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Correlation Between Oxidative Stress, SIRT1 Serum Level, and eGFR on Elderly

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Abstract: The aging network kidney causes Oxidative Stress (OS) and damages the kidney. Studies of aging kidneys keep going growing by developing sirtuin as an antiaging. Sirtuin 1 (SIRT1) is a protein implicated in several disorders including diabetes functions as an anti-aging protein. Decreased eGFR in the elderly caused by his height prevalence factor risk disease kidney at an older age. The study aims to study the correlation between oxidative stress, SIRT1 serum levels, and eGFR in the elderly. The method used in this research is observational with the cross-sectional method. The sample in this study was the whole elderly who met the inclusion and exclusion criteria, totaling 30 people. Exclusion criteria are patients with glomerulonephritis, nephropathy obstruction, nephropathy sour veins, and obesity. All patients complied requirements asked to fill informed consent form. The inspection was carried out by urinalysis ultrasound kidney and assessing serum MDA levels which were found to be higher in this study. This study showed SIRT1 and eGFR levels decreased in the elderly. There was a negative correlation with moderate correlation strength between serum MDA levels and serum SIRT1 levels and a strong correlation between serum MDA levels and eGFR in the elderly. There was a positive correlation with a moderate correlation between serum SIRT1 levels and eGFR in the elderly. SIRT1 is suggested to be examined in elderly patients with decreased eGFR, even without comorbidity.

Keywords: Oxidative Stress; eGFR on Elderly; SIRT1 Serum Level

Introduction

The kidney is one of the body's very energetic organs so it's faster to experience aging. Disease aging kidneys are a very serious health problem seriously all over the world. Aging kidney depends on metabolism aerobics that makes kidneys full of free radicals free (Hong & Park, 2021). In addition, kidney aging is caused by age whereas in the elderly there are changes in the structure and function of the kidneys. The aging network kidney causes Oxidative Stress (OS) and damages the kidney. OS is an imbalance of oxidants and antioxidants that harm cells. OS cause disturbance signaling redox and regulation damage molecular (Singh, 2022). OS contributes to the emergence of type 1

and type 2 diabetes, neuropathic diabetes, and the development of chronic kidney disease (CKD) (Franzin et al., 2021). CDK is characterized by damaged kidneys, such as abnormalities in sediment urine, electrolytes, histology, albuminuria, structure kidney, and present history of a transplanted kidney. OS in CKD patients contributes to atherosclerosis, amyloidosis, and anemia. CDK can be identified through an inspection routine with serum profile chemistry and urine studies. OS is an important factor related to renal insufficiency with aging which can be identified through Malondialdehyde (MDA) markers.

Studies of aging kidneys keep going growing by developing sirtuin as an antiaging. Sirtuins have gained notoriety as molecules that reduce age-related diseases

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and slow down aging. The seven enzymes that make up the sirtuin family (Sirt1-7) are involved in a variety of antioxidant and OS-related processes and activities, including the repair and metabolism of DNA damage through histone and protein deacetylation. SIRT1 is a protein implicated in several disorders including diabetes functions as an anti-aging protein. Sirtuin 1 (SIRT1) is expressed by various cells in organs, especially in the kidney (cell interstitial medulla kidney), and has a role-specific effect of renoprotective. Several studies with animal tests have observed the effect of SIRT1 renoprotective. The NAD⁺-dependent deacetylase SIRT1 significantly protects the kidneys by controlling apoptosis, fibrosis, oxidative stress, inflammation, and aging processes. Many kidney disorders, including diabetic kidney disease and HIV-associated kidney disease, have been linked to Sirt1's renal protective impact. The specific role is to guard the integrity podosit glomerular basement membrane, increasing the synthesis of erythropoietin (EPO) and the angiotensin II receptor type 1 (AT1R) expression (Motonishi et al., 2015). OS is indicated by SIRT1 kidney overexpression and SIRT1 as biomarkers of OS. A medication for SIRT1 may be created to address both CKD and its side effects. Kidney function in patients with CDK can be tested by estimating glomerular filtration (eGFR) (Hong et al., 2020).

