



## Study on Muscle Cramps in End-Stage Renal Disease Patients on Hemodialysis and Analysis of Factors Contributing to Muscle Cramps including Magnesium

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### KEYWORDS

Muscle cramps, End-stage renal disease, Hemodialysis

### ABSTRACT:

**Background:** One of the most prevalent and potentially fatal illnesses affecting people worldwide is chronic kidney disease. This is characterized as one of the causes of illness and death of this century. Additionally, this has an impact on the patient's daily activities, such as their social life, freedom to work, and physical activity. Consequently, this is among the causes of cardiovascular disease and death.

**Material and methods:** This cross-sectional observational study conducted for 6 months from November 2023 to March 2024 in the nephrology department among 76 patients and blood samples were collected during muscle cramps in hemodialysis for Sodium, Potassium, Calcium, and Magnesium to assess an electrolyte change. A visual analog scale assessed the severity of muscle cramps at the time of muscle cramps. Self-made questionnaire was asked to patients regarding the incidence, frequency, management, severity, location, and time of muscle cramps. Patient's interdialytic weight gain, pre-dialysis blood pressure, post-dialysis blood pressure, and blood pressure during muscle cramps were recorded.

**Results:** The mean age of the patients in this study was 55.57. Hypertension (54.6%) is the major comorbidity and diabetic mellitus (37.3%) are the second most common comorbidity. The mean dry weight of the patients is 58.46 Kg in this study with a mean inter-dialytic weight gain is 3.65±1.20. 58 (77%) people majorly were on thrice-weekly dialysis, 16 (21%) people were on twice-weekly dialysis, and 1 (1%) patient was on once-weekly dialysis. 55 (73.3%) had muscle cramps at the end of the dialysis and 20 (26.7%) had muscle cramps at mid-session of dialysis. 33(44%) patients had a visual



analog scale score of 2, 30 (40%) patients had 3, 7 (9.3%) patients had 4, and 5 (6.6%) patients had 1 respectively. and no patients had a 5 visual analog scale score.

Conclusion: The frequency of muscle cramps caused on by increased blood flow (QB >300 ml/min), inter-dialytic weight gain, and ultrafiltration volume during dialysis.

## INTRODUCTION:

Chronic kidney disease is a most occurring and life-changing disease of the global population. This is distinguished as one of the causes of morbidity and mortality of this century. And this affects the patient's day-to-day life including physical activity, freedom to work, and social activity of an individual. so, this is one of the reasons for cardiovascular morbidity and mortality [1]. CKD is defined as the deterioration of kidney function over three months either with or without reduced glomerular filtration rate ( $\leq 60$  ml/min/1.73m<sup>2</sup>) and kidney injury markers include albuminuria ( $\geq 30$ mg/g or  $\geq 3$  mmol/g), evidence of abnormalities in urinary analysis, structural damage detected through imaging, and tubular disorders with electrolyte imbalance [2]. CKD is categorized into five stages based on estimated glomerular filtration rate and albumin creatinine ratio, serum biomarkers (Serum cystatin C) of the patients. Due to uncontrolled hypertension, increased glomerular stress due to hyperfiltration of protein in patients with a high protein diet, poor control of fluid intake, and uncontrolled glycemic index in patients with diabetic CKD progress to end-stage renal disease (ESRD) [1].

Under patient on end-stage renal disease (ESRD) and CKD stage V (estimated glomerular filtration rate  $< 15$  ml/min/1.73m<sup>2</sup>) with symptoms (uremia, hyperkalemia, metabolic acidosis, hyperphosphatemia, breathing difficulty, and uremic bleeding) will undergo renal replacement therapy (RRT) like, Renal transplantation, Peritoneal dialysis, and Hemodialysis. Hemodialysis is a process of clearing metabolic waste products from the blood through the principles of diffusion, ultrafiltration, and convection or solvent drag. A dialyzer or artificial kidney works as a native kidney with the help of a dialyzer membrane or artificial nephron in the process of the above-mentioned principles. Dialyzer membrane works by its characteristics including flux and efficiency [3]. Intradialytic muscle cramps in hemodialysis are an unavoidable and frequently occurring complication

