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Health Inequity Associated with Financial Hardship Among Patients with Kidney Failure: A Secondary Analysis --Manuscript Draft--

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Full Title:	Health Inequity Associated with Financial Hardship Among Patients with Kidney Failure: A Secondary Analysis
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Keywords:	chronic kidney failure; financial hardship, health equity, patient reported outcome measures; services utilization
Abstract:	Financial hardship is a common challenge among patients with kidney failure and may have negative health consequences. Therefore, financial status is regarded as an important determinant of health, and its impact needs to be investigated. This cross-sectional study aimed to identify the differences in patient-reported and clinical outcomes among patients with different financial status. 354 patients with end-stage kidney disease were recruited from March to June 2017 at two regional hospitals in Hong Kong. The Dialysis Symptoms Index and Kidney Disease Quality of Life-36 were used to evaluate patient-reported outcomes. Clinical outcomes were retrieved from medical records and assessed using the Karnofsky Performance Scale (functional status) and Charlson Comorbidity Index (comorbidity level). Patients were stratified using two dichotomised variables, employment status and income level, and their outcomes were compared using independent sample t-tests. In this sample, the employment rate was 17.8% and the poverty rate was 61.2%. Compared with other patients, increased distress associated with specific symptoms, a higher comorbidity level, and more emergency room visits were found in patients with poorer financial status. Unemployed patients reported a decreased physical quality of life, while low-income patients had a lower serum albumin concentration and a longer hospital stay than other patients (all p < 0.05). Financially underprivileged patients experienced health inequity in terms of impaired patient-reported and clinical outcomes. Attention needs to be paid to these patients by providing financial assessments and interventions. Additional research is warranted to understand the experience of financial hardship and examine equity in healthcare.
Order of Authors:	Marques Shek Nam Ng, RN, PhD
	Dorothy Ngo Sheung Chan
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Response to Reviewers:	We are pleased to re-submit the revised manuscript entitled 'Health Inequity Associated with Financial Hardship Among Patients with Kidney Failure: A Secondary Analysis' (Manuscript No.: PONE-D-22-21227). We would like to thank the Editor and Reviewer for their thoughtful comments on the manuscript. Our responses to each of the comments are provided below in italics. The suggested revisions have strengthened the report of preliminary evidence, which informs directions for future research in health equity and financial wellbeing of patients with kidney failure. Thank you for your attention and I look forward to hearing from you. Title/Abstract Line 5/20: Recommend using "kidney failure" rather than "end-stage kidney disease" per guidelines advanced by Levey et al. (2020) Levey AS, Eckardt KU, Dorman NM, Christiansen SL, Cheung M, Jadoul M, et al. Nomenclature for kidney function and disease: executive summary and glossary from a Kidney Disease: Improving Global Outcomes consensus conference*. Nephrology Dialysis Transplantation. 2020 Jul 1;35(7):1077–84.

Response: We revised the wordings (e.g., kidney failure, kidney care) accordingly.

Introduction

• Line 48: The authors state that patients may be required to cover 12-71% of dialysis costs out of pocket, but do not specify the nature of reimbursement at the hospitals in the study. This context would be especially helpful for understanding the impact of financial hardship on study participants. Also, I think it may be relevant to mention here that, as I understand it, public healthcare is virtually free and guaranteed in Hong Kong as this is not the case elsewhere.

Response: We added a description about Hong Kong's healthcare system in the Introduction section (p.4 lines 72-79).

• Lines 53-60: This section seems to emphasize the relationship between financial hardship and medical expenses, but I think the experience of economic oppression is more profound than that. I think the authors can do more to describe the local context of economic inequality in Hong Kong. I am not an expert in the region, though I think some relevant dynamics include issues of financialization, housing and spatial segregation, and immigration issues.

Response: Thanks for this very thoughtful comment. We added a description about Hong Kong's economic inequity in the Introduction section (p.4 lines 72-79).

Materials and Methods

- Line 71: Are you able to add details about the hospitals from which these data were collected? They are described as "regional hospitals" but are they public? Private? Response: We provided details about these hospitals in the Materials and Methods section (p.4 lines 82-84).
- Line 72: Please provide a citation where the inclusion and exclusion criteria are previously reported.

Response: Details of the original study can be found in the reference #16. We added the inclusion and exclusion criteria in the Methods section for better understanding of the study design (p.4 line 85-87).

• Lines 93-100: I am not sure that the Methods adequately account for all four instruments and analyses. I also imagine chi-squared analyses were conducted to assess for differences in patient demographics, but these are not reported in the Methods. Looking at Table 1, I see composite scores for the Kidney Disease Quality of Life-36, the Karnofsky Performance Scale, and the Charlson Comorbidity Index, in addition to several individual patient-reported outcomes. Do the patient-reported outcomes derive from the Dialysis Symptoms Index? If so, how and why were only a subsample of the 30 symptoms selected for reporting?

Response: We supplemented detailed accounts and references for the four instruments used in the Methods section (p.5 lines 92-110). To provide a fair comparison, we presented the results of all symptoms in the Dialysis Symptoms Index and other instruments in Table 1.

Results

• The authors report significant results but do not describe results that are not significant, which is important.

Response: Thanks for pointing out this issue. We stated non-significant results in the Results and Discussion sections (p.6 lines 138-139; p.7 lines 148-149) and included the statistics in the Table 1.

Discussion

- Lines 126-128: I am not sure that this is the most accurate summary statement given that (1) your results differ based on employment status and poverty level, and (2) not all patient-reported outcomes were significantly different between your groups. I would revise this summary statement to provide a more cautious interpretation of your results. Response: We revised the summary to precisely capture both significant and non-significant results (p.7 lines 148-152).
- Lines 132-133: Consider rephrasing to situate the statistics of your study population relative to the general population (e.g., "In this study, roughly half as many people were employed and three times as many lived below the poverty line relative to the general

population of Hong Kong").

Response: We revised the statements based on your suggestion (p.7 line 154).

• Lines 137-142: Do you think that people experiencing economic oppression are at higher risk of developing kidney failure or that undergoing hemodialysis impedes employment opportunities, which then leads to financial hardship? Some literature on this might be helpful to include in the introduction. This might also be worth mentioning in the limitations with respect to the need for longitudinal analyses.

Response: Thanks for your suggestion. We added this point about disparities in the Introduction section (p.3 lines 53-55). We also stressed the need for a longitudinal study to investigate the impact of financial hardship on the outcomes of patients with kidney failure (p.8 lines 181-183).

• Lines 159-160: Can you recommend additional factors affecting financial hardship (e.g., wealth, homeownership)?

Response: We made recommendations on additional factors based on our recent review (p.8 lines 180-181).

Table 1

• The origin of the patient-reported outcomes is not clear to me. Are these from the DSI? If so, why are there not 30?

Response: We substantially revised Table 1 to present all the results, regardless their statistical significance levels.

· What is the KDQOL-36 PCS vs. MCS?

Response: We are sorry about the confusion. We defined all the abbreviations in the legends and provided details of the instruments in the Methods section (p.5 lines 92-110).

• How did you choose serum albumin vs. urine microalbumin as a clinical outcome? Response: Serum albumin was chosen as an indicator of nutritional status but not disease progression. The data were retrieved from the laboratory results in the medical records. We analysed glomerular filtration rate to evaluate disease progression but no significant result was found (Table 1).

Additional Information:

Question Response

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This study was approved by the Joint CUHK-NTEC Clinical Research Ethics Committee (reference number: 2017.092). Written consent was obtained from all participants.

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- Include an approval number if one was obtained
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Health Inequity Associated with Financial Hardship Among Patients with Kidney Failure: A Secondary Analysis (Short Title: Health Inequity and Financial Hardship in Kidney Failure) Marques Shek Nam NG^{1*}, Dorothy Ngo Sheung CHAN¹, Winnie Kwok Wei SO¹ ¹The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, China *Corresponding author Email: marquesng@cuhk.edu.hk

Abstract

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Financial hardship is a common challenge among patients with kidney failure and may have negative health consequences. Therefore, financial status is regarded as an important determinant of health, and its impact needs to be investigated. This cross-sectional study aimed to identify the differences in patient-reported and clinical outcomes among patients with different financial status. 354 patients with end-stage kidney disease were recruited from March to June 2017 at two regional hospitals in Hong Kong. The Dialysis Symptoms Index and Kidney Disease Quality of Life-36 were used to evaluate patient-reported outcomes. Clinical outcomes were retrieved from medical records and assessed using the Karnofsky Performance Scale (functional status) and Charlson Comorbidity Index (comorbidity level). Patients were stratified using two dichotomised variables, employment status and income level, and their outcomes were compared using independent sample t-tests. In this sample, the employment rate was 17.8% and the poverty rate was 61.2%. Compared with other patients, increased distress associated with specific symptoms, a higher comorbidity level, and more emergency room visits were found in patients with poorer financial status. Unemployed patients reported a decreased physical quality of life, while low-income patients had a lower serum albumin concentration and a longer hospital stay than other patients (all p < 0.05). Financially underprivileged patients experienced health inequity in terms of impaired patientreported and clinical outcomes. Attention needs to be paid to these patients by providing financial assessments and interventions. Additional research is warranted to understand the experience of financial hardship and examine equity in healthcare.

