

IDENTIFICATION OF RISK FACTORS AND SYMPTOMS OF CHRONICKIDNEY DISEASE ON ELDERLY IN NURSING HOME 'X' PEKANBARU

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ABSTRACT

Introduction: At this time, Chronic Kidney Disease (CKD) is still a world health problem, CKD is usually undetected until it reaches the severe or terminal stage. CKD ranks 16th as a cause of death worldwide. Nationally, CKD has been the second largest expense following heart disease.

Purpose: This study was conducted to identify the symptoms and risk factors for chronic kidney disease in the elderly in social care institutions who are the population at risk.

Methods: A descriptive study was conducted on 38 elderly people aged ≥ 60 years who are residents of nursing home 'X'. The residents of the nursing home who met the criteria of inclusion were interviewed and identified the risk factors and symptoms of CKD by conducting interviews using the available questionnaires and physical examination. Data were collected and presented in frequency distribution table.

Results: from 38 respondents, 15 respondents had history of hypertension, 10 respondents had a history of diabetes mellitus, 16 respondents had history of smoking, 8 with history of NSAIDS use, and no one has history of kidney disease. The highest count of risk factor was found in 1 respondent (2.6%), meanwhile respondent with 1 and 2 risk factors was found in 11 respondents (28.9%). The most frequent symptom of CKD that appeared among respondents was decreased libido which 26 respondents experienced every day and the rarest symptom of kidney disease that appeared among respondents were restless legs which 35 respondents have never experienced.

Conclusion: Almost every respondent had risk factors of CKD with the most frequent distribution of risk factor is 1-2 risk factor/s in one respondent and the most frequent symptom among respondents is impotence/decreased libido.

Keywords: CKD, geriatric, risk factor, symptoms

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INTRODUCTION

Chronic Kidney Disease (CKD) is characterized by abnormalities in the structure or function of the kidneys shown by declining glomerular filtration rate (GFR) $<60\text{mL}/\text{menit}/1,73\text{m}^2$ that lasts more than 3 months. (KDIGO, 2013) Chronic kidney disease is caused by irreversible damage to the nephrons. Damage to the kidneys resulting from acute kidney disease, hypertension, or diabetes causes an increase in glomerular capillary pressure. (Chonchol and Kendrick, 2015).

Chronic kidney disease is one of the global health problems. According to the 2017 Global Burden of Disease report, in 2016, around 275.9 million people all over the world suffering from CKD, an increase of 87% compared to 1990, which was 147.6 million people. CKD is also the 16th cause of premature death worldwide. (Global Burden of Disease Collaborative Network, 2018) Based on the National Health and Nutrition Examination Survey (NHANES) report in 2007-2012, most CKD patients were in the age group > 60 years. In Indonesia, the prevalence of CKD in 2018 is at 0.38%, there is an increase of 0.18% compared to 2013 which was at 0.2%. Riau has a CKD prevalence of 0.3%, there is an increase of 0.2% compared to 2013 which was at 0.1%. (Center for Disease Control, 2013).

At the age above 50 years, the kidneys will experience a decrease in function which will lead to decreased kidney function, especially at the rate of glomerular excretion and decreased tubular function. Risk factors of developing chronic kidney disease are elder age, bad drinking water habits, diabetes, hypertension, and a history of previous kidney problems. In addition, old age, race, gender, smoking history, and several other risks also play a role in the incidence of CKD. (Levey and Coresh, 2012).

The initial stage of chronic kidney disease does not cause significant

symptoms. CKD symptoms in stage I-III remain unclear, therefore, CKD tends to be ignored until it reaches a more severe and advanced stage that already has more absolute symptoms. Those common symptoms including high blood pressure, changes in the amount of urination and the number of times you urinate in a day, blood in the urine, weakness, and difficulty sleeping, loss of appetite, headaches that are unable to concentrate, itching, shortness of breath, nausea, and vomiting, and swelling, especially of the feet and ankles and of the eyelids in the morning. (Almutary, Bonner and Douglas, 2013).

