Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2022 Apr 29; 10(B):944-948.
https://doi.org/10.3889/oamjms.2022.8859
eISSN: 1857-9655
Category: *B - Clinical Sciences*
Section: *Endocrinology*

Correlation between HbA1c and Triglyceride Level with Coronary Stenosis Degree in Type 2 Diabetes Mellitus with Coronary Heart Disease

Laily Adninta[1], Indranila Samsuria[2], Edward Kurnia Setiawan Limijadi[2]*

[1]Department of Clinical Pathology, Columbia Asia Hospital, Semarang, Central Java, Indonesia; [2]Department of Clinical Pathology, Faculty of Medicine, Diponegoro University, Semarang, Central Java, Indonesia

Edited by: Ksenija Bogoeva-Kostovska
Citation: Adninta L, Samsuria I, Limijadi EKS. Correlation between HbA1c and Triglyceride Level with Coronary Stenosis Degree in Type 2 Diabetes Mellitus with Coronary Heart Disease. Open Access Maced J Med Sci. 2022 Apr 29; 10(B):944-948. https://doi.org/10.3889/oamjms.2022.8859
Keywords: HbA1c; Triglycerides; Coronary stenosis; Type 2 DM with CHD
***Correspondence:** Edward Kurnia Setiawan Limijadi, Department of Clinical Pathology, Faculty of Medicine, Diponegoro University, Semarang, Indonesia. E-mail: edwardksl@fk.undip.ac.id
Received: 02-Feb-2022
Revised: 22-Mar-2022
Accepted: 20-Apr-2022

Funding: This research did not receive any financial support
Competing Interest: The authors have declared that no competing interest exists

Abstract

BACKGROUND: The mortality of coronary heart disease (CHD) in type 2 diabetes mellitus (DM) increased 2–4 times more than non-diabetics because of coronary stenosis. One of the risk factors for CHD in type 2 DM is dyslipidemia. Hypertriglyceridemia plays an important role in atherosclerosis coronary arteries theoretically.

AIM: This study analyzed the parameters of HbA1c and triglyceride levels with the stenosis severity of coronary artery that occurs in type 2 DM patients with CHD that has not been analyzed so far.

METHODS: This study was a cross-sectional observational analytic study. Forty patients of type 2 DM with CHD in Kariadi Hospital on September 2013 were recruited based on the inclusion and exclusion criteria. HbA1c level in plasma was measured by turbidimetric immunoassay method. Triglyceride level was measured by enzymatic methods. Coronary stenosis was based on coronary angiography result as percentage. Spearman correlation test was used and $p < 0.05$ was considered statistically significant.

RESULTS: Mean HbA1c and triglyceride levels were 8.89 ± 1.498 % and 220.97 ± 92.24 mg/dL. The correlation test between HbA1c and triglycerides (TG) level with coronary stenosis, respectively, was $p < 0.001$, $r = 0.665$; $p = 0.001$, $r = 0.501$. In addition, correlation between HbA1c and TG was $p = 0.002$, $r = 0.466$.

CONCLUSION: HbA1c and triglyceride levels increase in line with the increasing stenosis severity of coronary heart disease in patients with type 2 DM.

Introduction

Diabetes mellitus (DM) is a chronic degenerative disease with a prevalence that continues to increase from year to year [1]. DM is a group of metabolic diseases with characteristics of chronic hyperglycemia due to defects in insulin secretion, insulin work, or both [2], [3]. A study by Shaw showed that the prevalence of diabetes worldwide in the adult population aged 20–79 years was 6.4% in 2010, affected 287 million adults and was expected to increase to 7.7%, and will affect 439 million adults by 2030. The prevalence of DM in Indonesia in 2010 was estimated at 4.6% with the number of patients as many as 6,964,000 patients [4]. Type 2 diabetes is also known as adult type or non-dependent insulin type [5], [6]. The World Health Organization (WHO) predicts an increase in the number of DM patients in the next years, especially in Indonesia. The WHO predicted an increase in the number of patients from 8.4 million in 2000 to ± 21.3 million in 2030 [3].

Pathogenesis of type 2 DM is based on impaired insulin secretion by pancreatic beta cells and insulin work disorders due to insensitivity (resistance) of target tissue to insulin. The main cause of death in type 2 DM is coronary heart disease (CHD) of approximately 80% as a complication of DM [7], [8]. The mortality rate of CHD in patients with type 2 diabetes can increase 2–4 times more than those who are non-diabetic due to atherosclerotic lesions in people with type 2 diabetes, which makes the development process is faster [7], [8], [9], [10].

