

## Anxiety and depression in family caregivers of hemodialysis patients: Incidence, risk factors, and correlation

Akbar Zulkifli Osman<sup>1,2</sup>, Eska Agustin Putri Susanti<sup>2</sup>, Reza Ishak Estiko<sup>\*3</sup>, Meiza Fadhila Azzahra<sup>3</sup>, Andika Danendra Widyadhana<sup>3</sup>

<sup>1</sup>dr. Soehadi Prijonegoro Public Hospital, Sragen, Indonesia

<sup>2</sup>Department of Psychiatry, Faculty of Medicine, Universitas Islam Indonesia, Yogyakarta, Indonesia

<sup>3</sup>Faculty of Medicine, Universitas Islam Indonesia, Yogyakarta, Indonesia

Original Article

### ABSTRACT

#### ARTICLE INFO

##### Keywords:

Anxiety  
Chronic kidney disease  
Depression  
Family caregivers  
Hemodialysis

##### \*Corresponding author:

rezaestiko@gmail.com

DOI: 10.20885/JKKI.Vol14.Iss3.art6

##### History:

Received: June 6, 2023  
Accepted: December 3, 2023  
Online: December 30, 2023  
Copyright ©2023 Authors.

**Background:** Chronic kidney disease (CKD) imposes a significant global burden, with diabetes and hypertension being major contributors. In the severe stage, CKD patients require long-term hemodialysis (HD) treatment and rely on family caregivers for support. Caregivers often experience mental health challenges, including anxiety and depression, which can impact their quality of life and patient outcomes.

**Objective:** This study aimed to identify the anxiety and depression incidence in HD family caregivers at Soehadi Prijonegoro Regional Public Hospital (SPRPH), identify the risk factors associated with these conditions, and investigate the relationship between anxiety and depression

**Methods:** A cross-sectional analysis was carried out at the Hemodialysis Department from November 2022 to February 2023. Caregivers accompanying CKD patients undergoing HD participated voluntarily. Anxiety and depression levels were evaluated using the Hamilton Anxiety Rating Scale (HAM-A) and Hamilton Depression Rating Scale (HAM-D).

**Results:** Out of 106 participants, 66% were female. Most caregivers (99%) experienced anxiety, with 91% classified as mild and 8% as mild to moderate. Depression was reported by 42%, with 2% experiencing mild to moderate symptoms. Spearman's analysis revealed a significant correlation between anxiety and depression ( $p=0.000$ ). No specific caregiver characteristics were found to be associated with anxiety or depression.

**Conclusion:** Family caregivers of HD patients demonstrated a high incidence of anxiety and a lower prevalence of depression. Anxiety levels were correlated with depression levels. We did not identify specific risk factors for these mental health conditions among caregivers. These findings emphasize the need for mental health screening and appropriate management to improve the quality of life for HD family caregivers.

**Latar Belakang:** Penyakit ginjal kronik (PGK) merupakan penyakit global, dengan diabetes dan hipertensi sebagai penyebab utama. Pada tahap yang parah, pasien PGK memerlukan pengobatan hemodialisis (HD) jangka panjang dan membutuhkan dukungan pengasuh keluarga. Pengasuh sering mendapat tantangan kesehatan mental, termasuk kecemasan dan depresi, yang dapat mempengaruhi kualitas hidup mereka dan pasien.

**Tujuan:** Penelitian ini bertujuan untuk mengetahui insidensi kecemasan dan depresi pada pengasuh keluarga pasien HD di Rumah Sakit Umum Daerah Soehadi Prijonegoro, mengidentifikasi faktor risiko, dan menyelidiki hubungan antara kecemasan dan depresi.

**Metode:** Penelitian potong lintang dilakukan di Departemen Hemodialisis dari November 2022 hingga Februari 2023. Pengasuh yang mendampingi pasien PGK yang menjalani HD berpartisipasi secara sukarela. Tingkat kecemasan dan depresi dinilai menggunakan Hamilton Anxiety Rating Scale (HAM-A) dan Hamilton Depression Rating Scale (HAM-D).

