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The relationship between water intake and progressivity

Glomerular filtration rate of chronic kidney disease patients

MUNAQISAH[1], Haerani A RASYID[2], AMINUDDIN[2], Suryani AS'AD[2], Nurpudji A. TASLIM[2], Nur ASHARI[2]

1 Department of Nutrition, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia.
2 Clinical Nutrition Specialist Program, Department of Nutrition, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia.

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ABSTRACT

Introduction and objectives: The increasing incidence of chronic kidney disease in Indonesia and several previous studies assessing the relationship of water intake by evaluating all inputs including total daily water intake as well as output (urine volume) found that there is a role of fluid input on the progressivity of CKD which shows that patients who drink too much or little water tend to progress the failure of kidney function faster so we raised this study to determine and important implications for education of CKD patients regarding water intake.

Methods: This prospective observational study entails the enrollment of CKD stage 3a, 3b and 4 outpatients from Hypertension Kidney Poluclinic at Dr. Wahidin Sudirohusodo Hospital and Makassar Satellite Hospital, The search for research subjects from October to December 2023 (11 subjects), followed by observation and data collection lasted for a duration of 3 months (10 subjects) and was analyzed from March to April 2024. The daily average water intake was measured using a 2-liter tumbler and 24-hour urine volume was measured using a chamber pot and the results were recorded in a food diary. Creatinine levels (LFG) were collected from red blood cells and urine osmolarity from 24-hour urine.

Results: The correlation between average daily water intake and delta creatinine was r= 0.151 (p=0.677), average daily water intake and delta eLFG was r= -0.196 (p=0.588), average daily water intake and 24-hour total urine volume was r=0.625 (p=0.053), average daily water intake and delta urine osmolarity was r= 0.608 (p=0.062). A p-value exceeding 0.05 indicates an insignificant correlation.

Conclusions: The physiological function of the kidneys can still function properly as evidenced by the amount of water given where the more the amount of water drunk, the more the amount of urine and urine osmolarity decreases. This study has not been able to prove the research hypothesis with research limitations.

KEYWORDS

Hydration, Renal Function, Fluid Consumption, Kidney Health, Renal Insufficiency.

INTRODUCTION

Chronic kidney disease (CKD) represents a gradual deterioration in kidney function spanning months or years. According to the Kidney Disease Improving Global Outcomes (KDIGO) 2012 guidelines, CKD is characterized by an abnormality in kidney function or structure persisting for over three months, with consequential health implications, manifested through the presence of one or more signs of kidney damage or the kidney's impaired ability to carry out its functions[1-4].

CKD commonly coexists with hypertension and diabetes, necessitating patients to adhere to a regimen involving multiple medications, dietary restrictions, and fluid control. Adherence to dietary and fluid limitations is pivotal for CKD patients, with dietary adjustments playing a crucial role in preserving kidney function[4,5] Dietary modifications encompassing alterations in energy, macronutrient intake, minerals, and fluids have been

Correspondencia:
munamizwar@gmail.com
haeraniabdurasyid@yahoo.com

shown to significantly mitigate the heightened risks of mortality and morbidity associated with CKD[5].

The hydration aspect of nutrition warrants particular attention. Despite various guidelines recommending different daily water intakes, the evidence supporting these recommendations is relatively weak. Nevertheless, research has elucidated a correlation between water intake and kidney function, with adequate hydration potentially offering protection against kidney disease. Studies indicate that increased water intake is linked to a decreased risk of kidney disease, while consumption of sugary drinks may elevate the risk. Furthermore, higher water intake is associated with a reduced risk of kidney stone recurrence, whereas sugary drink consumption may heighten the recurrence risk[6-8].

Research conducted by Wagner et al. and several prior studies has highlighted the complex relationship between water intake and CKD progression, influenced by factors such as urine osmolarity and volume. While adequate water intake generally correlates with a lower CKD prevalence in the general population, findings in CKD patients may vary. Some studies suggest that elevated urine osmolarity, possibly due to insufficient fluid intake, could exacerbate kidney function decline, whereas others propose that reduced urine osmolarity, potentially resulting from increased fluid intake, might also accelerate CKD progression[6,9].

Classification of CKD is predicated on etiology, glomerular filtration rate (GFR) category, and albuminuria category. Determination of CKD etiology hinges on the presence or absence of systemic disease and the observation of kidney disorder localization or anatomical pathology findings[6,10-13].

