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

Manuscript Number:	PONE-D-22-21227R2
Article Type:	Research Article
Full Title:	Health Inequity Associated with Financial Hardship Among Patients with Kidney Failure: A Secondary Analysis
Short Title:	Health Inequity and Financial Hardship in Kidney Failure
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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 of 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 confirm these findings and understand the experience of financial hardship and health equity.
Order of Authors:	Marques Shek Nam Ng, RN, PhD
	Dorothy Ngo Sheung Chan
	Winnie Kwok Wei So
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. 1). Authors have used ttest to compare outcomes between two financial level groups. ttest does not account for confounders, therefore factors that authors identified should be interpreted only as markers not as those with independent effects. Therefore conclusions need to be cautious to be within that limitation. Response: Thanks for this kindly advice. The limitation related to the statistical methods was highlighted in the Discussion section.

2). Line 59/60. "Negative health outcomes, including depression, anxiety, lower health-related quality of life (HRQoL), and higher mortality risk, have been reported (9-11)". Is this statement referring to those with lower financial levels or those with CKD in general?

Response: The statement was revised to enhance clarity.

3). Line 81. How were patients selected? All the patients who met inclusion/exclusion criteria in these 2 hospitals during the recruitment period were included or was there any selection? How representative the participants to non-participants if there was a selection? Was there any reason (like sample size estimation) for selecting specifically N=354 patients?

Response: Further details about recruitment were provided in the Methods and Results sections.

4). Line 87-88. "... research assistant administered a questionnaire...". Please indicate what information were collected through this questionnaire. I assume this questionnaire was used to collect all patient-reported outcomes as opposed to assessing inclusion/exclusion criteria.

Response: The statement was revised to enhance clarity.

5). Line 82. "... patients were recruited from two public hospitals". Could you name these hospitals?

Response: The names of the hospitals were provided.

- 6). Line 89/90. "... approved by the institutional research boards of the university and the involved hospitals". Could you name these institutions? Response: This statement which is redundant was removed. The names of the IRBs involved were provided together with the reference numbers in the following statement.
- 7). Line 108-112. Please give references for weighted score version of Charlson Comorbidity Index and MDRD equation. Cited ref 23 not applicable for these measures.

Response: References were updated for the captioned instruments.

- 8). Line 124. 58.5% were male. Different percentage in table1. Response: Thanks for spotting out the inconsistency. The figure was checked against raw data and the numbers in Table 1 were revised.
- 9). Line 131-141. This paragraph included results of comparing individual symptoms used to derive DSI score. This is a concern for multiple reasons. First, DSI index has been validated as a summative measure, not for individual symptoms, as reported in lines 92-110. Therefore how correct this comparison of individual items? Why validated summative DSI score not compared between groups? Second, ttest need outcome measures to be in continuous scale, patient-reported responses for these individual symptoms are in categorical scales (ie, likert scale coded to numeric) rather than in continuous scale, therefore not suitable for ttest. If authors need to retain these individual symptoms comparisons as results they need a justification with supporting reference(s) on why ttest is suitable. As at present ttest is not an appropriate statistical method. Otherwise comparison has to be done using a statistical method appropriate for the data. Same comment applicable to the corresponding results in table 1. Response: Thanks for raising the statistical concerns. First, we added the comparison of DSI total scores in Table 1 for reference. The DSI not only generates a score to indicate the overall symptom burden, but it also provides a framework for assessing CKD-related symptoms, as demonstrated by good content validity and test-retest reliability of individual items in the original instrument (Weisbord et al., 2004). Of note, in a study by Weisbord et al. (2007), symptoms reported by patients and clinicians were compared based on the mean scores of individual symptoms. Second, it is implicitly assumed that the individual item scores of DSI are of interval scale data, otherwise it does not make sense to calculate a summative score for DSI. Indeed, it is common to report means and standard deviations of individual symptoms in previous studies (Almutary et al., 2016; de Rooji et al., 2022; Weisbord et al., 2007) and the item scores are not skewed. Therefore, we believe that t-test is appropriate to compare the severity levels of symptoms between groups.

References:

Almutary, H., Bonner, A., & Douglas, C. (2016). Which patients with chronic kidney disease have the greatest symptom burden? A comparative study of advanced CKD stage and dialysis modality. Journal of Renal Care, 42(2), 73-82.

de Rooij, E. N., Meuleman, Y., de Fijter, J. W., Jager, K. J., Chesnaye, N. C., Evans, M., ... & Hoogeveen, E. K. (2022). Symptom burden before and after dialysis initiation in older patients. Clinical Journal of the American Society of Nephrology, 17(12), 1719-1729.