Detecting risk factors and symptoms of CKD at the early stage can reduce morbidity and reduce the physical, psychological, and economic impact of chronic kidney disease, and can even slow or stop kidney damage. (the United States Renal Data System, 2015) Therefore this study aims to identify the risk factors and symptoms of chronic kidney disease on elderly in nursing home 'x' Pekanbaru.

METHOD

This research was conducted at Panti Sosial Tresna Werdha Khusnul Khotimah, Pekanbaru, and conducted from March to November 2020, after obtaining research ethics permit with ethical number B/198/UN.19.5.1.1.8/UEPKK/2019.

Subjects were all of the nursing home residents who met all of the inclusion criteria.

Participant selection criteria inclusion criteria included:

- 1) Ages ≥ 60 years,
- 2) Willing to take the blood sampling,
- 3) Willing to be a respondent.

Exclusion criteria in this study were:

- 1) Residents with mental illness,
- 2) Linguistic problem,
- 3) Bedridden.

This research conducted on variables which are hypertension, diabetes mellitus (DM), acute kidney injury (AKI), smoking,

consumed non-steroid anti-inflammatory drugs (NSAID), body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), blood glucose, and symptoms of CKD (itching, sleep disorder, loss of appetite, bone/joint pain, decreased concentration, shortness of breath, muscle cramps, restless leg, cold, polyuria, impotence/decreased libido, fatigue, and muscle weakness). This research used anamnesis of CKD's risk factors, questionnaire (Kidney Symptom Questionnaire: Development, Content Validation and Relationship with Quality of Life)(Brown *et al.*, 2017) , blood pressure measurement, BMI measurement, and blood glucose measurement. Statistical analysis was performed using SPSS statistics software version 25.

RESULTS

In this study, we found 38 elderly people who meet the research criteria. Table 1 shows the youngest age in this study was 60 years and the oldest 92 years, with 21 people (55.3%) male and 17 female (44.7%).

Table 1 Characteristics of respondents based on age and gender

Variables	Average	Min	Max	N	%
Age	73.37	60	90		
Gender					
Male				21	55.3
Female				17	44.7
Total				38	100

Table 2 Distribution of risk factors in respondents

Risk factors	N	%
Hypertension		
Yes	15	39.5
No	23	60.5
DM		
Yes	10	26.3
No	28	73.7
AKI		
Yes	0	0
No	38	100
Smoking		
Yes	16	42.1
No	22	57.9
NSAID		
Yes	8	21.1
No	30	78.9
BMI		
Underweight	5	13.2
Normal	20	52.6
Overweight	7	18.4
Obese	6	15.8
SBP		
Normal	11	28.9
Pre-hypertension	14	36.8
Hypertension grade I	10	26.3
Hypertension grade II	3	7.9
DBP		
Normal	21	55.3
Pre-hypertension	8	21.1
Hypertension grade I	5	13.2
Hypertension grade II	4	10.5
Blood glucose		
Normal	35	92.1
Hyperglycemia	3	7.9
Total	38	100

DM : diabetes mellitus, AKI : acute kidney injury, NSAID : nonsteroidal anti-inflammatory drugs, BMI : body mass index, SBP : systolic blood pressure, DBP : diastolic blood pressure

Table 2 shows the distribution of risk factors in respondents. 15 people have a history of hypertension, 10 people have a history of DM, 16 people used to smoke, 8 people have a history of using NSAID while no one has a history of AKI or other kidney problems.

We also measure the respondents' body mass index (BMI) by calculating the weight divided by height squared. There are 20 people with normal BMI, 5 were underweight, 7 were overweight and 6 people who are obese. The measurements of SBP result in 11 people with normal SBP, 14 are pre-hypertension, 10 are in the category of hypertension grade I, and 4 with hypertension grade II. While the measurements of DBP shows there are 21 people with normal DBP, 8 with pre-

hypertension, 5 with hypertension grade I, and 4 with hypertension grade II. As for the measurement of blood glucose, we found 3 people with hyperglycemia while the others are in the normal range.