Introduction

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The global burden of kidney failure is increasing. More than 2 million patients have been diagnosed and treated with life-sustaining dialysis therapy worldwide (1). In some countries, 2–3% of healthcare expenditures are used for managing kidney failure, and the demand for dialysis continues to surge (2). At the individual level, patients often experience financial hardship associated with high treatment costs, unemployment, and reduced income. Although many countries provide reimbursement for dialysis therapy, patients are required to cover 12–71% of the costs out of pocket (3). In addition, these patients have reduced productivity associated with disease-related disabilities. According to an international survey (4), less than 55% of haemodialysis (HD) and 68% of peritoneal dialysis (PD) patients are employed. Limited income due to decreased employment may amplify financial hardship among these patients (5). Financial hardship is a profound and significant determinant of health. In fact, higher burdens associated with kidney failure are found in countries that are less socioeconomically developed (1). From an individual perspective, patients utilize their personal resources to pay for their medical and other daily expenses, which may lead to the depletion of financial reserves or incurrence of debt (6). Evidence suggests that impaired financial well-being is associated with poor physical and psychological health in patients with chronic illnesses (7,8). Negative health outcomes, including depression, anxiety, lower health-related quality of life (HRQoL), and higher mortality risk, have been reported (9-11). These outcomes may be seen as the consequences of health inequity caused by social determinants, especially financial factors. Despite the impact of financial hardship on health, few studies have evaluated the relationships between this hardship and various health outcomes among patients with kidney failure (12). A better understanding of these relationships may advance our understanding of

health inequity among patients with kidney failure. Hence, in addition to financial aids, kidney care providers can proactively identify financially underprivileged patients and provide specific interventions that promote equal participation in daily life (13). Therefore, to explore directions for future research, the aim of this secondary analysis was to identify the differences in patient-reported and clinical outcomes between kidney failure patients with high and low financial status.

This study was conducted in Hong Kong, one of the financial centres in the Chinese territory. While this city has a relatively high per capita gross domestic product of 59,264 USD in 2020 (14), it is famous for the large wealth gap. Its latest Gini coefficient in 2016 reached 46.7, which reflected fair inequality within this 700-million population (15). In terms of the healthcare system, Hong Kong has a predominant public sector that provides over 90% of inpatient services and is largely subsidised by taxation (16). Despite the availability of subsidised services, patients with kidney failure are required to use out-of-pocket expenses to cover costs of dialysis consumables and self-financed drugs.

Materials and Methods

The cross-sectional data of 354 patients from a mixed-methods study were analysed (17). These patients were recruited from two public hospitals from March to June 2017.

These hospitals were serving populations with highest and lowest household incomes in Hong Kong (18). The inclusion criteria included: 1) adults diagnosed with kidney failure; 2) received any modality of dialysis therapy for three or more consecutive months; and 3) were willing to provide written consent. Those with active psychiatric disorders (e.g., schizophrenia, dementia) were excluded. After obtaining informed consent, a research assistant administered a questionnaire and reviewed electronic health records at the specialist clinic or the haemodialysis centre. This study was approved by the institutional research boards of the university and the involved hospitals. This study was approved by the Joint

CUHK-NTEC Clinical Research Ethics Committee (reference number: 2017.092). Written consent was obtained from all participants.

Instruments

Symptoms and HRQoL were selected as the patient-reported outcomes. The Dialysis Symptoms Index (DSI) was used to assess the distress levels of 30 symptoms experienced in the past month (19). A higher score indicates a higher level of distress. The Chinese version of the DSI demonstrated excellent content validity (0.99) and internal consistency (α = 0.87) (20). The Kidney Disease Quality of Life-36 was used to evaluate the HRQoL of patients (21). It consists of 24 disease-specific and 12 generic questions that can be divided into three subscales (symptom, burden, and effect of kidney disease) and two summary scores (physical and mental component summary). A higher score indicates better performance in the specific domain. Its Chinese version demonstrated good test-retest reliability (interclass correlation coefficient = 0.79–0.92) and acceptable internal consistency (α = 0.60–0.93) (22).

The clinical outcomes included the functional status, comorbidity level, healthcare service utilization, and biochemical parameters. The Karnofsky Performance Scale was used to evaluate functional status (23). A higher score indicates higher ability to perform activities of daily living (range: 0–100). The Charlson Comorbidity Index was used to assess the comorbidity level (23). Patients' relative burden of comorbidity is evaluated based on the weighted sum of 14 conditions (range: 0–33). Other clinical data, including healthcare service utilization and biochemical parameters, were retrieved from the patients' electronic health records. Glomerular filtration rate was estimated based on the Modification of Diet in Renal Disease (MDRD) equation.

Analyses

Background characteristics and outcomes were summarised using descriptive statistics (e.g., frequency, percentage, mean). Two dichotomized variables that reflected the

patient's financial status were created: employment status and income level. In terms of income level, those earning a monthly household income of \leq 10,000 HKD (approximately 1,290 USD) were regarded as below the poverty line, which is in line with the government's definition (18). After stratifying the patients by these variables, patient-reported and clinical outcomes were compared using independent sample t-tests. All analyses were conducted using SPSS version 25.0 (IBM Corp., Armonk, NY). A two-sided p-value of < 0.05 was considered as statistically significant.

Results

Of the 354 patients, 58.5% were male. The patients had a mean age of 60.9 years (Table 1). Most of the patients received PD (69.9%) and had been on dialysis for a mean of 51.6 months. Overall, 17.8% of the patients were employed, and 61.2% were below the poverty line. The education level significantly differentiated patients regardless employment status and income level ($p \le 0.001$). Compared with other patients, a larger proportion of employed patients had received kidney transplants (9.5%; p = 0.035), and a larger proportion of patients above the poverty line were married (76.6%; p = 0.01).

Table 1 presents the differences in patient-reported and clinical outcomes between groups. Compared with employed patients, those who were unemployed reported higher levels of tiredness (mean: 2.33), joint or bone pain (mean: 1.60), and trouble falling asleep (mean: 2.13) (all $p \le 0.033$). The KDQOL-36 Physical Component Summary scale scores (mean: 37.27) for unemployed patients were significantly lower than for employed patients (p = 0.011). Patients below the poverty line reported higher levels of dry mouth (mean: 1.63), dry skin (mean: 2.68), itching (mean: 2.76), and trouble staying asleep (mean: 2.07) than those above the poverty line (all $p \le 0.045$). Interestingly, patients with lower income had less severe sexual symptoms ($p \le 0.004$), namely a decreased interest in sex (mean: 0.41) and

difficulty becoming sexually aroused (mean: 0.37). However, no significant difference was found in scores of other KDQOL-36 sub-scales nor distress levels of other symptoms.

In terms of clinical outcomes, in general, patients with a poorer financial status had higher comorbidity levels (all $p \le 0.033$) and more emergency room (ER) visits in the past six months (all $p \le 0.008$) than other patients. In addition, patients below the poverty line had a lower serum albumin concentration (35.39 vs. 36.85 g/L; p = 0.004) and longer length of hospital stay (7.30 vs. 4.87 days; p = 0.040) than did patients with higher earnings.

Discussion

The findings from this secondary analysis suggest that patient-reported and clinical outcomes differ between patients with different financial statuses in terms of their employment and income level. Based on our preliminary findings, while no significant relationship was found between financial status and most patient-reported outcomes, patients who were unemployed or living below the poverty line reported higher distress associated with specific symptoms, higher comorbidity levels, and more health care utilization than other patients. Consistent with existing evidence (8-10), the impact of financial hardship on health disparities among patients with kidney failure warrants additional attention.