**Hasil:** Dari 106 partisipan, 66% adalah perempuan. Sebagian besar pengasuh (99%) mengalami kecemasan,

dengan 91% tergolong ringan dan 8% tergolong ringan hingga sedang. Depresi dilaporkan oleh 42%, dengan 2% mengalami gejala ringan hingga sedang. Analisis Spearman menunjukkan korelasi yang signifikan antara kecemasan dan depresi ( $p=0,000$ ). Tidak ada karakteristik pengasuh yang berhubungan dengan kecemasan atau depresi

**Kesimpulan:** Pengasuh keluarga HD menunjukkan tingkat insidensi kecemasan yang tinggi dan depresi yang lebih rendah. Tingkat kecemasan berkorelasi dengan derajat depresi. Kami tidak menemukan faktor risiko spesifik untuk kondisi kesehatan mental pengasuh. Temuan ini menekankan perlunya skrining kesehatan mental dan manajemen yang tepat untuk meningkatkan kualitas hidup pengasuh keluarga pasien HD.

## INTRODUCTION

The global toll of CKD has been substantially rising and unevenly distributed. The burden of diabetes and hypertension, considered the two leading drivers of CKD, has considerably increased over the past several decades. It is stimulated by demographic growth and, in some regions, tied to the diabetic pandemic. More of the CKD burden was in low and lower-middle-income countries.<sup>1</sup> Patient with CKD compromises multiple aspects of life, such as physical, financial, family, and social. This compromise forces them to adapt to the changes stemming from the diagnosis and progression of the disease. It makes the patient dependent on several forms of care and caregivers.<sup>2</sup>

The CKD is chronic and requires prolonged treatment with HD in a severe stage. Caregivers, especially family, must support all this patient aspect of life. Thus, caregivers and patients showed similar mental health conditions. They met the criteria for depression as a self-perceived condition where the symptoms got worse with time.<sup>2</sup> According to Kang et al., dialysis patient caregivers have the burden and a reduction in psychological health.<sup>3</sup> Caregivers experience high levels of anxiety and depression when patients also suffer from anxiety and depression. The depression level experienced by patients undergoing HD is similar to that of cancer patients because CKD disrupts daily activities and affects the life quality for both patients and their families.<sup>4</sup> Previous research suggests that patients undergoing HD have a negative emotional impact on their caregivers, making them susceptible to anxiety and depression. Caregivers often experience mental and physical fatigue, a strain on family

relationships, and a decline in social functioning.<sup>5</sup> Caregivers of patients undergoing HD have a low quality of life, which can lead to anxiety and depression.<sup>6,7</sup>

Until now, no study has shown the incidence of anxiety and depression in HD family caregivers at SPRPH, Sragen. A previous study by Hayun and Sudiro only showed the relationship between anxiety and family moral support in CKD patients.<sup>8</sup> It is crucial to know the incidence of anxiety and depression in HD caregivers at the hospital to screen their mental health and give proper management for them. This work objective is to know the anxiety and depression incidence in HD patient caregivers at SPRPH, the risk factors for anxiety and depression, and the relationship between anxiety and depression.

## METHODS

### Study design

A cross-sectional analysis was carried out at the Hemodialysis Department of SPRPH, Sragen, Indonesia, from November 2022 to February 2023.

### Population and sampling

The study included individuals who met the following criteria: voluntary participation, aged 16 years or older, family members of HD patients, and the ability to read and write. Approximately 661 patients underwent HD annually. Based on the sample size formula, a minimum sample size of 94 was determined with a 75% CI. The randomized sampling method was used. We recruited participants that met all the criteria above to take part. A total of 109 potential candidates were identified from the hospital records. Through random sampling, 94 eligible participants were selected and approached for voluntary participation.

### Data collection

The Indonesian translations of HAM-A and HAM-D were provided to caregivers accompanying their family members during routine HD sessions. Both HAM-A and HAM-D were in the public domain.<sup>9,10</sup> Ramdan shows that HAM-A is a valid and reliable tool to assess work-related stress.<sup>11</sup> The HAM-D is also considered a valid and sensitive clinimetric index.<sup>12</sup> The data were obtained from the participant with clinical interview and was interpreted by the psychiatrist.