LITERATURE REVIEW

Chronic Kidney Disease

Chronic kidney disease denotes a gradual deterioration in kidney function occurring over months or even years. According to the 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines, CKD is delineated as an anomaly in kidney function or structure persisting for more than three months, with health implications marked by the presence of one or more indicators of kidney damage, or whether such damage exists, and the kidneys' capacity to perform their functions[11-13].

The classification of CKD hinges on factors such as its underlying cause, the glomerular filtration rate (GFR) category, and the albuminuria category. The etiology of CKD is ascertained by assessing the presence or absence of systemic diseases and scrutinizing the location of kidney pathology or anatomical finding[10,14].

Stage 1 CKD: In this early stage, kidney function is mildly impaired. The estimated glomerular filtration rate (eGFR) is greater than or equal to 90 mL/min/1.73m². Stage 2 CKD: Kidney function is still relatively preserved, but eGFR ranges from 60 to 89 mL/min/1.73m². Stage 3a CKD: eGFR falls between 45 and 59 mL/min/1.73m². At this point, symptoms may become more noticeable, and patients are at moderate risk for progression. Stage 3b CKD: eGFR is between 30 and 44 mL/min/1.73m². This stage represents moderate to severe kidney function loss. Patients are at high risk for CKD progression and heart disease. Stage 4 CKD: eGFR ranges from 15 to 29 mL/min/1.73m². Stage 5

Table 1. Degree of CKD and Risk of Progression

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				**Persistent albuminuria categories, description and range**		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR Categories (ml/min/ 1,73 m²) Description and range	**G1**	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green, low risk (if no other markers of kidney disease, no CKD); yellow, moderately increased risk; orange, high risk; red. very high risk.

CKD: Also known as end-stage renal disease (ESRD), eGFR is less than 15 mL/min/1.73m² [9,11,15].

Water Needs in PGK

In human studies, several observational investigations have highlighted a positive correlation between increased water intake and enhanced kidney function. For instance, in a prospective cohort study involving 2000 Canadian adults without renal ailments, heightened urine volume at baseline corresponded with a decelerated renal decline during subsequent monitoring. Likewise, in two cross-sectional analyses of Australian and American cohorts, greater self-reported water consumption correlated with improved kidney function. Recently, researchers pinpointed chronic dehydration, stemming from hot climates, as a primary contributor to the chronic kidney disease (CKD) surge in Central America, thereby reinforcing the notion of the protective impact of increased water intake on kidney health. Nevertheless, conclusive evidence from rigorously designed and large-scale randomized controlled trials is warranted to ascertain whether elevated water intake can effectively mitigate the pace of kidney function decline[2,7,16].

Kidney function naturally diminishes with age, as the kidneys lose their capacity to concentrate urine, thereby indicating an augmented necessity for adequate water intake to uphold optimal kidney function (IOM, 2005; EFSA, 2010). Benelam & Wyness (2010) have documented numerous health advantages associated with sufficient water consumption among older adults, encompassing a reduction in falls and constipation. Furthermore, a review by Armstrong (2012) revealed hydration to be linked with diminished risks of chronic kidney disease, fatal coronary heart disease, hypertension, venous thromboembolism, cerebral infarction, and dental ailments, albeit the evidence remains somewhat tenuous and relies on limited studies. A particular cross-sectional study conducted in Australia highlighted a significantly reduced risk of chronic kidney disease among participants in the highest quintile of fluid intake (3.3 L/day) compared to those in the lowest quintile (1.7 L/day).(3,6,17)

Relationship Between Water Intake and GFR

Fluid consumption is beneficial for kidney function. Choi et al found an inverse linear relationship between fluid intake and CKD prevalence. The higher the fluid intake the lower the risk, with an intake of 3.3 L/day associated with a 30–50% reduction compared with an intake of 1.7 L/day. Several observational studies examined the role of water intake in the development of CKD. Two large studies report that higher fluid intake and urine volume can preserve kidney function. Clark et al in a prospective Canadian cohort of 2,148 participants followed up for 6 years showed that the estimated rate of decline in glomerular filtration rate (GFR) was inversely related to the increase in 24-hour urine volume. For each litre of increase in 24-hour urine volume from <1 L to >3 L (stratified by quartiles), the annual percentage decrease in GFR decreased by 1.3, 1.0, 0.8, and 0.5%, respectively[18-21].