Compared with the general population in Hong Kong, the employment rate in this study was halved and the poverty rate was three times higher (cf. employment rate: 34.9%; poverty rate: 21.4%) (18). This finding is an alarming sign that in this city, which is well known for economic inequality, financial hardship is very common among patients with kidney failure. Our findings indicate the negative impact of such hardship within this group. Consistent with our previous studies (8,25), financially underprivileged patients may experience a higher symptom burden in terms of tiredness, sleep disturbances, skin problems, and pain. There are some possible reasons for this relationship. As reported in one study (26), financially underprivileged patients may have fewer resources to pay for healthcare services,

especially preventive care. This may explain why patients with impaired financial well-being reported poorer outcomes, particularly a higher mean number of ER visits and length of hospital stay. Therefore, kidney care providers need to pay special attention to the financial needs of patients by incorporating appropriate assessments and interventions in routine care (12). Nevertheless, there is a need to examine equity in the healthcare system to ensure that essential services are provided regardless of a person's financial status. In addition, there may be a reciprocal relationship between financial hardship and outcomes. While symptoms and other outcomes are signs of deteriorating health, patients with a poorer symptom status or poorer outcomes may have a higher demand for healthcare services and a lower physical capacity for engaging actively in employment (27). These consequences lead to increased medical expenditures and decreased income, which eventually intensify financial hardship (6). A better understanding of the experience of financial hardship is warranted to explore the factors that modulate the relationship between financial hardship and health.

Our preliminary evidence reveals the consequences of health inequity and suggests directions for researching issues associated with financial hardship among patients with kidney failure. However, several limitations warrant consideration. Although cross-sectional data were analyzed and limited variables were evaluated, other factors that might confound the relationship between financial hardship and outcomes (e.g., financial aids, home ownership, personal savings, health spendings) were not controlled (8). In addition, the causal relationships among financial statuses, kidney failure, incapacity for employment, and health outcomes need to be examined using a longitudinal design. Of note, financial status was conceptualized in terms of employment status and income level only, which might inadequately reflect the full picture of financial well-being. Therefore, the following suggestions are made: 1) factors influencing financial hardship should be identified and controlled in further analyses; 2) a longitudinal study should be conducted to evaluate

changes in financial status and outcomes; and 3) a comprehensive conceptualization of financial hardship should be adopted.

Conclusion

Financial hardship is very common among patients with kidney failure, especially in Hong Kong, in terms of high percentages of unemployment and poverty. Our preliminary evidence suggests that this hardship may result in health inequity and manifest in impaired patient-reported and clinical outcomes. Additional research is warranted to understand the experience of financial hardship and the equity of the healthcare system.

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Financial Disclosure

The authors received no specific funding for this work.

Competing Interests Statement

The authors have declared that no competing interests exist.

Data Availability Statement

Data cannot be shared publicly because of privacy issues. Confidential data are available from the CUHK Research Data Repository for researchers whose work has been approved by an institutional review board. Request may be sent together with the research proposal and ethical approval to the corresponding author or the Repository (website: https://researchdata.cuhk.edu.hk / email: data@cuhk.edu.hk).

References

213

- 1. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of
- chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of
- 216 Disease Study 2017. Lancet 2020;395:709-33.
- 2. Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the
- sustainable development goals. Bull World Health Organ 2018;96:414-22.
- 3. van der Tol A, Lameire N, Morton RL, Van Biesen W, Vanholder R. An international
- analysis of dialysis services reimbursement. Clin J Am Soc Nephrol 2019;14:84-93.
- 4. Brown EA, Zhao J, McCullough K, Fuller DS, Figueiredo AE, Bieber B, et al. Burden of
- kidney disease, health-related quality of life, and employment among patients receiving
- peritoneal dialysis and in-center hemodialysis: findings from the DOPPS program. Am J
- 224 Kidney Dis 2021;78:489-500.
- 5. Morton RL, Schlackow I, Gray A, Emberson J, Herrington W, Staplin N, et al. Impact of
- 226 CKD on household income. Kidney Int Rep 2018;3:610-8.
- 6. Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients
- with cancer: understanding and stepping-up action on the financial toxicity of cancer
- treatment. CA Cancer J Clin 2018;68:153-65.
- 7. Altice CK, Banegas MP, Tucker-Seeley RD, Yabroff KR. Financial hardships
- experienced by cancer survivors: a systematic review. J Natl Cancer Inst
- 232 2017;109:djw205.
- 8. Ng MSN, Chan DNS, Cheng Q, Miaskowski C, So WKW. Association between financial
- hardship and symptom burden in patients receiving maintenance dialysis: a systematic
- review. Int J Environ Res Public Health 2021;18:9541.

- 9. Ikonomou M, Skapinakis P, Balafa O, Eleftheroudi M, Damigos D, Siamopoulos KC.
- The impact of socioeconomic factors on quality of life of patients with chronic kidney
- 238 disease in Greece. J Renal Care 2015;41:239-46.
- 239 10. Tao S, Zeng X, Liu J, Fu P. Socioeconomic status and mortality among dialysis patients:
- a systematic review and meta-analysis. Int Urol Nephrol 2019;51:509-18.
- 11. Chen J, Liu L, Chen J, Ng MS, Lou VW, Wu B, Jiang W, Jie Y, Zhu J, He Y. The cross-
- lagged association between depressive symptoms and health-related quality of life in
- patients receiving maintenance hemodialysis: a three-wave longitudinal study. Qual Life
- Res 2021;30:3463-3473.
- 12. Krishnan M. The importance of considering total patient economics for hemodialysis.
- 246 Kidney Int Rep 2019;4:365-6.
- 13. Kalantar-Zadeh K, Li PK, Tantisattamo E, Kumaraswami L, Liakopoulos V, Lui S, et al.
- Living well with kidney disease by patient and care-partner empowerment: kidney health
- for everyone everywhere. Clin Nephrol 2021;95:115-22.
- 250 14. Organisation for Economic Co-operation and Development. Gross domestic product
- 251 (GDP) [Internet]. 2022 [Accessed 25 December 2022]. Available:
- 252 https://data.oecd.org/gdp/gross-domestic-product-gdp.htm.
- 253 15. World Economics. Hong Kong's Gini coefficient [Internet]. 2016 [Accessed 25]
- December 2022]. Available from: https://www.worldeconomics.com/Inequality/Gini-
- 255 Coefficient/Hong%20Kong.aspx.
- 16. Schoeb V. Healthcare service in Hong Kong and its challenges: the role of health
- professionals within a social model of health. China Perspect 2016;4:51-58.
- 17. Ng MSN, Miaskowski C, Cooper B, Hui YH, Ho EHS, Mo SKL, et al. Distinct symptom
- experience among subgroups of patients with ESRD receiving maintenance dialysis. J
- 260 Pain Symptom Manage 2020;60:70-9.

- 18. Government of the HKSAR. Hong Kong poverty situation report 2019 [Internet]. 2019
- [Accessed 30 March 2022]. Available from: https://www.
- povertyrelief.gov.hk/eng/pdf/Hong_Kong_Poverty_Situation_
- 264 Report_2019.pdf.
- 19. Weisbord SD, Fried LF, Arnold RM, Rotondi AJ, Fine MJ, Levenson DJ, Switzer GE.
- Development of a symptom assessment instrument for chronic hemodialysis patients: the
- Dialysis Symptom Index. J Pain Symptom Manage 2004;27:226-240.
- 20. Ng MSN, So WKW, Wong CL, Hui YH, Ho EHS, Choi KC, et al. Stability and impact of
- symptom clusters in patients with end-stage renal disease undergoing dialysis. J Pain
- 270 Symptom Manage 2020;59:67-76.
- 21. Hays RD, Kallich JD, Mapes DL, Coons SJ, Amin N, Carter WB, Kamberg C. Kidney
- Disease Quality of Life Short Form (KDQOL-SFTM), version 1.3: a manual for use and
- scoring [Internet]. 1997 [Accessed 30 March 2022]. Available from:
- https://www.rand.org/health-care/surveys_tools/kdqol.html.
- 275 22. Chow SKY, Tam BML. Is the kidney disease quality of life-36 (KDQOL-36) a valid
- instrument for Chinese dialysis patients? BMC Nephrol 2014;15:1-7.
- 23. Péus D, Newcomb N, Hofer S. Appraisal of the Karnofsky performance status and
- proposal of a simple algorithmic system for its evaluation. BMC Med Inform Decis Mak
- 279 2013;13:1-7.
- 24. Hemmelgarn BR, Manns BJ, Quan H, Ghali WA. Adapting the Charlson Comorbidity
- Index for use in patients with ESRD. Am J Kidney Dis 2003;42:125-32.
- 282 25. Ng MSN, Wong CL, Choi KC, Hui YH, Ho EHS, Miaskowski C, So WKW. A mixed
- methods study of symptom experience in patients with end-stage renal disease. Nurs Res
- 284 2021;70:34-43.

26. Essue BM, Wong G, Chapman J, Li Q, Jan S. How are patients managing with the costs
of care for chronic kidney disease in Australia? A cross-sectional study. BMC Nephrol
2013;14:5.
27. Ng MSN, Wong CL, Ho EHS, Hui YH, Miaskowski C, So WKW. Burden of living with
multiple concurrent symptoms in patients with end-stage renal disease. J Clin Nurs
2020;29:2589-601.