## Data analysis

Data were analyzed using IBM's statistical program for social science version 25. Incidences were analyzed using descriptive analysis, while the bivariate analysis used Spearman correlation and Chi-square to assess risk factors.

## Ethics

The SPRPH Ethical Committee has approved this study (077/Etik-Crssp/XI/2022). Participants were informed about the study's objectives and procedures, and written consent was obtained prior to data collection.

## RESULTS

This study obtained 106 participants with no drop-outs. Age spread between 16 to 75 years

old (median 45 and mean  $43.77 \pm 1.364$  y.o.) with middle-age 40-64 y.o. were highest among all ages (59.4%). Most caregivers were female (66%). Most worked as homemakers (34%), followed by employees (32.1%). High school education had the highest number (45.3%). Half the caregivers were the patients' spouses (50%), and nearly all lived together (82.1%). Both patients' sick time (88.7%) and the caregivers' time (87.7%) for accompanying patients were above three months mainly (Table 1). The mean of the patient's sick time was  $27.83 \pm 3.172$  months, while the caregivers giving patients care was  $25.76 \pm 3.164$  months. The mean of the patient's sick time was  $27.83 \pm 3.172$  months, while the caregiver giving patients care was  $25.76 \pm 3.164$  months.

Table 1. Family caregiver characteristics (N=106)

	Characteristics	Frequency (n)	Percentage (%)
Age	Adolescence (10-19 y.o.)	5	4.7
	Young adult (20-39 y.o.)	30	28.3
	Middle-age (40-64 y.o.)	63	59.4
	Geriatric group (>64 y.o.)	8	7.5
Gender	Female	70	66
	Male	36	34
Job	Labor	25	23.6
	Teacher	3	2.8
	Homemaker	36	34
	Student	4	3.8
	Retired	4	3.8
	Employee	34	32.1
Education	Not educated	5	4.7
	Elementary	22	20.8
	Middle school	20	18.9
	High school	48	45.3
	Bachelor/Diploma	11	10.4
Relation	Child	38	35.8
	Grandchild	2	1.9
	Parent	6	5.7
	Spouse	53	50
	Sibling	7	6.6
Live together	No	19	17.9
	Yes	87	82.1
Patient's sick time	<3 months	12	11.3
	$\geq 3$ months	94	88.7
Caregiver time	<3 months	13	12.3
	$\geq 3$ months	93	87.7

To evaluate the anxiety and depression level, all family caregivers were tested by HAM-A and HAM-D. Both normality tests show abnormal dispersion ( $p < 0.05$ ). Before we interpreted the score, using Spearman correlation methods, we observed a substantial correlation between the anxiety and depression scores with  $p = 0.000$  and a correlation coefficient of 0.491. Almost all the family caregivers had anxiety (99%), with 91% being mild and 8% mild to moderate. On the other hand, half of the caregivers had no depression

symptoms (56%), while 42% had mild and the rest 2% had mild to moderate depression (Figure 1).

Finally, we analyzed the rate of anxiety and depression with the characteristics of family caregivers. In Spearman's nonparametric correlation, we found that there's no relationship between anxiety and depression with age, gender, job, level of education, relation, living together, patient's sick time, or caregiver time ( $p > 0.05$ ) (Table 2).

