PROSPECTIVE EVALUATION OF CLINICAL PROFILE AND TREATMENT OUTCOME OF PATIENTS PRESENTING WITH POLYARTHRITIS DIAGNOSED AS RHEUMATOID ARTHRITIS

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ABSTRACT

Introduction: Polyarthritis is a common presentation of patients attending medicine outpatient department. Among various causes Rheumatoid arthritis is the commonest and a well established case has distinct characteristic features. However the early presentation of this disease has not been clear thus leading to delay in treatment. The objectives of this study was to identify the various causes of polyarthritis in our clinical practice, discuss the varied clinical presentation of rheumatoid arthritis including early Rheumatoid arthritis and to evaluate the treatment response during one year follow up.

Methods: Prospective longitudinal study conducted in a teaching hospital over a two years period

Results: Rheumatoid arthritis was the commonest cause of polyarthritis (77.8%) with a period prevalence of 0.7%. Early presentation included atypical features like asymmetry, unilateral presentation, manifesting within 2 months to 2 years of diagnosis. 43% (n=18) of the patients had swelling and tenderness in overused joints 1.5 years prior to full clinical manifestation. Flitting or migratory joint pain not considered to be a feature of rheumatoid arthritis was also present in 14.3% (n=6) patients with mean duration of 1.5 years prior to full blown presentation. MCPJ (metacarpophalyngeal joints) and PIP (proximal interphalyngeal joints) were involved in 90%. Treatment response with Methotrexate as a single DMARD was good as compared with DAS 28 ESR score.

Conclusions: RA is a common arthritis with varied clinical presentation. Recognition of early symptoms is needed for early diagnosis and initiation of DMARD. Methotrexate as a DMARD is effective and should be initiated early.

Key Words: Rheumatoid arthiris, Polyarthiris, DMARD.

INTRODUCTION

Joint Pain is one of the common complaints of patients visiting a clinician. Apart from nonspecific arthralgia, a significant number of patients present with inflammatory arthritis. Inflammatory arthritis is a condition characterized by pain and swelling in the joints associated with limitation of movements. The most common cause of chronic inflammatory arthritis is rheumatoid arthritis (RA) with a worldwide prevalence of 0.5% -1% of adult population[1]. Typically beginning in multiple small joints of the hands and feet in a symmetric fashion, RA has many variations, including months or years of recurrent monoarthritis (palindromic rheumatism)[2] before a typical pattern evolves. Disease duration of 12 weeks or more is strongly predictive of persistent RA[3]. The symmetry of RA

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is sometimes overemphasized, and it must be appreciated that this is a general, rough symmetry. RA can have unilateral manifestation[4,5] and early RA may have varied presentations not abiding with the American College of Rheumatology (ARA) criteria or the American College of Rhematological Diseases (ACR, 1988) criteria [6].

Though RA is the most common cause of polyarthritis, many other causes are also encountered time and again. While some of the arthritis like Ankylosing spondylitis is difficult to treat and also very difficult to prevent from progressing, others like arthritis due to rheumatic fever, gout can be prevented and treated[7,8]. In this context tuberculosis is worth mentioning in Asian population. It can present with symmetrical polyarthritis known as Poncets disease[9, 10]. It responds to antitubercular therapy and heals without residual disease. Rheumatoid arthritis can also be remarkably controlled with disease modifying drugs, if detected early and treated before joint damage has occurred [11,12].

Even though arthritis is common, study in this field is lacking in our country. Only recently have few specialist trained in rheumatology, started rheumatologic practice in Nepal. We do not have practice guide lines and management protocol as our cohorts of patients have not been studied. Hence a need for prospective study of this group of patient was needed.

The aim of this study was to diagnose various types of arthritis encountered in our population and to evaluate the various clinical presentations of rheumatoid arthritis. Early rheumatoid arthritis that does not exactly fit into the ACR[13, 14] criteria is largely missed and treated as nonspecific arthritis. We also want to evaluate the clinical presentation of this group of patients and highlight the early presentation. Similarly as the onset and progress of joint deformity and destruction in RA is directly related with early diagnosis and therapy this study also tries to assess the response of anti-rheumatoid drugs in our patients with use of locally available drugs.

