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Assessment of Upper and Lower Limb Muscle Function in Elderly Patients with Chronic Kidney Disease

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ABSTRACT

Background:

Chronic kidney disease (CKD) is recognized as a leading public health problem worldwidewhich is more prevalent in the elderly population.However, there is paucity of studiesinvestigating muscle function in older adults with CKD.This study aimed to assess the function of upper and lower limb muscles in elderly patients with CKD.

Methods

A case-control study was conducted, including 73 patients with CKD and 73 healthy individuals as a control group. Patients were subdivided into two groups; 37 predialysis patients and 36 patients on regular hemodialysis.History was taken, blood pressure, anthropometric measures, handgrip strength (HGS), timed up and go test(TUGT) were assessed anda blood sample was withdrawn for measuring complete blood count, random blood sugar, lipid profile, renal and liverfunction tests.

Results

There is a significant decreasein HGS and a significant prolongation of TUGT in CKD patients as compared to the control group.PredialysisCKD patients have significantly higher HGS and less prolonged TUGT as compared to patients on regular hemodialysis.Both hemoglobin and albumin are positively correlated with HGS and inversely correlated with TUGT.Fasting triglycerides are inversely correlated with HGS. A highly significant inverse correlation was found between HGS and TUGT.

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Conclusions

There is a significant decline in upper and lower limb muscle function in CKD patients and this decline seems to be more obvious in lower limb muscles.The decline in muscle function is more evident in the hemodialysis than in the predialysis CKD patients.

Keywords: *Chronic kidney disease- Elderly- Muscle strength- Sarcopenia*

I. INTRODUCTION

Weakness in muscle strength in older adults is a common problem and is associated with physical disability and functional limitation.1Many studies have reported that low muscle strength is a predictor of all-cause mortality and cardiovascular death.2The maintenance of functional independence is the uppermost health priority reported by patients with chronic kidney disease (CKD).3

Patients with CKD, even at the early stage of the disease, have a reduced quality of life,including physical quality of lifeas compared to the general population.4 CKD may also predispose individuals to reduced exercise capacity and consequent muscle atrophy.5

It is not well recognized whether the patient is influenced by treatment with chronic dialysis or whether decreased physical activity (PA) is an inherent characteristic of end-stage renal disease (ESRD).6 While some literature suggests that PA is decreased in the CKD stage 5 non-dialysis patients due to fatigue related to uremic disorders, associated comorbidity, and pre-existent lifestyle factors,7 others indicate that PA is adequately maintained in a cohort of CKD stages 4–5 patients.8Furthermore, theoretically, dialysis treatment may ameliorate PA on non-dialysis days because of partial correction of the uremic state. However, the treatment may cause fatigue and results in a sedentary lifestyle even on dialysis days.9

The use of handgrip strength (HGS) as a biomarker of health status is upheld by research demonstrating a cross-sectional association between HGS and the strength of other muscle actions of both healthy and diseased adults,10 Based on this research and the applicability of hand-grip dynamometry, the measurement of HGS has been widely accepted as a singular indicator of overall muscle strength.11McGrath et al.12recently supported this adoption by reporting that stand-alone HGScan be considered as an umbrella assessment of the body systems that contribute to strength capacity, and a panoptic estimation of muscle strength that is representative of overall health status. Despite this adoption, clinicians and scientists should be cautious in using HGS as an indicator of overall muscle strength as there is evidence that HGSalone may not always be reflective of overall strength,13 and may provide a better evaluation of overall strength if used in conjunction with a measure of lower limb strength.14

The Timed Up and Go test (TUGT) is a commonly used screening tool for falls risk in the inpatient and the community setting reflecting lower limb muscle strength.15

The question of which limb muscles are more affected in CKD patients and the discrepancy in the literature regarding the correlation between the anthropometric measures and HGS strongly motivated us to construct this work.

II. MATERIAL AND METHODS

We obtained approval for performing this study from the Institutional Review Board, and written informed consent was takento all enrolledindividuals.

Criteria for inclusion into the study included elderly predialysis CKD patients and elderly ESRD patients on regular hemodialysis with age ≥65 years.Criteria for exclusion included patients with acute kidney injury, diabetes mellitus, end-organ failure, malignancies, connective tissue disease, acquired immunodeficiency syndrome, dementia, limb amputation, metallic implant, or hand/ knee osteoarthritis. Also, we excluded those whoare using walkers or wheelchairs and those who used drugs that cause muscle weakness.