The structure and operation of the kidneys are altered in the elderly, such as CKD which causes a decrease in the number of nephrons which results in a decrease in GFR and renal plasma flow (Dybiec et al., 2022). In the diagnosis, grading, and prognosis of CKD cases, estimation of the glomerular filtration rate (eGFR) is crucial. GFR was used as a determinant function of kidney disease, diagnosing, staging, managing CKD, confirming disease prognosis kidney chronic, and decisive dose drug. GFR is a condition of the glomerulus filtering plasma to produce ultrafiltrate. The measurement of GFR frequently uses the biochemical marker creatinine, which serum and urine testing can identify. The amount of blood plasma cleared of creatinine per unit of time is known as Creatinine Clearance (CrCl) The results of previous studies (Coresh et al., 2007) show that 38% of elderly aged 70 years or over, have an eGFR < 60 ml/min/1.73 m². Several researchers argue that decreased eGFR as a result of aging is normal and should not be confused with CKD in the absence of other abnormalities (Glassock, 2007). Decreased eGFR in the elderly caused by his height prevalence factor risk disease kidney at an older age (Stevens, 2008). The study aims to study the correlation between oxidative stress, SIRT1 serum levels, and eGFR in the elderly. This research is a new study that examines

the correlation between OS, SIRT1 serum levels, and eGFR in the Elderly.

Method

Cross-sectional observational research methodology is the approach employed in this study. The study was conducted for 6 months at two hospitals in the city of Padang, West Sumatra, Indonesia. The two hospitals are the M. Djamil General Hospital part outpatient and Inpatient Installations for Internal Medicine and Reksodiwiryo Hospital. The population in this research is the elderly who are outpatients and inpatients in the internal medicine department at both hospitals. Thirty older participants who met the inclusion and exclusion criteria made up the study's sample. Exclusion criteria are patients with glomerulonephritis, nephropathy obstruction, nephropathy sour veins, and obesity.

All patients complied requirements asked to fill informed consent form. The inspection was carried out urinalysis, and ultrasound kidney. Examination laboratory covers Glucose Fast Blood (GFB), glucose blood 2 hours postprandial, acidic urate, total cholesterol, HDL, LDL, triglycerides, urea, creatinine, and eGFR. Furthermore, serum levels of MDA and SIRT1 were tested. The Statistical Package for the Social Sciences (SPSS) version 22.0 was used to do analysis statistics. Correlation absolute will give value $r = 1$, very strong (0.8-1.0), strong (0.6-0.79), moderate (0.4-0.59), weak (0.0-0.39). Correlation is considered significant if $p < 0.05$.

Result and Discussion

Research on the relationship between oxidative stress, serum SIRT1 levels, and eGFR in the elderly has been completed. The study was conducted for 6 months at two hospitals in the city of Padang, West Sumatra, Indonesia, and used a sample of 30 people.

The Characteristics of Elderly

Gender, age, body mass index (BMI), systolic and diastolic blood pressures, level of fasting blood glucose (FBG), 2-hour postprandial blood glucose (PPG), uric acid, total cholesterol, HDL cholesterol, low-density lipoprotein (LDL) cholesterol, triglycerides, urea, and creatinine were evaluated characteristics in this study, which included 15 male and 15 female patients (Tabel 1).

Table 1. Characteristics of Elderly Patients

Characteristics	n (%)	Mean (SD)
Gender		
Males	15 (50)	
Females	15 (50)	
Age (year-old)		67.83 (5.54)
BMI (kg/mm ²)		21.08 (0.99)
SBP (mmHg)		132.17 (7.50)
DBP (mmHg)		71.67 (4.79)
FBG (mg/dl)		88.50 (5.84)
PPG (mg/dl)		180.80 (11.86)
Uric acid (mg/dl)		5.72 (0.51)
Total cholesterol (mg/dl)		179.43 (9.81)
HDL cholesterol (mg/dl)		48.50 (6.37)
LDL cholesterol (mg/dl)		110.47 (12.66)
Triglycerides (mg/dl)		115.73 (12.37)
Urea (mg/dl)		40.20 (5.54)
Creatinine (mg/dl)		1.69 (0.48)

