**Evaluation of Neuropathic Pain in Rheumatoid Arthritis Patients: Relation to Clinical and Laboratory findings**

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**1.Introduction**

Rheumatoid A chronic autoimmune systemic illness of an inflammatory origin, arthritis (RA) affects synovial joints as well as other parts of the body [1]. According to earlier research [2], RA affects 39.19 percent of the global population.

In addition to its joint manifestations, RA may have extraarticular manifestations in any organ system, and these manifestations may occur prior to the development of arthritis itself. Entrapment neuropathy, a complication of proliferative synovitis, is the most prevalent neurological symptom of rheumatoid arthritis (3).

Neurological issues affect around a third of individuals throughout their lifetimes

3.

Compressive neuropathy, distal sensory neuropathy, and mixed sensorimotor neuropathy are the most prevalent types of peripheral nerve involvement in rheumatoid arthritis (4).

Neuropathy in rheumatoid arthritis may be caused by vasculitis with typical axonal loss and accumulation of immune complexes and the fixation of complement5. The walls of the arteries show fibrinoid type arteritis and immunological globins as symptoms (6).

Individuals with rheumatoid arthritis may confuse neurological symptoms with those of joint illness, making it difficult to detect the existence of peripheral neuropathy in these patients. When a patient has a serious joint condition, it is difficult to evaluate the neurological system (5). Thus, our present research is aimed at assessing the incidence and pattern of neuropathy in rheumatoid arthritis and correlating it with clinical parameters and other extraarticular involvement (2).

To evaluate neuropathic pain in individuals with rheumatoid arthritis (RA) who are experiencing neuropathic symptoms. 2. Objective.

**Methods:**

**3.Patients**

**Inclusion criteria:**

This study was carried out on sixty RA patientsACR/EULAR criteria for RA categorization were met by all patients who were at least 18 years of age.. At Benha University Hospitals, they were selected from the Rheumatology, Rehabilitation outpatient clinic.

The control group consisted of twenty seemingly healthy volunteers of the same age and sex as the patients.

Nerve conduction studies of the median nerve, ulnar nerve, common peroneal nerve, and sural nerves were carried out on all patients and controls in order to determine whether or not they had any abnormalities.

ESR, CRP, CBC, Liver, Kidney Functions, RF, FBS, 2h PPBS are all required for the study.

Treatment history, including earlier use of steroids and DMARDs (disease-modifying antirheumatic medications), was recorded. All patients had their hands x-rayed to look for joint erosions, and the results were tallied using the Larsen score, which ranges from 0 to 160. (9). Latex agglutination testing was used to quantify the rheumatoid factor. RA patients were assessed using the Stanford Health Assessment Questionnaire Disability Index (HAQ-D1). [10] A total of eight questions are asked, all of which revolve to the participant's regular physical activity. To look for tibial and peroneal neuropathies, the Tinsel sign was used. Detecting median neuropathy, Phalen's sign was used. The visual analogue scale (VAS) was used to measure pain (VAS). [11)

**4.Results**

Sixty Our research included people with RA. The electrophysiological detection of peripheral neuropathy was found in around 74.3 percent of the patients. Phalen's sign was positive in 5 (8.3%) of 44 RA patients with peripheral neuropathy, whereas Tinsel's sign was positive in 13 of 44. (29.5 percent ). It's shown in [Table 2].

Motor abnormalities occurred in eight of the RA patients with peripheral neuropathy (18.2%). Patient's age was substantially greater than that of those without peripheral neuropathy among those with RA with peripheral neuropathy, with a mean of 57.5 years. Patients with neuropathy had an average of 17 years of disease compared to 5 years for those without neuropathy [Table 1].

