

ORIGINAL ARTICLE

Assessment of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) Use in Chronic Kidney Disease (CKD) Patients in Khartoum North Teaching Hospital

Mhdia Elhadi DafaAlla Osman¹, Sara Al-Sadiq Salih², Nasrin E. Khalifa^{3,4}, Weiam Hussein^{5,6}, Weam M. A. Khojali^{5,7}, Salma Ahmed Ali Babiker⁸, Reem Falah Alshammari⁹, Halima Mustafa Elagib^{*10,11}

¹Department of Clinical Pharmacy, College of Pharmacy, University of Hail, Hail 2240, KSA.

² Faculty of pharmacy, Omdurman Islamic University, Sudan.

³ Department of Pharmaceutics, College of Pharmacy, University of Hail, Hail 2240, KSA.

⁴Department of Pharmaceutics, Faculty of Pharmacy, University of Khartoum, Khartoum 11115, Sudan.

⁵ Department of Pharmaceutical Chemistry, College of Pharmacy, University of Hail, Hail 2240, KSA.

⁶Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Aden University, 6075/Aden, Yemen

⁷ Department of pharmaceutical Chemistry, Faculty of Pharmacy, Omdurman Islamic University, Sudan

⁸Family Physician, Family Medicine, Ha'il University Clinics, University of Ha'il / Saudi Arabia

⁹Department of Family and Community Medicine, College of Medicine, university of Ha'il, KSA.

¹⁰ Department of Pharmacology, College of Medicine, University of Ha'il, KSA.

¹¹ Department of Pharmacology, Faculty of Pharmacy, Omdurman Islamic University, Sudan

Corresponding Author

Dr. Halima Mustafa Elagib

E-mail: halimaelagibwork@gmail.com

ABSTRACT

Non-steroidal anti-inflammatory drugs (NSAIDs) are among the most widely used of all therapeutic agents worldwide. They are frequently prescribed for pain in a number of medical conditions and used as OTC drugs. All currently available NSAIDs have significant unwanted effects in renal system causing CKD. The aim of this study to investigate the use of NSAIDs in chronic kidney disease (CKD) patients in Khartoum North Teaching Hospital. A descriptive hospital base study done in Khartoum North Teaching Hospital in a period from November 2017 to February 2018. The sample taken was 140 patients in renal refer clinic. All patients were interviewed directly using questionnaire for demographic data, patterns and reasons for taking NSAIDs before and after dialysis. The data was analyzed by SPSS version 20. 91% of patients were using NSAIDs as painkiller for headache and 35% took NSAIDs as OTC drugs. The study has shown that 20% of patients have HNT.55% used NSAIDs on need but 14% according to prescription.39 % of patients took NSAIDs after dialysis mainly for pain.10% of patients had family history of CKD.NSAIDs analgesics were widely used and frequently taken inappropriately and dangerously and users were generally unaware of the potential complication like CKD.

KEYWORDS: Assessment; Chronic, Kidney; Disease; NSAIDs

Received 24.05.2023

Revised 01.07.2023

Accepted 21.08.2023

How to cite this article:

Mhdia Elhadi DafaAlla Osman· Sara Al-Sadiq Salih· Nasrin E. Khalifa, Weiam Hussein, Weam M. A. Khojali· Salma Ahmed Ali Babiker , Reem Falah Alshammari Halima Mustafa Elagib. Assessment of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) Use in Chronic Kidney Disease (Ckd) Patients in Khartoum North Teaching Hospital. Adv. Biores. Vol 14 [5] September 2023; 21-28

INTRODUCTION

Pain relief is dependent on the type of pain (nociceptive or neuropathic pain). Non-opioid analgesics, such as nonsteroidal anti-inflammatory drugs, are used to treat mild to moderate arthritic pain (nociceptive pain). NSAIDs are a class of chemically distinct drugs with antipyretic, analgesic, and anti-inflammatory properties [1]. NSAIDs can cause ulcers, internal bleeding, kidney failure, and an increased risk of heart

attack and stroke [2.]Even infrequent use of NSAIDs may result in acute kidney failure [3]. In 2002, the National Kidney Foundation (NKF) established a definition and classification of CKD through the Kidney Disease Outcome Quality Initiative (KDOQI). According to the guidelines, CKD is defined as either kidney damage or a glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m² for at least three months [4].Chronic Renal Failure (CRF) is a progressive, irreversible kidney failure in which the body fails to maintain metabolic and electrolytic balance, resulting in uremia, metabolic acidosis, anemia, electrolyte imbalances, and endocrine disorders. Diabetes, hypertension, glomerulonephritis, and polycystic kidney disease are the most common causes [5]. In light of the foregoing, our goal is to investigate the use of (NSAIDs) in (CKD) patients at Khartoum North Teaching Hospital from November 2017 to January 2018. Furthermore, we will assess the use of over used (NSAIDs) in (CKD) patients. To assess the relationship associated with the excessive use of (NSAIDs) in (CKD) patients.

