ORIGINAL ARTICLE

PREVALENCE OF CARPAL TUNNEL SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS ASSOCIATION WITH DISEASE SEVERITY

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Background: Rheumatoid arthritis (RA) is an auto-immune inflammatory arthritis globally affecting 1% of the population. This study was conducted to see prevalence of carpal tunnel syndrome in patients of RA and its association with disease severity. **Methods:** One-hundred-fifty-four patients aged 21–80 years, of both gender, with RA were enrolled using non-probability consecutive sampling technique. Patients were divided into two groups of 77 each: active disease group (DAS-28 score >3.2) and LDA/remission group (DAS-28 score ≤3.2). RA was defined according to the 2010 ACR Diagnostic Criteria for Rheumatoid Arthritis. Disease severity of RA was determined according to DAS-28 score. Carpal tunnel syndrome (CTS) was diagnosed clinically by specific symptoms and clinical signs. Data were analysed using SPSS-25. **Results:** Mean age of the patients was 43.6±13.7 years, 102 (66.3%) were female. Mean disease duration was 8.3±6.1 years, and mean DAS-28 score was 4.3±2.1. RA factor was positive in 98 (63.7%) and Anti-CCP antibody in 79 (51.3%). CTS was present in 49 (31.8%) patients. On stratification, CTS was seen in 32 (41.5%) patients with active disease compared with 17 (22.1%) patients with LDA/remission. No statistical association of CTS was seen with age, gender, disease duration, RA factor positivity, Anti-CCP antibody positivity and disease severity. **Conclusion:** Carpal Tunnel Syndrome was seen in about one-third patients with RA but no statistically significant association was seen with age, gender, disease duration, RA factor or Anti-CCP positivity and disease activity.

Keywords: Rheumatoid Arthritis, DAS-28 Score, Carpal Tunnel Syndrome, Tinel Sign, Phalen Sign

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INTRODUCTION

Rheumatoid arthritis (RA) is a commonly seen auto-immune inflammatory arthritis globally occurring in up to 1% of the population.[1] RA is primarily a joint disease but can have extra-articular features and abnormal immune responses. Due to chronic inflammation, abnormalities in composition and quality of circulating blood cells can cause lymphopenia with raised neutrophils, thrombocytosis and normochromic anaemia, which are useful as markers of inflammation.[2] The plethora of cytokines, auto-antibodies and immune complexes production, deficiencies of growth factors, reduced life span, deficiency of platelet functions and complications of medicine toxicity can help to explain the changes in blood components in longstanding systemic inflammation.[2] Components of circulating blood cells are often employed in evaluating severity of inflammation. To estimate presence and severity of inflammatory conditions ESR and CRP are usually used but their use is restricted due to limitations such as low specificity and reflection of short-term inflammation only. Various non-inflammatory factors such as gender, anaemia, fibrinogen levels, plasma viscosity and hypergammaglobulinemia, confound the use of these markers.[3]

Disease severity in RA is generally assessed by the DAS-28 score at baseline and follow up, which is calculated by the swollen joint count, tender joint count, patient global assessment on VAS and ESR.[4,5] RA is heralded by infiltration of inflammatory cells in the synovium leading to continuous destruction of joints, cartilage and bone.[6] Various cytokines that affect granulopoiesis, anaemia and neutrophil homeostasis including granulocyte colony-stimulating factor, IL-17 and IL-23 are raised in active RA and correlate with disease activity.[7] Many active RA patients have leucocytosis and thrombocytosis.