Table 3 Total of risk factors in respondents

Total Risk Factors	N	%
0	2	5.3
1	11	28.9
2	11	28.9
3	4	10.5
4	8	21.1
5	1	2.6
6	1	2.6
Total	38	100

Table 3 shows that the highest total of risk factors suffered by the respondents are 6 risk factors. There are 11 respondents (28.9%) with one risk factor and 11 respondents (28.9%) with two risk factors.

Table 4 Distribution of symptoms in respondents

Symptoms	Frequency									
	0		1		2		3		4	
	N=38	%	N=38	%	N=38	%	N=38	%	N=38	%
Itching	19	50.0	1	2.6	2	5.3	6	15.8	10	26.3
Sleep disorder	18	47.4	2	5.3	5	13.2	1	2.6	12	31.6
Loss of appetite	21	55.3	0	0	5	13.2	5	13.2	7	18.4
Bone/joint pain	18	47.4	3	7.9	1	2.6	3	7.9	13	34.2
Decreased concentration/vigilance	16	42.1	1	2.6	3	7.9	5	13.2	13	34.2
Shortness of breath	28	73.7	1	2.6	3	7.9	3	7.9	3	7.9
Muscle cramps/stiffness	18	47.4	4	10.5	2	5.3	4	10.5	10	26.3
Feet can't stay still	35	92.1	2	5.3	1	2.6	0	0	0	0
Cold	24	63.2	2	5.3	3	7.9	3	7.9	6	15.8
The desire to urinate frequently	22	57.9	3	7.9	0	0	2	5.3	11	28.9
Impotence/decreased libido	3	7.9	0	0	2	5.3	7	18.4	26	68.4
Fatigue	5	13.2	1	2.6	6	15.8	11	28.9	15	39.5
Muscle weakness	19	50.0	2	5.3	1	2.6	6	15.8	10	26.3

0 : Never, 1 : Less than 1 time a week, 2 : 1-2 times a week, 3 : Several times a week, 4 : Everyday

Table 5 Frequency of symptoms in respondents

Symptoms	Impact											
	0		1		2		3		4		5	
	N=38	%	N=38	%	N=38	%	N=38	%	N=38	%	N=38	%
Itching	19	50.0	2	5.3	2	5.3	3	7.9	8	21.1	4	10.5
Sleep disorder	18	47.4	3	7.9	0	0	0	0	10	26.3	7	18.4
Loss of appetite	21	55.3	1	2.6	1	2.6	7	18.4	6	15.8	2	5.3
Bone/joint pain	18	47.4	2	5.3	1	2.6	6	15.8	7	18.4	4	10.5
Decreased concentration/vigilance	16	42.1	2	5.3	2	5.3	6	15.8	8	21.1	4	10.5
Shortness of breath	29	76.3	0	0	0	0	1	2.6	5	13.2	3	7.9
Muscle cramps/stiffness	18	47.4	2	5.3	1	2.6	6	15.8	6	15.8	5	13.2
Feet can't stay still	35	92.1	1	2.6	2	5.3	0	0	0	0	0	0
Cold	24	63.2	3	7.9	2	5.3	5	13.2	3	7.9	1	2.6
The desire to urinate frequently	22	57.9	3	7.9	1	2.6	2	5.3	2	5.3	8	21.1
Impotence/decreased libido	3	7.9	24	63.2	5	13.2	4	10.5	2	5.3	0	0
Fatigue	5	13.2	0	0	5	13.2	5	13.2	18	47.4	5	13.2
Muscle weakness	19	50.0	0	0	3	7.9	2	5.3	6	15.8	8	21.1

0 : No symptoms, 1 : Not disturbing, 2 : Slightly disturbing, 3 : Moderate, 4 : Disturbing, 5 : Very disturbing

Table 4 shows that the most frequent symptom among respondents is Impotence/decreased libido, 26 respondents (68.4%) experience this symptom everyday. Followed by other symptom, fatigue, 15 respondents (39.5%) experience this symptom everyday. The rarest symptom among respondents is restless leg (feet that can't stay still), 35 (92.1%) respondents never experience this symptom.

Although Table 4 shows that the most frequent symptom is impotence/decreased libido, the most undisturbed symptom is impotence/decreased libido, 0 resident (0%) residents feel undisturbed by this symptom. While the most disturbing symptom is sleep disturbance, 7 residents (18,4%) feel disturbed by this symptom.

