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Clinico-demographic Profile of Undifferentiated Inflammatory Arthritis Patients

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ABSTRACT

Background: Undifferentiated inflammatory arthritis is a group of inflammatory joint diseases that do not fulfil the classification criteria for any other rheumatic or connective tissue disorders. This study aims to describe the clinical, demographic and serological features of undifferentiated inflammatory arthritis cases presenting at a tertiary level rheumatology centre from Nepal.

Methods: A descriptive cross-sectional study conducted at National Centre for Rheumatic Diseases, Kathmandu, Nepal which represents a midterm analysis of the undifferentiated inflammatory arthritis registry maintained at the centre. Patients more than 18 years of age, who consented for the study having least one swollen or tender joint were enrolled. Ethical approval was obtained from Nepal Health Research Council.

Results: A total of 1120 patients were enrolled in the study out of which 941 (84%) were females. The mean age at diagnosis was 46.0±12.8 years and most of them were in overweight range (mean BMI: 27.0±5.8) with 818 (73%) patients having BMI more than 24.0. Patients mostly had low disease activity at presentation (DAS 28 score of 2.5±0.8). Other markers of inflammation and patient reported outcome measures (health assessment questionnaire, patient global assessment and visual analogue scale) were also in the moderate range. Seropositivity for anti-citrullinated peptides and anti-nuclear antibodies was seen in 5 (0.45%) and 43 (3.8%) patients respectively. Majority of patients were non-smokers (77%). Inflammatory arthritis on musculoskeletal ultrasonography was seen in 638 (57%).

Conclusions: Undifferentiated inflammatory arthritis was more common in overweight females. Serological markers and smoking status are not common features in these patients.

Keywords: Early arthritis; Nepal; undifferentiated arthritis.

INTRODUCTION

Undifferentiated inflammatory arthritis (UDIA) is a group of inflammatory joint diseases that do not fulfil the classification criteria for any other rheumatic or connective tissue disorders.[1]The clinical features of UDIA can be myriad and confusing; but the presence of inflammatory joint disease usually mandates some form of disease modifying therapy even in the absence of definite diagnosis.[1, 2]

Though many of the early cases (<3months duration) progress to rheumatoid arthritis, significant number may still persist in undifferentiated form for a prolonged period.[3] This group of disorders is still poorly understood and little data is available on their clinical, serological features and the natural history.

Increasing number of cases are being diagnosed as UDIA in Nepal and this study aims to describe the clinical, demographic and serological features of UDIA cases presenting at a tertiary level rheumatology centre from Nepal.

METHODS

This was a descriptive cross-sectional study conducted at the rheumatology out-patient department of National Centre for Rheumatic Diseases, Kathmandu, Nepal. The study represents a midterm analysis of the UDIA registry maintained at the centre. This registry is a part of UDIA cohort planned to be studied for outcome over 5 years. Ethical approval was provided by Nepal Health Research Council for study of the cohort of UDIA patients (registration no 166/2018). A convenience sampling method was used and consecutive patients diagnosed

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as undifferentiated arthritis by the rheumatologist were enrolled in the study registry from July 2015. A sample size of 425 was calculated based on the estimated population prevalence of 50percent and a power of the study of 95%.[4]

Patients more than 18 years of age, who consented for the study and who had at least one swollen or tender joint were enrolled in the cohort. Those who fulfilled the criteria for rheumatoid arthritis, spondyloarthropathy, lupus, scleroderma or any other connective tissue disorder and those who were already under treatment for established rheumatic disease at baseline were excluded. Those with trauma, mechanical joint lesions, osteoarthritis, crystal arthropathies or septic arthritis and those with only axial symptoms were also excluded from the cohort.

Baseline data were taken by rheumatologists, medical officer and trained research officer. Baseline demographic data included age, gender, height, weight, body mass index (BMI), education level, smoking status and disease duration. Education level was classified as illiterate, primary, secondary and higher education. Smoking status were recorded as either current and ex-smoker or non-smokers. The trained assessors performed the 28 swollen joint counts (SJC), 28 tender joint counts(TJC) and administered the patient-reported outcomes like translated and validated Nepali health assessment questionnaire (HAQ),[5] patient global assessment (PGA) and visual analogue score (VAS) for pain and morning stiffness. Investigations were sent for determining erythrocyte sedimentation rate (ESR, Westergren's method), C-reactive protein (CRP, ELISA), anti-citrullinated peptide antibodies (ACPA, ELISA) and anti-nuclear antibody (ANA, ELISA). As most of the cases are known to progress to rheumatoid arthritis, and no validated outcome or activity measure for UDIA are available yet, disease activity score (DAS) 28 was used to measure the disease activity.