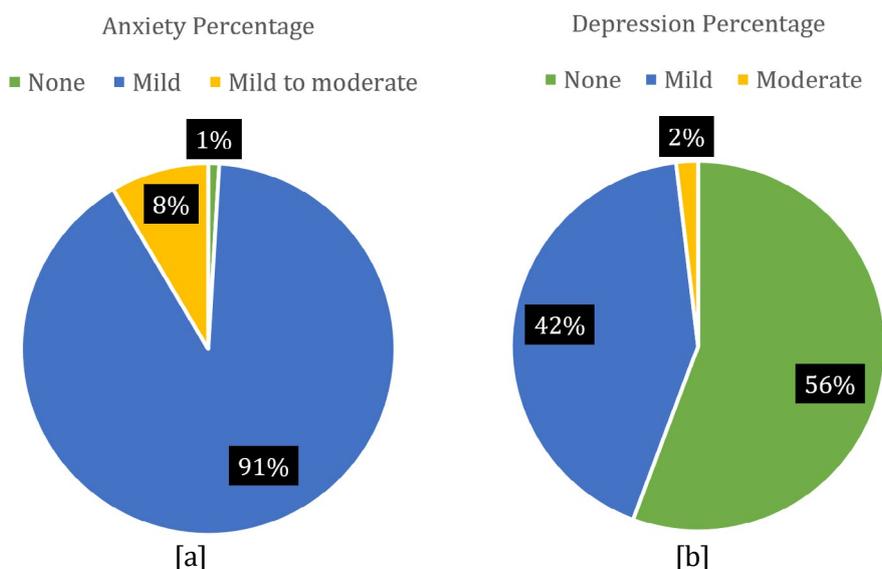


Figure 1. The percentage of [a] anxiety and [b] depression among family caregivers of hemodialysis patients

Table 2. Family caregiver characteristics.

	Age	Gender	Job	Edu	Relation	Live together	Patient's sick time	Caregiver time
Anxiety								
Correlation Coefficient	0.117	-0.112	-0.011	0.026	0.081	0.037	-0.009	-0.001
Sig. (2-tail)	0.233	0.251	0.909	0.793	0.410	0.704	0.930	0.992
Depression								
Correlation Coefficient	-0.07	-0.032	-0.043	-0.103	-0.025	0.055	0.025	0.049
Sig. (2-tail)	0.477	0.745	0.665	0.295	0.797	0.577	0.802	0.615

We analyzed the risk factors consisting of gender, living together, patient's sick time, and family caregiver time, which contribute to anxiety and depression appearance using the Chi-square analysis. The same finding as before, we didn't find any characteristic that appears to be the risk factor for anxiety or depression among family caregivers of HD patients ( $p > 0.05$ ).

**DISCUSSION**

Our study revealed that most family caregivers for HD patients experienced anxiety (99%) and depression (44%). A notable positive correlation was observed between anxiety and depression levels in caregivers, indicating that heightened anxiety corresponded to increased depression. Most participants fell within the 40-64 age group. Females constituted most caregivers (66%), many of whom were spouses and homemakers.

Notably, no significant correlations were found between demographic factors such as age, gender, occupation, education level, relationship to the patient, cohabitation, patient's sickness duration, or caregiver's time, and the levels of anxiety and depression.

We found that the rate of anxiety in family caregivers of HD patients was 99%, with 91% being mild and 8% mild to moderate. In comparison, depression 42% had mild, and the remaining 2% had mild to moderate depression. Hemodialysis patients are usually accompanied by caregivers who provide care for them. Caregivers are responsible for handling pre-HD administration, reminding patients to take medication, and monitoring their food and drink intake. Caregivers who have been caring for and accompanying patients for a long time tend to experience anxiety at a rate of 28% and depression at 18%. Also, anxiety in caregivers tends to increase by 42.3%, and the rate of depression increases by 17.6% when patients also experience anxiety and depression.<sup>13</sup> These findings indicate that some caregivers in the study experience anxiety and depression.

Another study conducted by Mashayekhi et al. explains that long-term treatment and the life satisfaction of patients with CKD can easily cause caregivers to experience stress.<sup>14</sup> Previous research shows that out of the total caregivers, 37.4% experienced a high and very high level of burden, while 42.7% experienced a moderate level of stress. A noteworthy adverse correlation exists between the cumulative burden of caregiving scores and life satisfaction ( $p < 0.001$ ). Caregivers of hemodialysis patients experience a high level of burden, which harms their quality of life. Consequently, this burden affects their social, economic, physical, and psychological well-being.<sup>15</sup> A study by Khalil et al. stated that one out of three caregivers experiences anxiety and depression. The time spent on caregiving for 24 hours daily is a strong factor associated with anxiety and depression. Caregivers spending time both at home and in the HD unit significantly impact the anxiety score on the Hospital Anxiety and Depression Scale (HADS) with  $p = 0.37$ , HADS depression score with  $p = 0.15$ , and are significantly associated with both anxiety and depression with  $p = 0.049$ .<sup>16</sup>

