ORIGINAL ARTICLE

Proportion of Peripheral Neuropathy in Newly Diagnosed Rheumatoid Arthritis - A Single Centre Retrospective Observational Study

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Abstract

Background Rheumatoid arthritis (RA) patients are more prone to develop neurological dysfunction; thus, it is important to recognize peripheral neuropathy in them. Since there are very few studies to exhibit the prevalence of peripheral neuropathy in newly diagnosed RA in Eastern part of India, our study will help to find out the proportion of peripheral neuropathy among newly diagnosed RA patients.**Material & Methods** Sixty patients who were newly diagnosed with RA classified by ACR/EULAR criteria for RA 2010 and who had a Nerve Conduction Study done within 3 months of diagnosis were randomly selected and a retrospective observational study was done to look for presence of peripheral neuropathy.**Results** 30% of study population had electrophysiologically detected peripheral neuropathy. Entrapment neuropathy was the most common type of neuropathy seen. Presence of neuropathy in RA patients is found to significantly increase with increase in DAS28 ESR score (Odd's ratio - 2.092). Disease duration and RF positivity also have association with neuropathic involvement.**Conclusion** It's observed that even in early RA a significant number of patients were found to have peripheral neuropathy. Early detection of high disease activity and its treatment accordingly, or prevention of escalation of disease activity can be helpful in preventing morbidity arising from neuropathy.

Key Words

Rheumatoid Arthritis, Peripheral Neuropathy, Nerve conduction study

Introduction

Rheumatoid arthritis is a chronic autoimmune syndrome associated with several genetic, epigenetic, and environmental factors affecting the articular joints contributing to cartilage and bone damage. [1] The primary target organ is synovium of the joints. [2] The disease is more common in females as compared to males in a 3:1 ratio. [3] Patients usually present with pain and swelling of the symmetrically involved joints. [4] It is the most common inflammatory arthritis, affecting 0.24% to 1% of the general population worldwide. [5] The lab diagnosis is done by detecting serum IgM RF, anti-CCP antibodies, ESR and CRP level. Autoantibodies are both pathologic and diagnostic in RA. [6,7]

The extra articular manifestations in RA are neurological, cardiac, pulmonary, renal and hematologic abnormalities. Peripheral neuropathy is the most common nervous system complication in RA. [8] It occurs secondary to entrapment, vasculitis and drug toxicity. Most of the patients with

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peripheral neuropathy have had subclinical involvement which can be detected by Nerve Conduction Study (NCS). NCS may be considered as an important tool for early detection of peripheral neuropathy in case of RA.[9] Entrapment neuropathies are diagnosed in approximately half of RA patients with severe peripheral disease and subcutaneous nodules. [10] The estimated prevalence of Carpal Tunnel Syndrome (CTS) in the general population is 220 per 100,000 while it is twice as high in the RA population. [11, 12] It may even be the presenting sign of RA. [8] Ulnar neuropathy is the next most common compressive neuropathy followed by Tarsal Tunnel Syndrome (TTS). [13]

As the RA patients are more prone to develop neurological dysfunction, it is important to recognize peripheral neuropathy in RA patients. There are very few studies to exhibit the prevalence of peripheral neuropathy in newly diagnosed RA in Eastern part of India. Our study aims to study the proportion of peripheral neuropathy among RA patients reporting to a tertiary hospital.

Materials and Methods

This is a retrospective, observational, hospital-based study carried out on a total number of 60 patients at a tertiary care centre in Eastern India. Patients who were newly diagnosed with RA and who had an NCS done within 3 months of diagnosis of RA were selected by simple random sampling from hospital records after obtaining institutional ethical committee clearance.

All patients who satisfied ACR/EULAR classification criteria 2010 (ACR- American College of Rheumatology; EULAR- European League Against Rheumatism) for diagnosis of RA (a total score of 6 from the joint, serology, duration and acute phase reactant variables) were included in the study. Patients having neuropathy due to possible secondary causes including diabetes mellitus, leprosy, HIV, vasculitis, SLE, Sjogren's, alcoholism, vitamin deficiency, kidney disorders, toxin induced, amyloidosis, local trauma were excluded. Serological tests such as complete hemogram, RF by Latex Agglutination test (with concentrations above 15 IU/ml recorded as positive), anti-CCP antibodies assayed using ELISA (with 15 IU/ml as the threshold for positive result), CRP, ESR and FBS were done. Disease activity score (DAS28 ESR) was used to measure the disease activity in patients with RA with the available recommended software. NCS was performed on median, ulnar, posterior tibial, peroneal and sural nerves for assessing peripheral neuropathy for each participating patient. Data analysis was done with statistical methods including multiple logistic regression, odd's ratio. Data was then represented in simple measures of frequency, percentage, mean and SD and then analyzed by suitable tables and charts.