Tabel 1 presents the characteristics of 30 elderly people. Characteristics include gender, age, blood pressure, body mass index, fasting blood sugar levels, 2-hour postprandial blood sugar, uric acid, urea, and creatinine levels. In this study, there were 15 males and 15 females. The mean age was 67.83 (5.54) years, and the average body mass index was 21.08 (0.99) kg/m². The mean systolic blood pressure was 132.17 (7.50) mmHg, while the mean diastolic blood pressure was 71.67 (4.79) mmHg. The average FBP is 88.50 (5.84) mg/dl, and the average PPG is 180.80 (11.86) mg/dl. The average uric acid level was 5.71 (0.51) mg/dl. On examination of the lipid profile, the average total cholesterol level was 179.43 (9.81) mg/dl, the average HDL level was 48.50 (6.37) mg/dl, the average LDL was 110.47 (12.66) mg/dl, the average TG 115.73 (12.37) mg/dl. Furthermore, the average urea level was 40.20 (5.54) mg/dl, and the average creatinine was 1.69 (0.48) mg/dl.

MDA Serum Levels In Elderly

The Saphiro-Wilk normality test showed the mean MDA serum levels in this study are distributed normally. The mean value of MDA serum levels in the elderly is 4.57 (1.86) nmol/L (Tabel 2).

Table 2. MDA serum levels in elderly

Variable	n	Mean (SD)
MDA serum (nmol/L)	30	4.57 (1.86)

SIRT1 Serum Levels In Elderly

The result of the Saphiro-Wilk normality test showed SIRT1 serum levels in this study are not distributed normally. In this study, the median SIRT1

serum levels in the elderly is 2.15 ng/μl, with the lowest score being 1.1 ng/μl and the highest score being 6.5 ng/μl (Tabel. 3).

Table 3. SIRT1 serum levels in Elderly

Variable	N	Median (Minimum-Maximum)
SIRT1 Serum (Ng/μl)	30	2.15 (1.1- 6.5)

eGFR In Elderly

The result of the Saphiro-Wilk test for normality showed that data for eGFR value in this study is distributed normally. In this study, we found the mean eGFR in the elderly is 37.35 (10.19) ml/min/1.73m² (Tab. 4). This means that the eGFR in the elderly is below normal (90 ml/min/1.73m² or higher) so it can be said that the elderly sampled suffer from kidney disease. GFR is the total amount of ultrafiltrate produced by the glomeruli in both kidneys in 1 minute.

Table 4. Estimated eGFR in the Elderly

Variable	n	Mean (SD)
eGFR (ml/min/1.73m ²)	30	37.35 (10.19)

Correlation Between MDA Level With SIRT1 Serum In Elderly

The result of the analysis correlation between MDA level with SIRT1 serum in the elderly showed there is a significant correlation in the elderly (p < 0.05) with a direction to negative correlation and moderate correlation (correlation coefficient r = 0.551) (Figure. 1). This showed that there is a statistically significant relationship between the two variables.

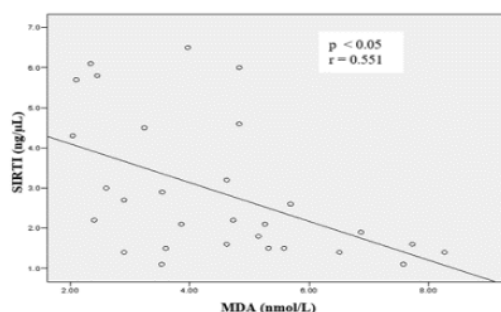


Figure 1. Correlation of MDA Serum Levels and SIRT1 In Elderly

Correlation Of MDA Serum Levels EGFR In Elderly

Correlation analysis in this study used the Pearson correlation test with 1 confidence interval < 0.05. The result of the analysis correlation between MDA serum levels and eGFR in the elderly showed there is a significant correlation (p < 0.05) with a direction to

negative correlation and strong correlation (correlation coefficient $r = 0.633$). This showed that there is a statistically significant relationship between the two variables.

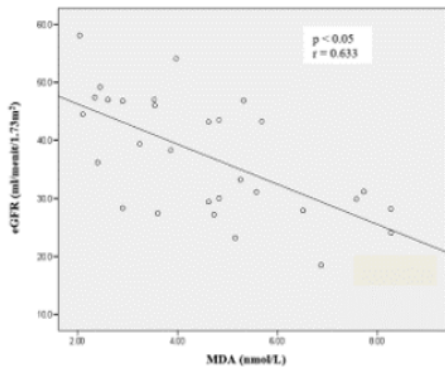


Figure 2. Correlation of MDA Serum Levels and eGFR in Elderly

Correlation Of SIRT1 Serum Levels And EGFR In Elderly

The correlation analysis that was used in this study is Spearman correlation with a confidence interval 0.05. The result of the analysis shows there is a significant correlation between SIRT1 serum levels and eGFR in the elderly ($p < 0.05$) with a direction to positive correlation and moderate correlation (Figure. 3). This showed that there is a statistically significant relationship between the two variables.

