250.00

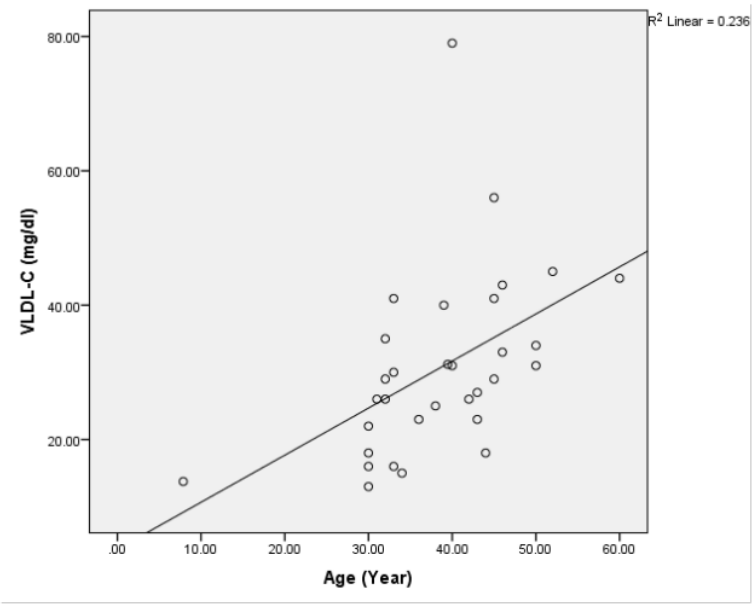

R² Linear = 0.849
400.00
300.00
200.00
100.00
.00
TG(mg/dl)
20.00
40.00
60.00
80.00
VLDL-C (mg/dl)

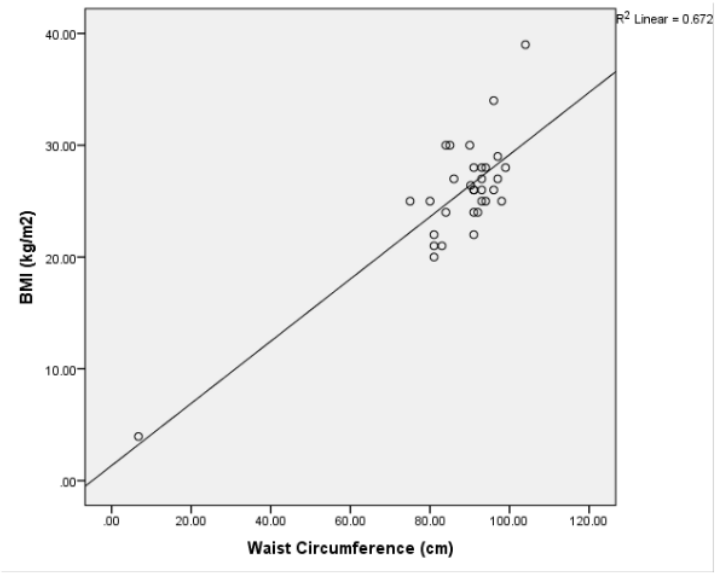

R² Linear = 0.222
400.00
300.00
200.00
100.00
.00
TG(mg/dl)
.00
10.00
20.00
30.00
40.00
50.00
60.00
Age (Year)