Results

A total of 60 patients were collected from hospital records.30% of study population had electrophysiologically detected peripheral neuropathy.10% of the study population had axonal type of neuropathy while demyelinating type constituted 5% and 3.3% had mixed type. Entrapment neuropathy was the most common type of neuropathy seen with a prevalence of 11.7% (as shown in *Table 1*). Among the patients with neuropathy (total 18), CTS was present in 33.33% and TTS in 5.55%. Sensory neuropathy occurred in 38.89% while 22.2% had sensory motor neuropathy (as in *fig 1*). The odds of presence of neuropathy in RA patients were calculated and shown in *Table 1*.

Discussion

Peripheral neuropathy is among the major cause of morbidity in Rheumatoid Arthritis patient, arising from compressive and non-compressive causes. Entrapment neuropathy is the most common form of neuropathy in RA, and CTS the most prevalent form. [10] Clinical and sub clinical patients can be detected by NCS for management accordingly. In our study, presence of neuropathy in RA patients is found to significantly increase with increase in DAS28 ESR score (Odd's ratio 2.092). Patients with RA may have electrophysiologic findings

Table 1. Demographic, Clinical and Neurological Parameters in the Study Population (n=60)

Demographic Details	
Age (mean ± S.D.)	44.38 ± 10.18 years
Clinical Details	
Tender joint count (mean ± S.D.)	4.85 ± 2.57
Swollen joint count(mean ± S.D.)	3.22 ±2.23
Patient global assessment (mean ± S.D.)	40.75 ±23.07
ESR (mean ± S.D.)	47.83 ± 21.96
CRP(mean ± S.D.)	23.13 ± 11.08
Hb (mean ± S.D.)	10.80 ±1.56
DAS 28 ESR (mean ± S.D.)	4.83 ± 1.06
High (DAS28 ESR >5.1)	26 (43.3%)
Moderate (DAS28 ESR 3.2-5.1)	31 (51.7 %)
Low (DAS28 ESR <3.2)	2 (3.3%)
Remission	1 (1.7%)
Rheumatoid factor	34.08 ± 14.58
Type of Neuropathy Detected	
A) Axonal	6 (33.3 %)
B) Demyelinating	3 (16.67%)
C) Mixed	2 (11.1 %)
D) Entrapment	7 (38.9 %)

Table 2. Multiple Logistic Regression Showing Covariates of Presence of Neuropathy in RA Patients

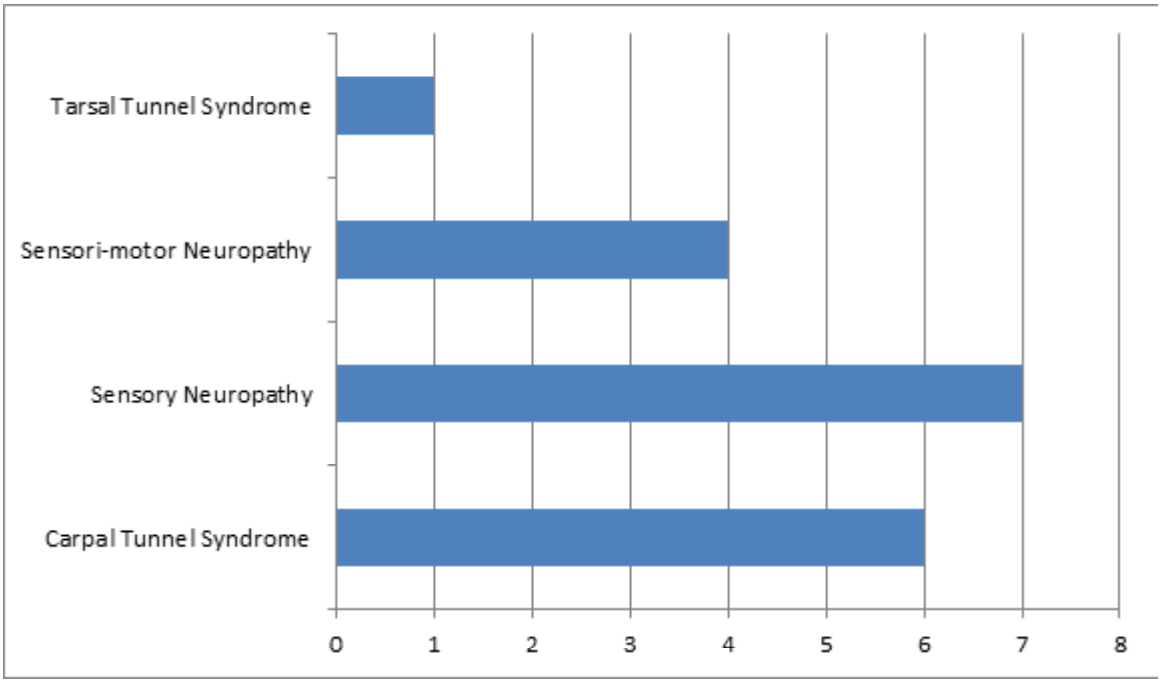
	Exp(B)OR	**95% C.I. upper/lower**	**Adjusted OR**	**95% C.I. Upper/lower**
Age	1.026	0.958/1.099	0.967	0.512/2.300
Gender	1.202	0.200/7.231	0.004	0.000/8.091
Hb	0.720	0.412/1.259	0.493	0.011/2.406
CRP	0.980	0.894/1.074	1.021	0.574/3.221
RF	**2.052**	**1.23/18.291**	**1.132**	**1.096/22.673**
Anti CCP titre	0.313	0.023/4.265	0.026	0.003/5.621
DAS28ESR	**3.485**	**1.039/11.686**	**2.092**	**1.237/8.014**

