Original Article

Musculoskeletal Ultrasound Findings in Children with End-Stage Renal Disease on Regular Hemodialysis.

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ABSTRACT

Introduction: Children with chronic kidney disease (CKD) often have musculoskeletal issues, which may be attributed to either chronic kidney disease-mineral and bone abnormalities (CKD-MBD) or dialysis-associated amyloidosis (DRA).

Aim of the study: This study aimed to assess the use of musculoskeletal ultrasonography in detecting any anomalies in the musculoskeletal system of children with end-stage renal disease (ESRD) undergoing regular hemodialysis.

Methods: A retrospective cohort study was carried on twenty-five children with ESRD on regular hemodialysis for more than six months in comparison to twenty-five children with CKD on conservative treatment of matched age and sex. Patients with ESRD on regular hemodialysis < 6 months duration, patients with rheumatological diseases, patients with metabolic diseases and diabetic patients were excluded**.** All patients were subjected to complete history taking and complete clinical examination especially musculoskeletal system examination. Musculoskeletal ultrasound (MSUS) was performed for all patients on joints of upper and lower limbs. Serum β_2 Microglobulin (β_2M) was also performed by HP-AFS/3 specific protein analyzer. Another blood sample was collected for serum parathormone hormone (PTH), serum ionized calcium, serum phosphorus and serum 25-OH Vitamin D.

Results: Arthralgia, growth impairment and bone abnormalities were considerably greater in dialytic patients than in non-dialytic patients (P=0.002, P=0.001, P=0.034). Significant differences in joint number and synovitis severity were seen in the dialytic group for MSUS (P<0.001). The dialytic group had bone erosions, enthesopathy, and CTS (P=0.037). MSUS results showed a substantial positive connection with dialysis time, PTH, and β2M (P<0.001) and a negative correlation with serum ionized calcium and 25-OH Vitamin D (P<0.001).

Conclusion: Children with ESRD on regular hemodialysis had more MSUS findings than CKD children on conservative treatment, which were related to the prolonged duration of dialysis, higher levels of PTH, β2M, and lower levels of serum ionized calcium and serum 25-OH Vitamin.

Keywords: Musculoskeletal Ultrasound; End-stage renal disease; Hemodialysis

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INTRODUCTION

According to the guidelines set by the Kidney Disease Improving Global Outcomes (KDIGO) foundation, chronic kidney disease (CKD) is defined as the presence of two factors: a glomerular filtration rate (GFR) lower than 60 mL/min/1.73m^2 and a urinary albumin/creatinine ratio higher than 30 mg/g. These factors must be accompanied by abnormalities in kidney structure or function that persist for a period of more than three months. End-stage renal disease (ESRD) is the fifth and last stage of CKD development. It is characterized by a GFR of less than 15 mL/min/1.73m^2. Renal replacement treatment is necessary in this circumstance **[1]**.

Hemodialysis (HD) is one of replacement therapy in which body waste products are removed, but this is associated with increased or decreased levels of some chemical parameters and despite the progress in HD techniques, musculoskeletal disorders remain a major problem in HD patients **[2, 3].**

High frequency musculoskeletal diseases connected to HD are sometimes found, with rates ranging up to 78% and 70% **[3].** These conditions include dialysis-associated arthropathy and chronic kidney disease-mineral and bone disorders (CKD-MBD). This may be attributed to either one or a combination of the following systemic components: The abnormalities that can occur in individuals undergoing dialysis include: (a) disruptions in the metabolism of calcium, phosphorus, parathormone hormone (PTH), or vitamin D, (b) disturbances in bone turnover, mineralization, volume, linear growth, or strength, (c) calcification of blood vessels or other soft tissues, (d) amyloidosis caused by the accumulation of β2 microglobulin fibrils when low flux dialyzers are used, (e) protein energy malnutrition resulting from catabolism induced by hemodialysis, characterized by muscle wasting, and (f) infection caused by the use of dialyzer membranes that are not compatible with the patient's biology **[4, 5].**

The diagnosis of changes in biochemical parameters resulting from dialysis is determined by clinical and laboratory assessments. Nevertheless, these assessments are unable to determine the magnitude of musculoskeletal involvement properly. Imaging modalities like ultrasound can immediately see and accurately measure this condition. Over the years, musculoskeletal ultrasound (MSK-US) has been referred to as the stethoscope of this profession by several rheumatologists **[6].** The objective of this research was to detect any abnormalities in the musculoskeletal system of children with end-stage renal illness who get regular hemodialysis using musculoskeletal ultrasonography.

METHODS

This retrospective cohort analysis was conducted in the Nephrology Unit of the Pediatric Department at our University Hospitals from January 2022 to January 2023. The study was ethically approved on 35253/2/22.

Fifty children with CKD were included in this study and were divided into two groups: Group I (Dialytic) included 25 children with ESRD.

Inclusion criteria: Individuals between the ages of 1 and 18 who have ESRD who have been receiving regular hemodialysis for more than 6 months. The patients were receiving hemodialysis three times per week, using both the Fresenius 4008S and 5008S dialysis machines from Germany. Each dialysis session lasted for three to four hours. The blood flow rate was calculated based on

the formula 2.5 x weight (kg) + 100ml/min. Polysulphane hollow fibre dialysers with surface areas suitable for the patients' needs were used, including F3 (0.4 m^2), F4 (0.7m^2), F5 (1.0m^2), and F6 (1.2m^2). Utilized were dialysis solutions containing bicarbonate.