We conducted a matched case-control study. Cases were selected from the Geriatric Unit in association with the Nephrology Unit of Internal Medicine Department in the period from June 2019 to June 2020.

Our study included 73 patients with CKD and 73 healthy individuals as a control group. Patients were subdivided into two groups; 37 predialysis patients and 36 patients on regular hemodialysis.

All participants were subjected tofull history taking, thorough physical examination,and anthropometric measures including mid-upper arm circumference (MAC), mid-calfcircumference (MCC), and body mass index (BMI). Also, all participants underwent an assessment of HGS and TUGT.

A handheld dynamometer (Jamar Hydraulic hand dynamometer; 5030J1, USA)was used to assess HGS. The dynamometer is held in the dominant hand with the arms by the sides of the body. For patients on hemodialysis, the non-fistula arm was used as there are concerns of bleeding if the patient overexerts.The participantwas asked to squeeze the dynamometer using maximum isometric effort. No other body movement was allowed. The better performance of three trials was recorded.16

TUGT is done by asking the individual to stand up from 44 to 47 cm high chair without using the arms, walk three meters, turn around, walk back, and sit down. Timing begins when the person starts to rise from the chair and ends when he returns to the chair and sits down.17

Laboratory investigations:

Two blood samples were collected from each participant after an overnight of 12 hours. The first sample was collected in a glass tube containing Ethylenediaminetetraacetic acid (EDTA) for complete blood count using an automated hematology analyzer, SYSMEX XN-1000. The second sample was collected in a dry tube without anticoagulant then; it was immediately centrifuged and kept in a freezer at minus 80 degree Celsius. It was handled by the automated chemiluminescence method with the IMULITE DPC Medlab system. Serum creatinine, urea, total bilirubin, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total plasma protein were measured with the Roche enzymatic method (Roche Cobas c501 chemistry analyzer, Roche Diagnostics). Glomerular filtration (GFR) was estimated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.Lipid profiles were tested via the selective solubilization method (AU5400 analyzer, Beckman Coulter, CA, USA). Fasting blood sugar was measured using the glucose oxidase and peroxidase method.

Statistical analysis

All data were collected, tabulated, and statistically analyzed using SPSS 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA) and MedCalc 13 for Windows (MedCalc Software BVBA, Ostend, Belgium). Continuous data were described as the mean ± standard deviation, mean, range and the categorical data were described as a percentage. An independent student t-test was used to compare two groups that have normally distributed data. Percent of categorical variables were compared with the Chi-square ($\chi 2$) test. Correlations between variables were done by using the Pearson correlation coefficient. $P< 0.05$ was considered to be statistically significant, $P< 0.01$ was considered to be highly statistically significant.

III. RESULTS

Regarding age, sex, smoking status, and anthropometric measures, no significant difference was found between cases and controls (tables 1 and 2).

Table (1): Age, sexand smoking statusdistribution between the studied groups

		Cases (n = 73) No.(%)	**Control (n = 73) No.(%)**	**Test**	**P value**
Age	**Mean ± SD (years)**	67.1±3.5	66.9±2.8	T=0.233	0.407
	Range	65 – 79	65-79		
Sex	**Male**	40 (54.8%)	35 (47.9%)	$\chi 2$=0.685	0.407
	Female	33(45.2%)	38 (52.1%)		
Smoking status	**Current**	12 (16.4%)	9 (12.3%)	$\chi 2$=1.14	0.563
	Former	14 (19.2%)	11(15.1%)		
	Never	47 (64.4%)	53 (72.6%)		

n: number;X2:Chi-square test; P < 0.05: statistically significant; P < 0.01: highly statistically significant; SD: standard deviation

Table 1 showsno significant difference between the studied groups regarding age, sex and smoking status.