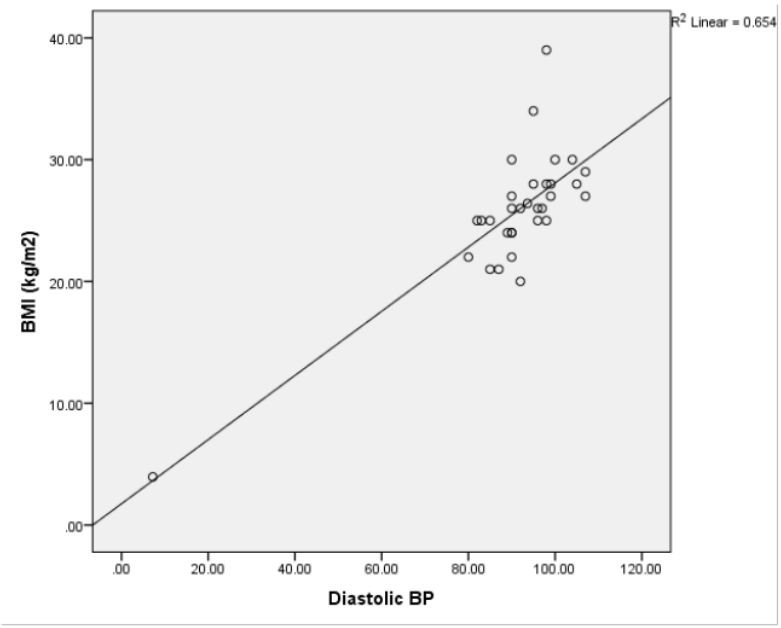

R² Linear = 0.565
Non-HDL-C (mg/dl)
T.Chol (mg/dl)
250.00
200.00
150.00
100.00
50.00
.00
.00
50.00
100.00
150.00
200.00
250.00
300.00

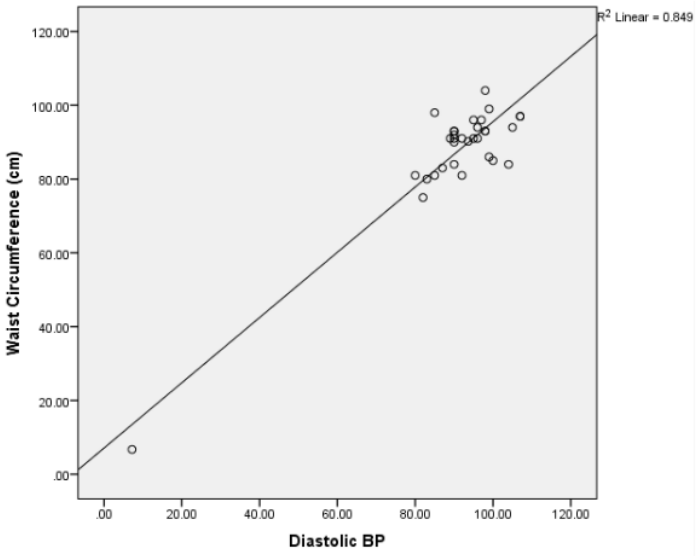

R² Linear = 0.566
Non-HDL-C (mg/dl)
LDL-C (mg/dl)
250.00
200.00
150.00
100.00
50.00
.00
.00
50.00
100.00
150.00
200.00
250.00

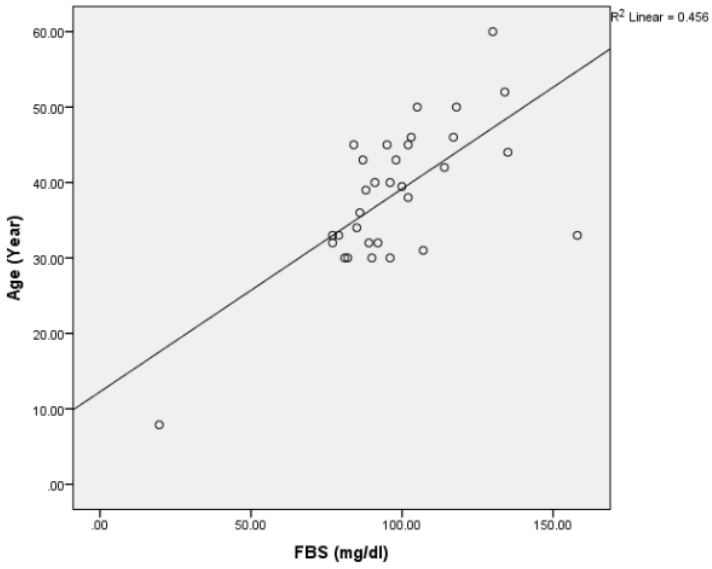

R² Linear = 0.252
Non-HDL-C (mg/dl)
250.00
200.00
150.00
100.00
50.00
.00
.00
10.00
20.00
30.00
40.00
50.00
60.00
Age (Year)

