Prevalence of Fatigue and Risk of Fall Among Elderly with Chronic Kidney Disease

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ABSTRACT

Background: One of the most often reported symptoms in people with chronic kidney disease (CKD) is fatigue. Additionally, fall is thought to be a marker of frailty and disability among them.

Objectives: To determine the prevalence of fatigue and risk of fall among elderly patients with CKD.

Subjects and methods: A cross sectional study included 100 elderly patients, Males and females aging 60 years or more that were recruited from Ain Shams University Hospitals, 50 patients on regular hemodialysis and 50 patients diagnosed with chronic renal impairment. All patients were subjected to Comprehensive Geriatric Assessment (CGA) with assessment of cognition, depression, risk of fall, balance, fatigue, past medical history, associated comorbidities and laboratory investigations. **Results:** The mean age among the studied population was 66.89±6.41 years, the prevalence of depression was 66%. The most common comorbidities were hypertension (HTN) (84%), diabetes (DM) (66%). On assessment of fall by Timed Up and Go (TUG) test, (45%) of the participants had risk of fall, which was more prevalent in haemodialysis group (54%); whereas by one leg balance test (51%) of them had risk of fall, which was more prevalent in haemodialysis group (72%), and on assessment of fatigue by Multidimensional Assessment of Fatigue (MAF) it was found that (68%) of the participants were fatigue positive, which was more prevalent in haemodialysis group (82%).

Conclusion: Almost half of elderly patients with CKD had high risk of falls and about two third of them experienced fatigue, which was more prevalent in patients on haemodialysis.

Keywords: Chronic Kidney Disease, MAF, Falls, Haemodialysis, Balance, TUG.

INTRODUCTION

It is expected that in USA, the population aged 65-year-old and older will be more than double between 2012 and 2060; rising from 43.1 million to 92 million **[1].** Chronic Kidney Disease (CKD) is more prevalent in the elderly population as reports indicate that one in three elderly patients will have estimated glomerular filtration rate (eGFR) below 45 ml/min/1.73 m^2 **[2].**

It was evident that patients with CKD, whether on dialysis or not, are at risk of falls **[3,4]**. In participants with CKD, falls are regarded as a critical source of injury and morbidity **[5]**, as they may be caused by physical function deficiencies, such as slowed gait and balance, that are common in this population **[6]**. Additionally, it has been found that slower gait speed was correlated with the fear of falls in elderly **[7]**. Even if there are no fractures as a result of the fall, the patient may still sustain other fall related injuries such as head injuries, bruises or fall phobia which would eventually affect their mobilization **[8]**. Fatigue can be defined as a multiplex, multidimensional, subjective experience that binds both psychological and physical symptoms together. Patients describe it as severe and persistent tiredness, lack of energy, exhaustion and weakness that is counterintuitive to their degree of exertion, and it interferes with physical functioning **[9].** Furthermore, it is considered a usual symptom in patients with chronic medical illnesses, including CKD patients requiring dialysis **[10],** and also an exhausting symptom in patients with CKD not on dialysis **[11].**

Approximately 66 to 75 % of patients with CKD experience fatigue, with almost quarter of them reporting severe symptoms **[12],** it differs in its prevalence according to the measurement instruments used and treatment modality. Not to forget that it is independently linked to dialysis initiation in patients with CKD, hospitalization and mortality **[11].** The pathophysiology of fatigue in CKD has many factors and includes decreased oxygen delivery to tissues, anaemia, lactic acidosis, chronic metabolic acidosis, sarcopenia, hyperphosphatemia, depression, and obstructive sleep apnea **[12].** So, the aim of our study was to determine the prevalence of fatigue and risk of fall among elderly patients with CKD.

SUBJECTS AND METHODS

A cross sectional study included 100 elderly patients, males and females aging 60 years or more that were recruited from inpatient ward and outpatient clinics in Ain Shams University Hospitals, 50 patients on regular hemodialysis and 50 patients diagnosed with chronic renal impairment (serum creatinine≥2).