In another study, Strippoli et al. in 2011 conducted two cross-sectional Australian population-based studies. The proportion of participants who completed a food frequency questionnaire (FFQ) and had a GFR measurement was 2,744/3,654 (75.0%) for the first survey and 2,476/3,508 (70.6%) for the second survey. CKD occurs in 12.4-23.5% of men and 14.9-28.7% of women (mean age 66.4-65.4 years). Participants in the highest quintile of fluid intake (3.2 L/day) had a significantly lower risk of CKD (odds ratio 0.5; 95% CI 0.32 to 0.77, p for trend=0.003). There was a significant inverse linear relationship between self-reported daily fluid intake volume and CKD prevalence. They concluded that higher fluid intake appeared to protect against CKD[22].

The relationship between water intake and estimated glomerular filtration rate (GFR) has been investigated in several observational studies and results have been mixed. In a retrospective analysis of adult patients with CKD in the Modification of Diet in Renal Disease study, higher urine volumes were associated with greater reductions in GFR, however, this association was not significant after controlling for the use of diuretics and antihypertensive medications. In contrast, in a prospective cohort study of adults free of CKD at study entry, higher urine volumes at baseline were associated with a slower decline in GFR over 7 years and those with the largest urine volumes (>3L/day) did not show a rapid decline in GFR (defined as a decline≥5%/year)[23-27].

METHODS

Research design

This research is a prospective observational study of CKD stage 3a, stage 3b and stage 4 outpatients at the Hypertension Kidney Polyclinic at Dr Wahidin Sudirohusodo Hospital Makassar and Makassar Satellite Hospital

Place and time

This study was conducted at Dr. Wahidin Sudirohusodo Hospital Makassar and Makassar Satellite Hospital, where the search for research subjects from October to December 2023, followed by observation and data collection lasted for 3 months and data were analyzed from March to April 2024.

Research Sample

The research sample was the total sampling of CKD patients who met the inclusion criteria and were accessible to researchers during the research period

Inclusion Criteria

CKD stage 3a, 3b and 4 patients who seek treatment at the RSWS Polyclinic or Makassar Satellite Hospital. Age >18 years.

The estimated glomerular filtration rate (GFR) is between 15-60 mL/minute/1.73 m2 at Prodia Makassar Laboratory. No hemodialysis and no history of previous kidney transplantation. Patients can communicate well, understand and provide written consent to participate in this research

Exclusion Criteria

There has been education by doctors to limit the volume of water intake. Symptoms of oliguria in the last 1 week. Currently taking antidiuretics. Gastrointestinal diseases or disorders (diarrhea, vomiting, inflammatory bowel disease and gastrointestinal bleeding) and respiratory diseases. Pregnant or breastfeeding. The subject has clinical symptoms of oedema or ascites. Subject died.

Research Procedures

The sample consisted of 10 participants. Data collection was carried out in 2 stages. First, screening is carried out to find samples, then samples are determined that meet the inclusion and exclusion criteria,

Second, collecting data from all variables to be studied, where water intake data uses a 2 liter tumbler to measure daily water intake by filling the 2 liter tumbler completely with water every day when the subject wakes up in the morning (for example at 5 am) then water intake, including when the subject wants to make juice/tea/coffee, is taken from the tumbler and the rest is recorded (at 5 am the next day) in the food diary, then every 1 working day and 1 weekend every week for 3 months (24 recording times). Data on 24-hour urine volume using a urine bedpan by discarding the first urine, then the next urine until the first urine the next day is collected using a urine bedpan and recording the 24-hour urine volume in litres in the *food diary* (for example: 1/9/2023 at 7 am urine is collected until 2/9/2023 at 7 am), then every 1 weekday and 1 weekend every week for 3 months (24 recordings).

Measurement of urea/creatinine (GFR) levels was carried out at the beginning and end of the study by taking blood samples at the Prodia Makassar Laboratory where before inserting the syringe, the blood collection location was cleaned with an alcohol swab and then left to dry. Ensure that the stabbing site is free from wounds and scars. The blood taken is venous blood through the median cubital vein or through a double lumen catheter. 5 ml of blood was taken and stored in a sample tube without EDTA. Urine osmolarity measurements were carried out at the beginning and end of the study where 24 hour urine samples were collected and collected by discarding the first urine, then the next urine until the first urine the next day was collected using bagged urine which had been provided by the Prodia Makassar laboratory (for example: 1/9 /2023 at 8 am urine is collected until 2/9/2023 at 8 am) and the 24 hour urine volume is recorded in liters, then the pot containing the urine is taken to the Makassar Prodia laboratory which will then be sent to the Harapan Kita Heart Hospital laboratory, Jakarta for analyzed.