Table (2): Comparison of anthropometric measures between cases and controls

	Cases (n = 73)	**Control (n = 73)**	**T test**	**P value**
	Mean ± SD Range	**Mean ± SD Range**		
Weight(kg)	74.3 ± 15.4 65-100	75.4 ± 16.1 64-98	0.421	0.673
Height (cm)	168.6 ± 12.6 155-187	167.2 ± 10.67 158 – 184	0.724	0.470
BMI(kg/m^2)	25.1 ± 4.4 22 – 34	25.5 ± 4.36 22 – 33	0.551	0.582
MAC(cm)	24.5±3.2 20-30	25.2±3.6 22-30	1.24	0.216
MCC(cm)	25.3±1.2 22-27	25.8±1.8 22-29	1.97	0.0502

BMI: body mass index; MAC: mid upper arm circumference; MCC: mid-calf circumference; n: number; P< 0.05: statistically significant; P< 0.01: highly statistically significant; SD: standard deviation.

Table 2 shows no significant difference between the studied groups regarding anthropometric measures.

Table (3): Distribution of blood pressure measurements betweenthe studied groups

	Cases (n = 73)	**Control (n = 73)**	**T test**	**P value**
	Mean ± SD Range	**Mean ± SD Range**		
Systolic BP (mm Hg)	144.13 ± 21.76 110 – 185	131 ± 14.1 105 – 150	2.408	0.016

Diastolic BP (mm Hg)	85.37 ± 10.7 85 (80 – 105)	79.5 ± 9.01 80 (65 – 90)	2.293	0.022

BP: blood pressure; n: number; P< 0.05: statistically significant; P< 0.01: highly statistically significant; SD: standard deviation.

Table 3 shows a significant difference between the two studied groups as regards to blood pressure measurements with blood pressure being higher in patients with CKD.

Table (4): Laboratory investigations in the studied groups

	Cases (n = 73)	**Control (n = 73)**	**T test**	**P value**
	Mean ± SD **Range**	**Mean ± SD** **Range**		
Hb (g/L)	108 ± 11 80.0-117	129.0± 21.0 115.0 – 160.0	7.56	<0.001
Creatinine (umol/L)	680.7 ± 335.9 539.2– 919.4	79.6 ± 17.7 53.0– 106.1	56.97	<0.001
Urea(mmol/L)	44.3 ± 18.5 25.7 – 85.0	7.1 ±0.7 3.6 – 8.9	27.84	<0.001
eGFR (ml/min)	11.8 ± 6.7 2.9 – 24.3	118.0 ± 18.9 95.0– 154.0	51.09	<0.001
ALT(units/L)	17.8 ± 2.4 16.0– 24.2	19.0 ± 0.5 16.1– 26.0	13.005	<0.001
AST(units/L)	19.9 ± 1.4 13.0– 26.0	21.2 ± 1.2 16.0– 29.0	32.705	<0.001
Total plasma protein(g/L)	73.6 ± 2.6 65.0 – 80.0	74.8 ± 4.4 65.0– 80.0	4.603	0.005

Serum albumin(g/L)	38.2 ± 2.8 33.0 – 44.0	39.2 ± 2.9 35.0 – 45.0	4.49	0.036
HDL(mmol/L)	1.2 ± 0.1 0.9 – 1.4	1.5 ± 0.1 1.2 – 1.8	18.381	<0.001
LDL(mmol/L)	3.4 ± 0.1 2.9-3.8	3.1 ± 0.2 1.6 – 2.8	12.586	<0.001
Fasting triglycerides (mmol/L)	1.9 ± 0.2 1.6 – 2.3	1.1 ± 0.2 0.7 – 1.2	18.003	<0.001
Total cholesterol(mmol/L)	4.8. ± 0.6 4.0 – 5.7	4.8 ± 0.4 3.6 – 5.7	0.428	0.733

ALT: alanine aminotransferase; AST: aspartate aminotransferase; eGFR: estimated glomerular filtration rate; Hb: hemoglobin; HDL: high density lipoprotein; LDL: low density lipoprotein; n: number; P< 0.05: statistically significant; P< 0.01: highly statistically significant

Table 4 shows that Hb, ALT, AST, serum total protein, albumin, HDL and eGFR are significantly lower in patients with CKD while serum creatinine, urea, LDL and triglycerides are significantly higher in patients with CKD

Table (5): Comparison of handgrip strength (HGS) in cases and controls

	Cases (n = 73) **Mean ± SD** **Range**	**Control (n = 73)** **Mean ± SD** **Range**	**T test**	**P value**
HGS (Kg)	30.1 ± 3.9 24 – 35	34.8 ± 3.2 32 – 38	2.67	0.008

HGS: handgrip strength; n: number; P< 0.05: statistically significant; P< 0.01: highly statistically significant; SD: standard deviation.

