Original Article

Evaluation of Renal Supportive Care by Assessment of Symptoms, Quality of Life and Functional Status

Md. Ashraful Alam[1], Md. Ayub Ali Chowdhury[2] , Md. Masud Iqbal[3], Kazi Shahnoor Alam[4], Md. Babrul Alam[5], Md. Raquib Morshed[6], S.M. Nafeez Imtiaz[7], Nazia Afrin Siddiqui[8], Md. Shahadat Hossain[9]

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Abstract

Introduction*: Like other chronic diseases, CKD patients experience a high symptom burden, reduced quality of life and poor functional status. Identification of these symptoms, measurement of quality of life (QOL) and functional status of these patients by using validated tool and taking necessary steps accordingly is an important aspect of renal supportive care.* ***Objective****: Assessment of symptom burden, QOL and functional status in CKD patients (including those on maintenance hemodialysis) and healthy individuals.* ***Materials and Methods****: This cross-sectional study was conducted in the department of Nephrology of National Institute of Kidney Diseases and Urology, Dhaka from July 2018 to June 2019.The study involved 135 CKD patients (stage 1-5 including those on maintenance hemodialysis) and 30 healthy volunteers. Their demographic profiles were recorded in a data sheet and some routine blood tests were done which included CBC, urine R/E, serum creatinine, serum urea, serum calcium, serum inorganic phosphate and serum uric acid. Symptom burden was assessed by using Palliative Care Outcome Scale-Symptom Renal (POS-S:Renal) survey, QOL was assessed by using Short Form - 36 survey and functional status was assessed by using Kornofsky Performance Status Scale (KPSS). CKD staging was done by Kidney Disease Improving Global Outcome (KDIGO) (2012) criteria. For the purpose of analysis and discussion, CKD patients were further divided into earlier stage (Stage 1-3) and advanced stage (Stage 4-5). SPSS-22.0A software version was used for data analysis.* ***Results****: In this study, it was found that symptom burden was high and quality of life and functional status was reduced in all stages of CKD (mostly in hemodialysis patients) compared to healthy individuals. There was a negative correlation between the glomerular filtration rate (GFR) and symptom burden of the patients. As GFR declined, patient experienced more symptom burden. The most prevalent symptoms reported were weakness, poor mobility, pain and feeling anxious among all stages of CKD. Weakness and poor mobility were also the most severe symptoms in all study population*

1. *Assistant Professor, Department of Nephrology, Enam Medical College & Hospital, Savar, Dhaka*
2. *Former Professor, Department of Nephrology, National Institute of Kidney Diseases & Urology (NIKDU)*
3. *Former Professor, Department of Neohrology, NIKDU*
4. *Professor, Department of Nephrology, NIKDU*
5. *Professor, Department of Nephrology, NIKDU*
6. *Registrar, Department of Nephrology, NIKDU*
7. *Associate Consultant of Nephrology, Japan East West Medical College & Hospital*
8. *Assistant Professor, Department of Nephrology, US-Bangla Medical College & Hospital*
9. *Assistant Registrar, Department of Nephrology, NIKDU*

Correspondence *Md. Ashraful Alam, Email: shuvonikdu@gmail.com*

except in healthy individuals where pain was the most prevalent and severe symptom. The mean number of symptoms and total symptom severity score were highest in hemodialysis patients compared with other groups. There was a positive correlation between GFR and quality of life and functional status of patients. All components of physical component summary (PCS) and mental component summary (MCS) score of quality of life and score of functional status decreased as GFR decreased. Regarding biochemical values, there was a positive correlation of serum calcium, serum albumin and hemoglobin level with GFR and a negative correlation of serum phosphate with GFR. ***Conclusions****: High symptom burden, reduced QOL and poor functional status was observed in all stages of CKD and mostly in dialysis patients. Renal supportive care should be applied from the earlier stages for reduction of symptom burden and improvement of QOL and functional status.*