Research Subject Consent

This research has received approval from the Health Research Ethics Commission (KEPK) of the Faculty of Medicine, Hasanuddin University with Number: 824/UN4.6.4.5.31/PP36/2023 and a research license from Human Resources, Education and Research of RSUP. Wahidin Sudirohusodo with Number: DP.04.03/D.XIX.2/22321/2023 and a research license from the manager of education and research at UNHAS Hospital with Number: 13669/UN4.24.1.1/PT.01.04/2023.

Data analysis

The data obtained is collected based on the type of data and then the appropriate statistical method is selected. Correlation test with Pearson if the data is normally distributed or Spearman correlation if the data is not normally distributed. The data normality test uses Shapiro Wilk because the sample is < 50.

RESULTS

The research findings are presented in Table 2, which outlines the characteristics of the sample under observation, including the number of individuals (n) and the percentage (%) for each variable category. The mean age of the participants was 52.70 years, with a standard deviation of 10.26 years, indicating the spread of data from the mean. The median age, representing the middle value in the data set, was 54 years. The age distribution ranged from 40 to 67 years, with most participants falling within a similar age range.

The average Body Mass Index (BMI) was 23.60, with a standard deviation of approximately 3.77. The median BMI was 23.80, with values ranging from 17.20 to 30.30. Regarding gender (JK), out of the total 10 individuals, 7 (70%) were men and 3 (30%) were women. In terms of employment status, 7 (70%) were employed, while 3 (30%) were not.

Regarding health habits, 5 individuals (50%) were smokers, and an equal number were non-smokers. Only 2 individuals (20%) reported alcohol consumption, while the remaining 8 (80%) did not. Hypertension (HT) was prevalent among 9 individuals (90%), while 1 (10%) did not have hypertension. Diabetes Mellitus (DM) affected 3 individuals (30%), while 7 (70%) did not have it. Similarly, only 1 individual (10%) experienced nasopharyngeal carcinoma (NPC), hyperuricemia, and dyslipidemia, respectively, while the majority did not have these conditions.

Figure 1 depicts the correlation between average daily water intake and delta creatinine, indicating a weak positive correlation (0.151) with a p-value of 0.677. Figure 2 illustrates

Table 2. Characteristics of research subjects

Characteristics		n (%)
Age		52.70 [10.26]
BMI		23.60 [3.77]
Gender	Man	7 (70.0)
	Woman	3 (30.0)
Work	Work	7 (70.0)
	Doesn't work	3 (30.0)
Smoke	Yes	5 (50.0)
	No	5 (50.0)
Alcohol	Yes	2 (20.0)
	No	8 (80.0)
Hypertension	Yes	9 (90.0)
	No	1 (10.0)
Diabetes	Yes	3 (30.0)
	No	7 (70.0)
Nasopharyngeal carcinoma	Yes	1 (10.0)
	No	9 (90.0)
Hyperuricemia	Yes	1 (10.0)
	No	9 (90.0)
Dyslipidemia	Yes	1 (10.0)
	No	9 (90.0)
Total		10 (10.0)

Data are presented as n (%) or mean [SD].

the correlation between water intake and glomerular filtration rate delta, showing a weak negative correlation (-0.196) with a p-value of 0.588. Figure 3 displays a relatively strong positive correlation (0.625) between water intake and 24-hour urine output, with a p-value of 0.053. Figure 4 demonstrates a strong negative correlation (0.608) between water intake and urine osmolarity delta, although the p-value (0.062) is slightly above 0.05, suggesting insignificance

DISCUSSION

Based on the analysis of Figure 1, it is evident that there is no significant correlation between average daily water intake and creatinine levels (r = 0.151, p = 0.677). Despite the lack of statistical significance, there appears to be a weak positive correlation between water intake and creatinine levels, suggesting that higher water consumption is associated with a slight decrease in creatinine values. However, it's important to note that water intake does not directly impact changes in creatinine levels. Creatinine is a byproduct of muscle metabolism excreted by the kidneys, commonly used as an indicator of kidney function. The findings indicate that other factors such as physical activity, diet, or underlying health conditions may play a more significant role in determining creatinine levels[15,28-31].

