



Scandic Journal of Advanced Research and Reviews

ISSN: 2703-965X CODEN (USA): SJARCA

Cross Ref DOI: [dx.doi.org/10.55966/sjarr](https://doi.org/10.55966/sjarr)

Journal homepage: [http://: www.sjarr.com](http://www.sjarr.com)

Prevalence of chronic kidney disease-associated pruritus, and association with depression among hemodialysis patients in Khyber Pakhtunkhwa

Hamad Ahmad Khan¹, Muhammad Naeem² and Raheela Begum³

1, Senior registrar, Nephrology Department Gajju Khan Medical College Swabi, ahmadkhan_hammad@yahoo.com

2, Medical officer, Dhq teaching Hospital Swabi, FCPS Medicine. naeem317swb@gmail.com

3, PhD Scholar Psychology Department, Shaheed Benazir Bhutto Women University of Peshawar. raheelaanjum57@gmail.com

Scandic Journal of Advanced Research and Reviews, 2022, 2(02), 001–012

Article DOI: <https://doi.org/10.55966/sjarr.2022.2.2.0031>

Abstract

Chronic kidney disease-associated pruritus (CKD-aP), formerly known as the uremic pruritus, is commonly observed in the patients with the hemodialysis. This study aimed to determine the prevalence of the Ckd-aP and to associate it with depression in hemodialysis patients. A multicenter cross-sectional study was conducted on the patients of CKD-aP Khyber Pakhtunkhwa, from March 2021 to March 2022. This research was conducted at multiple hospitals in the Khyber Pakhtunkhwa (different hospitals such as Hayat Abad Medical Complex, Zia Medical complex, Irfan General Hospital, and others). The sample size for this research was 1000, of which 700 were confirmed patients with the CKD-aP. Research shows that the prevalence of CKD-aP is higher in males than in females. This disease creates a negative impact on mental health and causes a range of depressive disorders, among diseased persons.

Keywords.

Chronic kidney disease-associated pruritus (CKD-aP), diseased, and depression.

Introduction

Chronic kidney disease-associated pruritus (CKD-aP), is formerly known as uremic pruritus. Pruritus is a persistent condition that is dominantly discerned in patients with CKD. (2) Previous studies conducted reported more than 50% of the disease's prevalence, all over the world. CKD also called chronic kidney failure entails a restrained loss of kidney function. For instance, kidney filters mediate the wasting of surplus fluid from the blood, which is then eliminated from the body with the urine. CKD ends with excess release, electrolyte imbalance, and other serve consequences. (3) Initial stages mark the diseases with the symptoms of vomiting, weakness, sleep problems, appetite loss, weakness, muscle cramps, high blood pressure, chest pain, itchy skin, and other things. (4) CKD may be the result of certain kind of diseases which causes a disproportion of the fluid particularly high blood pressure, type 1, and type 2 diabetes, interstitial nephritis, glomerulonephritis, polycystic kidney diseases, vesicoureteral reflux, and prolonged urinary tract obstruction due to the cancers, and kidney stones. Whereas CKD-ap is the form of itching that last more than 6 weeks and is called chronic pruritus. Sometimes it is considered as the treatment side effects that badly impact the patient mood, relationship, self-esteem, and quality of life. (5) Research reported that chronic kidney disease-associated pruritus is majorly observed in the people who experience dialysis. (6)

Furthermore, pruritus is reported in patients that do not use dialysis, but that are suffering from improper kidney functions. (7) These patients belong to the CKD stages 3-5, with the enhancement of the prevalence along with the intensifying function of the kidney. (8) Studies show that more than 40% of the patients reported intense itching. This itching ranges from moderate level to severe levels in the patients. CKD-aP is thought to be the agglomeration of the uremic released toxins that is due to the lower quality hemodialysis of the patients, and the developing decline ratio of the renal function. (9) Another major cause of the CKD-aP is a higher level of calcium, phosphorous, and parathyroid hormone, all of them are reported in different studies to cause pruritus'. (10) Also, some vitamin deficiency such as vitamin A, and

other causes skin issues in chronic kidney failure. (11) This led to the systematic inflammation or the inflammation of the skin. Furthermore, some of the studies reported that the immune system mediates the rapid production of cytokines particularly IL-2, IL-6, mast cells, and the T lymphocytes resulting in skin itching. (12)

