Media Kesehatan Masyarakat Indonesia
Volume 19 Issue 1 2023
DOI : 10.30597/mkmi.v19i1.20424
Website : http://journal.unhas.ac.id/index.php/mkmi

Factors Associated with Chronic Kidney Insufficiency Stage: A Cross-Sectional Study

Siti Fadlilah[1*], Nazwar Hamdani Rahil[2], Uswatun Khasanah[2], Santi Damayanti[2], Ariyanto Nugroho[3], Fika Lilik Indrawati[4]
[1]School of Nursing, Taipei Medical University, Taiwan
[2]Nursing Program Study, Faculty of Health Science, Universitas Respati Yogyakarta, Indonesia
[3]Public Health Program Study, Faculty of Health Science, Universitas Respati Yogyakarta, Indonesia
[4]School of Nursing, National Taipei University of Nursing and Health Sciences, Taiwan
[*]Authors Correspondence:d432111018@tmu.edu.tw, sitifadlilah@respati.ac.id/085710844204

ARTICLE INFO

Article History:
Received Sept, 10th, 2022
Accepted Feb, 21st, 2023
Published online Mar, 31st, 2023

Keywords:
CKI;
CKD;
diabetes mellitus;
hypertension;
smoking behaviours;

ABSTRACT
Chronic Kidney Insufficiency (CKI) is a kidney disorder that occurs for at least three months and can become a chronic kidney disease. Many risk factors can cause CKI related to individual characteristics and lifestyle. The purpose is to determine the relationship between age, gender, diabetes mellitus, hypertension, smoking, and consumption of energy supplements with CKI stage in a selected hospital in Indonesia. This research was an analytic observational quantitative with a cross-sectional design. The number of samples was 325 patients using the accidental sampling technique. The instrument used creatinine results and Glomerular Filtration Rate calculations based on laboratory tests, questionnaires, and observation sheets. Bivariate analysis with Chi-Square. Most of the respondents in the CKI stage V (38.8%), late elderly (35.4%), male (56.9%) had a history of diabetes mellitus (55.4%), hypertension (67.7%), did not smoke (78.5%), and does not consume energy supplements (62.5%). Bivariate analysis showed a meaningful relationship between age (X^2=8.52, p=0.019), history smoking behaviour (X^2=7.12, p=0.026), diabetes mellitus (X^2=4.39, p=0.037, and hypertension (X^2=7.99, p=0.026) with CKI stage. Age, smoking behaviour, history of diabetes mellitus, and hypertension were associated with the CKI stage.

INTRODUCTION

The number of Chronic Kidney Disease (CKD) patients increases and cause serious health problems. The number of CKD patients from 1990 to 2017 was 697.5 million and Estimates of CKD sufferers in is 37 million 2021 in the United States.[1,2] CKD was ranked 12th as the highest cause of death in 2017; 1.2 million CKD patients died.[3] The incidence of CKD in Indonesia also increases yearly. The number of new patients in 2017 was 30,831 and became 66,433 in 2018, active patients from 77,892 to 132,142.[4] The prevalence of CKD increased from 1.8 to 3.8 in 2018.[5]

CKD patients will experience impaired renal clearance, fluid and Na accumulation, Ca and P imbalances, anaemia, and uremic bone disorders. The decreased function causes the kidneys unable to eliminate toxic metabolic wastes and excess body fluids. This condition requires the patient to undergo dialysis for life. Dialysis is considered if the patient's Glomerular Filtration Rate (GFR) is less than 15 ml/1.73m^2.[6] The ideal frequency of hemodialysis is 2-3 times per week, with 4-5 hours per procedure.[7]

CKD can be caused by other diseases, including hypertension,[8,9] diabetes mellitus,[10] other kidney diseases, SLE, and other unknown causes. The other risk factors include age, gender, smoking history,[11] and consumption of energy supplements.[12] Previous studies have shown more CKD sufferers in adults than in other age groups, more often in men than women, and more often in blacks than in whites.[13,14,15] Previous studies examined patients who had been diagnosed with End-Stage Renal Disease, in contrast to this study uses patients with Chronic Kidney Insufficiency (CKI) and presents data in the form of a description of the stage.

CKD is a health problem with the second-highest cost from the Indonesian Social Security Administration data after heart disease. Therefore, the incidence of CKD must be controlled, and action is needed to reduce the risk of CKD occurrence. One way to prevent CKD is to know the risk factors and control them. Based on these data, researchers are interested in researching factors related to the stage of CKI.

