



Original article

Dimensions of quality of life in the different stages of chronic kidney disease patients – A cross-sectional study

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ABSTRACT

Background: Chronic Kidney Disease (CKD) is an emerging disease that causes morbidity, mortality and affects patient's quality of life (QoL). **Objectives:** To assess and compare dimensions of QoL in the different stages of CKD patients and also to identify the factors affecting QoL. **Data and methods:** A cross-sectional study was carried out for a period of 8 months in the Dept. of Nephrology. The inclusion criterion of the study is patients above 18 years age diagnosed with CKD stage 3–5 and patients undergoing maintenance haemodialysis. The patients were assessed for QoL using European-QoL-5-dimensional (EQ-QoL-5D) and visual analog scale (VAS) questionnaires. **Results:** Out of 210 patients, most of the patients were in the age group 51–65 years (43.33%) and the mean age of study population was 52 ± 16.04 . In the present study, most of the patients were males (79.04%). The most common comorbidities were hypertension (90%) and 51% of diabetes mellitus (DM). The mean EQ-5D index scores of the CKD stage 3, 4, 5 and 5D patients were 0.77 ± 0.09 , 0.67 ± 0.10 , 0.62 ± 0.12 and 0.50 ± 0.15 and the mean VAS scores for these stages were 74.10 ± 7.68 , 66.52 ± 10.90 , 66.45 ± 8.80 and 55.04 ± 12.82 respectively. **Conclusion:** The most commonly affected domains were usual activities (79%), pain (76.20%) and anxiety/depression (71.91%). Factors such as age (> 65 yrs), BMI (Underweight and Obese), educational background (Illiterate), Unemployment, domiciliary status (Rural), number of medications (> 11) had significant association with EQ-5D index and VAS scores ($p=0.000$). It was found that QoL was impaired in stage 5D compared to other stages ($p=0.000$).

1. Introduction

The prevalence of Chronic Kidney Disease (CKD) is increasing worldwide and is a global problem due to the hasty increase in common risk factors such as hypertension (HTN) and diabetes mellitus (DM).^{1,2} In India, the prevalence of CKD is 17.2% and 6% in stage 3 and above.³ Mortality from cardiac disease is projected to be 8–10 times more in CKD patients as compared to non-CKD patients.⁴ QoL is an important measure of how the disease affects patients' lives. CKD patients have decreased quality of life (QoL) compare to healthy controls. QoL is an important marker to assess the disease burden and can also be used to evaluate the treatment effectiveness and predict risk for adverse outcomes.⁵ A comprehensive study on factors influencing the QoL will render valuable perspicacity for the nephrologists to improve the QoL of patients. Nevertheless, the studies that assess the QoL and factors affecting CKD patients in developing countries are less.⁶ The aim of the

study was to assess and compare the dimensions of QoL in the different stages of CKD patients and also to identify the factors affecting QoL.

2. Data and methods

2.1. Study design and setting

A cross sectional study was conducted among CKD patients for a period of 8 months from September 2017–April 2018. This study was conducted in the outpatient of department of Nephrology, Justice K.S. Hegde Charitable Hospital, Deralakatte, Mangaluru.

2.2. Ethical issues

Prior to the initiation of study ethical clearance was obtained from the Institution Ethics Committee (NGSMIPS/IEC/11/2017-18),

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Table 1
Demographic characteristics of CKD patients.

