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Assessment of correlation between lipid ratios and body mass index in patients with type 2 diabetes mellitus in Sarajevo, Bosnia and Herzegovina

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Objective. Studies that have evaluated correlation between body mass index (BMI) and novel lipid indices such as triglycerides (TG)/ high-density lipoprotein-cholesterol (HDL-C), total cholesterol (TC)/HDL-C, and low-density lipoprotein cholesterol (LDL-C)/HDL-C in type 2 diabetes mellitus (T2DM) are scarce. Hence, the aim of the present study was to explore the correlation between BMI and novel lipid indices in Bosnian patients with T2DM.

Methods. Present study included 117 patients with T2DM (mean age: 66.51 years) and 68 controls (mean age: 68.37 years). BMI was calculated as weight/height^2. Lipids were measured by standard methods. TG/HDL-C, TC/HDL-C, and LDL-C/HDL-C ratios were separately calculated. The differences between the groups were assessed by Student's t-test or Man Whitney U test. Correlations were determined by Spearman's test.

Results. In a total sample of T2DM patients, 41.0% were overweight and 44.4% were obese. In the control group, 51.5% of subjects were overweight and 25.0% were obese. In T2DM group, a significant correlation was observed between BMI and HDL-C, LDL-C, TG/HDL, TC/HDL-C, and LDL-C/HDL-C ratios. In the control group, there was a significant correlation found between BMI and HDL-C, TG, TG/HDL, TC/HDL-C, and LDL-C/HDL-C-ratios. Correlation between BMI and other lipid parameters in T2DM and the control group was not determined.

Conclusion. The present study showed significant correlation between BMI and novel lipid indices in both T2DM patients and the control group of subjects. Possible explanation for the observed results might be prevalence of overweight and obese participants in this study sample. Since novel lipid indices are used in the prediction of cardiometabolic risk, results obtained in the present study have valuable clinical implications.

Keywords: body mass index, type 2 diabetes mellitus, obesity, lipids, dyslipidemia, TG/HDL ratio, TC/HDL ratio, LDL-C/HDL-C ratio

Type 2 diabetes mellitus (T2DM) is the most common occurring type of diabetes. It is a chronic metabolic disorder characterized by insulin resistance and relative insulin deficiency or secretion, which leads to hyperglycemia. T2DM is also referred as an age-related disease as it is not inherited, but acquired. The fact that it is inherited can be due to factors such as genetics, sedentary lifestyle, diet, urbanization, and many other aspects (DeFronzo et al. 2015).

T2DM is an expanding global health problem closely linked to the epidemic obesity. It presents as a complex net of connections with body mass index

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(BMI) as well as lipid ratios. A high BMI, especially in reference to central adiposity, plays a pivotal role in insulin resistance and the onset of T2DM. The impact of BMI classification, including overweight and various grades of obesity on the risk of T2DM in the real-world practice, is a well-investigated topic (Garber 2012).

Adipose tissue secretes adipokines and inflammatory cytokines, which contribute to the chronic inflammation and disrupted glucose homeostasis. Adipokines are bioactive molecules that are secreted by adipose tissue. Adipokines include, among others, leptin, adiponectin, and resistin. These bioactive molecules are involved in various physiological processes, which include energy metabolism, inflammation, and insulin sensitivity (Cheng and Yu 2022).

The obesity pandemic has progressed rapidly and to such an extent due to high calorie diets. This pandemic obesity is confirmed as a high-risk factor for T2DM as well as metabolic syndrome. The combination of obesity and metabolic syndrome concurring with T2DM has birthed the term "diabesity". These two health crises coexist and often exacerbate one another. Obesity, especially central adiposity, contributes to insulin resistance, which is an essential mechanism in the pathogenesis of T2DM. The health implications regarding diabesity encompass increased risks of cardiovascular disease, neuropathy as well as nephropathy and retinopathy, which all contribute to increased diabetes morbidity and mortality. The management hereof is thus pivotal as it requires an integrated approach, which include lifestyle modifications, medical interventions, and close monitoring of adverse health effects in order to improve the overall quality of life for affected individuals (Pinchevsky et al. 2020).