Table 5 shows that HGS is lower in CKD patients as compared to control group with highly significant difference

Table (6): Comparison ofTimed Up and Go Test between cases and controls

	Cases (n = 73)	**Control (n = 73)**	**T test**	**P value**
	Mean ± SD Range	**Mean ± SD Range**		
TUGT(seconds)	15.5 ± 1.5 12 -22	7.8 ± 1.2 6 – 10	34.61	<0.001

n: number; P< 0.05: statistically significant; P< 0.01: highly statistically significant; TUGT: timed up and go test

Table 6 shows that TUGT is more prolonged in CKD patients than in the control group with highly significant difference

Table (7): Correlations of hand grip strength (HGS) and Timed Up and Go Test (TUGT) with other variables in the whole subjects.

Variable	**HGS**		**TUGT**	
	r	**P**	**r**	**P**
Age	0.102	0.311	0.104	0.304
Gender	-0.011	0.913	-0.055	0.587
BMI	0.172	0.087	0.128	0.203
SBP	0.027	0.792	-0.029	0.772
DBP	0.060	0.555	0.042	0.676
MAC	0.108	0.285	0.175	0.081
MCC	0.195	0.052	0.103	0.307
Hb	0.349	<0.001**	-0.205	0.041*
WBCs	-0.068	0.501	0.139	0.167
Platelets	-0.026	0.794	-0.159	0.115

blood urea	-0.006	0.956	0.023	0.821
Serum creatinine	0.026	0.796	0.108	0.285
ALT	-0.066	0.516	-0.001	0.995
AST	0.000	0.997	0.013	0.894
Serum albumin	0.452	<0.001**	- 0.275	0.006**
Total bilirubin	0.010	0.925	0.092	0.360
Total cholesterol	-0.087	0.392	0.110	0.274
Triglycerides	-0.293	0.003**	-0.183	0.068
HGS	-	-	-0.278	0.005**
TUGT	-0.278	0.005**	-	-
**. Correlation is highly significant at the 0.01 level (2-tailed).				
*. Correlation is significant at the 0.05 level (2-tailed).				

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; DBP: diastolic blood pressure; Hb: hemoglobin; HGS: handgrip strength; MAC: mid upper arm circumference; MCC: mid-calf circumference; SBP: systolic blood pressure; TUGT: timed up and go test; WBCs: white blood cells.

Table 7 shows a high significant positive correlation between HGS and both Hb and albumin levels and a high significant inverse correlation between HGS and fasting triglycerides. Both serum albumin and Hb are negatively correlated with TUGT. Highly significant inverse correlation is found between HGS and TUGT.

Table (8): comparison of Handgrip strength (HGS) and Timed Up and Go test (TUGT) between pre-dialysis and hemodialysis patients

	Predialysis patients (n = 37)	**Hemodialysis patients (n = 36)**	**T test**	**P value**
	Mean ± SD Range	**Mean ± SD Range**		

HGS (kg)	30.6 ± 2.4 25 – 35	29.1 ± 2.3 24 – 33	2.766	0.004
TUGT (seconds)	14.8 ± 1.3 12 – 17	16.3 ± 1.3 14 – 22	4.496	<0.001

HGS: handgrip strength; n: number;P < 0.05: statistically significant; P < 0.01: highly statistically significant; SD: standard deviation; TUGT: timed up and go test

Table 8 shows HGS is significantly higher in predialysis patients as compared to patients on regular hemodialysis while TUGT was prolonged in hemodialysis patients as compared to predilaysis patients with high significant difference

Figure (1) showing a highly significant inverse correlation between handgrip strength and timed up and go test; HGS: handgrip strength; TUGT: timed up and go test

