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STUDY ON THE PREVALENCE OF PERIPHERAL NEUROPATHY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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ABSTRACT :

Background: The incidence and prevalence of Chronic Kidney Disease is increasing slowly. The affected groups are predominantly elderly individualS, diabetics and patients with systemic hypertension. Peripheral Neuropathy among CKD patients is the most common neurological complication of uremia, but still it is an under estimated problem adversely affecting the patient's quality of life.It is more often a silent burden for the patient, progressively affecting his/her quality of life. It is sometimes overlooked as the treating physicians are occupied with other uremia related complications and also there is a dearth of literature regarding the diagnostic criteria and management of this condition. It is further amplified by the lack of availability of a simple screening tool for peripheral neuropathy in CKD. Hence this study aims to establish the prevalence of peripheral neuropathy among patients with CKD in our Hospital.

Methods: Data was collected from patients attending the Department of General Medicine of Sree Mookambika Institute of Medical sciences, kanyakumari, tamil nadu, from march 2023 to september 2024. This study was carried out in chronic kidney disease patients attending hemodialysis unit and patients admitted as in-patients in our medical wards in the department of General medicine.A total sample of 100 patients were studied After prior Institutional Ethical clearance and obtaining informed consent, the participants satisfying the inclusion criteria were asked detailed history and clinical examination was performed according to the well-designed proforma cited below. The presence of neuropathy was assessed using Michigan Neuropathy Screening Instrument (MNSI) Scores with Semmes-Weinstein monofilament(10g) and Diabetic neuropathy symptom score(DNS).Weight,height and waist of the individual patients were measured and BMI was calculated and recorded in all the cases.

Results: The mean age of the study subjects was 47.87 years. Most of the patients belonged to the age group 40-70years.Out of 100 cases,there were 58 (58.0%) males and 42(42.0%) females.The Male to Female sex ratio was 1.38:1.Sixty patients out of 100 patients were on Hemodialysis whereas 40 patients belonged to the non-HD group. The prevalence of peripheral neuropathy in CKD patients assessed by

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MNSI was 64%.The prevalence of clinical Uremic distal symmetrical sensory-motor peripheral neuropathy assessed by MNSI in the CKD on HD population was 71.66%.

Conclusion: Uremic neuropathy is the most common neurological complication in patients with uraemia. The condition is not restricted to patients with ESRD,but it is more prevalent in patients with stage V CKD. MNSI physical assessment could be used as a simple bed side examination to determine the presence or absence of uremic peripheral neuropathy.

Keywords: Chronic Kidney Disease, Michigan neuropathy screening instrument, Peripheral neuropathy, Uremic neuropathy.

INTRODUCTION:

In the ever changing field of medicine, chronic kidney disease and its complications are on the uptrend in terms of incidence and prevalence and remains as a major cause of morbidity and mortality in developing and developed nations alike. It will remain to be so in the forth coming years. Much emphasis has been placed on the increased cardiovascular risk and electrolyte abnormalities that accompany chronic kidney disease but uremic neuropathy as a complication has always received less attention. The dreaded neurological complication is usually the uremic encephalopathy or a vascular event that accompanies hypertension.

The term uremic neuropathy denotes neuropathy either central or peripheral that is due to the extended effects of the spectrum of uraemia, a condition that loosely translates to accumulation of organic waste products that would be actively filtered by a normal kidney1.

Asbury KA1 in his own words said “The fact that chronic renal failure may be associated with polyneuropathy is not generally appreciated and is practically not documented in the medical literature. In the briefest possible terms, the neurological disease may be defined as follows: It began with painful burning sensation of the feet, followed by slowly progressive numbness and weakness. The feet and legs were affected more than the hands and arms, and the distal segments more than the proximal”. It was only after this our understanding of uremic peripheral neuropathy gradually increased.

Withstanding the therapeutic advances, most neurological complications of the uremic state fail to respond adequately to treatment.Despite routine haemodialysis, many neurological complications seldom improve in majority of the cases. A vast spectrum of pathophysiological processes are included in chronic kidney disease (CKD), which almost always progressively lead to abnormal kidney function along with worsening glomerular filtration rate. The development of neuropathy is most common when eGFR falls below 12mL/minute/1.73m2 BSA2,3.