DISCUSSION

Based on the results of the study, it was found that 15 people had a history of hypertension and 23 others had no history of hypertension. Data from the Center for Disease Control and Prevention (CDC) shows that 20% of hypertensive patients can suffer from CKD. (Centers for Disease Control and Prevention, 2019) Based on a case-control study conducted at the West Java Big Education Hospital, as many as 30.7% of patients with CKD have hypertensive comorbid diseases. From this study, it was concluded that hypertension was the most common comorbid disease suffered in all samples. (Indrayanti *et al.*, 2019) Individuals with a history of hypertension are 3.2 times more likely to develop CKD. This is because high blood pressure in hypertensive people can increase intraglomerular pressure. High intraglomerular pressure can cause damage to the glomerulus both structurally and functionally. (Pranandari and Supadmi, 2015).

The results of this study found that 10 people had a history of DM, while 28 other people had no history of DM.

Research conducted at Dr. Mohammad Hoesin Hospital in Palembang, the 300 samples of CKD patients who were taken, 61 of them had a history of diabetes mellitus. The results of this study concluded that diabetes mellitus was the second largest risk factor for developing CKD after hypertension. After conducting a bivariate analysis, it was found that diabetes mellitus had a significant relationship with the incidence of CKD (OR = 4; $p < 0.05$). (Hervinda, Novadian and Tjekyan, 2014) Hyperglycemia in DM sufferers can cause changes in renal hemodynamics that cause mechanical stretching, pressure on endothelial cells and mesangium, activation of complex biochemical pathways that increase extracellular matrix production, hyperglycemia-induced injury, as well as damage and loss of podocytes, these changes cause internal damage. selective glomerular capillary permeability. (Wang, Jardine and Perkovic, 2014).

Based on the results of the study, it was found that all the elderly had no previous history of kidney disease. A history of kidney disease is a risk factor for the incidence of CKD. A recent meta-analysis of 82 studies showed an increased risk for hospitalized patients with AKI experiencing new or progressive CKD (HR 2.67, 95% CI 1.99–3.58). (See *et al.*, 2019). This is due to a maladaptive repair in AKI which involves many pathophysiological processes. When the damage to the kidneys is greater than the compensatory response, there will be a failure in the tissue repair process. Angiogenesis is disturbed and the cell cycle becomes dysfunctional, this leads to the development of chronic kidney disease. (Kurzhausen *et al.*, 2020).

Based on the results of this study, 22 people had no history of smoking, and 16 people with a history of smoking. A total of 16 people with a history of smoking had a greater risk of developing CKD than non-smokers.

This is supported by a cross-sectional study conducted by Yacoub *et al.*, where approximately 43% of CKD patients have ever smoked regularly. From this study, it was found that in CKD patients, 56 people still smoke regularly and 30 people have a history of smoking regularly. Current smokers had an increased risk of developing CKD (OR = 1.63 $p = 0.02$, 95% CI = 1.08-2.45), while people who had a history of smoking had no statistically significant difference. (Yacoub *et al.*, 2010) Nicotine activates the $\alpha 7$ nicotinic acetylcholine receptors ($\alpha 7$ nAChR) in the proximal tubule and triggers the biosynthesis of profibrotic and proinflammatory cytokines that accelerate the development of CKD. (Rezonzew *et al.*, 2012).

Based on the results of the study, there were more elderly who did not have a history of NSAID use, namely 30 people, while 8 people had a history of NSAID use. Another study by A. Ingsathit *et al.* found the results of 626 people with CKD in Thailand, as many as 48.33% had a history of using NSAIDs. (Ingsathit *et al.*, 2010) Based on research by Hsu *et al.* there is a relationship between the use of NSAIDs and the risk of developing CKD. The results showed that respondents who had a history of using NSAIDs ≥ 90 days had an increased risk of CKD by 32%. (Hsu *et al.*, 2015) The use of NSAIDs may cause decreased renal perfusion due to inhibition of prostaglandin synthesis. (Lefebvre *et al.*, 2020) When there is a reduction in blood flow to the kidneys, prostaglandins are to prevent ischemia. With the presence of NSAIDs, there will be a disturbance in the balance between vasoconstriction and renal vasodilation, causing ischemia and decreased renal filtration. (Wu and Huang, 2018).

