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Evaluation of Lipid Profile in Patients with Ischemic Heart Disease

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Abstract

Ischemic heart diseases (IHDs), like coronary artery disease, remain a significant global health burden. While established risk factors such as low-density lipoprotein cholesterol (LDL) and hypertension are well-recognized, the role of triglyceride (T.G.) and high-density lipoprotein cholesterol (HDL-c) remains complex and multifaceted. This work was designed to examine the role of the T.G./HDL-c ratio in the IHD group and their effect on the effect of age, gender, and biomass index (BMI).

Method: A total of 90 samples, including 60 samples (30 male, 30 female) for the IHD patients group with an age range of 40-85 years, and 30 samples (15 male, 15 female) for the control group with matching age ranges, were randomly selected. Lipid profile parameters (HDL, LDL, VLDL, T.G., Cholesterol) were estimated according to Kit Shenzhen Mindray Bio—Medical Electronics—Germany's manual procedure. Then, the ratio TG/HDL-C was calculated.

Results: IHD patients illustrated a significant increase in the mean levels of all lipid profile panels, including [total cholesterol (T.C.), triglyceride (T.G.), LDL, and the ratio of T.G./HDL-c], except HDL, which was lower in patients group compared to the healthy control. The level of T.G./HDL-c was increased in IHD patients with increasing BMI associated with the healthy participants; it was also elevated in male IHD patients than in IHD female patients.

Conclusion: The ratio of T.G./HDL-c represents a valuable indicator for valuing IHD risk and personalized therapeutic approaches. Future research should delve deeper into the underlying mechanisms and refine strategies for effectively managing T.G./HDL-c for improved IHD prevention and management.

Key points:•Elevated T.G./HDL-c ratio, rather than individual T.G. or HDL-c levels alone, emerges as a stronger predictor of IHD risk. This ratio reflects increased atherogenic lipoprotein burden (high T.G.) and impaired cholesterol efflux capacity (low HDL-c).

•Mechanisms underlying the adverse effects of high T.G./HDL-c involve:

•Increased inflammation and oxidative stress

•Remnant lipoprotein formation and plaque instability

•Impaired endothelial function and vascular relaxation

•Increased postprandial lipemia and triglyceride-rich lipoprotein accumulation

•Heterogeneity exists within both T.G. and HDL-c, further influencing IHD risk. Particle size and apolipoprotein composition of these lipoproteins play crucial roles.

•Therapeutic strategies targeting T.G./HDL-c should consider diverse mechanisms and individual patient profiles. Lifestyle modifications, lipid-lowering medications, and novel HDL-raising therapies hold potential.

تقدير مستويات الدهون في مرضى نقص تروية القلب

الملخص

ان أمراض القلب الإقفارية(IHDs) ، مثل مرض الشريان التاجي، عبئًا عالميًا كبيرًا على الصحة. في حين أن عوامل الخطر المعروفة مثل الكوليسترول الدهني منخفض الكثافة (LDL) وارتفاع ضغط الدم معروفة جيدًا، فإن دور الدهون الثلاثية (TG) والكوليسترول البروتيني عالي الكثافة (HDL-c) لا يزال معقدًا ومتعدد الأوجه. صمم هذا العمل لفحص دور نسبة TG/HDL-c في مجموعة IHD وتأثرها بالعمر والجنس ومؤشر كتلة الجسم .(BMI) شملت الدراسة ٩٠ عينة ٦٠: عينة(٣٠رجال,٣٠ نساء) كمجموعة مرضى IHD تتراوح أعمارهم بين ٤٠ و ٨٥ عامًا، و ٣٠ عينة (١٥ رجال ,١٥ نساء) تم اختيارها عشوائيًا كمجموعة تحكم بنفس الفئة العمرية. تم تقدير معايير ملف الدهونات(HDL ، LDL، VLDL، TG، الكوليسترول(وفقًا للإجراء اليدوي لمجموعة .Shenzhen Mindray Bio- Medical Electronics- Germany ثم تم حساب نسبة, .TG/HDL-C أظهر مرضى IHDزيادة ملحوظة في متوسط مستويات جميع لوحة ملف الدهونات بما في ذلك]الكوليسترول الكلي(TC) ، الدهون الثلاثية(TG) ، LDLونسبة] TG/HDL-cباستثناء HDL الذي تبين أنه أقل في مجموعة المرضى مقارنة بالمجموعة الضابطة الصحية. زادت نسبة TG/HDL-c في مجموعة IHDمع زيادة مؤشر كتلة الجسم مقارنة بالمجموعة الضابطة الصحية، كما زادت أيضًا لدى الذكور من مرضى IHD مقارنة بمرضى IHD الإناث. نستنتج من ذلك ان نسبة TG/HDL-c علامة قيمة لتقييم مخاطر IHD والنهج العلاجية الشخصية. ينبغي أن تتعمق الأبحاث المستقبلية في الآليات الأساسية وصقل الاستراتيجيات لإدارة TG/HDL-c بشكل فعال لتحسين الوقاية من IHD وإدارتها .

