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Original Article

Prediction of cardiovascular risk factors and metabolic syndrome in adults from Saudi Arabia using the logarithm of triglyceride/HDL-cholesterol ratio

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ABSTRACT

Objective: Cardiovascular diseases (CVD) are the leading cause of death globally. Metabolic syndrome (MtS) is a risk factor that increases the likelihood of CVD. The atherogenic index (AIP), calculated as the logarithm of the ratio of triglycerides (TG) to high-density lipoprotein cholesterol (HDL) cholesterol in plasma, is a valuable marker for highly atherogenic small dense low-density lipoprotein cholesterol particles. This study aimed to explore MtS prevalence and investigate the potential of using the AIP as a predictor for CVD risk factors in adults from the Qassim region of Saudi Arabia.

Methods: The cross-sectional study enrolled 589 participants from public hospitals in nine major cities who completed a detailed questionnaire on health, diet, and lifestyle. Anthropometric measurements and some clinical parameters were measured.

Results: The findings indicated a significant prevalence of MtS (37.5%) among participants from the Qassim Area, which was higher in males (39.9%) than females (34.9%). Nevertheless, a significant prevalence was shown for CVD risk factors among participants, with hyperglycemia (78.1%), hypertriglyceridemia (39.0%), hypo-HDL-cholesterolemia (38.9%), and hypertension (21.6%) being common. The AIP's performance in identifying CVD risk factors showed a receiver operating characteristic value of 0.909 ($P < 0.001$). The optimal cutoff value for the AIP was determined to be 0.468, demonstrating high sensitivity (84.8%) and specificity (78.6%).

Conclusion: Incorporating AIP into clinical practice could enhance CVD risk prediction compared to using lipid profiles alone. These findings suggest that there is a high prevalence of MtS among adults in the Qassim region of Saudi Arabia. Further longitudinal studies are needed to recommend AIP as a robust tool for predicting CVD in clinical settings.

Keywords: CVD, High-density lipoprotein, metabolic syndrome, Qassim Region, triglycerides

Introduction

Cardiovascular diseases (CVD) are considered the main cause of death in the world in general and in Saudi Arabia as well. These clusters of diseases are interrelated with abnormalities in the plasma lipid profile, or what is called dyslipidemia.[1] Moreover, it was shown that metabolic syndrome (MtS) increased the likelihood of developing CVD in individuals at high risk.[2] The main components of MtS are central obesity, high blood pressure, glucose intolerance, dyslipidemia of high triglycerides (TG), and low high-density lipoprotein cholesterol (HDL). It was found that the presence of at least three of the aforementioned components is commonly accepted to detect MtS.[3] In dyslipidemia, the lipid profile in the blood shows high levels of low-density lipoprotein cholesterol (LDL), TG, and total cholesterol (TC) and low levels of HDL.[4] The prevalence of dyslipidemia in many countries is considered high.[5] In Saudi Arabia, a high prevalence of dyslipidemia was also observed.[6-8] It was shown that high levels of LDL and low levels of HDL are the most important risk factors for predicting CVD.[9,10] In addition, the lipoprotein particles' size is also important in the process of atherogenicity. In some studies, there was a strong association between small and dense LDL particles and CVD.[11] These small and dense LDL particles are weakly bound to LDL receptors and have the ability to be oxidized more easily than large LDL particles. Therefore, these small, dense LDL particles are more atherogenic than the other LDL particles.[11,12] Nevertheless, it was observed that small and dense LDL particles are highly predominant in the blood of CVD patients, even with a normal level of LDL.[12] In

addition, previous reports have found an association between small, dense HDL particles and the increased risk of CVD.[13] The early detection of dyslipidemia is essential for the proper management of CVD. It will help prevent the development of atherosclerosis. Several research trials were done to find the proper predictor of CVD risk factors. The common screening tests for dyslipidemia are TC and HDL.[14] In addition, the levels of TG are also important.[15] Moreover, it has been found that the TG/HDL ratio increases in CVD patients.[16] Therefore, the TG/HDL ratio is used for the prediction of the increased risk of CVD and diabetes mellitus in patients with CVD.[17] On the other hand, there was a correlation between the logarithm of the ratio TG/HDL and the particle size of HDL and LDL.[15] The measurement of particle sizes of both LDL and HDL is too complicated to be applied in clinical practice. Instead, the atherogenic index of plasma (AIP) is calculated from this formula (log[TG/HDL]).[18] The result of the AIP accurately reflected the existence of atherogenic, small, dense LDL and HDL particles. It is considered a sensitive predictor of CVD risk.[15] Therefore, this study was designed to explore the ability of AIP to predict CVD risk factors in a sample from the Qassim Region of Saudi Arabia.

