VOLUME-9, ISSUE-1, JANUARY-2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Medicine

DIFFERENCES OF GAMMA GLUTAMYL TRANSFERASE IN CORONARY HEART DISEASE PATIENTS WITH MORE THAN EQUAL 70% OCCLUSION AND LESS THAN 70% OCCLUSION

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ABSTRACT

Background: Coronary heart disease (CHD) is a cumulation of plaque in the heart arteries that can cause heart attacks. CHD is one of the main and first causes of death in developed and developing countries, including Indonesia. It is estimated that throughout the world, CHD in 2020 became the first most frequent killer of 36% of all deaths, twice as high as cancer deaths. Currently Gamma Glutamyl Transferase (GGT) is a prognostic marker of death and reinfarction in patients with patients Coronary Artery Disease (CAD) and there is a relationship of GGT with the prognosis of CAD patients undergoing angiography.

Methods: The study was conducted by cross sectional method. The study subjects were 60 male and female CHD patients who were treated and treated at the hospital in the Department of Cardiology FK-USU / H. Adam Malik Hospital Medan, which was enforced by history, physical examination, angiography and laboratory and underwent coronary angiography. GGT examination uses Architect c8000.

Results: A total of 60 CHD patients in this study found that GGT values were greater in the ≥70% group compared with occlusions <70% with p = 0.003.

Conclusions: This study showed a significant difference in the values of GGT with occlusion ≥70% and <70% occlusion.

KEYWORDS : Gamma glutamyl transferase, Coronary heart disease

BACKGROUND

Coronary Heart Disease is a complex disease where there is a cumulation of plaque in the coronary arteries that causes decreased and blocked blood flow in one or more arteries that surround and supply blood to the heart which causes chest pain and discomfort because the heart muscle does not get enough blood so slowly It will eventually weaken the heart muscle and cause heart failure and arrhythmias (1,2).

In Indonesia it is reported that CHD (which is classified as a circulatory system disease) is the main and first cause of all deaths, which is 26.4%, this number is four times higher than the mortality rate due to cancer (6%). In other words, approximately one in four people who died in Indonesia caused by CHD (3).

Various risk factors have an important role in the emergence of CHD from metabolic aspects, hemostasis, immunology, infection, and many other interrelated factors. The heart is able to contract without stopping thanks to the supply of energy materials continuously. The supply of energy in the form of oxygen and nutrients flows through a blood vessel called a coronary artery. If the blood vessels narrow or become blocked the process of transportation of energy materials will be disrupted (4).

Gamma-glutamyl transferase (GGT) is an enzyme found on the external surface of various cell types. GGT is present in all cells except erythrocytes, but there are variations in GGT activity according to the development of each cell (5). In mammals, GGT is a dimeric glycoprotein with a molecular weight of 68kDa. GGT activity is known to be higher in secretory cells and has absorption functions such as the kidneys, biliary system, intestine, and which is known to be greatest in the luminal surface of the ductus epididimis (6).

GGT activity also occurs very intensively in bile, hepatocytes, and cholangiocytes (6). GGT is no longer merely a marker of excessive alcohol consumption or of liver disease. GGT is on the outer surface of cells and plays a role in glutathione catabolism (GSH) by hydrolyzing the -glutamyl group between glutamate and cysteine. This reaction forms cysteine-glycine moieties which will enter intracellular through the membrane dipeptidase as precursor of GSH resintesis. GGT activity is found in carotid artery atheroma and coronary artery plaques (5).

The function of GGT in cells is thought to be related to the function of amino acid transport in the gamma-glutamyl cycle. However, it cannot be ascertained by the fact that humans with GGT deficiency do not all get amino acid transport disorders. An important function of GGT in human physiology is the breakdown of glutathione, an important antioxidant in the human body (7).

It is further known that cystein-glysin derivates derived from GSH hydrolysis by GGT induce the formation of reactive oxygen species (ROS) as occurs in LDL oxidation in vitro. This fact supports the basic pathophysiology of the direct role of GGT on oxidative processes in plaque and the progression of coronary artery disease (8,9).

Increased levels of GGT are associated with inadequate antioxidants and increased oxidative stress. (10). High levels of GGT in circulation can also be said to be a marker of inflammation that is significantly associated with an increase in the inflammatory process (11).

MATERIALS AND METHODS

This study was carried out in a cross sectional manner conducted for 5 months from November 2018 to April 2019, of 60 CHD patients treated and outpatient in cardiology at HAM General Hospital Medan, who had gone through the process of inclusion and exclusion. Where the inclusion criteria consisted of CHD patients who had been confirmed by physical, laboratory, ECG and coronary angiography. Exclusion criteria in this study were CHD patients with a history of heavy alcohol drinkers, impaired liver function, who had performed PCI and who had received statins.

RESULTS

Of the 60 CHD patients who participated in the study, 33 of the total sample were male (55%) and the remaining 27 (45%) were female. The overall study participants had a median age of 53.5 years. The youngest age is 42 years and the oldest is 71 years. (Table 4.1).

Table 4.1 Characteristics of Research Subjects

Variable	n (%)
Gender	
• Male	33(55)
• Female	27(45)
Age (mean/min/max)	54.95/42/71

Table 4.2 Measurement characteristics for each occlusion group greater or equal to 70% and 70% smaller.

Variable	Occlusion ≥ 70%	Occlusion < 70%	p
Age	57,86±6,55	52,03±5,92	0,001
Total Cholesterol	214,06±34,27	156,03±39,59	0,000
HDL	45,03±5,54	34,40±9,82	0,000
LDL	135,73±31,98	96,26±26,77	0,000
Triglyceride	160,20±68,80	140,10±54,51	0,183

There is an age difference between the occlusion group greater or equal to 70% with 70% smaller with a value of p = 0.001.