1. Introduction

Cardiovascular disease is the chief cause of death worldwide, and ischemic heart disease is the top one. However, risk factors for Ischemic heart diseases are adaptable and avoidable; it is not well explored in the local context. (Brodmann *et al.*, 2020) . The most significant risk factors were adaptable and avoidable, among which nutritional and interactive risk factors were central (Organization, 2009). Lipids and lipoproteins have a crucial influence on the origination and development of Cardiac Vascular Disease (CVD) by revenues of their cellular synthesis, transportation, assemblage, degradation, oxidation, and plasma concentrations (Yu *et al.*, 2019). Many studies confirmed the associations of lipid profiles with the risk of significant adverse cardiovascular outcomes in patients with heart disease (Zhao, Wang and Qin, 2021)

The blood cholesterol level was well-known as the first straight relation between flowing lipids and cardiac diseases. Amplified cholesterol levels are linked with an enlarged 10-year risk of cardiovascular death from 3.8% to nearly 19.6% in men with a pre-existing cardiac disease. Patients with atherosclerotic plaques show a relationship with 45% higher plasma oxidized LDL concentrations as matched with control participants. Additionally, patients with elevated total LDL have a 3.7 times higher risk of coronary artery calcification than those with lower LDL (Prado, Shugg and Backstrand, 2011). Epidemiological researches also connect the proportions of other lipids with cardiac disease risk, representing that enlarged plasma T.G. levels are related to a 14% increase in cardiac disease risk in men and a 37% increase in cardiac disease risk in women, individually, which is credited to a greater frequency of myocardial infarction, stroke, and total mortality. Patients with a TG/HDL ratio >3.5 have an unadjusted hazard risk of cardiac disease mortality (Vega *et al.*, 2014). The correlation of the TG/HDL proportion and cardiovascular risk likened to serum HDL levels is more precise than individual values because it relates to the negative impression of T.G.s and the positive impression of HDL on cardiac diseases. (De Backer *et al.*, 2019) Chronic inflammatory progressions can raise the risk of CVDs. Current indication proposes that arrhythmogenic diseases comprising atrial fibrillation, arrhythmogenic cardiomyopathy, and cardiac sarcoidosis can have an inflammatory constituent. Autoimmune and inflammatory-mediated cytokines, including IL-1, IL-6, and TNFα control the expression of ion channels by acting on cardiomyocytes, causing a reduction of Potassium (K+) and a rise of calcium (Lazzerini *et al.*, 2018)

IHD is a prolonged inflammatory disease of the arterial wall and has been revealed to be TNF-driven. A probable positive link of TNF with ischaemic stroke (Shah *et al.*, 2018)

The fundamental mechanism for TNF-driven atherothrombosis might be through a diversity of suggested mechanisms, including favorable effects on circul1ating lipids, insulin resistance, endothelial dysfunction, leucocyte staffing, oxidative stress, vasodilation, or coagulation (Nair *et al.*, 2022). Tumor necrosis factor-α (TNF-α) is a multifunctional flowing cytokine derived from endothelial and smooth muscle cells and macrophages linked with coronary atheroma. Initially recognized as a factor that stimulated hemorrhagic necrosis in transplanted tumors, TNF-α is involved in several cardiovascular processes (Yuan *et al.*, 2020)

Recent studies in literature showed a significant association between elevated TG/HDL-C ratio levels and various clinical conditions. The authors reported a significant correlation between TG/HDL-C ratio and arterial stiffness (Chen and Dai, 2018). In another study, authors concluded that elevated TG/HDL-C ratio could predict the development of type 2 Diabetes mellitus in the Korean population (Lim, Lee and Lee, 2020). The TG/HDL-C ratio indicates the severity of CHD. In 2014, research done by Yunke et al. reported that the harshness of coronary heart disease accompanied the TG/HDL-C ratio and may cause new-onset heart failure incidents (Yunke, Guoping and Zhenyue, 2014). Moreover, Chen et al. documented that elevated TG/HDL-C ratio levels were associated with greater cardiovascular event risk in Chinese people. All these conditions are related to metabolic, inflammatory, and vascular disturbances such as H.T. (Chen *et al.*, 2020).