OR- Odd's Ratio, C.I- Confidence Interval, Hb- Hemoglobin, CRP -C-reactive protein RF- Rheumatoid Factor, CCP - Cyclic Citrullinated Peptide, DAS -Disease Activity Score ESR - Erythrocyte Sedimentation Rate

of peripheral nerve damage, even in the absence of clinical evidence of peripheral nerve involvement and NCS would be useful in identifying these patients. An alternative explanation for the presence of neuropathy may be drug induced neuropathy caused by methotrexate and hydroxychloroquine, the possibility of which is very rare because the study was conducted in all patients within 3 months of diagnosis and initiation of treatment or any other rare causes for peripheral neuropathy which we haven't screened for.

Mean (SD) age of onset in this was 44.38[10-18], with females accounting for 81.7% of study population (*Table 1*). 30% of study population had electro physiologically detected peripheral neuropathy which was in agreement with the study by Kyung *et al* showing 33% of the population with peripheral neuropathy. [14] In the study population, 10 out of 18 patients with peripheral neuropathy showed involvement of upper limb only, 3 had only lower limb involvement, 5 had involvement of both limbs. 10% of the study population had axonal type of neuropathy while demyelinating type constituted 5% and 3.3% had mixed type (*Table 1*). The study by Agarwal V *et al*

Fig 1. Graphical Comparison of the Different Neuropathies Detected in the Population



supports this showing prevalence of demyelinating neuropathy to be 5%. [15] 11.6% had sensory neuropathy, 6.6% had combined sensorimotor type of neuropathy (*Fig 1*). This result is validated by the studies by Sivri *et al* [16] and Conn *et al* [17] which stated that the prevalence of sensorimotor neuropathy in RA patients ranged from 1-18%. Sensory neuropathy was found to be commoner in this study which is in accordance with study by Maiuolo *et al.* [18]

Applying Logistic Regression , Odds of presence of neuropathy in RA patients is found to be significantly increased for raised DAS28 ESR titre rise, after adjusting for R Factor, Anti CCP titre, Hb, CRP, Age, Gender (Odds Ratio = 2.092) (*Table 2*). The results are supported by the study by Bavrak et al which found a significant relationship among polyneuropathy, duration of RA and DAS28 values and that rise in DAS28 score was associated with a three-fold increase in the risk of polyneuropathy. [19] Three other studies also showed disease duration, disease activity and RF positivity to be associated with neuropathic involvement.[16,20]

The critical relevance of these findings is that early detection of high disease activity and its treatment accordingly, or prevention of escalation of disease activity can be helpful in preventing morbidity arising from neuropathy. The study however, suffers the limitation of small sample size and also this hospital-based study may not represent the whole population of Eastern India.

Conclusion

Presence of neuropathy in RA patients is found to significantly increase with increase in DAS28 ESR score. Patients with RA may have electro physiologic findings of peripheral nerve damage, even in the absence of clinical evidence of peripheral nerve involvement and NCV studies would be useful in identifying these patients. Early detection of high disease activity, its early treatment and prevention of disease activity from becoming high by suitable measures can prevent complications like neuropathy.

Further research should be conducted in this field, in order to better understand the disease activity and its correlation with onset of neuropathy.

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Conflicts of Interest
There are no conflicts of interest.

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