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Etiology and outcome of mono-articular arthritis: a follow up study

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ABSTRACT

Background: Monoarthritis is a common rheumatological complaint. Inspite of investigations, many cases remain undiagnosed. Prompt investigation and treatment is important in acute arthritis especially septic arthritis else joint destruction, permanent disability or even death can result. This study was conducted to etiologically categorise patients as inflammatory, non-inflammatory and infective arthritis and to study the outcome.

Methods: This observational prospective study conducted at a tertiary care hospital in Mumbai enrolled 40 patients above the age of 12 yrs presenting with first episode of mono-articular arthritis. They were treated with standard treatment guidelines and followed up every 3 monthly for one year. Outcome was assessed using ESR, CRP values and Health Assessment Questionnaire.

Results: Mean age at diagnosis was 38 years with a male to female ratio of 1.4:1. Acute and chronic mono-articular arthritis cases were 16.2% and 83.7% respectively. Knee joint was most commonly involved (38%). Etiologically inflammatory, infectious and non-inflammatory cases were 59.5%, 29.7% and 10.8% respectively. In 21% cases etiology was tuberculosis. 27% evolved into oligoarthritis over one year. The serial ESR, CRP values and Stanford Health Assessment Questionarre scores decreased significantly across all etiological groups with treatment.

Conclusions: Knee is the most commonly affected joint in mono-articular arthritis. Tuberculosis is the most common etiology. Irrespective of the etiology, if patients are treated according to standard guidelines promptly mono-articular arthritis has a good response to therapy as assessed by the health assessment questionnaire (HAQ) and serial measurements of proinflammatory markers like ESR, CRP.

Keywords: Mono articular arthritis, Septic, Inflammatory, Tubercular, HAQ-DI

INTRODUCTION

Monoarticular arthritis is a common presentation in a rheumatology clinic. While many patients have self-limited conditions, there are several urgent conditions that must be diagnosed promptly to avoid significant morbidity or mortality.^{1,2} These "red flag" diagnoses include septic arthritis, acute crystal-induced arthritis (e.g., gout) and fracture.¹⁻³ Monoarticular arthritis can be classified further upon the duration of symptoms as.^{4,5}

Acute: single joint involvement of < 2 weeks duration.

Chronic: single joint involvement > 2 weeks duration.

The major causes of acute mono-articular symptoms include trauma, septic arthritis, crystal-induced arthritis, systemic rheumatic diseases like RA. 1,3,5 Most common causes of chronic monoarthritis are indolent infections like tuberculosis, fungal infections and inflammatory arthritis like RA, chronic gout, sero-negative spondyloarthropathy, and at times osteoarthritis. 3,6 Many polyarthritic disorders can initially present as a monoarthritis. A study by Mjaavatten MD et al conducted in patients with recent onset arthritis in fact found

monoarticlar involvement (38.3%) more common than oligo or polyarticular (34.1% and 24.6% respectively.⁷

The evaluation of a monoarticular arthritis should first aim at ruling out septic arthritis because of the capacity of some infectious agents to destroy cartilage rapidly and then should proceed to ascertain if the complaint is inflammatory or non-inflammatory in nature, acute or chronic in duration, and localized (mono-articular) or widespread (poly-articular) in distribution to narrow the diagnostic possibilities. Detailed clinical examination, arthrocentesis and analysis of synovial fluid or synovial biopsy, gram staining and culture of synovial fluid etc. as well as measurement of proinflammatory markers like ESR, CRP help to reach diagnosis. Inspite of extensive investigations at times the etiology remains uncertain in few patients even after long term follow up.^{6,7}

Inflammatory arthritis is suggested by inflammatory pain (morning stiffness >30 min, systemic symptoms, local signs of inflammation), and supporting laboratory evidence of raised values of pro inflammatory markers like ESR, CRP etc while noninflammatory arthritis lacks these findings.³ Synovial fluid analysis helps to distinguish between these entities on the basis of appearance, leucocyte count, crystal detection etc.⁵