Amplified levels of triglycerides in the blood result in blood viscosity, which is augmented, which leads to a disturbance of blood flow.' The blood vessels so the heart works harder to pump' blood and raise blood pressure (Neama and Shwaikh, 2024). Hypercholesterolemia can also result in the accumulation of cholesterol in the arterial lumen, denoted as atherosclerosis, and causes artery tightening, inurement, and stiffness; this is what leads to raised peripheral vascular resistance and increased pressure (Kaidah *et al.*, 2020)

Enlarged plasma triglyceride levels are related to the build-up of large, triglyceride-rich VLDL-VLDL1(Adiels *et al.*, 2008). The liver can vary the number of lipids overloaded onto the rising lipoprotein particle in the endoplasmic reticulum, and depending on triglyceride obtainability, it can collect and secrete particles that range in size from VLDL1 to LDL (Sundaram and Yao, 2010).

Kinematic surveys have established that the metabolic destiny of flowing VLDL particles is a function of their size and lipid and apoprotein arrangement, especially their apoE and apoCIII content (Sacks, 2015). LDL subfraction

dissemination is also obviously affected by plasma triglyceride levels. A number of investigators have revealed that the concentration of small, dense LDL (LDL-III) rises meaningfully when triglyceride increases above about 1.5 mmol/l, and there is a mutual drop in LDL-II, the most abundant subfraction in regular participants (Krauss, 2010) (Boren *et al.*, 2020).

Conversely, apoCIII is the primary controller of plasma lipid concentrations. Its role in triglyceride transportation and as a latent interference target has been studied lately (Taskinen and Borén, 2016). Overproduction of apoCIII is related to elevated triglyceride levels. There are several ways in which apo CIII can affect triglyceride metabolism. It has been described as improving VLDL assemblage and exudation in the liver, preventing the action of lipoprotein lipase, henceforward slowing VLDL lipolysis, and perhaps delaying the straight clearance of VLDL fragments by receptors (Adiels *et al.*, 2019).

2. Materials and Methods

The samples were collected in Karbala (Imam AL Hussein Medical City and Imam Al-Hassan Al-Mujtaba Hospital); a total of 90 samples, including 60 samples from the IHD patients group with an age range of 40-85 years, and 30 samples were randomly selected as the control group with matching age rang. The Ethical Committee reviewed and approved the study's protocol, and all participants or their relatives gave written informed consent. A sample of 5 ml blood was withdrawn, allowed to clot for 1 hour, centrifuged at 3000 xg, then serum was separated after 15 min of the centrifugation and finally stored at - 80 °C until the biochemical assessment was performed.

Lipid profile parameters (HDL, LDL, VLDL, T.G., Cholesterol) were estimated according to Kit Shenzhen Mindray Bio-Medical Electronics- Germany's manual procedure. Then, the ratio TG/HDL-C was calculated.

Statistical analysis: All subjects' survey data were entered into a data sheet and given a serial identifier number. Numerous entrance was used to evade errors. The association between the analyzed parameters was assessed using Pearson regression, and a 95% Confidence Interval Range was planned by a non-conditional logistic regression. Significant differences in categorical variables among the parameters were established through analytical statistical tests. Results of all hypothesis tests with p-values <0.05 (two-sided) were considered statistically significant.