Evaluating the lipid profiles has been limited to the estimation of the conventional lipid profiles such as triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and total cholesterol (TC). These alone are inadequate to characterize the lipid abnormalities as they could appear normal in some patients and yet these patients are still at risk of developing cardiovascular diseases (Superko and King 2008).

A new approach in the estimation of cardiovascular risk factor encompasses estimations of Castelli's Risk Index–I (CRI–I), Castelli's Risk Index–II (CRI–II), atherogenic coefficient, cholesterol index (CHOL Index), and the atherogenic index of plasma that all have been shown to be useful and effective in risk prediction of conditions such as coronary artery disease, diabetes mellitus, dyslipidemia, metabolic syndrome, hypertension, obesity, atherosclerosis, and even stroke (Bhardwaj et al. 2013).

Abnormally high lipid ratios are metabolically interrelated and have been shown to be associated with insulin resistance. This association is principally evident in the context of metabolic syndrome, obesity and T2DM, where lipid abnormalities and insulin resistance coexist and amplify one another. The mechanisms underlying the association include lipid-induced insulin resistance, adipocyte dysfunction, chronic inflammation, lipid accumulation in non-adipose tissues as well as mitochondrial dysfunction (Wilcox 2005).

It is of high importance to understand the interplay between high lipid ratios and insulin resistance as they have significant clinical implications. Since studies that evaluated correlation between BMI and novel lipid indices such as TG/HDL-C, TC/HDL-C and LDL-C/HDL-C used in cardiometabolic risk prediction are limited, the aim of the present study was to explore the correlation between BMI and novel lipid indices in Bosnian patients with T2DM.

Material and Methods

Subjects. All patients that were recruited (117 patients), as defined by American Diabetes Association, regularly attended the Out-Patient Family Medicine Clinic "Višnjik" in Sarajevo, Bosnia, and Herzegovina. They all were receiving antihypertensive and anti-diabetic therapies, but some were also receiving anti-lipidemic drugs and/or aspirin for at least the previous 6 months. None of the patients were current smokers and consumers of alcohol and exclusion criteria were: the presence of sustained acute and chronic infections, hepatic or renal disease, malignancy, diabetic nephropathy and retinopathy, as well as other endocrine dysfunctions.

There were 68 apparently healthy participants in the control group with no history of hyperlipidemia, coronary heart diseases, hypertension, T2DM or any other endocrine dysfunctions. Subjects of the control group did not receive any medication (such as corticosteroids, vitamins supplements, hormone replacement therapy, antioxidant formulations, and thiazolidinediones), which may affect endothelial function and/or insulin resistance. None of the control group subjects were current smokers and consumers of alcohol.

All subjects had given written informed consent. Investigations were carried out in accordance with the Declaration of Helsinki as revised in 2013. The study was approved by the Ethical Committee of the Medical Faculty, University of Sarajevo.

Blood sampling. Blood sampling was done in the morning after an overnight fast and after a 30-min rest in a semi-recumbent position. It was done using the vacutainer technique and without stasis.

Blood chemistry analysis. An immunoturbidimetric method (TINIA; Siemens Healthcare Diagnostics Ltd, Camberley, United Kingdom) was used for measuring HbA1c with a normal range 4.8–6.0%. The LDL-C were calculated using the Friedewald formula, while standard enzymatic methods were used for measuring the TC, HDL-C and TG levels. TG/HDL-C, TC/HDL-C and LDL-C/HDL-C ratios were separately calculated. All biochemical tests were performed at Institute for Clinical Chemistry and Biochemistry, University of Sarajevo Clinics Centre.

Anthropometric measurements. The weight and height of each subject were measured to calculate BMI. The height was measured in centimeters by a portable stadiometer (seca 213; seca®). Subject was asked to stand on a horizontal surface in footwear with their feet together. The horizontal slider of the stadiometer was placed on the top of the head. Two centimeters were deducted from the recorded value to compensate for the mentioned footwear. Weight was measured in kilograms using a digital scale (BS-03; Shenzhen J and E Electronics Co., Ltd.). The subjects' weight was measured whilst wearing light casual clothing. BMI of each subject was calculated. The calculation was as follows: weight/height^2. BMI was expressed in kg/m^2.