Based on the results of the study, there were 5 people (13.2%) underweight, 20 people (52.6%) with normal BMI, 7 people (18.4%) overweight, and 6 people

(15.8%) obese. Based on data from case studies conducted in the Framingham Heart Study, 152 (34.5%) of 441 CKD cases had a BMI ≥ 30 kg / m² when diagnosed with CKD. (McMahon *et al.*, 2014) Obesity increases the risk of the incidence of major risk factors for chronic kidney disease (CKD), such as diabetes and hypertension which have a direct impact on the development of CKD and End-Stage Renal Disease (ESRD). (Kovesdy *et al.*, 2017) Obesity can contribute to the pathogenesis of kidney damage through inflammation, oxidative stress, and endothelial dysfunction, prothrombotic states, hypervolemia, and adipokine derangements. (Mirrakhimov, 2012) Excess visceral adipose tissue can lead to activation of the sympathetic nervous system and the renin-angiotensin system resulting in a feedback loop whereby obesity-induced decline in renal function leads to the development of hypertension, resulting in further damage to the kidneys. (Hashimoto *et al.*, 2015).

Research in South Korea states that individuals with a systolic blood pressure of 130-139 mmHg and ≥ 140 mmHg have a 1.30 and 1.79 times higher risk of having an incidence of CKD G3-G5 compared to systolic blood pressure of 120-129 mmHg. (Chang *et al.*, 2020) This study is in accordance with the theory which states that the kidney as the main target organ is affected by an increase in blood pressure. Hypertensive nephrosclerosis is the second most common cause of kidney failure. Long-term elevations in blood pressure can lead to decreased renal function through a variety of mechanisms. (Chang *et al.*, 2020) Most guidelines recommend a target blood pressure $< 140/90$ mmHg as the primary prevention of CKD. (Whelton *et al.*, 2018).

Studies on the risk factors for CKD in Nigerians reveal that there is a significant difference in blood pressure between the CKD patient group and the control group. In the group of patients with CKD, diastolic blood pressure

ranges from 100-130 mmHg. The study concluded that the more severe the level of hypertension, the greater the risk of developing kidney damage. (Nwankwo, Wudiri and Akinsola, 2010) In an increase in systolic and diastolic blood pressure, there is an increase in sympathetic nerve activity which plays a role in worsening hypertension and kidney disease. (Bae *et al.*, 2019).

The results showed that 35 people had a blood glucose <200 mg/dl while 3 others had a blood glucose \geq 200 mg/dl. Blood glucose examination is performed as early detection of DM. (Centers for Disease Control and Prevention, 2019) Therecommended tests for screening for DM are HbA1c, fasting blood sugar, or oral glucose tolerance test (OGTT). (Isfeedvajani, 2018) Based on the CDC, DM is the most dominant risk factor for CKD. (Centers for Disease Control and Prevention, 2019).

Result of this study show most of the respondents have one or two risk factors with the percentage of 28.9% for each group. While the highest number of risk factors suffered by the respondent are 6 risk factors with the percentage of 2.6%. Knowing the risk factors of CKD and implementing screening for high-risk populations will increase early detection for CKD. Thus, it will allow people to do initiate treatment for those modifiable risk factors. (Kazancioğlu, 2013).

Research at Leicester General Hospital on CKD stage 1-5 patients using the LUSS questionnaire with a mean age of 60.5 ± 1.0 years, it was found that the most commonly reported symptoms were muscle weakness with a frequency (75%) decreased appetite (58%), bone pain/joints (56%), itching (56%) and dyspnea (49%). 24 Another study at the University of Pittsburgh in stage 4 CKD patients reported that the most common symptoms were fatigue or lack of energy (78%), dry skin (53%), difficulty sleeping (44%), pruritus (44%), and bone or joint pain (39%). (Brown *et al.*, 2017).

