

تأثير نوعية المياه المتناولة على وظائف الكلى لدى مرضى الكلى: دراسة في غرب ليبيا

أ.سالم علي إبراهيم عتيق

قسم المختبرات، كلية التكنولوجيا الطبية، جامعة الجفارة، ليبيا

salemateeg13@gmail.com

The impact of the quality water intake on renal functions in kidney disease patients: A study in Western Libya

Salem Ali Ibrahim Ateeg

Department of Laboratories, Faculty of Medical Technology, Al-Jaffara University, Libya

تاريخ النشر: 2023-12-26

تاريخ القبول: 2023-12-15

تاريخ الاستلام: 2023-11-23

الملخص:

نظرا لارتفاع معدلات الإصابة به وانتشاره في جميع أنحاء العالم، وفي أماكن محددة في ليبيا، فقد اكتسبت أمراض الفشل الكلوي أهمية متزايدة بين الباحثين. على الرغم من أن هذا المرض يمكن أن يحدث نتيجة للتأثير المشترك لعوامل الخطر الوبائية والكيميائية الحيوية والتمثيل الغذائي والوراثي، فإن أحد العوامل المهمة التي تم أخذها في الاعتبار في هذه الدراسة هو استهلاك المياه الجيد. يمكن أن تشير تركيزات الكرياتينين ونيروجين اليوريا في الدم (BUN) إلى وظيفة الكلى. هدف الدراسة: تهدف الدراسة الحالية إلى تقييم نوع مياه الشرب التي يستهلكها مرضى الكلى بانتظام عن طريق قياس تركيز الكرياتينين واليوريا في عينات البلازما والبول.

المنهجية: شملت الدراسة 97 مريضاً من مركز الزاوية لأمراض الكلى ومستشفى الزهراء في ليبيا، مقسمين إلى أربع فئات عمرية. وأجابوا على استبيان حول معلوماتهم الشخصية، ونوعية مياه الشرب، ومستويات اليوريا والكرياتينين بعد غسل الكلى. تم جمع عينات الدم، ثم نسجها في جهاز الطرد المركزي. تم تحليل البيانات باستخدام Microsoft Excel وجمعها من المعلومات الشخصية. النتيجة+. ووجدت الدراسة أن 25.77% من العينة في الزاوية كانوا إناث، بينما في الزهراء 18.18% إناث. وفي الزاوية بلغت نسبة الذكور 23.70% من العينة، بينما بلغت نسبة الذكور في الزهراء 28.86%. وكشفت الدراسة أن الفئة العمرية 35-55 سنة كانت لها النسبة الأعلى (46.39%)، تليها الفئة العمرية 55+ (40.20%)، ثم الفئة العمرية 15-35 سنة (13.40%)، على ألا تقل الفئة العمرية عن 15 سنة. قامت الدراسة بتقييم وظائف الكلى عن طريق تقدير محتوى اليوريا والكرياتينين في الدم. أظهرت النتائج زيادة معنوية في مؤشرات وظائف الكلى بعد غسل الكلى، في حين لم يلاحظ أي فرق كبير في مستويات الكرياتينين. ووجدت الدراسة أن معظم المرضى يحتاجون إلى غسل الكلى ثلاث مرات أسبوعياً بسبب الفشل الكلوي، اعتماداً على شدة المرض ومرحلته. الاستنتاج: يحتاج مرضى الكلى في غرب ليبيا إلى مياه شرب نظيفة وآمنة لمنع تدهور حالة مريض الكلى. هناك حاجة إلى إجراء أبحاث لتقييم تأثير جودة المياه على صحة الكلى، ويوصى بإجراء تجربة عشوائية أكبر.

الكلمات الدالة: أمراض الكلى، جودة مياه الشرب، وظائف الكلى، مياه الشرب وتأثيرها على أمراض الكلى، الفشل الكلوي.

Abstract

Introduction: owing to its rising incidence and prevalence throughout the world, and in specific places in Libya, kidney failure diseases has gained increasing significance among the researcher. In spite of this disease can occurs as a result of the combined influence of epidemiological, biochemical, metabolic, and genetic risk factors, one of the important factors that considered in this study is quality water consumption. Creatinine concentrations and blood urea nitrogen (BUN) can indicate renal function. **Aim of study:** The aims of present work were to assess the water drinking type that regularly consumed by kidney patients by measuring of creatinine and urea concentrations in plasma and urine samples.