Moving on to Figure 2, the correlation analysis between average daily water intake and glomerular filtration rate (GFR) indicates a weak negative correlation (r = -0.196, p = 0.588). Although the correlation is not statistically significant, there appears to be a trend towards a weak negative relationship between water intake and changes in GFR values. However, this suggests that there is minimal correlation between total water intake and changes in GFR, which is an important parameter in assessing kidney function[9,15].

Regarding Figure 3, the research findings demonstrate that higher water intake correlates with increased urine production. Clinically, this suggests that individuals with higher water intake tend to excrete more urine, indicating healthy kidney function. However, in patients with kidney failure, decreased urine production may result from increased water intake, leading to fluid retention. Changes in body fluid requirements, such as physical activity or environmental conditions, can also influence the relationship between water intake and urine production[2,9,15].

Moving to Figure 4, a strong negative correlation is observed between average daily water intake and urine osmolarity (r = -0.608, p = 0.062). This indicates that higher water intake leads to lower urine osmolarity, suggesting dilution of urine. However, despite the numerical strength of the correlation, the p-value suggests that this relationship does not reach statistical significance. Hence, while there is a trend towards a relationship between water intake and changes in urine osmolarity, further statistical evidence is required to validate this conclusion[9,27].

In conclusion, while there are trends suggesting associations between water intake and various kidney function parameters, additional research with larger sample sizes and controlled factors is needed to establish conclusive evidence. Notably, Hebert et al.'s study underscores the importance of fluid intake in kidney disease progression, emphasizing the role of urine osmolality and volume in delaying kidney disease progression, even in patients without polycystic kidney disease (PKD)[8].

LIMITATIONS

The sample taken was a sample of new patients diagnosed with stage 3a, 3b and 4 CKD so the number of subjects successfully recruited was small.