The estimated prevalence of CKD in India is around 0.78% -0.8%3,4. The rate of which is increasing slowly1. A rough age adjusted incidence of CKD stage V or End Stage Renal Disease (ESRD) is around 151 and 232 per million population respectively5. Uraemia is a clinical syndrome involving abnormalities with fluid, electrolyte, hormone balance and metabolic abnormalities. These abnormalities develop in

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parallel to the deterioration of renal function. Uremic peripheral neuropathy is one of the severe and disabling complications in patients with chronic kidney disease. Charcot6 in 1880 suspected the existence of uremic neuropathy and Nearly more than half a century later, after the introduction of haemodialysis and renal transplantation in the early 1960s the investigations gathered steam.

Uremic neuropathy encompasses a wide variety of manifestations of which distal symmetrical sensory motor peripheral neuropathy is the commonest. The severity of uremic peripheral neuropathy increases with decrease in glomerular filtration capacity. The neuropathy is a dying back neuropathy or central-peripheral axonopathy associated with secondary demyelination. The clinical and pathological features of uremic peripheral neuropathy were described in detail by Adams, Victor and Asbury in 1962. Dyck7 and colleagues established the current concept of uremic neuropathy in 1971 on the basis on their wide nerve conduction studies in vivo and in vitro and on light and electron microscopy8. They were able to demonstrate axonal shrinkage with quantitative histology. Myelin sheaths were involved out of proportion to axonal involvement. The dysfunction of the neuron resulted in a decrease in the diameter of the axon, rearrangement of myelin, and in the end complete degeneration of the axon. The uremic peripheral neuropathy manifestation in patients are variable ranging from paraesthesia, pain, weakness and atrophy of lower limbs, muscle cramps, restless legs to sometimes features mimicking Guillain-Barre like. Renal replacement therapy has resulted in halting of the symptoms of uremic peripheral neuropathy or even reversal but sometimes there might not be any improvement at all. The rate of reversibility depends on various parameters such as duration of symptoms, type of renal replacement therapy, frequency of dialysis and so on. Renal transplant provides the best possible results out of all the current therapies available aimed at alleviating uremic peripheral neuropathy. This study is primarily aimed at estimating the prevalence of peripheral neuropathy in patients with CKD in a tertiary care hospital including those on renal replacement therapy.

AIM AND OBJECTIVES OF THE STUDY:

- To study the prevalence of peripheral neuropathy in patients with chronic kidney disease
- To determine the prevalence of Peripheral Neuropathy and associated factors in relation to the stage of CKD.

MATERIALS AND METHODS:

Data was collected from patients attending the Department of General Medicine of Sree Mookambika Institute of Medical sciences, kanyakumari, tamil nadu, from march 2023 to september 2024. inclusion criteria All patients irrespective of age and sex with the chronic kidney disease.,eGFR<60ml/min/1.73^2 determined byMDRD formula (186.3 x (Creatitine in mg/dl)$^{-1.154}$ x (Age)$^{-0.203}$ x (0.742 if female),Ultrasound abdomen evidence of CKD(increased renal cortical echogenicity, reduced renal cortical thickness or reduced renal length <9cm).

Exclusion criteria are Patient denying Consent.Patients who had a renal transplant,Patient with other known

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cause of peripheral neuropathy such as,Hypothyroidism, Alcoholism, Diabetes Mellitus, Tuberculosis, Hansen's disease, Patients on drugs having peripheral neuropathy as established toxicity, malignancy and vitamin B12 deficiency.

Statistical analysis was done using the statistical package for social sciences (SPSS).Different statistical methods were used as appropriate. Mean ± SD was determined for quantitative data and frequency for categorical variables. The independent t- test was performed on all continuous variables. The normal distribution data was checked before any t-test. The Chi-Square test was used to analyze group difference for categorical variables. In logistic regression models, age was adjusted for estimation of each or all the independent effects of hypertension, ischemic heart disease and diabetes mellitus . A p- value < 0.05 was considered significant.

