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COMPARISON OF GAMMA GLUTAMYL TRANSFERASE SERUM LEVELS IN PATIENTS WITH 5D CHRONIC KIDNEY DISEASES WITH STADIUM 3 AND 4 CHRONIC KIDNEY DISEASE

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Abstract

Background:

Chronic Kidney Disease (CKD) is a global public health problem with increased prevalence and incidence of kidney failure, poor prognosis and high costs. Therefore the aim of this study is to look at the characteristics of patients with CKD and the comparison of serum GGT levels in patients with chronic 5D kidney disease with patients with chronic kidney disease St 3 - 4. So they can find out the mortality rate of patients with CKD 5D with CKD st 3-4.

Method:

This study used a cross sectional data collection method to assess serum GGT levels in patients with 5D chronic renal failure and stage 3 - 4. chronic kidney disease as many as 49 samples for patients with stage 5D chronic kidney disease and patients with stage 3 and 4 chronic kidney disease

Results:

In this study the characteristics of CKD patients by sex were obtained by men as many as 55 people (56.1%), and female sex as many as 43 people (43.9%). From this study, the age of the youngest CKD patient was 26 years and the oldest age was 74 years. In this study also found the cause of CKD was hipertensi as many as 53 patients (54.1%), diabetes militus as many as 43 patients (43.9%), and nephrolithiasis as many as 2 patients (2.0%). And also obtained the results of a significant difference between the GGT levels of 5D CKD patients and CKD st 3-4 patients ($p = <0.001$).

Conclusion:

Characteristics of CKD patients based on sex obtained by men more than women. From this study also obtained the youngest age of CKD patients is 26 years and the oldest age is 74 years.

There is a significant difference between the GGT levels of patients with CKD 5D and CKD st 3-4.

Introduction

Chronic Kidney Disease (CKD) is a condition in which there is a decrease in kidney function due to chronic and irreversible damage to the renal parenchyma. Someone is diagnosed with chronic kidney disease if there is an abnormality and damage to the kidneys for 3 months or more which is characterized by a decrease in kidney function by 78-85% or the glomerular filtration rate (LFG) of less than 60 ml / min / 1.73m² with or without abnormalities in the kidneys. CKD is one of *non-communicable disease* that needs attention because it is public health problem with the incidence rate is quite high dan have big effect for morbidity, mortality dan the economic public because maintenance cost are quite high.^{9,12}

Gamma – Glutamyl Transferase (GGT) is one of enzyme on serum, that works in the first line proces degradation ekstraselular glutathione (GSH).Glutathione is the main antioxidant mammalian cells that play an important role in the protecting cell from the oxidant. If stres oxidatif increased, glutathione need also increased; If glutathione level low, than the damage due to stress oxidative will be increased.^{16,22}

Because of that, the GGT estimated to have an important role in some of kind tissue or the organ. Example, the kidney, if the kidney damage occurs so the GGT play a role in the process *reactive oxygen species* (ROS) especially *superoxideanions* that *nitric oxide* will decrease and than the *renal blood flow* and filtration glomerulus rate will be low.^{16,24}



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From this concept, so we do the research about content ratio GGT pasien CKD 5D with the pasien CKD st 3-4. Our result research contribution with the prognostic streght level for the result in the pasien hemodialisa. (Park et al,2015). GGT play the role relevant on the prediction risk mortality on the end stage renal disease, with the level GGT leaning to the right with median value 20 UI / L.^{16,22}

Methods

This study is an observational cross sectional study which performed at Haji Adam Malik General Hospital Medan with permission from Research Ethics Committee of the Faculty of Medicine, Universitas Sumatera Utara-RSHAM. Subjects were recruited from April to June 2019 consecutively. The inclusion criteria were patients who were clinically confirmed age >18 years old, patient with history CKD level 5D and CKD level 3, and patient who were willing to take part in this research.

Study Procedure

The population who occupy criteria will be included in the research, before that we do the inform consent for the research. The ingredients used in this research is blood serum from mediana vein cubiti. For GGT test, the serum must keep in the temperature 2-8⁰C, the sample maximum keep in 7 days dan the temperature -20⁰C sample stable only 1 years. The GGT test will be do with enzymatic metode colorimetric test.