Weisbord, S. D., Fried, L. F., Arnold, R. M., Rotondi, A. J., Fine, M. J., Levenson, D. J., & Switzer, G. E. (2004). Development of a symptom assessment instrument for chronic hemodialysis patients: The Dialysis Symptom Index. Journal of Pain and Symptom management, 27(3), 226-240.

Weisbord, S. D., Fried, L. F., Mor, M. K., Resnick, A. L., Unruh, M. L., Palevsky, P. M., ... & Arnold, R. M. (2007). Renal provider recognition of symptoms in patients on maintenance hemodialysis. Clinical Journal of the American Society of Nephrology, 2(5), 960-967.

- 10). Abstract line 32. "... increased distress associated with specific symptoms,...". Methods section says dialysis symptom index (DSI) is derived from kidney symptoms, and higher DSI indicates higher distress. If so, above statement is obvious by definition, therefore I wonder why it is worth reporting as a result. Response: The meaning of the captioned phrase means distress 'originated from specific symptoms.' We did not imply a statistical association between distress and
- 11). Table1. Please remove all asterisks and associated footnote because they are redundant.

Response: All asterisks and footnotes were removed accordingly.

specific symptoms. The statement was revised to enhance clarity.

12). Table1. Please check the correctness of the reported SD (0.11) for age for unemployed group.

Response: The figures were checked against raw data and the number in the Table 1 was revised.

13). Table1. Please mention Clinical visits and ER attendance are counted over what period. I could not find that in methods section. Please make sure method section includes how each of the reported measure was measured.

Response: The duration of capturing clinical/ER visits and lengths of hospital stay were added in the Methods section and Table 1.

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This study was approved by the Joint CUHK-NTEC Clinical Research Ethics Committee (reference number: 2017.092), HKEC Research Ethics Committee (reference number: HKEC-2017-008), and KCC/KEC Research Ethics Committee (reference number: KC/KE-17-0016/ER-3) prior to data collection. Written consent was obtained from all participants.

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- Include the approval number and/or a statement indicating approval of this research
- Indicate the form of consent obtained (written/oral) or the reason that consent was not obtained (e.g. the data were analyzed anonymously)

Animal Research (involving vertebrate animals, embryos or tissues)

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- Include an approval number if one was obtained
- If the study involved non-human primates, add additional details about animal welfare and steps taken to ameliorate suffering
- If anesthesia, euthanasia, or any kind of animal sacrifice is part of the study, include briefly which substances and/or methods were applied

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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 of 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 confirm these findings and understand the experience of financial hardship and health equity.

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 in patients with kidney failure who are socioeconomically disadvantaged (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). This sample size was estimated to generate sufficient data for the latent class analysis in the original study. These patients were recruited at the dialysis clinics of Pamela Youde Nethersole Eastern Hospital and United Christian Hospital 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. Given that the complete patient lists could not be generated due to privacy issues, a convenience sampling method was used.

A research assistant approached patients in the clinics and screened for eligibility. After explaining the study and obtaining informed consent, the research assistant administered a questionnaire containing a demographic form and the instruments. Then, electronic health records were reviewed at the dialysis clinics. This study was approved by the Joint CUHK-NTEC Clinical Research Ethics Committee (reference number: 2017.092), HKEC Research Ethics Committee (reference number: HKEC-2017-008), and KCC/KEC Research Ethics Committee (reference number: KC/KE-17-0016/ER-3) prior to data collection. 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 (24). 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 in past six months 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 (25).

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 424 patients approached, 22 did not meet eligibility and 48 declined to participate. Among the consented 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, overall symptom burden, 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 (8,26), 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 (27), 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 (28). 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.

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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). Given these methodological limitations, findings should be interpreted as markers of potential influences of financial status on patient outcomes. 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. However, given the methodological limitations, additional research is warranted to confirm these findings and understand the experience of financial hardship and health equity.

Acknowledgements

The authors would like to express their gratitude to Dr Stephen Mo, Ms Eva Ho, Dr Sunny Wong, Ms Yun Ho Hui, and the staff members of the study sites for their assistance in data collection.

Financial Disclosure

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213 The authors received no specific funding for this work.