MATERIAL AND METHOD

This research is a quantitative with an observational analytic survey using a cross-sectional design. The study was conducted at the Prambanan Regional General Hospital, Yogyakarta, Indonesia. The independent variables were age, gender, history of diabetes mellitus, history of hypertension, smoking and consumption of energy drinks. CKI's stage became the dependent variable. The research was held from July to December 2020. The total population used patients' data in hemodialysis units, internal medicine rooms, and internal medicine outpatients in 2019, which amounted to 929. Determination of the number of samples used the Slovin formula;

$$n = \frac{N}{\mathrm{N}\ (\mathrm{d}^2) + 1}$$

With details n = number of samples; N = number of the population; d = precision, researchers used 5.0%. Based on the calculation, the minimum sample required is 280 people. The number of respondents who participated in the study were 325 patients. The sampling technique used accidental sampling. The inclusion criteria were patients with CKI problems who were willing to be respondents. Exclusion criteria were history of routine use of analgesics and non-steroidal anti-inflammatory drugs (NSAIDs), tuberculosis and HIV/AIDS, urinary tract infections, and urinary tract stones.

The research instrument was an observation sheet to record age (in years), gender (based on Identity Card), diabetes mellitus (doctor's diagnosis), and hypertension history (doctor's diagnosis). The observation sheet was filled in based on the data contained in the medical record. Another instrument was a questionnaire to measure the variables of smoking history and history of consuming energy supplements. The CKI stage uses an examination of creatinine levels with fasting (at least 8 hours) venous blood samples according to the SOP written in the observation sheet. It calculates the GFR value using the formula:

$$GFR\ \left(\frac{ml}{minute}\right) = \frac{(140 - age)\ x\ weight\ (kg)}{72\ x\ serum\ creatinine}$$

In women, the result is multiplied by 0.85. The unit of GFR is ml/minute/1.73 m^2. The results of the calculation of the CKI stage are divided into 5, normal (GFR 90), Stage I (GFR 60-89), Stage II (GFR 45-59), Stage III (GFR 30-44), Stage IV (GFR 15-29), and Stage V (GFR < 15). Three assistants assisted data collection with the minimum criteria for nursing a Diploma in Nursing education and a working period of 7 years. Researchers explain the purpose, benefits, and process of the research. Researchers also explained what should and should not be done during the research process. Respondents signed informed consent as evidence of agreeing to participate in the study. The study was conducted after obtaining ethical clearance from the Ethics Commission of Universitas Respati Yogyakarta 140.3/FIKES/PL/VII/2020 and research permission from the Director of the Prambanan Hospital with Number 070/494. Univariate analysis using frequency distribution and the bivariate test using Chi-Square.

RESULTS

Age data is categorized into six stages according to the Ministry of Health of the Republic of Indonesia, namely late adolescence (17-25 years), early adulthood (26-35 years), late adulthood (36-45 years), early elderly (46-55 years), late elderly (56-65 years), very late elderly (65 years and over). Table 1 showed the most common is in the late elderly (35.38%) and males (56.92%). Most had a history of diabetes mellitus (55.38%) and hypertension (67.69%). The majority of respondents did not have a history of smoking (38.15%) and did not consume energy supplements (62.46%).

Table 2 shows that the percentage of stage CKI increases with age; the elderly, late and very late elderly show the incidence of stage V > 20%. Based on gender, male and female respondents were mainly in Stage V, at 28.0% and 10.8%. Most patients with diabetes mellitus and hypertension had Stage V, with 34.8% and 34.2%, respectively. Patients who do not smoke show the highest percentage of Stage I (17.7%), while cigarette consumption shows more stage V events than non-smokers. The incidence of stage I CKI mainly was in people who did not take stamina-enhancing supplements (6.5%). The incidence of stage V showed almost the same results between consuming supplement stamina and not consuming.

Based on the results of the bivariate test, the independent characteristics-age, is related to the CKI stage (X^2=8.52, p=0.019). At the same time, however, gender does not show a significant relationship (X^2=1.96, p=0.259). History of diabetes mellitus and hypertension was associated with the stage of Chronic Kidney Insufficiency (X^2=4.39, p=0.037 and X^2=7.99, p=0.023). The patient's lifestyle related to the CKI stage was smoking behaviour (X^2=7.12, p=0.026), while the consumption of stamina enhancing supplements showed no correlation (X^2=2.70, p=0.184).