RESULTS:

PREVALENCE OF UREMIC PERIPHERAL NEUROPATHY

DISTRIBUTION OF UPN IN THE STUDY POPULATION:

In the study population out of 100 patients, 64 patients were found to have clinical uremic peripheral neuropathy.The distribution of uremic neuropathy in different sub groups of study population is as follows.

Out of 100 patients 4 (4.0%)patients belonged to STAGE III CKD out of which 1 patient (25% prevalence) patient was clinically found to have peripheral neuropathy.17(17.0%) patients belonged to stage IV CKD group out of which 6 patients (35.29% prevalence) clinically tested positive for peripheral neuropathy.The CKD stage V group which includes both patients on HD and patients not on HD treatment had the highest number of patients at 79(79.0%) out of which 57 patients (72.15% prevalence) clinically tested positive for peripheral neuropathy.

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DISTRIBUTION OF UPN IN CKD SUBCLASSES

	Clinical UPN -ve	Clinical UPN +ve	Total
CKD stage III	3	1	4
CKD stage IV	11	6	17
CKD stage V	22	57	79
TOTAL	36	64	100

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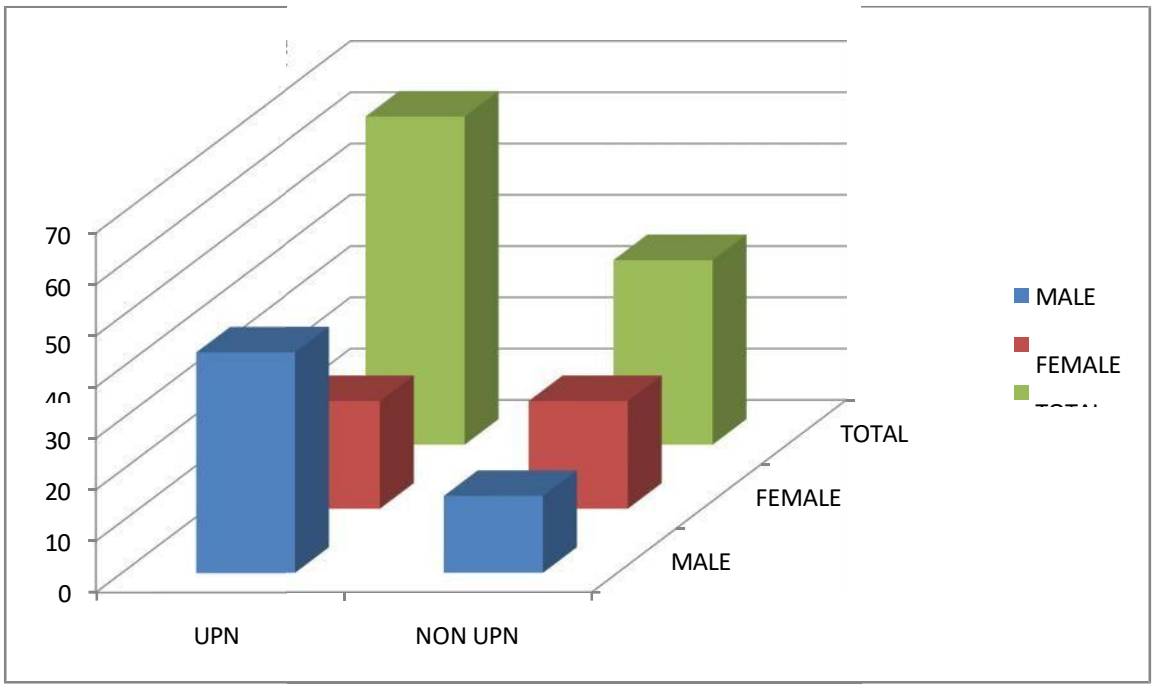
CHART 4: DISTRIBUTION OF UPN IN CKD SUBCLASSES



PERIPHERAL NEUROPATHY IN STAGE IV CKD:

There were a total of 17 cases who belonged to CKD stage IV, of which there were 4 male and 13 females.Out of the 17 patients 6 patients were diagnosed with peripheral neuropathy.The prevalence of peripheral neuropathy was 35.29%(p value <0.01).Among males the prevalence was 50% and among females the prevalence was