Outcome of mono-arthritis may be in the form of complete remission or evolution into oligo or polyarthritis with or without systemic disease and residual deformity. There are few prospective studies, especially in Asian patients evaluating the etiology and outcome in patients with initial presentation of monoarticular arthritis. Hence, we conducted this study to assess the aetiology and outcome of patients presenting for the first time with mono-articular arthritis in the rheumatology clinic in a tertiary care hospital, to categorise patients as Inflammatory, Non-inflammatory and Infective arthritis and assess response to treatment using HAQ.

METHODS

This prospective, observational study was conducted at department of Medicine at tertiary care Hospital, Mumbai after the Institutional ethics committee approval. Total 40 patients above the age of 12 years with mono-articular arthritis presenting for the first time to the rheumatology clinic and/ or those who were admitted in medical units were enrolled in the study after taking Informed consent. Sample size was decided by random sampling method.

Mono-articular involvement was defined by single joint involvement with two out of three features namely, swelling restricted to the joint, pain or tenderness of the joint and limitation of joint movement. Traumatic arthritis and soft tissue rheumatism (tendinitis, bursitis, strain, sprain, osteomyelitis) patients and those who lost follow up (n=3) were excluded from the study. Thus, 37 patients were followed up every three monthly for a period of one year.

Detailed history, physical examination and examination of joints for pain, swelling, tenderness, local warmth and limitation of joint movement was carried out followed by necessary radiological and laboratory investigations at the first visit. Systemic involvement in the form of presence of fever, generalized body ache, fatigue, anemia, generalized lymphadenopathy serositis, weight loss, Raynaud's phenomenon etc were noted. Specific organ involvement such as hepatosplenomegaly, renal, gastrointestinal cardiovascular and respiratory involvement, uveitis etc was noted at presentation and during follow up. ESR and CRP was measured for all patients at first and last visit. Procedures like aspiration of joint fluid for microscopic analysis of leucocyte count, gram stain, crystals identification, culture etc were done as required to establish the etiology. Synovial biopsy, Joint MRI, Rheumatoid factor, anti CCP antibody, HLA B27 were done as required.

Standard diagnostic criteria and treatment guidelines were followed. Therapeutic procedures like synovectomy, joint replacement, arthrodesis was done by orthopedic surgeon with combined decision of Rheumatologists and Orthopedic surgeon. For tubercular arthritis where AFB smear or culture was negative, clinical features and other relevant investigations such as MRI of joint, lymphocyte predominant synovial fluid along with elevated ADA were used for supporting the diagnosis.

Patients were categorized as inflammatory/infective/noninflammatory on the basis of clinical features and laboratory evidence. Inflammatory disorders were identified by any of the four cardinal signs of inflammation (erythema, warmth, pain, or swelling), systemic symptoms or elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) levels and inflammatory type of morning stiffness (>30 min). Noninflammatory disorders were identified by pain without synovial swelling or warmth, absence of inflammatory or systemic features, daytime gel phenomena rather than morning stiffness and normal (for age) or negative laboratory investigations such as ESR and CRP. Infective etiology was identified by features of inflammation along with joint aspirate positive for Gram stain or culture, polymorphs >70% or WBC count >50,000/mm.³

Outcome of mono-articular arthritis was assessed by Stanford Health using 2-page Assessment Questionnaire carried out at each three monthly follow up; and ESR, CRP values at the initiation and at 1 year of treatment. Stanford Health Assessment Questionnaire measures improvement in physical disability, pain relief and overall wellbeing in day today life with physical and mental wellbeing by using Health Assessment Questionnaire-Disability Index (HAQ-DI), Visual Analogue Scale (VAS) and Patient's Global Scale (PGS). Scores of 0 to 1 are generally considered to represent mild to moderate difficulty, 1 to 2 moderate to severe disability, and 2 to 3 severe to very severe disability.⁸

Statistical analysis was done by unpaired t-test and ANOVA test using Microsoft Excel and GraphPad software.