Table 1. Characteristics of Respondent

Characteristics	n = 325	%
Age		
Late adolescence	15	4.62
Early adulthood	15	4.62
Late adulthood	35	10.77
Early elderly	76	23.38
Late elderly	115	35.38
Very late elderly	69	21.23
Gender		
Men	185	56.92
Women	140	43.08
Diabetes Mellitus		
Yes	180	55.38
No	145	44.62
Hypertension		
Yes	220	67.69
No	105	32.31
Smoking Behaviour		
No	124	38.15
Mild	62	19.08
Moderate	75	23.08
Severe	64	19.69
Consumption of Energy Supplements		
No	203	62.46
Not Every Day	97	29.85
Every Day	25	7.69
Chronic Kidney Insufficiency Stage		
Stage I	24	7.38
Stage II	34	10.46
Stage III	50	15.38
Stage IV	91	28.00
Stage V	126	38.77

Source: Primary Data, 2020

DISCUSSION

The early stages of CKI have not caused real signs and symptoms, so many do not know. Although asymptomatic, functionally, the body has increased urea and creatinine levels.[16] If there are no symptoms, it is infrequent for patients to check their conditions at health facilities; patients will come when they have complaints. Stage V patients will experience more severe signs and symptoms due to progressively damaged kidney function. The kidneys can no longer maintain fluid and electrolyte balance and cannot dispose metabolic waste.[17] Following the results of this study, patients with stage V must undergo hemodialysis to clear waste metabolites.

The study results prove that not only can CKI attack elderly but also other various ages, as in this study, it is known that it can strike in late adolescence. Age is one of the non-modifiable factors that play a role in the progression of CKI, especially in old age.[18] The study results are in line with previous studies that more CKD incidence is in elderly than younger people.[19,20] Decreased estimated glomerular filtration rate (eGFR) in older people is one of the risk factors for high CKI cases at that age.[21] In addition, for several other reasons for the high prevalence of comorbid conditions (such as prostatic hypertrophy or congestive heart failure), drugs and medical interventions for the treatment of comorbid conditions can cause or influence the development of CKI.[22] The results also showed that more men were diagnosed with CKI than women. Men are at greater risk than women regarding lifestyle, work, and sex hormones.[23] In line with previous research that most CKD sufferers are male.[24] The results showed that gender was not related to the stage of CKI; both men and women had the same chance of developing CKI. The results of the study are in line with Harris's research which states that the gender is not associated with the incidence of CKD.[25]

Table 2. Factors Associated with Chronic Kidney Insufficiency Stage

Variables	Chronic Kidney Insufficiency Stage												$X^2(p)$
	Stage I		Stage II		Stage III		Stage IV		Stage V		Total		
	n	%	n	%	n	%	n	%	n	%	N = 325	%	
Age													
Late adolescence	1	0.3	2	0.6	3	0.9	3	0.9	6	1.8	15	4.6	
Early adulthood	2	0.6	1	0.3	2	0.6	6	1.8	5	1.5	15	4.6	
Late adulthood	4	1.2	5	1.5	7	2.2	6	1.8	13	4.0	35	10.8	8.52
Early elderly	7	2.2	8	2.5	15	4.6	24	7.4	21	6.5	71	23.1	(0.019)
Late elderly	4	1.2	13	4.0	15	4.6	37	11.4	46	14.2	115	35.4	
Very late elderly	6	1.8	5	1.5	8	2.5	15	4.6	35	10.8	69	21.5	
Gender													
Men	7	2.2	13	4.0	10	3.1	64	19.7	91	28.0	185	56.9	1.96
Women	17	5.2	21	6.5	40	12.3	27	8.3	35	10.8	140	43.1	(0.259)
Diabetes Mellitus													
Yes	4	1.2	5	1.5	13	4.0	45	13.8	113	34.8	180	55.4	4.39
No	20	6.2	29	8.9	37	11.4	46	14.2	13	4.0	145	44.6	(0.037)
Hypertension													
Yes	11	3.4	13	4.0	22	6.8	63	19.4	111	34.2	220	67.7	7.99
No	13	4.0	21	6.5	28	8.6	28	8.6	15	4.6	105	32.3	(0.023)
Smoking Behaviour													
No	22	6.8	27	8.3	46	14.2	19	5.8	10	3.1	124	38,2	
Mild	1	0.3	3	0.9	2	0.6	26	8.0	30	9.2	62	19,0	7.12
Moderate	1	0.3	2	0.6	1	0.3	22	6.8	49	15.1	75	23,1	(0.026)
Severe	0	0.0	2	0.6	1	0.3	24	7.4	37	11.4	64	19,7	
Consumption of Energy Supplements													
No	21	6.5	23	7.1	31	9.5	65	20.0	63	19.4	203	64,5	2.70
Not Every Day	2	0.6	9	2.8	11	3.4	17	5.2	58	17.8	97	29,8	(0.184)
Every Day	1	0.3	2	0.6	8	2.5	9	2.8	5	1.5	25	7,7	