Carpal tunnel syndrome (CTS) is a common entrapment neuropathy involving upper limb. In the United States, CTS is seen in up to 19% of the population.[8] Risk factors of CTS include diabetes mellitus, thyroid dysfunction, industrial workers, chronic alcoholism, increasing age, pregnancy, malignancy, female sex, and inflammatory conditions.[8,9] It has been postulated that 1 in every 5 patients who have symptoms of pain, tingling and numbness in the hands have CTS on clinical examination and nerve conduction studies. The most characteristic finding of CTS is non-inflammatory fibrosis and thickening of sub-synovial connective tissue.[9,10] Age and movement associated trauma to the synovium and the flexor tendons in the carpal tunnel

leads to degeneration and increase in volume which in turn cause compression of median nerve resulting in CTS.[10] Inflammatory conditions such as RA can cause CTS by teno-synovitis of the flexor tendons and synovitis of the radio-carpal joint which leads to median nerve compression.[11]

Smerilli *et al*[12] reported CTS to be present in 26.3% and Subasi *et al*[13] reported CTS in 13.2% of RA patients. Karadag *et al*[14] reported CTS in RA as 17.0%. RA patients who had CTS had increasing age, disease duration, diabetes mellitus, worse HAQ-DI score, worse CTS patient global score, severe Boston symptom severity and poor functional status scores.[14] However there was no difference in prevalence of CTS depending on disease severity of RA.[14] Data regarding prevalence of CTS in Pakistan is scare. The link of CTS and disease severity in chronic arthritis is not strongly established. The aim of this study was to document the prevalence of CTS in RA and its association with disease.

MATERIAL AND METHODS

This cross-sectional study was done at Department of Medicine, Jinnah Hospital, Allama Iqbal Medical College Lahore, Pakistan from January to December 2022. Approval from Institutional Ethical Review Board was obtained. RA was defined according to the 2010 ACR diagnostic criteria for rheumatoid arthritis.[15] Disease severity of RA was determined according to DAS-28 score.[16] Active disease was labelled as DAS-28 score >3.2 and low disease activity/remission as DAS-28 score ≤3.2. Carpal tunnel syndrome was diagnosed clinically as the presence of specific symptoms on history (pain, numbness, burning and tingling primarily in the thumb and index, middle and ring fingers) and presence of clinical signs on examination (Tinel sign and Phalen Sign). Tinel sign was performed by percussing over the Median nerve and considered positive when a sensation of tingling or 'pins and needles' was elicited in the distribution of the nerve over thumb and index, middle and ring fingers.[17] Phalen's sign involves flexing the wrist to 90 degrees for 1 minute while maintaining the shoulder in neutral and elbow in extension; and symptoms are elicited in the median nerve distribution to indicate CTS.[18] Keeping margin of error as 5% and confidence interval of 95% a sample size of 154 was required keeping expected frequency as 17.0%.[14]

Patients currently or in last 12 weeks on steroids and biologic DMARDS, chronic diseases including hypertension, diabetes mellitus, coronary artery disease, chronic renal failure, chronic obstructive pulmonary disease, haematologic diseases and malignancy, and patients with pregnancy or breast feeding were excluded from the study.

A total of 154 patients aged 21 to 80 years, of both gender, with Rheumatoid Arthritis were enrolled using non-probability consecutive sampling technique. After informed consent, demographic information, e.g., age, sex, socioeconomic status, duration of disease, educational status, along with medical history to ask for symptoms of CTS (pain, numbness, burning and tingling primarily in the thumb and index, middle and ring fingers) was obtained from each participant. Patients were then divided into two groups with 77 participants each. In active disease group, patients having DAS-28 score >3.2 were included who were either treatment naïve or had stopped taking conventional DMARDs for more than 12 weeks. In low disease activity/remission group, patients taking conventional DMARDs with DAS-28 score ≤3.2 were included. All clinical parameters of DAS-28 were assessed and each patient was then examined for CTS (Tinel Sign and Phalen Sign). Standard treatment as per hospital protocol was given to all patients.

SPSS-25 was used for data entry and analysis. For numerical quantitative variables, mean and standard deviation were calculated. For qualitative variables, frequency and percentage were calculated. Chi-square test was applied and $p \leq 0.05$ was considered as statistically significant.