Key words*: Chronic kidney dissease; Quality of life; Glomerular filtation rate*

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Introduction

Chronic kidney disease (CKD) is a global health issue and patient suffering from chronic kidney disease (CKD) is growing rapidly mainly due to the rising incidence of diabetes mellitus (DM) and hypertension. Like other chronic diseases, CKD also represents a considerable burden for patients, often due to numerous disturbing symptoms, especially in advanced stages of the disease.[1,2] The average number of symptoms per patient varies between 6 and 20 symptoms[3] and the most common symptoms are fatigue, pain, pruritus, sleep disturbance**,** and reduced appetite[3,4]. Most of the researches done on the end stage renal disease (ESRD) patients who were on maintenance hemodialysis showed a high symptom burden and reduced quality of life (QOL). But only a very few researches have been carried out to assess symptom burden and quality of life in other CKD patients specially who are not yet on renal replacement therapy (RRT) although these patients group also have a high symptom burden and reduced QOL.

There is evidence that patients with advanced CKD (stage 4−5) who do not require RRT report a similar number of symptoms of comparable severity[4-6]. Generally kidney patients tend to under-report their symptoms and are therefore often inadequately treated. In addition, symptoms of kidney patients are not assessed frequently and often poorly recognized. Ideally, symptoms should be routinely assessed and this assessment should be done without waiting for patients to raise them. Conventionally in case of dialysis patients, treatment i**s** mainly focused on dialysis, which leads to a poor quality of life. But in fact, dialysis can relieve some symptoms and at the same time it can also add to symptoms**.** Due to high symptom burden, CKD patients also experience a reduce quality of life. The symptom burden of CKD has a negative correlation with health-related quality of life **(**HRQOL**)**[1,7] and associated with increased morbidity and mortality rates.[8]

Subjective symptom assessment rather than objective clinical assessments should be a fundamental component of quality care for ESRD patients.[9] Like other chronic diseases, CKD patients have a poor functional status and therefore have a poor prognosis. So proper systematic assessment of symptoms, QOL and functional status are very important in managing CKD population (both dialysis and non-dialysis patient). To enhance the standard of care, it is currently identified that supportive care principles need to be incorporated into routine care of these patients.

Renal supportive care simply means the palliative care for patients who are suffering from kidney disease. Like palliative care in oncology, the aim is to reduce sufferings as the disease progresses.[10]

But actualy 'renal supportive care' is a broad term. It does not only mean stopping dialysis and provide the hospice/terminal care as most people imagine.

Ideally renal supportive care includes routine symptom assessment and management, managing complications of disease, taking action for retardation of progression of disease, identification prognosis of disease, shared decision making regarding initiation, continuation, withholding or stopping dialysis and advance care planning and also provides support for psychosocial and spiritual needs. It should be started from the presentation of illness along with curative/ remittive care. Kidney supportive care can be given to patients with acute kidney injury or chronic kidney disease including renal failure those are treated with either dialysis or transplantation. It includes but not limited to end-of-life care and this care is provided by a collaboration of nephrologists, palliative care specialists, nurses, dieticians, social workers and chaplains[9,10].