3. Results

A total of (60) participants were included in this study. The clinical demographic characteristics and laboratory parameters of the study groups were summarized in Table (1). The mean age of the IHD cases was 60.4± 13.7 years. The BMI mean of patients was (25.7± 3.6) while in the control group was (26.8± 3.6); as a risk factor, both groups were categorized using the body mass index (BMI) according to the traditional World Health Organization as shown in Figure (1). Results also demonstrated the Medical History, Type of medications, and Blood Pressure as Systolic / Diastolic (mm Hg), which was divided into subgroups based on the latest guidelines of the American College of Cardiology, American Heart Association, and the European Society of Cardiology, European Society of Hypertension blood pressure (Brodmann *et al.*, 2020)

Table 3: Demographic and Clinical Characteristics of the Study Population

Variables		Patients	Control
Age (Years)		60.4± 13.7	53.2± 9.6
Sex (Male/ Female) No.(%)		30/ 30	15/15
BMI (Kg/m^2)		25.7± 3.6	26.8± 3.6
Medical History	**Family History (Yes/ No)**	5/ 55	1/ 29
	Gastric intestinal disorder (Yes/ No)	7/ 53	2/ 28
	Smoking status (Yes/ No)	18/ 42	1/29
Type of Treatment	Tenormin	11	/
	Diostar	16	/
	Concor	6	/
	Capoten	7	/
	Tansartan	6	/
	Atacand	1	/
	No Treatment	13	/
Blood Pressure Systolic / Diastolic (mm Hg)	Normal Blood Pressure	12	11
	Elevated Blood Pressure	6	/
	Hypertension, stage 1	9	7
	Hypertension, stage 2	33	12

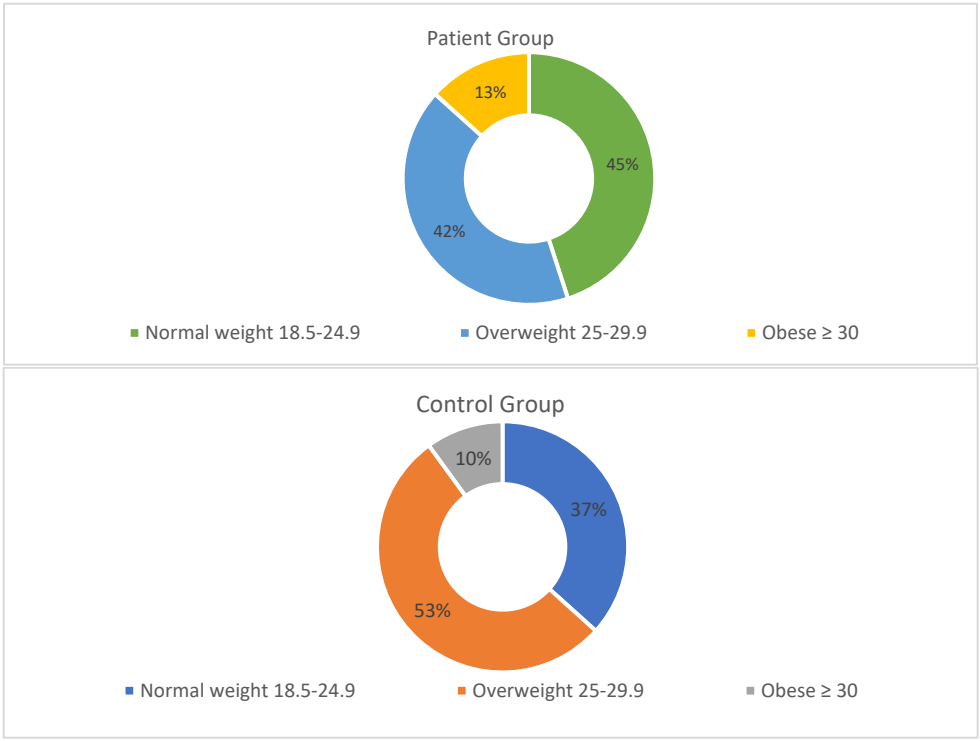

Figure 1: Subgroups of Body Mass Index (BMI) According to the Traditional World Health Organization (WHO)

A box plot was used to screen data dissemination by exhibiting the data quartiles and averages. Box plots show the five-number summary of a data set, including the least score, first (lower) quartile, median, third (upper) quartile, and maximum score. Concerning the valuation of biomarkers levels in IHD patient groups matched to the healthy control, Figures (2 & 3) demonstrated a significant accumulative in the mean levels of all lipid profile panels comprising [total cholesterol (T.C.), triglyceride (T.G.), LDL, and T.G./HDL-c ratio] except HDL which was found to be lesser in patients group compared to the healthy control. The mean levels of T.C., T.G., and LDL in IHD patients were (202.7, 137.48, and 33.98)
respectively, while in the control group were (175.6, 123.27, and 26.9) mg/dl.