RESULTS

Out of the 154 patients enrolled in our study, 102 (66.3%) were females and 52 (33.7%) were male having mean age 43.6±13.7 years. Seventy-three (47.4%) patients were younger than 40 years old, 51 (33.1%) were aged 41–60 years and 30 (19.5%) were older than 61 years. Mean duration of disease was 8.3±6.1 years with 89 (57.5%) having duration of disease greater than 3 years. Mean ESR was 33.1±24.2 mm/1st hr. Mean VAS score, tender joint count, swollen joint count and DAS-28 score were 3.5±3.2, 4.6±5.1, 2.4±2.7 and 4.3±2.1 respectively. RA Factor was positive in 98 (63.7%) and Anti-CCP antibody was seen in 79 (51.3%). Carpal Tunnel Syndrome was present in 49 (31.8%) patients. Comparison of clinical parameters with regards to disease severity group of Rheumatoid Arthritis is shown in Table-1 and no statistically significant association of disease severity was seen with age (p=0.102), gender (p=0.981), duration of disease (p=0.253) and RA factor positivity (p=0.432) and Anti-CCP antibody positivity (p=0.096).

On stratification, Carpal Tunnel Syndrome was seen in 32 (41.5%) patients with active disease compared with 17 (22.1%) patients with LDA/remission. No statistically significant association of Carpal Tunnel Syndrome was seen with age (p=0.709), gender (p=0.118), duration of disease (p=0.580), RA factor positivity (p=0.431), Anti-CCP antibody positivity (p=0.402) and disease severity (p=0.107) as shown in Table-2. Among the 77 patients with active disease, 43 (55.8%) were females and 34 (44.2%) male having mean age 42.3±14.3 years. Thirty-

nine (50.7%) patients were younger than 40 years old, 25 (32.5%) were aged 41–60 years and 13 (16.8%) were older than 60 years. Mean duration of disease was 8.3±5.2 years with 42 (54.5%) patients having duration of disease greater than 3 years. Mean ESR was 46.3±21.3 mm/1st hr. Mean VAS score, tender joint count, swollen joint count and DAS-28 score were 7.1±1.8, 6.9±3.9, 4.7±2.8 and 5.8±1.4 respectively. RA Factor was positive in 47 (61.1%) and Anti-CCP antibody was seen in 34 (44.2%).

Among the 77 patients with LDA/remission, 59 (76.7%) were females and 18 (23.3%) male having mean age 46.5±13.7 years. Thirty-four (44.2%) patients were younger than 40 years old, 26 (33.7%) were aged 41–60 years and 17 (22.1%) were older than 60 years. Mean duration of disease in years was 8.2±6.4 with 47 (61.0%) patients having duration of disease more than 3 years. Mean ESR was 12.4±4.4 mm/1st hr. Mean VAS score, tender joint count, swollen joint count and DAS-28 score were 1.1±1.3, 1.0±1.4, 0.5±1.0 and 2.8±0.9 respectively. RA Factor was positive in 41 (61.0%) and Anti-CCP antibody was seen in 34 (44.2%).

In the LDA/Remission group, 25 (32.5%) patients were being treated with methotrexate alone, 18 (23.4%) with leflunomide alone, 12 (15.6%) with methotrexate and hydroxychloroquine combination, 10 (13.0%) with methotrexate and leflunomide combination, 7 (9.0%) with sulfsalazine alone and 05 (6.5%) with methotrexare and sulfasalazine combination.

Table-1: Comparison of clinical parameters according to disease activity of rheumatoid arthritis

Clinical parameters	Disease activity	
	LDA/Remission	Active disease
Mean age (Years)	46.5±13.7	42.3±14.3
Mean Duration of disease (Years)	8.2±6.4	8.3±5.2
Mean ESR (mm/Hr)	12.4±4.4	46.3±21.3
Mean VAS score	1.1±1.3	7.1±1.8
Mean Tender joint count	1.0±1.4	6.9±3.9
Mean Swollen joint count	0.5±1.0	4.7±2.8
Mean DAS-28 score	2.8±0.9	5.8±1.4
Age groups		
<40 Years	34 (44.2%)	39 (50.7%)
40–60 Years	26 (33.7%)	25 (32.5%)
>60 Years	17 (22.1%)	13 (16.8%)
Gender		
Female	59 (76.7%)	43 (55.8%)
Male	18 (23.3%)	34 (44.2%)
Duration of disease		
≤3 years	30 (39.0%)	35 (45.5%)
>3 years	47 (61.0%)	42 (54.5%)
RA Factor status		
Positive	51 (66.2%)	47 (61.0%)
Negative	26 (33.8%)	30 (39.0%)
Anti-CCP antibody status		
Positive	45 (58.5%)	34 (44.2%)
Negative	32 (41.5%)	43 (55.8%)
Carpal tunnel syndrome		
Present	17 (22.1%)	32 (41.5%)
Absent	60 (77.9%)	45 (58.5%)