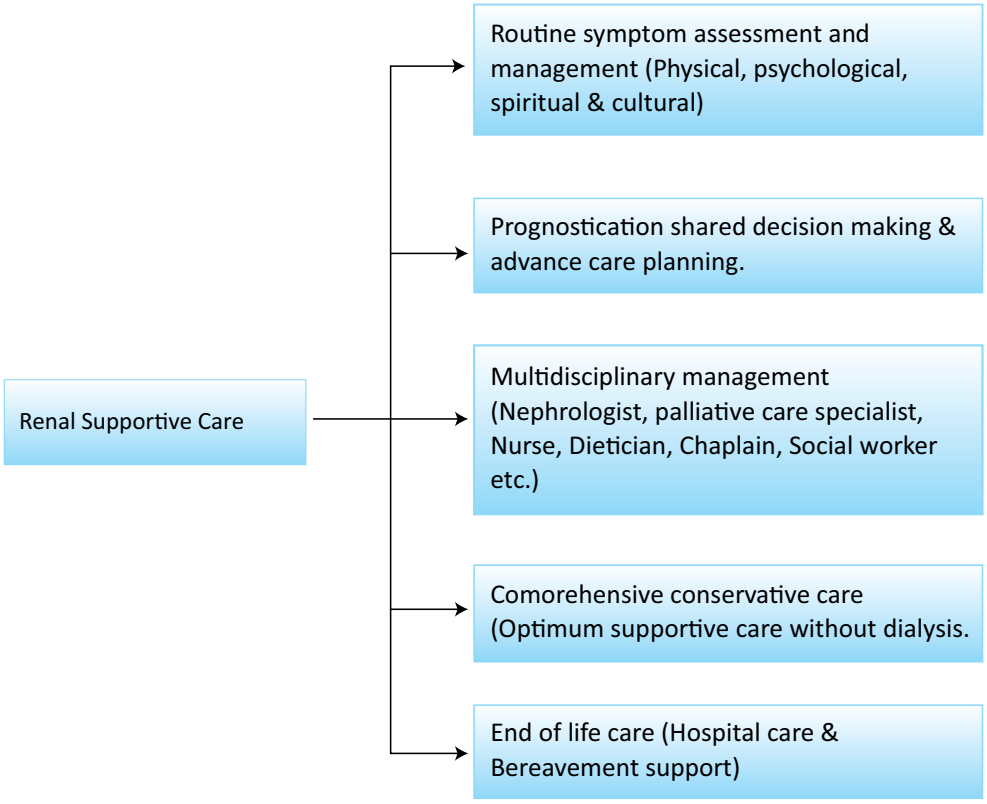

Fig 1. Domains of renal supportive care (adapted from Gelfand et al[10])

Materials and Methods

This cross-sectional study was done from July 2018 to June 2019 in the department of Nephrology of National Institute of Kidney Diseases and Urology, Dhaka. Total 135 CKD patients (stage 1−5 and also who are on maintenance hemodialysis) and 30 healthy volunteers were included in this study. CKD staging was done by using Kidney Disease Improving Global Outcome (KDIGO) (2012). For the purpose of analysis, study population were divided into four groups: earlier stage CKD (stage 1−3), advanced stage CKD (stage 4−5), hemodialysis (HD) patients and healthy individuals. Exclusion criteria included age less than 18 years, HD patients on temporary access, peritoneal dialysis patients and presence of active infection, active malignancy, active coronary artery disease (e.g., MI, unstable angina) within last 6 months, pregnancy, advanced dementia, advanced cirrhosis, refractory psychiatric illness or active alcohol abuse. Symptom burden, quality of life and functional status were assessed in all groups by using validated tool. Demographic characteristics and some biochemical data like serum hemoglobin, calcium, phosphorus, albumin, uric acid and creatinine were also recorded.

Assessment of symptoms, quality of life and functional status

Symptom burden was assessed by using Palliative Care Outcome Scale – Symptom Renal (POS-S: Renal), a symptom inventory tool specially designed and validated for CKD patients. It consists of total 17 symptoms during the last seven days and the severity of each symptom is marked as 'none', 'slight', 'moderate', 'severe' or 'overwhelming'. Patient completed the survey by himself. In addition, the tool provides an opportunity to list the main problem over the last seven days. We used the Short Form-36 (SF-36) health survey to assess the quality of life. The SF-36 survey consists of 8 dimensions (physical functioning, physical role functioning, pain, general health, emotional well-being, role emotional, social function and energy/fatigue) and two component summary scores (Physical Component Summary, PCS and Mental Component Summary, MCS). Higher scores indicate better QOL. Karnofsky Performance Status Scale (KPSS) was used to assess the functional status of study population. KPSS has three alphabetical groups (A, B and C) to identify patient's ability to work, perform normal activities and take care of themselves. These three groups are further classified into 11 categories, which cover all possible functional levels from completely normal (100) to dead (0). Validation of POS-S: Renal and KPSS in Bengali language was done by doing back translation and also by doing pilot study. SF-36 has already been used in several studies in our country.

