Research article

Prevalence of peripheral neuropathy and its electrophysiological types in patients with systemic lupus erythematosus at Kenyatta National Hospital

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Abstract

Background: Peripheral neuropathy, one of the neuropsychiatric syndromes of Systemic Lupus Erythematosus (SLE), occurs in 2% to 36% of patients. It has been associated with high disease activity indices and poor quality of life scores. Studies have demonstrated benefits of early identification and treatment on the severity and progression of neuropathy. There is paucity of data on neurological manifestations of SLE in Africa.

Objective: To determine the prevalence of peripheral neuropathy using clinical evaluation and Nerve Conduction Studies (NCS) and to describe its electrophysiological types using NCS; to determine and correlate quality of life with presence of peripheral neuropathy among SLE patients attending Kenyatta National Hospital (KNH), Rheumatology Clinic.

Design: This was a cross-sectional study of SLE patients attending Rheumatology outpatient clinic at KNH.

Methods: Fourty eight patients with a diagnosis of SLE as per the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria who were 18 years and above were included in the study. Socio-demographic data and clinical information were obtained from the patients medical records. Structured history and clinical examination was performed on all patients. Lupus quality of life questionnaire was administered and nerve conduction studies performed on all patients.

Results: The overall prevalence of peripheral neuropathy was 60.4% (29 out of 48). Of these 27.1% were symptomatic for peripheral neuropathy and had abnormal nerve conduction studies while 25% were symptomatic for peripheral neuropathy and had normal nerve conduction studies. The other 8.3% had abnormal nerve conduction studies despite being asymptomatic. The most common nerve conduction pathology was demyelination 9 (52.94%, n=17). However excluding 5 patients found to have Carpal tunnel syndrome, then demyelination was 4 (23.52%, n=17), while axonopathy was found in 5(29.41% n=17) of the patients. The most prevalent nerve conduction syndromes was motor neuropathy (52.94%, n=17). There was a significant correlation between the presence of peripheral neuropathy with lower quality of life scores involving the domains of physical health (p=<0.001), pain (p=0.012), planning (p=0.003), and fatigue (p=0.005).

Conclusion: There is a high prevalence of peripheral neuropathy among SLE patients, with variable clinical and electrophysiologic presentation. Quality of life scores are lower in affected patients.

Key words: Peripheral neuropathy, SLE, Kenya, Neuropsychiatric, Africa

Introduction

Systemic Lupus Erythematosus (SLE) is a prototypic chronic inflammatory autoimmune disease with a wide spectrum of clinical presentation affecting almost all organs and tissues, including the nervous system. Neurological manifestations, occurs in 10% - 90% of SLE patients [1-4]. In Africa there is paucity of data on the prevalence of neurological disorders among SLE patients. Genga *et al*[5] in Kenya reported a prevalence of 19% while Wadee *et al*[6] from South Africa reported a prevalence of 15.9%. These low numbers of neurological disorders was mainly represented by patients with stroke, new onset seizures, psychosis and did not include neuropathies.

Peripheral neuropathy in SLE is one of the neuropsychiatric syndromes defined by the 1999 revised American College of Rheumatology as acute inflammatory demyelinating radiculopathy (Guillen –Barre Syndrome), autonomic disorder, mononeuropathy–single/multiplex, myasthenia gravis, cranial neuropathy, plexopathy and polyneuropathy[7]. Recent studies now show that small fiber neuropathy not described in 1999 ACR

case definitions of neuropsychiatric syndromes to be common in SLE patients while plexopathy and Guillen-Barre syndrome uncommon[8,9].

Peripheral neuropathy is thought to occur in 2% to 36% of patients with systemic lupus erythematosus. In Africa there is not much data on prevalence and clinical associations of peripheral neuropathy with SLE. However Gbané-Koné *et al*[10] in Cote d' Voire , and Genga *et al*[11] in Kenya have reported cases of peripheral neuropathy. Oomatia *et al*[8] and Brundusa *et al*[12] associated peripheral neuropathy in SLE with a high disease activity indices and poor quality of life scores.

Materials and methods

This was a hospital based cross-sectional study conducted from May 2018 to July 2018, in the Rheumatology out-patient clinic at the Kenyatta National Hospital, Nairobi. The study commenced after obtaining all the necessary ethical approvals from the institutional review board. All patients aged 18 years and above fulfilling the 2012 SLICC classification criteria for SLE diagnosis were eligible for the study. Patients were excluded if they were amputees, had history of traumatic involvement affecting the nerves, had foot ulcerations, as well as those known to have other known causes of peripheral neuropathy such as mixed connective tissues disease, diabetes mellitus, history of heavy alcohol consumption, chronic renal failure and pernicious anaemia. All participants gave an informed written consent. Consecutive sampling method was applied.