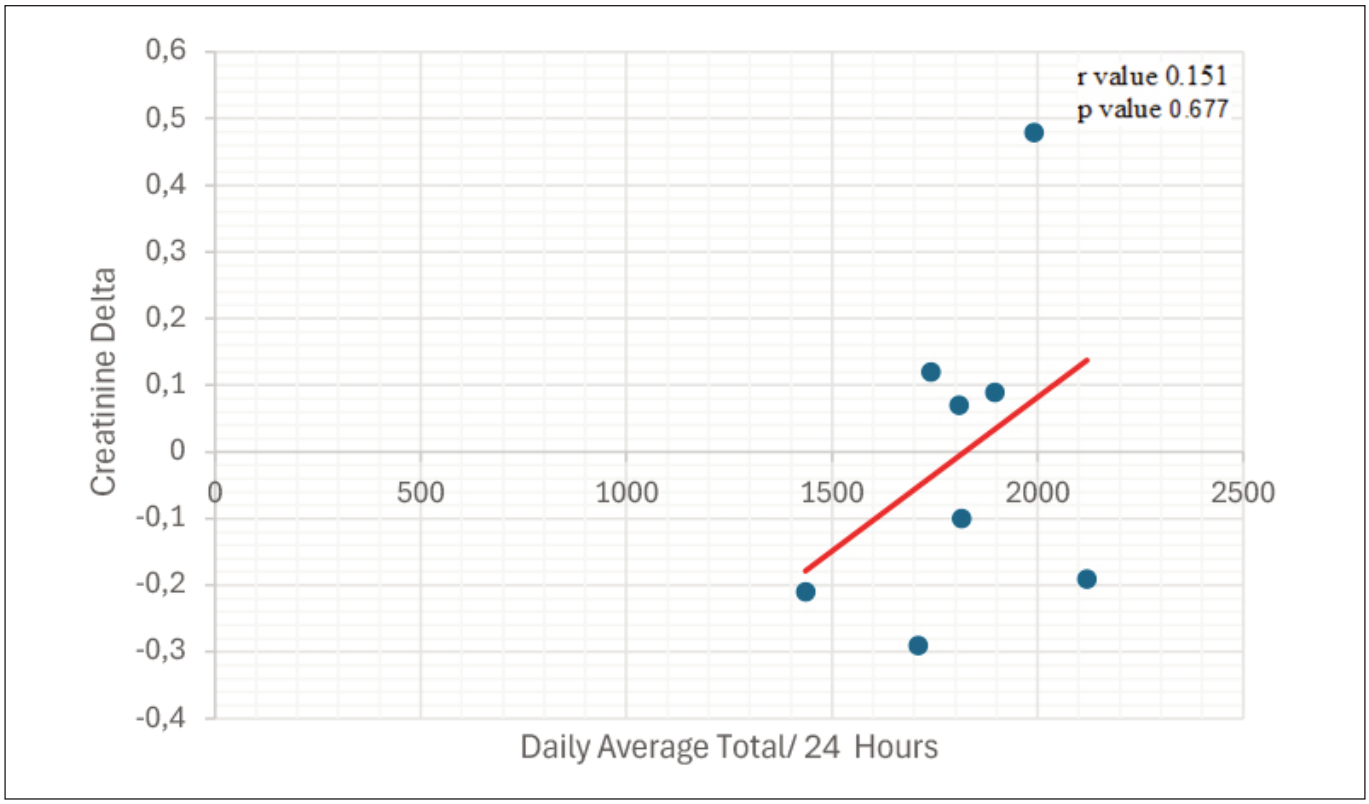

Figure 1. Correlation between average daily water intake and delta creatinine

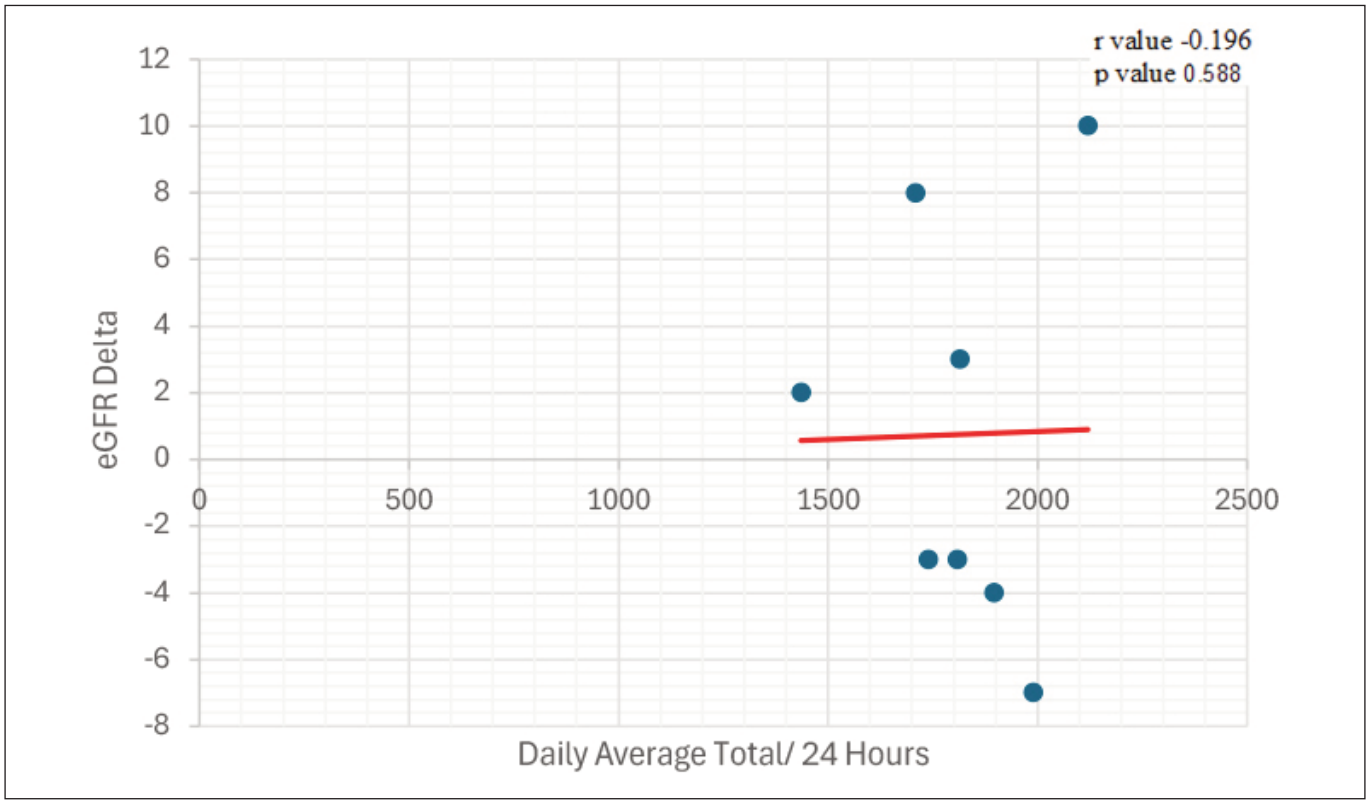

Figure 2. Correlation between