Inclusion criteria included those with glomerular filtration rate (GFR) ≤ 60 mg/min/1.73m^2. Exclusion criteria included those with GFR more than 60 mg/min/1.73 m^2 and with severe cognitive impairment. All patients were subjected to Comprehensive Geriatric Assessment with history taking and clinical examination, cognitive function assessment by Mini-Mental Status Examination (MMSE) **[13]**, assessment of depression using Geriatric Depression Scale (GDS-15) **[14]**, and assessment of balance by one leg balance test **[15].** Assessment of fatigue was done by Multidimensional Assessment of Fatigue (MAF) [The MAF is a 16-item scale that assesses four aspects of fatigue: degree and intensity, discomfort it causes, time of exhaustion (over the previous week, when it first appeared, and any variations), and its effects on different daily activities (household chores, cooking, bathing, dressing, working, socializing, sexual activity, leisure and recreation, shopping, walking, and exercising). We didn't finish the test if the person didn't

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become fatigued. If they reported weariness in the previous week, we finished the test using a numerical rating scale for items 1 and 4-14 and item 2 (1 = mild to 10 = severe), and item 3 (1 = no distress, 10 = significantly distressing). For Timing items 15 and 16, categorical replies (1–4) were available [16].

Assessment of gait speed and fall by the Timed Up and Go test (TUG) [17], calculation of body mass index (BMI), and laboratory investigations (kidney function test, complete blood count, electrolytes) were also done.

Ethical considerations:

All of the patients taking part in this trial provided their informed permission. The Research Review Board of the Geriatrics and Gerontology Department and the Ethical Committee of the Faculty of Medicine at Ain Shams University both examined and approved the study methodology. The Declaration of Helsinki, the World Medical Association's code of ethics for studies involving humans, guided the conduct of this work.

Statistical Analysis

In order to analyze the data acquired, Statistical Package for the Social Sciences (SPSS), version 20 was used to execute it on a computer. The quantitative data were presented in the form of the mean, standard deviation, and range. The qualitative data were presented as frequency and percentage. The independent student's t test (T) was used to compare the parametric quantitative data while data with non-parametric distribution was compared using Mann-Whitney test. Pearson Chi-Square test was used to assess qualitatively independent data. The significance of a P value of 0.05 or less was determined.

RESULTS

The mean age among our studied group was 66.89±6.41 years, 57% were males, 67% were married, and 32% were smokers. The mean MMSE score was 26.25±2.21 and it was higher in CKD patients not on dialysis than those on dialysis. The prevalence of depression was 66% with mean score 5.88±1.77 with no statistically significant difference between both groups.

The most common comorbidities were hypertension (HTN), diabetes (DM), ischemic heart disease (IHD), osteoporosis (OP), heart failure (HF), and history of fall (**Table 1).**

Table (1): Comparison between CKD and haemodialysis group regarding comorbidities