Variables	Stages of CKD				All the CKD patients (n = 210), %		
	CKD - 3 (n = 20), %	CKD - 4 (n = 21), %	CKD - 5 (n = 47), %	CKD - 5D (n = 122), %			
Age groups (Years)	< 35	7(35%)	2(9.52%)	17(36.17%)	13(10.65%)	39(18.6%)	
	35–50	2(10%)	5(23.80%)	14(29.78%)	24(19.67%)	45(21.42%)	
	51–65	8(40%)	9(42.85%)	16(34.04%)	58(47.54%)	91(43.33%)	
	> 65	3(15%)	5(23.80%)	–	27(22.13%)	35(16.7%)	
Age (Mean ± SD)		47.55 ± 19.13)	56.57 ± 16.64	41.65 ± 13.12	56.07 ± 14.52	52 ± 16.04	
Gender	Male	16(80%)	18(85.71%)	36(76.59%)	96(78.68%)	166(79.04%)	
	Female	4(20%)	3(14.28%)	11(23.40%)	26(21.31%)	44(20.95%)	
Domiciliary status	Rural	17(85%)	16(76.19%)	26(55.31%)	89(72.95%)	148(70.50%)	
	Urban	3(15%)	5(23.80%)	21(44.68%)	33(27.04%)	62(29.50%)	
Employment status	Employed	8(40%)	12(57.14%)	26(55.31%)	27(22.13%)	73(34.80%)	
	Unemployed	12(60%)	9(42.85%)	21(44.68%)	95(77.86%)	137(65.20%)	
Marital status	Married	14(70%)	20(95.23%)	36(76.59)	109(89.34%)	179(85.23%)	
	Unmarried	5(25%)	1(4.76%)	11(23.40%)	13(10.65%)	30(14.28%)	
	Widow	1(5%)	–	–	–	1(0.47)	
Educational background	Illiterate	6(30%)	4(19.04%)	6(12.76%)	65(53.27%)	81(38.60%)	
	Primary	7(35%)	3(14.28%)	8(17.02%)	24(19.67%)	42(20.00%)	
	Secondary	5(25%)	9(42.85%)	16(34.04%)	14(29.78%)	44(21.00%)	
	Graduate	2(10%)	5(25%)	17(36.17%)	19(40.42%)	43(20.50%)	
Body mass index (BMI)	Underweight (≤18.5)	–	–	6(12.76%)	112(91.80%)	118(56.19%)	
	Normal (18.5–24.9)	19(95%)	19(90.47%)	33(70.21%)	7(5.73%)	78(37.14%)	
	Overweight (25–29.9)	1(5%)	2(9.52%)	–	–	3(1.42%)	
	Obese(≥30)	–	–	8(17.02%)	3(2.45%)	11(5.23%)	
BMI (Mean ± SD)		21.09 ± 4.19	21.28 ± 4.19	22.18 ± 5.85	17.52 ± 4.63	19.28 ± 4.66	
Co-morbidities	HTN	Yes	18(90%)	17(80.95%)	43(91.48%)	111(19.98%)	189(90%)
		No	2(10%)	4(19.04%)	4(8.51%)	11(9.01%)	21(10%)
	DM	Yes	9(45%)	17(80.95%)	22(46.80%)	59(48.36%)	107(51%)
		No	11(55%)	4(19.04%)	25(53.19%)	63(51.63%)	103(49%)
	IHD	Yes	3(15%)	4(19.04%)	3(6.38%)	22(18.03%)	32(15.20%)
		No	17(85%)	17(80.95%)	44(93.61%)	100(81.96%)	178(84.80%)
Number of medications per prescription	≤5	16(80%)	4(19.04%)	7(14.89%)	12(9.83%)	39(18.57%)	
	5–8	4(20%)	14(66.66%)	29(61.70%)	82(67.21%)	129(61.42%)	
	9–11	–	3(14.28%)	7(14.89%)	18(14.75%)	28(13.33%)	
	≥11	–	–	4(8.51%)	10(8.19%)	14(6.66%)	
(Mean ± SD)		4.65 ± 2.41	7.52 ± 2.41	7.53 ± 2.47	8.09 ± 2.26	7.580 ± 2.41	

BMI - Body Mass Index, HTN - Hypertension, DM - Diabetics Mellitus, IHD - Ischemic Heart Disease, SD- Standard Deviation, CKD- Chronic Kidney Disease.

Mangaluru, Karnataka, India. Patients were recruited after obtaining the informed consent from the patients.

2.3. Study criteria

The inclusion criterion of the study was Patients above 18 years age diagnosed with CKD stage 3–5 and patients undergoing maintenance haemodialysis (HD). Kidney transplantation (KT), peritoneal dialysis (PD), patients shifted from KT or PD to haemodialysis, pregnant and lactating women were excluded from the study.

