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ORIGINAL

Differences in Gamma-Glutamyl Transferase and High-Sensitivity C-Reactive Protein Levels Between Type 2 Diabetes Mellitus with and without Vascular Complications

Diferencias en los niveles de transferasa gamma glutamilo y proteína c reactiva de alta sensibilidad entre diabetes mellitus tipo 2 con y sin complicaciones vasculares

Nahlida Rahmah[1], Puspa Wardhani[2], Yessy Puspitasari[2], Soebagijo Adi Soelistijo[3]

[1]Master of Basic Medical Sciences Student, Faculty of Medicine, Airlangga University. Surabaya, Indonesia.
[2]Department of Clinical Pathology, Faculty of Medicine, Airlangga University. Surabaya, Indonesia.
[3]Department of Internal Medicine, Faculty of Medicine, Airlangga University. Surabaya, Indonesia.

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Corresponding author: Puspa Wardhani

ABSTRACT

Introduction: type 2 diabetes mellitus (T2DM) is a metabolic disease that causes microvascular and macrovascular complications and increases mortality. Oxidative stress and inflammation play a role in the pathogenesis of (T2DM). Gamma-glutamyl transferase (GGT) and high-sensitivity C-Reactive Protein (hs-CRP) levels as oxidative stress and inflammation markers help detect the high risk of developing T2DM complications.
Objectives: analyzing the differences in GGT and hs-CRP levels between T2DM with and without vascular complications predicts the sensitivity and specificity for the detection of T2DM vascular complications.
Method: the cross-sectional study involved 19 patients with vascular complications of T2DM and 19 patients with T2DM without complications. Using patient serum samples, GGT and hs-CRP levels were measured using the TMS24i device.
Results: the T2DM vascular complications group increased GGT and hs-CRP values. GGT and hs-CRP levels between T2DM with and without vascular complications were significant. The macrovascular (CHD) group had a higher GGT value than the microvascular group, there was a substantial difference in GGT between the two research subjects. On the other hand, there was no significant difference in hs-CRP. Logistic regression analysis found that the duration of T2DM and GGT influenced the risk of T2DM vascular complications. Analysis (ROC) showed GGT had (AUC=0,691) and hs-CRP (AUC=0,706).
Conclusions: GGT plays a role in risk detection (CHD) compared to microvasculature. Significant differences in GGT and hs-CRP between T2DM with and without vascular complications and vascular complications of T2DM increase the values of GGT and hs-CRP.

Keywords: Diabetes Mellitus Type 2; Vascular Complications; Gamma-Glutamyl Transferase; High-Sensitivity C-Reactive Protein.

RESUMEN

Introducción: la diabetes mellitus tipo 2 (DM2) es una enfermedad metabólica que causa complicaciones microvasculares y macrovasculares y aumenta la mortalidad. El estrés oxidativo y la inflamación desempeñan un papel en la patogénesis de la DM2. Los niveles de gamma-glutamil transferasa (GGT) y proteína C reactiva de alta sensibilidad (hs-CRP) como marcadores de estrés oxidativo e inflamación ayudan a detectar el alto riesgo de desarrollar complicaciones de DM2.

Objetivos: analizar las diferencias en los niveles de GGT y PCR-us entre DM2 con y sin complicaciones vasculares predice la sensibilidad y especificidad para la detección de complicaciones vasculares de DM2.
Método: el estudio transversal involucró a 19 pacientes con complicaciones vasculares de DM2 y 19 pacientes con DM2 sin complicaciones. Utilizando muestras de suero de pacientes, se midieron los niveles de GGT y hs-CRP utilizando el dispositivo TMS24i.
Resultados: el grupo de complicaciones vasculares de DM2 aumentó los valores de GGT y PCR-as. Los niveles de GGT y PCR-us entre DM2 con y sin complicaciones vasculares fueron significativos. El grupo macrovascular (CHD) tuvo un valor de GGT más alto que el grupo microvascular; hubo una diferencia sustancial en GGT entre los dos sujetos de investigación. Por otro lado, no hubo diferencias significativas en la PCR-us. El análisis de regresión logística encontró que la duración de la DM2 y la GGT influyeron en el riesgo de complicaciones vasculares de la DM2. El análisis (ROC) mostró que tenía GGT (AUC=0,691) y hs-CRP (AUC=0,706).
Conclusiones: la GGT juega un papel en la detección de riesgo (CHD) en comparación con la microvasculatura. Las diferencias significativas en GGT y hs-CRP entre DM2 con y sin complicaciones vasculares y las complicaciones vasculares de T2DM aumentan los valores de GGT y hs-CRP.