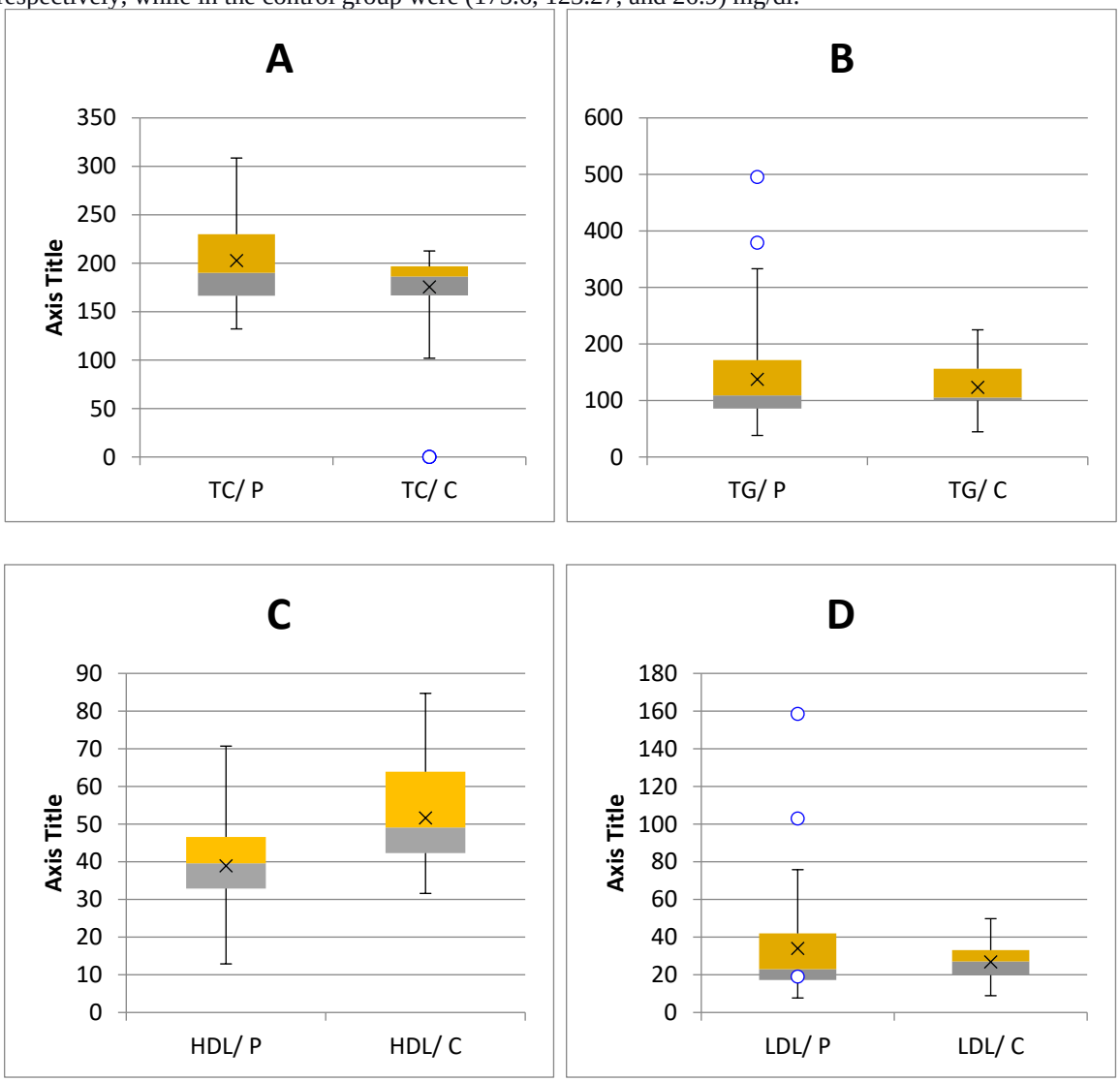

Figure 2: Boxplot for the Dispersal of Lipid Profile Board (A) Total Cholesterol (B) Triglyceride (C) High-Density Lipoprotein (D) Low-Density Lipoprotein in IHD Patients and Control Groups