Methods

Study design and sample

A cross-sectional descriptive study was designed and conducted during 2020 and 2021. Adults from different areas in the Qassim region of Saudi Arabia were recruited. Subjects were asked to complete a questionnaire containing questions about their health status, eating habits, and lifestyle, followed by clinical and anthropometric measurements.

Ethical approval and participants' recruitment

The sample size was calculated according to Sharma *et al*. (2020).[19] After recruitment, 589 participants accepted to join the study and signed the consent form. This study was approved by the research ethics committee at Qassim General Health Affairs (Approval#1443-409404). Participants were recruited from 9 different areas (Buraidah, Unaizah, Ar-Rass, Al Bukairiyah, Al-Khabra, Uyun Al-Jawa, Badaya'a, Al-Asyah, and Al Mithnab) in the Qassim region of Saudi Arabia. The inclusion criteria included people aged 18 years and above who live in the Qassim area. The exclusion criteria included subjects diagnosed with cancer or mental disorders and subjects who declined to be a part of the study.

Questionnaire

A structured questionnaire was adopted from previous published work and designed to collect self-reported information on age, gender, health status, dietary behaviors and characteristics, and eating habits.

Anthropometric measurements and clinical parameters

The anthropometric measurements and the blood pressure of the participants were recorded. Clinical parameters (lipid profile, fasting glucose) were measured using commercial kits (Human Inc., Germany). All determinations were carried out according to the manufacturer's instructions.

Statistical analysis

Data analysis was performed using SPSS (version 22), and descriptive statistics are presented as mean±standard deviation or proportions. The sample descriptive procedure was used for continuous variables and the sample crosstabs were used for categorical or ordinal variables. Receiver operating characteristic (ROC) curve analysis was used. The optimal cutoff value for the log (TG/HDL) ratio was defined as the point at which the sensitivity and specificity were at their maximum. A student's t-test was performed to compare lipid profile, fasting glucose, and blood pressure values between male and female results. The level of significance was set at $P < 0.05$.

Results

The demographics of the study population are shown in Table 1. As can be noticed, most participants were from Buraidah (29.2%), Unaizah (14.3%), and Ar-Rass (13.2%), as they are the main large cities in the Qassim region. About 47% of the participants were in the age range between 30 and 49 years, followed by the age range from 17 to 29 years (31.9%) and the age range from 50 to 59 years (12.1%). In addition, 52.3% were male, and 46.7% were females. Most

Table 1: Demographics of the study population

Characteristics	Total (*n*=589)	Male (*n*=308)	Female (*n*=281)
City in Qassim Region			
Buraidah	172	88	84
Unaizah	84	34	50
Ar-Rass	78	48	30
Al Bukairiyah	41	19	22
Al-Khabra	42	15	27
Uyun Al-Jawa	53	27	26
Badaya'a	42	24	18
Al-Asyah	38	26	12
Al Mithnab	39	27	12
Age			
17-29	188	82	106
30-39	161	100	61
40-49	117	59	58
50-59	71	47	24
>=60	52	20	32

of the participants were working in the governmental sector (40.7%) or studying (12.9%).

The status of some medical complications among the study population is presented in Table 2. As it can be observed, most of the participants were overweight or obese (27.2% and 43.3%, respectively), while only 26.8% and 2.7% were in the normal body mass index or underweight, respectively.

Moreover, most of the study sample had risk factors for CVD (62.6%). They were having hyperglycemia (78.1%), hypertriglyceridemia (39.0%), hypo-HDL-cholesterolemia (38.9%), and hypertension (21.6%). It can also be noticed from Table 1 that most of the overweight and obese participants were males, while most of the underweight and normal-weight participants were females. In addition, participants suffered from different medical complications (hyperglycemia (78.1%), hypertriglyceridemia (39.0%), hypo-HDL-cholesterolemia (38.9%), and hypertension (21.6%)) [Table 2]. It was found that 62.6% of participants were suffering from CVD risk factors (high LDL, low HDL, and high TG levels).

Table 3 presents some measurements and characteristics of participants with and without CVD risk factors (high LDL + low HDL + high TG levels).

It can also be noticed from Table 3 that the participants with CVD risk factors showed higher values of body weight, waist circumference, TC, TG, and LDL, systolic and diastolic blood pressure, and fasting glucose when compared with normal participants ($P < 0.001$). In addition, ratios of TC/HDL, TG/HDL, and Log (TG/HDL) showed a significant difference ($P < 0.001$) between participants with and without CVD risk factors.