among other complications. Muscle cramps during dialysis are because of High ultrafiltration rate, Use of low dialysate sodium, High dry weight, Hypovolemia, Elevated serum creatinine phosphokinase, Hyponatremia, Hypocalcemia, Hypomagnesemia, Carnitine deficiency [4,5]. The patient who is undergoing hemodialysis occasionally will face intradialytic complications. Including, Hypotension, muscle Cramps, Nausea and Vomiting, Hypertension, Headache, Pruritis, Fever and Chills, Dialyzer Reaction, Dialysis Disequilibrium Syndrome, Air embolism, and Hemolysis [6]. Usually, dialysate magnesium levels are similar to blood magnesium levels. Any disequilibrium between blood and dialysate levels (low magnesium) will cause muscle cramps [7,8]. Sodium levels in dialysis patients is a main predictor of cardiovascular morbidity and mortality along with increased blood pressure. In normal healthy kidney will maintain normal sodium, and ECF volume by natriuresis but in renal failure, individual need skillful and experienced doctors [9]. Carnitine plays a role in the transport of fatty acid from mitochondria to the cytoplasm through the carnitine shuttle. This helps in ATP production and prevents from persistent muscle cramps due to hypocalcemia. But in carnitine deficiency fatty acid is not transported from mitochondria to cytoplasm and this leads to a deficiency of ATP to retrieve the hypocalcemia from sarcoplasmic release, and this persists the muscle cramps [6]. Hence the aim of this study is to the assess the intra-dialytic muscle cramps among ESRD patients and determine the contribution factor of muscle cramp with magnesium during dialysis.

## OBJECTIVES:

1. To assess the level severity and incidence of muscle cramps using a visual analogue scale and Questionnaire.
2. To assess the level of intra-dialytic muscle cramps using blood investigation
3. To assess the contribution of intra-dialytic muscle cramps with magnesium levels during dialysis.



## MATERIALS AND METHODS:

This was a cross-sectional observational study conducted for 6 months from November 2023 to March 2024 in the nephrology department at the haemodialysis unit in SRM Medical College Hospital and Research Centre, Kattankulathur, Chennai after getting institutional ethical committee clearance (SRMIEC-ST0523-463). The sample size was 73 patients calculated based on this formula  $n = Z^2 \alpha^2 p \cdot q/d^2$ . After obtaining written informed consent, the patients on maintenance Haemodialysis above the age of 18 years old were included in the study. Patients who underwent Renal transplantation, Patients on Peritoneal Dialysis and with history of Acute Kidney Injury (AKI) were excluded.

**Data collection procedure:** Patient's blood samples were collected during muscle cramps in haemodialysis for Sodium, Potassium, Calcium, and Magnesium to assess an electrolyte change. A visual analog scale assessed the severity of muscle cramps at the time of muscle cramps. Self-made questionnaire was asked to patients regarding the incidence, frequency, management, severity, location, and time of muscle cramps. Patient's interdialytic weight gain, pre-dialysis blood pressure, post-dialysis blood pressure, and blood pressure during muscle cramps were recorded along with ultrafiltration volume. Patient's geographical data such as age, BMI, dry weight, and comorbidity were included. The other parameters collected were Pre-dialysis serum albumin, Medication history, Time of muscle cramps, Frequency of dialysis and Temperature.

**Statistical Analysis:** Statistical analysis was done using SPSS V.25 software and various analytical techniques were used. Mean and standard deviation were used for normal distribution data. The Pearson correlation method was used to study the correlation with other variables.

## RESULTS:

The mean age of the patients in this study was 55.57 and the majority were from the age group of 46-64 (41.3%). About 62.7% were male participants in this study. Hypertension (54.6%) is the major comorbidity presented in patients in this study, and hypertension and diabetic mellitus (37.3%) are the second most common comorbidity, and the least presented are hypothyroidism, hyperparathyroidism, and lupus nephritis (8.0%). The mean BMI was 23.09 Kg/m<sup>2</sup> which is overweight according to WHO Classification. The mean dry weight of the patients is 58.46 Kg in this study with a mean interdialytic weight gain is 3.65±1.20. The mean systolic blood pressure of pre-HD was 153.33±19.34 mmHg, during muscle cramps was 138±24.49 mmHg, and post-HD was 153.20±18.39 mmHg. Pre-HD's mean diastolic blood pressure was 88.13±9.68 mmHg, during muscle cramps was 84.13±11.75 mmHg, and post-HD was 86.13±8.37 mmHg. The mean laboratory value of sodium levels of 134.24±2.59 mmol/L, potassium levels of 3.75±0.50 mmol/L, magnesium levels of 2.60±0.68 mg/dl, and calcium levels of 10.547±0.998 mg/dl (**Table 1**).