Competing Interests Statement

215 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

223

- 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
- 226 Disease Study 2017. Lancet 2020;395:709-33.
- 227 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
- 234 Kidney Dis 2021;78:489-500.
- 5. Morton RL, Schlackow I, Gray A, Emberson J, Herrington W, Staplin N, et al. Impact of
- 236 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
- 239 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
- 242 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
- 248 disease in Greece. J Renal Care 2015;41:239-46.
- 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
- 254 Res 2021;30:3463-3473.
- 255 12. Krishnan M. The importance of considering total patient economics for hemodialysis.
- 256 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.
- 260 14. Organisation for Economic Co-operation and Development. Gross domestic product
- 261 (GDP) [Internet]. 2022 [Accessed 25 December 2022]. Available:
- 262 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-
- 265 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
- 270 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_
- 274 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
- 280 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.
- 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
- 289 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. Levey AS, Coresh J. Greene T, Stevens LA, Zhang Y, Hendriksen S, Kusek JW, van
- Lente F, Chronic Kidney Disease Epidemiology Collaboration. Using standardized serum
- creatinine values in the modification of diet in renal disease study equation for estimating
- 295 glomerular filtration rate. Ann Int Med 2006;145,247-54.

26. Ng MSN, Wong CL, Choi KC, Hui YH, Ho EHS, Miaskowski C, So WKW. A mixed 296 methods study of symptom experience in patients with end-stage renal disease. Nurs Res 297 2021;70:34-43. 298 27. Essue BM, Wong G, Chapman J, Li Q, Jan S. How are patients managing with the costs 299 of care for chronic kidney disease in Australia? A cross-sectional study. BMC Nephrol 300 2013;14:5. 301 28. Ng MSN, Wong CL, Ho EHS, Hui YH, Miaskowski C, So WKW. Burden of living with 302 multiple concurrent symptoms in patients with end-stage renal disease. J Clin Nurs 303 2020;29:2589-601. 304

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

	Ov	erall	Unemployed		Employed				Below Po	overty 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	%		p	N	%	N	%		p
Male	207	58.5%	164	56.4%	43	68.3%		0.082	128	59.0%	79	36.4%		0.806
Married	243	68.6%	206	70.8%	37	58.7%		0.061	138	63.6%	105	76.6%		0.010
Secondary education	231	65.3%	177	60.8%	54	85.7%		< 0.001	127	58.5%	104	75.9%		0.001
Peritoneal dialysis	255	72.0%	212	72.9%	43	68.3%		0.461	158	72.8%	97	70.8%		0.682
History of transplantation	16	4.5%	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	11.33	52.63	11.00	6.51	< 0.001	63.36	11.51	57.10	11.51	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	34.16	23.03	36.07	22.03	31.32	24.73	1.41	0.163	36.18	21.75	33.69	23.81	0.99	0.323
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	t	<i>P</i>	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 in 6 months	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 in 6 months	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 in 6 months	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

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 of 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 confirm these findings and understand the experience of financial hardship and health equity.

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 in patients with kidney failure who are socioeconomically disadvantaged (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). This sample size was estimated to generate sufficient data for the latent class analysis in the original study. These patients were recruited at the dialysis clinics of Pamela Youde Nethersole Eastern Hospital and United Christian Hospital 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. Given that the complete patient lists could not be generated due to privacy issues, a convenience sampling method was used.

A research assistant approached patients in the clinics and screened for eligibility. After explaining the study and obtaining informed consent, the research assistant administered a questionnaire containing a demographic form and the instruments. Then, electronic health records were reviewed at the dialysis clinics. This study was approved by the Joint CUHK-NTEC Clinical Research Ethics Committee (reference number: 2017.092), HKEC Research Ethics Committee (reference number: HKEC-2017-008), and KCC/KEC Research Ethics Committee (reference number: KC/KE-17-0016/ER-3) prior to data collection. 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 (24). 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 in past six months 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 (25).

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 424 patients approached, 22 did not meet eligibility and 48 declined to participate. Among the consented 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, overall symptom burden, 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 (8,26), 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 (27), 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 (28). 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.

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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). Given these methodological limitations, findings should be interpreted as markers of potential influences of financial status on patient outcomes. 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. However, given the methodological limitations, additional research is warranted to confirm these findings and understand the experience of financial hardship and health equity.

Acknowledgements

The authors would like to express their gratitude to Dr Stephen Mo, Ms Eva Ho, Dr Sunny Wong, Ms Yun Ho Hui, and the staff members of the study sites for their assistance in data collection.