Statistical analysis

Categorical variables are presented by number or frequency (n) and percentage (%). Numerical variables are represented by mean and standard deviation for normally distributed data, if data not normally distributed, the data shown by median. Compare the level GGT we used the T test unpaired when the data normal contribution. If the data not normality contribution, used *Mann Whithney Test*. All the data were analyzed using computer statistic software, the p value <0.05 was said to be statistically significant.

Results

In this research the characteristic patiens from the gender male 55 people (56.1%), and from the female 43 people (43.9%). From this research we get the younger age 26 years old and the oldest 74 years old. From this research the causes of CKD is Hypertension 53 patients (54.1%), diabetes militus 43 patients (43.9%), and nefrolitiasis 2 patients (2,0%).

Table 4.1 Characteristics of CKD Patients

Variable	N	Percentage (%)	Median (Min-Max)
Genders			
Male	55	56.1	
Female	43	43.9	
Age			55.00 (26.00 - 74.00)
20 – 29	3	3.1	
30 – 39	11	11.2	
40 – 49	23	23.5	



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50 – 59	31	31.6
60 – 69	25	25.5
Etiology		
DM	43	43.9
HT	53	54.1
Nefrolitiasis	2	2.0

From the measurement result obtained average result level ureum from all the patients research is 75.90 mg/dL with standard deviation 46.00 and the result median mean 77 mg/dL with the lowest level ureum 15 mg/dL and the highest level ureum 197 mg/dL. The average creatinine from all the patients research is 3.94 mg/dL with standard deviation 1.28 and the result median mean 3.77 mg/dL with the lowest level creatinine 1.24 mg/dL and the highest level creatinine 7.40 mg/dL.

Table 4.2 Measurement Data Ureum and Creatinine from all the patient PGK

Variabel	Mean ± SD	Median (Min - Max)
ureum (mg/dL)	75.90 ± 46.00	77.00 (15.00 - 197.00)
Creatinine (mg/dL)	3.94 ± 1.28	3.77 (1.24 - 7.40)

Measurement data by the tool average GGT from all the patients research is 301.08 U/L with standard deviation 105.47 and median rate 314.00 U/L with the lowest GGT 130.00 U/L and the highest GGT 449.00 mg/dL.

Table 4.3 Measurement Data GGT from all the patient PGK

Variable	Median (Min - Max)
GGT (U/L)	314.00 (130.00 - 449.00)

Using the Mann Whitney test to assess the comparison between the levels of ureum and creatinine in patients with CKD 5D patients with patients with CKD St. 3-4 obtained $p = <0.001$. This shows that there is a significant difference between the levels of ureum and creatinine in patients with CKD 5D and patients with CKD St 3-4.

Table 4.4 Comparison of urea and creatinine levels in 5D CKD patients with CKD St 3-4 patients

Variable	Mean ± SD	Median (Min-Max)	p Value
Ureum (mg/dL) PGK st 3-4	114.63 ± 30.47	102.00 (54.00-197.00)	0.000
Ureum (mg/dl) PGK 5D	37.18 ± 30.47	32.00 (15.00-79.00)	
Kreatinin (mg/dl) st 3-4	3.41 ± 0.79	3,42 (2.13-4.91)	
Kreatinin (mg/dl) 5D	4.48 ± 1.46	4.60 (1.24-7.40)	

*Mann Whitney test



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Using the Mann Whitney test to assess the comparison between the GGT levels of CKD 5D patients and CKD patients st - 3-4 obtained p value = <0.001. This shows that there is a significant difference between the GGT levels of 5D CKD patients and STK 3-4 patients.

Table 4.5 Comparison of GGT levels of 5D CKD patients with STK 3-4 patients

Variable	Kategori CKD		P Value
	PGK stage 3-4	PGK 5D	
	Median(Min-Max)	Media(Min-Max)	
GGT levels Serum (U/L)	211,89(130,00-354,00)	399,00(215,00-449,00)	<0.001*