Inflammation results in heat, and pain to the body parts which causes the patients to scratch the area and sometimes results in bleeding. (13) The body increases the production of the pruritogens such as IL-31, and histamine, which are associated with itching, and potentially end with neurogenic pruritis. Immune cells and skin cells simulate the perceptive peripheral sensory nerve fibers. Then in the dorsal root itch signal is transferred, then in the dorsal horn, then in different brain regions, which mediated the scratching. So, the association of the perceptive itching with the neurogenetic citing consequence in the CKD-aP. (14)

It is more than itching, as it enhances the rate of mortality and morbidity, and decreases the quality of the life. (15) On both peritoneal dialysis, and hemodialysis CKD-aP is influenced similarly. In some of the research, it is reported that this disease is present in post-renal transplants with a prevalence of 12%. The pathophysiology of this condition is complicated and involves a range of mechanisms. (16) The etiology of the disease is also complex and needs the presence of some particular factors that are linked with increasing the chance of causing CKD-aP. For instance, hepatitis c results in the use of arteriovenous graft. This needs vascular access for the hemodialysis. Moreover, dry skin is also considered for the pathogenesis of the disease. As dry skin is the process that causes alterations in the skin pH and enhances the urea excretion on the skin. Pathogenesis is also because of the opioid receptor. The study reported that patients treated with difelikeflain show pruritus relief. Some of the immune dysregulations are also responsible such as inflammatory markers like C-reactive protein are observed in the patients with the CKD-aP. (17)

For treatment purposes, numerous agents are reported. This medical expert takes the history of the patients and mediates the treatment process by suggesting some suitable moisturizers. Other studies reported the antihistamine, steroids, ultraviolet B, and opioid receptors as the agents for the treatment.(18) Acupuncture and acupressure for treating uremic pruritis are also reported that suggest positive results. (19)

This itching and severe pain for a longer duration cause the patients to wake up late at night. It is unbearable, make the patients aggressive, and developed mood swings. Eventually, it causes depression. Duration, types, and severity of depression vary from patient to patient. (20) Major types of the depression that are observed in the diseased person include the major depressive disorder which lasts longer more than two weeks, psychotic depression which ends in hallucinations, delusions it is more severe form it causes the patients to feel, hear, and sense different things because they disrupted the sleep cycle. Also, persistent depressive disorder is observed in people which lose interest in daily activities, and this ends in more than two years. (21)

In this study, we determine the prevalence of the CKD-aP and associated it with the types of depression. As depression is quite common in these diseases, none of the previous studies report that. So, this study will be greatly beneficial in terms of understanding the patient condition of the mind. So, the patient will be treated accordingly.

Methodology.

A multicenter cross-sectional study was conducted on the patients of CKD-aP Khyber-Pakhtunkhwa. Pruritus influence in terms of depression was determined in the patients that go through hemodialysis from March 2021 to March 2022. this research was conducted at multiple hospitals in the Khyber Pakhtunkhwa (different hospitals such as Hayat Abad Medical Complex, Zia Medical complex, Irfan General Hospital, and others). The sample size for this research was 700 confirmed patients with CKD-aP.

Inclusion, and Exclusion criteria.

Patients who were suffering from the CKD-aP in both genders and undergoing hemodialysis were selected. Also, patients who report some type of depression were included in the study. However, the patient who does not report depression were not included in the research project.

Procedure

More than 700 (1000) patients were included in this research. The sample size was based on a confidence interval of 95% and with a precision of 5%. while the patients were undergoing the hemodialysis, we approach the patients. Patients signed the

informed consent forms and confirmed their willingness to be a part of the research. Data were collected from the patients in which their medical history, CDK-aP, and depression-related question were asked. To understand the severity of depression in the patients, we designed a questionnaire that asks about the patient's lifestyle, diet intake, questions related to sleep disturbance, depression symptoms, and other things.

As mentioned above the research was conducted at the dialysis center of the department of Nephrology, in different hospitals such as Hayat Abad Medical Complex, Zia Medical complex, Irfan General Hospital, and others. This research project was approved by the research board Kyber Pakhtunkhwa. Later on, the ethical, and review board also approved the study. Nephrologists in the above-mentioned hospital referred the patients to participate in the study. The patients were divided into two groups. 1st group is those who were suffering from CDK-aP disease, level 1-3, this group includes 400 people, 2nd group target the CDK-aP disease with the 4-5 level.