Musculoskeletal ultrasonography with power Doppler (MSUS) scanning was performed in all new cases enrolled after January 2018 when this diagnostic modality became available in Nepal. The initial MSUS findings were recorded as normal, degenerative (reduced and/or irregular cartilage and osteophytes), periarticular disease (tenosynovitis, tendonitis, enthesitis, bursitis) and inflammatory arthritis (synovial hypertrophy, effusion and increased power Doppler uptake).

Simple descriptive statistical analysis was performed using SPSS version 21 (IBM corp., USA).

RESULTS

A total of 1120 patients diagnosed as UDIA were enrolled in the study. Among them, 941 (84%) were females. The mean age at diagnosis was 46.0±12.8 years and most of the patients were in overweight range (mean BMI 27.0±5.8) with 818 (73%) patients having BMI more than 24.0 kg/m2.

The median disease duration was 96 weeks at presentation. Majority of the patients presented to the rheumatologist after 1 year of disease onset 638 (57%), whereas only 168 (15%) presented within first 3 months of symptom onset. Other sociodemographic profiles are shown in Table 1 and education levels shown in figure 1.

Patients mostly had low disease activity at presentation as evidenced by mean DAS 28 score of 2.5 ± 0.8. Other markers of inflammation (ESR, CRP) and patient reported outcome measures (HAQ, PGA and VAS) were also in the moderate range (Table 1).

Table 1. Clinico-demographic profile of study participants at baseline (n=1120)

Parameters	N (%)
Age (years) Mean ± SD	46.0±12.9
Gender n (%)	Male - 179(16) Female - 941(84)
*BMI (Mean ± SD)	27.0±5.8
Disease Duration n (%)	< 3 months- 168(15) 3-12 months- 314(28) >12 months- 638(57)
†CRP in mg/dL Median (Range)	2.4 (0.6 - 170.2)
‡ESR (Mean ± SD) mm in 1st hour	25.4 ± 13.2
§VAS Pain(Mean ± SD)	4.4±2.5
Nepali ǁHAQ (Mean ± SD)	1.4 ± 0.3
¶PGA (Mean ± SD)	4.2 ± 2.4
**TJC Mean ± SD	2.3±1.9
††SJC Median (Range)	0 (0 - 16)
‡‡DAS 28- CRP Mean ± SD	2.5± 0.8

*BMI: body mass index; †CRP: C-reactive protein; ‡ESR: erythrocyte sedimentation rate; §VAS: visual analogue score; ǁHAQ: health assessment questionnaire; ¶PGA: patient global assessment; **TJC: tender joint count; ††SJS: swollen joint count; ‡‡DAS 28-CRP: disease activity score 28-CRP

Seropositivity for anti-citrullinated peptides was seen in only 5 (0.45%) patients whereas ANA positivity was seen in 43 (3.8%) patients. Inflammatory markers like elevated CRP (>6mg/dl) and ESR (>20mm) were seen in 616 (55%) and 670 (59.8%) patients respectively. Majority of patients presenting with symptoms were non-smokers (77%) and among those who had history of smoking 15% left smoking for more than a year (Figure 3).

Majority of patients had inflammatory arthritis 638

(57%) on MSUS of the affected joints and 168 (15%) had involvement of periarticular structures only (Figure 2).

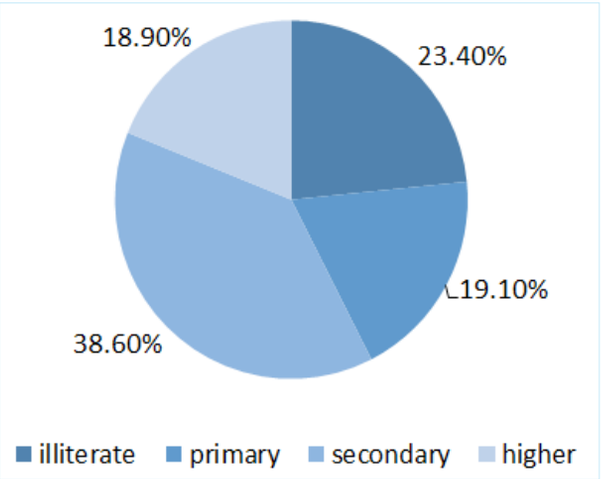

Figure 1. Percentage of patients in each education strata (n=1120).