Exclusion criteria: Patients with ESRD on regular hemodialysis < 6 months duration, patients with rheumatological diseases, patients with metabolic diseases or diabetic patients.

Group II (Non-dialytic) included 25 children with CKD (G1-G4) according to KDIGO foundation guidelines **[7].** Patients with comorbidities like those suffering from rheumatological diseases, septic arthritis or diabetes were excluded.

All patients were subjected to the following: Complete History taking, Complete clinical examination including anthropometric measurement, blood pressure measurement and musculoskeletal system examination**.** Laboratory investigations were done including serum phosphorus, serum ionized calcium serum 25-OH vitamin D **[8]** and serum β2 Microglobulin **[9]** and radiological examination by musculoskeletal ultrasound Examination **[10].**

The patients underwent examination in the ultrasound unit of the Physical Medicine, Rehabilitation & Rheumatology Department of Tanta University Educational Hospital using SAMSUNG MEDISON equipment.

-Model: UGEO H60. -Power: 100-240 V. 50/60 Hz. -Made in: Korea. -MFG date: 2013.01

Joint Scan approach: Hip, Knee (Lateral parapatellar recesses and Medial parapatellar recesses), Ankle (Anterior Longitudinal), MTP joints / IP joints, Shoulder (Supraspinatus tendon and subacromial bursa and Supraspinatus tendon and subacromial bursa), Elbow (Anterior Humeroulnar Longitudinal and Posterior Longitudinal), Wrist (Dorsal Longitudinal Midline and MCP joints / IP joints) and Carpal tunnel (transverse scan) **Figure 1**. MSUS can recognize most of the secondary forms of CTS with a sensitivity and specificity equal to those of electrophysiological tests. In CKD patients, it occurs mainly due to amorphous amyloid deposition. Imaging criteria for detection of CTS on ultrasonography include:

(A)Swelling of the median nerve: This can be assessed at varying levels within the carpal tunnel.

(B)Flattening ratio (FR): Usually the median nerve is swollen in the proximal tunnel and flattens in the distal tunnel. This is measured by the FR.

(C)Palmer bowing of the flexor retinaculum: This is seen secondary to increased pressure in the carpal tunnel.**[11]**

Statistical analysis

The data were inputted into the computer and analyzed using the IBM SPSS software program, namely version 20.0. The location of IBM Corp is Armonk, NY. Quantitative data were represented using numerical values and percentages. The Shapiro-Wilk test was used to confirm the normality of the distribution. The quantitative data were characterized using several statistical measures, including the range (minimum and maximum values), mean, standard deviation, median, and interquartile range (IQR). The significance of the acquired findings was assessed using a significance threshold of 5%. The tests used were the Chi-square test, Fisher's Exact or Monte Carlo correction, Student t-test, Mann-Whitney test, ANOVA test, Kruskal-Walli’s test, and Pearson correlation test.

Figure 1: Ultrasound equipment used in the study

RESULTS

There was no significant difference between the two studied groups regarding demographic data. The age of children in Group I (dialytic group) was between 3 and 17 years, with a mean of 10.2 ± 3.39. In Group II (non-dialytic group), it was between 3 and 16, with a mean of 9.68 ± 3.37. As regards the Male: Female Ratio, it was

1.08: 1. Anthropological measurements were slightly affected in the dialytic group than in the non-dialytic one.

The most common cause of renal disease in our studied children was congenital anomalies of kidney and urinary tract (CAKUT) represents about (52%), followed by steroid-resistant nephrotic syndrome (SRNS) (36%), hemolytic uremic syndrome (HUS) (8%), nephritic syndrome (NS) (4%). Regarding CKD stage , G5 represented about (50%) of all studied children . While G1, G2 , G3a , G3b and G4 represented about (8% , 12% , 12% ,8% and 10%) of all studied children respectively.

Dialytic children started dialysis at ages between 1 and 14 years, with a mean of 7.82 ± 3.75. (88%) of total dialytic children dialysed with high-flux dialyzers, while only (12%) dialysed with medium-flux dialyzers. The duration of dialysis ranged between 8 and 84 months, with a mean of 30.24 ± 17.08. Musculoskeletal manifestations including (arthralgia, muscle spasm, joint limitation, growth impairment, bone deformities and history of bone fractures) were significantly observed in dialytic children. Arthralgia was the most common complaint in both groups. **Figure 2.** As regard to PTH, serum phosphorus and β_2 microglobulin, they were significantly higher in dialytic children. While serum ionized calcium and 25-OH vitamin D were significantly lower in dialytic children. **Table 1**