All participants had a clinical history and a targeted neurological examination done. Lupus quality of life questionnaire was administered and nerve conduction study was carried out by a qualified neurologist with experience in electrophysiological studies on all participants.

Peripheral neuropathy was defined both clinically and electrophysiologically as: presence of a symptom, and or a sign, with or without impairment in nerve conduction studies or such impairment without a sign or symptom. All the NCS were carried out at room temperature on a Nihon Cohden Machine and the Median, Ulnar, Peroneal, Tibial and Sural nerves tested.

Data was coded, entered and managed in a Microsoft Access 2013 database. Statistical analysis was done using Statistical Package for Social Sciences version (SPSS) 25.0. Data was summarized into proportions for categorical variables, and into means (SD) or medians for the continuous variables. Prevalence of peripheral neuropathy was analyzed and presented as proportions with 95% confidence interval. Chi-square test was used to check for association between patient profile with the presence of peripheral neuropathy. A p value of less than or equal to 0.005 was considered statistically significant.

Lupus quality of life was scored and analyzed using a standard scoring system resulting in scores between 0 to 100. Health related quality of life was correlated with peripheral neuropathy using chi-square analysis.

Results

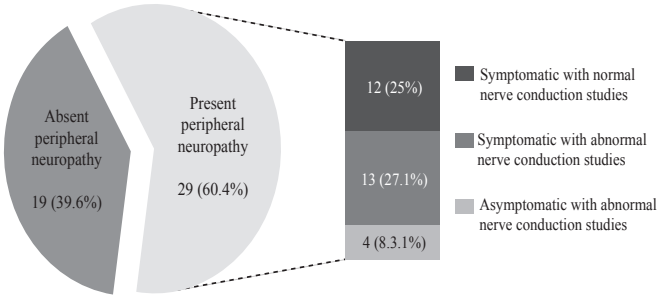
In a period of 3 months (May 2018 to July 2018), 48 patients with SLE were recruited into the study. The entire study population comprised of females whose mean age was 37.9 years (SD 11.92, SEM 1.72). The median duration of disease since diagnosis was 27.5 months (IQR 12.0-60.0). The most commonly used disease modifying agents was hydroxychloroquine at 97.9%, with a mean duration of usage of 38.46 months as outlined in Table 1.

Table 1: Medications taken by study participants (n=48)

Medication	Yes (%)	Mean duration of treatment (months)	SD
NSAIDs	17.1	27.27	32.98
HCQ	97.9	38.46	38.59
Leflunomide	4.2	43.5	40.31
MTX	14.6	24.86	31.46
Cyclosporine	0	0	0
MMF	25.0	24.19	15.90
AZA	37.5	35.24	46.85
Steroids	85.4	41.9	42.21
Biologics	0	0	0

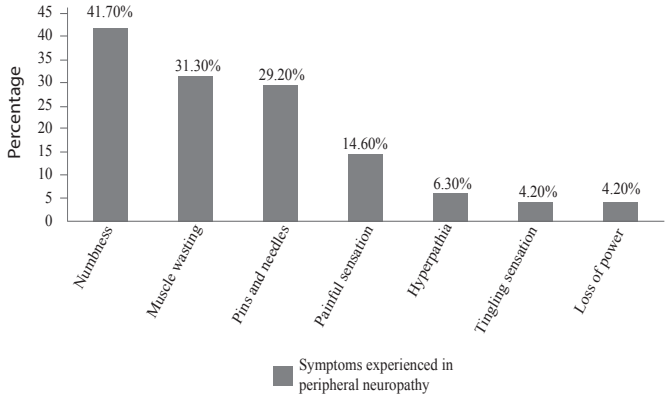
The overall prevalence of peripheral neuropathy in this population was 60.4%. Of these 27.1% were symptomatic with abnormal nerve conductions studies, while 25% were symptomatic with normal nerve conduction studies. Eight point three per cent were found to be asymptomatic with abnormal nerve conduction studies, as shown in Figure 1.

Figure 1: Prevalence of peripheral neuropathy and its presentation in the study participants (sample population n=48)



The frequencies of various neurological symptoms experienced at the time of presentation are shown in Figure 2. The most common symptoms complaint was numbness at 41.7%. Some patients had more than one complaint in terms of the symptoms.