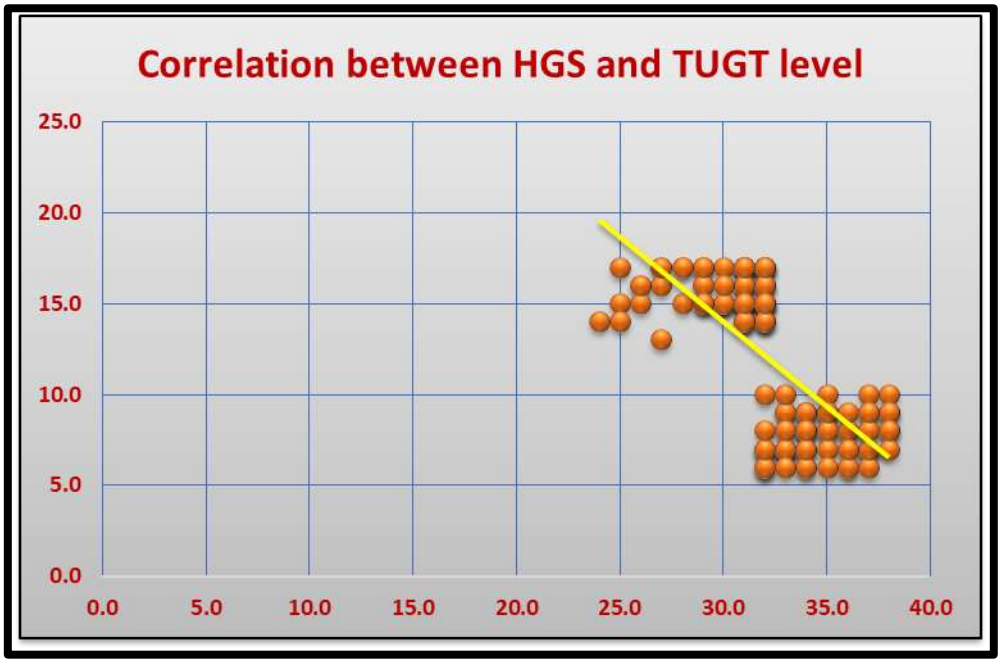

Figure (1): Negative correlation between HGS and TUGT.

Regarding blood pressure (BP), both systolic and diastolic BP were significantly higherin patients with CKD as compared to healthy participants (144.13 ± 21.76 vs131 ± 14.1, p= 0.016 respectively for systolic BP and 85.37 ± 10.7 vs79.5 ± 9.01, p=0.022 respectively for diastolic BP) as shown inTable 3.

Hemoglobin concentration (Hb%), ALT, AST, serum total protein, albumin, HDL,and eGFRwere significantly lower in patients with CKD while serum creatinine, urea, LDL, and triglycerides were significantly higher in patients with CKD as shown in Table 4.

HGS was lower in CKD patients as compared to the control group with a highly significant difference (30.1 ± 3.9 vs34.8 ± 3.2, p=0.008, respectively) as shown in Table 5. TUGT was more prolonged in CKD patients than in the control group with a highly significant difference (15.5 ± 1.5 seconds vs. 7.8 ± 1.2 seconds, p<0.001, respectively) as shown in Table 6.

There was a highlysignificant positive correlation between HGS and both Hb and albumin levels(r=0.349, p<0.001 for Hb and r=0.452, p<0.001 for albumin) and a highlysignificant inverse correlation between HGS and fasting triglycerides (r=-0.293, p=0.003). Both serum albumin and Hb were negatively correlated with TUGT (r=-0.275, p=0.006 for albumin and r=-0.205, p=0.041for Hb). A highly significant inverse correlation was found between HGS and TUGT(r=-0.278, p=0.005) (table 7 and figure 1).

HGS was significantly higher in predialysis patients as compared to patients on regular hemodialysis (30.6 ± 2.4 vs29.1 ± 2.3, p=0.004, respectively) as shown in Table 8.

TUGT was more prolonged in hemodialysis patients than inpredilaysis patients with a highly significant difference (16.3 ± 1.3vs14.8 ± 1.3, p<0.001, respectively) as shown in Table 8.