Financial Disclosure

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213 The authors received no specific funding for this work.

Competing Interests Statement

215 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

223

- 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
- 226 Disease Study 2017. Lancet 2020;395:709-33.
- 227 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
- 234 Kidney Dis 2021;78:489-500.
- 5. Morton RL, Schlackow I, Gray A, Emberson J, Herrington W, Staplin N, et al. Impact of
- 236 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
- 239 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
- 242 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
- 248 disease in Greece. J Renal Care 2015;41:239-46.
- 249 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
- 254 Res 2021;30:3463-3473.
- 255 12. Krishnan M. The importance of considering total patient economics for hemodialysis.
- 256 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.
- 260 14. Organisation for Economic Co-operation and Development. Gross domestic product
- 261 (GDP) [Internet]. 2022 [Accessed 25 December 2022]. Available:
- 262 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-
- 265 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
- 270 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_
- 274 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
- 280 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.
- 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
- 289 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. Levey AS, Coresh J. Greene T, Stevens LA, Zhang Y, Hendriksen S, Kusek JW, van
- Lente F, Chronic Kidney Disease Epidemiology Collaboration. Using standardized serum
- creatinine values in the modification of diet in renal disease study equation for estimating
- 295 glomerular filtration rate. Ann Int Med 2006;145,247-54.

26. Ng MSN, Wong CL, Choi KC, Hui YH, Ho EHS, Miaskowski C, So WKW. A mixed 296 methods study of symptom experience in patients with end-stage renal disease. Nurs Res 297 2021;70:34-43. 298 27. Essue BM, Wong G, Chapman J, Li Q, Jan S. How are patients managing with the costs 299 of care for chronic kidney disease in Australia? A cross-sectional study. BMC Nephrol 300 2013;14:5. 301 28. Ng MSN, Wong CL, Ho EHS, Hui YH, Miaskowski C, So WKW. Burden of living with 302 multiple concurrent symptoms in patients with end-stage renal disease. J Clin Nurs 303 2020;29:2589-601. 304

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

	Ov	Overall Unemployed			Emp	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	%		p	N	%	N	%		p
Male	207	58.5%	164	56.4%	43	68.3%		0.082	128	59.0%	79	36.4%		0.806
Married	243	68.6%	206	70.8%	37	58.7%		0.061	138	63.6%	105	76.6%		0.010
Secondary education	231	65.3%	177	60.8%	54	85.7%		< 0.001	127	58.5%	104	75.9%		0.001
Peritoneal dialysis	255	72.0%	212	72.9%	43	68.3%		0.461	158	72.8%	97	70.8%		0.682
History of transplantation	16	4.5%	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	11.33	52.63	11.00	6.51	< 0.001	63.36	11.51	57.10	11.51	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	34.16	23.03	36.07	22.03	31.32	24.73	1.41	0.163	36.18	21.75	33.69	23.81	0.99	0.323
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	t	P	Mean	SD	Mean	SD	t	P
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 in 6 months	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 in 6 months	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 in 6 months	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

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.

1). Authors have used ttest to compare outcomes between two financial level groups. ttest does not account for confounders, therefore factors that authors identified should be interpreted only as markers not as those with independent effects. Therefore conclusions need to be cautious to be within that limitation.

Response: Thanks for this kindly advice. The limitation related to the statistical methods was highlighted in the Discussion section.

2). Line 59/60. "Negative health outcomes, including depression, anxiety, lower health-related quality of life (HRQoL), and higher mortality risk, have been reported (9-11)". Is this statement referring to those with lower financial levels or those with CKD in general?

Response: The statement was revised to enhance clarity.

- 3). Line 81. How were patients selected? All the patients who met inclusion/exclusion criteria in these 2 hospitals during the recruitment period were included or was there any selection? How representative the participants to non-participants if there was a selection? Was there any reason (like sample size estimation) for selecting specifically N=354 patients? *Response: Further details about recruitment were provided in the Methods and Results sections.*
- 4). Line 87-88. "... research assistant administered a questionnaire...". Please indicate what information were collected through this questionnaire. I assume this questionnaire was used to collect all patient-reported outcomes as opposed to assessing inclusion/exclusion criteria.

Response: The statement was revised to enhance clarity.

- 5). Line 82. "... patients were recruited from two public hospitals". Could you name these hospitals? *Response: The names of the hospitals were provided.*
- 6). Line 89/90. "... approved by the institutional research boards of the university and the involved hospitals". Could you name these institutions?