Caring for patients with CKD, especially in stage V or terminal stage, poses a significant psychological burden for caregivers due to the

various challenges they have to face. These challenges include the impact of HD treatment, which lasts for 4-5 hours, 2-3 times per week and throughout the patient's lifetime, the risk of infections and complications, the length of hospital stays, economic burden, and increased psychological pressure, especially when the caregiver is a family member of the patient.<sup>17</sup> The burden on caregivers worsens when patients have limitations in caring for themselves due to functional and cognitive impairments secondary to CKD. Other factors that increase the risk of depression include caregiver difficulties in employment leading to job loss or early retirement, the caregiver's relationship with the patient's deteriorating behavior and psychological attitudes, as well as adverse life events.<sup>18</sup>

In this study, we found a significant correlation between anxiety and depression among family caregivers with a positive correlation coefficient, characterized by a positive correlation coefficient, signifying that increased anxiety corresponds to increased depression levels. It is well known that anxiety and depressive disorders are commonly encountered mental health disorders, and they can mutually influence each other, as global survey data reports that 45.7% of individuals with severe depressive disorder have experienced one or more anxiety disorders throughout their lifetime. These disorders can co-occur simultaneously, with 41.6% of individuals experiencing severe depression for 12 months also having one or more anxiety disorders for the same duration. Individuals with comorbid anxiety and depression are often rooted in underlying anxiety-prone personality traits, such as social phobia (20-70%), panic disorder (50%), Post-Traumatic Stress Disorder (PTSD) (48%), and generalized anxiety disorder (43%).<sup>19</sup>

Anxiety can also be a risk factor for depression occurring 12-14 years later. Individuals with both disorders often engage in avoidance behaviors as a form of self-protection and to reduce discomfort.<sup>20</sup> It is because anxiety is perceived as something that makes individuals feel uneasy due to external threats. Avoidant tendencies result in a lack of positive life experiences, making individuals easily pessimistic and losing hope for the future, thus making them vulnerable to depression.<sup>21</sup> Triggers for depression in anxious individuals are often attributed to recurring stressful factors or heavy, burdensome thoughts, such as the Corona virus

disease (COVID-19) pandemic, where individuals fear contagion and tend to limit their activities to maintain health.<sup>22</sup> It is noteworthy that our study occurred three years after the announcement of the COVID-19 pandemic by the Indonesian government, and during this time, community activity restrictions were still in effect.<sup>23</sup>

Most family caregivers in this study were middle-aged adults 40-64 y.o. (59.4%) with a median of 45 and mean age of  $43.77 \pm 1.364$  y.o. A previous study by Gerogianni et al. also shows the same result, with middle-aged adults becoming the majority of all ages. The middle age of the participants was 54.34, and half of the sample's age ranged from 43.9 to 66.28.<sup>24</sup> High depression rates are observed in middle-aged individuals in developed countries, possibly due to the dual caregiving responsibilities they undertake, caring for both parents and children. This generation of caregivers tends to have children later in life, leading to simultaneous care tasks and increased vulnerability to depression.<sup>25</sup>

Most of our participants were female, with a percentage of 66%, while male 34%. Gerogianni et al. also conducted a study with 414 patient-caregiver pairs, finding that 76.3% (n = 316) of the caregivers were female.<sup>24</sup> Anxiety and depressive disorders are more prevalent in women than men, with an estimated ratio of 2:1 compared to men during the reproductive years. Anxiety and depression are more prevalent in females compared to males, starting from the age of four and continuing into the age group over 60. Several studies have reported structural and functional differences in the brain, such as the prefrontal cortex, hippocampus, and amygdala, which regulate cognitive function, memory, and anxiety. Women experiencing anxiety have an impact on blood pressure and heart rate compared to men.<sup>26</sup>