Palabras clave: Diabetes Mellitus Tipo 2; Complicaciones Vasculares; Gamma-Glutamil Transferasa; Proteína C Reactiva de Alta Sensibilidad.

INTRODUCTION

The increase in hyperglycemia or blood sugar is a characteristic of metabolic diseases caused by type 2 diabetes, insulin secretion, insulin, or both abnormalities.[1] According to World Health Organization (WHO) data, type 2 diabetes mellitus (T2DM) is a direct cause of 1,5 million deaths in 2019 and is associated with several microvascular and macrovascular issues that might contribute to rising morbidity and mortality. Microvascular complications (nephropathy 7,7 %, neuropathy 17,6 %, retinopathy 2,7 %) and macrovascular consequences (coronary artery disease 5,4 %, cerebrovascular 5,4 %, peripheral arteries 0,5 %) were reported in Indonesia by the International Diabetes Federation (IDF, 2021). Every patient with T2DM should have their risk of developing complications from the disease evaluated, according to the American Diabetes Association.[2]

The liver is important in regulating glucose metabolism, so liver function indicators are often used as markers of developing T2DM.[3] Gamma-glutamyl transferase (GGT) is a glycoprotein that plays a role in the catabolism of extracellular glutathione (GSH), mainly produced in the liver, with an important role in response to cellular stress conditions. Serum GGT levels are often used as markers for oxidative stress and liver dysfunction, which are related to glucose metabolism and the pathogenesis of T2DM. GGT levels measured early in T2DM patients can help detect individuals at high risk for diabetes complications.[4] Further research shows that GGT has the potential to be used to predict diabetes complications.[5]

The mechanism of blood vessel damage due to hyperglycemia occurs through 4 pathways, namely, the main aldose reductase pathway, the second Advanced Glycation End-product (AGE) pathway, the third Protein Kinase C (PKC) pathway, and the fourth hexosamine pathway which is accompanied by increased oxidative stress.[6] Hyperglycemia accompanied by oxidative stress can activate NF-kß which causes the release of cytokines such as (IL-6), (TNF-α) in hepatocytes which can be detected with hs-CRP. The hs-CRP test is very sensitive and indicates an increase in sensitive inflammatory activity. CRP is a protein produced by the liver during the acute phase in reaction to inflammation.[5] The hs-CRP test is very sensitive and indicates a sensitive increase in inflammatory activity.[7] Diabetics have higher hs-CRP levels and show microvascular and macrovascular changes.[8] The incidence of T2DM is currently increasing, and the lack of efficient predictors still limits the early management of high-risk patients, so further research on GGT and hs-CRP is still needed.[9]

Increased GGT and hs-CRP, based on several studies, occur in patients with DM. Very little research has been conducted in Indonesia. The research aims to predict the sensitivity and specificity of GGT and hs-CRP levels as a high-risk detection of vascular problems of T2DM by comparing the levels of these markers across individuals with and without vascular difficulties.

METHOD

Research design, sampling, and data collection

The research method used analytical observational (cross-sectional) which was carried out at the Internal Medicine Clinic at Airlangga University Hospital, Surabaya, Indonesia. This study was conducted on 38 patients, including 19 patients with vascular complications of T2DM and 19 patients with T2DM without complications who had been diagnosed, collected from July to September 2024.

Inclusion criteria, Patients who have been diagnosed with DMT2, Research subjects aged ≥ 18 – 60 years, The patient is in good condition, cooperative, and willing to participate in the research by signing an informed consent

to participate in the research. Exclusion Criteria, Research subjects suffering from autoimmune diseases such as SLE, rheumatoid arthritis, etc., Research subjects with chronic infections such as tuberculosis, hepatitis, etc., Research subjects with impaired liver function, Research subjects who consumed anti-inflammatory drugs such as corticosteroids, NSAIDs, etc. The Ethics Committee of Airlangga University Hospital Surabaya has approved this research with the number 100/KEP/2024. Written consent was obtained from all subjects participating in the study before specimen collection was taken.