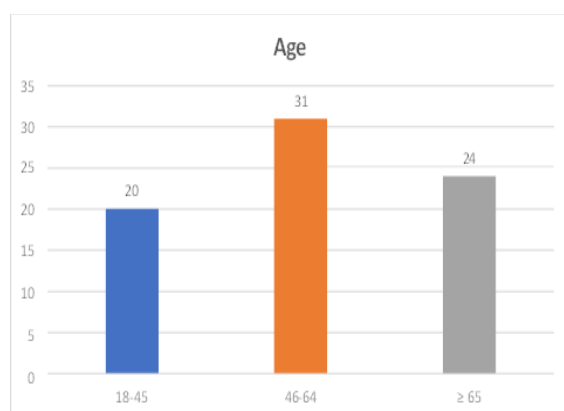
VARIABLE	MEAN	STANDARD DEVIATION
Age (Years)	55.57	13.56
Male (%)	62.7	-
Female (%)	37.3	-
Height (cm)	158.63	9.01
Hypertension (%)	54.6	-
Hypertension and Diabetic mellitus (%)	37.3	-
Others (%)	8.0	-
UF Volume (ml/min)	3.61	0.95
Interdialytic weight gain (Kg)	3.65	1.20
BMI (Kg/m <sup>2</sup> )	23.09	4.48



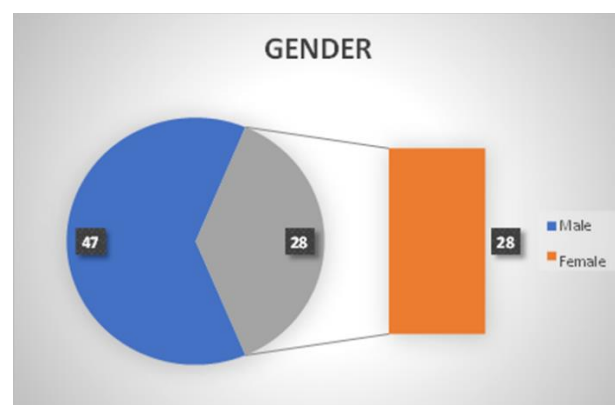
Dry weight (Kg)	58.46	13.74
Blood pressure pre-HD systolic (mmHg)	153.33	19.34
Blood pressure pre-HD diastolic (mmHg)	88.13	9.68
Blood pressure post-HD systolic (mmHg)	153.20	18.39
Blood pressure post-HD diastolic (mmHg)	86.13	8.37
Blood pressure during cramps systolic (mmHg)	138.00	24.49
Blood pressure during cramps diastolic (mmHg)	84.13	11.75
Temperature (°F)	97.30	1.21
Albumin (G/dl)	3.82	0.53
Sodium (mmol/L)	134.24	2.59
Potassium (mmol/L)	3.75	0.50
Calcium (mg/dl)	10.547	0.998
Magnesium (mg/dl)	2.60	0.68

**Table 1:** Demographic variables of the patients in this study

The incidence of muscle cramps with age distribution among 75 people. In this 41% of the people ranging from 45-64. Which is the highest among 75 people. The second highest is 32% of the people ranging more than or equal to 65. A minority of the people ranging from 18-45 about 26%. The mean age of the patients was  $55.57 \pm 13.56$  (Figure 1). Among 75, 47 (62.7%) were male and 28 (37.3%) were female (Figure 2).



**Figure 1:** Age Distribution



**Figure 2:** Gender Distribution

Among 75 people the majority of them had hypertension 41 (54.6%), 28 (37.3%) people had hypertension with diabetic mellitus, and 6 (08.0%) people had one of these comorbidities (hypothyroidism, lupus nephritis, and hyperparathyroidism) (Table 2).