Hormones are one of the factors that can influence anxiety. Women have estrogenic and progesterone hormones that affect neurotransmitters associated with anxiety. In contrast, men have testosterone hormone with an anxiolytic effect by reducing stress responses and suppressing the Hypothalamic-Pituitary-Adrenal (HPA) axis activity.<sup>27</sup> This explains why gonadal hormones play a role in women's higher prevalence of anxiety levels. Fluctuations in estrogenic and progesterone during the menstrual cycle affect the reactivation of the HPA axis and feedback response

to glucocorticoids and Gamma-aminobutyric acid (GABA), resulting in a less stable hormonal balance than in men, contributing to anxiety.<sup>28</sup>

Most family caregivers in this study were females, spouses of the patients, and worked as homemakers. The patients might be the breadwinners, responsible for the family's financial well-being. However, with the patient now diagnosed with end-stage CKD and requiring HD routinely, all the responsibilities have shifted to his wife to do all the work, including the family wage earner and homemaker, and accompany the patient to the HD center, thus putting pressure on her mental health.

Our study didn't find any correlation between age, gender, job, level of education, relation, living together, patient's sick time, or caregiver time with anxiety and depression. Wiesel et al. have shown the same result; age did not show any association with depression in both univariate and multivariable analyses. Therefore, age did not emerge as a significant forecaster of depression. Furthermore, this study indicated that gender did not moderate the correlation between age, anxiety, and depression.<sup>29</sup> Converse from our study, other previous studies have shown a relationship between risk factors such as low increased caregivers' age, poor financial condition, comorbidities, the time spent on care every 24 hours, and lack of social support to the development of anxiety as well as depression.<sup>7,13,30</sup> Pio et al. found that time of care contributes to the risk of both anxiety and depression.<sup>31</sup> Geroganni et al. also found that depression and anxiety were associated with demographic factors such as low levels of education.<sup>30</sup> The divergent outcomes in our research may be attributed to differences in sample characteristics, variations in measurement tools, or distinct contextual factors such as location. The samples of works by Bawazier et al. and Pio et al. comprised caregivers of HD patients residing in the major metropolitan city of Jakarta, Indonesia.<sup>13,31</sup> Whereas our study was conducted in the rural regency of Sragen. These geographic differences led to varying stress levels, which could have influenced the mental health results.<sup>32,33</sup>

The limitation of this study was the relatively small sample size, which might restrict its generalizability. Thus, a larger sample size would provide more representative results. Also, this study utilized a cross-sectional design, which only

provides a snapshot of the participants' mental health at a specific time. Longitudinal studies would allow for a better understanding of the dynamic nature of anxiety and depression in HD caregivers over time. By using cross-sectional methods, this study did not include a control group of caregivers who do not care for HD patients. A control group would have allowed for a better comparison and understanding of the specific impact of caregiving on anxiety and depression. The gender proportion in our study sample indicates more female caregivers than male caregivers, as the sample was collected at a single time and place without classifying the gender. This imbalance could introduce bias, potentially affecting the observed incidence rate higher among female caregivers. Further research could observe the findings with gender classification to minimize the bias, and more findings appear. Lastly, our study was carried out in one hospital, limiting the findings to other healthcare settings or regions. Including multiple centers and diverse populations would enhance the study's external validity.

## CONCLUSION

This current study highlights the high incidence of anxiety and mild depression in family caregivers of HD patients. The findings support previous research indicating the significant emotional burden experienced by caregivers in the context of CKD. The study also revealed a positive correlation between anxiety and depression, suggesting that these conditions often coexist and influence each other.

## CONFLICT OF INTEREST

The authors declare that there are no potential conflicts of interest concerning the authorship and publication of this article.

## ACKNOWLEDGEMENT

The authors acknowledge dr. Soehadi Prijonegoro Regional Public Hospital for supporting the authors in this study

## AUTHOR CONTRIBUTION

AO and ES provided conceptualisation, study design, data collection, and manuscript review. RE did conceptualisation, study design, data generation and collection, manuscript preparation,

manuscript review, and manuscript revision. MA and AD did data collection and manuscript preparation. All authors read and approved the final manuscript.