GTT and hs-CRP analysis

The hs-CRP and GGT test Each subject's venous blood was drawn and placed in a standard tube. Centrifugation was used to separate the serum for 15 minutes at 3000–4000 rpm. GGT levels were examined using the kinetic photometric method and hs-CRP using the turbidimetric method. GGT and hs-CRP tests used the TMS24i instrument with Gamma-GT FS reagent (Szasz mod) for the GGT test and Nanopia 1&2 CRP reagent for the hs-CRP test. This instrument automatically calculates the GGT concentration in U/L and the hs-CRP concentration in mg/L. GGT and hs-CRP levels were examined in the Clinical Pathology Laboratory of Airlangga University Hospital, Surabaya.

Statistical analysis

SPSS software, namely SPSS 22. Continuous data are presented using mean values and standard deviations (SD), while frequencies and percentages are used to describe variable categories. The Mann-Whitney test was used to assess the differences in GGT and hs-CRP between two groups, namely T2DM with vascular complications and T2DM without complications, and to assess the differences in GGT and hs-CRP between macrovascular (CHD) and microvascular complications. Logistic regression analysis was used to identify contributing factors that influence the occurrence of vascular complications in T2DM patients. Receiver Operator Characteristics (ROC) analysis was used to measure the Area Under Curve (AUC), sensitivity, and specificity of the 2 tests, namely GGT and hs-CRP. A p-value <0,05 was considered statistically significant.

RESULTS

Demographic characteristics

A total of 38 subjects participated, 19 subjects with T2DM with vascular complications and 19 subjects with T2DM without vascular complications. Variations in individual characteristics showed that both study groups had comparable age, blood pressure (systolic and diastolic), fasting blood glucose (FBS), and postprandial blood glucose (PPBG) and did not differ significantly. For categorical variables and according to Chi-Square, women had a greater majority than men. When compared with the T2DM group without complications, patients with T2DM for > 5 years were more in the T2DM group with complications. A history of not smoking had a higher proportion compared to a history of smoking in all study subjects. The variables of gender and history of hypertension had a higher prevalence (p < 0,05), while the duration of T2DM and smoking status did not differ significantly across study groups (table 1).

Table 1. Demographic characteristics of research subjects

Characteristics of research subjects	Total	DMT2 with complications	DMT2 without complications	p-Value
N	38	19	19	
Age (Years)d	53,50 (33-60)	54 (36 - 60)	53 (33 - 60)	0,814a
Gender, n (%)				0,097c
Man	15 (39,5 %)	10 (52,6 %)	5 (26,3 %)	
Woman	23 (60,5 %)	9 (47,4 %)	14 (73,7 %)	
Duration of DMT2				0,049c*
< 5 Years	22 (57,9 %)	8 (42,1 %)	14 (73,7 %)	
> 5 Years	16 (42,1 %)	11 (57,9 %)	5 (26,3 %)	
Smoking, n (%)				1,000c
Smoke	5 (13,2 %)	3 (15,8 %)	2 (10,5 %)	
Do not smoke	33 (86,8 %)	16 (84,2 %)	17 (89,5 %)	
History of Hypertension, n (%)				0,044c*
Hypertension	24 (63,2 %)	15 (78,9 %)	9 (47,4 %)	
Normal	14 (36,8 %)	4 (21,1 %)	10 (52,6 %)	

Systolic (mmHg)e	149,32±15,07	152,16±11,49	146,47±17,81	0,252b
Diastole (mmHg)	85,03±10,36	87,89±9,50	82,16±10,63	0,088b
GDP (mg/dl)d	180,08±62,33	195,47±73,08	164,68±46,32	0,131b
GDPP (mg/dl)e	261,53±98,18	286,79±111,37	236,26±77,87	0,114b

[a]Mann Whitney, bIndependent T-test, cChi-Square, *significant p < 0,05, dMedian (Min-Max), eMean±SD. GDP: fasting blood glucose, postprandial blood glucose (PPG)