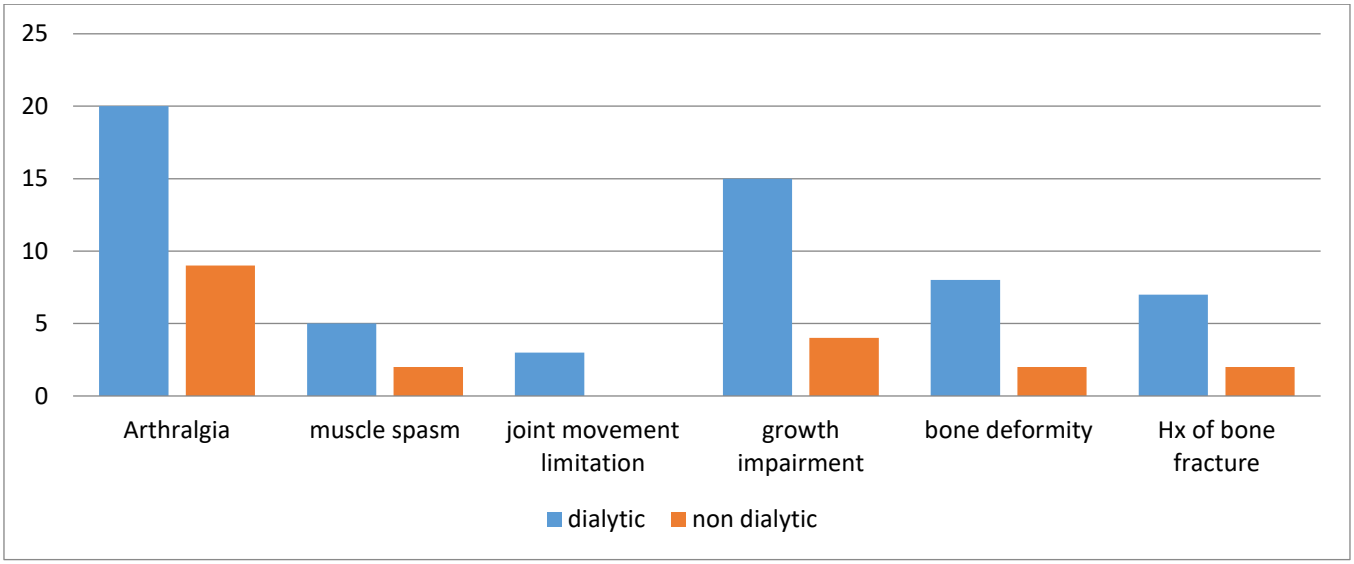

Figure 2: Comparison between musculoskeletal complaints in two studied groups.

Table 1: Comparison between the two studied groups according to laboratory investigations

Data		Group I	Group II	T-Test	
				t	P-value
PTH (pg/ml)	Min. – Max.	128 - 995	55 - 167	-7.328	<0.001*
	Mean ±SD	435.80 ± 237.46	85.00 ± 30.03		
Serum Ionized Calcium (mmol/L)	Min. – Max.	0.6 - 1.1	0.9 - 1.3	2.330	0.024*
	Mean ±SD	0.97 ± 0.12	1.05 ± 0.09		
Serum Phosphorus (mg/dL)	Min. – Max.	3.7 - 11.7	3.6 - 6.8	-2.469	0.017*
	Mean ±SD	6.26 ± 1.72	5.31 ± 0.88		
Serum 25-OH Vit D (ng/ml)	Min. – Max.	14 – 34	15 - 41	2.609	0.012*
	Mean ±SD	23.72 ± 5.81	28.52 ± 7.13		
Serum β_2 microglobulin (mg/l)	Min. – Max.	22 – 41	1 - 3.5	-30.681	<0.001*
	Mean ±SD	31.77 ± 4.75	2.29 ± 0.66		

Data are presented as Mean ± SD or range, * significant p value ≤ 0.05, PTH: parathormone hormone.
25-OH vitamin D: 25hydroxy vitamin D

There was significant difference in musculoskeletal ultrasound findings between two studied groups. Number of joints affected per case in dialytic children was 3 – 15 with median 8 (6.0 – 10.5) varied between (grade 1, 1 to 2 and 2 to 3) while in non dialytic children it was 0 – 10 with median 2 (0.0 – 4.5) with only grade 1 severity. In dialytic children only , bone erosion , enthesopathy and CTS represented about (16%) of cases for each. **Table 2.**

There was a significant difference in thickness of median nerve at carpal tunnel level between the two studied groups. Cross sectional area of both right and left median nerve were significantly larger in dialytic group than non-dialytic one. **Table 3.** Number of joints affected per case had significant positive correlation with "CKD stage, PTH, β_2 microglobulin and duration of dialysis " and significant negative correlation with serum ionized calcium, and serum 25-OH vitamin D. **Table 4 & Figure 3.**

Table 5 shows Comparison between the two studied groups according to median nerve cross-sectional area. While **Table 6** emphasizes the Correlation between the numbers of joints affected per case and CKD stage, age of diagnosis, HD duration and laboratory data in all the studied cases.

Table 2: Comparison between the two studied groups according to musculoskletal ultrasound findings

		Group I	Group II	test	P value
Number of joints affected per **case**	Min. – Max.	3 - 15	0 - 10	U=-7.187	<0.001*
	Median (IQR)	8 (6.0 – 10.5)	2 (0.0 – 4.5)		
Severity	Grade 1	7(28%)	17(68%)	χ^2=30.167	<0.001*
	Grade 1 to 2	16(64%)	0(0%)		
	Grade 2 to 3	2(8%)	0(0%)		
Bone erosions		4(16%)	0(0%)	χ^2=4.348	0.037*
Enthesopathy		4(16%)	0(0%)	χ^2=4.348	0.037*
Carpal tunnel syndrome (CTS)		4(16%)	0(0%)	χ^2=4.348	0.037*

Data are presented as Mean ± SD or frequency (%), * significant p value ≤ 0.05. SD :standard deviation

Table 3: Classification of synovitis According to grey scale mood with MSUS **[12]**

Synovitis grade	Definition
Grade 0	No synovial hypertrophy (SH) independently of the presence of effusion
Grade 1	SH with or without effusion up to level of horizontal line connecting bone surfaces
Grade 2	SH with or without effusion extending beyond joint line but with upper surface convex (curved downwards) or hypertrophy extending beyond joint line but with upper surface flat
Grade 3	SH with or without effusion extending beyond joint line but with upper surface flat or convex (curved downwards).

