

Effect of Garlic (*Allium Sativum*) Extract on Hemoglobin Levels in Chronic Hemodialysis Patients

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EFFECT OF GARLIC (*ALLIUM SATIVUM*) EXTRACT ON HEMOGLOBIN LEVELS IN CHRONIC HEMODIALYSIS PATIENTS

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ABSTRACT

Introduction: CKD patients undergoing hemodialysis have increased inflammatory biomarkers. Anemia in CKD is associated with an advanced degree of inflammation while undergoing chronic hemodialysis. Garlic (*Allium sativum*) has anti-inflammatory and antioxidant effects, which are expected to improve the degree of inflammation in CKD patients. This study aims to assess the effect of garlic extract on hemoglobin levels in patients undergoing chronic hemodialysis. **Method:** This study was an experimental study with a double-blind, randomized clinical trial design. This study was a crossover, randomized, placebo-controlled, double-blind trial. The study subjects were 40 stages 5 CKD patients undergoing chronic hemodialysis, randomly divided into two groups, namely the group that received 1000 mg of garlic extract per day (2x500 mg) for six weeks and the group that received placebo, then a 2-week wash-out period. And after that, the two groups were given alternate treatment. Statistical analysis was carried out using the SPSS version 25.0 program. **Result:** A total of 40 subjects participated in the study, 57.5% male. The mean age of the subjects was 48.6 (26-59) years. The results showed that there was a significant difference in Hb levels in the garlic group ($p = 0.047$), where the increase in Hb was from 10.2 (9.2–11.8) mg/dl to 10.23 (8.9–11.6) mg/dl while in the placebo group, there was a decrease in Hb from 10.18 (9.6 – 11.2) mg/dl to 10.05 ± 0.52 mg/dl. **Conclusion:** Garlic extract can reduce levels of inflammation which can then increase hemoglobin levels.

Keywords: Chronic Kidney Disease, Hemodialysis, Hemoglobin, *Allium Sativum*.

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INTRODUCTION

According to Kidney Disease Improving Global Outcomes (KDIGO) in 2012, CKD is defined as abnormalities in kidney structure or function, for > 3 months, with implications for health (Group, 2009). According to the Indonesian Renal Registry (IRR) in 2017, the proportion of the etiology or basic disease of CKD patients is hypertension which ranks first at 36% and diabetic nephropathy or known as diabetic kidney disease is second place (IRR, 2017). In chronic kidney disease (CKD) patients undergoing hemodialysis, there is an increase in proinflammatory cytokines, including IL6, CRP, Haptocidin, TNF- α , and Ferritin (Bacci et al., 2018) (Amore & Coppo, 2002).

Anemia is a common complication of chronic kidney disease (CKD) and is associated with reduced quality of life and increased morbidity and mortality (Portolés et al., 2021). Anemia is more frequent and severe at decreased glomerular filtration rate (eGFR) (Fadhilah, 2016). Cross-sectional analysis of data from the National Health and Nutrition Examination Survey (NHANES) in 2007-2008

² and 2009-2010 revealed that anemia was twice as common in patients with CKD as in the general population (15.4% vs. 7.6) (Zota et al., 2014). The prevalence of anemia increases with the development of CKD: 8.4% in stage 1 to 53.4% in stage 5.

Garlic has several bioactive compounds (Moulia, 2018). The main organosulfur component of garlic is γ -glutamyl-S-alkyl-cysteine, which can be hydrolyzed and oxidized to S-alkyl-cysteine sulfoxide (alliin). Garlic extract has biological activity, especially as an anti-inflammatory and antioxidant (Ried & Fakler, 2014) (El-Saber Batiha et al., 2020). A previous study found that giving garlic extract to patients with chronic kidney failure with CAPD reduced the proinflammatory cytokines IL-6 and TNF- α (Kendenan et al., 2021). The anti-inflammatory and antioxidant effects of garlic are expected to improve the degree of inflammation in CKD patients so that they can improve hemoglobin levels. This study aims to assess the effect of garlic extract on hemoglobin levels in patients undergoing chronic hemodialysis at RSUP Dr. Mohammad Hoesin Palembang.

¹ METHODS

This study used a *Randomized, Controlled, Double-Blind Crossover Trial design*. This study was a crossover, randomized, placebo-controlled, double-blind trial. The study subjects were 40 stages 5 CKD patients undergoing chronic hemodialysis, randomly divided into two groups, namely the group that received 1000 mg of garlic extract per day (2x500 mg) for six weeks and the group that received a placebo, then a 2-week wash-out period. And after that, the two groups were given alternate treatment. The study was conducted in the Hemodialysis Room of Dr. Moh Hoesin Hospital, Palembang. Data collection was carried out in January 2022. Each subject received informed consent before data collection. The inclusion criteria included all chronic hemodialysis patients undergoing routine hemodialysis twice a week with a duration of 4-5 hours each session, more than three months and a maximum of 2 years, aged ≥ 18 years to 60 years, willing to participate in the study by signing an informed consent form. Consent. Exclusion criteria included patients suffering from acute infections, receiving steroid therapy, suffering from autoimmune diseases, suffering from fluid overload, being infected with Covid 19, and being allergic to garlic. Each subject had blood drawn before hemodialysis after administering garlic extract or placebo.

Sampling was carried out by blocking selection. Patients who were going to undergo hemodialysis who met the inclusion criteria were taken as samples with numbers 1,2,3,4 based on the order in which the patients arrived until they met the specified number. Determining whether the model was included in the garlic extract group or the placebo group was carried out by a third party; the researchers and patients needed to learn.