After taking the written consent form from the participants, a questionnaire regarding disease severity, and depression was filled out by the patients. Enrolled patients were 700 patients. We determined the prevalence of the chronic kidney diseases that are associated with pruritus. Among them 400 patients with the stages of 1-3, and 300 patients with the stages of 4-5. Also, the ratio of the depression was determined in both groups.

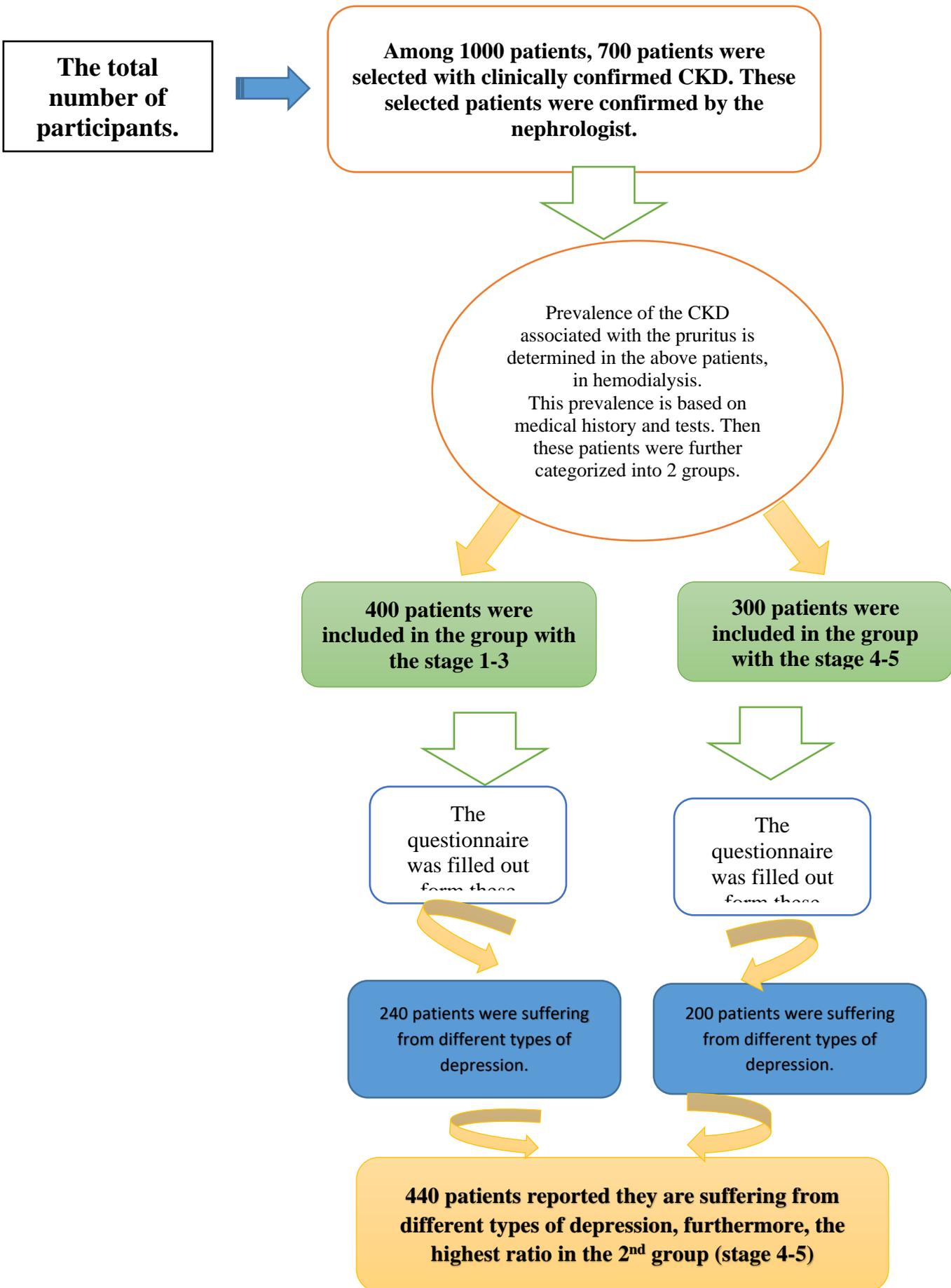


Figure 1. Flowsheet of complete research methodology.