## LIST OF ABBREVIATION

CKD: Chronic Kidney Disease; GABA: Gamma-aminobutyric Acid; HADS: Hospital Anxiety and Depression Scale; HAM-A: Hamilton Anxiety Rating Scale; HAM-D: Hamilton Depression Rating Scale; HD: Haemodialysis; HPA: Hypothalamic-Pituitary-Adrenal; PTSD: Post-Traumatic Stress Disorder; SPRPH: Soehadi Prionegoro Regional Public Hospital.

## REFERENCES

1. Xie Y, Bowe B, Mokdad AH, Xian H, Yan Y, Li T, et al. Analysis of the global burden of disease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016. *Kidney Int.* 2018;94(3):567–81.
2. Pereira B dos S, Fernandes N da S, de Melo NP, Abrita R, Grincenkov FR dos S, Fernandes NM da S. Beyond quality of life: A cross sectional study on the mental health of patients with chronic kidney disease undergoing dialysis and their caregivers. *Health Qual Life Outcomes.* 2017;15(1):1–10.
3. Kang A, Yu Z, Foo M, Chan CM, Griva K. Evaluating burden and quality of life among caregivers of patients receiving peritoneal dialysis. *Peritoneal Dialysis International.* 2019;39(2):176–80.
4. Gilbertson EL, Krishnasamy R, Foote C, Kennard AL, Jardine MJ, Gray NA. Burden of care and quality of life among caregivers for adults receiving maintenance dialysis: A systematic review. *American Journal of Kidney Diseases.* 2019;73(3):332–43.
5. Nipp RD, El-Jawahri A, Fishbein JN, Gallagher ER, Stagl JM, Park ER, et al. Factors associated with depression and anxiety symptoms in family caregivers of patients with incurable cancer. *Annals of Oncology.* 2016;27(8):1607–12.
6. Sajadi SA, Ebadi A, Moradian ST. Quality of life among family caregivers of patients on hemodialysis and its relevant factors: A systematic review. *Int J Community Based Nurs Midwifery.* 2017;5:206–18.
7. Shukri M, Mustofai MA, Md Yasin MAS, Tuan Hadi TS. Burden, quality of life, anxiety, and