Statistical Analysis

The study consists of four groups: healthy control, CKD 1−3, CKD 4−5 and hemodialysis group. Differences among these groups in demographic characteristics, clinical variables, mean number of symptoms and total symptom severity score, QOL and fuctional status were assessed by using ANOVA test and unpaired t-test for continous variables and Chi-square test for categorical variables to measure the level of significance, where p-value < 0.05 was considered as statistically significant. Bonferroni test was done to identify the statistical significant difference of mean number of symptoms and total symptom severity score among all groups. Correlation between eGFR and mean number of symptoms and total symptom severity score was also seen is this study.

Results

Patient Characteristics

A total of 165 patients were evaluated. Out of them, 105 were pre-dialysis (non-dialysis) CKD (stage 1−5) patients, 30 were hemodialysis (HD) patients and the rest 30 were healthy individuals. The pre-dialysis CKD patients were divided into two groups: earlier stage CKD (Stage1−3) that included 44 patients and advanced stage CKD (Stage 4−5) that included 61 patients. The mean age of CKD patients (pre-dialysis and HD group) was 53.5 years and mean age of healthy people was 47.9 years. Of this cohort, 60.6% were male and 39.4% were female. The probable primary disease was DM in 40.9% of the patients, the other probable primary diseases were hypertension (37.2%), GN (4.4%), ADPKD (2%), renal stone (2%) and unknown (20%). The mean eGFR was 23.4 mL/min/1.73m^2 in CKD (pre-dialysis and HD) patients and 95.5 mL/min/1.73m^2 in healthy controls. Values of the serum calcium and serum albumin levels gradually declined as eGFR decreased from earlier stage to HD group and value of the serum phosphate level changed in opposite direction. Serum uric acid level was lower and hemoglobin level was higher in earlier stage compared to advanced stage of CKD. Demographic data shows below.

Table II shows prevalence of symptoms among all study population. Prevalence of all symptoms (except pain and changes in skin) were increased from earlier stage (stage 1−3) to hemodialysis group and was lowest in healthy group. The prevalence of pain was highest in earlier stage compared with other groups and prevalence of changes in skin was higher in earlier stage compared to advanced stage (stage 4−5). Weakness, poor mobility, pain and feeling anxious were the most prevalent symptoms that were observed in all CKD stages including hemodialysis. Pain, constipation and difficulty in sleeping were the most prevalent symptoms in healthy individuals.

Table III shows the severity (from moderate to overwhelming) of symptoms among all study population. Weakness and poor mobility were the two

most severe symptoms observed in all groups except healthy individuals, where pain was the most severe symptom. There was also an increasing of severity of most symptoms (except pain and change in skin) from earlier stage to advanced stage like the prevalence and was highest in hemodialysis group. Severity of pain was similar in earlier stage and HD patients and slightly higher in advanced stage. Severity of change in skin was higher in earlier stage compared to advanced stage and was highest in HD group.

Table I: Descriptive statistics of clinical parameters of study population (n=165)

Variables	Control (n=30)	CKD (1-3) (n=44)	CKD (4-5) (n=61)	HD (n=30)	p-value
Demographic data					
Age (years)	48 ± 11	54 ± 10	54 ± 10	52 ± 10	0.040
Gender					
Male	16 (53)	33 (75)	33 (54)	16 (53)	0.108
Female	14 (47)	11 (25)	28 (46)	14 (47)	
Serum creatinine (mg/dL)	0.8 ± 0.2	1.5 ± 0.3	3.9 ± 1.5	10.9 ± 2.6	0.001
Calcium (mg/dL)		9.9 ± 1.2	9.4 ± 1.5	8.6 ± 1.8	0.001
PO_4 (mg/dL)		3.9 ± 0.6	4.6 ± 1.5	5.0 ± 2.1	0.010
Albumin (mg/dL)		5.3 ± 0.9	4.7 ± 1.2	3.6 ± 0.7	0.001
Uric acid (mg/dL)		6.1 ± 1.3	6.8 ± 1.3	6.2 ± 1.4	0.026
Hemoglobin (g/dl)		11.9 ± 1.4	10.3 ± 1.5		0.001

Table II: Prevalence of symptoms among study population (n=165)