*Mann Whitney test

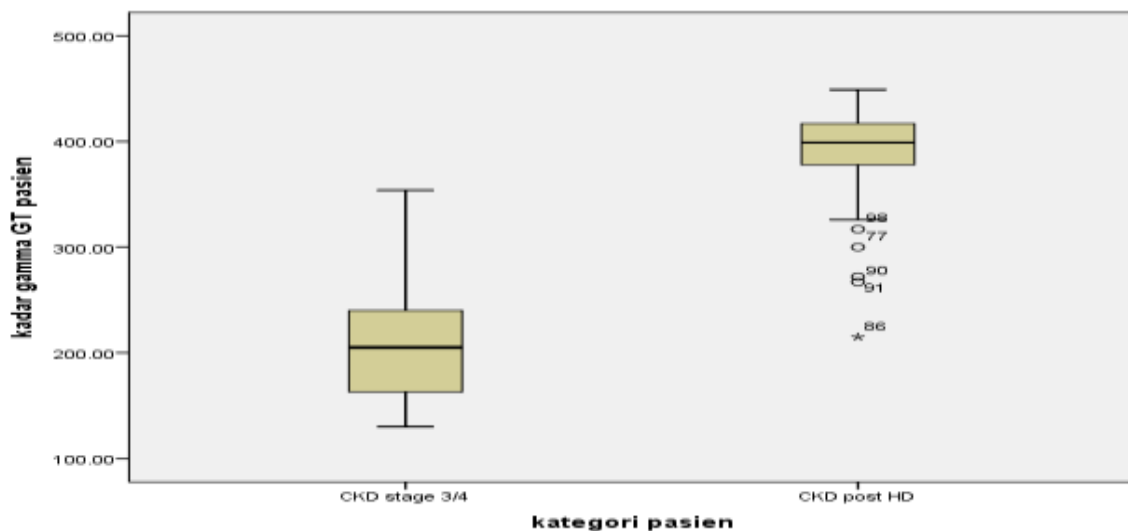


Figure 4.2 Comparison of GGT levels of 5D CKD patients with CKD st 3-4 patients

Discussion

Oxidative stress (OS), defined as a disturbance in the pro / antioxidant balance, is dangerous for cells due to excessive generation of reactive oxygen species (ROS) and nitrogen (RNS). When balance is not disturbed, OS has a role in physiological adaptation and signal transduction. However, excessive amounts of ROS and RNS cause oxidation of biological molecules such as lipids, proteins, and DNA. Oxidative stress has been reported in kidney disease, due to antioxidant depletion and increased ROS production. Kidney is a very metabolic organ, rich in oxidation reactions in the mitochondria, which makes it vulnerable to damage caused by OS, and several studies have shown that OS can accelerate the development of kidney disease. Also, in patients at an advanced stage of chronic kidney disease (CKD), increased OS is associated with complications such as hypertension, atherosclerosis, inflammation, and anemia.^{7,23}

The primary role of cellular glutamyltransferase (GGT) is to metabolize extracellular reduced glutathione (GSH), allowing precursor amino acids to be assimilated and reused for intracellular GSH synthesis. Recent experimental studies have shown that cellular GGT can also be involved in the generation of reactive oxygen species (ROS) in the presence of iron or other transition metals. Although the relationship between cellular GGT and serum GGT is unknown and serum GGT activity has been commonly used as a marker for excessive



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alcohol consumption or liver disease, our epidemiological study series consistently shows that serum GGT in its normal range may be the initial and sensitive enzymes associated with stress oxidative. Increased serum GGT within the normal range of laboratory values may be an early and sensitive marker for oxidative stress. Serum GGT may be useful in studying oxidative stress-related problems in both epidemiological and clinical settings.^{8,24}

This study is a cross sectional study that aims to determine the comparison of GGT levels between with CKD 5D patients with patients with CKD st. 3-4. In this study the characteristics of CKD patients by sex were obtained by men as many as 55 people (56.1%), and female sex as many as 43 people (43.9%). From this study, the age of the youngest CKD patient was 26 years and the oldest age was 74 years. In this study also found the cause of CKD was HT as many as 53 patients (54.1%), DM as many as 43 patients (43.9%), and nephrolithiasis as many as 2 patients (2.0%).

In this study, the characteristics of CKD patients consist of 55 male (56,1%) and 43 female (56,1%). From this study, the age of the youngest CKD patient was 26 years old and the oldest age was 74 years. This study also found that CKD patients caused by hypertension, DM, and nephrolithiasis were 53 patients (54.1%), 43 patients (43.9%), and 2 patients (2.0%) consecutively.