RESULTS

Total 40 cases of above age 12 years were enrolled in the study. Three patients were excluded due to loss of follow up. Hence 37 patients were studied and followed up every 3 monthly over a period of one year.

Mean age at presentation was 38 years with maximum (56%) patients in the range of 22-55 years with male to female ratio of 1.46:1 (Males=59%, Females =41%).

Joint pain was the main presenting feature of monoarticular arthritis seen in 35 (91.89%) patients followed by limitation of joint movement in 28 (75.67%) patients and swelling or tenderness of joint in 19 (51.35%) patients.

Irrespective of the etiology of arthritis, knee joint was most commonly involved in mono-articular arthritis (Table 1).

Table 1: Joint involvement at presentation in monoarticular arthritis.

Joint type	Number of cases (n/37)	%
Knee joint	14	37.8
Hip joint	5	13.5
Ankle joint	5	13.5
Shoulder joint	4	10.85
Elbow joint	3	8
MTP joint	3	8
Dip joint	1	2.7
Sternoclavicular joint	1	2.7
MCP joint	1	2.7
Total	37	100

On the basis of etiology, all cases were categorized into 3 broad classes: Inflammatory, Infective and Non-inflammatory as depicted in Table 2. Inflammatory arthritis was most common type comprising 59.5% cases, 29.7% cases of infective arthritis and 10.8% cases of non-inflammatory type of mono-articular arthritis. Among the infectious category, tuberculous arthritis was most common. Among the inflammatory category, crystal induced arthritis was most commonly seen. Pigment induced arthritis (pigmented villonodularsynovitis) and chronic hypertrophic synovitis were found to be rarest, each accounting 2.7% cases. All the cases under Non-inflammatory category were due to Osteoarthritis.

Chronic arthritis was more common than acute. 16.2% of cases (n=6/37) presented with acute mono-articular arthritis while 83.7% (n =31/37) had chronic mono-articular arthritis (Table 3).

Table 2: Etiological classification of mono articular arthritis-infectious, inflammatory, and Non-inflammatory arthritis.

Etiology	Number of cases (n/37)	%	Total	
Infectious arthritis				
Tuberculous arthritis	8	21.6		
Staphylococcal septic arthritis	2	5.4	11/37 (29.7%)	
Streptococcal septic arthritis	1	2.7		
Inflammatory arthritis				
Crystal induced arthritis (gout)	6	16.2	22/37	
Rheumatoid arthritis (RA)	5	13.5	(59.5%)	
Juvenile idiopathic arthritis (JIA)	3	8.1		
Seronegativespondyloa	arthropathy (SS	A)		
Psoriatic arthritis (PSA)	1	2.7		
Enteropathy associated arthritis	1	2.7		
Undifferentiated SSA	4	10.8	4/37	
Chronic hypertrophic synovitis (HS)	1	2.7	(10.8%)	
Pigmented villonodularsynovitis (PVS)	1	2.7		
Non-inflammatory				
Osteoarthritis (OA)	4	10.8		
Total	37	100	100%	

Table 3: Classification of arthritis as per duration of symptoms.

Type of arthritis as per duration of symptoms	No. of patients	Total	
Acute			
Septic arthritis	3	6	
Acute gout	3		
Chronic			
Tuberculous arthritis	8		
Chronic gout	3		
Rheumatoid arthritis (RA)	5		
Juvenile idiopathic arthritis (JIA)	3	31	
Seronegative spondyloarthropathy	6	31	
Chronic hypertrophic synovitis	1		
Pigmented villonodularsynovitis	1		
Osteoarthritis	4		

Systemic symptoms were present in eight patients (21.6%) as a presenting complaint in the form of fever, weight loss, fatigue (Table 4).

Table 4: Manifestations of mono-articular arthritis (other Joint involvement/ systemic/ organ involvement).