Symptoms	Stage 1-3 n (%)	Stage 4-5 n (%)	HD n (%)	Healthy individuals n (%)
Pain	38 (86)	48 (79)	22(73)	17(57)
Shortness of breath	8 (18)	19 (31)	19 (63)	
Weakness	38 (86)	52 (96)	30 (100)	5 (16.7)
Nausea	13 (30)	30 (49)	20 (67)	2 (7)
Vomiting	3 (7)	7 (12)	12 (40)	
Poor appetite	19 (43)	41 (67)	24 (80)	8 (27)
Constipation	26 (59)	41 (64)	20 (67)	12 (40)
Mouth problems	5 (11)	8(13)	7(23)	1(3)
Drowsiness	20 (46)	39 (64)	23 (77)	
Poor mobility	32 (73)	54 (98)	30 (100)	
Itching	14 (32)	21 (34)	14 (47)	7 (23)
Difficulty sleeping	30 (63)	40 (66)	25 (83)	13 (43)
Restless legs	15 (34)	28 (46)	18 (60)	5 (17)
Feeling anxious	38 (86)	32 (95)	30 (100)	3 (10)
Feeling depressed	10 (23)	41 (67)	30 (100)	1 (3)
Changes in skin	10 (23)	13 (21)	23 (77)	1 (3)
Diarrhoea	4 (9)	9 (15)	8 (27)	1 (3)

Table III: Severity of symptoms among study population (n=165)

Symptoms	Stage 1-3 n (%)	Stage 4-5 n (%)	HD n (%)	Healthy individuals n (%)
Pain	22 (50)	31 (52)	15 (50)	2 (7)
Shortness of breath	2 (5)	8 (13)	10 (33)	
Weakness	25 (57)	47 (89)	30 (100)	
Nausea	6 (14)	10 (17)	15 (51)	1 (3)
Vomiting	2 (4)	3 (5)	6 (20)	
Poor appetite	11 (25)	30 (49)	22 (73)	
Constipation	12 (28)	30 (50)	15 (50)	1 (3)
Mouth problems	2 (5)	4 (7)	1 (3)	
Drowsiness	3 (7)	12 (20)	21 (70)	
Poor mobility	18 (41)	49 (81)	30 (100)	
Itching	5 (11)	9 (15)	10 (33)	1 (3)
Difficulty sleeping	17 (39)	26 (43)	20 (67)	1 (3)
Restless legs	4 (9)	19 (31)	13 (43)	
Feeling anxious	8 (18)	20 (45)	27 (90)	
Feeling depressed	4 (9)	8 (13)	26 (87)	
Changes in skin	6 (14)	6 (10)	15 (50)	
Diarrhoea	2 (5)	6 (10)	5 (17)	

The mean number of symptoms (out of 17) in study population were 2.5±1.4 in healthy control, 7.3 ± 3.0 in CKD 1−3 and 9.2 ± 2.4 in CKD 4-5 patients and 11.8 ± 2.0 HD patients. The total symptom severity score (out of 68) were 2.9 ± 1.8 in healthy controls, 2.9 ± 1.8 in CKD 1−3, and 16.4 ± 6.1 in CKD 4−5 patients and 26.1 ± 6.6 in HD patients. So, the mean number of symptoms and total symptom severity score were increased from healthy individuals to hemodialysis group. There is statistically significant difference (p-value<0.001) of mean number of symptoms and total symptom severity score among all groups when Bonferroni test was applied. There was negative correlation between eGFR and mean number of symptoms and total symptom severity score among all study population as shown below.

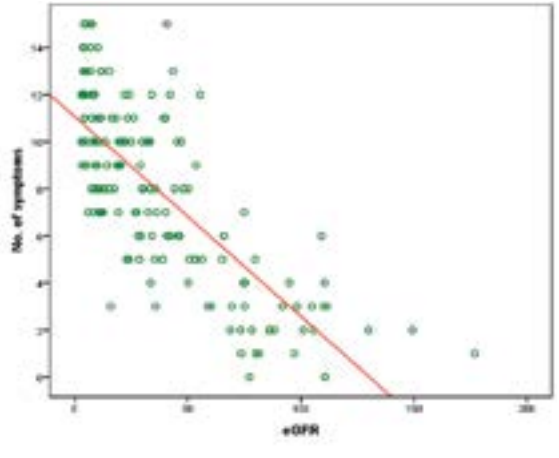

Fig 2. Negative correlation between number of symptoms and eGFR (r=-0.763; p=<0.001)