SH: synovial hypertrophy MSUS: musculoskeletal ultrasound

Table 4 : ROC curve between dialytic and non dialytic group.

	Cutoff	Sens.	Spec.	PPV	NPV	Accuracy
Number of joints affected	**>4**	**96.00**	**76.00**	**80.0**	**95.0**	**91.3%**

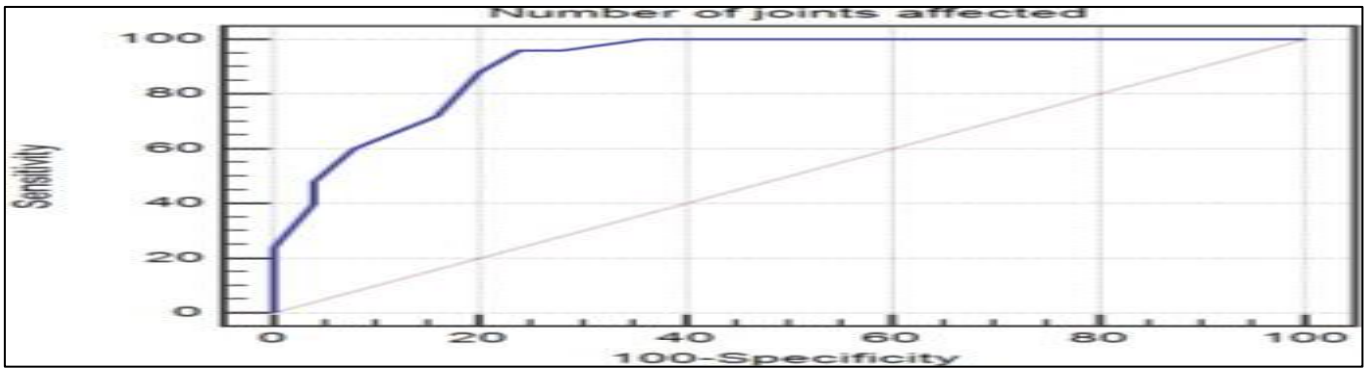

Figure 3: The most affected joint was knee followed by elbow in both groups.

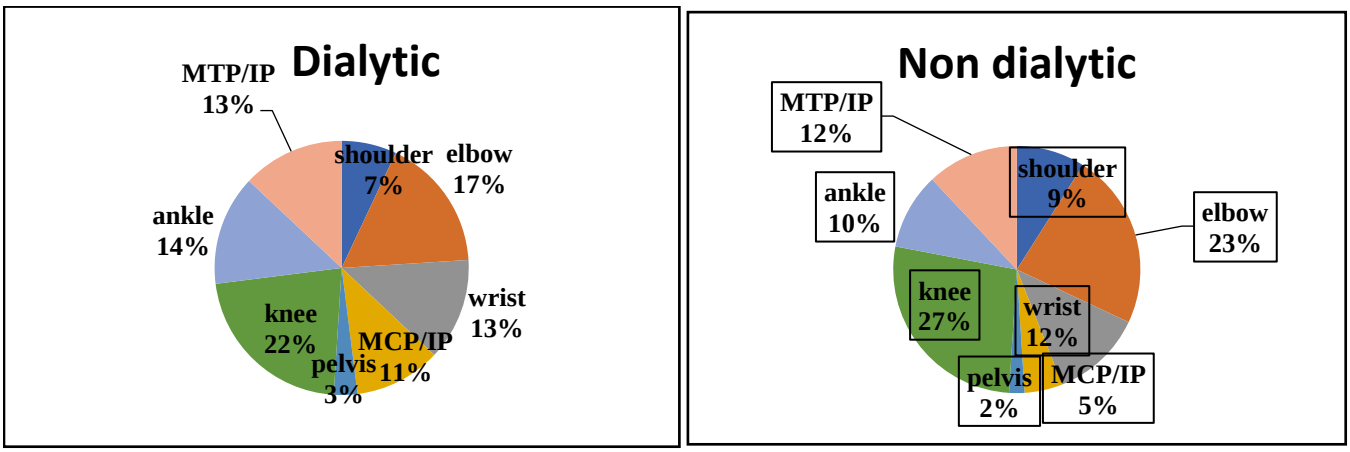

Figure 4: Comparison between affected joints distribution in two studied groups

Table 5: Comparison between the two studied groups according to median nerve cross-sectional area
Data are presented as Mean ± SD or range, * significant p value ≤ 0.05. CSA: cross sectional area.

Median nerve (CSA) for age(mm²)		Group I	Group II	T-Test	
				t	P-value
Right	Min. – Max.	2.9 - 7	2.9 - 5.7	-2.877	0.006*
	Mean ±SD	5.26 ± 0.89	4.59 ± 0.75		
Left	Min. – Max.	2.7 - 6.2	2.8 - 5.4	-2.510	0.016*
	Mean ±SD	4.97 ± 0.84	4.42 ± 0.71		

Table 6: Correlation between the numbers of joints affected per case and CKD stage, age of diagnosis, HD duration and laboratory data in all the studied cases

		Number of cases		Number of joints affected per case	Test	
		N	%	Median (IQR)	Test	P-value
CKD stage	G1	4	8%	0 (0-0.25)	Kw = 35.853	<0.001*
	G2	6	12%	0 (0-0.75)		
	G3a	6	12%	2 (0.5-2.75)		
	G3b	4	8%	2 (2-2.5)		
	G4	5	10%	7 (7-8)		
	G5	25	50%	8 (6-10)		
					r	P-value
Age of diagnosis (Years)					-0.005	0.973
PTH (pg/ml)					0.777	<0.001*
Serum Ionized ca (mmol/L)					-0.522	<0.001*
Serum Phosphorus (mmol/L)					0.261	0.067
Serum 25-OH, Vit D (ng/ml)					-0.671	<0.001*
Serum β_2 microglobulin (mg/l)					0.799	<0.001*
Duration of dialysis (months)					0.661	<0.001*