Methodology: The study involved 97 patients from Zawiya Nephrology Centre and Al-Zahra Hospital in Libya, divided into four age groups. They answered a questionnaire about their personal information, drinking water quality, and urea and creatinine levels after dialysis. Blood samples were collected, then spun in a centrifuge. Data was analysed using Microsoft Excel and collected from personal information. **Result.** The study found that in Zawiya, 25.77% of the sample was female, while in Zahra, 18.18% was female. In Zawiya, 23.70% of the sample was male, while in Zahra, 28.86% was male. The study revealed that the age group aged 35–55 had the highest percentage (46.39%), followed by those aged 55+ (40.20%), and those aged 15–35 (13.40%), with no age group less than 15 years. The study assessed kidney function by estimating urea and creatinine content in blood. Results showed significant increases in renal function markers after dialysis, while no significant difference was observed in creatinine levels. The study found that most patients require dialysis three times a week for kidney failure, depending on the severity and stage of the disease. **Conclusion:** Kidney patients in Western Libya require clean, safe drinking water to prevent kidney patient deterioration. Research is needed to assess water quality's impact on kidney health, and a larger random offer trial is recommended.

Keywords: Kidney disease, drinking water quality, kidney function, drinking water and its effect on kidney disease, kidney failure.

Introduction

In many nations, kidney disease is one of the main causes of death and disability (Mascha et al 2006). According to Eduardo et al. (2015). it is brought on by a slow and progressive deterioration of kidney function caused by several conditions, including infections, autoimmune disorders, diabetes, endocrine disorders, cancer, and hazardous chemicals. It is frequently brought on by aftereffects from more serious illnesses. While chronic kidney failure develops gradually over weeks, months, or years, acute kidney failure happens fast and unexpectedly. In the latter case, the kidneys gradually stop functioning, leading to the development of end-stage renal disease (ESRD) (Al-Hisnawi and Salih, 2014; Noor et al., 2014).

High blood pressure can harm the blood arteries that supply the kidneys with waste products like excess cellular fluids, making it one of the main causes of kidney failure. In the end, ESRD can result from excessive blood pressure (Azra 2014).

Clinical Significance

The degree to which the glomerulus filters creatinine is determined by measuring the amounts of creatinine in plasma and urine. Creatine is produced internally by the body and is readily filtered by the glomerulus. As a result, creatinine can be employed as a renal clearance endogenous measurement. The renal system can no longer remove as much creatinine when the GFR is lowered, as in renal disease. A drop in GFR results from this and plasma creatinine levels are increased. It is crucial to remember that measuring plasma levels by itself is an invalid method of assessing renal function. Moreover, a normal plasma creatinine level does not always indicate that the kidneys operate normally (Turney, 2013).

Although it is less specific than creatinine, blood urea nitrogen (BUN) is another analyte that can measure renal function. Since blood urea nitrogen is influenced by several variables, including the patient's hydration level, a high-protein diet, and protein synthesis variables, it is not a recommended marker for clearance. BUN alone is insufficient as a marker for the Glomerular Filtration Rate (GFR). However, BUN can be utilized as an analyte to distinguish

between pre- and post-renal increases in plasma (Non-protein Nitrogen) NPNs when paired with plasma creatinine (also known as the creatinine / BUN ratio).⁸ The kidneys' primary functions are maintaining fluid volume and maintaining the body's pH and composition within physiological ranges. Enormous anatomical and functional kidney units known as "nephrons" are responsible for this overall. (Ahmad, 2013).

Vital kidney units that sift blood are called nephrons. The ultrafiltration preparer permits irrelevant plasma proteins to enter while removing plasma like ultrafiltration, therefore sifting a Bowman capsule containing glomeruli, proteins, and other expanding glomerular elements. At first, every nephron is a kidney molecule.

The GFR sifting rate is one of the scales of renal work. The glomerular filtration rate depicts the stream rate of separated liquid passing through the kidney. Rate of excretion of creatinine The amount of blood plasma that has been freed of creatinine per time unit is known as CCr or CrCL, and it may be an important measure of GRF rounding. Because of creatinine emission, which cimetidine can prevent, creatinine clearance exceeds GFR. GFR and CCr can be precisely determined by comparing the amounts of chemicals in the blood and urine, or they can be assessed using formulas based on the blood test result. The results of these tests—eGFR and eCCr—are used to assess the kidneys' function. Chronic kidney disease is categorised based on albuminuria, the cause of kidney illness, and GFR classifications. The normal bodily surface zone, or average GFR rate, falls between 90 and 120 ml min⁻¹ 1.73 m² in women over 40 years old and 100 to 130 ml min⁻¹ 1.73 m² in men. The GFR in children is determined by emptying 110 ml in 1.73 minutes 2 in ladies more youthful than 40 a long time of age. In children, GFR is measured by evacuating affront 110 ml min⁻¹ 1.73 m² to two a long time ancient in both genders, at that point continuously diminishes. After the age of 40, GFR slowly diminishes with age, by 0.4 1.2 ml (Mian and Schwartz 2017).