Clinical feature	Number of cases (n/37)	%
Involvement of other joints in one year	10	27.02
Systemic symptoms (involvement) at presentation	8	21.6
Specific organ involvement at presentation	4	10.8

All the 8 patients were cases of Infective arthritis of which 3 were cases of septic arthritis and 5 were cases of Tuberculous arthritis. Specific organ involvement at presentation was seen in four patients (10.8%) in the form

of interstitial lung disease (n=1), ulcerative colitis (n=1), renal failure (n=1) and pulmonary tuberculosis (n=1). None of the patients developed new onset systemic symptom or new organ involvement during a follow up period of one year. Ten cases (27.02%) had involvement of other joints along with primary affected joint mainly evolving into oligoarticular involvement.

However, none of our patients progressed to polyarticular arthritis and over a period of one year none had recurrence of arthritis in same joint. Response to the treatment was monitored with ESR, CRP measurement pretreatment and at 1 year follow up.

Table 5 depicts statistically significant reduction in these markers with treatment and this was seen across all etiological groups.

Table 5: ESR, CRP values pre and post treatment at 1 year follow up.

	N	Mean	SD	t value	P value	Significance
ESR1	37	35.62	16.76			Significant (m < 0.05)
ESR2	37	15.14	6.08	6.90	< 0.00001	Significant (p<0.05)
CRP1	37	13.60	7.98			S::::
CRP2	37	7.22	3.51	4.39	< 0.00001	Significant (p<0.05)

*ESR 1, CRP1: at presentation; ESR2, CRP2: at 1-year follow- up.

Table 6: Mean and standard deviation of HAQ, VAS and PGS values for mono-articular arthritis.

	N	Mean	SD	t value	P value	Significance
HAQ0	37	1.79	0.44			
HAQ1	37	1.34	0.48	4.10	0.000107	G::G:t
HAQ2	37	0.92	0.48	7.92	< 0.00001	Significant (<i>p</i> <0.05)
HAQ3	37	0.61	0.47	10.88	< 0.00001	(p<0.05)
HAQ4	37	0.37	0.47	13.28	< 0.00001	
VAS0	37	1.83	0.50			
VAS1	37	1.28	0.50	4.68	0.000013	G::f:t
VAS2	37	0.78	0.50	8.13	< 0.00001	Significant (p<0.05)
VAS3	37	0.47	0.43	11.27	< 0.00001	(p<0.03)
VAS4	37	0.23	0.35	14.19	< 0.00001	
PGS0	37	1.91	0.45			
PGS1	37	1.36	0.52	4.74	0.000011	G::G:t
PGS2	37	0.86	0.45	9.83	< 0.00001	Significant (p. 0.05)
PGS3	37	0.58	0.41	13.04	< 0.00001	(p<0.05)
PGS4	37	0.36	0.43	14.94	< 0.00001	

*Scores 0,1,2,3,4 in each category indicate at presentation, 3 months, 6 months, 9 months and 1 year follow up respectively.

Subjective improvement in symptoms which was assessed using the Stanford Health Assessment Questionnaire also showed significant reduction in disability and improvement in quality of life as suggested by statistically significant reduction in the HAQ-DI, VAS, PGS scores taken at 3 monthly follow ups upto 1 year as shown in Table 6.

As the scores of HAQ-DI, VAS, PGS were comparable at each visit, across the different etiological groups HAQ-DI score was used to monitor the response to treatment.

As depicted in chart 1, there is reduction in the HAQ-DI score across each etiological group on subsequent follow up.

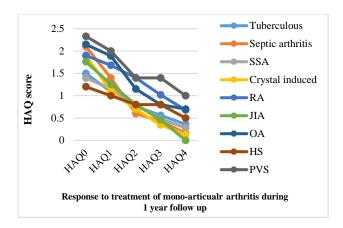


Figure 1: Assessment of etiology based response to treatment of mono-articular arthritis using HAQ-DI.