CHD, often called ischemic heart disease, is most often caused by atheroma plaque blockage (atherosclerosis) in the coronary arteries. Atherosclerosis causes narrowing of the coronary artery lumen (coronary stenosis/coronary artery stenosis), so the blood flow to the myocardial is disrupted and results in myocardial ischemia. When the plaque ruptures, a thrombosis process occurs. This series of events gives clinical manifestations ranging from stable angina pectoris to sudden death. Diagnostic tests to see the cause of CHD are obtained from invasive coronary angiography performed at cardiac catheterization. Invasive coronary angiography is used to determine the presence of coronary stenosis lesions (coronary arteries) in the heart and to know the extent of

stenosis which is the cause of CHD. The current invasive coronary angiography is a routine examination for the diagnosis of coronary artery disease (CAD), which is significant if stenosis is >50% in lumen diameter [11].

The development of atherosclerosis occurs gradually, and the process is complex, which is caused by interactions between risk factors, endothelial cell dysfunction, lipid oxidation, and lipid accumulation [12], [13]. One of the risk factors for CHD in type 2 DM is dyslipidemia. Diabetic dyslipidemia has characteristics of hypertriglyceridemia (HTG), increased very low density lipoprotein (VLDL), and small dense LDL [14], [15]. The role of triglycerides (TGs) as a risk factor for CHD has long been studied but until now it has not been determined whether TG increases are independent risk factors of CHD. Studies showed that an increase in the metabolism of triglyceride-rich lipoprotein (TGRLP) was important in the pathogenesis of atherosclerosis and could predict the presence of CHD. There is evidence that TGRLP has a pathologic role in possible atherothrombosis due to the endothelial damage [16]. High triglyceride levels in DM are caused by hyperglycemia as a manifestation of impaired carbohydrate metabolism, which, if it is not addressed immediately, will be followed by disorders of fat metabolism or dyslipidemia [17]. Diabetic dyslipidemia is a condition which is characterized by high levels of TG and cholesterol caused by diabetes, especially uncontrolled diabetes [14].

It has been widely known that type 2 DM has a relationship with the degree of hyperglycemia, an increased risk of mortality from microvascular complications, myocardial infarction, and macrovascular complications based on the previous studies [7], [18]. The process of coronary stenosis is an long process, occurring from a young age and developing for a long life. According to Diabetes Control and Complications Trial, variations in glucose profiles for several days cannot predict diabetes complications [18]. Glycosylated hemoglobin levels (HbA1c) can be predictors of CHD in DM patients and it is reported that good glucose control is associated with reduced risk of CHD. Reported increases in HbA1c levels are associated with an increased risk of CHD independently [19].

The study of Lee *et al.* concluded that patients with type 2 DM with high HbA1c variability could be an independent predictor of CAD with an average HbA1c level of more than 7% [18]. The study of Ertem *et al.* stated that there was no significant relationship between severity of CAD with HbA1c in patients with non-diabetic ACS [20]. The study of Yan *et al.*, assessing the relationship of lipid and HbA1c ratio in type 2 DM, concluded that there was no relationship between HbA1c and TG or HDL [21]. Petitti *et al.* in their study showed that there was a relationship between high HbA1c level and an increase in TG [22].

Existing study showed that HbA1c had a role in DM patients with CHD as well as HTG also played a role in the process of forming atherosclerosis in blockage of coronary arteries. This study analyzed the parameters of HbA1c and triglyceride levels with the stenosis severity of coronary artery that occurs in type 2 DM patients with CHD that has not been analyzed so far.

Methods

This study was an observational analytic study with cross-sectional approach conducted at Dr. Kariadi Central Hospital, Semarang, Indonesia, during September 2013. It had been approved by the Health Research Ethics committee of Faculty of Medicine, Diponegoro University/Dr. Kariadi Central Hospital, Semarang, number 415/EC/FK/RSDK/2013. All study subjects were requested to give written informed consent and patient's identity was confidential.

The subjects were 40 patients with type 2 DM with complications of CHD who received cardiac catheterization. CHD was diagnosed by a cardiologist based on a physical examination, an electrocardiogram, heart laboratory test, and a treadmill test.