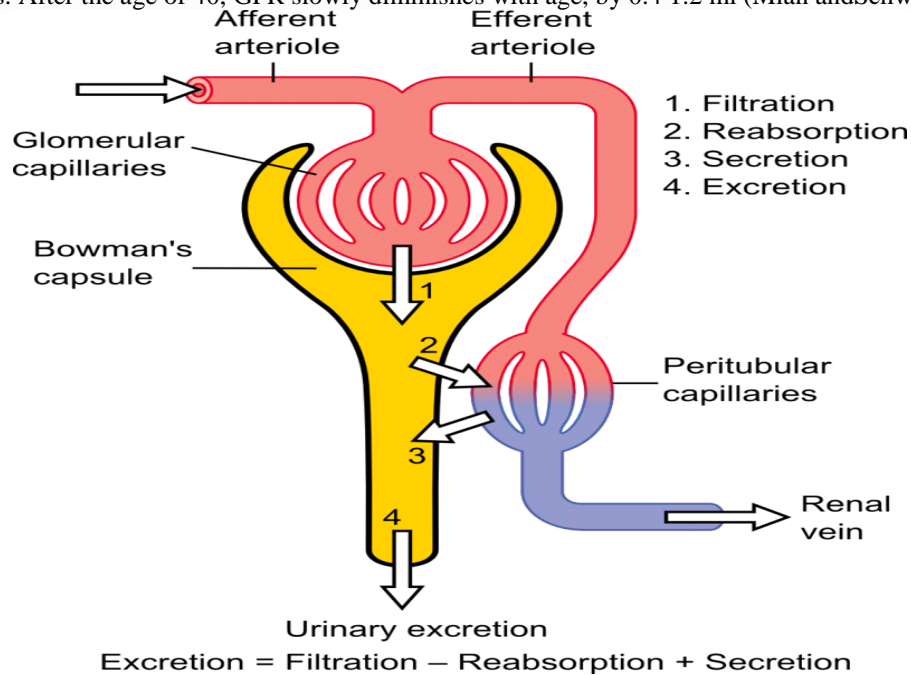


Figure 3 Schematic diagram of the nephron (yellow), relevant circulation (red/blue), and the four methods of altering the filtrate.

The section of the kidney's nephron's canal structure that connects Bowman's capsule and a loop of Henle is known as the proximal tubule. The brush border or striated border is an amazing feature of the proximal tubule. Furthermore, the nephron's surface epithelial cells are held in place by densely packed microvilli, which serve as a border that is clearly visible beneath the light-amplification lens and the brush border film BBM. According to Evan et al. (1983), the BBM of the renal proximal tubule is the crucial site for the reabsorption of certain solutes, such as amino acids, carbohydrates, and other supplements, as well as specific particles and minerals like Na and inorganic phosphate.

In BBM, the proximal tubes and auxiliary dynamic transport that actuates through the cell exchange of sodium particles are the taking after, which are reabsorbed particles and cations such as sodium, phosphate, sugars, amino acids, and others. The basal layer initiates dynamic transport from the luminal film deep down out of the epithelial cell (Holden et al., 2013).

Moreover, the dynamic movement of a shipper, sodium Na, is linked to the reabsorption of a small number of particles and solutes from the tubular depth by Na K ATPase, which is located on the basolateral side (Bonjour & Caverzasio 1984). All other types of transport, including Na K ATPase, rely on the exchange of Na, which is thought to be the kidney's primary function. This degradation of ATP occurs at the region of the anti-luminal layer. (Evan et al. 1983). Additionally, since the oxidative digestion system in mitochondria is often linked to ATP synthesis, it appears that either the oxidative digestion system or the oxygen pressure (pO₂) of the renal tubular cells are related to Na transport. O₂ take-up utilisation and Na reabsorption have established a coordinating direct link (Torelli et al. 1986). When tissue oxygen pressure, or Po₂, is switched, the cortico medullary slope seems to be reversed, meaning that Po₂ is significantly lower in the inner medulla than it is in the cortical tissue itself. Studies have shown that the major columns supporting the kidney's transport function include fatty acids, glutamine, lactate, citrate, and especially glucose (Stein 2012). As it happens, distinct nephron subsegments within completely separate kidney sections have varying capacities for both the substrate digestion system and solute and liquid transport. Examples include the renal medulla, which houses the anaerobic digestion system and glycolysis, and the renal cortex, which is mostly used by the aerobic oxidative digestion system. Additionally, gluconeogenesis has the ability to produce in the renal cortex (Hokamp et al., 2016).

