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Research Paper

Involvement of Joints and Deformity Pattern with Seropositivity in Rheumatoid Arthritis

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ABSTRACT
Introduction: *Rheumatoid Arthritis (RA) is an autoimmune systemic disease, which mainly attacks the joints and induces the inflammatory changes that thickens primarily the synovium resulting in swelling and severe pain in and around the joints. It starts with symmetrical pain, swelling and produces joint deformity. It also affects the cardio-respiratory system or other systems of body and eventually affects the quality of life.*
Objectives: *Our study aims to evaluate the relationship between the pattern of joint involvement and development of deformity with seropositivity in patients with Rheumatoid Arthritis. Data analysis was done by descriptive statistics, Chi-square test and Fisher's Exact text and p value < 0.05 was considered as statistically significant.*
Materials and Methods: *This cross sectional study was carried out in the Department of Medicine, Sir Salimullah Medical College and Mitford Hospital, Bangladesh, over a period of nine months from October 2016 to June 2017. A total of 100 patients with Rheumatoid Arthritis, aged above 18 years of either sex, diagnosed by criteria for Rheumatoid Arthrits set by the American College of Rheumatology (ARA) were included as study population.*
Results: *Mean age of patients was 37.3+9.8 years with higher prevalence in females, mostly housewives by occupation belonging to poor class. In the seropositive patients, bilateral symmetrical pain was the universal complaint of patients. Almost all patients suffered from bilateral carpal and metacarpophalangeal joint pain, bilateral tarsal and metatarsophalangeal joint pain was present in 93% patients, followed by 90% who suffered from bilateral wrist and ankle pain individually. Around 40% had bilateral elbow joint pain and 65% had both knee joint pain. Majority had swelling of joints of hand (98%), foot (86%), wrist (85%), ankle (80%) and knee (65%) bilaterally. Maximum 63% patients were found with joint deformity. Swan-neck deformity in index finger was present in 16% cases, in middle finger 46% and ring finger 38%. The boutonniere and Z-deformity of middle finger and thumbs were 7.9% and 4.8% respectively. Mean duration of swan neck, boutonniere and Z-deformity were 22.4±5.7, 15.6±5.8 and 6.0±2.1 months, respectively. About 9% patients had claw deformity of foot and 46% had bilateral wrist joints deformity. Mean duration of wrist and elbow deformities were 51.4±6.7, 12.0±4.5 months, respectively. Average hemoglobin, total count of WBC and ESR were 10.4±0.8 gm/dl, 8573±1794/mm^3 of blood and 86.6±14.9mm in 1st hour, respectively. None of the joint deformities like hand, elbow, wrist, foot were found to be associated with age and sex of the patients. Hand deformity was significantly higher with positive anti-cyclic citrullinated peptide (79.2%) compared with negative anti-cyclic citrullinated peptide antibody (p<0.001). Similarly, wrist joint deformity had higher affinity for positive Anti-CCP antibody (p=0.036). Patients with hand and wrist joint deformities were more prone to have positive RA tests (p<0.001 and p=0.048, respectively).*
Conclusion: *Patients of Rheumatoid Arthritis with hand and wrist joint deformities have significantly higher tendency to be seropositive (anti-CCP antibody and RA positive).*
KEYWORDS: *Rheumatoid Arthritis, Seropositivity, Deformity, Rheumatoid factor, Anti-cyclic citrullinated peptide.*
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I. INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune, long term disease of unknown aetiology[1]. It starts with pain, swelling and stiffness in joints[2]. Progression of the disease may vary and eventually lead to inability in performing daily activities[3]. The prevalence in women is thrice than men worldwide[4].

Rheumatoid arthritis mainly involves the symmetrical peripheral polyarthritis with synovium being the primary target[5]. It is associated with the production of autoantibody called rheumatoid factor (RF), anti-cyclic citrullinated peptide (anti-CCP). It has been investigated in several studies that, there is a positive relationship between autoantibody and disease activity[6]. Some studies reported that, anti-CCP is the only significant predictor for joint damage and seropositivity was significantly higher in RA patients with severe joint destruction than those with minimal joint destruction[7]. About 75% of patients with Rheumatoid Arthritis show hand deformity and 16% foot deformity[8]. Various types of deformity were noted such as, swan-neck, Boutonniere, Z-deformity of thumb, ulnar deviation, clawing of toes, ankylosis of joints etc[9,10,11].