DISCUSSION

Total 37 patients with acute or chronic onset symptoms of mono-articular arthritis were studied and followed up for a period of one year. Mean age at onset of arthritis was 38 years with a male to female ratio of 1.4:1. In a study by Jeong H et al the mean age was 42.8 years while a study by Uzma Rasheed et al, reported a younger average age of the patients (29.6 years) and maximum patients were between 31 -40 years. 9,2 The slight male preponderance in our study is consistant with previous studies by Mjaavatten MD and Jeong, H et al. 7,9 As studied before by Ma L et al, male preponderance is seen in gout, seronegative spodyloarthropathy. 1

Irrespective of the etiology of arthritis, knee joint was most commonly involved, in 37.8% (n=14). Previous studies have also shown more involvement of large joints especially the knee in cases with monoarticular presentation with 79% cases having large joint involvement and small joints like toes, fingers etc involved in only 21%. ^{2,6,10,11}

History of morning stiffness lasting more than one hour was seen in 14 (37.83%) patients which were of inflammatory type of arthritis. Noninflammatory arthritis cases did not show any of these features. As previous studies have noted, non-inflammatory disorders like osteoarthritis are often characterized by pain without warmth, absence of inflammatory or systemic features, daytime gel phenomenon rather than morning stiffness.³

Ten cases (27.02%) progressed to oligoarticular arthritis over follow up of one year. None of them evolved into polyarticular arthritis (>4 joints). New joint involvement during follow up was seen with seronegative spondyloarthropathy (n=3) and rheumatoid arthritis (n=1). According to previous studies polyarticular involvement during follow up was 14%. However the duration of follow up was 6-8 years as compared to a short term follow up in our study.

Among the acute arthritis group, infectious (septic) arthritis was the most common etiology followed by acute gouty arthritis. Earlier studies have shown the most common diagnoses in acute monoarthritis cases were gout (15%–27%) and septic arthritis (8%–27%), followed by osteoarthritis (5%–17%) and rheumatoid arthritis (11%–16%).^{4,12}

In the group with chronic arthritis, tuberculous arthritis was the most common cause found in our study, while few other previous studies have shown, rheumatoid arthritis and osteoarthritis or spondyloarthropathys as the most frequent diagnoses. 7,13 This difference can be attributed to the fact that in India, the prevalence of tuberculosis is still very high. Among the cases of osteoarticular TB, incidence of peripheral arthritis has been reported to be close to 30%. $^{\hat{1}4}$ Also, the sample size was smaller with majority patients of chronic arthritis. All tuberculous arthritis patients presented with an indolent form of disease with onset symptoms varying from 6 weeks to 2 years. A retrospective study done in Saudi Arabia suggested tuberculous arthritis as a forgotten cause of mono-articular arthritis due to under estimating the disease and difficulty in diagnosis, which requires tissue sampling.¹⁵ Knee was the most commonly involved joint in cases of tuberculous arthritis. Previous studies by Mohammed J. Al-Sayyad et al in Saudi Arabia, also described that extra axial osteoarticular tuberculosis involves large joints like hip, knee most frequently. 15,16 Of the 8 cases of tuberculous arthritis in our study, acid-fast staining was positive in one case, and cultures were positive for mycobacteria in 6 cases. Two cases required synovial biopsy for diagnosis of tuberculous arthritis. According to the literature, acid-fast staining of the fluid yields positive results in less than one-third of cases, and cultures are positive in 80%. Culture of synovial tissue taken at biopsy is positive in >90% of cases and shows granulomatous inflammation in most.³ In tuberculous arthritis, 4 cases who presented within 2 months of symptoms were completely cured with 9 months of anti-tuberculous treatment but remaining 4 cases who presented late (> 3 months) had some residual limitation in joint mobility. One case was posted for joint replacement due to deformity. This finding is consistant with previous studies on tuberculous arthritis suggesting successful treatment in active TB is influenced by establishing an early diagnosis and initiation of an appropriate treatment.¹⁷