Nephron, which is divided into several subsegments, is a structurally unique and practical contrast to Figure 3. Consequently, nephron heterogeneity expansion to the differentiation in renal function. According to Lise et al. (1987), the root and area of the nephrons inside the kidney's cortical location determine the inter- and intra-nephrotic heterogeneity in mammals. The superficial nephron is the one that emerges from the glomerulus in the shallow cortex, while the deep or juxtamedullary nephron originates from the deep cortical location. It has been discovered that these collections of nephrons are observable both physiologically and organizationally (Francois & Danielle 1985).

The review of the relationships between water intake, chronic kidney disease (CKD), and cardiovascular disease (CVD) in the general population revealed that CKD was more likely among those with lower than most notable total water intake. Additionally, the analysis discovered that CKD was associated with increased intakes of plain water but not other beverages. There was no correlation discovered between CVD and moo water admissions. The results suggest that increased intakes of water, particularly plain water, may have a protective effect on kidney function (Sontrop et al., 2013).

Drinking water from burrowed wells in CKDu endemic zones may be a significant source of nephrotoxic particle pollutants, according to research conducted in Sri Lanka. The Wewelketiya region's high levels of Pb and Cd exceeded Sri Lanka's water quality regulations. Fluoride concentrations also exceeded rational thresholds. Nevertheless, no water test in the reference range went above these bounds. This suggests that long-term exposure to high concentrations of metal particles and counterions puts people in these areas at risk for renal tissue damage (Perera et al., 2020).

High concentrations of heavy metals, such as blood lead (Pb), urine nickel (Ni), chromium Cr, manganese Mn, arsenic (As), copper (Cu), and cadmium (Cd), were linked to microalbuminuria, according to a study conducted in Southern Taiwan. The study also discovered that there were significant effects on proteinuria from the intuitive relationships between Pb and urine Cr and between Cd and Cu. According to Tsai et al. (2021).The quantities were discovered to be greater than the drinking water reasonable constraint set by the World Health Organisation. When compared to kidney patients who were not exposed, the biochemical markers, particularly urine N acetyl glycosaminidase, were observed to be greater in EKP patients. Higher correlations between As and Cd concentrations in water and urine tests were also discovered by the researcher (Arain et al., 2015). Another study looks at the levels of aluminium (Al) and cadmium (Cd) in ground water samples and assesses the risks to public health associated with high quantities of dangerous metals. In the southern part of Pakistan, a total of 200 samples were taken from patients with chronic kidney disease (CKD) and healthy control subjects. Manually drawing analytes in water and processing blood samples with corrosive chemicals were part of the extraction preparations. The samples were then desorbed using 2.0 mol L 1 HNO₃ in ethanol. An electrothermal nuclear retention spectrometer was used to determine the concentration of the extracted analytes (Panhwar et al., 2016).

The purpose of the study was to examine how routine drinking water replacement affected the kidney function of patients with chronic kidney disease (CKDu) in Sri Lanka's North Central Area. Consideration was given to an interventional study in which patients' renal function was assessed at 6-month intervals and regular drinking water was replaced with bottled spring water approved by Sri Lanka Standard for a period of 18 months. There was a noticeable decrease in the rate of disease transmission in the intervention group when compared to the non-intervention group. According to the study, drinking water on a regular basis may help slow the spread of the illness and urge intervention. More research is needed to determine how drinking water affects the CKDu popUltimately,

the impact of drinking water on kidney stone illness has not been thoroughly understood, especially in Libya. For the first time, this study will evaluate the effect of drinking water on renal patients in western Libya.

Aim of study

For the first time, this study aimed to examine the relationship between daily water consumption and kidney stone disease (KSD). Furthermore, the objective of this research is to compare the effects of drinking carbonated and healthy water versus regular water consumption by evaluating kidney function, measuring the level of Urea and Creatinine in serum and urine samples in Western Libya, and discussing the implications of these findings for patients with KSD and chronic kidney disease.

Methodology

Sample of the study

The size of samples was about of 97 cases of patients who regularly come to (Zawiya Nephrology Center) and (Al-Zahra Hospital) Nephrology Department in western Libya from 3/8/2023 to 20/8/2023.

Experimental Design

The study sample included 97 patients, divided into four age groups of both sexes. Where they answered a questionnaire prepared in advance consisting of personal information and information on the quality of drinking water, as well as urea and creatinine were taken after dialysis.