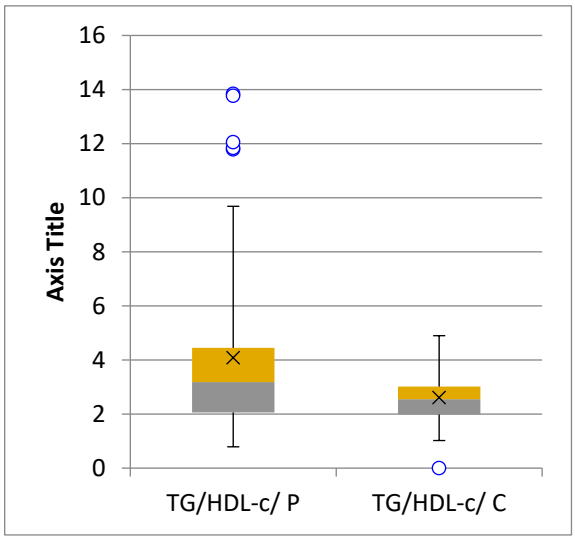

Figure 3: Boxplot for the Distribution of T.G./HDL-c Ratio in IHD Patients and Control Groups

The effect of BMI groups was also examined using the T.G./HDL-c ratio. Results illustrated that the serum level of T.G./HDL-c was enlarged in IHD patients with increasing BMI compared to the healthy control, as shown in Figure (4). In obese participants, the mean T.G./HDL-c ratio was (3.66) in IHD cases compared to (2.58) in the control group. This was agreed with another study that reported that lipid metabolism and the following dyslipidemia contribute to the formation of plaques in cardiovascular disease. (Kosmas *et al*., 2023)

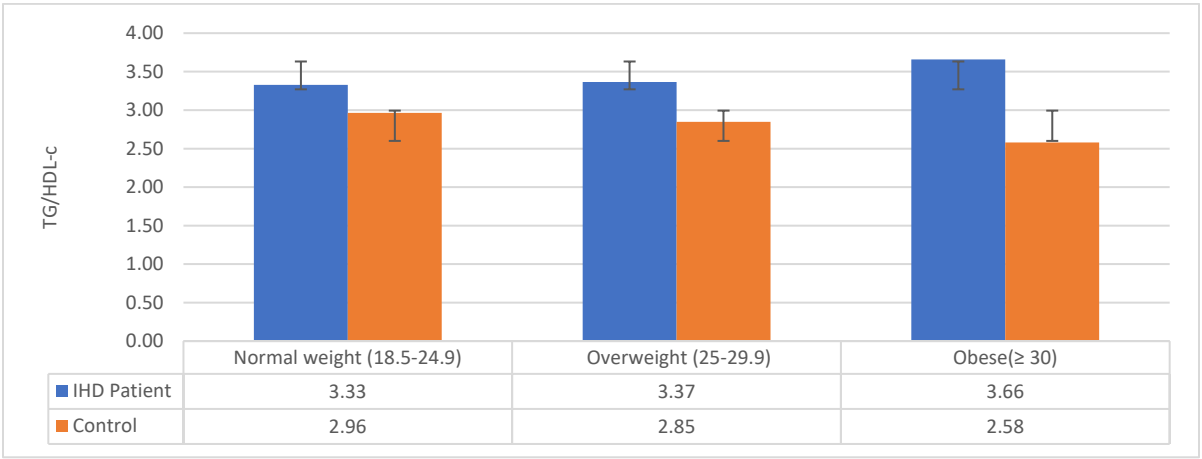

Figure 4: Mean Level of Serum T.G./HDL-c Ratio Based on the Body Mass Index in IHD Patients Compared to the Control Group

In both study groups, the participants' sex was subdivided into Male and Female groups. The effect of sex groups was examined with the biomarkers. Results illustrated that the T.G./HDL-c ratio serum level increased more in male IHD patients than in female IHD patients, as presented in Figure (5). The subclinical problem of coronary atherosclerosis accompanies a greater TG/HDL-C radionecrosis; sex differences in these relationships remain uncertain. (Patil *et al.*, 2020)