There is a difference in total cholesterol between occlusion groups greater or equal to 70% and less than 70% with a value of p = 0,000.

There is a difference in HDL between occlusion groups greater or equal to 70% and less than 70% with a value of p = 0,000.

There is an LDL difference between occlusion groups greater or equal to 70% and less than 70% with a value of p = 0,000.

There was no difference in triglycerides between occlusion groups greater or equal to 70% and less than 70% with a value of p = 0.183.

Table 4.3 Differences in Gamma GT with the Number of Vessels Experiencing Occlusion.

Variable	≥3 VD	< 3VD	p
GGT	34,16±18,18	21,33±8,03	0,003

There is a difference in Gamma GT in terms of the number of vessels involved with a value of P = 0.003.

Table 4.4 The difference in Gamma GT in occlusion greater or equal to 70% and less than 70%.

Variable	Occlusion ≥ 70%	Occlusion < 70%	p
GGT	34,16±18,18	21,33±8,03	0,003

There is a difference in Gamma GT between the occlusion group greater or equal to 70% and less than 70% with a value of p = 0.003.

DISCUSSION

This study involved 60 CHD patients who met the study criteria consisting of 33 men (55%) and 27 women (45%). In the study of Demircan et al 2009 found that more men suffer from CHD when compared with 148 patients (78%). The age of the patients in this study varied with the youngest population 42 years and the oldest 71 years. Demircan et al. 2009 also explained that the results of his study there was a relationship of age with the number of coronary arteries that were damaged. Where CHD patients with an average age of 57.9 years there is 1 coronary artery damage, while CHD patients with an average age of 62.9 years there are 2 to 3 coronary artery damage (12).

The causes of coronary heart disease include age and sex factors, with the incidence rate in men far more than in women but the incidence in women will increase after menopause around the age of 50 years. This is because the hormone estrogen has a protective effect against atherosclerosis, wherein people aged > 65 years found 20% of CHD in men and 12% in women (13).

Increasing age will also increase CHD patients, because blood vessels undergo progressive changes and take place continuously for a long period of time. The earliest changes begin at age 20 in the coronary arteries. Other arteries begin to modify only after the age of 40, occur in men aged 35-44 years and increase with age (13).

Risk factors involved in atherosclerosis such as high lipid profile, high blood sugar levels, endothelial dysfunction play an important role in the production of ROS in CAD pathomechanism. GGT is an enzyme in cell membranes that transfers gamma-glutamyl. The physiological role of GGT is to split the gamma-glutamyl amide bond from tripeptide and hydrolysis of extracellular GSH to produce cysteine and other thiol ingredients. In the process of atherosclerosis GGT can be slightly absorbed in LDL-c and LDL is oxidized in plaque (equivalent to the level of GGT) by reducing Fe (III) to active Fe (II). GGT is also involved in fibrous formation, plaque rupture and erosion, increased thrombotic aggregation and thrombosis (14).

The correlation mechanism of increased GGT activity with patients with coronary heart disease is closely related to the inflammatory process at the cellular level (15). A study conducted by Ruttmann et al 2005, they found a strong association between high GGT levels and cardiovascular mortality, and suggested that high GGT is an independent risk factor for cardiovascular disease.

The pathomechanism of GGT activity related to atheroscl erosis itself occurs at the cellular and molecular level. The breakdown of extracellular glutathione by GGT produces cysteine-glycine dipeptide which is a stronger reducing agent than glutathione. Cysteine-glycine dipeptide will reduce Fe3 + to Fe2 + which will consequently catalyze the formation of superoxide and hydrogen peroxide. This will trigger peroxidation reactions including LDL and will increase local prooxidants and inflammatory reactions. This reaction can be seen to occur in atherosclerotic plaque, and explains how GGT plays a role in the atherosclerotic process, plaque instability, and coronary ischemia events (16).

In line with the research conducted by Atar et al 2013, it was shown that GGT levels were strongly correlated for coronary artery calcification (p <0.001), patients who had high GGT levels were dominated by men (p <0.001), which had a strong correlation with smoking, diabetes and low HDL levels (p <0.001). In multivariate analysis of GGT, smoking, age can be an independent predictor of coronary calcification (17).

In a study conducted by Baars et al 2016, obtained GGT levels in ACS patients who had stenosis ≥ 50% with a mean value of 55.06 and a standard deviation of 0.72. GGT levels in ACS patients who had stenosis <50% with a mean value of 56.56 and a standard deviation of 1.66 and p value = 0.913. This shows that there is no significant difference in GGT between the stenosis group ≥50 and <50 (18).

In a study conducted by Arasteh et al 2018, it showed GGT levels in CHD patients who had occlusion 1 a.coronary with a mean value of 55.56, a standard deviation of 9.7 and p value 0.90. In CHD patients who experienced occlusion 2 a.coronary GGT levels were obtained with a mean value of 71.7, a standard deviation of 12.7 and p value = 0.90. Likewise in

CHD patients who had occlusion 3 a.coronary, GGT levels were obtained with mean 84.7, a standard deviation 13.4 p value 0.30 (14).

The ability to detect subjects at high risk for acute myocardial infarction (AMI) in a non-invasive way will reduce the need for intracardiac catheterization or PCI and complications related to these invasive measures. One of the liver enzymes, GGT, is linked to the risk of cardiovascular disease. Predictive values for potential liver serum markers to assess the severity of stenosis in AMI.

CONCLUSIONS

From this study, differences in GGT were obtained in more or equal to 70% and <70% occlusion of coronary arteries where GGT testing was reasonably priced and available in almost all laboratories.

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