The Likert scale (22) was used to determine the questionnaire. Diverse types of the parameters such as the types of depression, the severity of the depression, and lifestyle are set on the Likert scale analysis. We provide the instructions to the participants on how to fill the questionnaire, moreover, we provide the questionnaire during the different duration of the dialysis. As we want to analyze the influence of dialysis at various stages.

Results

Demographics of the patients n=1000

<i>Parameters</i>	<i>Total Number of the Patients</i> =1000	<i>Without Purities.</i> =300	<i>With purities.</i> =700
<i>Prevalence is based on gender Distribution.</i>			
<i>Male</i>	600 (60%)	200(33%)	400(77%)
<i>Female</i>	400(40%)	100(25%)	300(75%)
<i>Prevalence is based on the age</i>			
<i>18-30 Years.</i>	300	90	120
<i>31-60 Years.</i>	600	160	500
<i>60 Years Above.</i>	100	50	80
<i>Prevalence of pruritus based on stages.</i>			
<i>Stage 1-3</i>	28% of male	20% of female	
<i>Stage 4-5</i>	49% of male	40% of female	

Results show that the prevalence of chronic kidney diseases is more among the males 60%, than the females 40%. Also, among 600 males 400 show the influence of pruritus, which means that the prevalence of pruritus is 77% among males with

chronic kidney diseases. In females, 300 females show the pruritus effect after chronic kidney diseases which means that the prevalence is 75%. However, the prevalence of the CKD-aP is more in the age group of 31-60 years. Furthermore, the prevalence of CKD-aP is higher in stages 4-5.

Table 2. PSQI Questionnaire Responses.

Last month, at which time did you go to the bed?	Participants.
7 pm	30%
11 pm	44%
1 pm	4%
Do you feel hopelessness or emptiness?	45%
Do you feel frustrated, irritable, and anxiety	30%
Do you face sleep disturbances?	20%
You see different faces and the noises.	4%
You don't want to talk to anyone.	45%
You are hopeful about your medical condition.	33%
You feel negative about your family.	12%
You suddenly woke up late at night.	22%
You don't want to discuss your medical conditions.	32%
Do you have any thoughts related to suicide?	11%
You don't want to consume food properly.	2%
You overly think about the future.	64%
Your life is not fair to yourself.	32%
You sense the hallucinations and tell them to your doctors.	11%
You want to take a rest, but you can't.	2%

Table 3. Prevalence of the depression among the CKD-aP patients.

Types of depression	Severe Depression	Moderate Depression	Depression for 1 week.
Major depressive	58%	30%	12%

disorder			
Psychotic depression	15%	40%	45%
Persistent depressive disorder	60%	35%	5%

This table shows that prevalence of the persistent depressive disorders is more severe in the patients. Major depressive disorders are also commonly observed in patients. However, the prevalence of the psychotic disorder is less severe in diseased persons.

Discussion

CKD-aP is the most recurrent obstacle that is marked in hemodialysis patients. In the previous studies, the prevalence of the disease was determined that vary from 22% to 84%. This study also presents the prevalence of the disease while associating it with depression. This study provides the details of the prevalence based on the gender, diseases stages, and the age of the diseased person. In the study prevalence was 79%, however, in our study prevalence is 70%. (23,24) This prevalence has major relevancy among other diseases in Pakistan. As our study shows that the incidence of the diseases is more severe in the diseases stage 4-5. However, previous studies do not report the disease severity based on the states, they reported the severity of the disease based on the symptoms and other things.(25,26) We discussed depression and the types of depression in this stud. Furthermore, we analyze the prevalence that is based on the depression, we associated it with the CKD-aP. Also, the previous study determines the prevalence yet regarded with the sleep quality, and other diseases such as obesities, diabetes, and others. (26) However, we majorly focused on the depression prevalence among the CKD-aP. Previous studies show that the longer duration causes a severe impact on the health of the patients, after the hemodialysis. The current study also reported this by making two groups. Group 2 is presenting those patients that are suffering from the disease for a longer time. Our study shows that the prevalence is slightly higher in the males than the females, however, some of the studies reported that the female ratio is higher. Patients' data regarding the questionnaire tells that people face several kinds of sleeping difficulties. We determine that patient's lifestyle is badly influenced by this sleep disturbance which ends with depression. None of the studies associate the diseases with depression. We

also categorized the prevalence in types of depression, and we determined that the major depressive disorders and persistent depressive disorders are frequently observed in the patients. However, previous studies do not report any of these findings.