		Total	CKD	Haemodialysis	Test value	P-value	Sig.
		No. = 100	No. = 50	No. = 50			
DM	Negative	34 (34.0%)	6 (12.0%)	28 (56.0%)	21.569*	<0.001	HS
	Positive	66 (66.0%)	44 (88.0%)	22 (44.0%)			
HTN	Negative	16 (16.0%)	4 (8.0%)	12 (24.0%)	4.762*	0.029	S
	Positive	84 (84.0%)	46 (92.0%)	38 (76.0%)			
IHD	Negative	71 (71.0%)	41 (82.0%)	30 (60.0%)	5.877*	0.015	S
	Positive	29 (29.0%)	9 (18.0%)	20 (40.0%)			
HF	Negative	80 (80.0%)	46 (92.0%)	34 (68.0%)	9.000*	0.003	HS
	Positive	20 (20.0%)	4 (8.0%)	16 (32.0%)			
TIA	Negative	97 (97.0%)	50 (100.0%)	47 (94.0%)	3.093*	0.079	NS
	Positive	3 (3.0%)	0 (0.0%)	3 (6.0%)			
CVS	Negative	98 (98.0%)	50 (100.0%)	48 (96.0%)	2.041*	0.153	NS
	Positive	2 (2.0%)	0 (0.0%)	2 (4.0%)			
CLD	Negative	89 (89.0%)	46 (92.0%)	43 (86.0%)	0.919*	0.338	NS
	Positive	11 (11.0%)	4 (8.0%)	7 (14.0%)			
OP	Negative	79 (79.0%)	45 (90.0%)	34 (68.0%)	7.294*	0.007	HS
	Positive	21 (21.0%)	5 (10.0%)	16 (32.0%)			
FALL history	Negative	83 (83.0%)	47 (94.0%)	36 (72.0%)	8.575*	0.003	HS
	Positive	17 (17.0%)	3 (6.0%)	14 (28.0%)			
UI	Negative	95 (95.0%)	48 (96.0%)	47 (94.0%)	0.211*	0.646	NS
	Positive	5 (5.0%)	2 (4.0%)	3 (6.0%)			

*: Chi-square test; (CLD) chronic liver disease, (UI) urinary incontinence, (TIA) transient ischemic attacks.

Regarding assessment of risk of fall by (TUG) test, 45% of the participants were dependent and had risk of fall, which was more prevalent in hemodialysis group (54%). As regard balance assessment by one leg balance test, 51% of our participants had risk of fall, which was more prevalent in hemodialysis group (72%). The mean BMI of the participants was more in hemodialysis group than in CKD group (**Table 2).**

Table (2): Comparison between CKD and hemodialysis group regarding TUG test, balance, BMI

		Total	CKD	Hemodialysis	Test value	P-value	Sig.
		No. = 100	**No. = 50**	**No. = 50**			
TUG							
Score	**≤ 10 sec(normal)**	5 (5.0%)	2 (4.0%)	3 (6.0%)	4.000*	0.135	NS
	< 20 sec Independent	50 (50.0%)	30 (60.0%)	20 (40.0%)			
	≥ 30 sec dependent (fall risk)	45 (45.0%)	18 (36.0%)	27 (54.0%)			
Balance							
Score	**< 5 sec Fall risk**	51 (51.0%)	15 (30.0%)	36 (72.0%)	17.669*	<0.001	HS
	< 10 sec balance impairment	45 (45.0%)	32 (64.0%)	13 (26.0%)			
	> 10 sec Normal	4 (4.0%)	3 (6.0%)	1 (2.0%)			
BMI							
Score	**Mean ± SD**	27.69 ± 6.19	26.98 ± 5.28	28.41 ± 6.96	-1.157•	0.245	NS
	Range	17 – 45	17 – 38	17 – 45			

*:Chi-square test; •: Independent t-test

Regarding laboratory investigations it was found that mean Haemoglobin was significantly lower in hemodialysis group than CKD patients not on dialysis. Mean phosphorous level (PO_4) and serum creatinine (Cr) were significantly more in hemodialysis group (**Table 3).**

Table (3): Comparison between CKD group and hemodialysis group regarding lab findings

Labs		Total	CKD	Hemodialysis	Test value	P-value	Sig.
		No. = 100	**No. = 50**	**No. = 50**			
Haemoglobin (mg/dL)	**Mean ± SD**	9.69 ± 1.42	10.13 ± 1.39	9.26 ± 1.32	3.190•	0.002	HS
Serum Ca (units/mL)	**Mean ± SD**	8.52 ± 0.73	8.65 ± 0.60	8.40 ± 0.84	1.705•	0.091	NS
Serum PO_4 (mg/dL)	**Mean ± SD**	4.54 ± 1.1	3.97 ± 0.97	5.11 ± 1.27	-5.038•	<0.001	HS
Serum Na (mmol/L)	**Mean ± SD**	136.66 ± 6.58	137.02 ± 5.95	136.30 ± 7.20	0.545•	0.587	NS
Serum K (mEq/L)	**Mean ± SD**	4.49 ± 0.75	4.41 ± 0.72	4.56 ± 0.79	-0.994•	0.323	NS
Serum Cr (mg/dL)	**Mean ± SD**	4.20 ± 1.87	2.86 ± 0.1	5.55 ± 1.53	-10.351•	<0.001	HS