Figure 2: Symptoms experienced in peripheral neuropathy in the study population



Demyelination was the most common nerve conduction pathology detected among participants in this study with a prevalence of 9 (52.9%) out of 17 participants with abnormal nerve conduction studies. However, excluding 5 patients found to have Carpal tunnel syndrome, then the prevalence of demyelination was found to be lower with 4 (23.5%) study participants affected. Axonopathy was found in 5 (29.4%) of the study participants (n=17) (Table 2). Motor neuropathy was found to be the most common type of nerve conduction syndrome with 9 (52.9%) of the study participants affected (n=17) as shown in Table 2. No patient had mononeuritis multiplex as outlined in Table 2. Carpal tunnel syndrome was found in 5(29.4%) of the study participants (n=17).

The overall score for health related quality of life as determined by the LUPUS QOL questionnaire in our study participants was generally impaired quality of life in all the six domains. The domain with the lowest score was physical health (59.1). The summary of the findings are outlined in Table 3.

Table 3: Lupus QOL score of study population (n=48)

Transformed domain	Median (IQR)
Physical health	59.1 (53.1)
Emotional health	75.0 (33.3)
Pain	75.0 (29.3)
Planning	75.0 (58.3)
Fatigue	68.8 (37.5)
Burden to others	75.0 (23.3)

From the sample population, the correlations between presence of peripheral neuropathy and lower quality of life scores in the domains of Physical health, pain, planning and burdens to others were statistically significant as depicted on Table 4.

Table 2: Electrophysiological types of peripheral neuropathy in the study participants

Electrophysiological types	Variables	Frequency n=17	(%)
Nerve conduction pathologies	Demyelination	9	52.9
	Axonopathy	5	29.4
	Axonopathy & demyelinating	3	17.7
Nerve conduction syndromes	Motor	9	52.9
	Sensory- motor	5	29.4
	Sensory	3	17.37
	Mononeuropathy	8	47.1
	Mono-neuritis multiplex	-	-
	Carpal tunnel syndrome	5	29.4

Table 4: Association of peripheral neuropathy with quality of life of patients in the study

Variable	Peripheral neuropathy		X^2	Odds ratio	P value
	Yes n=29 (%)	No n=19 (%)			
Physical health (<80)	21 (72.4%)	4 (21.1%0	12.13	9.84	<0.001
Emotional health (<80)	19 (65.5%)	9 (47.4%)	1.66	2.11	0.212
Pain (<80)	15 (51.7%)	3 (15.8%)	6.32	5.71	0.012
Planning (<80)	17 (58.6%)	3 (15.8%)	8.66	7.56	0.003
Fatigue (<80)	20 (69.0%)	11 (57.9%)	0.62	1.62	0.433
Burden to others (<80)	19 (65.5%)	11 (57.9%)	8.01	11.10	0.005

*X^2- Chi Square results (Pearson's) on R software
*Significant associations are underlined in the table

Discussion

The overall prevalence of peripheral neuropathy in this population of SLE patients was found to be high at 60.4%. The prevalence of peripheral neuropathy in SLE in our study was higher than those that had been done worldwide in Europe and in Asia. This study defined peripheral neuropathy both clinically and electrophysiologically therefore yielding a high prevalence of peripheral neuropathy unlike the other studies that defined peripheral neuropathy either clinically only or electrophysiologically only.

Saigal *et al*[13] in North Asia found a prevalence of 36% (18 out of 50), after having defined peripheral neuropathy electrophysiologically, however they did not include those patients who were symptomatic for peripheral neuropathy and were found to have normal nerve conductions study. Khean *et al*[14] in South Asia found a high prevalence of 56% (28 out of 50) of patients with SLE to have abnormal nerve conduction studies; this high prevalence could have been attributed to external nerve compression in bed ridden patients as the study populations mainly comprised of in-patients, unlike our study that looked at ambulatory out-patients attending rheumatology out patient clinic. Brundusa *et al*[12] found a prevalence of 14%. This low prevalence was mainly because peripheral neuropathy was defined clinically as per the ACR nomenclature and case definition of neuropsychiatric manifestation of SLE.