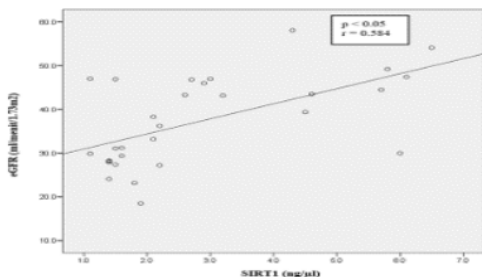


Figure 3. Correlation of SIRT1 serum levels and eGFR in Elderly

Discussion

The MDA level in this study is 4.57 (1.86) mmol/L, higher than the normal range (0.9-1.59 nmol/L) (Tab. 2). This can be caused by aging, which increases oxidative stress and free radicals. Free radicals resulting in damaged cells play an essential role in the aging process. This is supported by a study from (Shields et al., 2021) that proved age is the most potent risk factor for free radical accumulation. The RONS-induced damage buildup is thought to be the cause of age-related

functional deficits, according to the oxidative stress theory of aging (Zbroch et al., 2020). The results (Wan et al., 2023) showed that An increased risk of CDK in the elderly was linked to higher blood MDA levels. Oxidative damage can be caused by either an increase in Reactive Oxygen Species (ROS) production or a decrease in antioxidant defenses.

Proteins, nucleic acids, and other biological macromolecules can be cross-linked and polymerized by the primary by-product of lipid oxidation, MDA, which can also substantially compromise the functionality of crucial mitochondrial enzymes and the mitochondrial respiratory chain complex (Martemucci et al., 2022). Due to an increase in the end product of lipid peroxide and a decrease in antioxidant levels, diseases affecting the elderly are widespread. Oxidative stress is sparked by increased lipid peroxidation in the body, which leads to several illnesses including cancer, cardiovascular and neurogenic diseases, and CDK (Ito et al., 2019). The oxidative stress caused by peroxidation can be assessed using a variety of lipid peroxide end products, including malondialdehyde, oxidized low-density lipoproteins, isoprostanes, neuroprostanes, lipoperoxides, oxysterols (7-ketocholesterol, 7-hydroxycholesterol), and many others (Ali et al., 2022). The weights of the kidneys and thymus peaked earlier than MDA levels and the weights of other organs (Ahsani & Fidianingsih, 2018).

SIRT1 serum levels in this study are lower than the one by (Kumar et al., 2013), which is 4.82 (0.4) ng/ μ l. The result difference is caused by the difference in the sample, age range, and selection criteria of the samples. The study by (Kumar et al., 2013) also proved that the SIRT1 serum level in the elderly is lower compared to younger ones, which is 8.16 (0.87) ng/ μ l. A study of SIRT1 in mice compared the expression of SIRT1 in younger mice (6-month-old) with older mice (24-month-old). In this study, prominent SIRT1 expression is found in the nucleus and cytoplasm of renal tubules in younger mice, whereas in older mice, it showed decreased SIRT1 expression. This study also supports decreasing SIRT1 levels with advancing age (Kwon et al., 2015). SIRT1, also known as the master regulator, is now thought to be the key to the aging process. As people get older, their SIRT1 levels alter, becoming lower in the elderly. Long-term oxidative stress impairs transcription, post-transcription, and translation, and increases degradation, which is why SIRT1 levels dropped (Chen et al., 2020). According to (Kilic et al., 2015) older individuals had a considerable increase in their SIRT1 levels, while the whole population under study showed a significant positive connection between SIRT1 level and age.