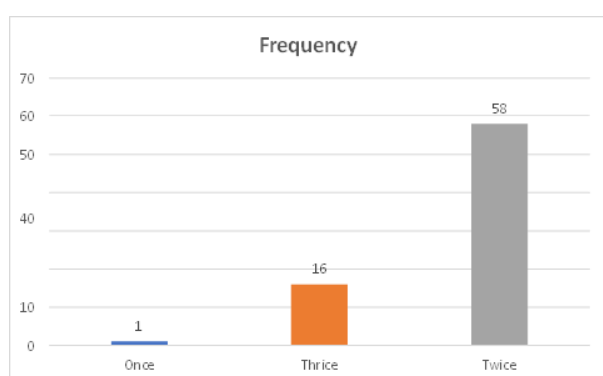
COMORBIDITIE S	FREQUENC Y	PERCEN T (%)
HTN	41	54.6
HTN AND DM	28	37.3



<b>OTHERS</b>	6	8.0
<b>Total</b>	75	100.0

**Table 2: Frequency and Percentage of Comorbidity Status**

Among 75 patients, 58 (77%) people majorly were on thrice-weekly dialysis, 16 (21%) people were on twice-weekly dialysis, and 1 (1%) patient was on once-weekly dialysis (**Figure 3**).



**Figure 3: Frequency of Dialysis**

Among 75 patients, 55 (73.3%) had muscle cramps at the end of the dialysis and 20 (26.7%) had muscle cramps at mid-session of dialysis. 27 (36.0%) had a normal BMI of 18.5-22.9, 19 (25.3%) were obese class II (25-29.9), 12 (16.0%) were underweight (<18.5), and obese class I (23-24.9) respectively, and 5 (6.7%) were obese class III ( $\geq 30$ ) (**Table 3**).

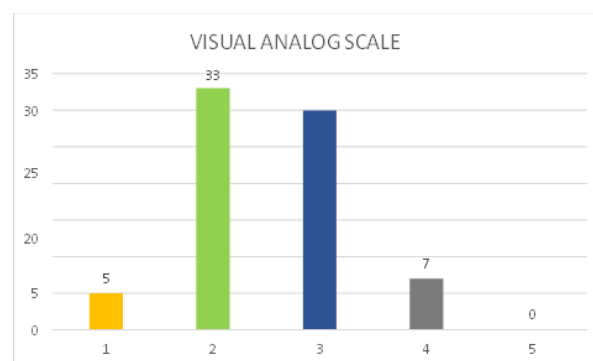
<b>BMI (Kg/m<sup>2</sup>)</b>	<b>FREQUENCY</b>	<b>PERCENTAGE (%)</b>
<18.5	12	16.0
18.5-22.9	27	36.0
23-24.9	12	16.0
25-29.9	19	25.3
$\geq 30$	5	6.7
<b>Total</b>	<b>75</b>	<b>100.0</b>

**Table 3: Percentage and frequency of BMI among the patients**

Among 75 patients, 28 (37.3%) patients were on 97-97.9 degrees Fahrenheit, 27 (36.0%) patients were on more than 98 degrees Fahrenheit, 13 (17.3%) patients were on 96-96.9 degrees Fahrenheit, and 7 (9.3%) patients were

on less than 96 degrees Fahrenheit and patients had a dialysis vintage of <5 years, 10 (13.3%) patients had a dialysis vintage of 5-10 years, and around 6 (8.0%) patients had a dialysis vintage of more than or equal to 10 years. respectively. 53 (70.7%) patients had muscle cramps with more than or equal to 300 ml/min, and 22 (29.3%) had muscle cramps with 250-300 ml/min. 35 (46.7%) patients had muscle cramps with interdialytic weight gain of 2-4.5 Kg, 20(26.7%) patients had muscle cramps with interdialytic weight gain of 1-2 Kg, 18 (24.0%) patients had muscle cramps with interdialytic weight gain of >4.5 Kg, and 2(2.7%) patients had muscle cramps with interdialytic weight gain of <1 Kg. 63 (84.0%) patients had muscle cramps even were on levocarnitine medication, and 12 (16.0%) patients had muscle cramps without levocarnitine medication.