Blood pressure measurements. Arterial blood pressure was measured by a standard mercury-column sphygmomanometer (SCH 11B; Smart Care). Subjects were asked to remain in a seated position. Prior to measurements, subjects rested for 5 min. One hand was positioned at the level of the heart. The sphygmomanometer cuff was positioned around the upper arm and inflated. Using a stethoscope, while decreasing the pressure of the sphygmomanometer, systolic blood pressure (SBP) was recorded. This is the pressure, at which the first Korotkoff sound could be heard. Diastolic blood pressure (DBP) was recorded when Korotkoff sounds were no longer audible.

Statistical analysis. The Kolmogorov-Smirnov test of normality was used to test the distributions of variables. To compare the difference between normally distributed variables the Unpaired Student's t-test was used. The Mann-Whitney U test was used to compare differences between groups for variables that were not normally distributed. Spearman's test assessed correlations. A p value of less than 0.05 was considered statistically significant. All statistical analyses were conducted using the software, SPSS for Windows (version 19:0; SPSS, Chicago, IL, USA).

Results

The baseline characteristics of study participants are shown in Table 1. There was a statistically significant difference in values of TC (p=0.014), LDL-C (p=0.023), and smoking (p=0.046) between the groups. Statistically high significant difference was established in gender (p=0.003) as well as the values of BMI (p=0.003), HDL-C (p=0.001), TG (p=0.001), fasting blood glucose (FBG) (p=0.001), glycated hemoglobin (HbA1c) (p=0.001), and SBP (p=0.001) between the groups. Significant difference in age (p=0.280) and values of DBP (p=0.076) between groups was not observed.

The lipid ratios in the study participants are shown in Table 2. There was a statistically significant difference in the value of TG/HDL-C ratio (p=0.001), but there was no significant difference neither in the value of TC/HDL-C ratio (p=0.063) nor in the value of LDL-C/HDL-C ratio (p=0.290) between T2DM patients and control group of subjects.

The correlation between BMI and lipid ratios is shown in Table 3. There was a significant positive correlation between BMI and TG/HDL-C ratio in the T2DM group (rho=0.257, p=0.005) and in the control group (rho=0.403, p=0.001). A significant positive correlation between BMI and TC/HDL-C ratio was observed both in the T2DM (rho=0.361, p=0.001) and the control group (rho=0.358, p=0.003). There was a significant positive correlation between BMI and LDL-C/HDL-C ratio in the T2DM group (rho=0.335, p=0.001) as well as in the control group (rho=0.314, p=0.009).

The correlation between BMI and standard lipid indices is shown in Table 4. The results demonstrate that there was no statistically significant correlation between BMI and TC neither in the T2DM (rho=0.181, p=0.051) nor in the control group (rho=0.127, p=0.303). There was a statistically significant negative correlation between BMI and HDL-C in the T2DM group (rho=-0.254, p=0.006) as well as in the control group (rho=-0.341, p=0.004). A significant positive correlation was observed between BMI and LDL-C in the T2DM group (rho=0.210, p=0.023), but there was no statistically significant correlation between BMI and LDL-C in control group (rho=0.148, p=0.228). The results show a significant positive correlation between BMI and TG in the control group (rho=0.374, p=0.002), but not a significant correlation between BMI and TG in the T2DM group (rho=0.157, p=0.091).

Discussion

A vast body of evidence has demonstrated a significant correlation between traditional lipid profiles and BMI in patients with T2DM. BMI is a powerful and reliable anthropometric measure of body fat that is derived from a patient's height and weight. Individuals who have a BMI between 18.5–24.9 kg/m² are considered healthy whereas those with a BMI between 25.0–29.9 kg/m² are regarded as overweight and any BMI over 30 kg/m² is classified as obese. Both T2DM and dyslipidemia are well established contributors to cardiovascular disease. This necessitates attentive management and monitoring in order to decelerate disease progression (Beyene et al. 2023).