IV. DISCUSSION

CKD has received increasing attention as a major public health problem around the world.[18] The burden of CKD was not only reflected in the needs for life-long dialysis or renal replacement therapy when entering ESRD, but also highlighted in association with a higher risk of morbidity (especially due to cardiovascular disease), mortality, hospitalization, and cognitive dysfunction.[19]

Besides carrying negative prognostic effectsin general and selected diseased populations, involvingolder ones, CKD also has negative effects in terms of functional disability, including impaired physical performance, frailty, and sarcopenia.[20]

Muscle strength is an important determining factorof healthy aging. A declinein muscle mass and strength is known to worsenbody function. Weakness in muscle strength in older adults is a common problem and is associated with physical disability and functional limitation.[1]

Our study included 73 CKD patients, as well as 73 healthy participants, as a control group.

The muscle strength of the upper limb was assessed using the HGS test, and our results showed that the patients with CKD had a significantly lower HGS value in comparison to the healthy participants.

In agreement with our results, Taşoğluet al.[21] reportedsignificantly low HGS values in 148 CKD patients as compared to 40 healthy participants. Also in agreement with our results, a very recent study by Turon-Skrzypinskaet al.[22]found significantly low mean HGS values in 30 CKD patients as compared to healthy participants.

In partial agreement with our results, Tran et al.[23]reported in their study on 330 nondisabled community-dwelling adults aged ≥ 65 years (134 (40%) had CKD and 196 (60%) had not) that patients with CKD, the HGS was non

significantly low when compared to those with no CKD. Also,Roshanravanet al.[24]reported a non-significant change in HGS in CKD patients as compared to normative values, a finding that is recently reported also by Toyama et al.[25]

In our study, the muscle strength of the lower limb was assessed by using the TUGT and our results showed that the patients with CKD had prolonged TUGT value in comparison to the healthy participants with a highly significant difference.

Taşoğluet al.[21]reported a significant prolongation in TGUT in their CKD patients as compared to healthy participants (p= 0.001), a result that is similar to ours. Also, Roshanravanet al.[24] previously reported significantly prolonged TUGT in CKD patients in comparison to normative values.

Ortega-Pe´rez de Villar et al.[26]showed in their study of 71 end-stage CKD patients receiving hemodialysis therapy, that the relative reliability of TGUT for patients undergoing hemodialysis is excellent (intraclass correlation coefficient = 0.96), therefore suggesting that this was an appropriate test for assessing this aspect of physical function in CKD patient groups. Additionally, this was the only test that correlated with the inverse creatinine values of the sample.

In partial agreement with our results using a different tool to assess lower limb muscles, Broers et al.[6]assessed lower limb muscle strength by using the gait speed test and noticed a significant change in CKD patients as compared to healthy participants.

In the systematic review done by Zemp et al.,[27]all the studies showed that CKD patients had a significantly slower gait speed, both at self-selected and at maximal walking speed in comparison to age-matched healthy controls. They attributed their finding tothe association of gait speed in CKD patients with physical, cognitive,sensory, and metabolic capacities and because all of these factors are influenced by CKD severity, slowing down of walking speed seems a logical consequence.[27]

Contrarily, Toyama et al.[25]found a non- significant change in gait speed among CKD patients.

In our results, the level of statistical significance ($p<0.001$) of the prolongation of TUGT time (mean nearly doubled) was more powerful than the level of statistical significance ($p= 0.008$) of the decrease in HGS values (mean decreased by about 13%), in cases as compared to the control. This may suggest that deterioration of lower limb muscle function is more than that in upper limb muscle function in our CKD patients.

This agrees with Roshanravanet al.[24]who reported that measures of lower extremities performance (including TUGT) were at least 30% lower than predicted, but HGS value was relatively preserved in their 384 CKD patients. They found that each –second longer TUGT was associated with an 8% higher risk of death.

Recently, Alyet al.[28] also found that lower limb muscle function (reflected by TUGT and gait speed) was more affected than upper limb muscle function (reflected by HGS values) in 80 CKD patients. Alyet al.[28]suggested a minimal role of upper limb muscles in gross mobility tasks, and hence lower extremity strength may be better associated with functional activities in comparison to the upper limb. More recently, Wyngaertet al.[29] reported that impairment of physical function is especially pronounced in lower limb muscle strength in CKD patients. Also,

Zanottoet al.[30]found that HGS differed insignificantly between fallers and non-fallers CKD patients, while a significant difference was noted as regards TUGT.