Table 1. Background Characteristics and Comparison of Patient-reported and Clinical Outcomes

	Ov	erall	Unem	Unemployed Employed		loyed			Below Po	verty Line	Above Po	verty Line		
	(N=	354)	(n=291)	; 82.2%)	(n=63;	17.8%)			(n=217; 61.3%)		(n=137; 38.7%)			
Background characteristics	N	%	N	%	N	%		р	N	%	N	%		р
Male	207	56.7%	164	56.4%	43	68.3%		0.082	128	59.0%	79	36.4%		0.806
Married	243	66.6%	206	70.8%	37	58.7%		0.061	138	63.6%	105	76.6%		0.010*
Secondary education	231	63.3%	177	60.8%	54	85.7%		<0.001**	127	58.5%	104	75.9%		0.001*
Peritoneal dialysis	255	69.9%	212	72.9%	43	68.3%		0.461	158	72.8%	97	70.8%		0.682
History of transplantation	16	4.4%	10	3.4%	6	9.5%		0.035*	10	4.6%	6	4.4%		0.920
	Mean	SD	Mean	SD	Mean	SD	t	P	Mean	SD	Mean	SD	t	P
Age (years)	60.93	11.89	62.70	0.11	52.63	11.00	6.51	<0.001**	63.36	11.51	57.10	0.12	4.98	<0.001**
Month on dialysis	51.63	64.96	50.32	61.02	57.59	80.75	-0.80	0.503	52.01	57.28	51.05	75.53	0.13	0.899
Patient-reported outcomes	Mean	SD	Mean	SD	Mean	SD	t	P	Mean	SD	Mean	SD	t	P
Dialysis Symptoms Index														
Constipation	1.09	1.60	1.15	1.65	0.78	1.35	1.93	0.057	1.21	1.67	0.89	1.48	1.89	0.059
Chest pain	0.50	1.16	0.54	1.18	0.33	1.06	1.28	0.203	0.53	1.21	0.46	1.09	0.55	0.070
Nausea	0.79	1.39	0.74	1.35	1.02	1.54	-1.32	0.190	0.72	1.34	0.89	1.47	-1.08	0.282
Vomiting	0.65	1.34	0.64	1.33	0.70	1.40	-0.30	0.765	0.61	1.27	0.72	1.45	-0.70	0.485
Diarrhea	0.71	1.34	0.70	1.36	0.73	1.30	-0.16	0.876	0.76	1.43	0.61	1.20	1.08	0.283
Decreased appetite	1.18	1.55	1.21	1.57	1.05	1.49	0.75	0.453	1.21	1.52	1.14	1.60	0.41	0.685
Cramps	1.43	1.62	1.41	1.62	1.54	1.62	-0.60	0.552	1.43	1.62	1.43	1.62	-0.01	0.991
Edema	0.97	1.36	0.93	1.35	1.14	1.40	-1.10	0.271	0.98	1.38	0.96	1.33	0.17	0.864
Shortness of breath	1.07	1.49	1.09	1.51	1.00	1.45	0.43	0.668	1.06	1.51	1.09	1.48	-0.14	0.888
Dizziness	0.96	1.46	0.99	1.46	0.83	1.50	0.79	0.430	0.97	1.45	0.94	1.49	0.16	0.870
Restless legs	0.60	1.32	0.64	1.36	0.43	1.10	1.17	0.243	0.54	1.21	0.71	1.47	-1.13	0.261
Limb numbness	1.04	1.53	1.08	1.55	0.87	1.44	0.95	0.342	1.06	1.53	1.00	1.54	0.39	0.700
Tiredness	2.23	1.66	2.33	1.65	1.79	1.65	2.34	0.020*	2.21	1.64	2.28	1.70	-0.39	0.700
Coughing	1.35	1.56	1.40	1.60	1.14	1.34	1.31	0.195	1.39	1.61	1.29	1.47	0.56	0.576
Dry mouth	1.49	1.56	1.54	1.58	1.24	1.43	1.38	0.164	1.63	1.60	1.26	1.46	2.22	0.027*
Joint/bone pain	1.51	1.75	1.60	1.75	1.08	1.69	2.14	0.033*	1.55	1.74	1.43	1.77	0.64	0.522
Headache	0.73	1.29	0.76	1.30	0.60	1.28	0.868	0.352	0.76	1.35	0.68	1.20	0.61	0.543
Muscle soreness	1.25	1.55	1.30	1.56	1.03	1.48	1.23	0.220	1.27	1.53	1.22	1.57	0.29	0.775

D. CC 1.	1.05	1.50	1.00	1 ~ 1	0.00	1.05	0.02	0.255	1.05	1.50	1.04		0.04	0.065
Difficulty concentrating	1.05	1.50	1.08	1.54	0.89	1.35	0.93	0.355	1.05	1.50	1.04	1.51	0.04	0.967
Dry skin	2.42	1.73	2.42	1.78	2.40	1.51	0.10	0.918	2.68	1.68	1.99	1.73	3.72	<0.001**
Itching	2.58	1.74	2.66	1.76	2.21	1.62	1.86	0.063	2.76	1.75	2.28	1.70	2.58	0.010*
Worrying	1.05	1.56	1.06	1.57	1.02	1.55	0.20	0.845	1.05	1.59	1.05	1.52	-0.01	0.998
Feeling nervous	0.88	1.46	0.90	1.48	0.79	1.45	0.54	0.592	0.89	1.51	0.88	1.42	0.08	0.933
Trouble falling asleep	2.02	1.98	2.13	1.99	1.51	1.87	2.26	0.024*	2.12	1.99	1.85	1.97	1.29	0.200
Trouble staying asleep	1.92	1.88	2.00	1.89	1.54	1.76	1.76	0.080	2.07	1.86	1.66	1.88	2.01	0.045*
Feeling agitated	1.03	1.52	1.06	1.54	0.89	1.50	0.80	0.426	1.11	1.55	0.91	1.50	1.20	0.229
Feeling sad	0.86	1.43	0.92	1.47	0.60	1.21	1.79	0.076	0.95	1.48	0.72	1.34	1.49	0.138
Feeling anxious	0.78	1.35	0.79	1.35	0.75	1.38	0.22	0.828	0.81	1.36	0.74	1.35	0.47	0.640
Decreased interest in sex	0.56	1.28	0.54	1.29	0.70	1.20	-0.92	0.361	0.41	1.08	0.82	1.51	-2.99	0.003*
Difficulty getting sexually	0.53	1.27	0.48	1.25	0.73	1.33	-1.40	0.164	0.37	1.51	0.77	1.52	-2.92	0.004*
aroused														
KDQOL-36														
Symptom of kidney disease	78.20	15.02	77.90	14.68	46.60	16.55	-0.81	0.417	77.84	15.07	78.77	14.99	-0.57	0.571
Effect of kidney disease	71.73	19.45	72.52	19.53 22.24	68.11 31.85	18.84	1.64	0.103	71.79	19.13	71.65	20.03	0.07 -1.18	0.947 0.239
Burden of kidney disease PCS	30.54 37.87	21.70 9.54	30.26 37.27	22.24 9.61	40.65	19.14 8.74	-0.524 -2.57	0.600 0.011*	29.46 37.51	22.07 9.56	32.25 38.45	21.06 9.50	-1.18 -0.90	0.239
MCS	48.54	10.84	48.80	11.05	47.36	9.86	0.96	0.340	47.88	10.98	49.58	10.59	-1.44	0.367
		SD				9.80 SD				10.98 SD		10.39 SD		0.131 P
Clinical Outcomes	Mean		Mean	<i>SD</i>	Mean		t	P	Mean		Mean		t	
KPS	88.59	13.43	87.56	14.07	93.33	8.61	-4.24	<0.001**	87.65	13.79	90.07	12.75	-1.66	0.098
CCI	1.83	2.00	1.98	2.05	1.14	1.64	3.05	0.002*	2.01	1.85	1.55	2.20	2.14	0.033*
Clinical visits	1.21	2.22	1.13	2.03	1.59	2.93	-1.19	0.240	1.18	2.32	1.26	2.07	-0.36	0.718
ER attendance	0.60	1.12	0.68	1.20	0.24	0.56	4.43	<0.001*	0.72	1.28	0.42	0.80	2.68	0.008*
Days of hospital stay	6.36	11.33	6.28	11.11	6.73	12.41	-0.28	0.781	7.30	12.17	4.87	9.72	2.06	0.040*
GFR $(mL/min/1.73m^2)$	5.45	2.26	5.50	2.32	5.21	1.95	0.92	0.359	5.53	2.25	5.32	2.27	0.85	0.397
Serum albumin (g/L)	35.96	4.68	35.73	4.74	36.98	4.28	-1.91	0.054	35.39	4.83	36.85	4.30	-2.88	0.004*
Serum calcium (mmol/L)	2.28	0.19	2.28	0.20	2.28	0.16	0.03	0.973	2.27	0.20	2.29	0.19	-1.03	0.302
Serum phosphate (mmol/L)	1.78	0.55	1.77	0.56	1.82	0.54	-0.60	0.548	1.74	0.55	1.84	0.56	-1.59	0.113
Hemoglobin (g/dL)	10.27	2.79	10.31	2.98	10.12	1.67	0.48	0.631	10.29	1.68	10.24	3.94	0.15	0.878