30.76% which was statistically significant χ^2=10.999 ,p value=0.004(<0.01)

CKD IV & UPN

CKD STAGE IV	UPN +ve	UPN -ve	TOTAL
MALES	2(50%)	2(50%)	4
FEMALES	4(30.76%)	9(69.23%)	13

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TOTAL	6(35.29%)	11(64.70%)	17

DNSS and CKD SUBCLASSES

DNSS SCORE	CKD STAGE			TOTAL
	III	IV	V	
0	4	14	59	77
1	0	3	17	20
2	0	0	2	2
3	0	0	1	1
Total	4	17	79	100

DNSS SENSITIVITY AND SPECIFICITY

Statistic	Formula	Value
Sensitivity	$\frac{a}{a+b}$	35.94%
Specificity	$\frac{d}{c+d}$	100.00 %

The DNSS had a sensitivity of 35.94% and a specificity of 100%.This makes DNSS a poor screening test, hence it could not be used in early diagnosis of uremic peripheral neuropathy.

DISCUSSION:

Uremic neuropathy is the commonest complication of the uremic syndrome and is defined as a predominantly distal sensory-motor polyneuropathy that predominantly affects the distal segments more so in the lower limbs than in the upper limbs which may occasionally present as a mononeuropathy due to compression, trauma or ischemia9-10. The condition is often a silent burden among patients with CKD affecting the quality of life

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considerably. The prevalence of peripheral neuropathy due to uraemia may range from 70-100% in patients with End stage renal disease10-14.Among the non- dialysis population,one study noted the prevalence to be 70%15.Patients start experiencing subtle symptoms of uremic neuropathy during stage 3 CKD with peripheral neuropathy prominently affecting stage 4 and ESRD.

Hundred adult patients with CKD stage 3 or more were included in the present study.They were patients attending the HD ward for thrice weekly dialysis or patients admitted in the medical wards of our institution.The mean age of the study population was 47.87years with a male to female ratio of 1.38:1.The mean duration of uremic symptoms was 28.69 months.

In a study by Jedras M et al16, conducted in 51 patients on chronic hemodialysis, more males were found to be have sensory-motor neuropathy when compared to women,whereas women were found to have more prevalent autonomic neuropathy when compared to men. Madhusudhana Babu et al in his study on 74 patients who were not on dialysis found that when compared to younger age group patients aged
more than 65years were affected by peripheral neuropathy.In his study he also noted that the prevalence of peripheral neuropathy increases among males if eGFR is <15ml/min/1.73m2.

In our study males were significantly more affected by peripheral neuropathy when compared to females.This was observed in CKD stage V group(eGFR<15) both in patients on HD and in patients not on HD.This finding extended to stage IV CKD and stage III CKD groups.These findings were statistically significant in our study.
In our study it was found that patients aged ≥60 years were predominantly affected by uremic neuropathy which was statistically very significant(pvalue<0.01).Even though Nerve conduction studies are the gold standard diagnostic modality for uremic neuropathy,The nature and the lack of such facilities impedes the early diagnosis.
There are studies which claim that simple screening tools like MNSI scores and Neuropathic symptom scores which is a validated tool for diabetic neuropathy will also provide an early window of opportunity to diagnose the presence of uremic neuropathy without having to undergo nerve conduction studies which will pave way for earlier management.

Mambelli E et al18,conducted a study on 225 dialysis patients to determine the prevalence of uremic neuropathy. In their study, all causes inducing secondary neuropathy were excluded.MNSI scores and Electroneurography of the lower limb was conducted to compare the sensory nerve conduction velocities and sensory nerve action potential results with MNSI results.37 patients(16.4%) were identified to have uremic neuropathy. There was a significant correlation between MNSI scores (>or equal to 3) between MNSI physical assessment and SCV(r2=0.1959;p<0.034) as well as SNAP(r2=0.3454;p=0.027) both measured by ENG. He concluded the study by saying that MNSI could represent a valid and simple clinical-instrumental screening test for the early diagnosis of Uremic neuropathy in view of an early therapeutic approach.
In our study of 100 patients which includes CKD patients from stage III to stage V with or without on hemodialysis. The smallest score obtained was 2 and the largest score obtained was 7 with a mean score of 2.580±2.069. two patients(2%) have scored MNSI scores between < 2.5 out of 10 and 58 patients(58%) had scored between 3-5.5 out of 10.
Further breaking down,1 patient(25% prevalence) from CKD stage III had scored >3 in

