Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 376 - 387
Received 05 May 2021; Accepted 01 June 2021.

Impact of Comorbidities on Health-Related Quality of Life in Patients with Different Stages of Chronic Kidney Disease in Babil Governorate, Iraq

Mohammed Saad Abdullah[1], Assistant prof. Suhair Mohammed Hassoun[2]

[1,2]Middle Technical University, College of Health & Medical Technology, Baghdad, Iraq.

mohammedsaad0093@gmail.com

Abstract

Background: Chronic kidney disease is associated with different comorbid conditions. Most persons with mild-to-moderate CKD reported reductions in at least one health-related quality of life (HRQOL) domain, which was independently associated with comorbidities.

Objectives: The present study aims to assess the impact of comorbidities on HRQOL in patients with stage3-5 chronic kidney disease (CKD) in Babil Governorate, Iraq.

Methods: A cross-sectional study among adults with CKD (eGFR<60 mL/min/1.73m^2) has been used. Participants diagnosed with CKD stage 3-4 by physicians and adult patients diagnosed with end-stage renal disease (ESRD) receiving haemodiaylsis (HD) treatment in Kidney Centers at Marjan Medical City and Imam-Alsadiq General Hospital were enrolled. Each participant completed the Kidney Disease Quality of Life (KDQoL™-36) questionnaire, which is comprised of two composite measures of physical and mental health and 3 kidney disease specific subscales. Analysis of data was carried out using the available statistical package of SPSS-27.

Results: A convenience sample of 206 patients were studied with a mean age of 55.2 (SD = 14.7) years and more than half 109 (52.9%) were males. Most of the participants (43.2%) had two comorbidities. The three most common comorbidities were hypertension (83.5%), diabetes mellitus (42.7%), cardiovascular disease (45.6%).The Meanscores for overall HRQOL, physical component summary, mental component summary, symptom/problem list, effects of kidney disease and burden of kidney disease scales were (58.1±13), (38.1±27.9), (52.9±18.7), (70.1±11.7), (76.5±13.4), and (30.2±31.2), respectively. A Kruskal-Wallis test revealed a statistically significant difference between overall HRQOL score and CKD stages, $\chi^2(2) = 100.51$, $p = 0.000$. Overall HRQOL score were lower in stage 5 HD in comparison to stage 4 and stage 3. A significant reduction in overall HRQOL score with increase number of comorbidities, $\chi^2(3) = 9.10$, $p = 0.028$. Among comorbidities, cardiovascular disease, chronic respiratory disorder, HCV infection were associated with overall HRQOL score, p value < 0.05.

Conclusion: Comorbidities considerably impair the HRQOL among CKD patients. over ninety percent of patients with CKD had comorbidities. Regular organization of health education awareness programs on the prevention of CKD and its associated comorbidities among the general public should be done.

Keywords: comorbidities, health-related quality of life, chronic kidney disease.

Introduction

Kidney diseases have risen from the world's 13th leading cause of death to the 10th(World Health Organization, 2020). Chronic kidney disease (CKD) has been redefined in the new millennium

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 376 - 387
Received 05 May 2021; Accepted 01 June 2021.

as any alteration of kidney morphology, function, blood, or urine composition lasting for at least 3 months (Versino & Piccoli, 2019). Chronic kidney disease (CKD) is a public health problem worldwide(A S Levey et al., 2007), with a high global prevalence between 11 to 13% (Hill et al., 2016).In Iraq, the prevalence of ESRD was 74 per a million of population (pmp)(Ali et al., 2018).

Chronic kidney disease is associated with different comorbid conditions,that is an important driver of the adverse clinical and economic consequences associated with CKD (Tonelli et al., 2015). Comorbidity is the presence of a co-existing or additional condition or disease in addition to the specific disease of interest (Barnett et al., 2012). The total burden of medical comorbidity among CKD patients was significantly higher than those without CKD (Chartier et al., 2018). In Iraq, high prevalence rates of comorbidity among end-stage kidney disease including hypertension (35.2%), heart failure (4.57%), ischemic heart disease (10.56%) and cerebrovascular accident (0.7%)(Askar et al., 2019).

Mostpatients with mild-to-moderate CKD reported reductions in at least one health-related quality of life (HRQOL) domain, which was independently associated with comorbidities(Fraser et al., 2020). HRQOL is an indicator of the impact of a condition on a patient's life and well-being (Pagels et al., 2012). Analysis of HRQOL surveillance data can identify subgroups with relatively poor perceived health and help to guide interventions to improve their situations and avert more serious consequences (Centers for Disease Control and Prevention, 2018).

Most of the global burden of chronic kidney disease (CKD) is occurring in low- and middle-income countries (LMICs) (Stanifer et al., 2016). In Iraq, previous studies on CKD patients have been limited. However, most of these studies assessed HRQOL of patients with the end-stage kidney disease, and not provided sufficient information about pre-dialysis stages or comorbidities (Alhajim, 2017; Askar et al., 2019; Dhaidan, 2018; Kadhim, 2019; Qader & Naqshbandi, 2019). The present study aims to assess the impact of comorbidities on HRQOL among patients with stage 3–5 CKD in Babil Governorate, Iraq.