The aim of the study is to explore the pattern, type and demographic characteristics of involvement of joint deformities and their relationship with seropositivity in patients with Rheumatoid Arthritis.

II. MATERIALS AND METHODS

This is a prospective, cross sectional study conducted in the Department of Medicine, Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh over a period of nine months from October 2016 to June 2017, after approval from Ethical committee of Sir Salimullah Medical College and Mitford Hospital, Dhaka, Bangladesh. Written informed consent was taken from all patients. A total of 100 patients aged above 18 years, of either sex were enrolled in this study, by inclusion and exclusion criteria who willingly participated in the study and also fulfilled the American College of Rheumatology (ACR) criteria 2010. All cases were subjected to a complete history, clinical examination and laboratory investigations. Patients' demographic data were collected at the time of visit to the Medicine department of Sir Salimullah Medical College and Mitford Hospital, Bangladesh. Data was analyzed using software Statistical Package for Social Sciences (SPSS) version 20. Results are presented in tables and figures. Analytical study was done by descriptive statistics, Chi-square (χ^2) test and Fisher's Exact test with p value < 0.05 considered as statistically significant.

III. RESULTS

Demographic characteristics:

The mean age of patients was 37.3 ± 9.8 years. Figure 1(a) and 1(b) shows that most of the patients (76%) were females, housewives (72%) by occupation and belonged to poor class (56%).

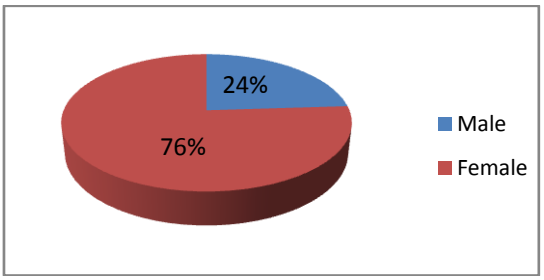

Figure 1(a): Gender distribution of patients

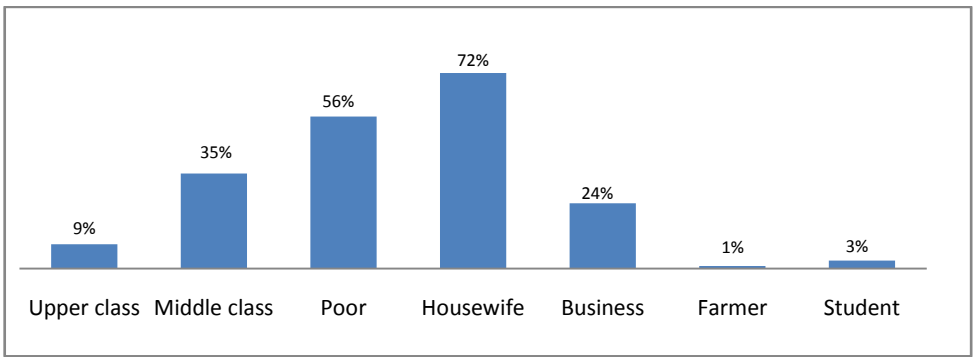

Figure 1(b): Distribution of patients by class and occupation

Figure 2 displayed that 100% of patients experienced bilateral carpal and metacarpophalangeal joint pain followed by 93% who suffered from bilateral tarsal and metatarsophalangeal joint pain, almost 90% complained of bilateral wrist and ankle pain individually. Over 40% complained pain in both elbow joints and 65% suffered from both knee joint pain. Shoulder joint pain was less commonly experienced.