Source: Primary Data, 2020

There are more patients who have a history of diabetes mellitus than those who do not. The study results are in line with previous studies that most of CKD patients have a history of diabetes mellitus.(10) Diabetes mellitus causes microvascular disease, one of which is impaired flow to the kidneys. Decreased blood flow causes diabetic nephropathy as a significant factor in terminal renal failure.[26] This study supports previous research that there is a relationship between the last patient's diabetes mellitus and the incidence of CKD.[27,28] However, the results are not following previous studies, that the diabetes mellitus variable is not associated with the incidence of CKD in patients on hemodialysis.[29]

The results showed more patients with a history of hypertension, in line with previous studies, that most CKD occurred in patients with a history of hypertension.[30] The study results prove the theory that hypertension is associated with CKD incidence. Hypertension causes vasoconstriction of the renal blood vessels so that the blood flow that carries nutrients and oxygen is impaired. This condition results in damage to the kidney cells. Old age can cause kidney nephrons to die and not function.[31] The study results are in line with previous studies; there is a significant relationship between hypertension and stadium of CKD.[9] The opposite effect in the Kalengkonga study was that there was no relationship between hypertension and the incidence of CKD.[32]

The risk of CKI increases along with cigarette consumption. Nicotine in cigarettes will enter and circulate through the bloodstream and undergo metabolism mostly in the liver and kidneys. Cigarettes have a stimulating effect on the sympathetic nerves. As a result of the race, there will be an increase in blood pressure, heart rate, and the build-up of catecholamines in the bloodstream. In the acute phase, the renal vasculature undergoes vasoconstriction, which increases the resistance of the renal vasculature. Resulting in a decrease of the glomerular filtration rate and filter fraction.[33] The results of the study support previous research stating that there is a relationship between a history of smoking and the incidence of chronic kidney failure.[8,34,35]

Research data shows that more patients do not have a history of consuming energy supplements. Energy drink supplements contain several psychostimulants, such as caffeine and amphetamines. Caffeine and taurine are contents of energy supplements that can harm kidneys. The diuretic effect is obtained due to increased blood flow to the kidneys and accelerates the glomerular filtration rate. In addition, it is also due to a reduction in the reabsorption process in the renal tubules.[36] Amphetamines trigger vasoconstriction of arteries leading to the kidneys, resulting in decreased blood flow to the kidneys resulting in reduced nutrients and oxygen needed by the kidneys. The lack of blood flow causes kidney cells to experience ischemia, stimulates inflammation, and ends with a decrease in blood-filtering power.[29]

This study showed no relationship between energy supplement consumption and CKI stage, in line with previous research that there was no relationship between energy supplement consumption and CKD.[37] Many food supplements are circulating in society, such as vitamins and minerals, plant ingredients and extracts, proteins and amino acids, omega-3 fatty acids, probiotics, and prebiotics.[38,39] The initial purpose of food supplements is to compensate for nutritional deficiencies. An unbalanced diet extends life and provides several benefits for disease.[39, 40] In this study, the self-questionnaire only asked about the habit of taking supplements but did not ask in detail about the type, duration, dosage, and content of the supplements. The unequal distribution of respondents between those who consumed and did not consume energy supplement drinks could be one of the factors in the study's results showing no relationship. On the other hand, the opposite results were shown by other studies, namely the relationship between consumption of energy drinks containing a combination of caffeine and taurine with the incidence of CKD.[12]

This study has several limitations since researchers does not limit the educational background and knowledge of the respondents, the instrument is made simple with a limited number of questions. This study results in the loss of some detailed information. Researchers did this to get a large number of respondents. This study shows data on the number of cigarettes and energy supplements consumed each day without more detailed information about these two behaviours. However, despite the limitations of this data collection, this study

applying a simple, economic and contact-free approach, most importantly, can produce significant results in a short period of time.