Methods

Study design and setting

A cross-sectional study was conducted to assess the impact of comorbidities on HRQOL among patients with stage 3-5 CKD attending Marjan Medical City and Imam-Alsadiq General Hospital in BabilGovernorate, Iraq. These hospitals, are a governmental institution that provides services to Iraqi citizens. Babil Governorate is about 125 kilometers south of Baghdad city, the capital of Iraq.

Study participants

Participants were eligible to participate in the study if they had been diagnosed with stages 3- 4 CKD by physicians and adult patients diagnosed with ESRD receiving HD treatment in Kidney Centers at Marjan Medical City and Imam-Alsadiq General Hospital were enrolled, were at least 18 years old, and were able to offer informed verbal consent.Data were collected between September 2020 and March 2021.

Sample size and Sampling technique

Sample size was 206 patients calculated according to Daniel's sample size formula for continuous {infinite} community (Charan & Biswas, 2013; Pourhoseingholi et al., 2013);prior studies

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 376 - 387
Received 05 May 2021; Accepted 01 June 2021.

also used similar sample size (Aggarwal et al., 2016a)(Pauly et al., 2020). In this study, Convenience samplingtechnique was used. Although it is a non-probability sampling method, it is the most applicable and widely used method in clinical research (Elfil & Negida, 2017).

Instruments

Socio-demographic, Clinical characteristics and Comorbidities: Participants in the study were asked to provide information about their age, gender, educational level, marital status, employment status, residence, and smoking habits. Clinical characteristics of the participants were obtained by reviewing and self-reporting medical records and laboratory results. These included durations of chronic kidney disease, serum creatinine, eGFR, weight, height and BMI. The serum creatinine was used to calculate eGFR by using CKD Epidemiology Collaboration (CKD-Epi) formula (Andrew S Levey et al., 2009). Patients reported the presence and type of major medical conditions (other than CKD) when asked, "Do you have any major medical conditions other than CKD? (yes/no)" followed by an open-ended item "if yes, please list the other major medical conditions that you have".

Health-Related Quality of Life: KDQOL™ is a disease-specific QOL questionnaire that was developed in 1994 to measure HR-QOL in patients with CKD (Hays et al., 1994). The overall KDQOL-36™ instrument consists of five dimensions: Physical Component Summary (PCS), Mental Component Summary (MCS), Burdens of Kidney Disease (BKD), Symptoms and Problems of Kidney Disease (SPKD), and Effects of Kidney Disease (EKD). Item scores were summed for each scale and transformed on a scale of 0 to 100 with a higher score indicating better HRQoL(Kidney Disease Quality of Life Working Group, n.d.). The overall mean score ≤50 and >50 was considered as lower and higher HRQOL, respectively (Kim et al., 2021).

Statistical analysis

Analysis of data was carried out using the available statistical package of SPSS-27.At first, normality tests were conducted for all the study continuous variables to inform selection of appropriate and robust statistical tests. Normality tests were conducted using Shapiro-Wilk test and Kolmogorov-Simonov (K–S) test for all the study continuous variables. Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values), median interquartile range (IQR). Mann-Whitney u testwas used to determine the differences of the overall HRQOL scorewith twocategorial variables. Kruskal-Wallis tests were used to determine if there are statistically significant differences between number of comorbidities on overall HRQOL score. The significance of difference of different percentages (qualitative data) was tested using Pearson Chi-square test (χ^2-test). Statistical significance was considered whenever the P value was equal or less than 0.05.

Results

Socio-demographic, clinical characteristics and comorbidities of study participants

Table 4.1: summarizes the socio-demographic and clinical characteristics of the participants. Of the total 206 participants, the average age of the study patients was 55.2 years (*SD* = 14.7),and the highest percentage was found among those aged between (41-60) years with 84 (40.8 %) participants, more than half of them were male 109 (52.9%), while 97 (47.1%) were female. Majority of them were married 184 (89.3%).Only 19 (9.8%) have attended a college or higher education. Regarding the employment among participants, the majority 143 (69.8%) were unemployed, while only 15 (7.3%) were employed. Most of the subjects were living in urban area 120 (58.3%) while the remaining live in

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 376 - 387
Received 05 May 2021; Accepted 01 June 2021.

rural area. Most of the participants 81 (39.3%) were in CKD Stage 5 (haemodialysis), 68 (33%) were in CKD Stage 4, and 57 (27.7%) were in CKD Stage 3. Their mean (±SD) body mass index (BMI) was (23.7±3.3) kg/m^2; 128 (62.1%) had normal BMI, followed by 63 (30.6%) with overweight BMI, 6 (2.9%) had obesity, and 9 (4.4%) were underweight. The mean (±SD) duration of having chronic kidney disease was (2.9±2.6) years. The mean (±SD)serum creatinine (mg/dl), eGFR (mL/min/1.73 m^2) were (4.8±3.5), (21.8±16.3),respectively. The three most common comorbidities were hypertension (83.5%), diabetes mellitus (42.7%), and cardiovascular disease (45.6%) as shown in (**Figure 1)**.

Table 1. Sociodemographic and clinical characteristics of participants.