2.4. Data collection and QoL assessment

Patients who met the inclusion criteria the demographic details include Age, gender, marital status, educational background, employment status, comorbidities, body mass index (BMI), social habits, domiciliary status, frequency of HD sessions per week and number of medications prescribed were collected from the medical records and patients. The patients QoL were assessed using the Euro-QoL-5D-5L (EQ-5D) and VAS questionnaires.⁷ Prior to the usage of validated versions of English, Kannada and Malayalam Euro-QoL-5D-5L and VAS questionnaires the permission was obtained from the Euro QoL group. The EQ-5D-5L QoL questionnaire consists of 5 questions related to mobility, self-care, usual activities, pain or discomfort and anxiety or depression. The EQ-VAS measures the patient's self-rated health on a vertical scale. The VAS score ranged from 0 to 100 in which the endpoints are marked as 100 "good health" and 0 as "worst health". The EQ-5D index scores were calculated using the EQ-5D-5L Crosswalk

Index Value Calculator.⁸

2.5. Statistical analysis

Categorical data are presented as frequency and percentage. Continuous variables are presented as mean and standard deviation. The association between the continuous variables (two groups) vs EQ-5D index; and VAS scores were assessed using independent sample *t*-test. The association between the continuous variables (more than two groups) vs EQ-5D index; and VAS scores were assessed using ANOVA test. The *p* value <0.05 was considered as statistically significant. The data was analysed in the SPSS version 20.0.

3. Results

Among 210 patients, the majority of the patients enrolled in the study belong to CKD stage 5D (58.1%), followed by stage 5 (22.4%). The patients undergoing HD (58.10%) outnumbered the non-dialysis (41.90%) patients. The age wise distributions of the CKD patients were in the range from 19 to 85 years, among which the highest proportion of patients were observed in the age group between 51 and 65 years (43.33%). The mean age of the study population was 52 ± 16.04. In gender wise distribution, male patients 166 (79.04%) outnumbered the female patients 44 (20.95%). Most of the patients were from rural (n = 148) area whereas remaining CKD patients were from urban area (n = 62). Overlooking the employment status, majority of patients were unemployed (65.20%), which was most commonly observed in CKD 5D (77.86%). Educational background varied in different patients

Table 2
Domains of QoL in various stages of CKD.

QoL Domains	Stages of CKD	All the CKD patients				
Mobility	Level	CKD - 3 (n = 20), %	CKD - 4 (n = 21), %	CKD - 5 (n = 47), %	CKD - 5D (n = 122),%	Number of patients (n = 210), %
	1	19(95%)	17(80.95%)	37(78.72%)	69(56.55%)	142(67.60%)
	2	1(5.00%)	4(19.04%)	10(21.27%)	42(34.42%)	57(27.10%)
	3	–	–	–	3(2.45%)	3(1.42%)
	4	–	–	–	6(4.91%)	6(2.85%)
Self-care	5	–	–	–	2(1.63%)	2(1.00%)
	1	20(100%)	16(76.19%)	32(68.08%)	45(36.88%)	113(53.80%)
	2	–	5(23.80%)	14(29.78%)	70(57.37%)	89(42.40%)
	3	–	–	1(2.12%)	5(4.09%)	6(2.90%)
	4	–	–	–	1(0.81%)	1(0.50%)
Usual Activities	5	–	–	–	1(0.81%)	1(0.50%)
	1	11(55%)	4(19.04%)	14(29.78%)	15(12.29%)	44(21%)
	2	6(30%)	10(47.61%)	15(31.91%)	47(38.52%)	78(37.10%)
	3	3(15%)	4(19.04%)	11(23.40%)	37(30.32%)	55(26.20%)
	4	–	3(14.28%)	7(14.89%)	20(16.39%)	30(14.30%)
Pain	5	–	–	–	3(6.38%)	3(1.40%)
	1	10(50%)	8(38.09%)	15(31.91%)	17(13.93%)	50(23.80%)
	2	10(50%)	10(47.61%)	24(51.06%)	48(39.34%)	92(43.80%)
	3	–	3(14.28%)	2(4.25%)	36(29.50%)	41(19.52%)
	4	–	–	6(12.76%)	15(12.29%)	21(10%)
Anxiety	5	–	–	–	6(4.91%)	6(2.85%)
	1	13(65%)	8(38.09%)	17(36.17%)	21(17.21%)	59(28.09%)
	2	5(25%)	10(47.61%)	15(31.91%)	57(46.72%)	87(41.42%)
	3	2(10%)	1(4.76%)	11(23.40%)	26(21.31%)	40(19.04%)
	4	–	2(9.52%)	4(8.41%)	15(12.29%)	21(10%)
	5	–	–	–	3(2.45%)	3(1.42%)

QoL-Quality of Life, CKD- Chronic Kidney Disease.

among which (61.4%) of them were literate which was most commonly observed in CKD 5D (65%), followed by 21% of them had secondary education. Majority of CKD patients were underweight (56.19%) and mean BMI of the study population was $19.28 \pm 4.66 \text{ kg/m}^2$. The most common co-morbidities were HTN (90%) followed by DM (51%) and others. Comparing the various stages of CKD patients, it was found that the majority of patients were alcoholic (29.50%). Majority of patients were married (85.23%), whereas 14.28% of patients were unmarried followed by 0.47% of widow. The mean number of medications per prescription was 7.58 ± 2.41 . The demographic characteristics of patients are summarized in Table 1.