The ROC curve results are shown in Figure 1. Areas under the ROC curve to identify risk factors for CVD were 0.909 ($P < 0.001$) for Log (TG/HDL). The optimal cutoff values of

Table 2: Status of some medical complications among the study population

Characteristics	Total (%, *n*=589)	Male (=308) (%)	Female (%, *n*=281)
BMI Status			
Underweight (BM I ≤18).	16 (2.7)	5 (1.6)	11 (3.9)
Normal weight (BMI >18 and ≤25).	158 (26.8)	68 (22.1)	90 (32.0)
Overweight (BM I >25 and <30).	160 (27.2)	99 (32.1)	61 (21.7)
Obese (BMI ≥30).	255 (43.3)	136 (44.2)	119 (42.3)
Hyperglycemia (Fasting glucose >110 mg/dL).	460 (78.1)	241 (78.2)	219 (77.9)
Hypertriglyceridemia (>150 mg/dL).	230 (39.0)	119 (38.6)	111 (39.5)
Hypo-HDL-cholesterolemia (<40mg/dL).	229 (38.9)	133 (43.2)	96 (34.2)
Hypertension (>140/85 mmHg).	127 (21.6)	65 (21.1)	62 (22.1)
Participants with CVD risk factors (High LDL, low HDL, and high TG levels).	369 (62.6)	198 (64.3)	171 (60.9)

Table 3: General characteristics of participants with and without CVD risk factors (high LDL+low HDL+high TG levels)

Characteristics	Total (*n*=589)	Participants with/without CVD risk factors		
		Normal (*n*=220)	CVD (*n*=369)	T-test
Weight (Kg).	78.88±20.66	70.3±17.7	84.0±20.6	***
Waist Circumference (cm).	89.71±13.63	83.7±11.2	93.3±13.7	***
Total Cholesterol, TC (mg/dL).	203.65±35.72	183.3±27.0	215.8±34.7	***
Triglycerides (mg/dL).	142.08±43.31	110±29.8	161.0±38.8	***
HDL (mg/dL).	44.58±11.95	50.6±13.8	40.9±8.9	***
LDL (mg/dL).	130.65±35.42	110.6±27.9	142.60±33.9	***
TC/HDL.	4.82±1.42	3.8±0.86	5.4±1.31	***
TG/HDL.	3.39±1.38	2.28±0.76	4.06±1.23	***
Log (TG/HDL).	0.491±0.198	0.327±0.182	0.589±0.131	***
Fasting Glucose (mg/dL).	132.39±32.78	120.5±24.6	139.4±35.0	***
Systolic blood pressure.	124.59±10.13	120.2±3.7	127.2±11.7	***
Diastolic blood pressure.	81.89±7.01	79.5±4.3	83.3±7.9	***

Values are means±SD. ***:*P*<0.001

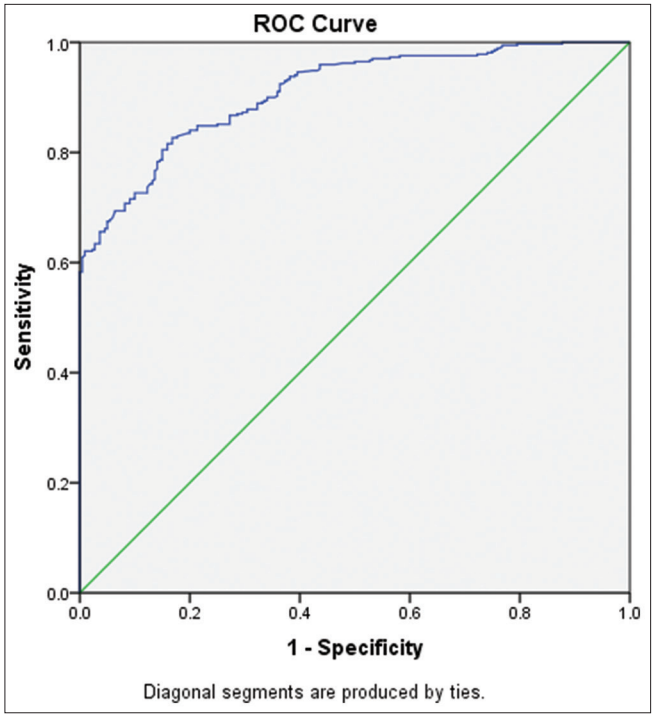

Figure 1: Sensitivity and specificity of logarithm TG/HDL ratio as a tool for prediction of CVD risk factors

the log (TG/HDL) ratio for risk factors of CVD prediction were 0.468, with a high sensitivity and specificity percentage of 84.8% and 78.6%, respectively.

Discussion

In this study, a high prevalence of MtS was found (37.5%) in the Qassim area of Saudi Arabia. On the other hand, we demonstrated that the log (TG/HDL) ratio is highly associated with CVD risk factors in a study population from Qassim Region, Saudi Arabia. The cutoff values of the log (TG/HDL) ratio for risk factors of CVD prediction were 0.468, with a high sensitivity and specificity percentage of 84.8% and 78.6%, respectively.