Characteristics	n	%
Age groups		
18-40	42	20.4
41-60	84	40.8
> 60	80	38.8
Mean ± SD (Range)	55.2±14.7 (18-90)	
Gender		
Male	109	52.9
Female	97	47.1
Educational level		
Illiterate / Primary	136	66
Intermediate / Secondary	51	24.8
College and higher	19	9.2
Marital status		
Married	182	88.3
Widowed	7	3.4
Divorced	3	1.5
Single	14	6.8
Employment status		
Employed	15	7.3
Unemployed	143	69.8
Retired	47	22.9
Residence		
Rural	86	41.7
Urban	120	58.3
Duration of CKD (years)		
< 1 year	40	19.4
1-4 years	126	61.2
≥ years	40	19.4
Mean ± SD	2.9±2.6	
BMI (kg/m^2)		
Underweight (<18.5)	9	4.4
Normal (18.5-24.9)	128	62.1
Overweight (25-29.9)	63	30.6
Obese (≥ 30)	6	2.9

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 376 - 387
Received 05 May 2021; Accepted 01 June 2021.

Mean ± SD	23.7±3.3	
CKD Stage		
G3a	27	13.1
G3b	30	14.6
G4	68	33
G5	81	39.3
Serum creatinine (mg/dl)		
Mean ± SD	4.8±3.5	
eGFR (mL/min/1.73 m^2)		
Mean ± SD	21.8±16.3	

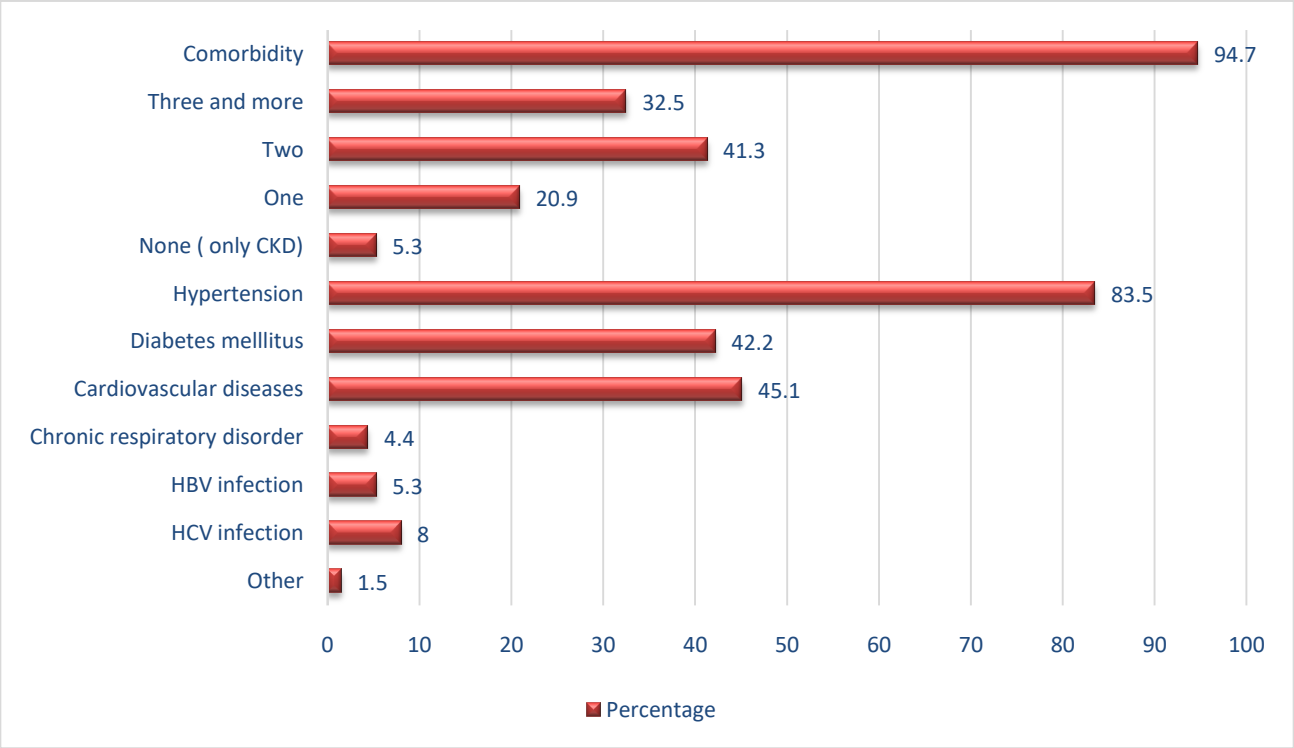

Figure 1: Comorbidities of patients with CKD.

Descriptive results of health-related quality of life among the study participants

Table 2: shows the Mean ±SD on the Kidney Disease and Quality of Life (KDQOL™-36). The overall Mean ± SD of HRQOL measured using the KDQOL-36™ among the participants was (58.1±13) ranging from (32.92-89.58), with (35%) of participants scored lower HRQOL. Higher (Mean ± SD) for the mental component summary (52.9±18.7), in compared to physical component summary (38.1±27.9). Among kidney disease specific sub-scales, higher mean score was the effects of kidney disease sub-scale (76.5±13.4), followed by symptoms/problems list sub-scale, and then the burden of kidney disease sub-scale (30.2±31.2).