- depressive symptoms among caregivers of hemodialysis patients: The role of social support. *The International Journal of Psychiatry in Medicine*. 2020;55(6):397–407.
8. Al Aziz IH, Sudiro S. Hubungan dukungan keluarga dengan tingkat kecemasan pada pasien gagal ginjal kronis yang menjalani hemodialisis di RSUD Dr. Soehadi Prijonegoro Sragen. *Jurnal Keperawatan Global*. 2017;2(1):56–61.
  9. Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol*. 1959;32(1):50–5.
  10. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23(1):56–62.
  11. Ramdan IM. Reliability and validity test of the Indonesian version of the Hamilton anxiety rating scale (HAM-A) to measure work-related stress in nursing. *Jurnal Ners*. 2018;14(1).
  12. Carrozzino D, Patierno C, Fava GA, Guidi J. The hamilton rating scales for depression: A critical review of clinimetric properties of different versions. *Psychotherapy and Psychosomatics*. S. Karger AG; 2020. p. 133–50.
  13. Bawazier LA, Stanley I, Sianipar W, Suhardjono. Anxiety and depression among caregivers of hemodialysis patients at the Indonesian national referral hospital. *Medical Journal of Indonesia*. 2018;27(4):271–8.
  14. Mashayekhi F, Pilevarzadeh M, Rafati F. The assessment of caregiver burden in caregivers of hemodialysis patients. *Materia Socio Medica*. 2015;27(5):333–6.
  15. Jafari H, Ebrahimi A, Aghaei A, Khatony A. The relationship between care burden and quality of life in caregivers of hemodialysis patients. *BMC Nephrol*. 2018;19:321.
  16. Khalil A, Khalifeh A, Al-Rawashdeh S, Darawad M, Abed M. Depressive symptoms, anxiety, and quality of life in hemodialysis patients and their caregivers: A dyadic analysis. *Japanese Psychological Research*. 2021;64(4):426–36.
  17. Taset AY, Martinez FLLL. Family caregivers-of patients with chronic renal failure terminal psychological stress. *MOJ Addiction Medicine & Therapy*. 2018;5(5):214–21.
  18. Hawamdeh S, Almari AM, Almutairi AS, Dator WLT. Determinants and prevalence of depression in patients with chronic renal disease, and their caregivers. *Int J Nephrol Renovasc Dis*. 2017;10:183–9.
  19. Jacobson NC, Newman MG. Avoidance mediates the relationship between anxiety and depression over a decade later. *J Anxiety Disord*. 2014;28(5):437–45.
  20. Hofmann SG, Hay AC. Rethinking avoidance: Toward a balanced approach to avoidance in treating anxiety disorders. *Journal of Anxiety Disorders*. 2018;55:14–21.
  21. Kalin NH. The critical relationship between anxiety and depression. *American Journal of Psychiatry*. 2020;177(5):365–7.
  22. Shek DTL, Chai W, Tan L. The relationship between anxiety and depression under the pandemic: The role of life meaning. *Front Psychol*. 2022;13:1059330.
  23. Menteri Dalam Negeri Republik Indonesia. Instruksi menteri dalam negeri no 1 tahun 2022 tentang pemberlakuan dan pembatasan kegiatan masyarakat level 3, level 2, dan level 1 Corona virus disease 2019 di wilayah Jawa dan Bali. Jakarta; 2022.
  24. Gerogianni G, Polikandrioti M, Babatsikou F, Zyga S, Alikari V, Vasilopoulos G, et al. Anxiety–depression of dialysis patients and their caregivers. *Medicina (Lithuania)*. 2019;55(5):168.
  25. Thrush A, Hyder A. The neglected burden of caregiving in low- and middle-income countries. *Disabil Health J*. 2014;7(3):262–72.
  26. Christiansen DM. Examining sex and gender differences in anxiety disorders. In: Durbano F, editor. *A fresh look at anxiety disorders*. Rijeka: IntechOpen; 2015.
  27. Pillerová M, Borbélyová V, Pastorek M, Riljak V, Hodosy J, Frick KM, et al. Molecular actions of sex hormones in the brain and their potential treatment use in anxiety disorders. *Frontiers in Psychiatry*. 2022; 13:972158.
  28. McHenry J, Carrier N, Hull E, Kabbaj M. Sex differences in anxiety and depression: Role of testosterone. *Frontiers in Neuroendocrinology*. 2014;35(1): 42–57.
  29. Weiss Wiesel TR, Nelson CJ, Tew WP, Hardt M, Mohile SG, Owusu C, et al. The relationship between age, anxiety, and depression in older adults with cancer. *Psychooncology*. 2015;24(6):712–7.
  30. Gerogianni G, Polikandrioti M, Alikari V, Vasilopoulos G, Zartaloudi A, Koutelekos I, et al. Factors affecting anxiety and depression in caregivers of hemodialysis patients. In: Vlamos P, editor. *GeNeDis 2020*. Cham: Springer International Publishing; 2021. p. 47–58.

31. Pio TMT, Prihanto JB, Jahan Y, Hirose N, Kazawa K, Moriyama M. Assessing burden, anxiety, depression, and quality of life among caregivers of hemodialysis patients in Indonesia: A cross-sectional study. *Int J Environ Res Public Health*. 2022;19:4544.
32. Prabha V, Rao V, Kannakabushanam G. A comparative study of anxiety and depression among adolescents from rural and urban areas. *Journal of Medical and Scientific Research*. 2017;5(1):29-32.
33. Razak R, Tumaji T, Khaqiqi Nantabah Z, Dwi Laksono A. Factor related to depression among elderly in urban rural areas in Indonesia. *Southeast Asian J Trop Med Public Health*. 2022;53(Suppl 2):233.