The most commonly affected QoL domains in the study populations were usual activities (79%), pain (76.20%) and anxiety and depression (71.91%). The detailed QoL domains affected in patients are summarized in Table 2. The mean EQ-5D index scores of the CKD stage 3, 4, 5 and 5D patients were 0.77 ± 0.09 , 0.67 ± 0.10 , 0.62 ± 0.12 and 0.50 ± 0.15 and the mean VAS score for these stages were 74.10 ± 7.68 , 66.52 ± 10.90 , 66.45 ± 8.80 and 55.04 ± 12.82 respectively.

By correlating different stages of CKD with EQ – 5D Index scores it was found that QoL of CKD stage 3 patients had better than stage 5 ($p = 0.000$) and 5D ($p = 0.000$). QoL of CKD stage 4 had better QoL than CKD stage 5D ($p = 0.000$). QoL of CKD stage 5 had better QoL than CKD 5D ($p = 0.000$). The CKD stage 5D had worse QoL compared to all other three stages of CKD ($p = 0.000$). The association between the demographic characteristics and EQ–5D Index scores are summarized in Table 3. Correlation of different stages of CKD with VAS score it was found that QoL of CKD stage 3 is better than stage 5D ($P = 0.000$). QoL of CKD stage 4 had better QoL than CKD stage 5D ($p = 0.000$). QoL of CKD stage 5 had better QoL than CKD 5D ($p = 0.000$). CKD stage 5D had worse QoL compared to all other three stages of CKD ($p = 0.000$).

The factors such as age, DM, BMI, education, unemployment, domiciliary status, duration of HD, number of medications had significant association with EQ–5D Index and VAS scores ($p = 0.000$). The association between the demographic characteristics and VAS scores are summarized in Table 4.

4. Discussion and conclusion

EQ-5D was used in several studies to assess the QoL among chronic diseases patients.⁹ In the present study, EQ-5D was used to compare the QoL dimensions of different stages of CKD patients. Overall the QoL was better in patients with CKD stage 3–4, followed by stage 5, and patients on haemodialysis. It was found that QoL was impaired in stage 5D compared to other stages ($p = 0.000$). Similar findings were found in the studies conducted by Pagel M et al., Eriksson E et al., reported that the QoL was impaired in stage 5D compared to other stages ($p = 0.000$).^{10,11} Eriksson E et al., also reported the better EQ-5D index and VAS scores for the CKD stages 3–5 and 5D than the present study.¹¹ Whereas in a study conducted by Kathib ST et al., reported comparatively less EQ-5D index and VAS scores and Sakthong P et al., reported the better EQ-5D index and VAS scores for the CKD-5D than present study.^{12,13}

In the study, the most commonly affected domains among the study population were usual activities (79%), pain (76.20%) and anxiety and depression (71.91%). The study conducted by Errikson E et al., reported that most commonly affected domains were pain (63.3%) and anxiety/depression (41.97%). In an another study conducted by Saffari M et al., reported that mobility (59.4%) was the most commonly affected domain followed by pain (47.8%).^{11,14}

In our study, most of the CKD patients were in the age group between 51 and 65 years (43.33%) and the mean age of the study population was 52 ± 16.04 . The EQ–5D index and VAS scores had strong association with age groups ($p = 0.000$). The results were in correspondence with the study conducted by Zyoud SH et al., where the mean age of the study population was 53.3 ± 16.2 . The study also reported that EQ–5D index ($p = 0.010$) and VAS scores ($p = 0.001$) had the strong association with age.¹ A study carried out by Pezeshki ML et al., reported that the mean age of the study population was 51.76 ± 17.37 . No significant association with age was found with kidney disease component (KDC) score¹⁵

In our study, it was found that male patients 166 (79.04%) outnumbered the female patients 44 (20.95%). Gender had no significant association with EQ–5D score ($p = 0.712$) and VAS score ($p = 0.633$). Similar results were shown in a study carried out by Cruz M et al.,

Table 3
Analysis of Demographic characteristics vs. EQ – 5D Index scores.