Table 2. Health-Related Quality of life (HRQOL) Scores in Sub-scales

Sub-scales	Mean ±SD	Minimum	Maximum	Score	Number	Percentage

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 376 - 387
Received 05 May 2021; Accepted 01 June 2021.

Physical component summary (PCS)	38.1±27.9	0	93.5	Low ≤ 50	138	67
				High >50	68	33
Mental component summary (MCS)	52.9±18.7	0	85	Low ≤ 50	86	41.7
				High >50	120	58.3
Burden of kidney disease (BKD)	30.2±31.2	0	100	Low ≤ 50	159	77.2
				High >50	47	22.8
Symptom/problem list (SPKD)	70.1±11.7	41.67	87.5	Low ≤ 50	16	7.8
				High >50	190	92.2
Effects of kidney disease (EKD)	76.5±13.4	43.75	100	Low ≤ 50	15	7.3
				High >50	191	92.7
Overall HRQOL score	58.1±13	32.92	89.58	Low ≤ 50	72	35
				High >50	134	65

Health-related quality of life and CKD stages

A Kruskal-Wallis test revealed a statistically significant difference between overall HRQOL score and CKD stages, $\chi^2(2) = 100.51$, $p = 0.000$. Overall HRQOL score were lower in stage 5 HD (Mean rank= 65.81) in comparison to stage 4 (Mean rank= 95.47) and stage 3 (Mean rank= 169.22) **(see Table 3, Figure 2).** There was positive correlation between e GFR (renal function indicator) and HRQOL among all sub-scales p value < 0.01. These results indicated that more advanced stages associated with reduced HRQOL.A Kruskal-Wallis H test showed that there was a statistically significant difference between overall HRQOL scores and employment status, marital status, and duration of chronic kidney disease, p value< *0.05*, Overall HRQOL score were lower in unemployed group (Mean rank= 95.06) in comparison to retired (Mean rank= 125,3).

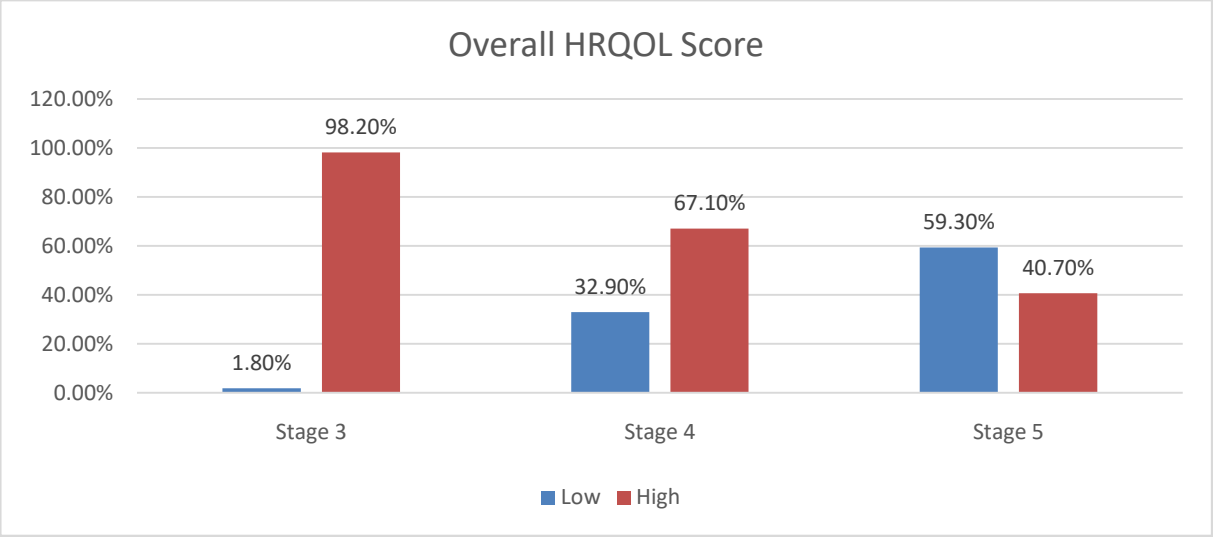

Figure 2. HRQOL in different CKD stages

Table 3:Overall HRQOL Score by CKD Stage

CKD Stages	Overall HRQOL score	*p* value *	Post-Hoc comparison **

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 376 - 387
Received 05 May 2021; Accepted 01 June 2021.

	Median	Mean Rank		
Stage3	72.22	169.22		Stage 5 < Stage 4, p = 0.007;
Stage 4	54.44	95.47	**0.000**	Stage 5 < Stage 3, p =0.000;
Stage 5	47.92	65.81		Stage 4 < Stage 3, p= 0.000

*The Kruskal-Wallis test was used to compare the mean rank across CKD stages.

** Comparisons significant at 0.05 level with Bonferroni correction. Only comparisons,> .05 are shown

Comorbidities and Health- Related Quality of Life.

A Kruskal-Wallis H test showed that there was a statistically significant difference in overall HRQOL score between the different number of comorbidities, $X^2(3) = 9.10$, $p = 0.028$, Overall HRQOL score were lower in three and more comorbidities group (Mean rank= 87.14) in comparison to one comorbidity group (Mean rank= 118.95) **(Table 4)**. These results indicated significant reduction in overall HRQOL score with increase number of comorbidities. participants with cardiovascular diseases, chronic respiratory diseases, and HCV infection were significantly associated with overall HRQOL score *p* value < 0.05**(Table 5)**.