In our study we found 3 patients with synovial fluid-culture proven septic arthritis, 2 caused by Staphylococcus aureus and one due to Streptococcus all involving large joints like knee. As per the available literature, most commonly involved joint in non gonococcal septic arthritis was knee (50%), followed by hip (20%), shoulder (8%), ankle (7%). 11,18 One case out of three had residual disability due to delay in seeking the treatment. Previous studies have therefore emphasized the need to evaluate and treat septic arthritis on

emergency basis due to the rapid cartilage destruction in non-gonococcal septic arthritis. 19,20

Among the 6 cases of crystal induced arthritis (gout), Four cases presented with 1st metatarsophalangeal (MTP) joint involvement, one with 1st distal interphalangeal (DIP) joint and one with ankle joint involvement. Four cases showed crystals in joint aspirate and remaining 2 were diagnosed on the basis of hyperuricemia, joint pain and risk factors. Except one case of chronic gout all achieved remission on treatment.

Rheumatoid arthritis cases were 5 out of total 37. Monoarticular presentation is rare in RA as per previous studies and when present usually involves large joints as studied previously by Sarazin J et al, a finding consistent in our study. They were diagnosed by clinical suspicion along with supporting evidence such as ESR/CRP/anti-CCP/Rheumatoid factor and treated with 2 drugs (hydroxychloroquine and methotrexate) or 3 drugs (hydroxychloroquine, methotrexate and oral low dose prednisolone) combination as per standard protocols. None of our proven cases of RA progressed to polyarthritis in one year follow up, although earlier studies report progression to polyarticular RA over 3-4 years in most cases. 21

Our study had 6 cases of SSA, who presented with chronic symptoms mainly involving knee joint and ankle joint, similar to previous studies showing mainly large joint involvement especially of lower extremity.³ Treatment with NSAIDs, sulfasalzine, low dose methotrexate and supportive measures resulted in remission in 5 out of 6 cases. Only 1 patient had residual joint involvement.

The response to treatment was assessed on the basis of changes in the ESR, CRP, HAQ-DI over the period of one year. We found a significant difference (p<0.05) between the values of ESR and CRP taken at baseline and at end of 1 year, thus indirectly indicating good response to therapy with significant reduction in inflammatory markers for disease activity. The serial Health Assessment Questionnaire recordings done every three monthly did not show significant improvement within first 3 months (p>0.05 for HAQ-DI, VAS and PGS) but during the subsequent visits they showed significant improvement in all parameters (p<0.001) i.e. HAQ-DI, VAS and PGS, thus indicating the subjective improvement in quality of life as perceived by the patients across all the etiological groups.

This could be due to the large proportion of our patients having chronic arthritis thus requiring treatment for more than 3 months to show a subjective improvement in symptoms. As suggested by previous studies by Bruce B, Fries JF, the application of HAQ helped to assess subjective improvement in disability and pain across various etiological classes of monoarthritis although initially evaluated only in cases of RA.²²

Our study may provide a reference for application to the Indian (South Asian Region) population. Additional studies with a larger study population and a longer duration of follow -up would provide better information into the outcome and evolution of monoarthritis.

CONCLUSION

Knee joint is most commonly affected in mono-articular arthritis followed by other large joints. As per etiopathogenesis, inflammatory arthritis is most common type of mono-articular arthritis followed by infectious and non-inflammatory type arthritis. Tuberculosis is the commonest cause of mono-articular arthritis followed by induced seronegative arthritis, spondyloarthropathy, rheumatoid arthritis. A high index of suspicion should be kept for tuberculosis especially in large joint monoarthritis with synovial fluid analysis for diagnosis. Using standard treatment guidelines and interventions, mono-articular arthritis has good response to therapy as assessed by sequential ESR, CRP values and Stanford HAQ. Long term follows up is required to assess evolution into oligo or polyarticular joint involvement.

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institutional ethics committee

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