The inclusion criteria were those over 20 years old, underwent cardiac catheterization, and willing to take part in the study, while the exclusion criteria were having hemoglobin abnormalities and taking regular dyslipidemia drugs.

The respondent's identity, smoking history, and physical examination were collected, and the respondents were taken for middle cubital venous blood as much as 3 cc of ethylenediaminetetraacetic acid (EDTA) blood and 3 cc in a plain tube. EDTA blood was immediately homogenized and HbA1c levels were then examined, while plain tubes were left for 30 min to get the serum and were then centrifuged with the speed of 3000 rpm for 5 min, then the serum was examined for the triglyceride levels in the laboratory of Dr. Kariadi Central Hospital. Plasma HbA1c levels, assessed by the turbidimetric immunoassay method (equipment, manufacturer, and country), were expressed as a percentage. Serum triglyceride levels were assessed by enzymatic method (equipment, manufacturer, and country), expressed in mg/dL. Subjects underwent cardiac catheterization to see the degree of stenosis of the coronary arteries by the cardiologist which was expressed in percentages then classified as stenosis if the heart block was more than 50%, non-significant stenosis if the heart block was <50%, and no stenosis if there was 0% blockage.

The collected data were in the form of interviews, physical examination, and laboratory examination. The collected data were edited, coded, and incorporated into computer programs. Bivariate statistical analysis was done using the Pearson relationship test. The significance level was $p < 0.05$.

Results

The average age of the subjects was 56.05 years with a standard deviation of 9.2 years. The sex of the study subjects was mostly male. The mean body mass index (BMI) value with the standard deviation of the study subjects was 24.88 ± 3.446 kg/m^2. Based on the BMI value for Asians, most of the study subjects were classified as obese. The characteristics of subject are present in Table 1.

Table 1: The characteristics of study subjects

Characteristics	n (%)
Sex	
Male	29 (72.5)
Female	11 (27.5)
Age (years), mean ± SD	56.05 ± 9.21
BW (kg), mean ± SD	65.97 ± 9.94
BH (cm), mean ± SD	162.77 ± 6.49
BMI (kg/m^2), mean ± SD	24.88 ± 3.44
Underweight	1 (2.5)
Normal	9 (22.5)
Pre-obese	14 (35.0)
Obese	16 (40.0)

SD: Standard deviation, BW: Body weight, BH: Body height, BMI: Body mass index.

The overall HbA1c levels of respondents in this study increased above normal. Respondents with a significant degree of stenosis had the highest HbA1c level compared with neither non-significant stenosis nor stenosis. The same situation occurred in triglyceride parameters where respondents with significant stenosis had the highest triglyceride levels (Table 2).

Table 2: The mean glycosylated hemoglobin and triglyceride levels based on stenosis severity of coronary artery in patients with type 2 diabetes mellitus and coronary heart disease

Stenosis severity (%)	Mean ± SD	
	HbA1c level (%)	TG level (mg/dl)
No stenosis	6.31 ± 1.303	128.00 ± 55.07
Non-significant stenosis	6.90 ± 0.458	126.00 ± 49.93
Stenosis	8.89 ± 1.498	220.97 ± 92.24

HbA1c: Glycosylated hemoglobin, DM: Diabetes mellitus, CHD: Coronary heart disease, TG: Triglyceride, SD: Standard deviation.

The analysis result of the relationship test (Tables 3 and 4) showed that both HbA1c and triglyceride levels were significantly associated with the degree of stenosis in patients with type two DM with complications of CHD.

Discussion

The results of the relationship test between HbA1c and coronary stenosis showed a strong positive relationship. This was in accordance with the study of Saleem *et al.* and Su *et al.* who concluded that there was a positive relationship between coronary stenosis and HbA1c [9], [23]. A study by Rivera *et al.* also concluded that the increased HbA1c level was related to the presence of coronary stenosis but in the non-DM population [24]. The role of glucose variability in the pathogenesis of atherosclerosis remains unclear.

Table 3: The relationship between glycosylated hemoglobin and triglyceride levels and stenosis severity of coronary artery disease in patients with type 2 diabetes mellitus and coronary heart disease

Parameter	Stenosis severity	
	r	p
HbA1c level (%)	0.665	< 0.001
TG level (mg/dl)	0.501	0.001

HbA1c: Glycosylated hemoglobin, TG: Triglyceride.