Research by Tanvir Chowdhury Turin et al., In 2012 found that gender differences in CKD development studies have been reported, with higher development rates for men. The results of Riskesdas 2013 also showed that the prevalence increased with age, with a sharp increase in the age group of 35-44 years compared to the age group of 25-34 years and the prevalence in men (0.3%) was higher than women (0.2%). Research by J.F Souza et al., 2008 found no significant differences were observed between groups regarding gender, namely 50.6% were women and 49.4% were men. In 2017, the etiological proportion or basic disease of 5 D CKD patients is hypertension, which ranks first 36% and diabetic nephropathy, known as diabetic kidney disease, is 29%, while nephrolithiasis ranks sixth from other causes of CKD, which is equal to 4% of Reports from IRR.

In this study the results of a significant difference between the GGT levels of 5D CKD patients and STK 3-4 patients. This is supported by a retrospective study on observations in groups of patients with CKD stage 4-5 pre-dialysis high and abnormal GGT levels are Frequent findings in patients with CKD.²⁷ In CKD patients who undergo hemodialysis tend to have higher levels of GGT, this is consistent with research conducted by J.F. Souza et al., 2008, where patients with CKD undergoing dialysis the mean value of GGT was 3 or 4 times above the reference limit. Likewise, other studies which state that serum GGT is significantly increased in CKD patients undergoing hemodialysis.²⁸

Conclusion

Characteristics of CKD patients based on sex obtained by males more than females. From this study also obtained the youngest age of CKD patients is 26 years and the oldest age is 74 years. There is a significant difference between GGT levels in patients with CKD 5D and CKD st. 3-4.

Suggestion

Further research needs to be done by calculating other variables that can also play a role in the increase in GGT in CKD. Longitudinal studies need to be done to see the relationship of GGT levels with mortality rates in CKD patients.

References

- [1] Anderson ME, Allison RD, Meister A. Interco version of leukotrienes catalyzed by purified gamma-glutamyl transpeptidase: concomitant formation of leukotriene D4 and gamma-glutamyl aminoacids. *Proc Natl Acad Sci USA*. 2014;79:1088-91.
- [2] Andrews NC. Disorders of iron metabolism. *N Engl J Med*. 2015;341:1986-95.
- [3] American Diabetes Association. (2014). *Diagnosis and Classification of Diabetes Mellitus*. *Diabetes Care* Volume 37, 581-590.