Factors influencing type 2 diabetes mellitus with vascular complications

The analysis was continued with a logistic regression test to determine the factors that influence the occurrence of vascular complications in patients with T2DM. The variables tested were variables that had a p-value <0,25, namely gender, duration of T2DM, history of hypertension, diastole, GDP, GDPP, GGT, and hs-CRP. The results of the logistic regression analysis of the variables of duration of T2DM and GGT had a significance value (P <0,05) which means that there is an effect of duration of T2DM and GGT on the risk of vascular complications in patients with T2DM (table 2). On the other hand, other parameters (gender, duration of T2DM, history of hypertension, diastole, GDP, GDPP, hs-CRP) were excluded because the results were insignificant or had no effect.

Table 2. Regression test analysis of factors influencing DMT2 with vascular complications

Independent variables	Standardized Coefficients	*P-value*	95 % Confidence Interval for B	
	Beta		Lower Bound	Upper Bound
Duration of DMT2	1,895	0,022*	1,307	33,852
GGT	0,039	0,020*	1,006	1,075

*Significant (p value <0,05) according to logistic regression analysis. GGT: Gamma-glutamyl transferase.

Differences between GGT and hs-CRP in T2DM patients with vascular complications and T2DM without complications

The measurement results showed that in both examinations, a p-value of <0,05 was obtained, which means that there was a difference in the GGT and hs-CRP examination values in DMT2 patients with and without vascular complications. The results of the GGT and hs-CRP examination values in DMT2 subjects with complications had significantly higher values compared to the DMT2 group without complications (table 3).

Table 3. Differences in GGT and hs-CRP values in type 2 diabetes mellitus patients with and without vascular complications

Group	n	GGT Value (U/L)	*p-value*	hs-CRP value (mg/L)	*p-value*
DMT2 with complications	19	42 (16 – 221)b	0,037a*	3,97 (1,14 – 67,65)b	0,030a*
DMT2 without complications	19	24 (5 – 92)b		1,83 (0,43 – 10,59)b	

[a]Mann Whitney, bMedian (Min-Max), *significant p < 0,05. GGT: Gamma-glutamyl transferase, hs-CRP: high-sensitivity C-Reactive Protein.

Differences between GGT and hs-CRP in patients with T2DM macrovascular (CHD) and microvascular (neuropathy, nephropathy, retinopathy) complications

The measurement results showed a significant difference in GGT between macrovascular complications and microvascular with (p = 0,044), and higher GGT values were obtained in macrovascular complications (CHD) compared to microvascular complications. While in hs-CRP statistical results showed no significant difference between macrovascular complications and microvascular with (p = 0,576) (table 4).

Table 4. Differences in GGT and hs-CRP values in type 2 diabetes mellitus patients with macrovascular (CHD) and microvascular (neuropathy, nephropathy, retinopathy) complications

Inspection	Macrovascular (CHD) (n=3)	Microvascular (Neuropathy, nephropathy, retinopathy) (n=16)	*p-value*
GGT (U/L)	120 (66 – 127)b	33 (16 – 221)b	0,044a*
Hs-CRP (mg/L)	1,92 (1,36 – 22,63)b	3,97 (1,14 – 67,65)b	0,576a

[a]*Mann Whitney*, bMedian (Min-Max), *significant p < 0,05. GGT: Gamma-glutamyl transferase, hs-CRP: high-sensitivity C-Reactive Protein.

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Receiver Operator Characteristics curve analysis of GGT and hs-CRP

According to the ROC curve analysis, the AUC for hs-CRP was the highest (AUC = 0,706), while GGT had the lowest (AUC = 0,691) as shown in table 5.

Table 5. AUC of GGT and hs-CRP parameters

Parameter	Area (AUC)	Std. Error	P value	Asymptotic 95 % Confidence Interval	
				Lower Bound	Upper Bound
GGT (U/L)	0,691	0,086	0,044	0,523	0,859
hs-CRP (mg/L)	0,706	0,084	0,030	0,542	0,871

GGT: Gamma-glutamyl transferase, hs-CRP: high-sensitivity C-Reactive Protein.