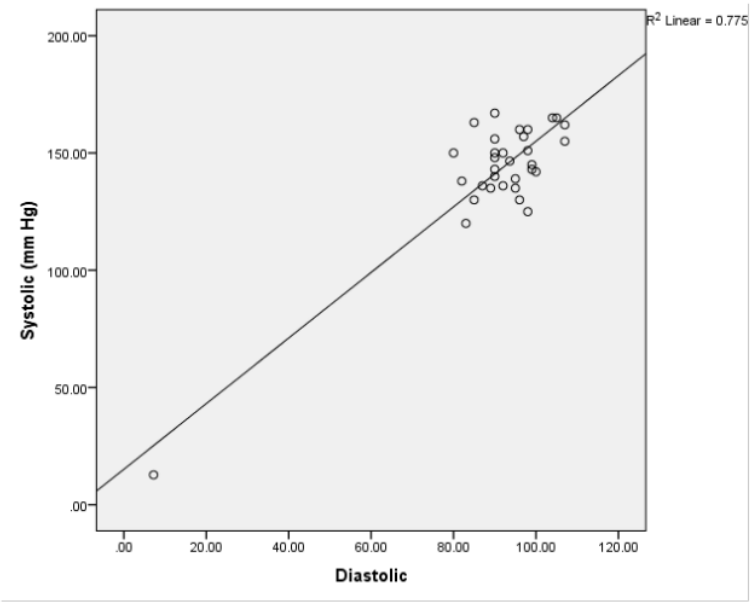

R² Linear = 0.236
VLDL-C (mg/dl)
80.00
60.00
40.00
20.00
.00
10.00
20.00
30.00
40.00
50.00
60.00
Age (Year)

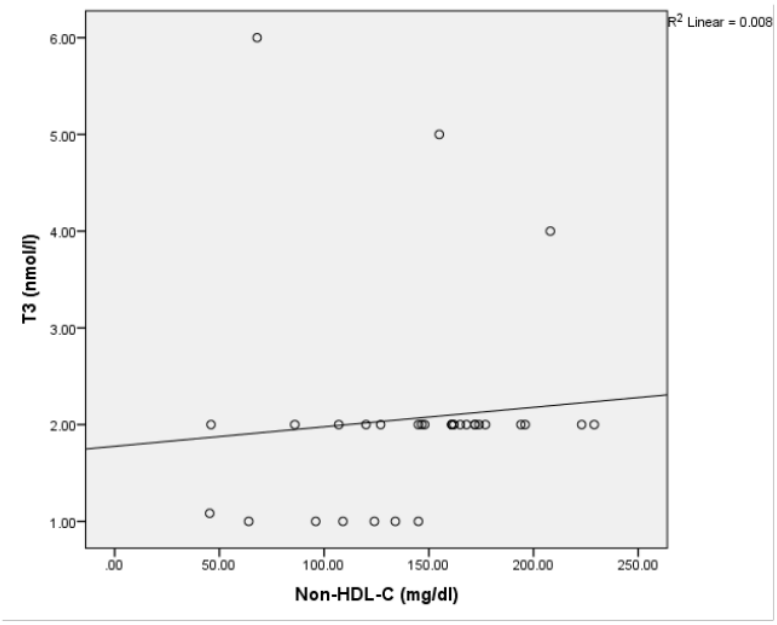

R² Linear = 0.672
BMI (kg/m2)
40.00
30.00
20.00
10.00
.00
.00
20.00
40.00
60.00
80.00
100.00
120.00
Waist Circumference (cm)