Based on the results of this study, it was found that the most common symptom was impotence/decreased libido. Decreased libido in patients with chronic kidney disease occurs due to disturbances in the hormonal system and also due to disorders of the sympathetic nervous system. Decreased arterial or venous supply from the penis and psychological effects can cause erectile dysfunction in men with chronic kidney disease. Chronic kidney disease causes arterial occlusion and causes weak blood flow to the penis as well as venous occlusion leading to the inability to have persistent erections. Chronic kidney disease also causes atherosclerosis and vascular disorders in the pelvic region, so that these vascular system problems lead to decreased erectile function or erectile dysfunction. Psychological factors also play an important role in the erectile function of people with chronic kidney disease. Life-threatening illnesses cause fear in the sufferer. Neurogenic disorders also occur in patients with chronic kidney disease. Patients undergoing hemodialysis generally experience disorders of autonomic innervation. This innervation disorder causes problems with the adrenergic and cholinergic neurotransmitters that regulate blood flow in the corpus cavernosa so that it is thought to cause erectile dysfunction. (Ahmad *et al.*, 2009).

This study reported that fatigue was experienced by 15 people (39.5%) of respondents every day. Several complex clinical factors, some of which can be modified, correlate with fatigue in patients with CKD, including a high burden of medical comorbidities, sedentary lifestyle, obesity, hypoalbuminemia, and use of sleeping pills. (Jhamb *et al.*, 2013) Based on research by Gregg *et al.* conducted in patients with non-chronic non-dialysis CKD, reported that of 266 respondents, 69.2% have symptoms of fatigue and 10.9% have severe symptoms of severe

fatigue. Fatigue arises as a result of various factors, such as insomnia, depression, pain, and drug use. (Moreh, Jacobs and Stessman, 2010),

This study reported that another disturbing symptom of kidney disease that was most prevalent in the nursing home was sleep disorder with a frequency of 12 (31.6%) who experiencing it. Research conducted by Tan et al. in CKD patients at China Medical University Hospital reported that 33.3% of CKD patients and in patients who had received hemodialysis therapy had sleep disturbances, the prevalence of sleep disorders increased to 46.7%. (Tan *et al.*, 2019) These symptoms can be caused by multifactorial causes including psychological disorders (depression, anxiety), lifestyle factors (coffee/nicotine use, sleep hygiene), treatment-related factors (dialysis time, napping, cytokine production, changes in thermoregulation, dialysis disequilibrium syndrome, circadian rhythm disorders, medication side effects) and intrinsic, specific kidney disease (anemia/obstructive sleep apnea/restless leg syndrome and other comorbidities, uremia, changes in neurotransmitter production). Sleep disorder is a common disorder that occurs in the elderly population, it is reported that 50% of the elderly suffer from sleep disorders. (Patel, Steinberg and Patel, 2018).

Restless leg syndrome (legs can't stay still) is a symptom that rarely appears in the elderly at the Tresna Werdha Khusnul Khotimah Social Home, Pekanbaru, with a frequency of 35 people (92.1%) never experienced these symptoms. The causes are related to iron deficiency, anemia, uremia leading to encephalopathy, and peripheral neuropathy. A study conducted on 66 at CKD stages 1-5 conducted by Lin et al. showed that 28.4% of CKD patients experienced these symptoms, but in early-stage CKD patients, only 9.9% had symptoms of restless leg syndrome. Respondents in this study were healthy

populations and none of them experienced a decrease in GFR stage 4-5. So, it is natural that the symptoms of restless leg syndrome were not found in the respondents of this study. (Mahaldar, 2014).

CONCLUSION

From the research of identification of risk factors and symptoms of chronic kidney disease on elderly in nursing home 'x', Pekanbaru, this research concluded that almost respondents had risk factor/s of CKD with the highest count of risk factors suffered by the respondents are 6 risk factors and the most frequent symptom among respondents is impotence/decreased libido. Thus, frequent screening test is absolutely needed, especially on risky population.