MATERIAL AND METHODS

This was a descriptive hospital-based study conducted at Khartoum North Teaching Hospital from November 2017 to February 2018. The sample consisted of 140 patients from a renal referral clinic. All patients with chronic kidney disease admitted to the study area during the study period, both sexes, were directly interviewed using a questionnaire for demographic data, patterns, and reasons for taking NSAIDs before and after dialysis, as well as information from the file contents. Patients under the age of 18 were barred from participating. Data was manually analyzed as well as using a computer-assisted program (SPSS version 20).

RESULTS

Patients Demographic Data

The majority of patients were in age group >60, females were greater than males and most of patients were unoccupied. Most of them were living in urban area as illustrated in table 1.

Table No.1. Patient's demographic data.

Variables	Frequency (Percentage) n=140
Age (years)	
(18-36)	28 (27.9%)
(36-45)	11 (10.7%)
(46-60)	28 (27.9%)
>60	33 (33.6%)
Gender	
Male	80 (57.1%)
Female	60 (42.9%)
Occupation	
Occupation	20 (14.3%)
Inoccupation	120 (85.7%)
Residence	
Rural	96 (68.6%)
Urban	44 (31.4%)

Urea creatinine

The majority of patients had high urea creatinine value of >0.8 mg/ml.

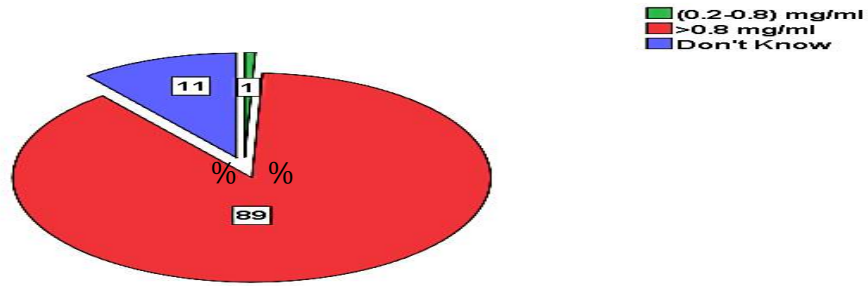


Figure No.1: Frequency percentage of urea creatinine value

Urea

Most of patients had urea level of > 43 mg/dl as shown in fig2.

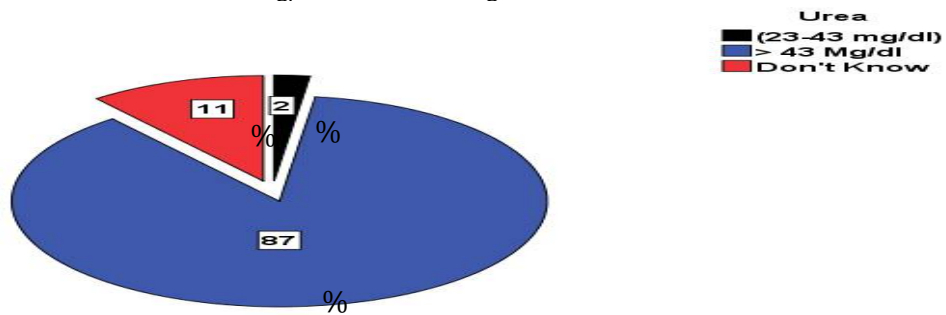


Figure No. 2: Percentage of urea level

Patient's Concomitants disease

Most of patients had HTN and DM while 17% have no disease.

Use of NSAIDs for pain

The majority of patients used NSAIDs as pain killer as shown in fig.3.