average daily water intake and glomerular filtration rate delta

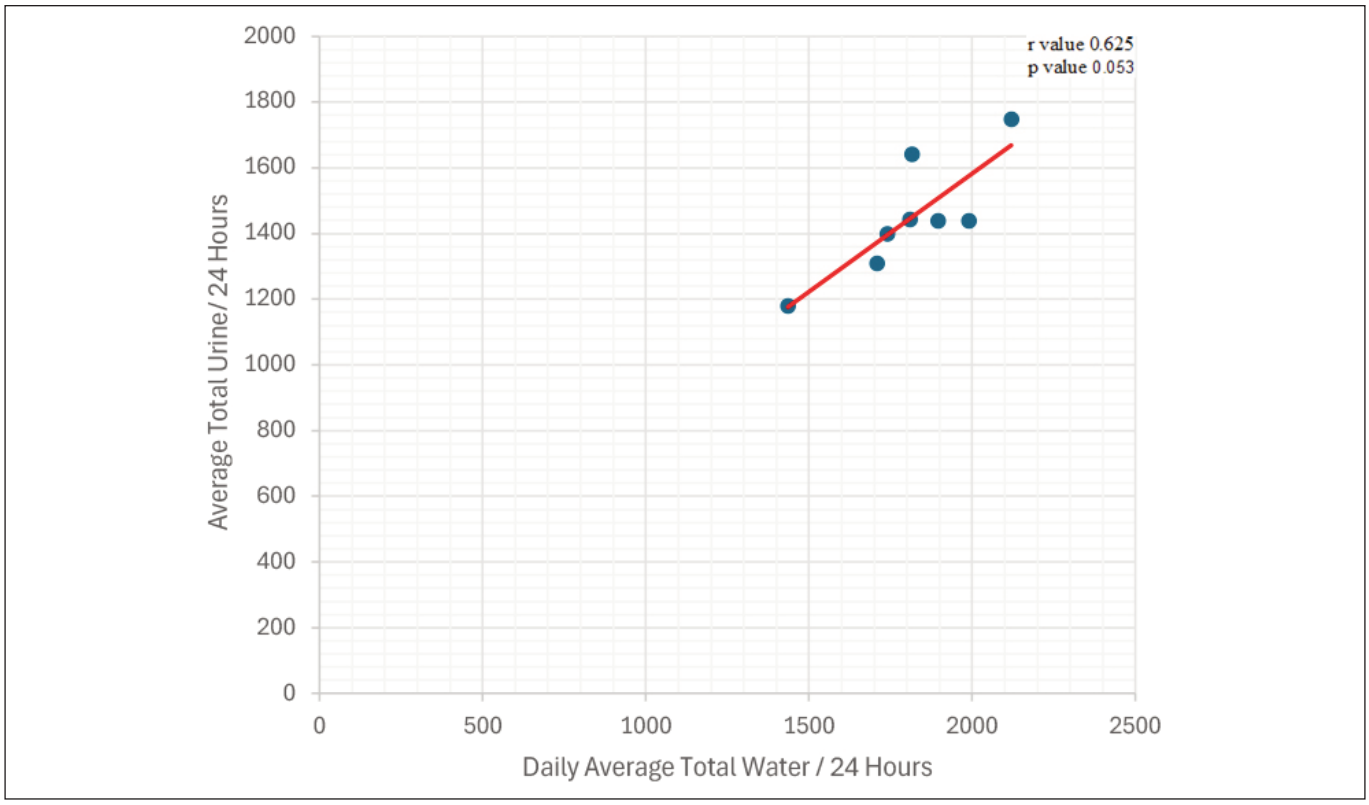

Figure 3. Correlation between average daily water intake and average 24 hour total urine