Table4. Number of Comorbidities by Overall HRQOL Score

Number of Comorbidities	Overall HRQOL Score		*p* value*	Post-Hoc Comparison**
	Median	Mean Rank		
None (CKD only)	64.44	94.68		
One	55.83	118.95	**0.028**	Three and more < One, *p* =**0.038**
Two	57.14	109.72		
Three and more	51.14	87.14		

*The Kruskal-Wallis test was used to compare the mean rank across different number of comorbidities.
** Comparisons significant at 0.05 level with Bonferroni correction. Only comparisons,> .05 are shown

Table5. Type of Comorbid Conditions by Overall HRQOL Score

Comorbid Conditions		Overall HRQOL Score		χ^2	*P* value*
		Low (≤50)	High (>50)		
		n (%)	n (%)		
Hypertension	Yes	57(33.1)	115(66.9)	0.193	0.66
	No	13(38.2)	21(61.8)		
Diabetes mellites	Yes	34(39.1)	53(60.9)	2.737	0.098
	No	36(30.3)	83(69.7)		
Cardiovascular diseases	Yes	39(41.9)	54(58.1)	8.559	**0.014**
	No	30 (26.8)	82(73.2)		
Chronic respiratory disorder	Yes	6(66.7)	3(33.3)	4.164	**0.041**
	No	64(32.5)	133 (67.5)		
HBV infection	Yes	6(54.5)	5 (45.5)	1.962	0.161
	No	64(32.8)	131(67.2)		
HCV infection	Yes	23 (48.9)	24(51.1)	5.238	**0.022**

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 376 - 387
Received 05 May 2021; Accepted 01 June 2021.

	No	47 (29.6)	112(70.4)

** Pearson's chi-squared (χ^2) test

Discussion

This study found that the number of comorbidities was statistically significant with reduced overall HRQOL score, patients with three and more comorbidities had a lower overall HRQOL scorein compared to other groups. This indicates that the higher the number of comorbidities, the lower the patients' HRQOL. Similar results were found in a study by Cha & Han (2020)which found that HRQOL-as calculated by the 12-item Medical Outcomes Study Short Form questionnaire- was significantly different based on the number of comorbidities (F=9.83, p<0.001) among 250 adults undergoing hemodialysis. These findings also consistent with a previous study byChiang et al. (2004) who found among 497 HD patients, HRQOL was measured by using the SF-36 questionnaire, less comorbid medical condition was predicted on a better physical component scale (PCS). Multimorbidity associated with adverse clinical outcomes In patients with CKD (Sullivan et al., 2020). Additionally, there was a significant association between number of comorbidities and CKD stages. These results indicated that higher burden of comorbidity in more advanced stages of CKD. These findings are consistent with a prospective study by W.-C. Lee et al. (2018), in which found that stages 3–5 CKD patients with at least three comorbidities at enrollment initiated dialysis earlier (hazard ratio (HR): 2.971) than patients without comorbidities.

Among comorbid conditions, participants with cardiovascular diseases, chronic respiratory diseases, chronic respiratory disorder and HCV infection were significantly associated with lower overall HRQOL score p value < 0.05. The same results from the Iraqi study byAlhajim (2017) reported that positive hepatitis serology was significantly associated with lower QOL (p< 0.05). However, a cross-sectional study conducted among CKD patients' stage 3–5 and patients undergoing maintenance haemodialysis assessed for QoL using European-QoL-5-dimensional (EQ–QoL-5D) and visual analog scale (VAS) questionnaires, the visual analog scale (VAS) score had a significant association with DM (p = 0.000), while no significant association on EQ–5D Index scores (Pauly et al., 2020). Whereas, Aggarwal et al., (2016), reported that diabetes mellitus and cardiovascular disease (CVD) had significantly lower scores on all HRQoL dimensions.

In this study, the overall HRQOL mean score was (58.1±13) ranging from. From the sub-scales, higher mean score was the effects of kidney disease sub-scale, followed by symptoms/problems list sub-scale, and then the burden of kidney disease sub-scale. These results indicated that the most affected domain was the burden of kidney disease (BKD) with (77.2%) of participants scored lower on this domain. Nearly similar results were shown in a study conducted in Ethiopia, where among 125 hemodialysis patients, using a standardized Kidney Disease Quality of Life (KDQOL™-36) questionnaire to assess HRQOL, the burden of kidney disease(BKD) subscale had the lowest mean score and the symptom/problem list subscale had the highest mean score (Kim et al., 2021). In a study conducted in turkey byAslan, (2018), the burden of kidney disease (BKD) had the lowest mean score, while symptom/problem list domain had the highest mean score.