Response: This statement which is redundant was removed. The names of the IRBs involved were provided together with the reference numbers in the following statement.

7). Line 108-112. Please give references for weighted score version of Charlson Comorbidity Index and MDRD equation. Cited ref 23 not applicable for these measures.

Response: References were updated for the captioned instruments.

8). Line 124. 58.5% were male. Different percentage in table 1.

Response: Thanks for spotting out the inconsistency. The figure was checked against raw data and the numbers in Table 1 were revised.

9). Line 131-141. This paragraph included results of comparing individual symptoms used to derive DSI score. This is a concern for multiple reasons. First, DSI index has been validated as a summative measure, not for individual symptoms, as reported in lines 92-110. Therefore how correct this comparison of individual items? Why validated summative DSI score not compared between groups? Second, ttest need outcome measures to be in continuous scale, patient-reported responses for these individual symptoms are in categorical scales (ie, likert scale coded to numeric) rather than in continuous scale, therefore not suitable for ttest. If authors need to retain these individual symptoms comparisons as results they need a justification with supporting reference(s) on why ttest is suitable. As at present ttest is not an appropriate statistical method. Otherwise comparison has to be done using a statistical method appropriate for the data. Same comment applicable to the corresponding results in table1.

Response: Thanks for raising the statistical concerns. First, we added the comparison of DSI total scores in Table 1 for reference. The DSI not only generates a score to indicate the overall symptom burden, but it also provides a framework for assessing CKD-related symptoms, as demonstrated by good content validity and test-retest reliability of individual items in the original instrument (Weisbord et al., 2004). Of note, in a study by Weisbord et al. (2007), symptoms reported by patients and clinicians were compared based on the mean scores of individual symptoms. Second, it is implicitly assumed that the individual item scores of DSI are of interval scale data, otherwise it does not make sense to calculate a summative score for DSI. Indeed, it is common to report means and standard deviations of individual symptoms in

previous studies (Almutary et al., 2016; de Rooji et al., 2022; Weisbord et al., 2007) and the item scores are not skewed. Therefore, we believe that t-test is appropriate to compare the severity levels of symptoms between groups.

References:

Almutary, H., Bonner, A., & Douglas, C. (2016). Which patients with chronic kidney disease have the greatest symptom burden? A comparative study of advanced CKD stage and dialysis modality. Journal of Renal Care, 42(2), 73-82. de Rooij, E. N., Meuleman, Y., de Fijter, J. W., Jager, K. J., Chesnaye, N. C., Evans, M., ... & Hoogeveen, E. K. (2022). Symptom burden before and after dialysis initiation in older patients. Clinical Journal of the American Society of

Nephrology, 17(12), 1719-1729.

Weisbord, S. D., Fried, L. F., Arnold, R. M., Rotondi, A. J., Fine, M. J., Levenson, D. J., & Switzer, G. E. (2004). Development of a symptom assessment instrument for chronic hemodialysis patients: The Dialysis Symptom Index. Journal of Pain and Symptom management, 27(3), 226-240.

Weisbord, S. D., Fried, L. F., Mor, M. K., Resnick, A. L., Unruh, M. L., Palevsky, P. M., ... & Arnold, R. M. (2007). Renal provider recognition of symptoms in patients on maintenance hemodialysis. Clinical Journal of the American Society of Nephrology, 2(5), 960-967.

- 10). Abstract line 32. "... increased distress associated with specific symptoms,...". Methods section says dialysis symptom index (DSI) is derived from kidney symptoms, and higher DSI indicates higher distress. If so, above statement is obvious by definition, therefore I wonder why it is worth reporting as a result.
- Response: The meaning of the captioned phrase means distress 'originated from specific symptoms.' We did not imply a statistical association between distress and specific symptoms. The statement was revised to enhance clarity.
- 11). Table1. Please remove all asterisks and associated footnote because they are redundant. *Response: All asterisks and footnotes were removed accordingly.*
- 12). Table 1. Please check the correctness of the reported SD (0.11) for age for unemployed group. *Response: The figures were checked against raw data and the number in the Table 1 was revised.*
- 13). Table 1. Please mention Clinical visits and ER attendance are counted over what period. I could not find that in methods section. Please make sure method section includes how each of the reported measure was measured. Response: The duration of capturing clinical/ER visits and lengths of hospital stay were added in the Methods section and Table 1.