Hyperglycemia is thought to induce oxidative stress and interfere with endothelial cell function by overproduction of reactive oxygen species (ROS), which results in coronary stenosis through several molecular mechanisms. *In vitro* studies showed that blood glucose fluctuations could activate nuclear factor-κB and protein kinase C (PKC) pathways, which result in excessive expression of adhesion molecules and formation of advanced glycation end-products [25], [26]. Several studies have shown that apoptosis in endothelial cells intermittently exposed to high blood glucose may be related to overproduction of ROS, through PKC-dependent activation of nicotinamide adenine dinucleotide phosphate oxidase and apoptosis through activation of the caspase cascade resulting in cell death due to its binding with the ligand, which will result in coronary stenosis through endothelial dysfunction [26], [27], [28].

Table 4: The relationship between glycosylated hemoglobin level and triglyceride level in patients with type 2 diabetes mellitus and coronary heart disease

Parameter	TG level (mg/dl)	
	r	p
HbA1c level (%)	0.466	0.002

HbA1c: Glycosylated hemoglobin, TG: Triglyceride.

The result of the relationship test between TG and coronary stenosis showed a moderate positive relationship. Some previous studies have not directly linked TG with coronary stenosis, but several recent studies have suggested that the increase in TG is independently related to the incidence of CHD. The Copenhagen male study at 8 years of follow-up reported that an increase in fasting TG was a strong independent risk factor for CHD [29], [30].

Increased plasma TG and TGRLP are risk factors for atherothrombosis. Some TGRLP can cause endothelial dysfunction that can potentially trigger atherothrombosis, including chylomicron from normal individuals as well as individuals with hyperlipoproteinemia and VLDL from individuals with elevated TG/HTG (HTG-VLDL). Endothelial cells bind and enter TGRLP from individuals with HTG with the effect of deterioration including a decrease in fibrinolytic capacity. HTG-VLDL inhibits plasminogen binding in endothelial cells and modulates PAI-1 release, thereby inhibiting plasmin formation [31]. Reaven suggested the existence of an insulin resistance syndrome wherein cardiovascular risk occurs more frequently. Insulin, pro-insulin like molecules, glucose, and VLDL TG directly stimulate transcription and secretion of PAI-1 in endothelial cells [32], [33], [34], [35].

The results of the Spearman test for the relationship between HbA1c and TG were found to be a moderate positive relationship. This was different from the results of the study of Yan *et al.* who concluded that there was no correlation between HbA1c and TG [21]. However, according to the study of Petitti *et al.*, there was a significant relationship between elevated triglyceride levels and increased HbA1c levels in DM population [22]. High triglyceride levels in type 2 DM caused by hyperglycemia which was a manifestation of impaired carbohydrate metabolism. Various metabolic disorders found in T2DM or in insulin resistance syndromes such as hyperglycemia which lead to atherosclerosis and dyslipidemia. Insulin resistance associated with type 2 diabetes has several effects on fat metabolism. In a state of insulin resistance, the sensitive hormone lipase in the adipose tissue will become active so that lipolysis of TG in the adipose tissue will increase, and this condition will produce excessive free fatty acids. Some free fatty acids will be taken to the liver as a raw material for forming TG. The state of insulin resistance, in the liver, will produce VLDL which is rich in TG [17].

This study did not analyze the study variables based on the characteristics of the respondents, especially the BMI. In addition, this study did not exclude comorbid disease from DM, namely, hypertension, and did not take into account the condition of patients who had undergone therapy for the complaints of heart disease or therapy for abnormal metabolic fat.

Conclusion

HbA1c and triglyceride levels increased in line with the increasing stenosis severity of CHD in patients with type 2 DM. These two parameters can be used as markers to evaluate patients with DM who can experience significant blockages and develop toward more severe heart disease.

Acknowledgments

We thank to laboratory technician of Dr. Kariadi Public Hospital for running the laboratory examination. We also thank to cardiologist of Dr. Kariadi Public Hospital for determining the stenosis degree of subject.