**Table1**Demographic, clinical, and extra-articular manifestation of patients of rheumatoid arthritis

|  |  |
| --- | --- |
| **Parameter** | **Frequency (%), n=60** |
| Gender (F/M) | 54/6 (90%/10%) |
| NSAIDS | 58 (96.7%) |
| Sulfasalazine (y/n) | 1(1.7%) |
| Methotrexate (y/n) | 52 (86.7%/21.3%) |
| Hydroxychloroquine (y/n) | 33 (55%) |
| Leflunomide (y/n) | 32 (53.3%) |
| Neuropathy | 44 (74.3%) |
| Motor abnormalities. | 12 (20%) |
| Tinel’s sign | 21 (35%) |
| Phalen’s sign | 5(8.3%) |
| Tendon reflex | 48(80%) |

**Table 2**Comparison of parameters of patients with RA with and without neuropathy

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | Patients with neuropathy (n=44) | Patients without neuropathy (n=16) | P | Parameter |
| Age (years) | 57.5 (50.25-60.0) | 24.0 (29.0-30.0) | 0.001 | Age (years) |
| Disease duration (years) | 18.0 (16.0-19.0) | 5.0 (4.0-6.75) | 0.000 | Disease duration (years) |
| RF positivity | 37(48.1) | 2(33.3%) | 0.001 | RF positivity |
| ESR | 55.0(55.0-75.0) | 45.0 (41.25-70.0) | 0.001 | ESR |
| Absence of tendon reflexes | 8 (18.2%) | 4 (25%) | 0.048 | Absence of tendon reflexes |
| Muscle weakness | 8 (18,2%) | 4 (25%) | 0.72 | UL, LL weakness |
| Tinel’s sign | 13 (29.5%) | 8 (50%) | 0.14 | Tinel’s sign |
| Phalen’s sign | 5(9%) | 0 (0%) | 0.001 | Phalen’s sign |
| HAQ-D1 (mean±SD) | 0.5 (0.5-1.0) | 1.0 (1.0-2.0) | 0.007 | HAQ-D1 (mean±SD) |
| Pain sensitivity (VAS: 0-10) | 5.0 (5.0-7.0) | 8.0 (6.0-9.0) | 0.001 | Pain sensitivity (VAS: 0-10) |
| Steroids | 26(59.1%) | 13(18.2%) | 0.11 |  |
| NSAIDS | 44(100%) | 14(87.5%) | 0.068 |  |
| Biological | 1(2.3%) | 0(0%) | 0.54 |  |
| Hydroquine | 32(72.7%) | 1(6.3%) | 0.001 |  |
| Leflunamide | 30(68.2%) | 2(12.5) | 0.001 |  |
| Mtx | 40(90.9%) | 12(75.2%) | 0.11 |  |
| salazopyrine | 0(0%) | 1(6.3%) | 0.093 |  |

RA: Disease activity score; Rheumatoid arthritis Rheumatoid factor: ESR stands for the erythrocyte sedimentation rate. Interstitial lung disease, or ILD, is the medical term for this condition. HAQ-D1: Disability Index of the Health Assessment Questionnaire; (Standard Deviation) Neuropathy Symptoms Score (NSS) and Visual Analog Scale (VAS)

DMARDS (methotrexate 90.9 percent, hydoxychloroquine 72.7, biological 2,3 percent, and sulfasalazine 0 percent) were used by the majority of patients with peripheral neuropathy in RA (68.2 percent) as compared to the other group.

However, there was no significant association between the prevalence of neuropathy and past usage of steroids or NSAIDs.

Neither the existence of neuropathy nor NSS was shown to be significantly correlated with this. With neuropathy, patients' health evaluation scores (HAQ-D1 and VAS) were considerably higher.

**5.Discussion**

Patients with neuropathic symptoms of rheumatoid arthritis (RA) were evaluated for neuropathic pain in this research. We also looked at how RA patients' overall well-being and pain levels were affected by peripheral neuropathy. Of the sixty RA patients in our investigation, electro-physiological evidence of peripheral neuropathy was found in 44 (74.3 percent).