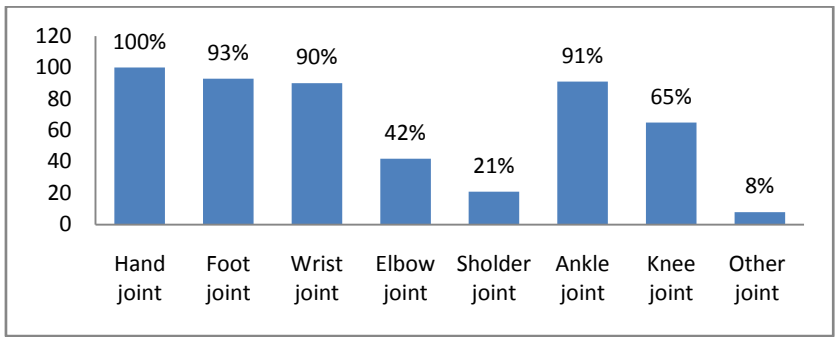

Figure 2: Distribution of joint pain

Figure 3 showed that majority (98%) of patients had swelling of hand joints, foot (86%), wrist (85%) and ankle (80%) bilaterally, followed by swelling in both sides of knee joints (63%). Elbow joint swelling was not frequently seen (20%).

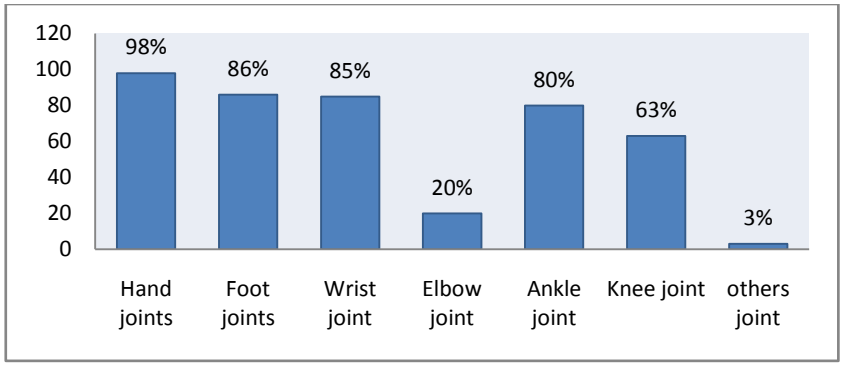

Figure 3: Distribution of joint swelling

Figure 4 revealed that, out of 100 patients, 63 of them had some form of joint deformity. Swan-neck deformity was present in all the 63 cases with 16% in index finger, 46% in middle finger and 38% in ring finger. Boutonniere and Z-deformity of middle and thumb fingers were 7.9% and 4.8% respectively. Nine out of hundred patients exhibited clawing deformity of foot. About 46% of patients had deformity of both wrist joints and 2% had elbow deformity. Table 1 displays the mean duration of swan neck, Boutonniere and Z-deformity were 22.4±5.7, 15.6±5.8 and 6.0±2.1 months, respectively. Mean duration of clawing deformity was 3.0±0.9 months, while of wrist and elbow deformities were 51.4±6.7 and 12.0±4.5 months, respectively.

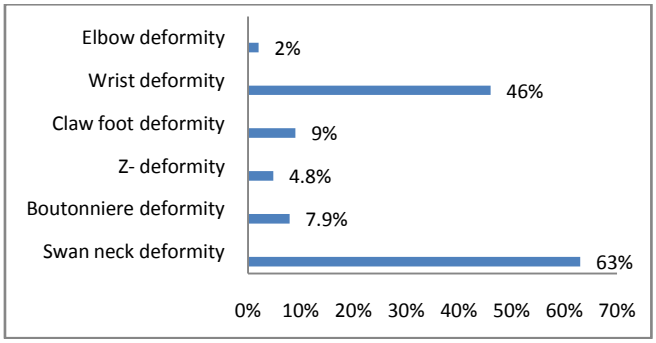

Figure 4: Pattern of joint deformity

Table 1: Mean duration of joint deformities

Duration of joint deformity	**Mean ± SD (months)**
Deformity of hand joint Swan neck deformity Boutonniere deformity Z deformity	 22.4 ± 5.7 15.6 ± 5.8 6.0 ± 2.1
Deformity of foot joint (clawing)	3.0 ± 0.9
Deformity of wrist joint	51.4 ± 6.7
Deformity of elbow joint	12.0 ± 4.5

Table 2 reveals the investigative findings where average hemoglobin, total count of WBC and ESR were 10.4±0.8 gm/dl, 8573±1794/mm^3 of blood and 86.6±14.9mm in 1st hour, respectively, and most of the patients were anaemic.