The present study, showed that the HD patients had significantly lower HRQOL score among most sub-scales p value < 0.05 except for the symptoms/problems list sub-scale p value > 0.05 in compared to the pre-dialysis patients. In addition, Participants with CKD stage 5HD were show significantly a lower overall HRQOL score than participants with CKD stage 3 and 4, $\chi^2(2) = 47.74$, p = .000. These results indicated that the HRQOL scores in most dimensions impaired progressively and

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 7, 2021, Pages. 376 - 387
Received 05 May 2021; Accepted 01 June 2021.

significantly across the groups with the lowest scores seen in group 5HD suggesting the need for support for patients at earlier as well as later stages of CKD. Dialysis complications, such as dietary limitations, limit social and leisure activities. Medical problems, financial pressure, marital problems, sexual dysfunction, emotional stress, and anxiety placed patients and their caregivers under extra pressure that impair their HRQOL. This pattern of results can be found in a cross-sectional study conducted in Australia, using the KDQoL-36 instrument to assess HRQOL and found that among 308 patients with co-morbid diabetes and chronic kidney disease in which, the mean scores of patients not on dialysis were significantly higher in compared to patients on dialysis p value < 0.05 except for the symptoms/problems list sub-scale *p* value > 0.05 (Zimbudzi et al., 2016). This pattern of results is also consistent with the previous literatures by (Aggarwal et al., 2016b; Al-Mansouri et al., 2021; Pagels et al., 2012).

Consistent with many previous studies (Ademola et al., 2020; Kim et al., 2021; Senanayake et al., 2020; Zimbudzi et al., 2016), in the present study, the participants scored higher in the MCS (52.9±18.7) than the PCS (38.1±27.9). This suggests that, despite the worsening physical conditions of CKD patients, their mental health is relatively preserved. Previous studies explained that this may result from patients adapting their expectations in response to their chronic illness (Chan et al., 2012; Seica et al., 2009).

The present study identified socio-demographic and clinical factors that may influence HRQOL in CKD patients. This study found that employment status, marital status, smoking status and duration of CKD were associated with overall HRQOL score. These results consistent with previous studies by (Al-Mansouri et al., 2021; Kim et al., 2021; Krishnan et al., 2020).

Conclusion

In this cross-sectional study of adults with CKD stages 3 to 5(HD). The three most common comorbidities such as hypertension, diabetes mellitus, and cardiovascular disease were common among these patients with stage 3-5 CKD. Majority of patients with CKD had comorbidities, patients with CKD stage 5 HD showed a higher percentage of comorbidity in compared to CKD stage 3 and 4, withsignificant reduction in overall HRQOL score with increase number of comorbidities. More than thirty percent of the participants scored lower HRQOL. Additionally, the study participants among all sub-scales of (KDQOL™-36) had significantly a higher HRQOL score for pre-dialysis patients but only non-significantly so for the symptoms /problems list sub-scale. Among comorbid conditions, participants with cardiovascular diseases, chronic respiratory diseases, HCV infection and chronic respiratory disorder were significantly associated with lower overall HRQOL score. There is a need for focused and comprehensive care for chronic conditions especially CKD, which is associated with multiple comorbidities. Regular organization of health education awareness programs on the prevention of CKD and its associated comorbidities among the general public should be done.

References

1. Ademola, B. L., Obiagwu, P. N., & Aliyu, A. (2020). Assessment of health-related quality of life of chronic kidney disease patients in aminu kano teaching hospital, Kano. *Nigerian Journal of Clinical Practice*, *23*(7), 906–911. https://doi.org/10.4103/njcp.njcp_589_19
2. Aggarwal, H. K., Jain, D., Pawar, S., & Yadav, R. K. (2016a). Health-related quality of life in different stages of chronic kidney disease. *QJM*, *109*(11), 711–716. https://doi.org/10.1093/qjmed/hcw054
3. Aggarwal, H. K., Jain, D., Pawar, S., & Yadav, R. K. (2016b). Health-related quality of life in different stages of chronic kidney disease. *QJM*, *109*(11),