Data are presented as Mean ± SD or frequency (%), * significant p value ≤ 0.05. CKD: chronic kidney disease., PTH: parathormone hormone. 25-OH vitamin D : 25hydroxy vitamin D

CASE STUDY

Case 1:

A 14-year-old boy with ESRD due to hypoplastic kidney on HD for 7 years complaining about knee arthralgia. **Figure 5**

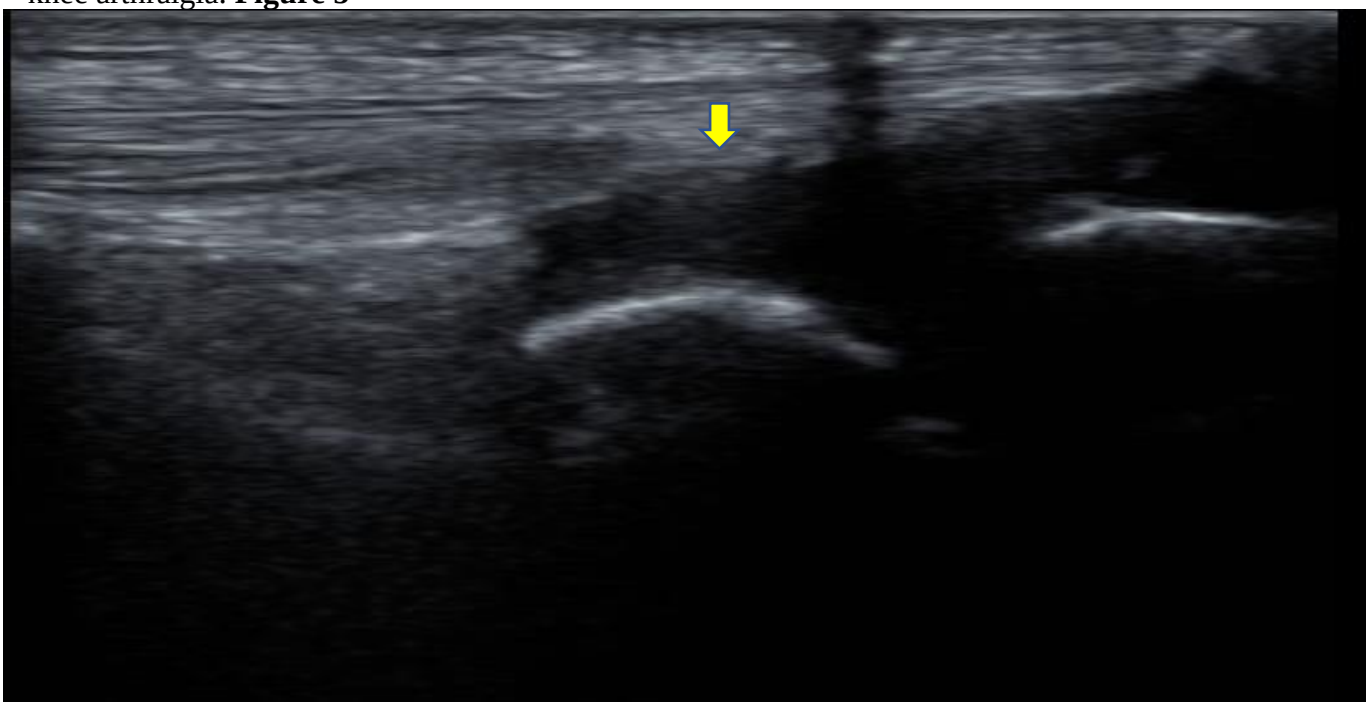

Figure 5: MSUS examination of right knee joint shows: grade 2 to 3 synovitis with minimal effusion.

Case 2:

A 17-year-old boy with ESRD due to Alport syndrome on HD for 3 years complaining about left knee arthralgia. **Figure 6**

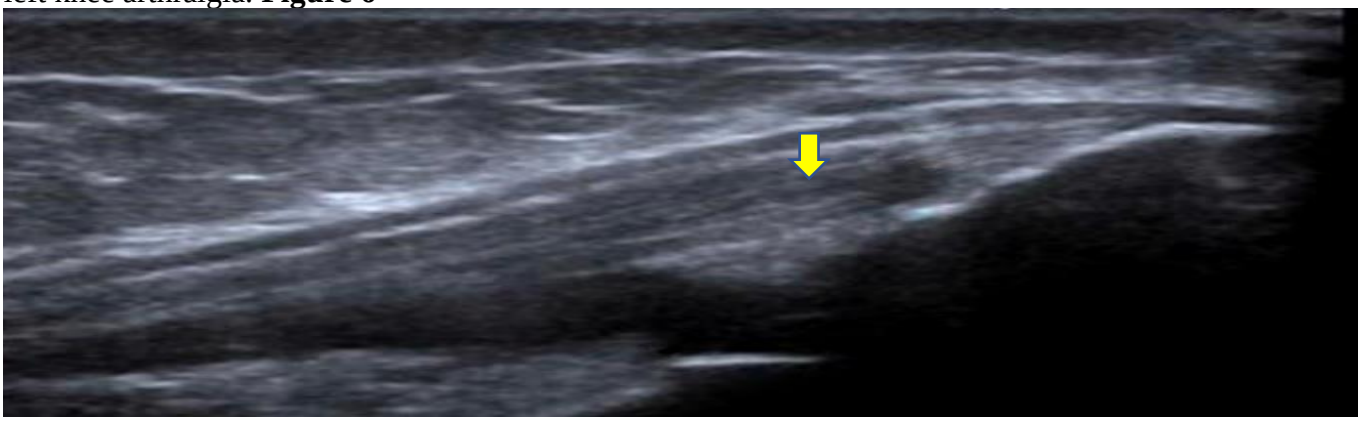

Figure 6: MSUS on left knee shows: Enthesopathy of quadriceps tendon at patellar insertion