^{*}P < 0.05; **P < 0.001

Abbreviations: CCI = Charlson Comorbidity Index; ER = Emergency room; GFR = Glomerular filtration rate; g/dL = Gram per deciliter; g/L = Gram per liter; KDQOL-36 = Kidney Disease Quality of Life-36; ; KPS = Karnofsky Performance Scale; MCS = Mental Component Summary; mL/min/1.73m² = milliliter per minute per 1.73 meter squared; mmol/L = millimole per liter; PCS = Physical Component Summary

Health Inequity Associated with Financial Hardship Among Patients with Kidney Failure: A Secondary Analysis (Short Title: Health Inequity and Financial Hardship in Kidney Failure) Marques Shek Nam NG^{1*}, Dorothy Ngo Sheung CHAN¹, Winnie Kwok Wei SO¹ ¹The Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, China *Corresponding author Email: marquesng@cuhk.edu.hk

Abstract

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Financial hardship is a common challenge among patients with kidney failure and may have negative health consequences. Therefore, financial status is regarded as an important determinant of health, and its impact needs to be investigated. This cross-sectional study aimed to identify the differences in patient-reported and clinical outcomes among patients with different financial status. 354 patients with end-stage kidney disease were recruited from March to June 2017 at two regional hospitals in Hong Kong. The Dialysis Symptoms Index and Kidney Disease Quality of Life-36 were used to evaluate patient-reported outcomes. Clinical outcomes were retrieved from medical records and assessed using the Karnofsky Performance Scale (functional status) and Charlson Comorbidity Index (comorbidity level). Patients were stratified using two dichotomised variables, employment status and income level, and their outcomes were compared using independent sample t-tests. In this sample, the employment rate was 17.8% and the poverty rate was 61.2%. Compared with other patients, increased distress associated with specific symptoms, a higher comorbidity level, and more emergency room visits were found in patients with poorer financial status. Unemployed patients reported a decreased physical quality of life, while low-income patients had a lower serum albumin concentration and a longer hospital stay than other patients (all p < 0.05). Financially underprivileged patients experienced health inequity in terms of impaired patientreported and clinical outcomes. Attention needs to be paid to these patients by providing financial assessments and interventions. Additional research is warranted to understand the experience of financial hardship and examine equity in healthcare.

Introduction

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The global burden of kidney failure is increasing. More than 2 million patients have been diagnosed and treated with life-sustaining dialysis therapy worldwide (1). In some countries, 2–3% of healthcare expenditures are used for managing kidney failure, and the demand for dialysis continues to surge (2). At the individual level, patients often experience financial hardship associated with high treatment costs, unemployment, and reduced income. Although many countries provide reimbursement for dialysis therapy, patients are required to cover 12–71% of the costs out of pocket (3). In addition, these patients have reduced productivity associated with disease-related disabilities. According to an international survey (4), less than 55% of haemodialysis (HD) and 68% of peritoneal dialysis (PD) patients are employed. Limited income due to decreased employment may amplify financial hardship among these patients (5). Financial hardship is a profound and significant determinant of health. In fact, higher burdens associated with kidney failure are found in countries that are less socioeconomically developed (1). From an individual perspective, patients utilize their personal resources to pay for their medical and other daily expenses, which may lead to the depletion of financial reserves or incurrence of debt (6). Evidence suggests that impaired financial well-being is associated with poor physical and psychological health in patients with chronic illnesses (7,8). Negative health outcomes, including depression, anxiety, lower health-related quality of life (HRQoL), and higher mortality risk, have been reported (9-11). These outcomes may be seen as the consequences of health inequity caused by social determinants, especially financial factors. Despite the impact of financial hardship on health, few studies have evaluated the relationships between this hardship and various health outcomes among patients with kidney failure (12). A better understanding of these relationships may advance our understanding of

health inequity among patients with kidney failure. Hence, in addition to financial aids, kidney care providers can proactively identify financially underprivileged patients and provide specific interventions that promote equal participation in daily life (13). Therefore, to explore directions for future research, the aim of this secondary analysis was to identify the differences in patient-reported and clinical outcomes between kidney failure patients with high and low financial status.

This study was conducted in Hong Kong, one of the financial centres in the Chinese territory. While this city has a relatively high per capita gross domestic product of 59,264 USD in 2020 (14), it is famous for the large wealth gap. Its latest Gini coefficient in 2016 reached 46.7, which reflected fair inequality within this 700-million population (15). In terms of the healthcare system, Hong Kong has a predominant public sector that provides over 90% of inpatient services and is largely subsidised by taxation (16). Despite the availability of subsidised services, patients with kidney failure are required to use out-of-pocket expenses to cover costs of dialysis consumables and self-financed drugs.

Materials and Methods

The cross-sectional data of 354 patients from a mixed-methods study were analysed (17). These patients were recruited from two public hospitals from March to June 2017.

These hospitals were serving populations with highest and lowest household incomes in Hong Kong (18). The inclusion criteria included: 1) adults diagnosed with kidney failure; 2) received any modality of dialysis therapy for three or more consecutive months; and 3) were willing to provide written consent. Those with active psychiatric disorders (e.g., schizophrenia, dementia) were excluded. After obtaining informed consent, a research assistant administered a questionnaire and reviewed electronic health records at the specialist clinic or the haemodialysis centre. This study was approved by the institutional research boards of the university and the involved hospitals. This study was approved by the Joint

CUHK-NTEC Clinical Research Ethics Committee (reference number: 2017.092). Written consent was obtained from all participants.

Instruments

Symptoms and HRQoL were selected as the patient-reported outcomes. The Dialysis Symptoms Index (DSI) was used to assess the distress levels of 30 symptoms experienced in the past month (19). A higher score indicates a higher level of distress. The Chinese version of the DSI demonstrated excellent content validity (0.99) and internal consistency (α = 0.87) (20). The Kidney Disease Quality of Life-36 was used to evaluate the HRQoL of patients (21). It consists of 24 disease-specific and 12 generic questions that can be divided into three subscales (symptom, burden, and effect of kidney disease) and two summary scores (physical and mental component summary). A higher score indicates better performance in the specific domain. Its Chinese version demonstrated good test-retest reliability (interclass correlation coefficient = 0.79–0.92) and acceptable internal consistency (α = 0.60–0.93) (22).

The clinical outcomes included the functional status, comorbidity level, healthcare service utilization, and biochemical parameters. The Karnofsky Performance Scale was used to evaluate functional status (23). A higher score indicates higher ability to perform activities of daily living (range: 0–100). The Charlson Comorbidity Index was used to assess the

to evaluate functional status (23). A higher score indicates higher ability to perform activities of daily living (range: 0–100). The Charlson Comorbidity Index was used to assess the comorbidity level (23). Patients' relative burden of comorbidity is evaluated based on the weighted sum of 14 conditions (range: 0–33). Other clinical data, including healthcare service utilization and biochemical parameters, were retrieved from the patients' electronic health records. Glomerular filtration rate was estimated based on the Modification of Diet in Renal

Disease (MDRD) equation.

Analyses

Background characteristics and outcomes were summarised using descriptive statistics (e.g., frequency, percentage, mean). Two dichotomized variables that reflected the

patient's financial status were created: employment status and income level. In terms of income level, those earning a monthly household income of \leq 10,000 HKD (approximately 1,290 USD) were regarded as below the poverty line, which is in line with the government's definition (18). After stratifying the patients by these variables, patient-reported and clinical outcomes were compared using independent sample t-tests. All analyses were conducted using SPSS version 25.0 (IBM Corp., Armonk, NY). A two-sided p-value of < 0.05 was considered as statistically significant.

Results

Of the 354 patients, 58.5% were male. The patients had a mean age of 60.9 years (Table 1). Most of the patients received PD (69.9%) and had been on dialysis for a mean of 51.6 months. Overall, 17.8% of the patients were employed, and 61.2% were below the poverty line. The education level significantly differentiated patients regardless employment status and income level ($p \le 0.001$). Compared with other patients, a larger proportion of employed patients had received kidney transplants (9.5%; p = 0.035), and a larger proportion of patients above the poverty line were married (76.6%; p = 0.01).