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- [4] Bandiara R. Penatalaksanaan anemi defisiensi besi pada pasien yang menjalani hemodialisis. Workshop: “Registrasi Unit Dialisis SeJabar“ PPGII Jabar di Hotel Papandayan Bandung, 25 Februari 2013 [cited 19 Jan 2016]. Available from: <http://pustaka.undap.ac.id>
- [5] Badan Penelitian dan Pengembangan Kesehatan. Riset Kesehatan Dasar 2013. Jakarta: Kemenkes RI; 2013.
- [6] Boccardo P, Remuzzi G, Galbusera M. Platelet dysfunction in renal failure. Seminars in thrombosis and hemostasis [Internet]. 2014 [cited 2014 Feb 2]; 30(5):579-589. Available from : PubMed Central.
- [7] Centers for Disease Control and Prevention (U.S.), National Center for Health Statistics (U.S.), National Vital Statistics System (U.S.)
- [8] National vital statistics reports : from the Centers for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System. DHHS publication no (PHS). Hyattsville, Md.: National Center for Health Statistics:v [Internet]. 2013 [cited 2014 Jan 11].
- [9] Conigrave KM, Saunders JB, Reznik RB, et al. Prediction of alcohol-related harm by laboratory test results. Clin Chem. 2013;39:2266-70
- [10] Chonchol, M., Spiegel, D.M., 2015. The Patient with Chronic Kidney Disease. In: Schrier, R.W., 6th ed. Manual of Nephrology. Philadelphia: Lippincott Williams and Wilkins, 177-186.
- [11] Crews DC, Plantinga LC, Miller ER, 3rd, et al. Prevalence of chronic kidney disease in persons with undiagnosed or prehypertension in the United States. Hypertension [Internet]. 2013 [cited 2015 sept 4]; 55(5):1102-1109.
- [12] De Boer I.H et al. Temporal Trends in The Prevalence of Diabetic Kidney Disease in The United States. Journal of the American Medical Association. 2011;305:2532-39.
- [13] D. T. Gilbertson, J. Liu, J. L. Xue et al., “Projecting the number of patients with end-stage renal disease in the United States to the year 2015,” Journal of the American Society of Nephrology, vol. 16, no. 12, pp. 3736–3741, 2015
- [14] Dugdale D. High Blood Pressure. medline plus 2014. Flack J, Peters S, Shafi T, Alrefai H, Nasser S, Crook E. Prevention of Hypertension and Its Complications: Theoretical Basis and Guidelines for Treatment. Journal of The American Society of Nephrology 2013;14:592- 598.
- [15] Fransisca, dkk. Penyebab Gagal Ginjal Rusak. Jakarta: Cerdas Sehat; 2014
- [16] Fishbane S, Pollack S, Feldman HI, et al. Iron indices in chronic kidney disease in the National Health and Nutritional Examination Survey 2000-2014. Clinical journal of the American Society of Nephrology : CJASN [Internet]. 2009 [cited 2014 Jan 13];4(1):57-61. Available from : PubMed Central.
- [17] Ghaban R, Staros EB. Gamma-Glutamyl transferase [Internet] 2013. [Cited 2014 March 10] Available from: <http://emedicine.medscape.com/article/2087891-overview>
- [18] Harrison D, Guzik T, Lob H, et al. Inflammation, Immunity, and Hypertension. Hypertension 2014;47:132-140.
- [19] Harrison. (2013). Jakarta: EGC
- [20] Hernaningtyas LFDP. Hipertensi, Obesitas Sentral, dan Diabetes Mellitus (Komponen Sindrom Metabolik) Sebagai Prediktor Kejadian Penyakit Ginjal Kronik : Studi Kohort Retrospektif Pada Penduduk Kecamatan Blahbatuh Gianyar Bali. Denpasar: Universitas Udayana; 2012.
- [21] Hoy, W.E., Hughson, M.D., Bertram, J.F., Douglas-Denton, R., Amann, K. Nephron number, hypertension, renal disease, and renal failure. J Am Soc Nephrol. 2015;16:2557–2564
- [22] Imai E, Horio M, Watanabe T, et al. Prevalence of chronic kidney disease in the Japanese general population. Clinical and experimental nephrology [Internet]. 2012 [cited 2014 Jan 2];13(6):621-630.
- [23] Claudia, T., Francesco, M.R., Jan, L.C.M., Maurizio, P., Giovanni, L.T., Francesca, M. Oxidative Stress as Estimated by Gamma-Glutamyl Transferase Levels Amplifies the Alkaline Phosphatase Dependent Risk for Mortality in ESRD Patient on Dialysis. Journal of Hindawi. 2016
- [24] Kristien, D., Asmin, A., Djalila, M., Ann, V.S., Francois, J., Bert, B. Oxidative stress in chronic kidney disease. Journal of Pediatric Nephrology. 2018
- [25] Duk-Hee, L., Rune, B., David, R.J. Is serum Gamma Glutamyl transferase a Marker of Oxidative Stress??. Journal of University of oslo USA. 2004
- [26] Tanvir, C.T., Marcello, T., Braden, J.M., Sofia, B.A., Pietro, R., Matthew, J., Brenda, R.M. Lifetime Risk of ESRD. Journal of university of Calgary Canada. 2012



INTERNATIONAL JOURNAL OF RESEARCH SCIENCE & MANAGEMENT

- [27] J.F Souza., L.A Miorin., C Longui., Y.A dos santos. Gamma-Glutamyl transferase Activity in Chronic Dialysis Patient and Renal Transplant Recipients With Hepatitis C Virus Infection. Journal of Elsevier. 2008
- [28] Fernando, C.F., Lilia, A., Miquel, A.B., Boris G.C., Enrique, L. Niveles sericos elevados de gamma-glutamyl transferase y fosfatase alkaline son predictors independientes de mortalidad en la enfermedad renal cronica estadio 4-5. Journal of Sociedad espanola de nefrologia.2016
- [29] R. Sowmi., M.E Sumathi., K.N Shashidhar., B.N Raghavendra Prasad. Association of serum gamma glutamyl transferase with lipid abnormalities in end stage renal disease. Journal of Elsevier. 2016.