33(44%) patients had a visual analog scale score of 2, 30 (40%) patients had 3, 7 (9.3%) patients had 4, and 5 (6.6%) patients had 1 respectively. and no patients had a 5 visual analogue scale score (**Figure 4**).



**Figure 4: Frequency and percentage of visual analog scale**

73 (97.3%) patients answered yes that they did get muscle cramps, and 2 (2.7%) patients answered no with experience of muscle cramps for the first time. 31 (41.3%) patients had muscle cramps within the last week, 16 (21.3%) patients had muscle cramps within the last two weeks, 10 (13.3%) patients had muscle cramps within the last day, 5 (6.7%) patients had muscle cramps greater than a month ago, and 2 (1.3%) patients had not experienced muscle cramps so far this dialysis period and that was their first experience of getting muscle cramps. 38 (50.6%) patients had muscle cramps on both dialysis and non-dialysis days, 35 (46.7%) patients had muscle cramps on dialysis days and 2 (2.7%) patients had not



experienced muscle cramps so far this dialysis period and that was their first experience of getting muscle cramps. 37 (49.3%) patients 35 patients experienced muscle cramps during dialysis, and 2 patients had not experienced muscle cramps so far. 8 (10.7%) patients experienced muscle cramps in the evening during non-dialysis day, 3 (4.0%) patients experienced muscle cramps on the morning, and 1 (1.3%) patient experienced muscle cramps on the afternoon on non-dialysis day. 42 (56%) patients experienced muscle cramps at the end of the dialysis, and 33 (44%) patients experienced muscle cramps during dialysis. 37 patients had given 8 out of 10 for the severity of muscle cramps from 1-10, 20 (26.7%) patients had given 7 for the severity, 14 (18.7%) patients had given 9 out of 10 for the severity, 3 patients had given 6 out of 10 for the severity, and 1 patient had given 5 out of 10 for the severity. 44 (58.6%) patients had experienced muscle cramps on leg, 24 (32%) patients had experienced muscle cramps on leg and arm, 4 (5.3%) patients experienced muscle cramps on arm, 2 (2.7%) patients had experienced muscle cramps on back and leg, and 1 (1.3%) patient had experienced muscle cramps on leg and abdomen. 39 (52%) patients had shared information regarding muscle cramps with a nephrologist, 34 (45.3%) patients had shared information regarding muscle cramps with a haemodialysis technologist, and 2 (2.7%) patients had not informed anyone regarding muscle cramps. 52 (69.3%) patients had sodium levels of 125-135 mmol/dl during muscle cramps, and 23 (30.7%) patients had sodium levels of 135-145 mmol/dl during muscle cramps. 29 (38.7%) patients had potassium levels of <3.5 mmol/dl during muscle cramps, 24 (32.0%) patients had potassium levels of 3.5-4.0 mmol/dl during muscle cramps, and 22 (29.3%) patients had potassium levels of >4.0 mmol/dl during muscle cramps. 40 (53.3%) patients had magnesium levels of 1.5-2.5 mmol/dl during muscle cramps, 20 (26.7%) patients had magnesium levels of 2.5-3.5 mmol/dl during muscle cramps, and 15 (20.0%) patients had magnesium levels of > 3.5 mmol/dl during muscle cramps. 47 (62.7%) patients had calcium levels of 10-11.5 mmol/dl during muscle cramps, 16 (21.3%) patients had calcium levels of 8-10 mmol/dl during muscle cramps, and 12 (16.0%) patients had calcium levels of > 11.5 mmol/dl during muscle cramps.

## DISCUSSION:

Renal replacement therapy (RRT) is one of the tools for patients with renal impairment. Among the RRT, Hemodialysis is a widely used modality around the world. This has some complications during hemodialysis sessions. Among those, muscle cramps is one of the complications occurring frequently during dialysis. Our observational cross-sectional study was done in the hemodialysis unit at SRM Medical College Hospital and Research Centre for 6 months from November 2023 to March 2024. The patients were recruited by fulfilling inclusion and exclusion criteria with ethical clearance. This study aimed to evaluate muscle cramps during 4-hour (240-minute) hemodialysis sessions by analyzing demographic data, patient comorbidities, inter-dialytic weight gain, and sodium, potassium, calcium, and magnesium levels. Muscle cramps were assessed using a visual analog scale and a questionnaire to determine the frequency and severity of cramps.