Laboratory measurements procedure

Urea, and creatinine were measured utilizing EasyLyte Also furthermore analyzer may be a totally mechanized, microprocessor-controlled electrolyte framework that uses ISE Particle Particular Terminal innovation to create electrolyte estimations. The EasyLyte Furthermore measures combinations of Na, K, Cl in entirety blood, serum, plasma, or urine.

Statistical analysis

Student's t-test was used to test for statistically significant differences in the different parameters, data were expressed as means±standard deviations. The p-values were checked to analyze whether the parameters differed significantly between the case and control areas by using Graphpad Instat software (GraphPad prism 8 Software). A p-value<0.05 was considered to be statistically significant.

2.3 Nipro Dialysis

The Nipro dialysis machine, also known as the Nipro Surdial X, could be a restorative gadget utilized for hemodialysis treatment. Hemodialysis may be a lifesaving treatment for patients with end stage kidney illness, where the machine makes a difference channel squander and overabundance liquid from the blood when the kidneys are incapable to do so.

The Nipro Surdial-X is outlined with progressed highlights to guarantee proficient and secure dialysis treatment. It consolidates a single pump framework for moved forward blood stream control and exactness amid the filtration prepare. The machine moreover offers exact ultrafiltration control to expel particular volumes of liquid from the patient s blood, decreasing the chance of liquid imbalance.

The Surdial-X comes with a user-friendly interface and clear show for simple route and observing. It utilizes progressed security highlights such as built in alerts for persistent security and non-invasive weight observing to avoid clotting or overabundance negative weight amid dialysis. By and large, the Nipro dialysis machine points to supply solid and viable hemodialysis treatment, making strides quiet results and quality of life for people with kidney disappointment.

Results and Discussion

Distribution of samples by city and gender

The samples were about 97 samples from the city of Zawiya and Al-Zahra, where patients frequented the kidney centres in these cities, where 52.57% were from the city of Zawiya and 47.42% from the city of Al-Zahra table (1), figure (1)

Table 1: Distribution of samples by city

	patients count	percent
Alzawia	51	52.57%
Alzahra	46	47.42%

Figure 1: Distribution of samples by city.

The percentage of females in the city of Zawiya was 25.77% of the total number of samples 97 (100%) while the percentage of females in the city of Zahra was 18.18%. As for the percentage of males, 23.70% in the city of Zawiya and 28.86% in Zahra, and the percentage of males in this study is higher than females.

Table 2: Distribution of samples by gender.

City	Female	percent	Male	percent
alzawia	25	25.77%	26	23.70%
alzahra	18	18.18%	28	28.86%

Figure 2: Distribution of samples by gender

Distribution of samples by age

The results of the study showed that the age period (35-55) was the largest percentage by about 46.39%, followed by the age period (55 years and more) by 40.20%, then the age period (15-35) by 13.40%, and no percentage was received for the age period (less than 15 years).

Table 3: Distribution of samples by age

Age	patients count	Percent
Less than 15	0	0%
15-35	13	13.40%
35-55	45	46.39%
55 and more	39	40.20%

Figure 3: Distribution of samples by age

The statistical results of Biomarkers of Renal Function (Serum Urea, Creatinine)

To assess kidney function, the content of urea in the blood and creatinine was estimated the results of biochemical tests carried out on the serum of patients are highlighted below.

Changes in levels of renal function markers in patients after dialysis are shown in (Table 4). Renal functional markers such as urea increased significantly compared to control ($P < 0.05$). As for the Creatinine the difference was not significantly different compared to the control value.

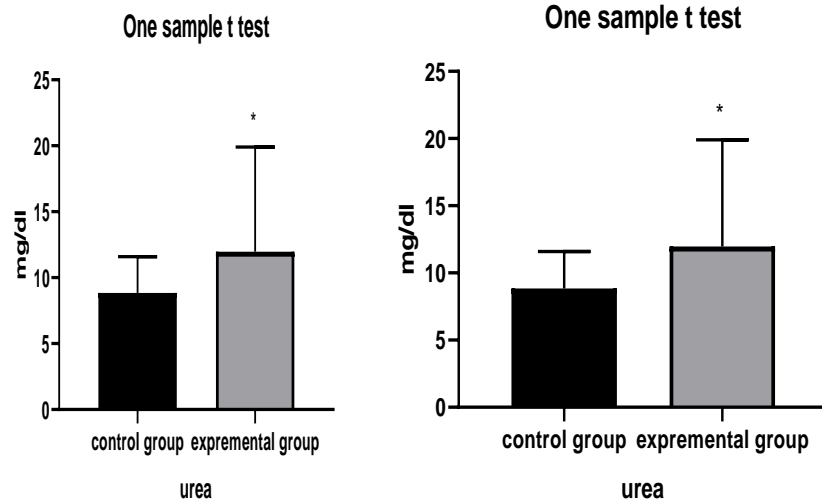
GrhaphPad prism 8 program was used to analyze this data