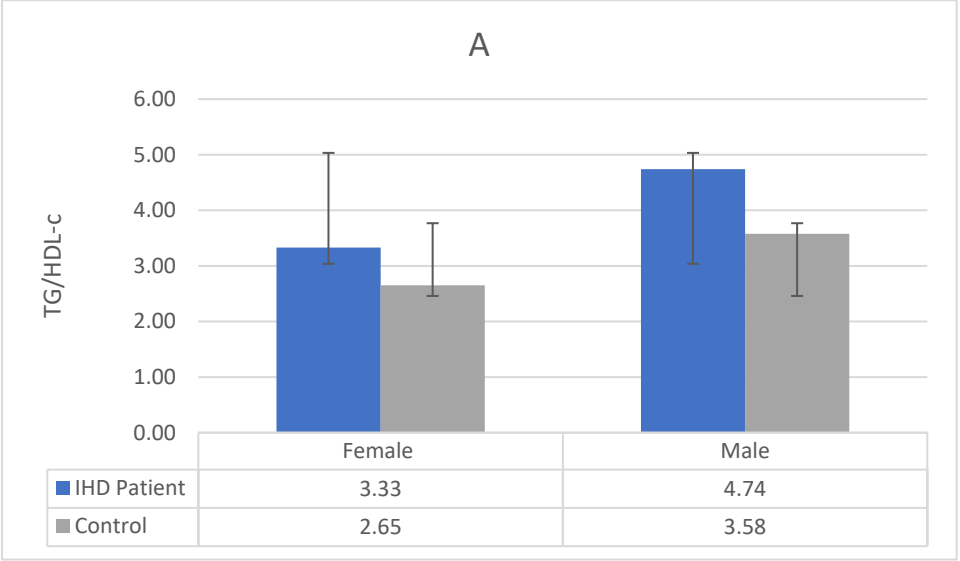

Figure 5: Mean Level of Serum T.G./HDL-c Ratio Based on the Sex in IHD Patients Compared to the Control Group

4. Discussion

Adipokines are highly deregulated by obesity and may control cardiovascular homeostasis (Boulet *et al.*, 2015). Adipose tissue can release free fatty acids (FFA) in the nearness and around the coronary arteries, moderating vascular receptiveness to vasoactive agents (Henrichot *et al.*, 2005) and revolving into an opposing lipotoxic, pro-thrombotic, and pro-inflammatory factor (IFNγ) to overexpress chemotactic cytokines. In addition, fatty tissue can discharge FFA into the bloodstream, alarming vascular homeostasis and endothelial dysfunction, which leads to an amplified risk of heart disease (González *et al.*, 2017).

Second, raised blood pressure leads to systemic arteriole spasm by increasing the penetrability of the vascular endothelium, delaying the interaction time of lipoproteins with the vascular wall, and decreasing endothelium-dependent vasodilation. Systemic arteriole spasm was proposed to raise the risk of heart disease (Yuan and Braun, 2017).

Third, blood pressure regulation is placed on endothelial function, which is controlled by the interaction of the renin–angiotensin–aldosterone system, adrenergic receptors, and metabolic reactions; these endothelial function-related mechanisms are also faithfully related to adipose tissue (Mu *et al.*, 2018). Also, obesity-related FFA constrains the sodium/potassium exchange pump and sodium-ATP pump, which increases smooth muscle tone, peripheral resistance, and blood pressure (Bell and Rahmouni, 2016).

In this study, the T.G./HDL-c ratio was amplified enormously in the IHD group compared to the control; these results were consistent with another finding. Since abnormal lipid panel (HDL-C <40 mg/dl in men and <50 mg/dl in women and T.G.≥150 mg/dl) was considered as a central define of metabolic syndrome (Belete *et al.*, 2021) and felt a brilliant predictor of chief hostile cardiovascular proceedings (Qiao-Yu *et al.*, 2022).

For the previous decade, widespread research has been showing concerning the interlink between T.G.s and other lipoproteins, yet it has not been entirely productive. (Nur Zati Iwani *et al.*, 2022). Patients in the maximum quartile of TG/HDL-C ratio had the uppermost rate of opposing cardiovascular proceedings with excellent TG/HDL-C ratio might raise the risk of ISR via amplified insulin resistance, endothelial dysfunction and atherosclerosis, oxidative stress, pro-inflammatory status, and proliferation of vascular smooth muscle cells (Kundi *et al.*, 2017)

The mechanisms fundamental to the correlation between TG/HDL-C ratios and IHD patients remain unidentified. An earlier study presented significant relations between TG/HDL ratio rises and fractional esterification rates of cholesterol in plasma exhausted of apoB lipoproteins. Many factors have been established to raise the serum concentrations of T.G. and HDL-C, and the TG/HDL-C ratio was involved in poor glycemic control (Hermans, Ahn and Rousseau, 2010)