Based on Tab.4 the result is corresponding with literature that stated a decrease of eGFR of about 1

ml/min/1.73 m² starting from the age of 40 and a reduction in kidney parenchymal density by 1% every year (Nitta et al., 2013). Many studies found there is decreasing in GFR without any comorbidities in elderly. The preliminary study of the Baltimore Longitudinal Study of Aging observed serial GFR levels in 254 healthy males aged 22 to 97 years old. This study found a decrease in mean GFR of about 0.75 ml/min/1.73 m² every year. The elderly without comorbidities will also experience a decrease in eGFR caused by physiological aging. A decreased eGFR in the elderly does not always indicate some disease manifestations (Epstein, 1996). Several studies have found that adult GFR declines with age (Granerus & Aurell, 1981). In contrast to the results of other studies which state that GFR is influenced by gender, where women's GFR is higher (Poggio et al., 2009) is lower or the GFR value is the same between men and women.

Based on Figure 1, the correlation analysis that was used is the Spearman correlation test with a confidence interval < 0.05. The result of this study fits the literature about the theory of aging, which states that OS is an essential factor associating kidney dysfunction with aging. Specific end products of the process can measure OS because free radicals cannot last long in circulation. The results (Hardiany et al., 2020) showed that the MDA level in the younger group (60-70 years) was slightly higher than in the older group (> 70 years). The aging process affects the structure and function of the kidney (aging kidney), such as kidney vasculature, filtration rate, and tubulointerstitial function. This can explain why the prevalence of chronic kidney disease most commonly happens in the elderly (Denic et al., 2016). SIRT1 is considered to play an essential role in maintaining the balance of the oxidant and antioxidant mechanisms, which is essential aging.

In Figure 2, it can be seen the correlation between serum MDA levels and eGFR in old age. The correlation analysis used was the Pearson correlation test, and the degree of confidence was < 0.05. The results of the analysis showed that there was a significant correlation between serum MDA levels and eGFR in the elderly (p < 0.05) with a negative correlation direction and strong correlation strength (correlation coefficient r = 0.633). Similar studies (Li et al., 2012) have shown that Plasma MDA levels reveal oxidative stress, which is related to the prevalence of MIKF and CKD. High levels of MDA in plasma may link the deterioration of kidney function with age, despite placing a growing burden on the kidney and encouraging a cyclical process of oxidative stress in the body. Oxidative stress was probably a mediator in the relationship between urinary Cd level and reduced eGFR in the general population. These findings imply that kidney impairment brought on by

Cd exposure in the general population can be very well predicted by eGFR (Kim et al., 2019).

Based on Figure 3, it can be seen that there is a correlation between SIRT1 serum levels and eGFR in the elderly. The correlation analysis that was used in this study is Spearman correlation with a confidence interval < 0.05. The results of the analysis showed that there was a significant correlation between serum SIRT1 levels and eGFR in old age. The correlation analysis used was Spearman's correlation test and the degree of confidence was < 0.05. The results of the analysis showed that there was a significant correlation between serum SIRT1 levels and eGFR in the elderly (p < 0.05) with a positive correlation and moderate correlation strength (correlation coefficient r = 0.584). Low SIRT1 levels in the elderly will result in oxidative stress increases, inflammation increases, apoptosis increases, autophagy decreases, Endothelial Nitric Oxide Synthase (ENOS) levels decrease and AT1R expression increases. This causes a disruption in the structure and function of the kidney which can be assessed by a decrease in the glomerular filtration rate (GFR) (Ogura et al., 2021).

Conclusion

This study discusses the correlation of oxidative stress, serum SIRT 1 level, and the estimation of glomerular filtration rate in the elderly. OS in this study was represented by assessing serum MDA levels which were found to be higher in this study. In contrast, this study showed SIRT1 and eGFR levels decreased in the elderly. Furthermore, there was a negative correlation with moderate correlation strength between serum MDA level and serum SIRT1 levels and a strong correlation between serum MDA levels and eGFR in the elderly. Meanwhile, there was a positive correlation with a moderate correlation between serum SIRT1 levels and eGFR in the elderly. SIRT1 serum is suggested to be examined in elderly patients with decreased eGFR, even without comorbidity. As a follow-up, further research is needed regarding the use of SIRT1 activators to increase serum SIRT1 levels.

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Author Contributions

HH contributed to the conceptualization and data curation; EV contributed to Writing-review & editing; Alexander Kam contributed to methodology; RA contributed to writing-original draft.

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Conflicts of Interest

The authors declare no conflict of interest.

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