Table 1 presents the differences in patient-reported and clinical outcomes between groups. Compared with employed patients, those who were unemployed reported higher levels of tiredness (mean: 2.33), joint or bone pain (mean: 1.60), and trouble falling asleep (mean: 2.13) (all $p \le 0.033$). The KDQOL-36 Physical Component Summary scale scores (mean: 37.27) for unemployed patients were significantly lower than for employed patients (p = 0.011). Patients below the poverty line reported higher levels of dry mouth (mean: 1.63), dry skin (mean: 2.68), itching (mean: 2.76), and trouble staying asleep (mean: 2.07) than those above the poverty line (all $p \le 0.045$). Interestingly, patients with lower income had less severe sexual symptoms ($p \le 0.004$), namely a decreased interest in sex (mean: 0.41) and

difficulty becoming sexually aroused (mean: 0.37). However, no significant difference was found in scores of other KDQOL-36 sub-scales nor distress levels of other symptoms.

In terms of clinical outcomes, in general, patients with a poorer financial status had higher comorbidity levels (all $p \le 0.033$) and more emergency room (ER) visits in the past six months (all $p \le 0.008$) than other patients. In addition, patients below the poverty line had a lower serum albumin concentration (35.39 vs. 36.85 g/L; p = 0.004) and longer length of hospital stay (7.30 vs. 4.87 days; p = 0.040) than did patients with higher earnings.

Discussion

The findings from this secondary analysis suggest that patient-reported and clinical outcomes differ between patients with different financial statuses in terms of their employment and income level. Based on our preliminary findings, while no significant relationship was found between financial status and most patient-reported outcomes, patients who were unemployed or living below the poverty line reported higher distress associated with specific symptoms, higher comorbidity levels, and more health care utilization than other patients. Consistent with existing evidence (8-10), the impact of financial hardship on health disparities among patients with kidney failure warrants additional attention.

Compared with the general population in Hong Kong, the employment rate in this study was halved and the poverty rate was three times higher (cf. employment rate: 34.9%; poverty rate: 21.4%) (18). This finding is an alarming sign that in this city, which is well known for economic inequality, financial hardship is very common among patients with kidney failure. Our findings indicate the negative impact of such hardship within this group. Consistent with our previous studies (8,25), financially underprivileged patients may experience a higher symptom burden in terms of tiredness, sleep disturbances, skin problems, and pain. There are some possible reasons for this relationship. As reported in one study (26), financially underprivileged patients may have fewer resources to pay for healthcare services,

especially preventive care. This may explain why patients with impaired financial well-being reported poorer outcomes, particularly a higher mean number of ER visits and length of hospital stay. Therefore, kidney care providers need to pay special attention to the financial needs of patients by incorporating appropriate assessments and interventions in routine care (12). Nevertheless, there is a need to examine equity in the healthcare system to ensure that essential services are provided regardless of a person's financial status. In addition, there may be a reciprocal relationship between financial hardship and outcomes. While symptoms and other outcomes are signs of deteriorating health, patients with a poorer symptom status or poorer outcomes may have a higher demand for healthcare services and a lower physical capacity for engaging actively in employment (27). These consequences lead to increased medical expenditures and decreased income, which eventually intensify financial hardship (6). A better understanding of the experience of financial hardship is warranted to explore the factors that modulate the relationship between financial hardship and health.

Our preliminary evidence reveals the consequences of health inequity and suggests directions for researching issues associated with financial hardship among patients with kidney failure. However, several limitations warrant consideration. Although cross-sectional data were analyzed and limited variables were evaluated, other factors that might confound the relationship between financial hardship and outcomes (e.g., financial aids, home ownership, personal savings, health spendings) were not controlled (8). In addition, the causal relationships among financial statuses, kidney failure, incapacity for employment, and health outcomes need to be examined using a longitudinal design. Of note, financial status was conceptualized in terms of employment status and income level only, which might inadequately reflect the full picture of financial well-being. Therefore, the following suggestions are made: 1) factors influencing financial hardship should be identified and controlled in further analyses; 2) a longitudinal study should be conducted to evaluate

changes in financial status and outcomes; and 3) a comprehensive conceptualization of financial hardship should be adopted.

Conclusion

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Financial hardship is very common among patients with kidney failure, especially in Hong Kong, in terms of high percentages of unemployment and poverty. Our preliminary evidence suggests that this hardship may result in health inequity and manifest in impaired patient-reported and clinical outcomes. Additional research is warranted to understand the experience of financial hardship and the equity of the healthcare system.

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Competing Interests Statement

The authors have declared that no competing interests exist.

Data Availability Statement

- 207 Data cannot be shared publicly because of privacy issues. Confidential data are available
- 208 from the CUHK Research Data Repository for researchers whose work has been approved by
- an institutional review board. Request may be sent together with the research proposal and
- ethical approval to the corresponding author or the Repository (website:
- 211 https://researchdata.cuhk.edu.hk/email: data@cuhk.edu.hk).

References

212

- 1. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of
- chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of
- 215 Disease Study 2017. Lancet 2020;395:709-33.
- 216 2. Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the
- sustainable development goals. Bull World Health Organ 2018;96:414-22.
- 3. van der Tol A, Lameire N, Morton RL, Van Biesen W, Vanholder R. An international
- analysis of dialysis services reimbursement. Clin J Am Soc Nephrol 2019;14:84-93.
- 4. Brown EA, Zhao J, McCullough K, Fuller DS, Figueiredo AE, Bieber B, et al. Burden of
- kidney disease, health-related quality of life, and employment among patients receiving
- peritoneal dialysis and in-center hemodialysis: findings from the DOPPS program. Am J
- 223 Kidney Dis 2021;78:489-500.
- 5. Morton RL, Schlackow I, Gray A, Emberson J, Herrington W, Staplin N, et al. Impact of
- 225 CKD on household income. Kidney Int Rep 2018;3:610-8.
- 226 6. Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients
- with cancer: understanding and stepping-up action on the financial toxicity of cancer
- treatment. CA Cancer J Clin 2018;68:153-65.
- 7. Altice CK, Banegas MP, Tucker-Seeley RD, Yabroff KR. Financial hardships
- experienced by cancer survivors: a systematic review. J Natl Cancer Inst
- 231 2017;109:djw205.
- 8. Ng MSN, Chan DNS, Cheng Q, Miaskowski C, So WKW. Association between financial
- hardship and symptom burden in patients receiving maintenance dialysis: a systematic
- review. Int J Environ Res Public Health 2021;18:9541.

- 9. Ikonomou M, Skapinakis P, Balafa O, Eleftheroudi M, Damigos D, Siamopoulos KC.
- The impact of socioeconomic factors on quality of life of patients with chronic kidney
- 237 disease in Greece. J Renal Care 2015;41:239-46.
- 238 10. Tao S, Zeng X, Liu J, Fu P. Socioeconomic status and mortality among dialysis patients:
- a systematic review and meta-analysis. Int Urol Nephrol 2019;51:509-18.
- 11. Chen J, Liu L, Chen J, Ng MS, Lou VW, Wu B, Jiang W, Jie Y, Zhu J, He Y. The cross-
- lagged association between depressive symptoms and health-related quality of life in
- patients receiving maintenance hemodialysis: a three-wave longitudinal study. Qual Life
- 243 Res 2021;30:3463-3473.
- 12. Krishnan M. The importance of considering total patient economics for hemodialysis.
- 245 Kidney Int Rep 2019;4:365-6.
- 13. Kalantar-Zadeh K, Li PK, Tantisattamo E, Kumaraswami L, Liakopoulos V, Lui S, et al.
- Living well with kidney disease by patient and care-partner empowerment: kidney health
- for everyone everywhere. Clin Nephrol 2021;95:115-22.
- 249 14. Organisation for Economic Co-operation and Development. Gross domestic product
- 250 (GDP) [Internet]. 2022 [Accessed 25 December 2022]. Available:
- 251 https://data.oecd.org/gdp/gross-domestic-product-gdp.htm.
- 15. World Economics. Hong Kong's Gini coefficient [Internet]. 2016 [Accessed 25]
- December 2022]. Available from: https://www.worldeconomics.com/Inequality/Gini-
- 254 Coefficient/Hong%20Kong.aspx.
- 255 16. Schoeb V. Healthcare service in Hong Kong and its challenges: the role of health
- professionals within a social model of health. China Perspect 2016;4:51-58.
- 17. Ng MSN, Miaskowski C, Cooper B, Hui YH, Ho EHS, Mo SKL, et al. Distinct symptom
- experience among subgroups of patients with ESRD receiving maintenance dialysis. J
- 259 Pain Symptom Manage 2020;60:70-9.