Critical markers in the study of T2DM and its associated cardiovascular risk include elevated levels of LDL-C, FBG, TC, TG as well as HDL-C. This is emphasized in a study conducted in Ethiopia (Temesgen et al. 2020), where there were elevated levels of LDL-C, FBG, and TC in patients that had a BMI of ≥25 kg/m². Building on these findings, subjects in our study, both from the control and the T2DM groups, had BMI's, which exceeded 25 kg/m². Age, diet, and lifestyle of the patients in the control group are all factors that attribute to the increase in BMI. Notably, Bosnia and Herzegovina maintain an average daily caloric intake of 3100 calories. In adult women aged 18 years and over, 20.3% are living with obesity, while 19.4% of adult men in the same age group are similarly affected. Simultaneously, diabetes

Table 1
Baseline characteristics of study participants

Variables	T2DM group (n=117)	Control group (n=68)	p-value
Age (years)	66.51±9.89	67.93±5.53	0.280
Gender (male /female)	50.4% / 49.6%	27.9% / 72.10%	0.003
BMI [kg/m²]	29.00 (26.00–33.00)	27.00 (25.10–30.78)	0.003
TC [mmol/L]	5.60 (4.90–6.47)	6.00 (5.30–7.00)	0.014
HDL-C [mmol/L]	1.10 (0.89–1.30)	1.33 (1.09–1.46)	0.001
LDL-C [mmol/L]	3.50 (2.89–4.33)	4.08 (3.20–4.93)	0.023
TG [mmol/L]	1.96 (1.38–2.87)	1.54 (1.10–2.13)	0.001
FBG [mmol/L]	8.45 (6.75–10.06)	5.20 (4.80–5.87)	0.001
HbA1c [%]	7.40 (6.55–8.70)	5.70 (5.40–5.80)	0.001
SBP [mm/Hg]	140 (127.50–150.00)	120 (110–140)	0.001
DBP [mm/Hg]	80 (80–90)	80 (80–90)	0.076
Smoking (yes/no)	23.1% / 76.9%	36.8% / 63.2%	0.046

Abbreviations: BMI – body mass index; DBP – diastolic blood pressure; FBG – fasting blood glucose; HbA1c – glycated hemoglobin; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; SBP – systolic blood pressure; T2DM – type 2 diabetes mellitus; TC – total cholesterol; TG – triglyceride.

Table 2
Lipid ratios in study participants

Variable	T2DM group (n=117)	Control group (n=68)	p-value
TG/HDL-C ratio	1.95 (1.13–3.10)	1.18 (0.75–1.87)	0.001
TC/HDL-C ratio	5.05 (4.18–6.46)	4.75 (3.88–5.78)	0.063
LDL-C/HDL-C ratio	3.28 (2.47–4.54)	3.05 (2.47–3.88)	0.290

Abbreviations: LDL-C – low-density lipoprotein cholesterol; HDL-C – high-density lipoprotein-cholesterol; TC – total cholesterol; TG – triglycerides; T2DM – type 2 diabetes mellitus.

is estimated to impact 7.4% of adult women and 8.9% of adult men in the country (Global Nutrition Report 2024). In Bosnia and Herzegovina, the obesity and overweight prevalence rates are 17.9% and 53.8%, respectively (Jasar et al. 2021).

TG is another critical marker in the study of T2DM and its association with cardiovascular risks. This is due to TG's involvement in lipid metabolism and insulin resistance. Elevated TG levels are often indicative of dyslipidemia in individuals with T2DM and is a common metabolic abnormality. TGs are influenced by dietary intake of sugars and fats, but also linked to genetic predispositions and lifestyle factors. In T2DM insulin resistance contributes to the increased lipolysis in adipose tissue as well as enhanced hepatic production of triglyceride-rich lipoproteins. This results in elevated circulating TG levels (Ren et al. 2016).