Case 3:

A 13-year-old girl with ESRD due to SRNS on HD for 5 years complained about polyarthralgia, especially his knee joint. **Figure 7**

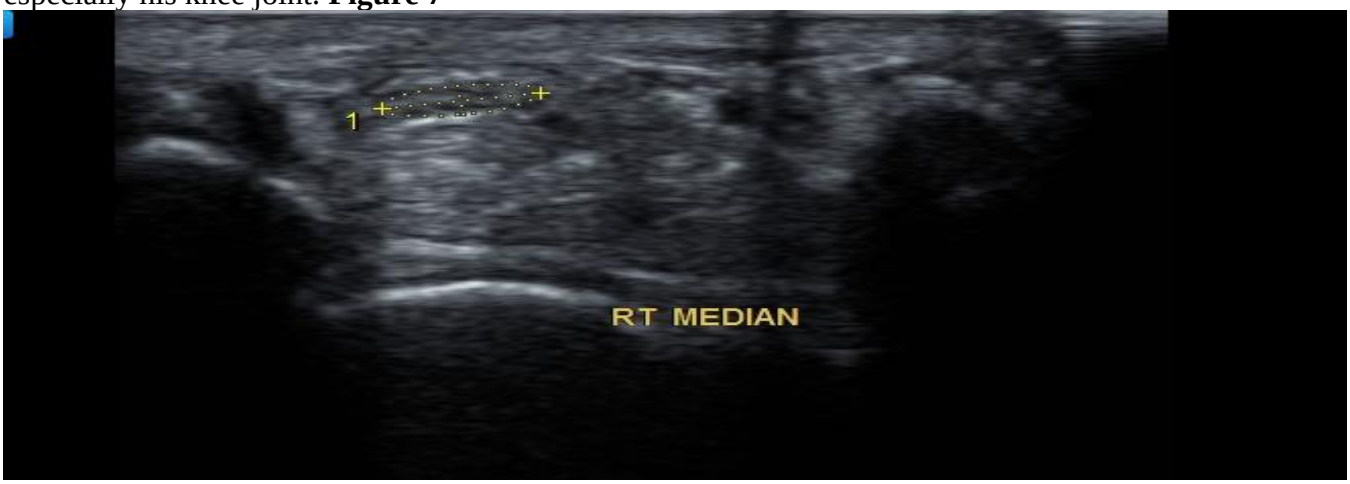

Figure 7: Accidental MSUS on right wrist joint shows: Thickened median nerve above normal indicating subclinical carpal tunnel syndrome

Case 4:

A 16-year-old girl with ESRD due to SRNS on HD for 3 years complained about polyarthralgia and muscle spasms. **Figure 8**

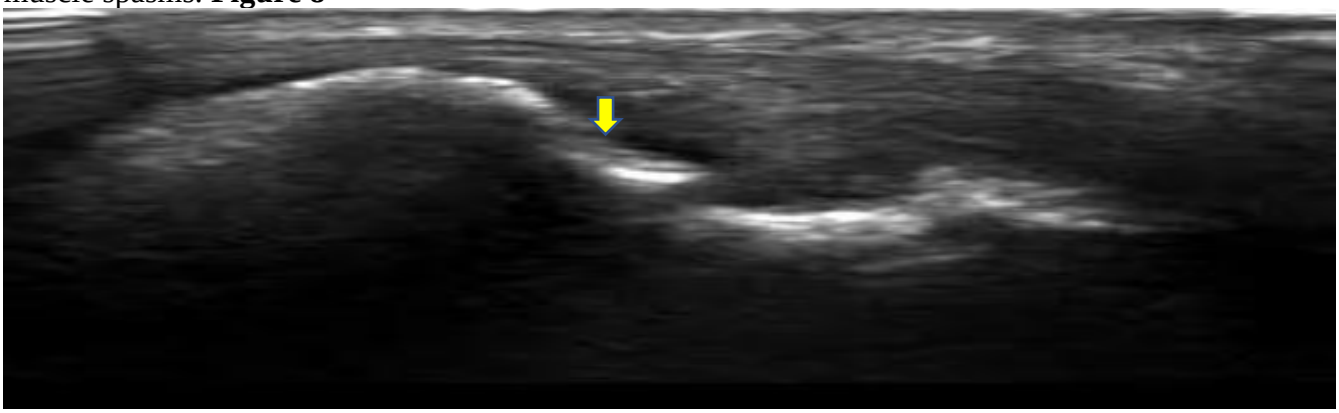

Figure 8: MSUS examination shows: Bone erosions and interrupted cortex of 1st metacarpophalangeal joint. 1st metacarpophalangeal joint spasm, joint limitation, growth impairment, bone deformities, and history of bone fractures.