- 18. Government of the HKSAR. Hong Kong poverty situation report 2019 [Internet]. 2019
- [Accessed 30 March 2022]. Available from: https://www.
- povertyrelief.gov.hk/eng/pdf/Hong_Kong_Poverty_Situation_
- 263 Report_2019.pdf.
- 19. Weisbord SD, Fried LF, Arnold RM, Rotondi AJ, Fine MJ, Levenson DJ, Switzer GE.
- Development of a symptom assessment instrument for chronic hemodialysis patients: the
- Dialysis Symptom Index. J Pain Symptom Manage 2004;27:226-240.
- 20. Ng MSN, So WKW, Wong CL, Hui YH, Ho EHS, Choi KC, et al. Stability and impact of
- symptom clusters in patients with end-stage renal disease undergoing dialysis. J Pain
- 269 Symptom Manage 2020;59:67-76.
- 21. Hays RD, Kallich JD, Mapes DL, Coons SJ, Amin N, Carter WB, Kamberg C. Kidney
- Disease Quality of Life Short Form (KDQOL-SFTM), version 1.3: a manual for use and
- scoring [Internet]. 1997 [Accessed 30 March 2022]. Available from:
- 273 https://www.rand.org/health-care/surveys_tools/kdqol.html.
- 22. Chow SKY, Tam BML. Is the kidney disease quality of life-36 (KDQOL-36) a valid
- instrument for Chinese dialysis patients? BMC Nephrol 2014;15:1-7.
- 23. Péus D, Newcomb N, Hofer S. Appraisal of the Karnofsky performance status and
- proposal of a simple algorithmic system for its evaluation. BMC Med Inform Decis Mak
- 278 2013;13:1-7.
- 24. Hemmelgarn BR, Manns BJ, Quan H, Ghali WA. Adapting the Charlson Comorbidity
- Index for use in patients with ESRD. Am J Kidney Dis 2003;42:125-32.
- 25. Ng MSN, Wong CL, Choi KC, Hui YH, Ho EHS, Miaskowski C, So WKW. A mixed
- methods study of symptom experience in patients with end-stage renal disease. Nurs Res
- 283 2021;70:34-43.

26. Essue BM, Wong G, Chapman J, Li Q, Jan S. How are patients managing with the costs
of care for chronic kidney disease in Australia? A cross-sectional study. BMC Nephrol
2013;14:5.
27. Ng MSN, Wong CL, Ho EHS, Hui YH, Miaskowski C, So WKW. Burden of living with
multiple concurrent symptoms in patients with end-stage renal disease. J Clin Nurs
2020;29:2589-601.

Table 1. Background Characteristics and Comparison of Patient-reported and Clinical Outcomes

	Ov	erall	Unem	Unemployed Employed		loyed			Below Po	verty Line	Above Po	overty Line		
	(N=	354)	(n=291)	; 82.2%)	(n=63;	17.8%)			(n=217)	; 61.3%)	(n=137; 38.7%)			
Background characteristics	N	%	N	%	N	%		р	N	%	N	%		р
Male	207	56.7%	164	56.4%	43	68.3%		0.082	128	59.0%	79	36.4%		0.806
Married	243	66.6%	206	70.8%	37	58.7%		0.061	138	63.6%	105	76.6%		0.010*
Secondary education	231	63.3%	177	60.8%	54	85.7%		<0.001**	127	58.5%	104	75.9%		0.001*
Peritoneal dialysis	255	69.9%	212	72.9%	43	68.3%		0.461	158	72.8%	97	70.8%		0.682
History of transplantation	16	4.4%	10	3.4%	6	9.5%		0.035*	10	4.6%	6	4.4%		0.920
	Mean	SD	Mean	SD	Mean	SD	t	P	Mean	SD	Mean	SD	t	P
Age (years)	60.93	11.89	62.70	0.11	52.63	11.00	6.51	<0.001**	63.36	11.51	57.10	0.12	4.98	<0.001**
Month on dialysis	51.63	64.96	50.32	61.02	57.59	80.75	-0.80	0.503	52.01	57.28	51.05	75.53	0.13	0.899
Patient-reported outcomes	Mean	SD	Mean	SD	Mean	SD	t	P	Mean	SD	Mean	SD	t	P
Dialysis Symptoms Index														
Constipation	1.09	1.60	1.15	1.65	0.78	1.35	1.93	0.057	1.21	1.67	0.89	1.48	1.89	0.059
Chest pain	0.50	1.16	0.54	1.18	0.33	1.06	1.28	0.203	0.53	1.21	0.46	1.09	0.55	0.070
Nausea	0.79	1.39	0.74	1.35	1.02	1.54	-1.32	0.190	0.72	1.34	0.89	1.47	-1.08	0.282
Vomiting	0.65	1.34	0.64	1.33	0.70	1.40	-0.30	0.765	0.61	1.27	0.72	1.45	-0.70	0.485
Diarrhea	0.71	1.34	0.70	1.36	0.73	1.30	-0.16	0.876	0.76	1.43	0.61	1.20	1.08	0.283
Decreased appetite	1.18	1.55	1.21	1.57	1.05	1.49	0.75	0.453	1.21	1.52	1.14	1.60	0.41	0.685
Cramps	1.43	1.62	1.41	1.62	1.54	1.62	-0.60	0.552	1.43	1.62	1.43	1.62	-0.01	0.991
Edema	0.97	1.36	0.93	1.35	1.14	1.40	-1.10	0.271	0.98	1.38	0.96	1.33	0.17	0.864
Shortness of breath	1.07	1.49	1.09	1.51	1.00	1.45	0.43	0.668	1.06	1.51	1.09	1.48	-0.14	0.888
Dizziness	0.96	1.46	0.99	1.46	0.83	1.50	0.79	0.430	0.97	1.45	0.94	1.49	0.16	0.870
Restless legs	0.60	1.32	0.64	1.36	0.43	1.10	1.17	0.243	0.54	1.21	0.71	1.47	-1.13	0.261
Limb numbness	1.04	1.53	1.08	1.55	0.87	1.44	0.95	0.342	1.06	1.53	1.00	1.54	0.39	0.700
Tiredness	2.23	1.66	2.33	1.65	1.79	1.65	2.34	0.020*	2.21	1.64	2.28	1.70	-0.39	0.700
Coughing	1.35	1.56	1.40	1.60	1.14	1.34	1.31	0.195	1.39	1.61	1.29	1.47	0.56	0.576
Dry mouth	1.49	1.56	1.54	1.58	1.24	1.43	1.38	0.164	1.63	1.60	1.26	1.46	2.22	0.027*
Joint/bone pain	1.51	1.75	1.60	1.75	1.08	1.69	2.14	0.033*	1.55	1.74	1.43	1.77	0.64	0.522
Headache	0.73	1.29	0.76	1.30	0.60	1.28	0.868	0.352	0.76	1.35	0.68	1.20	0.61	0.543
Muscle soreness	1.25	1.55	1.30	1.56	1.03	1.48	1.23	0.220	1.27	1.53	1.22	1.57	0.29	0.775