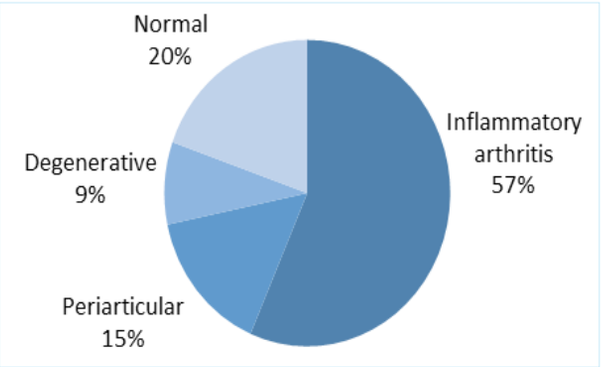

Figure 2. MSUS findings in UDIA.

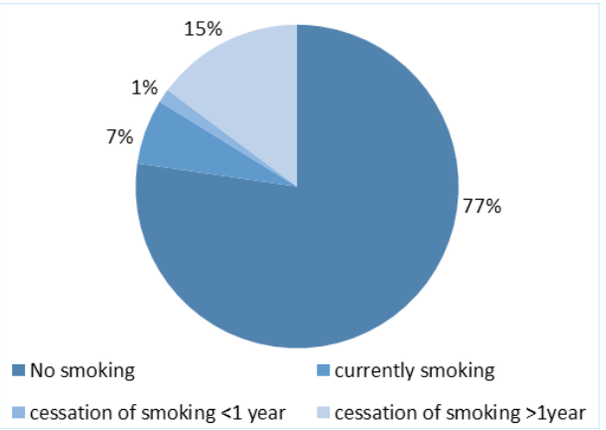

Figure 3. Smoking status among patients with UDIA.

DISCUSSION

It is a common experience of many rheumatologists, orthopedicians and internists to encounter cases of inflammatory arthritis that do not fit into any of the established diseases. Usually these cases are either early presentation of rheumatoid arthritis or any other systemic rheumatic disorder, or they might just remain undifferentiated without progression.[3, 6] Previous studies have tried to explore the clinical and serological features that can help to differentiate those early diseases into progressive or remitting groups.[6,7] Many have found presence of ACPAs and involvement of multiple joints as the important predictive factors for progression. The ACPA and ANA positivity rates were also significantly low as compared to patients with RA or any other defined connective tissue disorder like lupus or scleroderma. It is likely that those who are positive to these autoantibodies given definite diagnosis by this period of follow-up.[8, 9]

The study from Leiden cohort has given a prediction rule consisting of nine parameters to assess the risk of progression of these early undifferentiated arthritis cases to rheumatoid arthritis.[10]

Our study is an analysis of the inception cohort of UDIA patients enrolled to study their natural history and treatment outcomes from Nepal. Though the mean age of patients was almost same as of RA patients in most studies, most of the patients were females and the female to male ratio of approximately 5:1 exceeds the ratio for RA patients (3:1).[11,12] The majority of patients (57%) had disease duration of more than 1year with median disease duration of 1.8 years at presentation highlighting the fact that the cohort represented a group different from early RA (< 3 months) cases: patients who remained undifferentiated even after a period of 1 year follow-up.[3, 7]

Around 73% of patients were overweight but the study was not powered to identify whether being overweight is a risk factor for developing UDIA. A few prior studies have shown that a higher BMI has a worse disease outcome and a higher prevalence of co-morbidities in RA.[13,14] In contrast to RA patients, most patients (77%) were non-smokers. [15- 17]

The inclusion of patients with at least one swollen or tender joint of inflammatory nature ensured that the analysis included only those patients with inflammatory arthritis clinically. But not all patients had inflammation of the joints as seen by MSUS where 35% of patients had either normal findings (20%) or inflammation of soft-tissues (15%). Even the median CRP and ESR levels were not elevated in 45% and 40% patients respectively; and the mean DAS28-CRP score was in the remission range. These findings may suggest that most patients with UDIA have mild inflammatory features on investigation as compared to the clinical findings.[18]

Patient-reported outcome measures like Nepali HAQ,

PGA and VAS scores were only moderately elevated in these patients. These measures are known to be valid and responsive to the patient's disease activity and represents the overall health status of the patients.[19]

This study thus describes the clinical, demographic and serological features seen in patients with persistent UDIA. We have highlighted several salient features of UDIA that are different from RA, which is known to be the most common differential diagnosis and the most frequent outcome of these disorders.

CONCLUSIONS

UDIA represents a major group of patients presenting to early arthritis clinic. It constitutes a group of inflammatory joint conditions that do not fit into any of the diagnostic criteria for other diseases. In our study, UDIA was more common in overweight females. Presence of autoantibodies and smoking status are not common features in this group of patients.

CONFLICT OF INTEREST

None

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