Strength, and Limitations.

The strength of this study is that it is the 1st study in Pakistan that associated the CKD-aP with depression. As many people do not consider the patient's state of the mind. Another center is that it is a multicenter study that involved different centers. It is not particular to the one hospital or specific area.

Limitations of this study include the data collected from the patient. This study needs more in-depth data collection to report accurate major findings. However, CKD-aP is a very irritable disease, which makes the patients incredibly angry in small situations.

Conclusion.

Findings show that the prevalence of the CKD-aP is higher in males than in females. This disease creates a negative impact on mental health and causes a range of depressive disorders, among the patients. To suggest the treatment for the patients, it is beneficial to determine the patient's state of mind and suggest the treatment accordingly. Chronic kidney disease-associated pruritus (CKD-aP), is formerly known as uremic pruritus. Pruritus is a persistent condition that is dominantly discerned in patients with CKD. CKD may be the result of certain kind of diseases which causes a disproportion of the fluid particularly high blood pressure, type 1, and type 2 diabetes, interstitial nephritis, glomerulonephritis, polycystic kidney diseases, vesicoureteral reflux, and prolonged urinary tract obstruction due to the cancers, and kidney stones. CKD-aP is the form of itching that last more than 6 weeks and is called chronic pruritus. Major types of the depression that are observed in the diseased person include the major depressive disorder which lasts longer more than two weeks, psychotic depression which ends in hallucinations, delusions it is more serve form it causes the patients to feel, hear, and sense different things because they disrupted the sleep cycle.