One of the aims of our study was comparing HGS values and TGUT duration between pre-dialysis and dialytic CKD patients. In this regard, our results revealed a significant decrease in HGS and significant prolongation of TGUT in dialytic compared to pre-dialysis CKD patients, reflecting more decrease in upper and lower limb muscle function in dialytic compared to pre-dialysis CKD patients.

Goto et al.[31]reported in their study on 285 patients ≥ 65 years (196 patients at the time of dialysis initiation and 89 patients who chose maximal conservative management "MCM") in order to assess the prevalence of geriatric impairments and frailty in the elderly ESRD population, that the incidence of immobile patients was higher in dialysis patients in comparison to those who chose MCM. Also, the incidence of impaired TUGT was higher in dialysis patients than in the other patients' group.

In partial similarity to our results, Broerset al.[6] found a decline in HGS and gait speed in dialysis patients as compared to CKD-5 non-dialysis patients, but contrary to ours, this decline was non-significant.

In concordance to our results to some extent, Hirakiet al.[32]found a significant decrease in HGS and gait speed in stage 4 and 5 CKD patientsas compared to stage 2 and 3 CKD patients.

Contrarily, Taşoğluet al.[21]noticed a non-significant difference in HGS and TUGT between stage 3 CKD patients and stage 4 and 5 CKD patients. Recently,Toyama et al.[25]also reported a non-significant association between the severity of CKD and both HGS and gait speed.

In the present study, we found no significant difference between the studied groups as regards anthropometric measures, as well as no significant correlation between either HGS or TUGT and these measures.

On the other hand, Abdulanet al.[33]found a strong correlation between anthropometric measures and HGS in 80 patients with CKD hospitalized in a geriatric unit. Also, Birajdaret al.[34] found a significant correlation between HGS and MAC (r= 0.294, p= 0.007). Meanwhile, Alyet al.[28]found a significant negative correlation between TUGT and MCC (r -0.359, p= 0.02) in their 80 CKD patients. More recently, Lee et al.[34]in his study of 277 hemodialysis patients, also found that MAC was positively correlated with HGS and gait speed, although the statistical significance was marginal.

Differences in ethnicity, dialysis modalities, duration of dialysis, patient characteristics, sample size, using different cut-off values, and presence of comorbidities may explain these differences among the studies.

The decreased muscle strength and physical function in elderly CKD patients can be explained by several mechanisms responsible for these symptoms, such as hormonal imbalance, malnutrition, adenosine triphosphate (ATP) and glycogen depletion, metabolic acidosis and electrolyte imbalance, poor oxygen transport as a resultof anemia, lifestyle changes, muscle wasting, and weakness because of muscle fiber atrophy.[35]

Our results showed a significant negative correlation between HGS and TGUT (r = - 0.278, p= .005), a result that was near to that obtained by Nogueiraet al.[36](r= -0.456, p= 0.008) in their study of 122 CKD patients.

In contradiction to our results, Alyet al.[28] reported non-significant negative correlation between HGS and TUGT (r = - 0.039, p= 0.807) in their study of 80 CKD patients.

Regarding the correlation between HGS and other variables in the study, our results showed that there was a strong direct correlation between muscle strength assessed by HGS and Hb%.

Cesari et al.[37] who studied 909 elderly aged ≥ 65 years to detect whether Hb%is associated with differences in quantitative and qualitative measures of muscle and fat found that Hb%wasassociated with muscle mass (evaluated by peripheral quantitative computed tomography (pQCT) scan), a finding that is near to our result.

Penninx et al.[38] who examined the association between anemia & physical performance and muscle strength in 1156 older persons aged ≥ 65 years found that anemia was associated with poorer physical performance and lower muscle strength, a result that is consistent with our finding.

Also, Fukushimaet al.[39] detected a significant strong direct correlation between Hb% and muscle strength.

Our result showed also a strong direct correlation between muscle strength assessed by HGS and Albumin level.

In disagreement with our finding wereBirajdar et al.[34]who reported in their prospective observational cross-sectional study on 83 hemodialysis patients that there was no significant correlation between HGS and Hb%or albumin levels.

Our study showed also that there was a significant negative correlation between TUGT and both Hb and albumin levels.

In disagreement with our findings, Alyet al.[28] reported a non- significant correlation between TUGT and Hb%.