Similarly, GGT had sensitivity (0,632) and specificity (0,684), while hs-CRP had sensitivity (0,632) and specificity (0,632) (table 6).

Table 6. Analysis of the ROC curve: sensitivity and specificity of GGT and hs-CRP

Parameter	Positive if Less than or Equal to	Sensitivity	Specificity	1 - Specificity
GGT (U/L)	29,00	0,632	0,684	0,316
hs-CRP (mg/L)	2,0800	0,632	0,632	0,368

GGT: Gamma-glutamyl transferase, hs-CRP: high-sensitivity C-Reactive Protein.

DISCUSSION

Demographic Characteristics of Research Subjects

Type 2 diabetes mellitus (T2DM) is a metabolic disease characterized by high blood sugar levels (hyperglycemia) due to abnormalities in insulin secretion, insulin function, or both, which can cause microvascular and macrovascular complications. Most T2DM subjects with and without complications in the study were >53 years old. The prevalence of T2DM with complications is not only suffered by the elderly (>60 years), but those of productive age are at risk of experiencing it.[10] Research supports that as adults age, they are at increased risk of developing T2DM due to the combined effects of increased insulin resistance and impaired pancreatic function. Aging can reduce insulin sensitivity which can affect blood glucose levels.

This study found that research subjects who suffered from T2DM > 5 years were more dominant in the T2DM category with complications. This study found that a history of hypertension had a higher value in subjects with T2DM with complications.[11] 50 % to 75 % of patients with T2DM also suffer from hypertension, and a combination of both can lead to The development of microvascular and macrovascular complications is one of the main causes of morbidity and mortality. This study also found that the mean fasting glucose and postprandial glucose values were equally high in both categories, but in patients with T2DM with complications, they were higher than those without complications.[12] Research supports what causes T2DM to cause hypertension because blood vessels lose their ability to stretch, the amount of fluid in the body increases, insulin resistance, sugar accumulates in the body's cells and becomes fat. The combination of T2DM and hypertension can increase the risk of heart attack, stroke, kidney disease, and retinopathy.

Factors influencing T2DM with vascular complications

Previous research shows that the duration of T2DM and GGT levels has a significant impact on the possibility of blood vessel problems in T2DM patients, Due to the effects of chronic hyperglycemia, which damages blood vessels through oxidative stress and endothelial dysfunction, the duration of T2DM was substantially linked to the risk of vascular problems. Research Supports that complications occur over a longer period after the patient is diagnosed with type T2DM which is triggered by chronic hyperglycemia poor glycemic control and dyslipidemia. GGT levels are significantly associated with the development of T2DM, The process of inflammation and oxidative stress can explain this. Damage to DNA, proteins, and lipids from oxidative stress can set off cascades that impair the shape and functionality of pancreatic ß cells. GGT contributes to the antioxidant glutathione's extracellular breakdown, which raises the generation of ROS. GGT and oxidative stress are intimately associated because elevated serum GGT levels are necessary to preserve glutathione as an intracellular antioxidant.[13]

Duration of T2DM and GGT levels are significant factors in increasing the risk of vascular complications in patients with T2DM. These results are important for monitoring patients with T2DM who may require earlier

or more intensive intervention, including tighter glycemic control to prevent the development of vascular complications.

Differences in GGT in T2DM patients with vascular complications and T2DM without complications

The results of the examination of GGT and hs-CRP values in T2DM subjects with complications had significantly higher values in contrast to the group with T2DM who did not experience any problems, These results are consistent with the results obtained in the study. Stated that GGT levels increased in subjects with T2DM with complications compared to T2DM without complications. Higher GGT levels indicate greater oxidative stress, linked to insulin resistance and chronic inflammation. Based on the mean value, GGT increased in the T2DM group with vascular complications. Increased GGT levels are associated with an increased risk of diabetes complications such as diabetic nephropathy, retinopathy, neuropathy, and cardiovascular disease based on oxidative stress and inflammation that plays a role in the pathogenesis of T2DM complications, and are followed by poor glycemic control factors.[14]

There is substantial evidence that highlights the strong association between GGT and the development of T2DM. However, it is unlikely that serum GGT will enhance the prediction of T2DM risk beyond what is already provided by established risk factors. GGT testing has a limited role in predicting the risk of T2DM and is limited by screening policies. GGT can be a risk marker for T2DM. This helps to identify people with a high risk of developing T2DM, but it cannot be a primary predictor.[15,16]