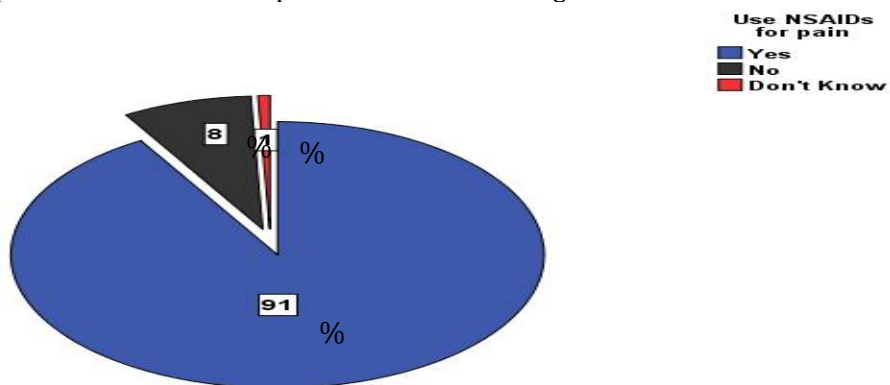


Figure No.3. Percentage of use NSAIDs for pain

Patterns of taking NSAIDs

Most of patients used NSAIDs sometimes followed by 22% took it always as shown in fig.4.

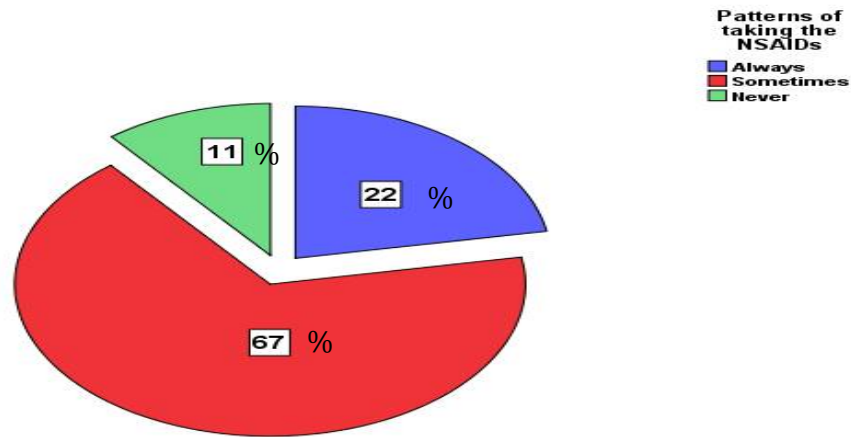


Figure No. 4. Percentage of patterns of taking NSAIDs

Reason for taking NSAIDs

The majority of patients took NSAIDs for headache as shown in fig.5.

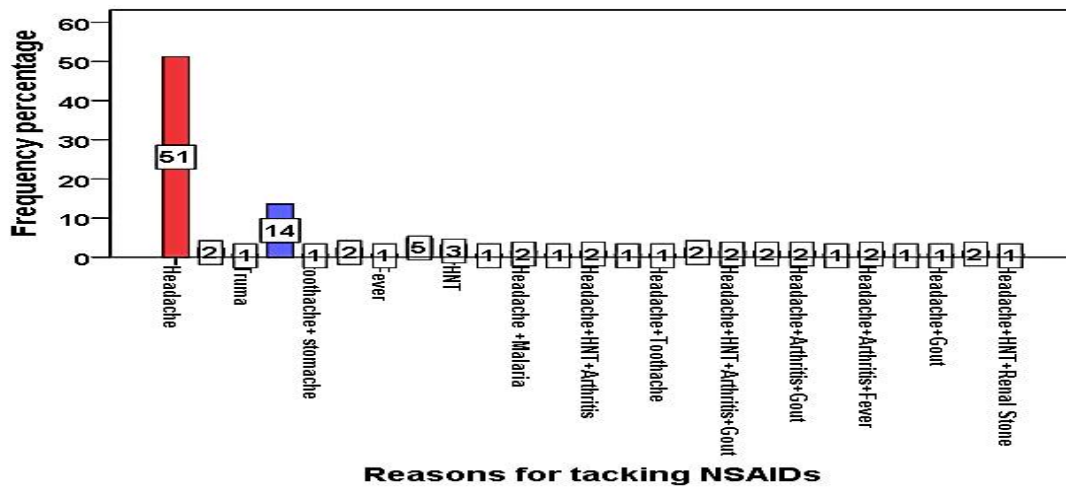


Figure No. 5. Percentage of reason for taking NSAIDs

Manners of taking NSAIDs

Most of patients took NSAIDs as over the counter drugs and 24 % by prescription as shown in fig.6.