Table 2: Findings of blood investigations (n=100)

Investigations	**Mean±SD**
Hemoglobin (gm/dl)	10.4±0.8
Total count of WBC (/mm^3)	8573±1794
ESR (mm at the end 1st hr)	86.6±14.9

Table 3 shows there were no association between the joint deformities (hand, foot, wrist and elbow) with age and sex of the patients with p>0.05 for both age and sex.

Table 3: Association between joint deformities with age and sex of patients

Joint deformity	**Age (years)**		**p-value**	**Sex**		**p-value**
	< 40 (n=53) n(%)	≥ 40 (n=47) n(%)		Male (n=24) n(%)	Female (n=76) n(%)	
Hand*	32(68.1)	31(58.5)	0.321^{ns}	13(54.2)	50(65.8)	0.304^{ns}
Foot$^{\#}$	2(4.3)	7(13.2)	0.112^{ns}	1(4.2)	8(10.5)	0.343^{ns}
Wrist*	18(38.6)	28(52.8)	0.146^{ns}	7(29.2)	39(51.3)	0.058^{ns}
Elbow	2(4.3)	0(0)	-	0(0)	2(2.6)	----

*****Chi-square test; #Fisher's Exact test; ^{ns}:non significant

Table 4 showed that, hand deformity was significantly higher in patients with positive anti-cyclic citrullinated peptide (79.2%) compared to that in patients with negative anti-CCP antibody (p<0.001). Similarly, wrist joint deformity tend to be significantly associated with positive Anti-CCP antibody (p=0.036).

Table 4: Association between anti-CCP antibody and joint deformity (n=100)

Joint deformity	**Anti-CCP antibody**		**p-value**
	Positive (n =77) n(%)	Negative (n =23) n(%)	
Hand	61(79.2)	2(8.7)	< 0.001^{*s}
Foot	9(11.7)	0(0)	-
Wrist	24(31.2)	2(8.6)	0.036^{*s}
Elbow	2(2.6)	0(0)	-

* Chi-square test ; ^{s} :significant

Table 5 demonstrated that patients with hand and wrist joints were more prone to have positive Rheumatoid Test (RA) tests (p < 0.001 and p = 0.048 respectively). There was a significant association between RA test and joint deformity (p<0.05).

Table 5: Association between RA test and joint deformity (n=100)

Joint deformity	RA test		p-value
	Positive (n=61) n(%)	Negative (n=39) n(%)	
Hand*	55(90.2)	8(20.5)	< 0.001*[s]
Foot	9(14.8)	0(0)	-
Wrist* (both)	41(67.2)	5(12.8)	0.048*[s]
Elbow (left)	2(3.3)	0(0)	-

*Chi-square test; [s] :significant

IV. DISCUSSION

Rheumatoid Arthritis is a chronic multi-system disabling disease with various manifestations frequently leading to physical and psychological dependence with considerable economic consequences. Thus, this study was conducted to evaluate the joint involvement and pattern of deformity and their relationship with seropositivity. The modern trend of Rheumatoid Arthritis treatment has been changed to start treatment as early as possible, based on the concept that early control of inflammation results in reduced joint damage[13]. It is, therefore, important to differentiate between RA and other forms of arthritis early after the onset of symptoms[14]. Although, the 1987 American College of Rheumatology classification criteria for RA are often used in clinical practice as diagnostic tool for RA, they are not well-suited for the diagnosis of early RA[15]. The ACR criteria rely heavily on the expression of clinical symptoms of RA, but in early RA these clinical parameters are often not manifested. Therefore, a specific and sensitive (serological) marker, which is manifested early in the disease, is needed. The marker should ideally be able to predict the erosive or non-erosive progression of the disease.

The present study revealed that RA is primarily a disease of early middle age (mean age 37.3±9.8 years) which was analogous to a similar study[16]. Females acquire the disease more often than the males (female to male ratio being roughly being 3:1) and over half (53%) of the patients were rural residents and of low socioeconomic class which were similar to other studies[14,15].