Variable	Frequency (n = 210)	EQ-5D index score Mean ± SD	p value			
Age	< 35	39	0.76 ± 0.07	0.000		
	35–50	45	0.61 ± 0.05			
	51–65	91	0.53 ± 0.09			
	> 65	35	0.38 ± 0.20			
Gender	Male	166	0.55 ± 0.16	0.712		
	Female	44	0.60 ± 0.15			
BMI	Underweight	118	0.51 ± 0.15	0.000		
	Normal	78	0.75 ± 0.51			
	Overweight	3	0.65 ± 0.13			
	Obese	11	0.50 ± 0.11			
Education background	Illiterate	81	0.44 ± 0.14	0.000		
	Primary	42	0.57 ± 0.11			
	Secondary	44	0.65 ± 0.10			
Employment status	Employed	73	0.69 ± 0.09	0.000		
	Unemployed	137	0.50 ± 0.15			
Domiciliary status	Rural	148	0.52 ± 0.15	0.000		
	Urban	62	0.67 ± 0.11			
Marital status	Married	179	0.54 ± 0.15	0.833		
	Unmarried	30	0.72 ± 0.14			
Smoking	Yes	37	0.51 ± 0.20	0.140		
	No	173	0.58 ± 0.15			
Alcohol	Yes	62	0.55 ± 0.16	0.352		
	No	148	0.57 ± 0.16			
No. of medications	< 5	39	0.65 ± 0.17	0.000		
	5–8	129	0.57 ± 0.14			
	9–11	28	0.52 ± 0.14			
	> 11	14	0.39 ± 0.22			
Comorbidities	HTN	Yes	189	0.56 ± 0.16	0.596	
		No	21	0.56 ± 0.16		
	DM	Yes	107	0.54 ± 0.17		0.185
		No	103	0.59 ± 0.14		
IHD	Yes	32	0.48 ± 0.13	0.430		
	No	178	0.58 ± 0.16			
Stages of CKD	CKD - 3	20	0.77 ± 0.09	0.000		
	CKD - 4	21	0.67 ± 0.10			
	CKD - 5	47	0.62 ± 0.12			
	CKD – 5D	122	0.50 ± 0.15			

BMI- Body Mass Index, HTN- Hypertension, DM- Diabetic Mellitus, IHD- Ischemic Heart Disease,CKD- Chronic Kidney Disease.

where male patients 108(56.5%) outnumbered the female patients 83 (43.45%) respectively. Whereas Xu RH et al., reported that gender has strong association with EQ-5D score (p<0.001) ^{16,17}

The most common comorbidities reported in the study were HTN (90%) and DM (51%). The VAS score had significant association with DM (p=0.000). Similar results were shown in studies carried out by Mujais SK et al., and Manavalan M et al., where, the most common comorbidities were HTN and DM. Mujais SK et al., showed significant association between the QoL scores with HTN and DM, whereas, Manavalan M et al., showed that KDC score has no significant association with HTN and DM ^{18,19}

In the present study, most of the patients were underweight (56.19%). VAS score and EQ – 5D score had significant association with BMI (p=0.000). These results are contradictory to the studies carried out by Zyoud SH et al., and Aggarwal HK et al., where, majority of the patients were at healthier levels. Zyoud SH et al., reported that BMI had significant association with EQ–5D score (p=0.047) whereas, Aggarwal HK et al., reported no significant association with BMI ^{1,20}

Majority of the patients were literates (61.4%) and educational status had significant association with EQ–5D score and VAS score (p=0.000). These results were similar to the studies conducted by Manavalan M et al., Pezeshki ML et al., where, they reported that most of the patients were literates and educational status had significant association with KDC scores, p values 0.00 and 0.04 respectively ^{15,19}

Majority of the patients in our study were unemployed (65.20%)

Table 4
Analysis of Demographic characteristics vs. VAS scores.