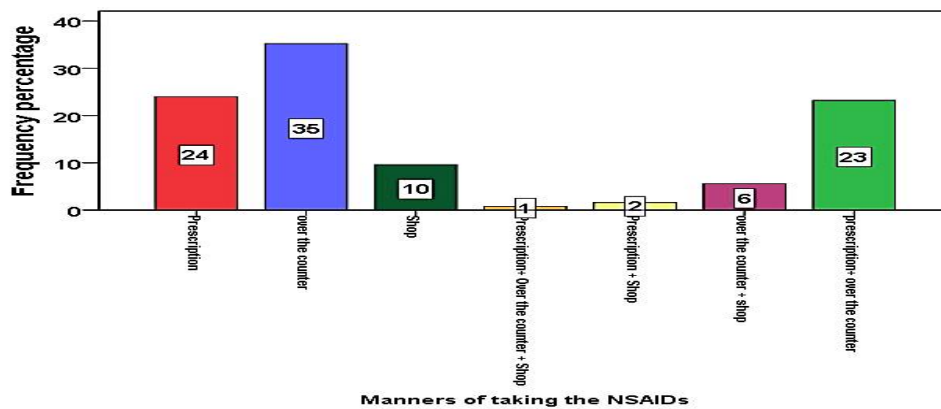


Figure No.6. Percentage of manners of taking the NSAIDs

Common NSAIDs used

Most NSAIDs used among the patients was paracetamol followed by aspirin as shown in fig.7.

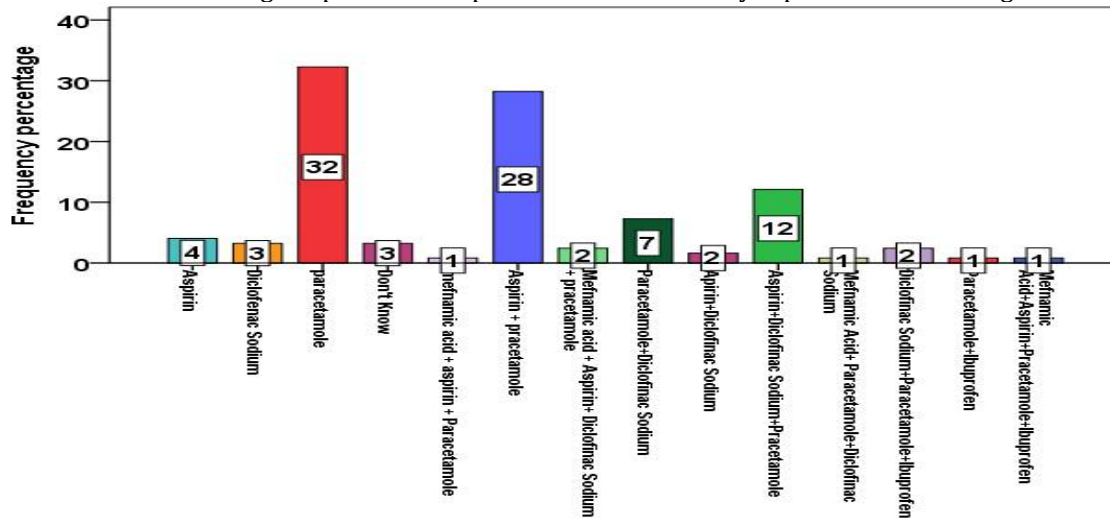


Figure No.7. Percentage of common NSAIDs used

Habits of taking NSAIDs

55% of the patients took NSAIDs on need and 14% according to doctor prescription. The most reason for taking NSAIDs after dialysis was pain.

Duration of taking NSAIDs

Most of patients took NSAIDs for > 2 years.

Taking NSAIDs after dialysis.

39 % of patients took NSAIDs after dialysis for the period of (1-5 days) as tablets, few of them took infusion or injection.. Only 16% used it for life. While the majority did not.

Patterns of taking NSAIDs after dialysis

The majority of those took NSAIDs were according to doctor prescription.

The most reason for taking NSAIDs after dialysis was pain.

Planning for renal transplant

The majority of patients did not plan for renal transplant.

Family history of CKD

The majority of patients did not have family history of CKD.