References

1. Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of Type 2 Diabetes – Global Burden of Disease and Forecasted Trends. J Epidemiol Glob Health. 2020; 10(1): 107–111.
2. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2012;35 Suppl 1:S64-71. https://doi.org/10.2337/dc12-s064
   PMid:22187472
3. Association of Indonesian Endocrinologist (PERKENI). Diabetes Mellitus, Guideline of Management and Prevention of Type 2 DM in Indonesia. Jakarta: Association of Indonesian Endocrinologist (PERKENI); 2006.
4. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract. 2010;87(1):4-14. https://doi.org/10.1016/j.diabres.2009.10.007
   PMid:19896746
5. Sylvia PA. Glucose Metabolism and Diabetes Melitus, Pathophysiology. 6th ed., Vol. 2. Jakarta: EGC; 2006. p. 1260-65.
6. Stephen MJ, Ganong WF. Disorders of the Endocrine Pancreas, Pathophysiology of Disease. 5th ed. USA: Lange; 2006. p. 521-2.
7. Adam John MF. Reducing cardiovascular risk. In: Type 2 Diabetes from the Lipidologist View, Textbook of Diabetes and Related Disorders. Makassar: Perkeni; 2004. p. 1-2.
8. Einarson TR, Annabel, Ludwig C, Panton UH. Prevalence of Cardiovascular Disease in Type 2 Diabetes: A Systematic Literature Review of Scientific Evidence from Across The World in 2007–2017. Cardiovasc Diabetol. 2018; 17: 83.
9. Su G, Mi S, Tao H, Li Z, Yang H, Zheng H, *et al.* Association of glycemic variability and the presence and severity of coronary artery disease in patients with type 2 diabetes. Cardiovasc Diabetol. 2011;10:19. https://doi.org/10.1186/1475-2840-10-19
   PMid:21349201
10. Raghavan S, Vassy JL, Lam HY, Song RJ, Gagnon DR, Cho K, et al. Diabetes Mellitus–Related All-Cause and Cardiovascular Mortality in a National Cohort of Adults. J Am. Heart Assoc. 2019;8:e011295.
11. Lily IR. Coronary heart disease. In: Cardiovascular Disease. Jakarta; Publishing Center of Medical Faculty of University of Indonesia; 2012. p. 119-223.
12. Libby P, Theroux P. Pathophysiology of coronary artery disease. Circulation. 2005;111(25):3481-8. https://doi.org/10.1161/CIRCULATIONAHA.105.537878
   PMId:15983262
13. Insull W Jr. The pathology of atherosclerosis: Plaque development and plaque responses to medical treatment. Am J Med. 2009;122 Suppl 1:S3-14. https://doi.org/10.1016/j.amjmed.2008.10.013
   PMid:19110086
14. Taskinen MR. Diabetic dyslipidemia: From basic research to clinical practice. Diabetologia. 2003;46(6):733-49. https://doi.org/10.1007/s00125-003-1111-y
   PMid:12774165
15. Ginsberg HN. Insulin resistance and cardiovascular disease. J Clin Invest. 2000;106:453-8. https://doi.org/10.1172/JCI10762
   PMid:10953019
16. Sungkar MA. Triglycerides: A independent risk factor of coronary heart disease. In: Sutikno T, Sodiqur R, editors. Atherosclerosis. Semarang: Diponegoro University; 2003. p. 37-42.
17. Parhofer KG. Interaction between Glucose and Lipid Metabolism: More than Diabetic Dyslipidemia. Diabetes Metab

J 2015;39:353-362.

18. Lee EJ, Kim YJ, Kim TN, Kim TI, Lee WK, Kim M, *et al.* A1c variability can predict coronary artery disease in patients with type 2 diabetes with mean A1c levels greater than 7. Endocrinol Metab. 2013;28(2):125-32. https://doi.org/10.3803/enm.2013.28.4.348

    PMid:24396666

19. Habib SS. Serum lipoprotein(a) and high sensitivity C reactive protein levels in Saudi patients with type 2 diabetes mellitus and their relationship with glycemic control. Turk J Med Sci 2013;43:333-8.