Correspondingly in our study, elevated TG levels were observed in T2DM group, which heightens their risk for cardiovascular disease. On the other hand, the control group maintained normal TG levels despite increased BMI. Both the T2DM and control groups demonstrated elevated TC, which indicates hyperlipidemia. Moreover, LDL levels were elevated and correlated with BMI in both groups. Accumulating LDL-C in arteries leads to plaque formation in individuals, which significantly increases cardiovascular disease risk (Jyotsna et al. 2023). HDL levels in both groups remained within normal ranges and negatively correlated with BMI. The obtained results are reinforcing the risk posed by low HDL-C levels for cardiovascular diseases (Assmann and Gotto 2004).

Castelli's Risk Index (CRI), which is calculated from TC, LDL, and HDL values is divided into CRI-I (TC/HDL-C ratio) as well as CRI-II (LDL-C/HDL-C ratio). CRI-I, referred to as the cardiac risk ratio, reflects the formation of coronary plaques with a diagnostic value as good as the determination of total cholesterol. CRI-II is an exemplary predictor of cardiovascular risk (Bhardwaj et al. 2013).

Apart from T2DM and its use determining pivotal cardiovascular risk factors, Castelli's indices are also commonly used within the sphere of coronary slow flow (CSF). These indices have emerged as crucial prognostic markers. Research conducted by Afsin et al. (2021) has investigated the predictive value of Castelli I (TC/HDL-C) and Castelli II (LDL-C/HDL-C) ratios in CSF patients. Their findings emphasize these indices as independent predictors of adverse cardiovascular outcomes like CSF. Once again highlighting the intricate link between lipid metabolism and coronary pathophysiology. Their study unravels that elevated Castelli ratios correlate significantly with increased cardiovascular risk. This promotes the necessity for these indices' incorporation into risk stratification algorithms and therapeutic strategies tailored for cardiovascular conditions such as CSF. Ultimately elucidating the clinical utility of Castelli indices beyond traditional lipid profiles, which enhances their role in optimizing patient care and outcomes in CSF management.

TC/HDL-C ratio, a novel lipid index, has been reported as a risk marker for both metabolic syndrome as well as cardiovascular disease. Crucial indicators for vascular risk are thus TC/HDL-C and LDL-C/HDL-C ratios. High TC/HDL-C and LDL-C/HDL-C ratios indicate heightened vascular risk due to the imbalance between protective lipoproteins and atherogenic lipoproteins (Millan et al. 2009). Our

Table 3
Correlation between BMI and lipid ratios in study participants

Variables	BMI	
	T2DM (n=117)	**Control group (n=68)**
TG/HDL-C ratio	rho=0.257 p=0.005	rho=0.403 p=0.001
TC/HDL-C ratio	rho=0.361 P=0.001	rho=0.358 P=0.003
LDL-C/HDL-C ratio	rho=0.335 p=0.001	rho=0.314 p=0.009

Abbreviations: BMI – body mass index; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; rho – Spearman correlation coefficient; T2DM – type 2 diabetes mellitus; TC – total cholesterol; TG – triglycerides.

Table 4
Correlation between BMI and standard lipid indices

Variables	BMI	
	T2DM (n=117)	**Control group (n=68)**
TC [mmol/L]	rho=0.181 P=0.051	rho=0.127 P=0.303
HDL-C [mmol/L]	rho=-0.254 P=0.006	rho=-0.341 P=0.004
LDL-C [mmol/L]	rho=0.210 P=0.023	rho=0.148 P=0.228
TG [mmol/L]	rho=0.157 P=0.091	rho=0.374 P=0.002

Abbreviations: BMI – body mass index; HDL-C – high-density lipoprotein cholesterol; LDL-C – low-density lipoprotein cholesterol; rho – Spearman correlation coefficient; T2DM – type 2 diabetes mellitus; TC – total cholesterol; TG – triglycerides.

study found a significant positive correlation between BMI and TC/HDL-C ratio in both T2DM and control groups. As the BMI increases so does the TC/HDL-C ratio. This correlation has been shown to be linked to ischemic heart disease risk and insulin resistance, associated with T2DM (Lemieux et al. 2001).

A study assessing the association between the TG/HDL-C ratio and the risk of T2DM among Chinese elderly participants in the Beijing longitudinal study of aging (Zheng et al. 2020), has shown that increased TG/HDL-C ratios are closely correlated with insulin resistance, which conclusively leads to T2DM. This study's findings are in accordance with our study, as we also report significant positive correlations between BMI and TG/HDL-C ratios in our study cohort.