The high prevalence of peripheral neuropathy in our study could also be explained by the late presentation of SLE patients in our set up and also our patients could have had a high disease activity index, which studies have found to correlate with the presence of peripheral neuropathy, though our study did not assess for disease activity index. Racial difference with genetic variability may also explain the wide discrepancy on the prevalence of peripheral neuropathy as most studies on prevalence of peripheral neuropathy were conducted in Europe, Asia and America. There was paucity of similar studies done in Africa.

Twelve (25%) patients with symptomatic peripheral neuropathy in our study were found to have normal nerve conduction studies; this probably represent patients who may have involvement of small diameter nerve fiber that is not picked on nerve conduction studies and these patients would benefit from either skin or nerve biopsy for confirmatory diagnosis. These results were comparable to other studies done by Oomatia *et al*[8] who found that 17.1% (14 out of 82) of SLE patients with peripheral neuropathy had small fiber neuropathy while Gøransson *et al*[9] found 13%. These studies performed punch skin biopsy to confirm the diagnosis however in our study skin and nerve biopsy were not performed. Oomatia *et al*[8] found that small fiber neuropathy was commonly observed in SLE patients than mononeuritis multiplex, plexopathies, and demyelinating neuropathies. Non length dependent small fiber neuropathy associated with skin biopsy result suggestive of dorsal root ganglion neuronal cell loss was reported by Oomatia *et al*[8]. Therefore small fiber neuropathies not included in the ACR neuropsyciatric case definations of peripheral neuropathies SLE is rather a common finding.

Thirteen (27.1%) patients with symptomatic peripheral neuropathy, had abnormal nerve conduction studies. This was similar to a study by Saigal *et al*[13] in North Asia where they found that 9 out of 18 patients with SLE were symptomatic for peripheral neuropathy and had nerve conduction study abnormality hence clinical peripheral neuropathy.

The remaining 4 (8.3%) patients in our study were asymptomatic and had abnormal nerve conduction studies, and represented a group of patients with sub-clinical peripheral neuropathy. This was almost similar to Saigal *et al*[13] who found that 9 out of 18 patients with peripheral neuropathy had sub-clinical peripheral neuropathy.

In our study, demyelination was found to be the most common type of nerve conduction pathology with 9 (59.9%) patients affected. In contrast to other studies done that found axonopathy to be the most common type of peripheral neuropathy[12-14]. However, on excluding 5 patients with Carpal tunnel syndrome, then the prevalence of demyelination was found to be lower at 4(8.33%) in this study, therefore comparable findings to the other studies that did not include Carpal tunnel syndrome. Five (29.4%) patients had axonopathy hence suggestive of vasculitic neuropathy as expected to occur in patients with SLE and this was consistent with what was found in previous studies[13].

Most of our patients had 9 (52.9%) had motor neuropathy as the most common type of peripheral neuropathy. This was similar to a study done by Saigal *et al*[13] who found that electrophysiological motor nerve parameters were frequently abnormal compared to sensory parameters.

Five (29.4%) patients had Carpal tunnel syndrome, which is mononeuropathy of the median nerve, representing patients who could have had active SLE disease with inflammation of wrist joint.

This study found that presence of peripheral neuropathy could have led to poor quality of life as concerns the domains in physical health, pain, planning and burdens to others. These findings were similar to a study by Brundusa *et al*[12] who found that patients with peripheral neuropathy had significantly lower SF 36 score especially in the physical components, hence poor quality of life.

Conclusion

This study demonstrates a high prevalence of peripheral neuropathy among SLE patients. Small fiber neuropathy which presents with symptoms and normal nerve conduction studies may be rather a common finding in SLE patients in our population. The proportion of patients with demyelination were substantially high

however excluding patients with Carpal tunnel syndrome then axonopathy was rather a common finding. Motor neuropathy was more prevalent. There was a correlation between presence of peripheral neuropathy with quality of life as concerns domains in physical health, pain, planning and burdens to others.

Study limitation

We were unable to exclude all confounding causes of peripheral neuropathy in our population due to resource limitation. Sural nerve biopsy and skin punch biopsy were not performed to further characterize the neuropathies in instances where nerve conduction study was non-revealing, due to financial constraints. Electromyogram was not conducted in our study due to time and resource limitation. This was a hospital based study therefore not generalizable.

Recommendations

A prospective study to determine the progression and outcome of peripheral neuropathy seen in SLE patients in our setting. Skin and nerve biopsy to be included in future studies especially in instances where nerve conductions studies were none revealing. Electromyogram to be incorporated in subsequent studies for confirmatory diagnosis of radiculopathy. Base line symptom screen for peripheral neuropathy in all SLE patients.

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