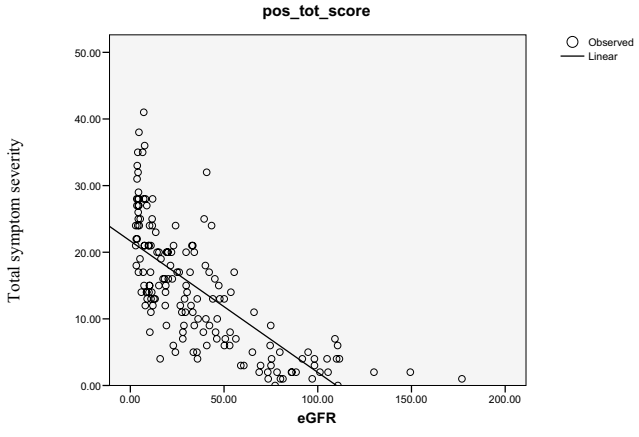

Fig 3. Negative correlation between estimated GFR and POS total symptom severity score in all study groups (r= -0.726, p=.01)

Score of PCS and MCS were higher in control group compared to other groups. Also it was noticeable that scores of all components of PCS and MCS gradually declined from earlier stage to hemodialysis (HD) group where the score was the lowest.

Regarding the functional status, the study result also followed the SF-36 survey results that means the functional status as measured by KPS scale was highest in control group and lowest in hemodialysis (HD) group. So it is seen that functional status gradually decreased from earlier stage to hemodialysis group.

Single pool Kt/V (equation used to assess the dailysis adequacy) was measured in 30 hemodialysis patients and 28 patients had Kt/V of at least 1.2 (target value is at least 1.2 or >1.2). So there was no association of Kt/V with symptom burden and QOL in hemodialysis patients in our study.

Table IV: Quality of life score domain in study population (n=165)

Quality of life score domain	Control (n=30)	CKD (1-3) (n=44)	CKD (4-5) (n=61)	HD (n=30)	p values
Physical functioning	94.5 ±7.5	71.2 ± 23.0	52.3 ± 19.5	32.2 ± 11.2	0.001
Role-physical	94.2 ±10.7	51.1 ± 35.3	25.6 ± 20.9	15.8 ± 12.2	0.001
Pain	84.3 ± 11.7	63.2 ± 21.5	59.9 ± 22.7	56.0 ± 25.0	0.001
General health	81.1 ± 9.5	63.6 ± 17.3	51.2 ± 12.6	32.6 ± 12.4	0.001
Emotional well-being	92.5 ± 4.7	84.5 ± 8.5	76.7 ± 10.0	53.3 ± 15.5	0.001
Role – emotion	99.7 ± 1.0	88.1 ± 31.6	80.2 ± 38.4	4.4 ± 11.5	0.001
Social function	95.8 ± 9.5	78.8 ± 27.1	57.4 ± 24.3	36.6 ± 16.4	0.001
Energy/fatigue	86.0 ± 7.0	71.3 ± 11.4	60.2 ± 9.5	41.2 ± 14.6	0.001
PCS	88.3 ± 9.1	62.3 ± 20.8	47.3 ± 12.5	34.1 ± 10.2	0.001
MCS	93.5 ± 4.7	81.3 ± 15.9	68.3 ± 15.8	33.9 ± 11.4	0.001

Table V: KF score domain in study population (n=165)

KF	Control (n=30)	CKD (1-3) (n=44)	CKD (4-5) (n=61)	HD (n=30)	p values
Karnofsky score	98.3 ± 3.8	90.0 ± 7.5	82.4 ± 8.5	66.3 ± 9.9	0.001

Discussion

This study examined the symptom burden, quality of life and functional status in different stages of CKD patients including hemodialysis and healthy control by using validated tool.