Differences in hs-CRP in T2DM patients with vascular complications and T2DM without complications

This study shows that there is a significant difference in hs-CRP levels between T2DM with and without vascular complications, and hs-CRP levels were higher in T2DM with complications than in T2DM without complications. This finding is in line with the results of previous research. Stated that hs-CRP levels increased in subjects with T2DM with complications compared to subjects with T2DM without complications.[14] Research Chuengsamarn, 2017, Stated that increased hs-CRP can increase the development of microvascular and macrovascular complications caused by uncontrolled glycemic and metabolic components resulting in increased production of inflammatory cytokines, including IL-6, and TNF-α in hepatocytes which can be examined with hs-CRP as a marker of inflammation.[17]

Study Lainampetch, 2019, Stated that a combination of increased CRP, IL-6, and TNF-α showed a close relationship in increasing the risk of T2DM and the risk of T2DM complications.[18] IL-6 is a pro-inflammatory cytokine that is produced by immune cells as well as adipocytes, or fat cells., where increased levels of IL-6 stimulate the liver to produce hs-CRP which functions as a marker of increased inflammatory activity, this is in line with research Kalyan, 2024 Stated that increased IL-6 correlates with worse renal outcomes in T2DM patients and also plays a role in the inflammatory process of T2DM complications.[19] An uncontrolled increase in blood sugar levels (hyperglycemia) in diabetes sufferers causes the immune system's response to slow down when exposed to disease germs. High hs-CRP levels can indicate inflammation in the body, which can be caused by various conditions such as infection, autoimmune disorders, or disease. Chronic. These hs-CRP levels can also be a risk factor for cardiovascular disease.

Differences in GGT in patients with T2DM macrovascular complications (CHD) and microvascular (neuropathy, nephropathy, retinopathy)

Vascular complications of T2DM are divided into two main types, namely microvascular and macrovascular complications. This study found higher GGT levels in patients with (CHD) compared to microvascular complications, although in microvascular there was also an increase in GGT levels. This may be due to the stronger role of oxidative stress in large blood vessel damage compared to small blood vessels.

The results of this study are by the research. Guan, 2023, Stated that higher GGT levels were associated with CHD risk in the T2DM patient population. Macrovascular complications occur in large blood vessel damage, such as in coronary heart disease, associated with atherosclerotic plaque formation and lipid deposition in the blood vessel wall.[20] GGT activity significantly contributes to the pro-oxidant effects of glutathione catabolites in the extracellular environment, facilitating their formation. Of atherosclerotic plaques in the carotid and coronary arteries that trigger LDL oxidation, which in the presence of iron has a higher concentration in atherosclerotic plaques than in normal arterial walls.[21]

The study Haydinger, 2023. Stated that Due to its high metabolic activity, the retina is relatively susceptible to oxidative stress. Microvascular complications such as diabetic retinopathy tend to be more associated with chronic hyperglycemia, which exacerbates oxidative stress and local inflammation, thus accelerating the increase in GGT.[22] Stated that increased serum GGT levels are a potential indicator of the risk of diabetic nephropathy. The main mechanism underlying increased GGT with microvascular complications is oxidative stress and endothelial dysfunction, which causes damage to small blood vessels. GGT as a marker of oxidative stress is more active in responding to endothelial cell damage in the brain, as in the kidneys and retina.[23]

Differences in hs-CRP in patients with T2DM macrovascular (CHD) and microvascular (neuropathy, nephropathy, retinopathy) complications

High-sensitivity C-reactive protein is a highly sensitive test that can detect inflammation at lower levels. This study found no significant difference between hs-CRP levels in patients with macrovascular (CHD) and microvascular complications (neuropathy, nephropathy, retinopathy). Endothelial dysfunction induced by oxidative stress causes stronger activation of inflammatory pathways, which contributes to increased hs-CRP. Chronic inflammation as well as activation of the innate immune system play a significant role in the development of diabetes as well as microvascular complications. Increased glucose levels result in microvascular changes and increase the production of inflammatory factors (IL-6, IL-8, and TNF-alpha) which play a role in triggering an inflammatory response, causing endothelial dysfunction and worsening diabetes.[5] A study by Lin, 2023, Showed that higher hs-CRP levels are a risk factor for diabetic nephropathy (DN) and may help identify T2DM patients at high risk for DN.[24]