METHOD

All patients presenting to the medical outpatient department of a medical college hospital with history of joint pain and swelling of more than two joints, for more than two weeks duration, were prospectively enrolled in the study period of April 2008 to April 2010. A detailed history was taken and examination done by a single experienced clinician. Patient characteristics included were mode of onset, duration of joint pain, morning stiffness, number of joints and joint areas involved, involvement of small joints of the hands and feet, presence or absence of axial joint involvement and sacroilitis, presence of tenderness, swelling and synovitis. All were assessed for presence of nodules, rash and extra-articular features including all system. For laboratory investigation complete blood count and ESR, and specific investigations were sent if needed on the first day and data entered on day eight after reports were collected. All patients with clinical diagnosis of rheumatoid arthritis were diagnosed as per The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis[4, 12] and those with early incomplete criteria were diagnosed with presence of seropositivity. Seropositivity defined as presence of RA factor (IgM)[13, 14,15,16,17]>60 units and or A-CCP[18,19,] (anti citrullinated cyclic peptide antibody), titer>15 units done by Elisa assay in a standard laboratory. Ankylosing Spondylitis and seronegative spondyloarthritis was diagnosed on the basis of presence of sacroilitis, buttock pain and nocturnal awakening with back pain, morning stiffness more than 30 minutes and family history[20]. Diagnosis of tuberculosis was considered if arthritis was present along with evening rise of temperature and showed positive mantoux test of > 20 mm with or without presence of erythema nodosum and phlyctenular conjunctivitis [9, 10]. Rheumatic fever was diagnosed by Jones criteria[21]. Arthritis with features of connective tissue diseases other than RA were grouped as other connective tissue diseases. Gouty arthritis and non specific reactive arthritis were grouped as ''others". All the patients with newly diagnosed rheumatoid arthritis were evaluated by DAS 28 ESR[22, 23, 24, 25, 26, 27, 28] score after six weeks of persistent arthritis[13] and started on methotrexate at loading dose of 15mg/week[28, 29]. Those who had long duration of disease and had DAS 28 >5.1 at presentation were started on more than two DMARD including hydroxychloroquine 400 mg and sulfasalazine 1gm[30, 31]. Follow up evaluation was done at 6 weeks, three months, six months and one year. All were instructed to visit in between if any drug complications arose or break through pain occurred. Treatment response in rheumatoid arthritis was defined as the improvement in DAS 28 score by > 1.2 from baseline score[23]. The dose of methotrexate was tapered if possible to lowest 7.5-10mg/week if sustained response was seen, after six months. The scoring was done at three, six and 12 months but comparison was done between the third and the 12 months score. They were allowed to have NSAID as needed but frequency restricted to 1-3 times per week and if frequency was more than that, was asked to report when short course steroid was initiated. Maximum dose of methotrexate was 20mg/week, Hydroxychloroquin was 400mg/day with Salphasalazine at 2gm per day. Patients having DAS score > 6.1 at the onset were allowed to have steroids[30, 31] for 7-10 days in a tapering dose. Steroid injections were allowed for few swollen joints at the time of follow up. All the data were entered in to the data sheet of SPSS version 17 and data analysis for relevant variables were done using descriptive statistics and t- test as required.

RESULTS

A total of 54 patients presenting with inflammatory polyarthritis were enrolled. Rheumatoid arthritis was the most common arthritis and constituted 77.8% (n=42) with a period prevalence of 0.7% and was followed by seronegative spondyloarthritis (Fig.1). Tuberculosis presenting as polyarthritis was consistently associated with fever, erythema nodosum and positive ulcerative mantoux test with reading >20mm. Mean age of the patients in RA group was 51.95±2.9 and non RA group was 31.92±6.13 (Fig 2). There were 32 females and 22 males in the study group. Female and male ratio in the rheumatoid group was 1.8:1 and 1.4:1 in non RA group. Clinical presentation and comparison between the RA and Non RA group is shown in Table1. Morning stiffness > 45mins, involvement of more than two joint areas, boggy synovial swelling of the joints and joint deformities were significantly present in the RA group (p>.05). Rheumatoid nodules were present in only 11.9% (n=5) of RA patients.

Patients presenting with early rheumatoid arthritis had varied clinical presentation (Table. 2) which manifested within a mean duration of two months to two years before diagnosis. Interestingly 43% (n=18) of the patients had swelling and tenderness in overused joints almost 1.5 years prior to full clinical manifestation. Flitting or migratory joint pain not considered to be a feature of rheumatoid arthritis was also present in 14.3% (n=6) patients with mean duration of 1.5 years prior to full blown presentation.