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REFERENCES

1. Ahmad, M. *et al.* (2009) 'Impact of renal transplantation on erectile dysfunction due to chronic renal failure in male patients.', *Journal of Ayub Medical College, Abbottabad : JAMC. Pakistan*, 21(1), pp. 69–71.
2. Almutary, H., Bonner, A. and Douglas, C. (2013) 'Symptom burden in chronic kidney disease: a review of recent literature.', *Journal of renal care*. United States, 39(3), pp. 140–150. doi: 10.1111/j.1755-6686.2013.12022.x.
3. Bae, E. H. *et al.* (2019) 'Association between systolic and diastolic blood pressure variability and the risk of end-stage renal disease', *Hypertension*, 74(4), pp. 880–887.
4. Brown, S. A. *et al.* (2017) 'Symptom

- burden in patients with chronic kidney disease not requiring renal replacement therapy', *Clinical Kidney Journal*, 10(6), pp. 788–796. doi: 10.1093/ckj/sfx057.
5. Center of Disease Control (2013) *Anthropometry Procedures Manual, National Health and Nutrition Examination Survey (NHANES)*. Atlanta.
 6. Centers for Disease Control and Prevention (2019) *Chronic kidney disease in the United States*. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention.
 7. Chang, T. I. *et al.* (2020) 'Associations of systolic blood pressure with incident CKD G3-G5: a cohort study of South Korean adults', *American Journal of Kidney Diseases*, 76(2), pp. 224–232.
 8. Chonchol, M. and Kendrick, J. (2015) 'The patient with chronic kidney disease', in *Schrier RW, ed. Manual of Nephrology*. 8th ed.
 9. Wolters Kluwer. Global Burden of Disease Collaborative Network (2018) *Global Burden of Disease Study 2017 (GBD 2017) All-cause Mortality and Life Expectancy 1950-2017*. Seattle, United State: Institute for Health Metrics and Evaluation (IHME).
 10. Hashimoto, Y. *et al.* (2015) 'Metabolically healthy obesity and risk of incident CKD', *Clinical Journal of the American Society of Nephrology*, 10(4), pp. 578–583.
 11. Hervinda, S., Novadian, N. and Tjekyan, S. (2014) 'Prevalensi dan faktor risiko penyakit ginjal kronik di RSUP Dr. Mohammad Hoesin Palembang', *Majalah Kedokteran Sriwijaya*, 46(4), pp. 275–281.
 12. Hsu, C. C. *et al.* (2015) 'Use of nonsteroidal anti-inflammatory drugs and risk of chronic kidney disease in subjects with hypertension: nationwide longitudinal cohort study', *Hypertension*, 66(3), pp. 524–533.
 13. Indrayanti, S. *et al.* (2019) 'Risk factors for chronic kidney disease: a case-control study in a district hospital in Indonesia', *Journal of Pharmaceutical Sciences and Research*, 11(7), pp. 2549–2554.
 14. Ingsathit, A. *et al.* (2010) 'Prevalence and risk factors of chronic kidney disease in the Thai adult population: Thai SEEK study', *Nephrology Dialysis Transplantation*, 25(5), pp. 1567–1575.
 15. Isfeedvajani, M. S. (2018) 'Diabetes mellitus type 2 screening guidelines', *International Journal of Medical Reviews*, 5(4), pp. 137–139.
 16. Jhamb, M. *et al.* (2013) 'Prevalence and correlates of fatigue in chronic kidney disease and end-stage renal disease: are sleep disorders a key to understanding fatigue?', *American journal of nephrology*, 38(6), pp. 489–495. doi: 10.1159/000356939.
 17. Kazancioğlu, R. (2013) 'Risk factors for chronic kidney disease: an update', *Kidney International Supplements*, 3(4), pp. 368–371. doi: 10.1038/kisup.2013.79.
 18. KDIGO (2013) 'Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease'. Available at: www.publicationethics.org (Accessed: 21 August 2020).
 19. Kovesdy, C. P. *et al.* (2017) 'Obesity and kidney disease: hidden consequences of the epidemic', *Kidney International*, 91(2), pp. 260–262. doi:10.1016/j.kint.2016.10.019.
 20. Kurzhausen, J. T. *et al.* (2020) 'AKI: an increasingly recognized risk factor for CKD development and progression', *Journal of Nephrology*, 33(6), pp. 1171–1187.
 21. Lefebvre, C. *et al.* (2020) 'Non-