Variable	Frequency (n = 210)	VAS scores (Mean ± SD)	p value			
Age	< 35	39	76.38 ± 4.14	0.000		
	35–50	45	67.55 ± 4.59			
	51–65	91	57.28 ± 7.89			
	> 65	35	42.42 ± 12.20			
Gender	Male	166	59.91 ± 13.10	0.633		
	Female	44	62.81 ± 13.70			
BMI	Underweight	118	0.56 ± 12.97	0.000		
	Normal	78	75 ± 5			
	Overweight	3	66.02 ± 12.03			
	Obese	11	56.27 ± 10.56			
Education background	Illiterate	81	49.04 ± 11.09	0.000		
	Primary	42	61.71 ± 9.17			
	Secondary	44	68.65 ± 7.18			
Employment status	Employed	73	70.54 ± 6.84	0.000		
	Unemployed	137	55.20 ± 12.76			
Domiciliary status	Rural	148	56.46 ± 12.83	0.000		
	urban	62	70.32 ± 8.19			
Marital status	Married	179	58.28 ± 12.51	0.000		
	Unmarried	30	73.36 ± 9.25			
Smoking	Yes	37	57.35 ± 15.16	0.156		
	No	173	61.24 ± 12.75			
Alcohol	Yes	62	60.50 ± 12.35	0.391		
	No	148	60.58 ± 13.65			
No. of medications	< 5	39	65.41 ± 14.29	0.000		
	5–8	129	61.30 ± 11.92			
	9–11	28	56.50 ± 13.20			
	> 11	14	48.28 ± 13.74			
Comorbidities	HTN	Yes	189	60.66 ± 12.89	0.771	
		No	21	59.57 ± 16.48		
	DM	Yes	107	57.79 ± 40		0.002
		No	103	63.42 ± 11.81		
IHD	Yes	32	51.78 ± 14.01	0.224		
	No	178	62.13 ± 12.51			
Stages of CKD	CKD - 3	20	74.10 ± 7.68	0.000		
	CKD - 4	21	66.52 ± 10.90			
	CKD - 5	47	66.45 ± 8.80			
	CKD – 5D	122	55.04 ± 12.82			

BMI- Body Mass Index, HTN- Hypertension, DM- Diabetic Mellitus, IHD- Ischemic Heart Disease, CKD- Chronic Kidney Disease.

and the employment status showed significant association with EQ-5D score (p = 0.000) but not with VAS score. This result is similar to the studies conducted by Kathib ST et al., Joshi U et al., and Pezeski ML et al., where more number of unemployed patients was reported and employment status had significant association with EQ-5D score (p = 0.001), WHO-QoL-BREF (p = 0.04), (KDC) scores (p = 0.02) respectively. Most of their patients were unemployed or stopped working due to their disease condition. ^{12,15,21}

In the present study, most of the patients were in rural areas (70.50%) and had strong association with EQ–5D score (p = 0.000). These results were in correspondence with the study carried out by Zyoud SH et al., where, higher number of patients were in rural areas (60.3%) and showed significant association with EQ–5D score (p = 0.004). A study carried out by Saffari M et al., reported that more patients were in urban areas (94.2%) which is in contrast to the study results, but showed significant association with EQ–5D score (p = 0.001). ^{1,14}

The mean number of medications prescribed per patient was 7.58 ± 2.41. The number of medications had significant association with EQ–5D index and VAS scores (p = 0.000). These results are in contrast to the study conducted by Zyoud SH et al., where, mean number of medications was 6.5 ± 2.8 whereas, number of medications had strong association with EQ–5D index scores (p = 0.010) and VAS score (p = 0.042).¹ The sample size of the study was small because the study duration was only 8 months and the cross-sectional study is difficult to interpret the association between the cause and effect were the

limitations of the study.

Majority of the patients were in the age group 51–65 years (43.33%). The mean age of study population was 52 ± 16.04 . The most commonly affected domains were Usual Activities (79%), Pain (76.20%) and Anxiety/Depression (71.91%). Factors such as age (> 65 yrs), BMI (Underweight and Obese), educational background (Illiterate), employment (Unemployed), domiciliary status (Rural), number of medications (> 11) had significant association with EQ-5D index and VAS scores ($p=0.000$). It was found that QoL was impaired in stage 5D compared to other stages ($p=0.000$).

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Authors' contribution

UVM and PS conceptualized the study and analysed the data. MP, NS and MLP interpreted the results. MP, NS and MLP wrote the final draft. All the authors read and approved the final draft.

Declaration of competing interest

None.

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