Peripheral neuropathy was shown to be associated with age, gender, and length of disease in our research (7.3:1.1 females to 1.1 men) This might be because RA is a disease that disproportionately affects women. A greater proportion of patients with neuropathy had Phalen's test deformity and a lower percentage had Tinel test or lack of tendon reflex than patients who did not have neuropathy.

While the majority of RA patients with peripheral neuropathy were using DMARDS, there was no significant correlation between the prevalence of neuropathy with previous usage of steroids or NSAIDS in our analysis.

According to our findings, rheumatoid factor positive was substantially related with peripheral neuropathy in our research.

Inflammatory indicators of disease activity (ESR) and peripheral neuropathy were shown to be significantly linked in our research.

Patients with neuropathy in rheumatoid arthritis are more likely to have functional impairment than those without it, according to our research. In addition, individuals with RA with neuropathy had a higher VAS pain score and a higher HAQ-D1 score. As a result, neuropathy, particularly in the elderly, is associated with overall health in RA patients.

Peripheral neuropathy was found in 74.3% of participants in our research, which was somewhat higher than the percentages found in earlier studies by Sim et al. (33%) and Biswas et al (39.19 percent ). Due to the inclusion of both old and new RA patients in our analysis, this discrepancy may be explained. In previous research, either newly diagnosed RA patients or only those with peripheral neuropathy symptoms were included. Patients exhibiting symptoms of peripheral neuropathy were included in Sim et al., but not in Biswas et al., which comprised 74 RA patients. [12,13]

Women outnumbered men in our survey by a ratio of 7.3 to 1. One explanation for this is because RA is a disease that disproportionately affects women. The findings of Sivri et al. were not in agreement with this connection between gender and peripheral neuropathy. [18,24] Peripheral neuropathy was shown to be more common in men, according to a study by Albani et al. [17]

According to our research, the older a person is, the more likely they are to suffer from peripheral neuropathy. As a result, in the elderly, RA is a secondary cause of peripheral neuropathy. Peripheral neuropathy is often misdiagnosed in the elderly population. Other than secondary reasons, peripheral nerves' architecture and function gradually deteriorate with age. These patients have a higher risk of falling than others. This might have a substantial impact on their daily routines and functional deterioration as they age. [19,20,21] This link was shown to be substantial by Bharadwaj et al. and Agarwal et al. [1,3] Contrary to popular belief, previous research found no link between the two. This may be due to the fact that the research' sample sizes are lower.

It was revealed that those with rheumatoid factor positive were more likely to have peripheral neuropathy. Albani et al. and Biswas et al. found the same thing. [13,17] However, this link has been disproved in the past by a slew of research. [22,23]

Bhardwaj et al. and Hamed et al. performed studies that indicated a substantial correlation between ESR and peripheral neuropathy in our research. Similar to DAS-28, the occurrence of peripheral neuropathy was shown to have a significant correlation. According to Rajesh et al., this was also found to exist. For further information, see page [25].

We discovered no link between the occurrence of neuropathy and past usage of steroids or NSAIDS in this investigation. According to earlier research, this was the case. [13,15,18] Patients with RA neuropathy who have functional impairment and disease activity are reported to be linked in previous research. RA patients with neuropathy had a higher pain score (VAS) as well. [26]

Patients with RA neuropathy exhibited higher HAQ-D1

requires a multidisciplinary approach to therapy. When it comes to treating these patients and enhancing their quality of life, the responsibility of a family medicine physician cannot be overlooked..[[27](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6396610/#ref27)]

**6.Conclusion**

* Peripheral Rheumatoid arthritis seems to have a wide range of symptoms, and nerve involvement is one of them. Because of the prevalence of subclinical rheumatoid arthritis, electrophysiological testing should be included into the normal examination of this condition.
* Peripheral neuropathy in RA is more likely in older patients and those with a longer history of the illness. This contributes to the functional limitations of the elderly population.

**7.References**

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