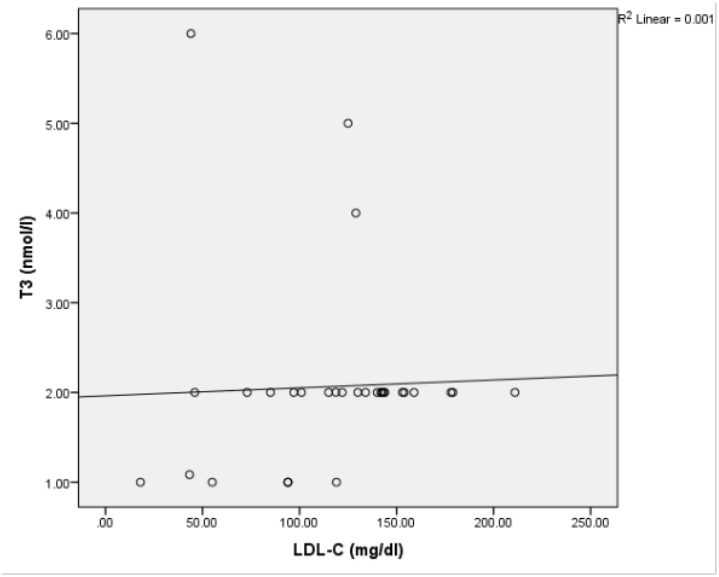

R² Linear = 0.654
BMI (kg/m2)
40.00
30.00
20.00
10.00
.00
.00
20.00
40.00
60.00
80.00
100.00
120.00
Diastolic BP

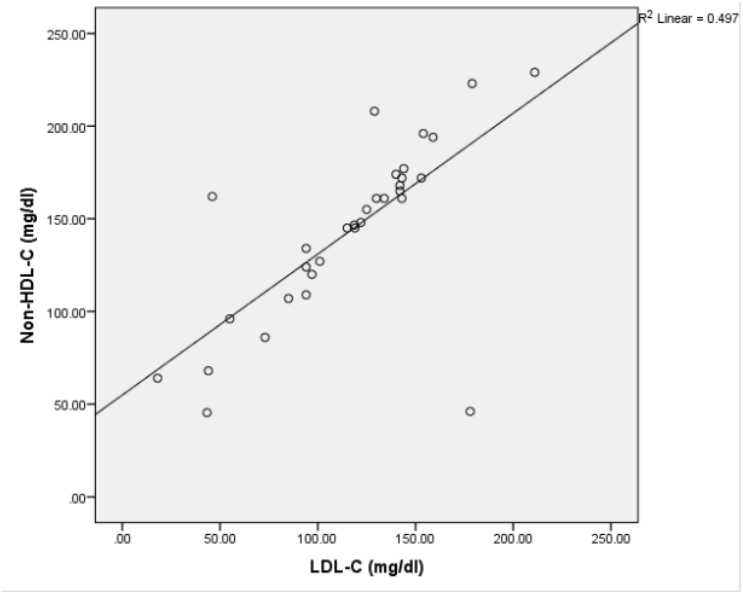

R² Linear = 0.849
Waist Circumference (cm)
Diastolic BP
120.00
100.00
80.00
60.00
40.00
20.00
.00
.00
20.00
40.00
60.00
80.00
100.00
120.00


R² Linear = 0.456
Age (Year)
FBS (mg/dl)
60.00
50.00
40.00
30.00
20.00
10.00
.00
.00
50.00
100.00
150.00


R² Linear = 0.775
Systolic (mm Hg)
200.00
150.00
100.00
50.00
.00
.00
20.00
40.00
60.00
80.00
100.00
120.00
Diastolic


R² Linear = 0.008
T3 (nmol/l)
6.00
5.00
4.00
3.00
2.00
1.00
.00
50.00
100.00
150.00
200.00
250.00
Non-HDL-C (mg/dl)


R² Linear = 0.001
T3 (nmol/l)
6.00
5.00
4.00
3.00
2.00
1.00
.00
50.00
100.00
150.00
200.00
250.00
LDL-C (mg/dl)


R² Linear = 0.497
Non-HDL-C (mg/dl)
250.00
200.00
150.00
100.00
50.00
.00
.00
50.00
100.00
150.00
200.00
250.00
LDL-C (mg/dl)

RESULT

The purpose of this study was to evaluate the lipid profile, FBS &BMI of patients with hypothyroidism& apparently healthy controls.

The parameters estimated were:

1) Lipid profile panels

2) Fasting blood sugar

3) BMI

4) Blood pressure

The parameter levels were compared with control levels, who are apparently healthy individuals.

The study observations were as follows-:

1) When compared to control subjects, the level of total cholesterol was considerably higher in cases (p=0.0001) (Table.3 & Fig.4).

2) When compared to control subjects, the level of triglycerides was considerably higher in cases (p=0.0444) (Table.3 & Fig.5).

3) When compared to control subjects, the level of non-HDL was considerably lower in cases (p=0.0001) (Table.3 & Fig.6)

4) When compared to control subjects, the level of LDL-C was considerably higher in cases (p=0.0001) (Table.3 & Fig.7).