In our study, weakness, poor mobility, pain and feeling anxious were the more prevalent symptoms that were observed in all stages of CKD including dialysis. Out of them, weakness and poor mobility were the most severe symptoms. Prevalence and severity of most of the symptoms increased as GFR decreased.

Brown et al[11] studied the symptom burden of CKD patients (stage 1−5, not on dialysis) by using Leicester Uremic Symptom Score (LUSS) scale and found excessive tiredness was the most reported symptom followed by sleep disturbance and pain in the bones/ joints. In our study, weakness and pain were also the prominent symptoms in all stages of CKD.

Brennan et al[12] and Murphy et al[6] both studied the symptom burden of patients with CKD stage 5 and

CKD stage 4-5 respectively, who were managed conservatively. Both studies used the POS:S:Renal scale and found that the two most prevalent symptoms were weakness and poor mobility. It is also similar to our findings. The other symptoms that were found in above two studies were also present in different proportions among different groups in our study. The two most prevalent symptoms were also the most severe in our study which also found in Brennan et al[12] study.

A systematic review was done by Murtagh et al[4] to identify the prevalence of symptoms in hemodialysis patients and they found that the most prevalent symptom was fatigue/tiredness (71%) along with other symptoms in different proportions like pruritus, constipation, anorexia, pain, sleep disturbance, anxiety, shortness of breath, nausea, restless leg syndrome, depression. In our study, the most prevalent symptoms in hemodialysis group were the weakness (100%), poor mobility (100%), anxiety (100%) and depression (100%) along with the other symptoms.

Our study found that the mean number of symptoms and the mean number of total symptom severity score gradually increased as GFR decreased.

Almutary et al[5] found that total symptom burden score, mean number of symptoms and mean overall symptom severity score were significantly higher in the hemodialysis group compared with advanced stages (Stage 4-5). Similarly, in our study the mean number of symptoms and the mean number of total symptom severity score was highest in hemodialysis group compared to other groups. Fatigue was one of the most prevalent and severe symptoms observed in hemodialysis group in our study which again coincides with the Almutary et al[5] study.

In this study, the other symptoms that were reported by the patients (other than main 17 score in POS-Scale: renal) was mostly the sex problem mainly in the form of reduced interest in sex in both hemodialysis and pre-dialysis patients. Problem about sex is one of important component of symptom assessing tool and this symptom is frequently reported in different studies among CKD population. Few patients also complained of vertigo and swelling of leg.

Regarding symptom burden between advanced stage and HD patients, Abdel-Kader et al[1] showed no difference in mean overall number of symptoms and total symptom severity score by using a different scale (dialysis symptom index, DSI). The study also assessed the QOL in two above-mentioned groups. The study found that overall physical well-being as measured by PCS was comparable to overall mental well-being as measured by MCS in both groups.

Cruz et al[13] also assessed the QOL and functional status in all stages of CKD (stage 1-5) including hemodialysis and found that QOL and functional status decreased in all stages of kidney disease, even in the early stages of disease. They found no association between the stages of disease and QOL. In our study, QOL and functional status also decreased in the earlier stage. But QOL and functional status gradually decreased as GFR decreased which does not coincide with the Cruz et al[13] study. The reason behind this dissimilarity may be due to a high prevalence and severity of depression and anxiety in hemodialysis patients, mostly due to chronic dialysis treatment which contributes to their symptom burden, poor QOL and poor functional status. In our study, hemodialysis patients had the highest prevalence and severity of anxiety and depression compared with other groups. Almutary et al[5] found that overall symptoms were more burdensome in the dialysis group, in particular among those receiving HD, which indicates that dialysis therapy may contribute to increased symptom burden.

In our study, it was also found that the value of serum calcium, serum albumin and hemoglobin gradually decreased as GFR decreased. On the other hand, serum phosphate and serum uric acid level was high in advanced stage compared with earlier stage. This biochemical abnormality may contribute to high symptom burden and reduced QOL in higher stages of CKD.

High symptom burden, reduced QOL and poor functional status affect all stages of CKD patients including hemodialysis. Validated tools can be used for regular assessment of these problems. At the same time, renal supportive care should be given from the

earlier stages of CKD for identification and alleviation of these problems.

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