•: Independent t-test

Regarding assessment of fatigue by Multidimensional Assessment of Fatigue (MAF) it was found that 68% of the participants were fatigue positive, which was significantly more prevalent in hemodialysis group than in CKD group. Fatigue during going to work, during sexual activity, having entertainment activities, and during walking and exercise was significantly more in hemodialysis group than in CKD group (**Table 4).**

Table (4): Comparison between two groups regarding Multi-dimensional Assessment of Fatigue (MAF)

		Total	CKD	Hemodialysis	Test value	P-value	Sig.
		No. = 100	No. = 50	No. = 50			
MAF	**Negative**	32 (32.0%)	23 (46.0%)	9 (18.0%)	9.007*	0.003	HS
	Positive	68 (68.0%)	27 (54.0%)	41 (82.0%)			
Q1 (degree of fatigue)	**Mean ± SD**	6.19 ± 1.31	6.19 ± 1.41	6.20 ± 1.21	-0.250‡	0.803	NS
	Range	2 – 10	3 – 10	2 – 10			
Q2 (severity of fatigue)	**Mean ± SD**	6.16 ± 1.11	6.22 ± 1.12	6.12 ± 1.13	-0.006‡	0.995	NS
	Range	2 – 10	2 – 10	2 – 10			
Q3 (distress of feeling fatigue)	**Mean ± SD**	6.37 ± 1.51	6.41 ± 1.45	6.34 ± 1.31	-0.167‡	0.867	NS
	Range	1 – 10	4 – 10	1 – 10			
Q4 housework	**Mean ± SD**	3.88 ± 0.81	3.48 ± 0.83	4.15 ± 1.01	-0.788‡	0.431	NS
	Range	0 – 10	0 – 9	0 – 10			
Q5 cooking	**Mean ± SD**	3.57 ± 0.62	3.22 ± 0.91	3.80 ± 0.64	-0.580‡	0.562	NS
	Range	0 – 10	0 – 9	0 – 10			
Q6 showering	**Mean ± SD**	3.88 ± 0.51	3.89 ± 0.61	3.88 ± 0.52	-0.039‡	0.969	NS
	Range	0 – 9	0 – 9	0 – 9			
Q7 dressing	**Mean ± SD**	3.87 ± 0.41	3.56 ± 0.51	4.07 ± 0.81	-0.583‡	0.560	NS
	Range	0 – 10	0 – 9	0 – 10			
Q8 working	**Mean ± SD**	1.51 ± 0.5	0.26 ± 0.05	2.34 ± 0.42	-3.044‡	0.002	HS
	Range	0 – 10	0 – 7	0 – 10			
Q9 visiting friends	**Mean ± SD**	2.21 ± 0.35	1.41 ± 0.41	2.73 ± 0.49	-1.707‡	0.088	NS
	Range	0 – 10	0 – 9	0 – 10			
Q10 sexual activity	**Mean ± SD**	1.60 ± 0.51	0.67 ± 0.14	2.22 ± 0.28	-2.193‡	0.028	S
	Range	0 – 9	0 – 7	0 – 9			
Q11 entertainment activities	**Mean ± SD**	1.28 ± 0.41	0.33 ± 0.07	1.90 ± 0.51	-2.485‡	0.013	S
	Range	0 – 9	0 – 9	0 – 9			
Q12 shopping	**Mean ± SD**	1.50 ± 0.11	0.70 ± 0.11	2.02 ± 0.31	-1.952‡	0.051	NS
	Range	0 – 10	0 – 10	0 – 9			
Q13 walking	**Mean ± SD**	1.63 ± 0.22	0.70 ± 0.12	2.24 ± 0.50	-2.310‡	0.021	S
	Range	0 – 10	0 – 10	0 – 10			
Q14 exercise	**Mean ± SD**	1.66 ± 0.31	0.63 ± 0.12	2.34 ± 0.53	-2.124‡	0.034	S
	Range	0 – 10	0 – 9	0 – 10			
Q15 (timing of fatigue)	**Mean ± SD**	3.16 ± 0.66	3.00 ± 0.55	3.27 ± 0.71	-1.942‡	0.052	NS
	Range	1 – 4	2 – 4	1 – 4			
Q16 (change in fatigue)	**Mean ± SD**	2.98 ± 0.42	2.92 ± 0.52	3.03 ± 0.61	-1.030‡	0.303	NS
	Range	1 – 4	1 – 4	1 – 4			