Table 4: the statistical results of groups

**significant at the 0.05 level*

	Group	Mean	Std. deviation	T-test	p-value
Urea	Control group	8.85	2.74	2.208	0.0297*
	Expremental group	11.96	7.93		
Creatinine	Control group	136.63	35.23	1.599	0.0566
	Expremental group	149.04	37.12		

Figure 4: the mean value urea and creatinine.



Kidney patients generally need access to clean and safe drinking water. Poor water quality, such as water contaminated with pollutants, heavy metals, or pathogens, can exacerbate kidney problems and lead to further health complications. It is crucial for kidney patients to avoid drinking water that may contain harmful substances. The source of drinking water in Western Libya could vary, ranging from tap water, underground water, or bottled water. Each source may have different levels of contamination or mineral content. Underground water sources, for instance, might have higher mineral content that could impact kidney health. Understanding the specific water sources and their quality is essential.

The samples were about 97 samples from the city of Zawiya and Zahra, conducted from 3/8/2023 to 20/8/2023. where patients frequented kidney centers in these cities, the percentage of patients in this study was from the city of Zawiya more than the city of Zahra and the proportions of males and females were different, where the percentage of females in the city of Zawiya was more than in the city of Zahra, while the percentage of males in the city of Zahra was more than in the city of Zawiya. due to the ratio of population between the two cities.

The age period (35-55) was the largest percentage of patients with kidney failure here could be several reasons Middle-aged adults in this age group may have engaged in unhealthy lifestyle behaviours such as poor dietary habits, lack of exercise, excessive alcohol consumption, or smoking, which are known risk factors for kidney disease. Chronic health conditions like hypertension and diabetes, Aging process, Delayed diagnosis It is important to note that the causes of kidney failure can vary among individuals and there may be additional factors contributing to the larger percentage of patients within this age range.

Through the results of the study and comparison of urea and Creatinine analysis samples for the control group that uses Well water for drinking and the experimental group that uses other sources of drinking water. We found that there was a statistically significant increase in urea, but for the Creatinine, there were no statistically significant changes. This is relatively consistent with the study of Clark *et al* (2017).

A study assessing the disease progression rate of kidney failure patients who switched to bottled spring water for 18 months and those who continued with their usual water found a reduced progression rate. Kidney function of subjects in both groups were monitored in terms of blood pressure, serum creatinine, serum calcium, serum phosphorus, hemoglobin, estimated glomerular filtration rate and urinary protein at 6 months intervals during the intervention and follow up periods. The study suggests further interventional studies to understand the general effect of drinking water on kidney failure patients (Siriwardhana *et al.*, 20018).

Many of the respondents on the questions do not drink the municipality's water and do not believe that the water in Libya is its security, and this is due to the count of confidence in the water sources in the country.

A high percentage of the respondents is not smoked, or they stopped smoking, and this indicates patients' awareness of the smoking relationship to public health. 14.43% of patients in the study suffer from obesity and many of them have chronic diseases such as high blood pressure and diabetes. The studies found that there is a

close relationship between kidney failure, obesity, diabetes and high blood pressure. Obesity, high blood pressure and diabetes are considered risk factors for kidney problems. Obesity increases blood pressure and affects kidney function, while diabetes can cause damage to the blood vessels in the kidneys. In addition, high blood pressure affects the blood vessels in the kidneys and increases the risk of kidney failure. Therefore, it is necessary to control obesity, high blood pressure and diabetes to maintain kidney health (Maric-Bilkan 2013; Hall et al.,2014).

25.77 % of patients have a family history with the disease and they have relatives from the first circle and the second have kidney failure. Some kidney diseases that lead to kidney failure can be hereditary, such as multiple renal cystic disease and polycystic kidney syndrome. If a family member has these diseases, there may be a high risk of kidney problems and the need for dialysis. However, it should be noted that not all cases of kidney failure are related to heredity.

Gene mutations in monogenic kidney diseases like Alport syndrome, thin basement membrane disease, and polygenic renal disorders like glomerulopathies and diabetic nephropathy are being studied. This knowledge could improve early diagnosis and provide new diagnostic and prognostic tools, especially in the growing number of ESRD patients (Stavljenić-Rukavina 2009).