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MNSI, six patient(35.29% prevalence) has scored >3 in MNSI. Finally among the CKD Stage V patients, 51 patients (64.55%) have scored >3 in MNSI.
Among the CKD V patients on HD ,43 patients(71.66% prevalence) had MNSI scores more than 3 and among CKD V patients not on HD 14 patients(73.68%) had MNSI scores >3.

The distribution of MNSI scores among different CKD subtype was statistically significant(χ^2=13.418 ,$p<0.05$).Our study reiterates the fact that MNSI could serve as a valid test to diagnose Uremic neuropathy with the view that early management may have a positive impact on the quality of life of the patient.

In a study by HK Aggarwal et al19 on 100 predialysis patients ,70% of patients had scored atleast 1 point in the T-Neuropathy symptom score with maximum score of 17109-111.The scores were found to correlate well with the increase in levels of serum creatinine107.Krishnan et al. in their study on 12 ESRD patients graded the neuropathic symptoms using modified NSS. Each symptom received a score of 1, and the number of symptoms present in each subset was summed to give a T-NSS. The maximum possible T-NSS was 9. All 12 patients reported symptoms of neuropathy (mean T- NSS, 1.9±0.2) . Majority of the patients had at least one neurological symptom (70%), as compared against the minority (30%) who were asymptomatic. 49% of the patients had a T-NSS of ≥2 while maximum score of 5 was elicited in 9% of the patients (mean T-NSS, 1.72±1.61).

The distribution of DNSS scores and Serum creatinine levels, eGFR levels and duration of CKD symptoms were statistically insignificant(p value>0.05).Thus our study concludes that oversimplified symptom scoring systems such as DNSS might not the best tool for diagnosing uremic neuropathy.T-NSS score and modified NSS score though laborious might be considered as an effective tool in screening uremic neuropathy.

H K Aggarwal et al,in their study on 100 patients found that prevalence of peripheral neuropathy increased with a raise in serum creatinine, This observation was confirmed in other studies as well.
In our study, The minmum serum creatinine observed was 1.7mgs% and the maximum was 11.3mgs% and a mean creatinine value of 5.33mgs%.The prevalence was 66% in patients with serum creatinine 6.1 to 9mgs% and in patients with serum creatinine ≥9.1 the prevalence was 100%($p<0.05$).

CONCLUSION:

The prevalence of clinical uremic peripheral neuropathy in a series of 100 chronic kidney disease patients which includes different stages of CKD ranging from stage 3 to stage 5 CKD including those on hemodialysis was **64%**.The prevalence of peripheral neuropathy in various subgroups of CKD stages were**25%** in stage III CKD ,**35.29%** in stage IV CKD and

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64.55% in stage V CKD.

Patients on Hemodialysis had a prevalence of **71.77%**,whereas patients not on hemodialysis who belonged to CKD stage 5group had a prevalence of **73.68%**.Clinical neuropathy occurred more commonly in males,older age groups(>60years), patients with longer duration of uraemic symptoms, elevated serum creatinine levels and decreasing eGFR levels.
The most common symptom was burning foot and the most common clinical sign observed was loss of ankle reflex.Prevalence of uremic neuropathy is high in patients with CKD.Since this condition occurs even in patients not requiring dialysis and worsens with increasing duration of symptoms, our study emphasises the need for active screening of uremic peripheral neuropathy in patients with CKD with simple diagnostic tools like MNSI so that early institution of treatment and further management may play a positive role in the life of CKD patients.

LIMITATIONS OF THE STUDY:

- The long mean duration of uremic symptoms in our patients was probably due to‘Recall bias’.
- The positive correlation between MNSI and Electroneuronography as seen by Mambelli et al, was observed in Italians.There are no reference studies done in Asian or in any other population groups. Further studies need to be done on different population subgroups in future.

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