DISCUSSION

The majority of examined participants fell into the age group of >60 years. Followed by the age group of 18 to 36 and the age group of 46 to 60.67% (N = 2339) of the participants were men, with a mean age of 50.4 % 16 years this in accordance with the findings of the study conducted by [1], which stated that information regarding the patient's age and sex was obtained for 91% (N = 3452) of the patients..

All renal care centers and subsystems shared many of these characteristics.

Regarding to sex in this study 32% of the patients were over the age of 60, 65% were between the ages of 20 and 59.13 % of patients under the age of 18 were affected (N = 85; 2.5%) and this in agreement of the study done by [7] found that male patients have a significantly higher prevalence of CKD and incidence rate of ESRD than female patients. This result may be due to the different risk factors for each gender. It was determined that, in relation to the illness, very few patients were working, and the majority of them were not. They must rest to avoid overworking and making CKD worse.

The study demonstrated that the majority of patients resided in rural areas. This could be due to a lack of doctors or dialysis centers in the rural area, as mentioned in the ([8] study, where some researchers found higher ESRD rates in rural counties than in urban ones.

The majority of patients in this study had a urea creatinine value of more than 0.8 mg/ml and a urea level of more than 43 mg/dl. This is in line with the conclusion of [9] in routine blood parameters, there were many differences between patients in the no severe and severe groups when they admitted. BUN count was higher in severe cases (46.0 vs. 23.8 mg/dL; P .001), and a higher BUN/Cr ratio (50.3% versus 24.2; WBC count was higher (8.1 vs. 6.0 10⁹/L; P.001), P = .001).

According to the data variable diseases and renal dialysis patients were among the 140 patients. The most common combination of HNT and other conditions, such as diabetes, kidney stones, dye poisoning, malaria, and arthritis, was HNT alone. Only a few people had ulcers. Some patients had HNT, arthritis, anemia, and a kidney stone at the same time. This match the findings of a study by [10] that found patients with advanced CKD (CKD stages 4–5) had a significantly higher risk of cardiovascular events than patients with early CKD (CKD stages 1–3). The NCL survey, on the other hand, found that 83% of patients had used over-the-counter painkillers. The findings of this study were similar to those of the NCL survey. The majority of patients took NSAIDs for pain either occasionally or always, which is related to how they were taken [11]. Musculoskeletal pain was found to be the most common OTC use of NSAIDs in this study, with 63.8% of consumers using NSAIDs as needed and 23.3% using the usual dose. Additionally, 79.2% of participants were unaware of the adverse effects of NSAIDs [12].

Among the patients, headache was the most common reason for taking NSAIDs.

According to data compiled by [13], the reasons for using nonsteroidal anti-inflammatory drugs (NSAIDs) were, in descending order, musculoskeletal pain (249 (41.5 %), headache (131 (21.8 percent), toothache (90 (15 %), dysmenorrhea (66 (11%), antiplatelet (29 (4.8%)), colic pain (26 (4.3%)), and fever (9 (1.5%)). In the rest of data, patients had more than one reason to take NSAIDs. For example, arthritis, fever, menstrual cycle, HNT. In this study, paracetamol, aspirin, diclofenac sodium, paracetamol, and mefenamic acid were the most commonly used NSAIDs. This could be attributed to the affordability of paracetamol in pharmacies as well as its widespread availability as over-the-counter (OTC) medications. Ibuprofen was the OTC that was used the most in the Roper and NCL survey, while aspirin was used a lot, which was different from findings of [11] and [13]. Additionally, non-prescription paracetamol was used more frequently in Denmark, The Netherlands, Poland, Sweden, and Norway than NSAIDs used in Germany, Italy, Finland, and Austria [14].

The majority of people took NSAIDs for more than two years, followed by periods of one to two years and months, respectively. People mentioned the time, but they did not say exactly how often or how much of the drug they took. This is in line with the same study done by [15], which found that 33 (13%) high-risk patients had used an over-the-counter NSAID. In the general population sample and the high-risk sample, more than 30% of OTC NSAID users had used the medication for more than seven days. In the general population and the high-risk sample, respectively, 9% and 3% of OTC NSAID users used a dosage that was higher than the daily maximum.

Our study found that the majority of patients did not take NSAIDs after dialysis, but a small number did. All patients underwent dialysis multiple times. After dialysis, a small number of patients were not aware of NSAIDs. This indicated that some patients might not experience pain at all, while others may, this was similar to a study done by [16] studied 87 patients and enrolled 62 (71%) of them, and he found that bone/joint pain, insomnia, mood swings, sexual dysfunction, paresthesia, and nausea were among the potentially treatable symptoms. Analgesics were only used by 45 percent of patients with joint or bone pain, according to the study. 53% of patients with nausea and 23% of patients with difficulty falling asleep reported receiving medication to alleviate this symptom.