Table-2: Comparison of qualitative clinical parameters according to Carpal Tunnel Syndrome

Clinical Parameters	Carpal Tunnel Syndrome		*p*
	Present	Absent	
Gender			
Female	38 (37.2%)	64 (62.8%)	0.118
Male	11 (21.2%)	41 (78.8%)	
Age			
≤40 years	27 (37.0%)	46 (63.0%)	0.709
41–60 years	14 (27.4%)	37 (72.6%)	
≥61 years	08 (26.7%)	22 (73.3%)	
Duration of disease			
≤3 years	21 (32.3%)	44 (67.7%)	0.580
>3 years	28 (31.5%)	61 (68.5%)	
RA Factor status			
Positive	34 (34.7%)	64 (65.3%)	0.431
Negative	15 (26.8%)	41 (73.2%)	
Anti-CCP Antibody status			
Positive	26 (33.0%)	53 (67.0%)	0.402
Negative	23 (30.7%)	52 (69.3%)	
Disease Severity			
LDA/Remission	22 (28.6%)	55 (71.4%)	0.107
Active Disease	27 (35.0%)	50 (65.0%)	

DISCUSSION

Carpal Tunnel Syndrome, a constellation of signs and symptoms, can result from various mechanisms which cause median nerve compression.[18] CTS in RA patients is usually due to inflammatory process whereas in idiopathic CTS inflammation is characteristically absent.[19,20] CTS can also be an initial presentation of RA. In the UK, Muller *et al*[21] conducted a retrospective case-control study to highlight that patients with CTS may go on to develop RA in the following two years after consultation, having odds ratio 2.96.[21]

In the present study 154 patients of RA were enrolled and CTS was seen in 49 (31.8%) patients. In Italy, Smerilli *et al*[12] reported CTS to be present in 26.3% patients of RA. In Turkey, Subasi *et al*.[13] reported CTS in 13.2% of RA patients. Karadag *et al*.[14] enrolled 100 of RA to document prevalence of Carpal tunnel syndrome as 17.0% using combination of history, examination and ultrasonography. In the present study there was no statistically significant association of CTS with age (p=0.709), gender (p=0.118), duration of disease (p=0.580), RA factor positivity (p=0.431) and Anti-CCP antibody positivity (p=0.402). Karadag *et al*[14] found that RA patients having CTS were older, had a longer disease duration, diabetes mellitus and poor functional status scores.[18] However there was no difference in prevalence of carpal tunnel syndrome depending on disease severity of RA.[14] In the present study, CTS was seen in 32 (41.5%) patients with active disease compared with 17 (22.1%) patients with LDA/remission. However there was no significant statistical association (p=0.107).

Splinting is usually recommended as first-line in patients with mild symptoms.[22] Corticosteroid injection into the carpal tunnel is indicated in moderate CTS to provide relief of symptoms, but the effect is usually temporary.[23] For patients not responding to conservative interventions, surgical release is recommended to decompress the median nerve.[24]

The present study has some limitations that it was a single centre study, had a relatively small sample size and enrolled out-patients only. Case-control or cohort studies are a better option.

CONCLUSION

Carpal Tunnel Syndrome is not an uncommon extra-articular manifestation of Rheumatoid Arthritis and was seen in almost one-third of the patients with Rheumatoid Arthritis It is relatively more common in patients with active disease. It is recommended that clinical assessment of CTS should be done routinely in patients with RA, so that lifestyle modifications and pharmacological treatment may be modified accordingly to control and reduce disease morbidity and disability. More work is recommended to find association of CTS and RA disease severity.

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