Our study was designed on a selection of cross-matched participants for age and gender to avoid the effect of these factors on our findings so, our results showed that there was no statistically significant difference between case and control groups as regard age and gender distribution with p-value = 0.911 and 0.407 respectively.

Regarding smoking habit, our results showed that in the case group; 64.4% of our patients were non-smokers, 16.4% were current smokers and 19.2% were ex-smokers. While in the control group 72.6% of them were non-smokers, 12.3% were current smokers and 15.1% were ex-smokers. There was no significant difference between both groups with p-value= 0.563.

In our study systolic and diastolic BP were significantly higher in the cases group than the control group; these results are in agreement with Ridao et al.[40] This can be attributed to several factors including sodium retention, volume excess, activation of the renin-angiotensin-aldosterone system, activation of the sympathetic nervous system, endothelium-derived vasoconstrictor substances, erythropoietin use, and pre-existent essential hypertension.[41]

Regarding liver functions tests, our results showed that serum ALT and AST were significantly lower in the case group as compared to the control group;in agreement with Sette and de Almeida Lopes[42] who reported that the serum aminotransferase levels were lower in the patients with ESRD on hemodialysis than in the patients with normal renal function.

A recent study by Latiweshet al.[43] concluded that serum AST and ALT levels tend to be reduced in CKD patients, particularly in those on maintenance hemodialysis.

The exact cause of low serum aminotransferase levels in CKD remains controversial, possible reasons include pyridoxine deficiency and/or the presence of an inhibitory substance in the uremic milieu.[42]

Also, Total plasma protein and serum albumin were significantly lower in the case group as compared to the control group; this can be due to one or more of the following factors; loss of appetite, diabetic gastroparesis, mechanical compression of stomach and intestine in polycystic kidney disease, Immobility and reduced ability to purchase food, inadequate dietary recommendations, Comorbidity, socioeconomic factors (e.g. poverty, social deprivation), depression, chronic inflammation, dialysis-associated amino acid, and protein loss, metabolic acidosis, inadequate dialysis dose, inadequate dental status, proteinuria and complications of dialysis (e.g. nausea, hypotension).[44]

Regarding Hb%, our results showed that patients in the cases group had significantly lower Hb% in comparison with those in the control group. This was in agreement with McClellan et al.[45] who reported that anemia was present in 47.7% of 5222 predialysis patients with CKD. Another study by Khan and Elderdery[46]also reported lower Hb% in CKD patients as compared to the control group.

This can be attributed to iron deficiency, vitamin B12 or folate deficiency, functional deficiency of iron (due to impaired iron utilization for erythropoiesis), effects of dialysis, bleeding because of platelet function defect, decreased synthesis of erythropoietin, decreased sensitization of erythroblasts to erythropoietin, and the effect of drugs used for treatment.[47]

Regarding lipid profile, our results showed that in comparison to the healthy participants, patients in the case group had a significantly lower HDL level and significantly higher LDL and Triglycerides levels, while regarding total cholesterol level there was no statistically significant difference between the case group and the control group.

These findings were in agreement with Tsimihodimoset al.[48] as they reported that dyslipidemia is a common complication of CKD, and lipid profile depends on the level of kidney function.

Also, de Boer et al.[49] reported that patients with CKD tend to have alterations in both HDL quantity and HDL quality, even a mildly impaired kidney function is associated with low HDL, which becomes progressively worse through ESRD.

Regarding HDL, CKD patients have decreased levels of apolipoproteins AI and AII, the main components of HDL, and impaired the activity of lecithin–cholesterol acyltransferase, the enzyme important for the esterification of free cholesterol in HDL, and increased the activity of cholesterol ester transfer protein (CETP), which supports the transfer of cholesterol esters from HDL to triglyceride-rich lipoproteins.[48]

Usually, patients with CKD have hypertriglyceridemia because of both the delayed catabolism and the increased hepatic production of triglyceride-rich lipoproteins (VLDL, chylomicrons, and their remnants).[50]

V. CONCLUSION

In conclusion, there is a significant decline in upper limb muscle function, as reflected by significant decrease in HGS in CKD patients and there is a significant decline in lower limb muscle function as reflected by a significant prolongation of TUGT in CKD patients. We concluded also that the decline in upper and lower limb muscle function is more evident in the hemodialysis than in the predialysis CKD patients.

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