5) When compared to control subjects, the level of FBS was considerably higher in cases (p=0.0700) (Table.3 & Fig.8).

6) When compared to control subjects, the level of BMI was considerably higher in cases (p=0.0001) (Table.3 & Fig.9).

DISCUSSION

Result showed that mean of BMI, WC, FBS, TSH, TC, TG, non-HDL-C, LDL-C, VLDL-C, SBP, and DBP were significantly elevated in cases compared to controls. However, mean of T3, T4, and HDL-C was found significantly low in cases compared to controls. Similarly, 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 the development of dyslipidemia (Alarcón-González et al 2021).

Elevated TSH readings surpassing the upper limit of the established reference range, along with evident and subtle hypothyroidism, are linked to lipid issues. The extent of TSH elevation typically shows an inverse relationship with the level of lipid irregularities. The specific pattern of observed lipid deviations can also be influenced by other factors, such as age, gender, and body mass index. Notably, the most compelling finding related to TSH elevation is the increase in low-density lipoprotein cholesterol. Both subtle and obvious hypothyroidism can witness a reversal of their lipid irregularities through the application of thyroid hormone therapy. In conclusion, recognizing hypothyroidism as a significant non-communicable ailment could potentially open avenues for research testing the hypothesis that thyroid hormone treatment, aimed at rectifying lipid irregularities associated with hypothyroidism, might enhance metabolic and cardiovascular outcomes due to the established connection between lipid irregularities and metabolic/cardiovascular diseases.(Jonklaas et al., 2023).

TC has shown a significant positive correlation with non-HDL-C ($r = 0.707$, $p<0.01$), and LDL-C ($r = 0.933$, $p<0.01$) among cases. Similarly, TG has shown a significant positive correlation with VLDL-C ($r = 0.918$, $p<0.01$), and age ($r = 0.421$, $p<0.05$) among cases. Non-HDL-C has shown a significant positive correlation with LDL-C ($r = 0.719$, $p<0.01$), and age ($r = 0.375$, $p<0.05$) among cases. VLDL-C has shown a significant positive correlation with age ($r = 0.450$, $p<0.05$) among cases. BMI has shown a significant positive correlation with WC ($r = 0.580$, $p<0.01$), and DBP ($r = 0.547$, $p<0.01$) among cases. WC has shown a significant positive correlation with DBP ($r = 0.538$, $p<0.01$) among cases. Age has shown a significant positive correlation with FBS ($r = 0.497$, $p<0.01$) among cases. SBP has shown a significant positive association with DBP ($r = 0.386$, $p<0.01$) among cases, shown in Table 2.

SUMMARY

Introduction: Hypothyroid can be defined as high amount of TSH and decreased amount 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

To find the association of non-HDL-C and cardiometabolic risk factors in patients with hypothyroidism.

OBJECTIVES

1. To estimate serum FBS and lipid profile in patients of hypothyroid patients and apparently healthy controls.
2. To estimate the BMI, waist circumference and blood pressure in patients of hypothyroid patients and apparently healthy controls.
3. To find the correlation between non-HDL-C and cardiometabolic risk factors in patients of hypothyroidism patients 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, total chol, tg, LDL-C, VLDL-C, TSH, SBP, & DBP was found significantly elevated in cases compared to control subjects ($p < 0.001$). However, mean of Non-HDL-C, T3, and T4 were found reduced in cases compared to control subjects ($p < 0.001$). Correlation analysis has shown that lipid abnormalities were significantly associated with obesity and hypertension in patients with hypothyroidism.

CONCLUSION

In the current study, it was found that the patients of hypothyroidism had considerably higher levels of total cholesterol, triglycerides, LDL, FBS, BMI & decrease Non-HDL levels as compared to the apparently healthy control. Numerous researches looked at the relationship between patients of hypothyroidism and their age, obesity, and cardiovascular disease. Therefore, increased levels of TC, TG, LDL-C, FBS, BMI & lower HDL indicate the presence of hypothyroidism, making it crucial to look at the lipid profile in patients of hypothyroidism, including lipid profile, W.C, FBS, and BMI.

The findings of this study may be useful in understanding how lipid profiles contribute to the pathophysiology of hypothyroidism.

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