711–716. https://doi.org/10.1093/qjmed/hcw054
4. Al-Mansouri, A., Al-Ali, F. S., Hamad, A. I., Ibrahim, M. I. M., Kheir, N., Ibrahim, R. A., AlBakri, M., & Awaisu, A. (2021). Assessment of treatment burden and its impact on quality of life in dialysis-dependent and pre-dialysis chronic kidney disease patients in Qatar. *Research in Social and Administrative Pharmacy*. https://doi.org/10.1016/j.sapharm.2021.02.010
5. Alhajim, S. A. (2017). Assessment of the quality of life in patients on haemodialysis in Iraq. *Eastern Mediterranean Health Journal*, *23*(12), 815–820. https://doi.org/10.26719/2017.23.12.815
6. Ali, A., Younis Majeed, Y., Hassan Al-Lami, F., & Baldawi, K. (2018). Haemodialysis services in Iraq in 2012: situation analysis, epidemiology and infrastructure. *Iraqi New Medical Journal July*, *4*(8), 91–99.
7. Askar, H. F., Athab, A. M., Shakir, S. A., & Ali, N. K. M. (2019). Renal Failure in Diyala Province. *Diyala Journal of Medicine*, *17*(2), 33–40.
8. Aslan, I. (2018). Applying KDQOL^{TM}-36 Form to CKD Patients. *Journal of Current Topics in Healthcare Management (COES&RJ-JHM)*, *1*(1), 11–21. https://doi.org/10.25255/jhm.2018.1.1.11.21
9. Barnett, K., Mercer, S. W., Norbury, M., Watt, G., Wyke, S., & Guthrie, B. (2012). Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. *The Lancet*, *380*(9836), 37–43. https://doi.org/10.1016/S0140-6736(12)60240-2
10. Centers for Disease Control and Prevention. (2018). *HRQOL Concepts | CDC*. https://www.cdc.gov/hrqol/concept.htm
11. Cha, J., & Han, D. (2020). Health-related quality of life based on comorbidities among patients with end-stage renal disease. *Osong Public Health and Research Perspectives*, *11*(4), 194–200. https://doi.org/10.24171/j.phrp.2020.11.4.08
12. Chan, R., Brooks, R., Steel, Z., Heung, T., Erlich, J., Chow, J., & Suranyi, M. (2012). The psychosocial correlates of quality of life in the dialysis population: a systematic review and meta-regression analysis. *Quality of Life Research*, *21*(4), 563–580.
13. Charan, J., & Biswas, T. (2013). How to calculate sample size for different study designs in medical research? *Indian Journal of Psychological Medicine*, *35*(2), 121–126. https://doi.org/10.4103/0253-7176.116232
14. Chartier, M. J., Tangri, N., Komenda, P., Walld, R., Koseva, I., Burchill, C., McGowan, K.-L., & Dart, A. (2018). Prevalence, socio-demographic characteristics, and comorbid health conditions in pre-dialysis chronic kidney disease: results from the Manitoba chronic kidney disease cohort. *BMC Nephrology*, *19*(1), 255. https://doi.org/10.1186/s12882-018-1058-3
15. Chiang, C.-K., Peng, Y.-S., Chiang, S.-S., Yang, C.-S., He, Y.-H., Hung, K.-Y., Wu, K.-D., Wu, M.-S., Fang, C.-C., & Tsai, T.-J. (2004). Health-related quality of life of hemodialysis patients in Taiwan: a multicenter study. *Blood Purification*, *22*(6), 490–498.
16. Dhaidan, F. A. (2018). Prevalence of end stage renal disease and associated conditions in hemodialysis Iraqi patients. *International Journal of Research in Medical Sciences*, *6*(5), 1515. https://doi.org/10.18203/2320-6012.ijrms20181279
17. Elfil, M., & Negida, A. (2017). Sampling methods in Clinical Research; an Educational Review. *Emergency (Tehran, Iran)*, *5*(1), e52. http://www.ncbi.nlm.nih.gov/pubmed/28286859
18. Fraser, S. D. S., Barker, J., Roderick, P. J., Yuen, H. M., Shardlow, A., Morris, J. E., McIntyre, N. J., Fluck, R. J., McIntyre, C. W., & Taal, M. W. (2020). Health-related quality of life, functional impairment and comorbidity in people with mild-to-moderate chronic kidney disease: a cross-sectional study. *BMJ Open*, *10*(8), e040286. https://doi.org/10.1136/bmjopen-2020-040286