The study indicated that most patients are dialysis 3 times a week. The number of times dialysis is required for kidney failure depends on the severity and stage of the kidney disease. In general, dialysis is a treatment option for individuals with end-stage renal disease (ESRD) or advanced kidney failure. The frequency of dialysis sessions can vary, but it is typically done multiple times per week. The exact number of dialysis sessions needed is determined by the healthcare provider based on the patient's specific condition and needs. It is important to follow the recommended dialysis schedule for effective management of kidney failure.

Conclusion

Kidney patients in Western Libya require clean, safe drinking water, and based on the findings of this study that showed significantly increased of kidney function markers, in particular urea. The results may be concluded that drinking water quality is essential for kidney patients in order to prevent kidney problems and health complications. Furthermore, to confirm findings of this study further investigations are required in several area and increase size of samples which considered as one of the important limitations in this study.

References

- Al-Hisnawi RA, Salih H. A study of some biochemical changes in patients with chronic renal failure undergoing hemodialysis Int. J. Curr. Microbiol. App. Sci. 2014; 3(5): 581-586.
- Aperia AC, Liebow AI. 1964. Implications of urine pO₂ for renal medullary blood flow. *American Journal of Physiology*, 206(3): 499-504.
- Aperia AC, Liebow AI. 1964. Implications of urine pO₂ for renal medullary blood flow. *American Journal of Physiology*, 206(3): 499-504
- Arain, M. B., Kazi, T. G., Baig, J. A., Afridi, H. I., Sarajuddin, Brehman, K. D., ... & Arain, S. S. (2015). Co-exposure of arsenic and cadmium through drinking water and tobacco smoking: risk assessment on kidney dysfunction. *Environmental Science and Pollution Research*, 22, 350-357.
- Azra K. Estimation of blood urea (BUN) and serum creatinine level in patients of renal disorder. *J Fundam Appl Sci*. 2014; 4:199-202.
- Bidwell GL III, Perkins E, Raucher D. A thermally targeted c-Myc inhibitory polypeptide inhibits breast tumor growth. *Cancer Lett* 319: 136–143, 2012. doi: 10.1016/j.canlet.2011.12.042. [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]
- Bonjour JP, Caverzasio JHC. 1984. Phosphate transport in the kidney. *Reviews of Physiology, Biochemistry and Pharmacology*, 100: 161- 21.
- Carpenter, D.O.; Bushkin-Bedient, S. Exposure to Chemicals and Radiation during Childhood and Risk for Cancer Later in Life. *J. Adolesc. Health* **2013**, 52, S21–S29. [CrossRef] [PubMed]