*:Chi-square test; ‡: Mann Whitney test

DISCUSSION

More research now shows that individuals with CKD in various stages experience a high symptom burden that negatively impacts their quality of life [(18)]. One of the most often noted symptoms in CKD patients is fatigue. Studies concentrating on fatigue among CKD patients who are not on dialysis are uncommon, limited by a small sample size, and a chosen demographic, despite the fact that there is a wealth of literature addressing the prevalence and severity of fatigue in the End-Stage Renal Disease (ESRD) community [(19, 20)]. Furthermore, no sizable research that compare the level of weariness in the two groups exist.

In our study, the prevalence of fatigue was almost 66%, being higher in CKD on dialysis as it reaches about 82%; this comes with many studies that report that the prevalence of fatigue in CKD patients ranged between 21-90%, and this prevalence increases with advancing CKD stages [(21)]**.** Furthermore, the same result in **Murtagh *et al.*** [(22)] study shows that fatigue is one of the most frequently recorded symptoms in CKD patients; it affects nearly 60–97% of patients on long-term renal replacement therapy and reaches 84% in CKD stage 5 patients. Nonetheless, other studies show different prevalence since these varying results are likely due to differences in instruments used, sample size, and other ethnic and genetic backgrounds[(11, 21, 23)]**.**

Also we found that severity of fatigue was almost the same in both CKD patients and those on dialysis with no statistically significant difference between them. This goes with **Jhamb *et al.*** [(18)] in their study**.**

It was absurd to find that patients with end-stage renal illness and advanced CKD not on dialysis experience weariness of a similar severity. Patients with CKD who are not dialysis reliant would be expected to be more physically active, functional, and less fatigued [(24)]. Therefore, it is possible to hypothesise that these subgroups' exhaustion may be caused by various underlying factors. It's possible that in dialysis-dependent patients, treatment-related factors have taken the place of kidney disease-related factors such pruritis and uremia that cause fatigue in non-dialysis dependent CKD patients.

Moreover, on addressing effect of fatigue on daily activities we found that fatigue during going to work, during sexual activity, having entertainment activities, and during walking and exercise, all being examples of physical fatigue and are related to muscle weakness and sarcopenia, were more in hemodialysis group than in CKD group. This can be explained by the presence of chronic metabolic acidosis in some CKD patients especially with low GFR can lead to rapid occurrence of exertional muscle fatigue and more functional impairment [(25)] affecting quality of life.