In Turkey, a study has reported higher mean serum levels of TG, TC, LDL-C alongside with lower HDL levels in T2DM patients (Ozder 2014). These results also align with our findings with the exception of HDL, which was normal in our T2DM group. A clear association between BMI and LDL-C as well as BMI and HDL-C was also proven in a Jordanian study (Dmour 2019) among obese T2DM participants. These results support our findings of a positive correlation between BMI and LDL-C in the T2DM group, but not in the control group.

A noteworthy study carried out in South India among T2DM patients with healthy BMI ranges identified increased TG and decreased HDL-C levels in the T2DM group, but not in their non-diabetic control group (Latha et al. 2023). Similarly, our study proved elevated TG in the T2DM group and normal levels in the control group. This is suggestive of a BMI-independent correlation between T2DM and TG. Normal HDL-C levels were observed in both of our groups, however, the T2DM group's 25th percentile range fell below the reference range. This warrants careful attention.

Contrastingly, a comparative study by Jain and Gupta (2019) have reported no significant correlation between BMI and LDL-C in either T2DM group or the control group. This demonstrates a disparity in comparison to our findings. A positive correlation between BMI and LDL-C in the T2DM group observed in our study indicates that elevated BMI is associated with increased LDL-C levels.

Present study provides valuable insights into the association between BMI and novel lipid indices among patients diagnosed with T2DM compared with the control group. The rigorous employment of methodology alongside stringent participant selection criteria enabled the complex interplay between anthropometric measurements and lipid metabolism to be elucidated. The integration of novel lipid indices such as TC/HDL-C, TG/HDL-C, and LDL-C/HDL-C ratios enabled an expansion upon conventional lipid parameters. This offers a nuanced perspective on cardiovascular risk assessment in T2DM. Consistent positive correlations between BMI and the novel lipid ratios emphasizes the potential of these lipid indices as predictive markers for cardiovascular morbidity in diabetic populations.

Limitations of our research include its cross-sectional design, which precludes establishing causality and the small non-generalizable sample size from a single Family Medicine Centre. Future research should evaluate existing morbidities such as cardiometabolic, vascular, and central nervous system diseases to explore their potential connections with obesity and novel lipid indices in T2DM patients. There are also many benefits that can be derived from more diverse study populations, including comparisons among different ethnicities (Kosmas et al. 2023). Additionally, incorporating advanced biomarkers and conducting longitudinal studies, which would further enhance the robustness and applicability of our findings.

Notwithstanding inherent study limitations, our findings accentuate the clinical relevance of comprehensive lipid profiling in guiding early intervention strategies as well as personalized management approaches focused on mitigating the progressive nature of the cardiometabolic diseases. Moreover, present study reinforces and draws attention to the significant correlations between BMI and novel lipid indices in both T2DM and control groups. This highlights the intricate link between these anthropometric measures and lipid metabolism. A higher BMI, which is prevalent in both the T2DM and the control groups, is associated with increased levels of LDL-C, TC, and TG, which contributes to amplified cardiovascular risk. These findings underscore the pivotal role of comprehensive lipid profiling, which includes novel indices such as TC/HDL-C, TG/HDL-C, and LDL-C/HDL-C ratios in predicting cardiovascular morbidity and mortality in diabetic cohorts. Despite the limitations such as its cross-sectional design and small sample size, the results advocate for the incorporation of these novel lipid indices into clinical practice.

Conclusion

The present study showed significant correlation between BMI and novel lipid indices in both T2DM patients and the control group of subjects. Possible explanation for the observed results might be prevalence of overweight and obese participants in this study sample. Since novel lipid indices reflect coronary plaque formation and are used as risk markers for cardiometabolic diseases as well as in the prediction of cardiovascular risk. Results obtained in the present study have also valuable clinical implications. Future research should aim to include more diverse populations and the employment of longitudinal studies to further elucidate these relationships and ultimately enhance the applicability of the present findings.

Conflicts of interest: *The authors declare no conflict of interests.*

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