All CKD patients undergoing hemodialysis at the RSMH Hemodialysis Unit, fulfilling the inclusion criteria and not meeting the exclusion criteria, will be randomized into two groups, namely the group that received garlic extract and the group that received placebo and then examined in stages. Garlic extract medicine (*allium sativum*) 2x500 mg capsules. This study consisted of two phases. In phase I, group A consisted of 20 samples that received garlic extract (from now on referred to as the garlic group), and group B consisted of 20 pieces that received a placebo. The results of both groups were observed for six weeks. This is followed by a 2-week wash-out period. Then in phase II, group A and group B received the alternate treatment.

Data processing and analysis using the SPSS 25 for Windows program. The data is presented in the form of tables and graphs. The information is tested to determine whether the distribution is normal; if the distribution is normal, then parametric and non-parametric tests are used if the data distribution is not normal. The data analysis plan will be carried out in three stages: univariate, bivariate, and multivariate. Univariate data is divided into numerical and categorical data. If numerical information uses the Shapiro-Wilk normality test and Levine's homogeneity test, and if it is normally distributed, then the data will be presented with the mean \pm standard deviation. It will be presented with the median (min-max) if it is not normally distributed.

The bivariate analysis will use the chi-square test on categorical data. It will use a T-test (if normally distributed) or Mann Whitney (if not normally distributed) on categorical and numerical data and then paired T-test (if normally distributed)) or Wilcoxon test (if not normally distributed) to see analysis before and after treatment. Multivariate will use post hoc analysis to analyze all independent and confounding variables that correlate with the dependent variable in this study. It is hoped that this confounding factor will not become a research bias.

RESULTS AND DISCUSSION

In Table 1, 40 subjects participated, dominated by 23 men, of which 12 people (60%) received garlic extract, while there were 17 women, of which eight people (40%) received garlic extract. Garlic extract in phase 1. The median age in the garlic group was 45.5(28-58) and 55(26-59) in the placebo group.

Table 1. General characteristics of research subjects

	Group			p. s
	Total (n=40)	Garlic (n=20)	Placebo (n=20)	
Age	48.6 (26-59)	45.5 (28-58)	55 (26-59)	0.001
Gender				
Man	23 (57.5%)	12 (60 %)	11 (55 %)	
Woman	17 (42.5%)	8 (40 %)	9 (45 %)	

p: p-value before and after treatment. p': p-value after treatment between groups. a) Paired T-test
b) Unpaired T-test, significant if $p < 0.05$

In Table 2. there is a significant difference in Hb levels in the garlic group ($p = 0.047$), where the increase in Hb from 10.2 (9.2–11.8) mg/dl to 10.23 (8.9–11.6) mg/dl while in the placebo group, there was a decrease in Hb from 10.18 (9.6 – 11.2) mg/dl to 10.05 \pm 0.52 mg/dl. Statistically, there was a significant difference between Hb in the garlic and placebo groups after treatment, with a p-value = 0.022.

Table 2. Characteristics of Hemoglobin Levels

	Group						
	Garlic (n=40)			Placebo (n=40)			p'
	Before	After	p.s	Before	After	p.s	
Hemoglobin	35.41 \pm 22.08	45.75 \pm 25.73	0.041a –	48.75 \pm 23.81	46.02 \pm 25.12	0.14a –	0.011b –

p: p-value before and after treatment. p': p-value after treatment between groups. a) Paired T-test
b) Unpaired T-test, significant if $p < 0.05$

The mean age of CKD patients undergoing chronic hemodialysis was 48.6 years, with the proportion mostly male. The average age of CKD patients differs from data from the Centers for Disease Control and Prevention (CDC), with an average age of 65 years (Hsu et al., 2016). The difference in age in the placebo group ($p = 0.001$) was signed between the garlic extract group and the placebo group, but patients would be crossover so that all subjects would receive the same treatment.

In the study of Ibrahim et al. (2014), there was an increase in the proinflammatory cytokines IL-6, CRP, and Hepsidin in CKD patients undergoing hemodialysis and was associated with decreased hemoglobin levels in the subjects (Ibrahim et al., 2014). In a study by Akchurin et al., it was found that increased IL-6 levels correlated with the incidence of anemia in subjects with CKD (Akchurin et al., 2019).

A study by Zare et al. (2019) in patients with continuous ambulatory peritoneal dialysis (CAPD) found a significant decrease in serum IL6 levels in 42 PD patients after eight weeks of garlic extract administration (Zare et al., 2019). Research by Kendenan M et al. (2019) also showed that with continuous ambulatory peritoneal dialysis (CAPD) in CKD patients, after giving 2x500 mg of garlic extract for six weeks, the results showed a decrease in IL-6, which was significant with ($p = 0.005$) compared to the placebo group (Kendenan et al., 2021).

In this study, it was found that garlic extract can reduce the inflammatory process and can further increase hemoglobin levels in CKD. In patients after giving onions, hemoglobin levels improved significantly compared to the placebo. This study follows previous research that hemoglobin is affected by inflammation, then patients undergoing hemodialysis experience a process of continuous activation of proinflammatory cytokines and an increase in proinflammatory cytokines such as CRP, TNF- α , Ferritin, and Hepsidin as an anti-inflammatory and antioxidant, Garlic extract plays an important role in reducing inflammation. According to research (Kendenan et al., 2021), there is a decrease in IL-6. Research (Ibrahim et al., 2014) has that CKD patients with high levels of IL-6, CRP, and Hepsidin are associated with anemia in CKD. This study proved that after giving garlic extract 2x500 mg for six weeks, there was an increase in hemoglobin levels in CKD patients with chronic hemodialysis.

CONCLUSION

Based on the study's results, the following conclusions are drawn from this study. There is effectiveness of garlic extract in increasing hemoglobin levels in patients with stage V CKD undergoing chronic HD at Moh Hoesin Hospital Palembang.

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