Macrovascular complications such as cardiovascular disease (CVD) including (CHD) and stroke are more related to the atherosclerosis process involving large blood vessels. The mechanism of the atherosclerosis process in T2DM involves many factors, including inflammation, insulin resistance, hyperglycemia, dyslipidemia, and oxidative stress.[25,26,27] Research result, Aryan, 2018 It was found that hs-CRP can be used to predict the occurrence of CHD and microvascular complications.[28]

Receiver Operator Characteristics curve analysis of GGT and hs-CRP

Receiver Operator Characteristics (ROC) curve analysis evaluates subjects known to have vascular complications from a population of T2DM patients with and without vascular complications. The test accuracy can be measured by the AUC accurately distinguishing between T2DM individuals with vascular complications and T2DM individuals without complications. A test that has 100 % sensitivity and specificity is the optimal test for disease diagnosis. The AUC for hs-CRP is the highest (AUC = 0,706), while GGT has the lowest (AUC = 0,691). The ability of GGT with an AUC value of 0,691 means that GGT has a fairly good ability to distinguish between T2DM patients with and without vascular complications, although not very strong. The GGT cut-off value is 29 U/L The sensitivity was 63,2 %, the specificity 68,4 %, so if the measurement value of a T2DM patient is > 29 U/L, the individual is classified as a T2DM patient with vascular complications.

The ability of hs-CRP with an AUC value of 0,706 indicates that hs-CRP can distinguish between patients with T2DM and without vascular complications quite well. The cut-off value for hs-CRP found was 3,08 mg/L, which means that if the value is > 3,08 mg/L then patients with T2DM are classified as patients with T2DM with vascular complications. The sensitivity of hs-CRP was 63,2 % and the sensitivity of 63,2 % was still relatively low, indicating that hs-CRP was less than optimal in detecting positive and negative conditions. If hs-CRP is used for diagnosis, it is necessary to add additional parameters or data to increase sensitivity and specificity. Research results Sharma, 2020, Showed that hs-CRP is more effective when combined with other biomarkers to improve accuracy. Other studies also stated that the combination of hs-CRP with other biomarkers such as GGT and HbA1c can provide more accurate diagnostic results.[29]

RESEARCH LIMITATIONS

This study's limitation is the absence of supporting laboratory examinations such as HbA1C, cholesterol, triglycerides, HDL, LDL, urea, and creatinine.

CONCLUSION

GGT plays a greater role in detecting the risk of macrovascular complications (CHD) than microvascular. In addition, there is a significant difference in GGT and hs-CRP between T2DM with and without vascular complications, and vascular complications of T2DM increase GGT and hs-CRP values.

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CONFLICT OF INTEREST

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AUTHORSHIP CONTRIBUTION

Conceptualization: Nahlida Rahmah.
Data curation: Nahlida Rahmah, Puspa Wardhani, Yessy Puspitasari, Soebagijo Adi Soelistijo.
Formal analysis: Nahlida Rahmah.
Research: Nahlida Rahmah.
Methodology: Nahlida Rahmah, Puspa Wardhani, Yessy Puspitasari, Soebagijo Adi Soelistijo.
Project management: Nahlida Rahmah, Puspa Wardhani, Yessy Puspitasari.
Resources: Nahlida Rahmah, Puspa Wardhani, Yessy Puspitasari, Soebagijo Adi Soelistijo.
Software: Nahlida Rahmah.
Supervision: Puspa Wardhani, Yessy Puspitasari, Soebagijo Adi Soelistijo.
Validation: Puspa Wardhani, Yessy Puspitasari, Soebagijo Adi Soelistijo.
Display: Puspa Wardhani, Yessy Puspitasari, Soebagijo Adi Soelistijo.
Drafting - original draft: Nahlida Rahmah.
Writing - proofreading and editing: Nahlida Rahmah, Puspa Wardhani.