In the rheumatoid group the MCPJ (metacarpophalyngeal joints) and PIP (proximal interphalyngeal joints) were involved in 90%, followed by wrist 80%, elbow 60% knee 60% (Table. 3). Para-articular site soft tissue involvement

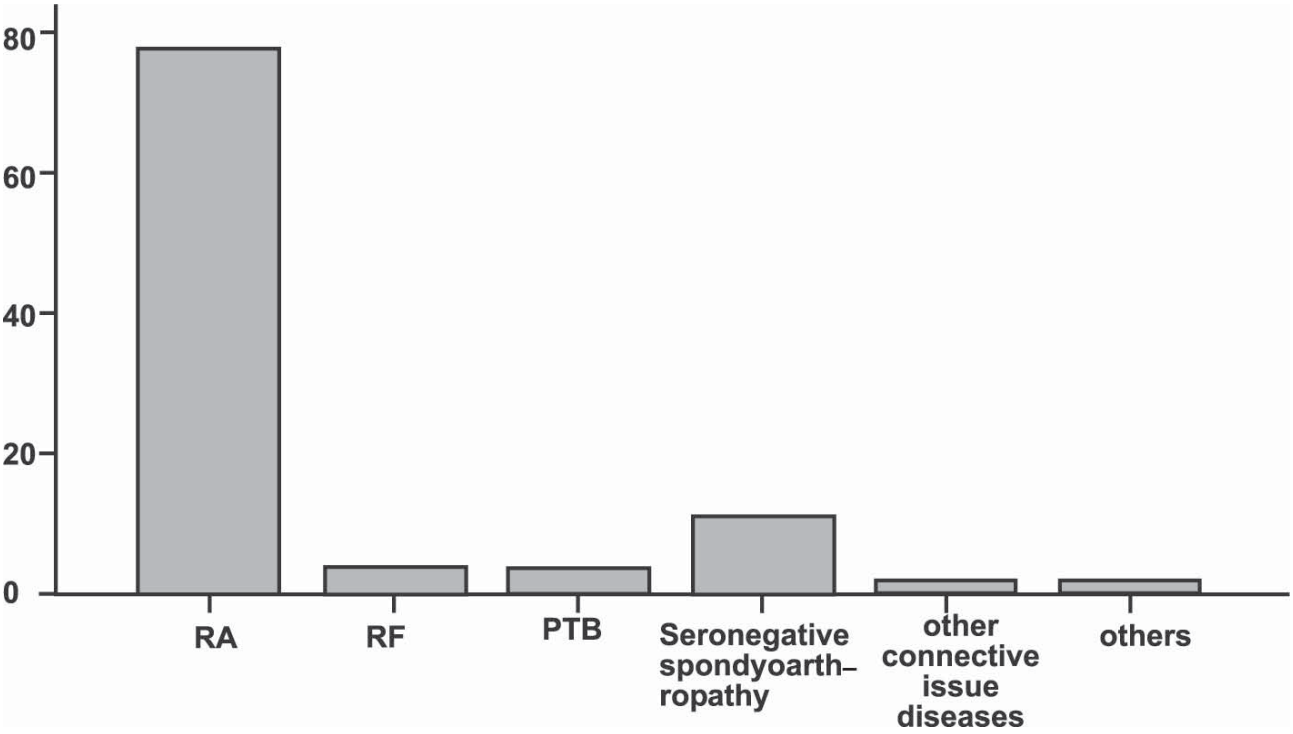

Fig: 1 Different causes and percentage of polyarthritis

manifested as repeated chest pain, upper back pain, throat and anterior neck pain sometimes confused as thyroiditis and pharyngitis. Extraarticular manifestations in our cohorts of RA cases were not significant. One patients had pericarditis and pericardial effusion. 9.5% (n=4) had sicca syndrome with severe dryness of eye proved by Schirmers tear test. Two patients had fine inspiratory crepts at ling bases without clinical symptoms and only mild evidence of restrictive lung disease in spirometry test. All these had disease duration of more than five years.

Regarding treatment Methotrexate as a DMARD was very effective and tolerated in our cohort of RA. None of the patients had to be discontinued due to side effects. Mean DAS 28 score on the second follow up was significantly lower (p=<.05) compared with the DAS 28 score on the first follow up (Table.4) similarly patients on one DMARD (methotrexate) had disease control comparable to more than two DMARD and increasing the number of DMARD did not show statistically significant disease control (p=0.95).