Difficulty concentrating	1.05	1.50	1.08	1.54	0.89	1.35	0.93	0.355	1.05	1.50	1.04	1.51	0.04	0.967
Dry skin	2.42	1.73	2.42	1.78	2.40	1.51	0.10	0.918	2.68	1.68	1.99	1.73	3.72	<0.001**
Itching	2.58	1.74	2.66	1.76	2.21	1.62	1.86	0.063	2.76	1.75	2.28	1.70	2.58	0.010*
Worrying	1.05	1.56	1.06	1.57	1.02	1.55	0.20	0.845	1.05	1.59	1.05	1.52	-0.01	0.998
Feeling nervous	0.88	1.46	0.90	1.48	0.79	1.45	0.54	0.592	0.89	1.51	0.88	1.42	0.08	0.933
Trouble falling asleep	2.02	1.98	2.13	1.99	1.51	1.87	2.26	0.024*	2.12	1.99	1.85	1.97	1.29	0.200
Trouble staying asleep	1.92	1.88	2.00	1.89	1.54	1.76	1.76	0.080	2.07	1.86	1.66	1.88	2.01	0.045*
Feeling agitated	1.03	1.52	1.06	1.54	0.89	1.50	0.80	0.426	1.11	1.55	0.91	1.50	1.20	0.229
Feeling sad	0.86	1.43	0.92	1.47	0.60	1.21	1.79	0.076	0.95	1.48	0.72	1.34	1.49	0.138
Feeling anxious	0.78	1.35	0.79	1.35	0.75	1.38	0.22	0.828	0.81	1.36	0.74	1.35	0.47	0.640
Decreased interest in sex	0.56	1.28	0.54	1.29	0.70	1.20	-0.92	0.361	0.41	1.08	0.82	1.51	-2.99	0.003*
Difficulty getting sexually aroused	0.53	1.27	0.48	1.25	0.73	1.33	-1.40	0.164	0.37	1.51	0.77	1.52	-2.92	0.004*
KDQOL-36														
Symptom of kidney disease	78.20	15.02	77.90	14.68	46.60	16.55	-0.81	0.417	77.84	15.07	78.77	14.99	-0.57	0.571
Effect of kidney disease	71.73	19.45	72.52	19.53	68.11	18.84	1.64	0.103	71.79	19.13	71.65	20.03	0.07	0.947
Burden of kidney disease	30.54	21.70	30.26	22.24	31.85	19.14	-0.524	0.600	29.46	22.07	32.25	21.06	-1.18	0.239
PCS	37.87	9.54	37.27	9.61	40.65	8.74	-2.57	0.011*	37.51	9.56	38.45	9.50	-0.90	0.367
MCS	48.54	10.84	48.80	11.05	47.36	9.86	0.96	0.340	47.88	10.98	49.58	10.59	-1.44	0.151
Clinical Outcomes	Mean	SD	Mean	SD	Mean	SD	<i>t</i>	P	Mean	SD	Mean	SD	t	<i>P</i>
KPS	88.59	13.43	87.56	14.07	93.33	8.61	-4.24	<0.001**	87.65	13.79	90.07	12.75	-1.66	0.098
CCI	1.83	2.00	1.98	2.05	1.14	1.64	3.05	0.002*	2.01	1.85	1.55	2.20	2.14	0.033*
Clinical visits	1.21	2.22	1.13	2.03	1.59	2.93	-1.19	0.240	1.18	2.32	1.26	2.07	-0.36	0.718
ER attendance	0.60	1.12	0.68	1.20	0.24	0.56	4.43	<0.001*	0.72	1.28	0.42	0.80	2.68	0.008*
Days of hospital stay	6.36	11.33	6.28	11.11	6.73	12.41	-0.28	0.781	7.30	12.17	4.87	9.72	2.06	0.040*
GFR $(mL/min/1.73m^2)$	5.45	2.26	5.50	2.32	5.21	1.95	0.92	0.359	5.53	2.25	5.32	2.27	0.85	0.397
Serum albumin (g/L)	35.96	4.68	35.73	4.74	36.98	4.28	-1.91	0.054	35.39	4.83	36.85	4.30	-2.88	0.004*
Serum calcium (mmol/L)	2.28	0.19	2.28	0.20	2.28	0.16	0.03	0.973	2.27	0.20	2.29	0.19	-1.03	0.302
Serum phosphate (mmol/L)	1.78	0.55	1.77	0.56	1.82	0.54	-0.60	0.548	1.74	0.55	1.84	0.56	-1.59	0.113
Hemoglobin (g/dL)	10.27	2.79	10.31	2.98	10.12	1.67	0.48	0.631	10.29	1.68	10.24	3.94	0.15	0.878

^{*}P < 0.05; **P < 0.001

Abbreviations: CCI = Charlson Comorbidity Index; ER = Emergency room; GFR = Glomerular filtration rate; g/dL = Gram per deciliter; g/L = Gram per liter; KDQOL-36 = Kidney Disease Quality of Life-36; ; KPS = Karnofsky Performance Scale; MCS = Mental Component Summary; mL/min/1.73m² = milliliter per minute per 1.73 meter squared; mmol/L = millimole per liter; PCS = Physical Component Summary

We are pleased to re-submit the revised manuscript entitled 'Health Inequity Associated with Financial Hardship Among Patients with Kidney Failure: A Secondary Analysis' (Manuscript No.: PONE-D-22-21227). We would like to thank the Editor and Reviewer for their thoughtful comments on the manuscript. Our responses to each of the comments are provided below in italics. The suggested revisions have strengthened the report of preliminary evidence, which informs directions for future research in health equity and financial wellbeing of patients with kidney failure. Thank you for your attention and I look forward to hearing from you.

Title/Abstract

• Line 5/20: Recommend using "kidney failure" rather than "end-stage kidney disease" per guidelines advanced by Levey et al. (2020)

Levey AS, Eckardt KU, Dorman NM, Christiansen SL, Cheung M, Jadoul M, et al. Nomenclature for kidney function and disease: executive summary and glossary from a Kidney Disease: Improving Global Outcomes consensus conference*. Nephrology Dialysis Transplantation. 2020 Jul 1;35(7):1077–84.

Response: We revised the wordings (e.g., kidney failure, kidney care) accordingly.

Introduction

• Line 48: The authors state that patients may be required to cover 12-71% of dialysis costs out of pocket, but do not specify the nature of reimbursement at the hospitals in the study. This context would be especially helpful for understanding the impact of financial hardship on study participants. Also, I think it may be relevant to mention here that, as I understand it, public healthcare is virtually free and guaranteed in Hong Kong as this is not the case elsewhere.

Response: We added a description about Hong Kong's healthcare system in the Introduction section (p.4 lines 72-79).

• Lines 53-60: This section seems to emphasize the relationship between financial hardship and medical expenses, but I think the experience of economic oppression is more profound than that. I think the authors can do more to describe the local context of economic inequality in Hong Kong. I am not an expert in the region, though I think some relevant dynamics include issues of financialization, housing and spatial segregation, and immigration issues.

Response: Thanks for this very thoughtful comment. We added a description about Hong Kong's economic inequity in the Introduction section (p.4 lines 72-79).

Materials and Methods

• Line 71: Are you able to add details about the hospitals from which these data were collected? They are described as "regional hospitals" but are they public? Private?

Response: We provided details about these hospitals in the Materials and Methods section (p.4 lines 82-84).

- Line 72: Please provide a citation where the inclusion and exclusion criteria are previously reported. Response: Details of the original study can be found in the reference #16. We added the inclusion and exclusion criteria in the Methods section for better understanding of the study design (p.4 line 85-87).
- Lines 93-100: I am not sure that the Methods adequately account for all four instruments and analyses. I also imagine chi-squared analyses were conducted to assess for differences in patient demographics, but these are not reported in the Methods. Looking at Table 1, I see composite scores for the Kidney Disease Quality of Life-36, the Karnofsky Performance Scale, and the Charlson Comorbidity Index, in addition to several individual patient-reported outcomes. Do the patient-reported outcomes derive from the Dialysis Symptoms Index? If so, how and why were only a subsample of the 30 symptoms selected for reporting?

Response: We supplemented detailed accounts and references for the four instruments used in the Methods section (p.5 lines 92-110). To provide a fair comparison, we presented the results of all symptoms in the Dialysis Symptoms Index and other instruments in Table 1.

Results

• The authors report significant results but do not describe results that are not significant, which is important. Response: Thanks for pointing out this issue. We stated non-significant results in the Results and Discussion sections (p.6 lines 138-139; p.7 lines 148-149) and included the statistics in the Table 1.

Discussion

• Lines 126-128: I am not sure that this is the most accurate summary statement given that (1) your results differ based on employment status and poverty level, and (2) not all patient-reported outcomes were significantly different between your groups. I would revise this summary statement to provide a more cautious interpretation of your results. *Response: We revised the summary to precisely capture both significant and non-significant results (p.7 lines 148-152).*

• Lines 132-133: Consider rephrasing to situate the statistics of your study population relative to the general population (e.g., "In this study, roughly half as many people were employed and three times as many lived below the poverty line relative to the general population of Hong Kong").

Response: We revised the statements based on your suggestion (p.7 line 154).

• Lines 137-142: Do you think that people experiencing economic oppression are at higher risk of developing kidney failure or that undergoing hemodialysis impedes employment opportunities, which then leads to financial hardship? Some literature on this might be helpful to include in the introduction. This might also be worth mentioning in the limitations with respect to the need for longitudinal analyses.

Response: Thanks for your suggestion. We added this point about disparities in the Introduction section (p.3 lines 53-55). We also stressed the need for a longitudinal study to investigate the impact of financial hardship on the outcomes of patients with kidney failure (p.8 lines 181-183).

• Lines 159-160: Can you recommend additional factors affecting financial hardship (e.g., wealth, homeownership)? *Response: We made recommendations on additional factors based on our recent review (p.8 lines 180-181).*

Table 1

- The origin of the patient-reported outcomes is not clear to me. Are these from the DSI? If so, why are there not 30? *Response: We substantially revised Table 1 to present all the results, regardless their statistical significance levels.*
- What is the KDQOL-36 PCS vs. MCS? Response: We are sorry about the confusion. We defined all the abbreviations in the legends and provided details of the instruments in the Methods section (p.5 lines 92-110).
- How did you choose serum albumin vs. urine microalbumin as a clinical outcome? Response: Serum albumin was chosen as an indicator of nutritional status but not disease progression. The data were retrieved from the laboratory results in the medical records. We analysed glomerular filtration rate to evaluate disease progression but no significant result was found (Table 1).