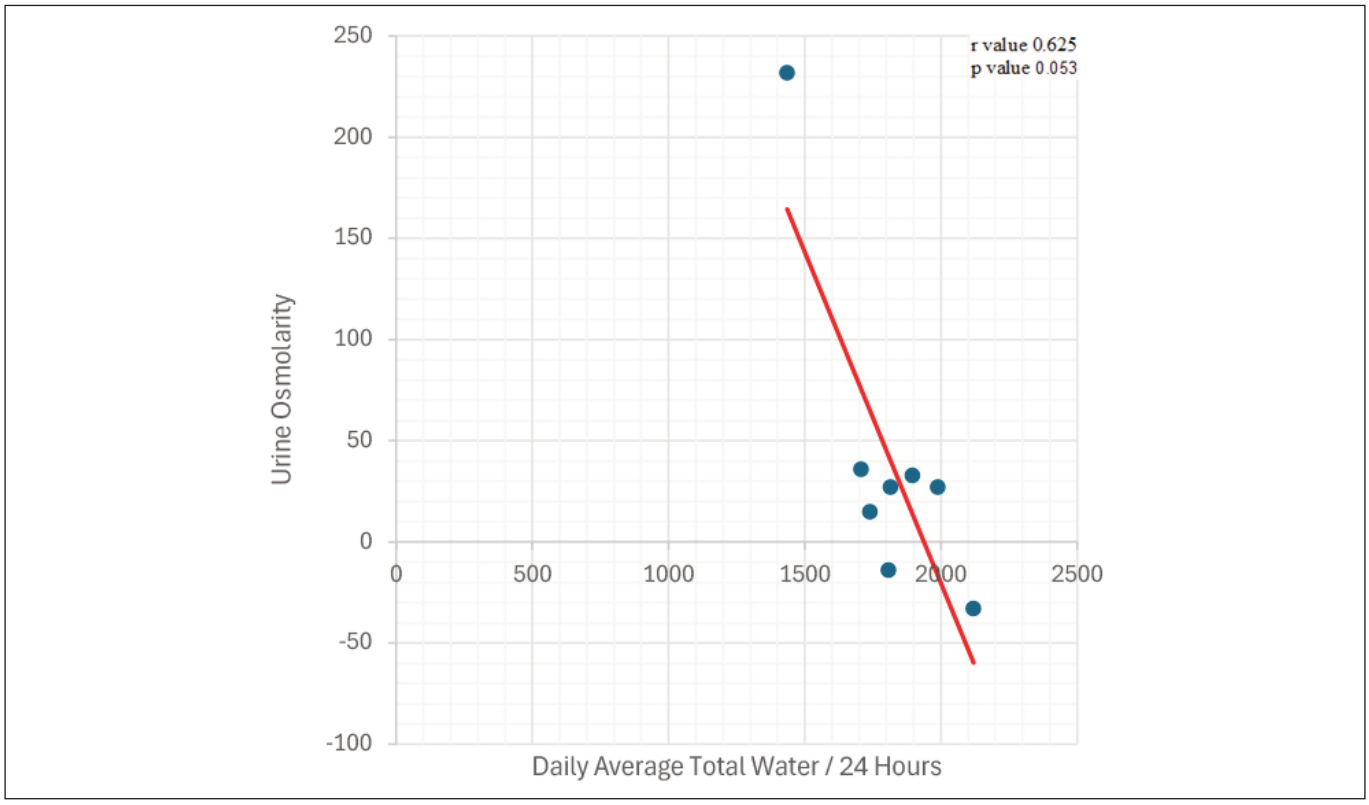

Figure 4. Correlation between average daily water intake and urine osmolarity delta

The study time was short so the number of patients could not meet the criteria 3.

CONCLUSION

The physiologically, kidneys can still function properly as evidenced by the amount of water given where the more the amount of water drunk, the amount of urine and urine osmolarity decreases[9,15].

This study has not been able to prove the research hypothesis about the relationship between water intake with 24-hour urine volume, urine osmolality and LFG progressivity of stage 3a, 3b and 4 CKD patients with research limitations.

RECOMMENDATION

Based on the results of this research, it can be recommended that further research needs to be carried out with more subjects and a longer time to assess water intake on the progressivity of LFG of CKD patients stages 3a, 3b and 4 so that it can provide more generalizable and accurate results.

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