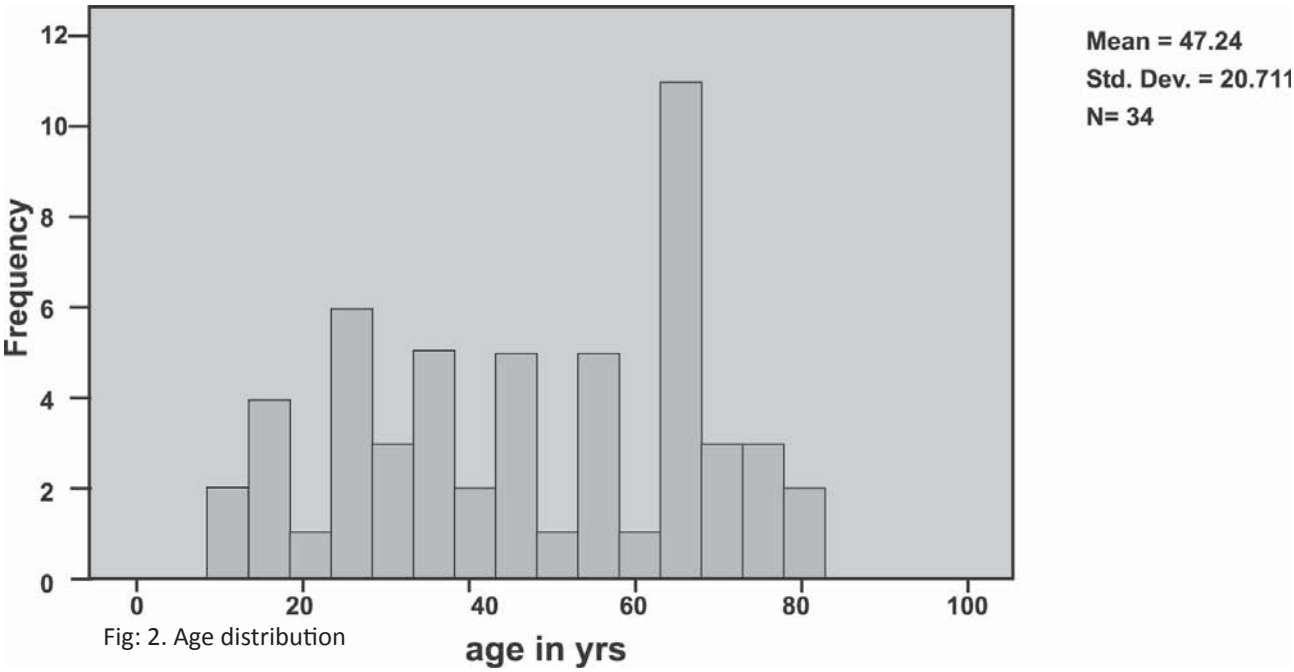

Fig: 2. Age distribution

Table 2: Early presentation of rheumatoid arthritis

Clinical profile **Mean age± SE**	**Parameters**	**Rheumatoid arthritis group N=42** **51.95 ± 2.9**	**Non rheumatoid arthritis group N= 12** **31.92 ± 6.13**	***p*=(x^2)**
Duration from onset Of typical presentation	<one year 1-5yrs >5yrs >10 yrs	**19** **8** **13** **2**	**10** **2** **0** **0**	**.077**
morning stiffness	No morning stiffness <30 mins >45 mins	**1** **8** **33**	**0** **10** **2**	**.042**
Axial joint involvement	Not involved Involved	**38** **4**	**4** **8**	**.00**
number of joint areas involved	<4 4-6 >6	**5** **12** **25**	**7** **4** **1**	**.001**
presence of boggy synovial swelling	**< 2** **2-4** **>4**	**6** **15** **21**	**7** **4** **1**	**.003**
deformity in the joints	**None** **<4** **>4**	**17** **8** **17**	**9** **1** **2**	**.006**
Nodules	**Absent Present**	**37** **5**	**7** **5**	**.019**
Fever at onset	**Absent** **Present**	**37** **5**	**9** **3**	**.26**
Flitting pain	**Absent** **Present**	**36** **6**	**7** **5**	**.038**
RA titre >60 iu/dl	**Present** **Absent**	**32** **10**	**2** **10**	**.001**

	Duration(mean) before diagnosis (years)	Symmetry Yes	No	No of patients n= (%)
Morning stiffness < 30 mins	1.5 yrs	4	3	7 (16.6)
Tenosynovitis of the hands with swelling	0.5 yrs	6	2	8(19)
Swelling and tenderness in overused joints	0.5 yrs		18	18 (43)
Supraspinatus tendinitis only	2.0 yrs		4	4 (9.5)
Acute severe polyarthritis	0.2yrs	4		4 (9.5)
Throat pain on swallowing and anterior neck pain	1.0yr	2		2 (5)
Flitting pain	1.5 yrs		6	6 (14.3)
Temporo-mandibular joint Joint arthritis	2.0yrs		7	7(16.6)
Chest pain with enthesitis on off	1yrs		3	3 (7.1)

Table : 3 Joints involvement in rheumatoid artrhitis

Joints involved	MCP, PIP	Wrists	Knees	Shoulders	Ankles	Feet	Elbows	Hips	TMJ	spine	Sternoclavicular joint	Para articular sites
%	90	80	60	60	30	36	64	24	10	5	2	27
Number	38	34	25	25	13	15	27	8	14	2	3	11

MCP: Metacarpophalangeal joint. PIP: Proximal Interphalangeal joint. TMJ: Temporomadibular joint.