DISCUSSION

The average age of the dialysis group patients in this research was 10.20 ± 3.39 years, and their ages varied from 3 to 17 years. They were thirteen males and twelve females, with a male-to-female ratio of 1.08 to 1.0. On the other hand, the average age of the patients in the non-dialysis group was 9.68 years, with a range of 3 to 16 years. They were thirteen males and twelve females, with a male-to-female ratio of 1.08 to 1.0.

The results agreed with those of Azarfar A et al. **[13],** who discovered that chronic renal failure was slightly more common in boys (56.4% vs. 43.6% of girls). This could be because boys are more likely to be born with kidney and urinary tract congenital defects (like posterior urethral valves) and SRNS, the most common cause of CKD and ESRD in children. Additionally, estrogen has a function in kidney repair and regeneration via its receptors, which contributes to its nephroprotective action in females.

Our study also showed that anthropometric measurements were slightly affected in the dialytic group than non-dialytic one, mostly due to dialysis related malnutrition. This is consistent with research undertaken by Lacquaniti et al. **[14]** and Casey et al. **[15]** which found that about one-third of dialysis patients have mild to moderate malnutrition, while 6-8% suffer from severe malnutrition. Modifiable iatrogenic variables of malnutrition include low dialysis adequacy resulting in uremia and metabolic acidosis, as well as amino acid loss linked with dialysis membranes and methods. Malnutrition in these individuals may be attributed to modifiable non-iatrogenic variables such as dietary insufficiency, inadequate caloric and protein intakes, poor appetite status, low food quality, and psychological and socioeconomic obstacles.

Regarding CKD causes, the most common cause in our patients was CAKUT (52%) followed by SRNS (34%), and obstructive uropathy was the most common congenital cause representing about (16%) of total causes. This agrees with Amanullah F et al. **[16]** and Masalskienė J et al. **[17]**, who found that the most frequent cause of CKD in their patients was CAKUT represented (49%, 37.9%) respectively. Safouh, H. et al. **[18]** also reported that the most common single cause of CKD was obstructive uropathy (21.7%) more than any other cause. This contradicts the findings of Afifi et al. **[19]** and Ghonemy et al. **[20]** which showed that hypertension and diabetes mellitus were the leading causes of ESRD in their respective patient populations. This disparity is mostly caused by the fact that these studies used bigger sample sizes and covered a variety of age groups and etiologies.

Regarding musculoskeletal manifestations among our CKD children, musculoskeletal complaints were more common in dialytic group than non-dialytic one. Arthralgia was the most common complaint in both groups. As regards dialytic group, they complained about arthralgia in (80%) of cases, muscle spasm (5%), growth impairment (60%) and bone deformities in (32%) of total cases. While in non-dialytic group; (36%) complained about arthralgia, muscle spasm in (8%), growth impairment in (16%) and bone deformities in (8%) of total cases. This was in agreement with El-Najjar et al. **[21]** who found that arthralgia was the most common symptom (25.3%)

among his total cases. In contrast Adle F et al. [22] found that muscle spasm especially carpopedal spasm was the most common musculoskeletal complaint (54%).

Regarding laboratory investigations in our present study, it was found that PTH, phosphorus was significantly higher in the dialytic group than non-dialytic one with (P.value <0.001, 0.017) respectively. While serum ionized calcium and 25-OH Vitamin D were significantly lower in the dialytic group than non-dialytic one with (P.value 0.024 and 0.012) respectively. This agrees with Patel S et al. [23] as there was increasing PTH levels with advanced CKD stage up to dialysis. However, there is disagreement regarding other lab findings as it was reported that there was no influence of CKD stage on 25-OH Vitamin D and serum phosphorus and ionized calcium, and their levels remained quietly constant in different CKD stages. This difference may be related to medication history and dietary supplementations and variations in group size.

Regarding β2 microglobulin levels in our present study, it was noticed that β2M levels is significantly higher in the dialytic group than non-dialytic one with (P.value <0.001). This agreed with Mumtaz A et al. [24] who reported that β2M levels were higher in his dialytic patients about 40-50 folds its levels in control group. This may be related to duration of dialysis, type of dialyzer and residual renal function to excrete this type of metabolite.

Regarding musculoskeletal system affection, the most common joint affected in both groups was the knees joint (22% and 27%) in dialytic and non-dialytic groups respectively. This agrees with El-Najjar et al. [21], Afifi W et al. [19], and Dosogi W et al. [25] who showed that the knee joint was the most commonly affected joint followed by the ankle joint. This can be explained by the nature of knee as large weight bearing joint with more friction.

Regarding musculoskeletal ultrasound findings, in dialytic group; all cases had affected joints with median 8 joints per case especially knee joints with severity of synovitis varying from grade 1 (28%), grade 1 to 2(64%) and grade 2 to 3(8%), bone erosions (16%) and enthesopathy (16%) all of them were quadriceps tendon. while in non-dialytic group only (68%) cases had joint affection with median 2 joints per case but with only grade 1 synovitis. These ultrasound findings may be strictly related to electrolytes and metabolites disturbance which worsen in advanced CKD stages up to dialysis. This agrees with Besar M et al. [26] who reported that synovial hypertrophy in the knee joint was the most common ultrasound finding in their cases, followed by tendinopathy of the biceps tendon. However, this is in discrepancy with Hruska et al. [27], and Murphey et al. [28] who reported that subperiosteal bone resorption was the most common radiological findings in 66% of patients.