- steroidal anti-inflammatory drugs in chronic kidney disease: a systematic review of prescription practices and use in primary care', *Clinical Kidney Journal*, 13(1), pp. 63–71.
22. Levey, A. S. and Coresh, J. (2012) 'Chronic kidney disease', *The Lancet*. doi: 10.1016/S0140-6736(11)60178-5.
 23. Mahaldar, A. R. (2014) 'Restless leg syndrome in chronic kidney disease', *Clinical Queries: Nephrology*, 3(1), pp. 5–8. doi: <https://doi.org/10.1016/j.cqn.2014.03.002>.
 24. McMahan, G. M. *et al.* (2014) 'Mid-Adulthood risk factor profiles for CKD', *Journal of the American Society of Nephrology*, 25(11), pp.2633–2641.
 25. Mirrakhimov, A. E. (2012) 'Obstructive sleep apnea and kidney disease: is there any direct link?', *Sleep and Breathing*, 16(4), pp.1009–1016. doi: 10.1007/s11325-011-0624-8.
 26. Moreh, E., Jacobs, J. M. and Stessman, J. (2010) 'Fatigue, function, and mortality in older adults.', *The journals of gerontology. Series A, Biological sciences and medical sciences*. United States, 65(8), pp. 887–895. doi:10.1093/gerona/glq064.
 27. Nwankwo, E. A., Wudiri, W. W. and Akinsola, A. (2010) 'Risk factors for the development of chronic kidney disease among Nigerians with essential hypertension', *Journal of Medical Sciences*. Asian Network for Scientific Information, 7(4), pp. 579–584. doi: 10.3923/jms.2007.579.584.
 28. Patel, D., Steinberg, J. and Patel, P. (2018) 'Insomnia in the Elderly: A Review.', *Journal of clinical sleep medicine: JCSM: official publication of the American Academy of Sleep Medicine*, 14(6), pp. 1017–1024. doi: 10.5664/jcsm.7172.
 29. Pranandari, R. and Supadmi, W. (2015) 'Faktor resiko gagal ginjal kronik di unit hemodialisis rsud wates kulonprogo', *Majalah farmaseutik*, 11(2), pp. 316–320.
 30. Rezonzew, G. *et al.* (2012) 'Nicotine exposure and the progression of chronic kidney disease: role of the $\alpha 7$ -nicotinic acetylcholine receptor', *American Journal of Physiology-Renal Physiology*, 303(2), pp. 304–312.
 31. See, E. J. *et al.* (2019) 'Long-term risk of adverse outcomes after acute kidney injury: a systematic review and meta-analysis of cohort studies using consensus definitions of exposure', *Kidney International*, 95(1), pp. 160–172
 32. Tan, L. H. *et al.* (2019) 'Prevalence of Insomnia and Poor Sleep in Patients with Chronic Kidney Disease: A Systematic Review', *Kidney International Reports*. Elsevier Inc, 4(7), p. S117. doi: 10.1016/j.ekir.2019.05.301.
 33. United States Renal Data System (2015) '2015USRDS Annual Data Report: CKD in the United States', 1.
 34. Wang, A. Y., Jardine, M. and Perkovic, V. (2014) 'Kidney disease in diabetes', in *Managing Cardiovascular Complications in Diabetes*. Oxford, UK: John Wiley & Sons, Ltd, pp. 58–86.
 35. Whelton, P. K. *et al.* (2018) 'Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary', *Journal of the American College of Cardiology*, 71(19), pp. 2199–2269.
 36. Wu, H. and Huang, J. (2018) 'Drug-induced nephrotoxicity: pathogenic mechanisms, biomarkers and prevention strategies', *Current Drug Metabolism*, 19(7), pp. 559–567.

37. Yacoub, R. *et al.* (2010) 'Association between smoking and chronic kidney disease: a case control study', *BMC Public Health*, 10(1), p. 731.