The logarithm of the ratio TG/HDL-C associates well with HDL particles' size and the fractional esterification rate of cholesterol by lecithin: cholesterol acyltransferase (LCAT) in plasma (Dobiášová *et al.*, 2011). The fractional

esterification level of cholesterol in plasma exhausted of apoB-containing lipoproteins reveals the reactivity of HDL to LCAT. It has been well-known that the molar ratio of the concentration of TG/HDL-C is meaningfully amplified in patients who have experienced a myocardial infarction, matched with age- and sex-paralleled control subjects (Dobiasˇova, 2004). It can be relieved by calculating the atherogenic index of plasma (AIP). It has been recurrently revealed that the AIP value (log[TG/HDL-C]) is strongly associated with the size of the lipoprotein particles. Therefore, the AIP value precisely indicates the attendance of atherogenic LDL particles, and it is also a sensitive predictor of coronary atherosclerosis and cardiovascular risk (Soška *et al*., 2012)

The influence of BMI was also established in the TG/HDL ratio; the ratio was amplified with cumulative BMI. These results were totally consistent with other research that showed that the TG/HDL-C ratio has been established to rise along with the increase of the BMI and waist circumference, and this ratio has elevated up to three times in obese persons. Numerous studies have defined the TG/HDL-C ratio as an insulin resistance indicator (Özkaya, Bavunoglu and Tunçkale, 2014). The ratio of triglyceride to high-density lipoprotein cholesterol (TG/HDL-C) can reveal the body's complete level of lipid metabolism, and it has been established to be a risk factor for numerous cardiovascular diseases (Chen *et al.*, 2020).

The mechanism may be associated with low levels of HDL-C that are unfavorable to regulating extracellular matrix rebuilding, cell differentiation, and proliferation (Prasad *et al.*, 2019). Its pathophysiological meaning may be connected to the amplified serum T.G. level irritating the reduced endothelial vasodilation function of aortic vessels. All at once, the study established that T.G. was meaningfully positively linked with the risk of cardiovascular proceedings and all-cause mortality. With the rise of T.G. levels, the occurrence of ischemic heart disease and ischemic stroke in the research subjects presented a significant upward drift (Bittner *et al.*, 2009).

Nevertheless, matched with the single blood lipid pointers of T.G. and HDL-C, it cannot ultimately reveal the overall level of blood lipids. TG/HDL-C ratio, as a joint blood lipid index, can be used as a simple, available, and dependable hematological index for expecting cardiovascular risk. The TG/HDL ratio has been revealed to be a strong predictor of total mortality, coronary heart disease occurrence, and cardiovascular mortality. It was not associated with critical predictive variables, including age, civilization, smoking, hypertension, diabetes, and severity of coronary heart disease (Drexel *et al.*, 2005). Caselli et al. (Caselli *et al.*, 2021) establish that low HDL-C levels and excellent TG/HDL-C ratios were risk factors for cardiovascular proceedings in patients with coronary heart disease. The ratio of TG/HDL-C can more precisely reflect the complete level of lipid metabolism in patients than the single blood lipid measurement results. So, using the ratio of TG/HDL-C as a predictor of cardiovascular proceedings in coronary heart disease can more precisely predict the remaining cardiovascular risk in patients with coronary heart disease. Studies have found that high levels of TG/HDL-C can lead to the development of abdominal aortic aneurysm, and it is positively correlated with the severity of the patient's disease (Ma *et al.*, 2019).

Many types of research have revealed that hypertriglyceridemia is an independent analyst of IHD and may be a more potent risk factor among gender (Sarwar *et al.*, 2007). Atherogenic dyslipidemia, the combined incidence of high triglycerides (T.G.) and low HDL-C, is linked to an intensely prognostic of CHD (Grundy *et al.*, 2005). The ratio of TG/HDL-C has been suggested as a simply available atherogenic indicator. Documents on the predictive value of the TG/ HDL-C ratio are restricted. The ratio intensely expected risk of myocardial infarction. Others have connected a high TG/HDL-C ratio to coronary atherosclerosis, reduced heart rate, and IHD incidence (Collaboration, 2005).

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