Anaemia plays an important role in developing fatigue in (CKD) patients and this was clear in our studied population as anaemia with mean HB level was 9.69 ±1.42 with lower level in hemodialysis group may contribute to more fatigue prevalence in this subgroup and this was confirmed by **Jhamp *et al.*** [(23)] in their study considering anemia one of the most common diseases associated with fatigue**.** In addition, it was found that correction of anaemia over time was associated with improvement in patient-recorded fatigue [(26)]. On the contrary, **McCann and Boore**[(27)] in their study stated that no association was found between anaemia and fatigue in CKD patients on haemodialysis**.**

Regarding common comorbidities in our studied group: the high prevalence of HTN, DM (84, 66% respectively) can lead to more fatigue as it was found that insulin resistance is allied with a low microvascular vasodilatory response and as diabetes is considered one of the most common causes of CKD it can share in the pathophysiology of muscle fatigue in CKD patients as reported in many studies [(28)]**.**

It was noted that prevalence of depression was 66% among our studied population with no significant difference between both groups, this high prevalence of depression in CKD patients was confirmed in many studies that correlated depression and fatigue in such population groups [(29, 30)]**.** Moreover, it was found in one study that 53% percent of the patients with CKD had depression confirmed by a PHQ-9 score ≥10 [(18)]**.** Fatigue was positively correlated with depression even after adjusting for other variables such as antidepressant medication use [(31)]**.** However, a causal relationship could not be confirmed yet.

In this study, we found that mean phosphorous level was 4.54±1.26 among our studied population, which was more in haemodialysis group than in CKD group not on dialysis and this hyperphosphatemia is thought to assist in developing muscular fatigue as reported by other studies through its effects on intracellular calcium by binding with calcium ions (which is important for excitation-contraction coupling and muscle contraction) and precipitate them as calcium phosphate in the sarcoplasmic reticulum. Therefore, absence of calcium ions can lead to fatigue sensation and poor exercise tolerance [(32)]**.**

Recurrent attacks of falls can be considered as a marker of frailty and disability in elderly and they become more obvious in patients with CKD [(33)]**.** On top of that, the relationships between the severity of kidney disease and slower gait speed, increase risk of fall and impaired balance, could be the result of decreased physical activity noticed in patients with CKD and the risk of fall is thought to be 4 to 5 times higher in patients with CKD than the general population [(20)]**.**

Additionally, we figured out that 45% of the participants were dependent and had risk of fall, and decrease gait speed which was more prevalent in hemodialysis group (54%) than in CKD group (36%) using Timed Up and Go test. Regarding balance assessment, by using one leg balance test we found that

51% of our participants had risk of fall, which also was more prevalent in hemodialysis group (72%), this was confirmed by **Wickstrom *et al.***[20] in their study, which showed that the prevalence of balance deficits was high in CKD group and impaired balance was increasing with kidney disease severity. It is known that decreased lower-extremity muscle strength has a negative effect on balance and gait in elderly whether residing in nursing home or in the community with increased risk of fall [34]. Also, an identical result was confirmed by **Song *et al.***[35]**,** in their study, which showed that low physical performance, as reported by decrease walking speed, was significantly correlated to increased CKD severity.

Our study had several strengths. Firstly, it confirmed a high prevalence of fatigue and high risk of fall in elderly patients with CKD with increasing prevalence in CKD patients on dialysis. Moreover, we used a validated fatigue questionnaire that focus on the multidimensional aspects of fatigue and their effect on daily activities. Secondly, we assessed depression in our patients by GDS15, which is a validated depression questionnaire confirming high prevalence of depression in our studied population. Subsequently, a causal relation between depression and fatigue in CKD patients may be suggested; however, more studies are needed to confirm such relation. Lastly, we analysed a wide range of comorbidities in patients with CKD, which may play a pivotal role in developing fatigue and increase risk of fall in such populations. So, proper treatment and early intervention strategies with psychological, nutritional and rehabilitation programs to improve balance, nutrition and depression with correction of anaemia in elderly with CKD can improve fatigue, decrease its prevalence and decrease risk of fall.

Limitation of our study can be seen in the absence of control elderly group with normal kidney function, which limited the study of the relationship between both fall and fatigue and CKD.

CONCLUSION

Almost half of elderly patients with CKD had high risk of falls and about two thirds of them experienced fatigue. Not to forget that this was more prevalent in patients on haemodialysis.

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