This study found that the majority of patients took NSAIDs over-the-counter, with 24 percent taking them on prescription. Additionally, the majority of patients (83 %) had HTN or diabetes mellitus, which may have contributed to the overestimation of NSAID side effects like ulcer. This coincides with the finding of [17] that patients with end-stage renal disease who are receiving hemodialysis had a high risk of ulcer bleeding. In these patients, diabetes mellitus, coronary artery disease, cirrhosis, and taking nonsteroidal anti-inflammatory medications were significant risk factors for ulcer bleeding.

According to the findings of this study, pain was the most common reason people took NSAIDs after dialysis, followed by disease and sometimes both.

As [18] mentioned in his study, aging HD patients are associated with a higher risk of PUB. Because of advanced bone disorders, neuropathies, and surgery, patients with CKD and ESRD may suffer from chronic pain. Concerning to the findings of our study, the majority of HD patients used NSAIDs in the form of tablets, with a few opting for injections and infusions. These findings correspond to the fact that HD patients used NSAIDs to alleviate pain, albeit in a variety of dosage forms. The researchers concluded that the topical route of administration has a significant amount of potential to serve as an efficient and risk-free method of administering aceclofenac for its local analgesic [19].

The majority of patients did not intend to undergo renal transplant. But a few did, and others were unsure whether or not they would. This may be due to the fact that the majority of patients are still undergoing follow-up and have not chosen when to begin transplantation. More than half did not had a family history of CKD, and few did not know that their family had CKD. Kidney transplants require special criteria [20]. This was inconsistent with [21] report that a significant increased risk associated with a positive

family history even after adjusting for age, sex, race, diabetes, hypertension, and socioeconomic status. This could be explained by the presence of additional risk factors or by patients sometimes denying the reality.

CONCLUSION

OTC analgesics, such as NSAIDs, are frequently taken incorrectly, and patients typically are unaware of their renal system side effects. Among elderly patients, diabetes and hypertension now account for the majority of CKD cases. Controlling CKD complications, particularly anemia, hypertension, dyslipidemia, and hyperproteinemia, as well as taking the right painkillers, has improved significantly. Nephrologists endeavor to give ideal treatment for deep-rooted cardiovascular gamble factors, regardless of whether this for the most part neglects to forestall the overabundance cardiovascular illness of CKD patients.

INFORMED CONSENT

Informed consent was obtained from all participants included in the study.

ETHICAL CONSIDERATION

Before beginning data collection, the study received ethical approval from the University, Khartoum State Ministry of Health Research Department, and permission to the patients' hospital files from the hospital authorities. A written consent was obtained from the patients.

ACKNOWLEDGEMENTS

The authors would like to thank University, Khartoum State Ministry of Health Research Department for their cooperation and guidance through the whole process, and we would like to thank all that were part of this study for taking their time to complete the survey.

AUTHOR CONTRIBUTIONS

All the authors contributed evenly with regards to data collecting, analysis, drafting and proofreading the final draft.

FUNDING

This study has not received any external funding

CONFLICT OF INTEREST

There are no conflicts of interest.

DATA AND MATERIALS AVAILABILITY

All data associated with this study are present in the paper.