We included 75 patients, 31 were predominately from the age group of 46-64 years (41.3%) and the mean age was (55.57±13.56). 47 patients were male (62.7%), 44 patients had muscle cramps on the lower extremities, and 55 (73.3%) patients experienced muscle cramps at the end of the dialysis session of 180-240 minutes. Aleksandra Parmakovsk, et al done "Frequency and severity of muscle cramps in chronic hemodialysis patients" had a similar variable associated with our study [10].

41 (54.6%) patients had hypertension as a comorbidity. 58 (77%) patients had muscle cramps when they were on thrice weekly dialysis. 59 (78.7%) had dialysis vintage of < 5 years. 53 (70.7%) had a blood flow rate of >300 ml/min with an incidence of muscle cramps. 35 (46.7%) patients had an inter-dialytic weight gain of 2-4.5 Kg with an incidence of muscle cramps. 63 patients had muscle cramps and were on levocarnitine. The mean systolic blood pressure of pre-HD was 153.33±19.34 mmHg, during muscle cramps was 138±24.49 mmHg, and post-HD was 153.20±18.39 mmHg. The mean diastolic blood pressure of pre-HD was 88.13±9.68 mmHg, during muscle cramps was 84.13±11.75 mmHg, and post-HD was 86.13±8.37 mmHg. We assessed the incidence and severity of muscle cramps by asking the questions related to muscle cramps, 31 patients answered that they had muscle cramps within the last week, and 17



(22.7%) patients would get muscle cramps twice a month. And 38 patients had muscle cramps on both and non-dialysis days. 26 (34.7%) patients mostly had muscle cramps at night time on non-dialysis days. 37 (49.3%) patients had given the severity score of muscle cramps [8].

According to Patrick G. Lynch, et al done "Magnesium and Muscle Cramps in End-Stage Renal Disease Patients on Chronic Hemodialysis" had a similar association that 41 (52%) patients were not reported to the nephrologist regarding the incidence of muscle cramps during dialysis which goes with our study [7]. 33 (44%) patients had a visual analogue scale score 2 out of 5 for the severity of muscle cramps.

Laboratory values of sodium, potassium, magnesium, and calcium were measured during muscle cramps, 52 (69.3%) patients had sodium levels of 125-135 mmol/L, 29 (38.7%) patients had potassium levels of <3.5 mmol/L, 40 (53.3%) patients had magnesium levels of 1.5-2.5 mg/dl, and 47 (62.7%) patients had calcium levels of 10-11.5 mg/dl. And, we found that there is an association between ultrafiltration and inter-dialytic weight gain with the p-value of (0.000), ultrafiltration volume with calcium levels with the p-value of (0.02), ultrafiltration volume with BMI with the p-value of (0.016), and comorbidity with inter-dialytic weight gain with the p-value of (0.045). No correlation between blood flow rate (BFR) and sodium levels with the p-value of (0.497), BFR with potassium levels with the p-value of (0.947), BFR with magnesium levels with the p-value of (0.968), and BFR with calcium levels with the p-value of (0.886).

## CONCLUSION:

The incidence of muscle cramps in the patients on maintenance hemodialysis in our center showed that 69.3% of patients had sodium levels of 125-135 mmol/L, 38.7% of patients had potassium levels of less than 3.5 mmol/L, 53.3% of patients had magnesium levels of 1.5-2.5 mg/dl, 62.7% of patients had calcium levels of 10-11.5 mg/dl, 46.7% of patients had inter-dialytic weight gain of 2-4.5 Kg. Based on our results, the incidence of muscle cramps caused by higher ultrafiltration volume, higher inter-dialytic weight gain, and blood flow (QB >300 ml/min) rate during dialysis.

## CONFLICT OF INTEREST:

The authors declare that they have no conflicts of interest.

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