Table 4: Drug response in Rheumatoid arthritis

Outcome group	Treatment response (n=)	DAS 28 ESR score Mean ±SE	Test of significance	Significance *P*=	95% CI
1.	DAS 28 at first follow up (n=42) DAS 28 at second follow up (n=42)	6.80±.22 3.52±.34	Paired sample correlation 4.28	.005	
2.	DAS 28 score difference in two group(n=42)	2.5±.24	One tailed t-test t=10.9 df=41	<.001	2.11-3.06
1.	DAS 28 score difference with one DMARD (n=28)	2.58±0.28	t=0.051 df=40	0.95	-1.05-1
2.	DAS 28 score difference with more than one (n= 14)	2.6±o.45			

DISCUSSION

Rheumatoid arthritis was the most common causes of inflammatory arthritis in our population. In our study the in hospital period prevalence was 0 .7% which is comparable to the prevalence in other studies. Females were more affected than male but the ratio was less than quoted in other studies[16, 17]. Among other causes of inflammatory arthritis, Spondylotic arthritis was the second most common as in other studies[18, 19]. Primary tuberculosis also presented as polyarthritis and was associated with boggy synovial swelling of multiple joints, mainly involving the wrist and ankle and was seen in young females. The presentation was typical of Poncet's reactive arthritis[20, 21].

Regarding clinical features in rheumatoid arthritis (Table.2), those presenting within one year of onset of joint pain had characteristic features. Significant number of patients presented with unilateral symptoms and had morning stiffness less than 30 mins. Some of the patients presented with chondral site pain like anterior neck pain with tenderness over the hyoid bone and cricoids cartilage and difficulty in swallowing. Temporomandibular arthritis[32] was the symptoms that had a prolonged onset with a mean duration of 1.9 years before full blown presentation. Low back pain was also present in some patients diagnosed as RA.

Joint involvement in RA was almost similar to other studies with the MCP and PIP involved in maximum number of patients (Table 3). However systemic and extra-articular manifestation was negligible in our cohort of patients with RA. Interestingly after one year follow up, two of our patients died. One male RA patient died due to pericardial tamponade and a female with coexistent COAD died due to bronchogenic carcinoma which manifested almost 6 months after the patients initiation on methotrexate, compelling us to diagnose RA presenting as a paraneoplastic syndrome[33].

Regarding treatment our group of patients responded very well to Methotrexate [29, 30] and there was not much difference between the one DMARD and more than one DMARD group[33, 34] (Table.4). Apart from intermittent diarrhea and oral ulcers none of the patients reported much adverse effect. Those patients responding to methotrexate did fine with good treatment response at a dose ranging from10mg/week to 15mg/week. Those not showing response and requiring repeated NSAID and short course steroid (7-10 days) for more than three times in six months period did not improve significantly (p=.95) with three DMARD.

Due to practical problem we did not use radiological score to evaluate the response which may be the major drawback of our study. Treatment response was assessed using DAS28 ESR score and the mean difference in the score after treatment was significantly better (Table.5). As the treatment response in the group with more than one DMARD were not statistically different and they had to be put on intermittent steroid we want to infer that these patients may be the ones to improve on biological agents[35]. But due to financial constraints and lack of fund we could not add biological agents to these patients and had to be satisfied with intermittent steroid and multiple DMARD though our study shows that they could have been managed on only methotrexate with intermittent steroid.

CONCLUSION

We conclude that RA is a very common disabling arthritis in our population, but reactive arthritis like tubercular arthritis may also present as polyarthritis similar to rheumatoid arthritis. Early presentation of RA may not fit in the typical ARA clinical criteria. Early diagnosis and treatment is essential to prevent joint damage. At this early stage serology may be helpful for diagnosis apart from the various presentations mentioned. Methotrexate is a very good drug for our population and adverse effect is not much. Since disease control is the goal of therapy intermittent steroid is very helpful. Patients not responding to multiple DMARD should be considered candidates for the biological agents along with methotrexate.

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