19. Hays, R. D., Kallich, J. D., Mapes, D. L., Coons, S. J., & Carter, W. B. (1994). Development of the Kidney Disease Quality of Life (KDQOLTM) Instrument. *Quality of Life Research*, *3*(5), 329–338. https://doi.org/10.1007/BF00451725
20. Hill, N. R., Fatoba, S. T., Oke, J. L., Hirst, J. A., O'Callaghan, C. A., Lasserson, D. S., & Hobbs, F. D. R. (2016). Global Prevalence of Chronic Kidney Disease – A Systematic Review and Meta-Analysis. *PLOS ONE*, *11*(7), e0158765. https://doi.org/10.1371/journal.pone.0158765
21. Kadhim, D. J. (2019). Research Article ó Quality of life of patients with end stage renal disease on haemodial- ysis comparing to patients underwent kidneys transplantation in Iraq. *Iraqi New Medical Journal*, *5*.
22. Kidney Disease Quality of Life Working Group. (n.d.). *Kidney Disease Quality of Life Instrument (KDQOL) | RAND*. Retrieved June 15, 2021, from https://www.rand.org/health-care/surveys_tools/kdqol.html
23. Kim, S., Nigatu, Y., Araya, T., & Dereje, N. (2021). Health Related Quality of Life (HRQOL) of Patients With End Stage Kidney Disease (ESKD) on Hemodialysis in Addis Ababa, Ethiopia: A Cross-Sectional Study. *Research Square*. https://doi.org/10.21203/rs.3.rs-254355/v1
24. Krishnan, A., Teixeira-Pinto, A., Lim, W. H., Howard, K., Chapman, J. R., Castells, A., Roger, S. D., Bourke, M. J., Macaskill, P., Williams, G., Lok, C. E., Diekmann, F., Cross, N., Sen, S., Allen, R. D. M., Chadban, S. J., Pollock, C. A., Turner, R., Tong, A., … Craig, J. C. (2020). Health-Related Quality of Life in People Across the Spectrum of CKD. *Kidney International Reports*, *5*(12), 2264–2274. https://doi.org/10.1016/j.ekir.2020.09.028
25. Lee, W.-C., Lee, Y.-T., Li, L.-C., Ng, H.-Y., Kuo, W.-H., Lin, P.-T., Liao, Y.-C., Chiou, T., & Lee, C.-T. (2018). The Number of Comorbidities Predicts Renal Outcomes in Patients with Stage 3–5 Chronic Kidney Disease. *Journal of Clinical Medicine*, *7*(12), 493. https://doi.org/10.3390/jcm7120493
26. Levey, A S, Atkins, R., Coresh, J., Cohen, E. P., Collins, A. J., Eckardt, K.-U., Nahas, M. E., Jaber, B. L., Jadoul, M., Levin, A., Powe, N. R., Rossert, J., Wheeler, D. C., Lameire, N., & Eknoyan, G. (2007). Chronic kidney disease as a global public health problem: approaches and initiatives - a position statement from Kidney Disease Improving Global Outcomes. *Kidney International*, *72*(3), 247–259. https://doi.org/10.1038/sj.ki.5002343
27. Levey, Andrew S, Stevens, L. A., Schmid, C. H., Zhang, Y. (Lucy), Castro, A. F., Feldman, H. I., Kusek, J. W., Eggers, P., Van Lente, F., Greene, T., & Coresh, J. (2009). A New Equation to Estimate Glomerular Filtration Rate. *Annals of Internal Medicine*, *150*(9), 604. https://doi.org/10.7326/0003-4819-150-9-200905050-00006
28. Pagels, A. A., Söderkvist, B., Medin, C., Hylander, B., & Heiwe, S. (2012). Health-related quality of life in different stages of chronic kidney disease and at initiation of dialysis treatment. *Health and Quality of Life Outcomes*, *10*(1), 71. https://doi.org/10.1186/1477-7525-10-71
29. Pauly, M., Mateti, U. V., Shenoy, P., Saj, N., & Philip, M. L. (2020). Dimensions of quality of life in the different stages of chronic kidney disease patients – A cross-sectional study. *Clinical Epidemiology and Global Health*, *8*(3), 797–801. https://doi.org/10.1016/j.cegh.2020.02.002
30. Pourhoseingholi, M. A., Vahedi, M., & Rahimzadeh, M. (2013). Sample size calculation in medical studies. *Gastroenterology and Hepatology from Bed to Bench*, *6*(1), 14–17. http://www.ncbi.nlm.nih.gov/pubmed/24834239
31. Qader, H., & Naqshbandi, V. (2019). Quality of Life of Patients Undergoing Maintenance Hemodialysis in Erbil City. *Erbil Journal of Nursing and Midwifery*, *2*(1), 19–25. https://doi.org/10.15218/ejnm.2019.03
32. Seica, A., Segall, L., Verzan, C., Văduva, N., Madincea, M., Rusoiu, S., Cristea, S., Ştefan, M.,

Şerbănescu, D., & Moroşanu, P. (2009). Factors affecting the quality of life of haemodialysis patients from Romania: a multicentric study. *Nephrology Dialysis Transplantation*, *24*(2), 626–629.

33. Senanayake, S., Gunawardena, N., Palihawadana, P., Senanayake, S., Karunarathna, R., Kumara, P., & Kularatna, S. (2020). Health related quality of life in chronic kidney disease; a descriptive study in a rural Sri Lankan community affected by chronic kidney disease. *Health and Quality of Life Outcomes*, *18*(1), 106. https://doi.org/10.1186/s12955-020-01369-1
34. Stanifer, J. W., Muiru, A., Jafar, T. H., & Patel, U. D. (2016). Chronic kidney disease in low- and middle-income countries. *Nephrology Dialysis Transplantation*, *31*(6), 868–874. https://doi.org/10.1093/ndt/gfv466
35. Sullivan, M. K., Rankin, A. J., Jani, B. D., Mair, F. S., & Mark, P. B. (2020). Associations between multimorbidity and adverse clinical outcomes in patients with chronic kidney disease: a systematic review and meta-analysis. *BMJ Open*, *10*(6), e038401. https://doi.org/10.1136/bmjopen-2020-038401
36. Tonelli, M., Wiebe, N., Guthrie, B., James, M. T., Quan, H., Fortin, M., Klarenbach, S. W., Sargious, P., Straus, S., Lewanczuk, R., Ronksley, P. E., Manns, B. J., & Hemmelgarn, B. R. (2015). Comorbidity as a driver of adverse outcomes in people with chronic kidney disease. *Kidney International*, *88*(4), 859–866. https://doi.org/10.1038/ki.2015.228
37. Versino, E., & Piccoli, G. (2019). Chronic Kidney Disease: The Complex History of the Organization of Long-Term Care and Bioethics. Why Now, More Than Ever, Action is Needed. *International Journal of Environmental Research and Public Health*, *16*(5), 785. https://doi.org/10.3390/ijerph16050785
38. World Health Organization (WHO). (2020, December 9). *The top 10 causes of death*. https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death
39. Zimbudzi, E., Lo, C., Ranasinha, S., Gallagher, M., Fulcher, G., Kerr, P. G., Russell, G., Teede, H., Usherwood, T., Walker, R., & Zoungas, S. (2016). Predictors of Health-Related Quality of Life in Patients with Co-Morbid Diabetes and Chronic Kidney Disease. *PloS One*, *11*(12), e0168491. https://doi.org/10.1371/journal.pone.0168491