CONCLUSION AND RECOMMENDATION

The results showed that the factors associated with the CKI stage were age, smoking behaviour, history of diabetes mellitus and hypertension. Meanwhile, gender and history of energy supplement consumption were not related to the CKI stage. People with hypertension and diabetes mellitus can be more vigilant in maintaining their health and avoiding factors that aggravate the CKI stage. Therefore, it is necessary to regularly check health-related blood sugar control, blood pressure and kidney function and implement a healthy lifestyle considering the signs and symptoms that do not appear in the early stages. Stage V patients are advised to routinely perform hemodialysis and comply with the management to avoid further complications.

ACKNOWLEDGMENTS

Researchers independently financed this research. Researchers would like to thank the Director of the Prambanan Regional General Hospital, Yogyakarta, Indonesia, for permission to conduct research. Researchers also thank all hospital staff who have helped the research process.

AUTHOR CONTRIBUTIONS

Study conception and design SF, NHR, and UK; Data collection SF, NHR, and UK; Data analysis and interpretation SD, AN, SF, UK, and FLI; Drafting of the article SF, NHR, UK, SD, and FLI; Critical revision of the article SF. SF = Siti Fadlilah; NHR = Nazwar Hamdani Rahil; UK = Uswatun Khasanah; SD = Santi Damayanti; AN = Ariyanto Nugroho; FLI = Fika Lilik Indrawati.

CONFLICTS OF INTEREST

There was no conflict of interest in this study.

REFERENCES

1. Prevention CfDCa. Chronic Kidney Disease in the United States, 2021 2021 [Available from: https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html
2. P A. What is the Global Prevalence of Chronic Kidney Disease (CKD)? 2021 [Available from: https://www.medscape.com/answers/238798-105274/what-is-the-global-prevalence-of-chronic-kidney-disease-ckd
3. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al. Global, Regional, and National Burden of Chronic Kidney Disease, 1990–2017: a Systematic Analysis for the Global Burden of Disease Study 2017. *The Lancet*. 2020;395(10225):709-733. 10.1016/S0140-6736(18)32279-7
4. Registry IR. 11th Report of Indonesian Renal Registry 2018. 2018 [Available from: https://www.indonesianrenalregistry.org/data/IRR%202018.pdf
5. Riskesdas K. Main Results of Basic Health Research (RISKESDAS). Journal of Physics A: Mathematical and Theoretical. 2018;44(8):1-200.
6. Chazot C, Jean G. End-Stage Kidney Patients Require Hemodialysis Therapy Full Start. *Blood Purification*. 2019;47(1-3):214-222.10.1159/000494582
7. Dai L, Lu C, Liu J, Li S, Jin H, Chen F, et al. Impact of Twice- or Three-Times-Weekly Maintenance Hemodialysis on Patient Outcomes: A Multicenter Randomized Trial. *Medicine*. 2020;99(20):e20202. 10.1097/MD.0000000000020202
8. Lee H, Kwon SH, Jeon JS, Noh H, Han DC, Kim H. Association Between Blood Pressure and the Risk of Chronic Kidney Disease in Treatment-Naïve Hypertensive Patients. *Kidney Res Clin Pract*. 2022;41(1):31-42. 10.23876/j.krcp.21.099
9. Liu X, Li F, Zheng Z, Li G, Zhou H, Zhang T, et al. Association of Morning Hypertension with Chronic Kidney Disease Progression and Cardiovascular Events in Patients with Chronic Kidney Disease and Hypertension. *Nutr Metab Cardiovasc Dis*. 2022;32(4):965-972. 10.1016/j.numecd.2021.12.021
10. Damtie S, Biadgo B, Baynes HW, Ambachew S, Melak T, Asmelash D, et al. Chronic Kidney Disease and Associated Risk Factors Assess-

ment among Diabetes Mellitus Patients at A Tertiary Hospital, Northwest Ethiopia. *Ethiopian Journal of Health Sciences*. 2018;28(6). 10.4314/ejhs.v28i6.3