The obtained results showed a higher prevalence of MtS among participants from Saudi Arabia (37.5%) than that of other Middle East countries such as Tunisia,[20] Oman,[21] and the United Arab Emirates,[22] as well as other Asian countries such as Korea and South Asia.[23,24] Moreover, the findings of the current study revealed a higher prevalence of MtS among men (39.9%) than women (34.9%). These obtained results are similar to those reported by others.[25] This could be explained by the tendency of men to be overweight (32.1% vs. 21.7%) or to have hypo-HDL-cholesterolemia (43.2% vs. 34.2%) than women, respectively.

Cholesterol is primarily transported in the circulation, surrounded by VLDL, LDL, and HDL particles, while TG is transported by VLDL particles. Thus, serum TC and TG levels reflect the serum concentrations of lipoprotein particles transporting them.[26] LDL is well-known to be the major atherogenic lipoprotein, and small VLDL and intermediate-density lipoprotein have also been identified to have atherogenic activity, as described by Ivanova *et al*. (2017).[27] Meanwhile, HDL has antiatherogenic activity by promoting the removal of lipid deposits from atherogenic vascular lesions and by having antioxidant and anti-inflammatory effects.[26] Dyslipidemia is considered an important risk factor for CVD. The high prevalence of dyslipidemia is showing a continuous increase in many countries.[28] Turk-Adawi *et al*. (2017)[29] found a high prevalence of dyslipidemia in most of the Gulf countries, such as Saudi Arabia. This high rate of dyslipidemia is encouraging researchers to find suitable early and easy screening tools for the detection of dyslipidemia as a CVD risk factor.

In fact, the elevation of LDL and the reduction of HDL levels in the blood are considered important risk factors for CVD.[9] Not only the levels but also the size of lipoproteins play a crucial role in the process of atherosclerosis formation.[30] The smaller LDL particles showed more ability in the development of atherosclerosis.[13] On the other hand, only the large and light HDL particles showed a protective ability against CVD and not the smaller HDL, which are believed to be linked with high CVD risk.[13,15] The formation of small and dense LDL and HDL particles is organized by the effect of cholesteryl ester transfer protein, which catalyzes the transfer of cholesteryl esters from HDL to ApoB-containing lipoproteins, resulting in smaller HDL.[31] In addition, the TG-rich LDL particles become smaller and denser due to the hydrolysis effect of hepatic lipase. These smaller LDLs become more atherogenic due to their ability to enter the arterial.[32] However, the logarithm of the TG/HDL ratio is found to be well correlated with the size of both LDL and HDL particles.

It has been recognized that the TG/HDL ratio is increased in patients with CVD.[33] Due to the difficulty of measuring particle sizes of LDL and HDL in clinical practice, the logarithm of the TG/HDL ratio can be calculated, as it shows a strong correlation with LDL and HDL particle size and the fractional rate of cholesterol esterification.[33] Hermans *et al*. (2012) found that log (TG/HDL) can be used to detect CVD risk factors and recognize deteriorating glucose homeostasis in Type 2 diabetic females. In another study, patients with a higher value of TG/HDL showed dyslipidemia, insulin resistance, and diabetes, which means a high risk of CVD.[34] Moreover, the TG/HDL ratio was strongly correlated with pre-diabetic and type-2 diabetes in CVD patients.[35]

In young adults, the TG/HDL ratio was considered an independent determinant of arterial stiffness.[36] They recommended using this ratio to help prevention of CVD in young adults. In Venezuela, Aguirre *et al*. (2018)[37] used the TG/HDL ratio as a predictor of CVD risk factors in adolescents. In Egypt, the TG/HDL ratio was used as a marker

of insulin resistance in overweight and obese Egyptian children older than five years instead of the insulin resistance index (HOMA).[38] In Mexico, the TG/HDL ratio was used for the diagnosis of metabolic syndrome in obese children.[39]

Along with dyslipidemia, the present study confirmed the high prevalence of overweight and obesity among the study participants (70.5%), which is in line with previous studies in Saudi Arabia[6] and Tabuk city,[1] which represent 78.8% and 71%, respectively, of the study participants from Saudi Arabia. However, it seems that overweight and obesity are a risk factor for CVD, as increased body weight beyond the normal body mass index range is associated with high levels of serum-free fatty acids that increase the production of circulated try glycerides, leading to hypertriglyceridemia.[1,40]

Furthermore, our findings are in line with other reports that found that the TG/HDL ratio has been advocated as a practical and helpful predictor to identify individuals at risk of dyslipidemia and MtS components.[41]

Conclusion

The log (TG/HDL) ratio could be useful as a marker for the prediction of CVD risk factors. More work is needed to repeat this predictor on other participants from other areas across Saudi Arabia to recommend using this marker for the prediction of CVD risk factors among the Saudi population.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors Contributions

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