- Cho S, Dong S, Parent KN, Chen M. Immune-tolerant elastin-like polypeptides (iTEPs) and their application as CTL vaccine carriers. *J Drug Target* 24: 328–339, 2016. doi: 10.3109/1061186X.2015.1077847. [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]
- Clark, W. F., Huang, S. H., Garg, A. X., Gallo, K., House, A. A., Moist, L., ... & Sontrop, J. M. (2017). The chronic kidney disease water intake trial: Protocol of a randomized controlled trial. *Canadian Journal of Kidney Health and Disease*, 4, 2054358117725106
- Coresh, J.; Selvin, E.; Stevens, L.A.; Manzi, J.; Kusek, J.W.; Eggers, P.; Van Lente, F.; Levey, A.S. Prevalence of Chronic Kidney Disease in the United States. *JAMA* **2007**, 298, 2038–2047. [CrossRef]
- Dai L, Lu C, Liu J, Li S, Jin H, Chen F, Xue Z, Miao C. Impact of twice- or three-times-weekly maintenance hemodialysis on patient outcomes: A multicenter randomized trial. *Medicine (Baltimore)*. 2020 May;99(20):e20202. doi: 10.1097/MD.00000000000020202. PMID: 32443343; PMCID: PMC7253701.
- Eduardo OC, Kaue A, Idania AA, *et al.* Influence of hemodialysis on the plasma concentration of adenosine deaminase in patients with chronic kidney disease. *J Bras Patol Med Lab*. 2015; 51:153-157.
- Evan AP, Vincet GH, Schwartz GJ. 1983. Development of solute transport in rabbit proximal tubule. II. Morphologic segmentation, *American Journal of Physiology*, 1245: F391-F407.
- Evan AP, Vincet GH, Schwartz GJ. 1983. Development of solute transport in rabbit proximal tubule. II. Morphologic segmentation, *American Journal of Physiology*, 1245: F391-F407.
- Francois H, Danielle C.1985. Functional segmentation of the nephron. In: *The Kidney: Physiology and Pathophysiology*, Seldin DW and Gibbisch G (editors). Raven Press, New York, pp. 519-529.
- Geng Q, Sun X, Gong T, Zhang Z-R. Peptide-drug conjugate linked via a disulfide bond for kidney targeted drug delivery. *Bioconjug Chem* 23: 1200–1210, 2012. doi: 10.1021/bc300020f. [PubMed] [CrossRef] [Google Scholar] [Ref list]
- George EM, Liu H, Robinson GG, Mahdi F, Perkins E, Bidwell GL III. Growth factor purification and delivery systems (PADS) for therapeutic angiogenesis. *Vasc Cell* 7: 1, 2015. doi: 10.1186/s13221-014-0026-3. [PMC free article] [PubMed] [CrossRef] [Google Scholar] [Ref list]
- Grant, M.K.; Goldizen, B.F.C.; Sly, P.; Brune, M.M.-N.; Neira, M.; Berg, M.V.D.; Norman, R.E. Health consequences of exposure to e-waste: A systematic review. *Lancet Glob. Health* **2013**, 1, e350–e361. [CrossRef]
- Hall, M. E., do Carmo, J. M., da Silva, A. A., Juncos, L. A., Wang, Z., & Hall, J. E. (2014). Obesity, hypertension, and chronic kidney disease. *International journal of nephrology and renovascular disease*, 75-88
- Hokamp, Jessica A., and Mary B. Nabity. "Renal biomarkers in domestic species." *Veterinary clinical pathology* 45.1 (2016): 28-56.
- Holden, J. A., Layfield, L. L., & Matthews, J. L. (2013). *The zebrafish: atlas of macroscopic and microscopic anatomy*. Cambridge University Press
- Hwang, S.-J.; Tsai, J.-C.; Chen, H.-C. Epidemiology, impact and preventive care of chronic kidney disease in Taiwan. *Nephrology* **2010**, 15 (Suppl. S2), 3–9. [CrossRef]
- Imai, E.; Horio, M.; Iseki, K.; Yamagata, K.; Watanabe, T.; Hara, S.; Ura, N.; Kiyohara, Y.; Hirakata, H.; Moriyama, T.; *et al.* Prevalence of chronic kidney disease (CKD) in the Japanese general population predicted by the MDRD equation modified by a Japanese coefficient. *Clin. Exp. Nephrol.* **2007**, 11, 156–163. [CrosRef]
- Inker, L.A.; Levey, A.S.; Pandya, K.; Stoycheff, N.; Okparavero, A.; Greene, T. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Early Change in Proteinuria as a Surrogate End Point for Kidney Disease Progression: An Individual Patient Metaanalysis. *Am. J. Kidney Dis.* **2014**, 64, 74–85. [CrossRef] [PubMed]

- Jha, V.; Garcia-Garcia, G.; Iseki, K.; Li, Z.; Naicker, S.; Plattner, B.; Saran, R.; Wang, A.Y.-M.; Yang, C.-W. Chronic kidney disease: Global dimension and perspectives. *Lancet* **2013**, *382*, 260–272. [CrossRef]
- Landrigan, P.J.; Sly, J.L.; Ruchirawat, M.; Silva, E.R.; Huo, X.; Diaz-Barriga, F.; Zar, H.J.; King, M.; Ha, E.H.; Asante, K.A.; *et al.* Health Consequences of Environmental Exposures: Changing Global Patterns of Exposure and Disease. *Ann. Glob. Health* **2016**, *82*, 10–19. [CrossRef] [PubMed]
- Levey, A.S.; De Jong, P.E.; Coresh, J.; Nahas, M.E.; Astor, B.C.; Matsushita, K.; Gansevoort, R.T.; Kasiske, B.L.; Eckardt, K.-U. The definition, classification, and prognosis of chronic kidney disease: A KDIGO Controversies Conference report. *Kidney Int.* **2011**, *80*, 17–28. [CrossRef] [PubMed]
- Lin Y, Li Y, Wang X, Gong T, Zhang L, Sun X. Targeted drug delivery to renal proximal tubule epithelial cells mediated by 2-glucosamine. *J Control Release* *167*: 148–156, 2013. doi: 10.1016/j.jconrel.2013.02.001. [PubMed] [CrossRef] [Google Scholar] [Ref list]
- Lise B, Nadine B, Marie till'. 1987. 11ccerogrcify of nephron anatomy. *Kidney International*, *31*: S25-S39.