11. Poudyal A, Karki KB, Shrestha N, Aryal KK, Mahato NK, Bista B, et al. Prevalence and Risk Factors Associated with Chronic Kidney Disease in Nepal: Evidence from a Nationally Representative Population-Based Cross-Sectional Study. *BMJ Open*. 2022;12(3):e057509. 10.1136/bmjopen-2021-057509
12. Ariyanto A, Hadisaputro S, Lestariningsih L, Adi MS. Several Risk Factors for Stage V Chronic Kidney Disease (CKD) in the Age Group Less Than 50 Years (Study at Dr. H. Soewondo Kendal Hospital and Dr.Adhyatma Hospital, MPH Semarang). *Jurnal Epidemiologi Kesehatan Komunitas*. 2018;3(1):1-6. https://doi.org/10.14710/jekk.v3i1.3099
13. Islam SMS, Salehin M, Zaman SB, Tansi T, Gupta RD, Barua L, et al. Factors Associated with Chronic Kidney Disease in Patients with Type 2 Diabetes in Bangladesh. *Int J Environ Res Public Health*. 2021;18(23). 10.3390/ijerph182312277
14. Paluch AE, Pool LR, Isakova T, Lewis CE, Mehta R, Schreiner PJ, et al. Association of Fitness with Racial Differences in Chronic Kidney Disease. *Am J Prev Med*. 2019;57(1):68-76. 10.1016/j.amepre.2019.02.016
15. Fadlilah S, Nekada Y, Dede C, Lanni F, Saleha L, Lestiawati E, et al. Interdialytic Weight Gain (IDWG) and Complications of Intradialisis among Hemodialized Patients. *International Medical Journal*. 2021;28(6).
16. Brookes EM, Power DA. Elevated Serum Urea-to-Creatinine Ratio is Associated with Adverse Inpatient Clinical Outcomes in Non-end Stage Chronic Kidney Disease. *Scientific Reports.* 2022;12(1):20827. 10.1038/s41598-022-25254-7
17. Chen TK, Knicely DH, Grams ME. Chronic Kidney Disease Diagnosis and Management: a Review. *Jama*. 2019;322(13):1294-1304. 10.1001/jama.2019.14745
18. Al-Wahsh H, Lam NN, Liu P, Quinn RR, Fiocco M, Hemmelgarn B, et al. Investigating the Relationship Between Age and Kidney Failure in Adults with Category 4 Chronic Kidney Disease. *Canadian Journal of Kidney Health and Disease*. 2020;7. https://doi.org/10.1177/2054358120966819
19. Toyama T, Kitagawa K, Oshima M, Kitajima S, Hara A, Iwata Y, et al. Age Differences in the Relationships Between Risk Factors and Loss of Kidney Function: a General Population Cohort Study. *BMC Nephrology*. 2020;21(1):1-9. 10.1186/s12882-020-02121-z
20. Ravani P, Quinn R, Fiocco M, Liu P, Al-Wahsh H, Lam N, et al. Association of Age with Risk of Kidney Failure in Adults with Stage IV Chronic Kidney Disease in Canada. *JAMA Network Open*. 2020;3(9):e2017150. 10.1001/jamanetworkopen.2020.17150
21. Tonelli M, Riella M. Chronic Kidney Disease and the Aging Population. *Brazilian Journal of Nephrology*. 2014;36:1-5. 10.4103/0971-4065.127881
22. Stevens LA, Viswanathan G, Weiner DE. Chronic Kidney Disease and End-Stage Renal Disease in the Elderly Population: Current Prevalence, Future Projections, and Clinical Significance. *Adv Chronic Kidney Dis*. 2010;17(4):293-301. 10.1053/j.ackd.2010.03.010
23. Valdivielso JM, Jacobs-Cachá C, Soler MJ. Sex Hormones and Their Influence on Chronic Kidney Disease. *Current Opinion in Nephrology and Hyper*tension. 2019;28(1):1-9. 10.1097/MNH.0000000000000463
24. Tomlinson LA, Clase CM. Sex and the Incidence and Prevalence of Kidney Disease. *Am Soc Nephrol*; 2019:1557-1559. 10.2215/CJN.11030919
25. Harris RC, Zhang M-Z. The Role of Gender Disparities in Kidney Injury. *Annals of Translational Medicine*. 2020;8(7). 10.21037/atm.2020.01.23
26. Nordheim E, Jenssen TG. Chronic Kidney Disease in Patients with Diabetes Mellitus.