In the present study, most of the patients had bilateral carpal and metacarpophalangeal joint pain. Bilateral tarsal and metatarsophalangeal joint pain (93%), bilateral wrist and ankle pain was present in each of the 90% cases. Over 40% complained of pain in both elbow joints, 65% in both knee pain joints. These data thus indicate that the symmetrical involvement of metacarpophalangeal, metatarsophalangeal joints and joints of hands and wrists are the most characteristic and early findings of RA[17]. The first symptoms are pain**,** swelling, and stiffness in the joints. Most commonly involved joints include hands, feet, wrists, elbows, and ankles, although other joints may also be involved[2,3,5]. The joints are affected in a symmetrical fashion[5]. Patients frequently experience painful joint stiffness when they first get up in the morning, lasting for an hour or so. Over time, the joints become deformed and the joints may be difficult to straighten, and affected fingers and toes may be permanently bent (flexed). The hands and feet may curve outward in an abnormal way[5,7]. RA lead to erosion of tendons in the wrist and fingers that can cause deformity and loss of function[18]. Synovitis of the elbow joint and inflammation and nodule formation in the extensor surface of the elbow are frequent as RA progresses. Mild flexion contractures occur in the early stages and, later in the disease, severe contractures may lead to functional disability[19]. And in patients with chronic RA, the shoulder joint space can contract and lead to rupture of the rotator cuff. Involvement of the knees is common and is often a primary occurrence in the early course of RA[20]. This is usually characterized by swelling and synovial effusion and thickening. Chronic and persistent synovitis can limit walking due to cartilage destruction, ligament laxity, joint instability, and contractures[2,21]. Inflammation of the small joints of feet is another common manifestation, with ankle joint involvement less common. Similarly to the MCP and PIP joints, the MTP joints are sites of early synovitis[22]. As the disease progresses, the synovitis in the MTP joints can lead to deformity as well as to pain and disability, particularly in the ball of the foot when bearing weight (i.e., standing, walking). The joints of the hind-foot (talus) may be involved, which can lead to heel pain and difficulty walking[23].

The flexion and pinch force of the fingers found that index and middle fingers were significantly stronger than the ring and little fingers. The earliest erosions in the MCP joints were found to occur in the index and middle fingers[24].

In the present study, Swan neck deformity was found in about 16% of patients of index finger, 46% middle and 38% ring finger. The boutonniere and Z-deformity were 7.9% and 4.8% respectively, in the middle and thumb fingers. The deformity of wrist appears first and that of elbow appears last. Majority (86%) of the patients were anaemic which were similar with several studies[5-11].

The anti-CCP was positive in 79.2% of patients with hand deformity, 11.7% with foot deformity, 31.2% with bilateral wrist deformity and 2.6% left elbow deformities. The proportion of positive RA test with bilateral hand and wrist deformities were significantly higher than those with negative RA test (90.2% vs. 20.5,

p<0.001 and 67.2% vs. 12.8%, p=0.048) which was similar to other research works[16,17,18]. Seropositive patients had more frequent involvement of hand joints, and higher involvement of number of joint counts than seronegative patients[18]. Furthermore, a report indicated that rheumatoid nodule was highly prevalent in seropositive patients[25]. As the factors related to poor prognosis in RA were checked, it was found that women with RF positive status, high ESR and CRP, anaemia, and rheumatoid nodule were associated with poor outcomes[26].

Finally, Anti-CCP and RA test are recognized biomarkers associated with RA that are incorporated in the current ACR classification guidance for RA diagnosis. The reviewed studies indicate that the two biomarkers are promising early diagnostic tests with the potential to support early, aggressive intervention using newer RA treatment options. RF (RA test) appears to be a strong predictor of erosive RA, making it a potentially important prognostic tool that could be used to inform patient management decisions. Additional prospective longitudinal research studies of the prognostic value of RF tests would help to validate this clinical application.

V. CONCLUSION

From this study and discussion it could be concluded that RA is primarily a disease of early middle age. Females acquire the disease more often than males. Symmetric involvement of the metacarpo-phalangeal, metatarso-phalangeal joints and joints of hands and wrists were the most characteristic and early findings of RA. Rheumatoid arthritis patients with hand and wrist joint deformities have significantly higher tendency to be seropositive (anti-CCP antibody and RA positive).

Conflict of interest

The authors declare that they have no conflict of interest.

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