20. Ertem AG, Bagbanci H, Kilic H, Yeter E, Akdemir R. Relationship between HbA1c levels and coronary artery severity in nondiabetic acute coronary syndrome patients. Turk Kardiyol Dern Ars. 2013;41(5):389-95. https://doi.org/10.1016/s0167-5273(13)70394-2

    PMid:23917003

21. Yan Z, Liu Y, Huang H. Association of glycosylated hemoglobin level with lipid ratio and individual lipids in type 2 diabetic patients. Asian Pac J Trop Med. 2012;5(6):469-71. https://doi.org/10.1016/s1995-7645(12)60080-7

    PMid:22575980

22. Petitti DB, Imperatore G, Palla SL, Daniel SR, Dolan LM, Kershnar AK, *et al*. Serum lipids and glucose control. Arch Pediart Adolesc Med. 2007;161:159-65. https://doi.org/10.1001/archpedi.161.2.159

    PMid:17283301

23. Saleem T, Mohammad KH, Abdel-Fattah MM, Abbasi AH. Association of glycosylated haemoglobin level and diabetes mellitus duration with the severity of coronary artery disease. Diabetes Vasc Dis Res. 2008;5(3):184-9. https://doi.org/10.3132/dvdr.2008.030

    PMid:18777491

24. Rivera JJ, Choi EK, Yoon YE, Chun EJ, Choi S, Nasir K, *et al.* Association between increasing levels of hemoglobin A1c and coronary atherosclerosis in asymptomatic individuals without diabetes mellitus. Coron Artery Dis. 2010;21(3):157-63. https://doi.org/10.1097/mca.0b013e328337ff9b

    PMid:20308881

25. Huo ZQ, Li HL, Gao L, Pan L, Zhao JJ, Li GW. Involvement of chronic stresses in rat islet and INS-1 cell glucotoxicity induced by intermittent high glucose. Mol Cell Endrocinol. 2008;291(1-2):71-8. https://doi.org/10.1016/j.mce.2008.03.004

    PMid:18485584

26. Quagliaro L, Piconi L, Assaloni R, Martinelli L, Motz E, Ceriello A. Intermittent high glucose enhances apoptosis related to oxidative stress in human umbilical vein endothelial cells: the role of protein kinase C and NAD(P)H-oxidase activation. Diabetes. 2003;52(11):2795-804. https://doi.org/10.2337/diabetes.52.11.2795

    PMid:14578299

27. Ceriello A, Esposito K, Piconi L, Ihnat MA, Thorpe JE, Testa R, *et al.* Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. Diabetes. 2008;57(5):1349-54. https://doi.org/10.2337/db08-0063

    PMid:18299315

28. Kim MK, Jung HS, Yoon CS, Ko JH, Jun HJ, Kim TK, *et al.* The effect of glucose fluctuation on apoptosis and function of INS-1 pancreatic beta cells. Korean diabetes J. 2010;34(1):47-54. https://doi.org/10.4093/kdj.2010.34.1.47

    PMid:20532020

29. Monnier L, Mas E, Ginet C, Michel F, Villon L, Cristol JP, *et al.* Activation of oxidative stress by acute glucose fluctuations compared with sustained chronic hyperglycemia in patients with type 2 diabetes. JAMA. 2006;295(14):1681-7. https://doi.org/10.1001/jama.295.14.1681

    PMid:16609090

30. Ginsberg HN. Hypertriglyceridemia: New insights and new approaches to pharmacologic therapy. Am J Cardiol. 2001;87(10):1174-80. https://doi.org/10.1016/s0002-9149(01)01489-8

    PMid:11356393

31. Eckel RH. The metabolic syndrome. In: Jameson JL, editor. Harrison's Endocrinology 2nd ed. Lancet: The McGraw-Hill Companies; 2010.

32. Sena CM , Pereira AM, Seiça R. Endothelial dysfunction - A Major Mediator Of Diabetic Vascular Disease. Biochimica et Biophysica Acta. 2013; 1832: 2216–2231.

33. Cullen P. Evidence that tryglycerides are an independent coronary heart disease risk factor. Am J Cardiol. 2000;86(9):943-9. https://doi.org/10.1016/s0002-9149(00)01127-9

    PMid:11053704

34. Gianturco SH, Bradley A. Pathophysiology of tryglyceride – Rich lipoprotein in atherothrombosis: Cellular aspect. Clin Cardiol. 1999;22 Suppl 6:II7-14. https://doi.org/10.1002/clc.4960221403

    PMid:10376191

35. Kohler HP, Grand PJ. Plasminogen-activator inhibitor type 1 and coronary artery disease. N Engl J Med. 2000;342(24):1792-801. https://doi.org/10.1056/nejm200006153422406

    PMid:10853003