Endocrine Connections. 2021;10(5):R151. 10.1530/EC-21-0097

27. Sukkar L, Kang A, Hockham C, Young T, Jun M, Foote C, et al. Incidence and Associations of Chronic Kidney Disease in Community Participants with Diabetes: a 5-year Prospective Analysis of the EXTEND45 study. *Diabetes Care*. 2020;43(5):982-990. 10.2337/dc19-1803
28. Nazzal Z, Hamdan Z, Masri D, Abu-Kaf O, Hamad M. Prevalence and Risk Factors of Chronic Kidney Disease Among Palestinian Type 2 Diabetic Patients: a Cross-Sectional Study. *BMC Nephrology*. 2020;21:1-8. https://doi.org/10.1186/s12882-020-02138-4
29. Lilia IH, Supadmi W. Risk Factors for Chronic Kidney Failure in Hemodialysis Units of Private Hospitals in Yogyakarta. *Majalah Farmasetika*. 2019;4:60-65. https://doi.org/10.24198/mfarmasetika.v4i0.25860
30. Georgianos PI, Agarwal R. Hypertension in Chronic Kidney Disease (CKD): Diagnosis, Classification, and Therapeutic Targets. *Am J Hypertens*. 2021;34(4):318-26. 10.1093/ajh/hpaa209
31. Weldegiorgis M, Woodward M. The Impact of Hypertension on Chronic Kidney Disease and End-Stage Renal Disease is Greater in Men Than Women: a Systematic Review and Meta-Analysis. *BMC Nephrology*. 2020;21(1):506. https://doi.org/10.1186/s12882-020-02151-7
32. Kalengkongan DJ, Makahaghi YB, Tinungki YL. Risk Factors Associated with Chronic Kidney Disease (CKD) in Patients Treated at the Liunkendage Tahuna Regional Hospital. *Jurnal Ilmiah Sesebanua*. 2018;2(2):100-114.
33. Jo W, Lee S, Joo YS, Nam KH, Yun HR, Chang TI, et al. Association of Smoking with Incident CKD Risk in the General Population: A Community-Based Cohort Study. *PLoS One*. 2020;15(8):e0238111. https://doi.org/10.1371/journal.pone.0238111
34. Choi HS, Han K-D, Oh TR, Kim CS, Bae EH, Ma SK, et al. Smoking and Risk of Incident End-Stage Kidney Disease in General Population: A Nationwide Population-based Cohort Study from Korea. *Scientific Reports*. 2019;9(1):19511. 10.1038/s41598-019-56113-7
35. Jo W, Lee S, Joo YS, Nam KH, Yun H-R, Chang TI, et al. Association of Smoking with Incident CKD Risk in the General Population: A Community-Based Cohort Study. *PloS One*. 2020;15(8):e0238111. https://doi.org/10.1371/journal.pone.0238111
36. Bigotte Vieira M, Magriço R, Viegas Dias C, Leitão L, Neves JS. Caffeine Consumption and Mortality in Chronic Kidney Disease: a Nationally Representative Analysis. *Nephrology Dialysis Transplantation*. 2019;34(6):974-980. 10.1093/ndt/gfy234
37. Díaz-López A, Paz-Graniel I, Ruiz V, Toledo E, Becerra-Tomás N, Corella D, et al. Consumption of Caffeinated Beverages and Kidney Function Decline in an Elderly Mediterranean Population with Metabolic Syndrome. *Scientific Reports*. 2021;11(1):1-13. 10.1038/s41598-021-88028-7
38. Tan EC, Eshetie T, Gray S, Marcum Z. Dietary Supplement Use in Middle-aged and Older Adults. *The Journal of Nutrition, Health & Aging*. 2022;26(2):133-138. 10.1007/s12603-022-1732-9
39. Wierzejska RE. Dietary Supplements for Whom? The Current State of Knowledge about the Health Effects of Selected Supplement Use. *International Journal of Environmental Research and Public Health*. 2021;18(17):8897. 10.3390/ijerph18178897
40. Crawford C, Brown LL, Costello RB, Deuster PA. Select Dietary Supplement Ingredients for Preserving and Protecting the Immune System in Healthy Individuals: A Systematic Review. *Nutrients*. 2022;14(21):4604. 10.3390/nu14214604