Regarding cross sectional area of median nerve, subclinical carpal tunnel syndrome was noticed only in (16%) of dialytic group with significant increase of median nerve in dialytic group than in non-dialytic one with (P.value 0.006 and 0.016) of both hands. This agreed with Besar M et al. [26], who reported carpal tunnel syndrome in only (3.2%) of their subjects and El-Najjar et al. [19] who found carpal tunnel syndrome only in 14.9% of patients. However, there was disagreement with Decianu R et al. [29] who found that carpal

tunnel syndrome was (66%) of his dialytic cases compared to (16%) of his non-dialytic control group. This variation may be attributed to the difference in size and age group of every study.

In our study, the number and severity of joint affection had a significant positive correlation with duration of dialysis. This agreed with Hage V et al. [3] who found that musculoskeletal manifestations are common among hemodialysis patients and increase with dialysis vintage and age. This can be due to the accumulation of more amyloid fibrils with longer duration of dialysis, especially with decreasing residual renal function over time. Also, the age-related inability to dissolve amyloid fibrils suggests the spread of musculoskeletal findings in older populations.

In our study, musculoskeletal ultrasound findings had a significant positive correlation with PTH level, and a significant negative correlation with serum ionized calcium and vitamin D level. This agreed with Afifi W et al. [19] who reported the prevalence of musculoskeletal manifestations in dialytic patients with deficient or insufficient vitamin D, low serum ionized calcium, and secondary hyperparathyroidism. This can be explained by the renal osteodystrophy state, in which the skeletal system is obviously affected by decreased vitamin D level and hypersecretion of parathyroid gland.

In our present study, we found that musculoskeletal ultrasound findings had a significant positive correlation with serum level of β2M. This was in agreement with Kamel SR et al. [30] who reported that sonographic features of dialysis-related amyloidosis are obviously associated with elevated serum levels of β2M. This can be explained by the deposition of β2M amyloid fibrils in joints, tendons, and synovial membrane.

LIMITATIONS OF STUDY

The Study Limitations were Small sample size and short durations of dialysis. MSUS is an effective and bedside method for assessment of musculoskeletal system affection should be compared to other advanced imaging modalities such as Joint MRI.

Other bone markers for assessment of bone density should be compared with β2M.

RECOMMENDATIONS

- Musculoskeletal system affection is common among CKD children and regular screening is recommended.
- Musculoskeletal Ultrasound has a great value in diagnosis of clinical and subclinical musculoskeletal affection in CKD children especially synovitis and carpal tunnel syndrome.
- However musculoskeletal affection was significantly related to long HD duration, further studies on large group of patients with longer HD duration to confirm musculoskeletal changes.
- Correlation of median nerve affection by MSUS with nerve conduction for assessment of type and severity of injury.

CONCLUSIONS

Children with ESRD on regular hemodialysis had more MSUS findings than CKD children, which were related to the prolonged duration of dialysis, higher levels of PTH, β2M, and lower levels of serum ionized calcium and serum 25-OH Vitamin.

ABBREVIATIONS

ACR	Albumin to creatinine ratio	**HUS**	Hemolytic uremic syndrome
ACTRIIA	Activin A type 2 receptor	**KDIGO**	Kidney disease improving global outcomes
AER	Albumin excretion rate	**LRP**	Lipoprotein receptor related protein
AGEs	Advanced glycogen end products	**MMP**	Matrix metalloproteinase
ANCA	Antineutrophil cytoplasmic antibody	**MSUS**	Musculoskeletal ultrasound
APC	Adenomatous polyposis coli	**NAANES**	National health and nutrition examination survey
CAKUT	Congenital anomalies of kidney and urinary tract	**NaPI**	Sodium dependent phosphate cotransporter
CaSR	Calcium sensitizing receptor	**NAPRTCS**	North American pediatric renal trials and collaborative studies
CKD	Chronic kidney disease	**NC**	Nephrocalcinosis
CKD-MBD	Chronic kidney disease- metabolic bone disorder	**OPG**	Osteoprotegrin
CSA	Cross sectional area	**PTH**	Parathormone hormone
DKK-1	Dickkopf-1	**QUS**	Quantitave ultrasound
DRA	Dialysis related33 amyloidosis	**RAAS**	Renin angiotensin aldosterone system
DSA	Destructive spondylarthropathy	**RANKL**	Receptor activator of nuclear factor JB ligand
DVL	Disheveled	**ROMK**	Renal outer medullary K+ channel
ESRD	End stage renal disease	**RRT**	Renal replacement therapy
FGF23	Fibroblast growth factor 23	**SRNS**	Steroid resistant nephrotic syndrome
FGFR	Fibroblast growth factor receptor	**TCF/LEF**	T cell factor/lymphoid enhancer binding factor
FRP	Frizzled receptor protein	**TMV**	Turnover mineralization volumeclassification
GFR	Glomerular filtration rate	**TRPC6**	Ubiquitous calcium entry channel
GN	Glomerulonephritis	**TRPV5**	Highly selective renal calcium entry channel
GSK	Glycogen synthase kinase	**VDR**	Vitamin D receptor
HD	Hemodialysis	**VSMC**	Vascular smooth muscle cells

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AUTHORS' CONTRIBUTIONS

The submitted manuscript is the work of the author & co-author.

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Conception and design of study: H.H.A.E

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STATEMENTS

Ethics approval and consent to participate.
This study was approved by Ethics Committee of Faculty of medicine, Tanta University, with the ethics code 35253. Also, written informed consent was obtained from the parent of the participating children.

Consent for publication
"Not applicable"

Availability of data and material
"Available for your request, anytime"

Conflict of interest
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