References

1. Agarwal P, Garg V, Karagaiah P, Szepietowski JC, Grabbe S, Goldust M. Chronic kidney disease-associated pruritus. *Toxins*. 2021 Aug;13(8):527.
2. Williams KA, Roh YS, Brown I, Sutaria N, Bakhshi P, Choi J, Gabriel S, Chavda R, Kwatra SG. Pathophysiology, diagnosis, and pharmacological treatment of prurigo nodularis. *Expert Review of Clinical Pharmacology*. 2021 Jan 2;14(1):67-77.
3. Almutary H, Bonner A, Douglas C. Symptom burden in chronic kidney disease: a review of recent literature. *Journal of Renal care*. 2013 Sep;39(3):140-50.
4. Mehta OP, Bhandari P, Raut A, Kacimi SE, Huy NT. Coronavirus disease (COVID-19): comprehensive review of clinical presentation. *Frontiers in Public Health*. 2021 Jan 15;8:1034.
5. Makar M, Smyth B, Brennan F. Chronic Kidney Disease-Associated Pruritus: A Review. *Kidney and Blood Pressure Research*. 2021 Sep 7:1-1.
6. Shirazian S, Aina O, Park Y, Chowdhury N, Leger K, Hou L, Miyawaki N, Mathur VS. Chronic kidney disease-associated pruritus: impact on quality of life and current management challenges. *International journal of nephrology and renovascular disease*. 2017;10:11.
7. Agarwal P, Garg V, Karagaiah P, Szepietowski JC, Grabbe S, Goldust M. Chronic kidney disease-associated pruritus. *Toxins*. 2021 Aug;13(8):527.
8. Kim D, Pollock C. Epidemiology and burden of chronic kidney disease-associated pruritus. *Clinical Kidney Journal*. 2021 Dec;14(Supplement_3):i1-7.
9. Qin, L., Zhang, J., Xiao, Y., Liu, K., Cui, Y., Xu, F., Ren, W., Yuan, Y., Jiang, C., Ning, S. and Ye, X., 2022. A novel long-term intravenous combined with local treatment with human amnion-derived mesenchymal stem cells for a multidisciplinary rescued uremic calciphylaxis patient and the underlying mechanism. *Journal of Molecular Cell Biology*.
10. Agarwal P, Garg V, Karagaiah P, Szepietowski JC, Grabbe S, Goldust M. Chronic kidney disease-associated pruritus. *Toxins*. 2021 Aug;13(8):527.
11. Chazot C, Steiber AL, Kopple JD. Vitamin metabolism and requirements in chronic kidney disease and kidney failure. In *Nutritional Management of Renal Disease 2022* Jan 1 (pp. 413-465). Academic Press.
12. Guzman-Sanchez DA, Ishiujii Y, Patel T, Fountain J, Chan YH, Yosipovitch G. Enhanced skin blood flow and sensitivity to noxious heat stimuli in papulopustular rosacea. *Journal of the American Academy of Dermatology*. 2017 Nov 1;57(5):800-5.
13. Nagappa AN, Kanoujia J. Community Pharmacy Services: Dispensing of Prescription, Home Medication Review, Treatments of Minor Ailments, Screening and Monitoring of Chronic Disease, and Maintaining of Patient Profile. In *Perspectives in Pharmacy Practice 2022* (pp. 111-142). Springer, Singapore.
14. Irie H, Kabashima K. The interaction between the immune system and the peripheral sensory nerves in pruritus. *International immunology*. 2021 Dec;33(12):737-42.
15. Elhag S, Rivas N, Tejovath S, Mustafa N, Deonarine N, Hashmi MA, Yerneni S, Hamid P. Chronic Kidney Disease-Associated Pruritus: A Glance at Novel and Lesser-Known Treatments. *Cureus*. 2022 Jan 11;14(1).
16. Cannata-Andía JB, Martín-Carro B, Martín-Vírgala J, Rodríguez-Carrio J, Bande-Fernández JJ, Alonso-Montes C, Carrillo-López N. Chronic kidney disease—mineral and bone disorders: pathogenesis and management. *Calcified Tissue International*. 2021 Apr;108(4):410-22.
17. Sharbin GK, Rash CJ. Characterizing nicotine withdrawal in smokers experiencing homelessness. *Journal of Substance Abuse Treatment*. 2022 Feb 19:108748.
18. Satoh T, Yokozeki H, Murota H, Tokura Y, Kabashima K, Takamori K, Shiohara T, Morita E, Aiba S, Aoyama Y, Hashimoto T. 2020 guidelines for the diagnosis and treatment of cutaneous pruritus. *The Journal of Dermatology*. 2021 Sep;48(9):e399-413.
19. Vernon MK, Swett LL, Speck RM, Munera C, Spencer RH, Wen W, Menzaghi F. Psychometric validation and meaningful change thresholds of the Worst Itching Intensity Numerical Rating Scale for assessing itch in patients with chronic kidney disease-associated pruritus. *Journal of patient-reported outcomes*. 2021 Dec;5(1):1-2.
20. Chen MH, Lin WC, Wu HJ, Bai YM, Li CT, Tsai SJ, Hong CJ, Tu PC, Cheng CM, Su TP. Efficacy of low-dose ketamine infusion in anxious vs nonanxious depression: revisiting the adjunctive ketamine study of Taiwanese patients with treatment-resistant depression. *CNS spectrums*. 2021 Aug;26(4):362-7.
21. Adeyemo T. *The Adjunctive Effects of Regular Preferred Exercise on Depressive Symptoms in Adults Suffering from Major Depressive Disorder* (Doctoral dissertation, University of Massachusetts Global).

22. Jebb AT, Ng V, Tay L. A review of key Likert scale development advances: 1995–2019. *Frontiers in psychology*. 2021 May 4;12:1590.
23. Kim D, Pollock C. Epidemiology and burden of chronic kidney disease-associated pruritus. *Clinical Kidney Journal*. 2021 Dec;14(Supplement_3):i1-7.
24. Hosseinzadeh M, Koohpayehzadeh J, Bali AO, Asghari P, Souri A, Mazaherinezhad A, Bohlouli M, Rawassizadeh R. A diagnostic prediction model for chronic kidney disease in internet of things platform. *Multimedia Tools and Applications*. 2021 May;80(11):16933-50.
25. Viscusi ER, Torjman MC, Munera CL, Stauffer JW, Setnik BS, Bagal SN. Effect of difelikefalin, a selective kappa opioid receptor agonist, on respiratory depression: A randomized, double-blind, placebo-controlled trial. *Clinical and Translational Science*. 2021 Sep;14(5):1886-93.
26. Rehman IU, Lai PS, Lim SK, Lee LH, Khan TM. Sleep disturbance among Malaysian patients with end-stage renal disease with pruritus. *BMC nephrology*. 2019 Dec;20(1):1-8.