REFERENCES

1. Karen Whalen, Carinda Feild,, Rajan Radhakrishnan, Lippincott Illustrated Reviews: (2019). Pharmacology Seventh Edition, 38: 1447
2. Ghosh R, Alajbegovic A, Gomes AV. (2015). NSAIDs and cardiovascular diseases: role of reactive oxygen species. *Oxidative medicine and cellular longevity*. 20:90.
3. Modig S, Elmståhl S. (2018). Kidney function and use of nonsteroidal anti-inflammatory drugs among elderly people: a cross-sectional study on potential hazards for an at risk population. *International journal of clinical pharmacy*. 40(4):870-7.
4. Hogg RJ, Furth S, Lemley KV, Portman R, Schwartz GJ, Coresh J, et al. (2003). National Kidney Foundation's Kidney Disease Outcomes Quality Initiative clinical practice guidelines for chronic kidney disease in children and adolescents: evaluation, classification, and stratification. *Pediatrics*. 111(6):1416-21.
5. Stavroula G. (2014). Psychological aspects in chronic renal failure. *Health science journal*. (2): 8:205-2014.
6. Ramón García-Trabanino , Zulma Trujillo , Ana Verónica Colorado d , Salvador Magana Mercadoc , Carlos Atilio Henríquezf. (2016). Prevalence of patients receiving renal replacement therapy in El Salvador in 2014. *Nefrología*. a. ;36(6):631-636.
7. Chang P-Y, Chien L-N, Lin Y-F, Wu M-S, Chiu W-T, Chiou H-Y. (2016). Risk factors of gender for renal progression in patients with early chronic kidney disease. *Medicine*. 95(30):1009
8. Fan ZJ, Lackland DT, Lipsitz SR, Nicholas JS, Egan BM, Garvey WT, et al. (2007). Geographical patterns of end-stage renal disease incidence and risk factors in rural and urban areas of South Carolina. *Health & place*. 13(1):179-87.

9. Ok F, Erdogan O, Durmus E, Carkci S, Canik A. (2021). Predictive values of blood urea nitrogen/creatinine ratio and other routine blood parameters on disease severity and survival of COVID-19 patients. *Journal of medical virology*. 93(2):786-93.
10. Jankowski J, Floege J, Fliser D, Boehm M, Marx N. (2021). Cardiovascular disease in chronic kidney disease: pathophysiological insights and therapeutic options. *Circulation*. 143(11):1157-72.
11. Wilcox CM, Cryer B, Triadafilopoulos G. (2005). Patterns of use and public perception of over-the-counter pain relievers: focus on nonsteroidal antiinflammatory drugs. *The Journal of rheumatology*. 32(11):2218-24.
12. Amirimoghadam P, Zihayat B, Dabaghzadeh F, Kiani K, Ebrahimi J, Ghazanfari M, et al.(2017). Evaluation and awareness of over the counter use of non-steroidal anti-inflammatory drugs. *J Appl Pharm Sci*:154-9.
13. Zhou Y, Boudreau DM, Freedman AN.(2014). Trends in the use of aspirin and nonsteroidal anti-inflammatory drugs in the general US population. *Pharmacoepidemiology and drug safety*. 23(1):43-50.
14. Dale O, Borchgrevink PC, Fredheim OMS, Mahic M, Romundstad P, Skurtveit S. (2015). Prevalence of use of non-prescription analgesics in the Norwegian HUNT3 population: Impact of gender, age, exercise and prescription of opioids. *BMC public health*. 15(1):1-9.
15. Koffeman AR, Valkhoff VE, Çelik S, W't Jong G, Sturkenboom MC, Bindels PJ, et al. (2014). High-risk use of over-the-counter non-steroidal anti-inflammatory drugs: a population-based cross-sectional study. *British Journal of General Practice*. 64(621):e191-e8.
16. Claxton RN, Blackhall L, Weisbord SD, Holley JL. (2010). Undertreatment of symptoms in patients on maintenance hemodialysis. *Journal of pain and symptom management*. 39(2):211-8.
17. Luo J-C, Leu H-B, Huang K-W, Huang C-C, Hou M-C, Lin H-C, et al. (2011). Incidence of bleeding from gastroduodenal ulcers in patients with end-stage renal disease receiving hemodialysis. *CMAJ*. 183(18):E1345-E51.
18. Lin X-H, Lin C-C, Wang Y-J, Luo J-C, Young S.-18. H, Chen P-H, et al. (2018). Risk factors of the peptic ulcer bleeding in aging uremia patients under regular hemodialysis. *Journal of the Chinese Medical Association*. 81(12):1027-32.
19. Dua K, Pabreja K, Ramana M. (2010). Aceclofenac topical dosage forms: in vitro characterization. *Acta pharmaceutica*. 60(4):467.
20. Kasiske BL, Zeier MG, Chapman JR, Craig JC, Ekberg H, Garvey CA, et al.(2010). KDIGO clinical practice guideline for the care of kidney transplant recipients: a summary. *Kidney international*. 77(4):299-311.
21. McClellan WM, Warnock DG, Judd S, Muntner P, Patzer RE, Bradbury BD, et al. (2012). Association of family history of ESRD, prevalent albuminuria, and reduced GFR with incident ESRD. *American journal of kidney diseases*. ;59(1):25-31.

Copyright: © 2023 Author. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.