ORIGINAL RESEARCH

Epidemiological profile of oligoarticular arthritis at a tertiary care centre of north India

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ABSTRACT
Arthritis involving two to four joints is commonly encountered in clinical practice and is termed as oligoarthritis. The profile of oligoarticular arthritis is less explored as compared to polyarthritis. Etiology of oligoarthritis ranges from infectious to non-infectious causes. The present study was done to explore the epidemiological profile of oligoarticular arthritis and identify the demographic, clinical and etiological factors which could help in the differentiation of infectious from non-infectious arthritis. It included 30 subjects with oligoarticular inflammatory arthritis who visited a tertiary care center of north India during Sept.2019 to Sept.2020. Standard diagnostic criteria were used for making diagnosis of arthritis in the subjects and the arthritis was categorized into infectious and non-infectious groups. The study design is a cross sectional, observational study. We found that maximum cases accounting to 20.0% had axial spondyloarthritis and the minimum being 3.3% were each with TB of hip joint and gout. Juvenile idiopathic arthritis accounted for 16.7%. Peripheral spondyloarthritis, RA and ReA, each of the three accounted for 13.3% of the cases and 10% subjects with SLE presented as oligoarthritis. The cases with septic arthritis constituted 6.7% of the whole chunk.
Keywords: epidemiological, oligoarticular, arthritis, India

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INTRODUCTION
Musculoskeletal pain is one of the common complaints with which patients present in outpatient clinics. Some of these patients turn out to be having arthritis. Polyarthritis e.g. rheumatoid arthritis has been widely studied. But the profile of oligoarticular arthritis is less explored. Arthritis involving two to four joints is commonly encountered in clinical practice and is termed as oligoarthritis. It's etiology ranges from infectiousto non-infectious causes. The present study was done to explore the epidemiology of oligoarticular arthritis and identify the demographic, clinical and etiological factors which could help in the differentiation of infectious from non-infectious arthritis.

AIM & OBJECTIVES
To study the epidemiological profile of oligoarticular arthritis at a tertiary care centre of north India.

MATERIAL & METHODS
This is a hospital-based, cross-sectional, observational study. It included a total of 30 patients who presented to the outpatient and inpatient services of our hospital between September 2019 and September 2020 with oligoarticular arthritis. Standard diagnostic criteria were used for making diagnosis of arthritis in the subjects and the arthritis has been categorized into infectious and non-infectious groups. Approval was obtained from the institutional ethics committee. All subjects gave written informed consent before enrolment in the study. Patients with clinically evident osteoarthritis, neuropathic joint disease and those with history of significant prior trauma to the bones or joints were excluded from the study. History taking and clinical examination were done as per a predefined questionnaire. Routine laboratory investigations were performed in all patients, which included routine haemogram, liver and renal function tests, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Apart from these, appropriate

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specific immunological and microbiological tests like IgM and IgG enzyme linked immunosorbent assay (ELISA) for brucellosis, human leucocyte antigen-B27 (HLA B-27), rheumatoid factor, anti-cyclic citrullinated peptide, angiotensin-converting enzyme (ACE) levels, urine for Chlamydial polymerase chain reaction assay (PCR), stool culture for *Shigella*spp. and *Salmonella* spp., stool for *C. difficile* toxin ELISA, synovial fluid for CBNAAT, Ziehl-Neelsen stain and Mycobacterial culture were performed according to the physician's discretion depending on the clinical presentation of the patient. All patients underwent a chest radiograph as well as a radiographic projection of the affected joints to look for erosions.Depending on the clinical scenario, magnetic resonance imaging (MRI) were performed on a case to case basis. Standard predefined specific criteria were used to assign a final diagnosis to the subjects. For the diagnosis of axial and peripheral spondyloarthritis, Assessment of Spondyloarthritis International Society (ASAS) classification criteria was used. Crystal-induced arthritis was diagnosed based on the presence of compatible clinical presentation and hyperuricemia with or without demonstration of crystals in the synovial fluid aspirate. Early rheumatoid arthritis was diagnosed as per the American College of Rheumatology/European League Against Rheumatism Criteria (ACR/EULAR, 2010). Systemic lupus erythematosus (SLE) was diagnosed according to the ACR classification criteria.

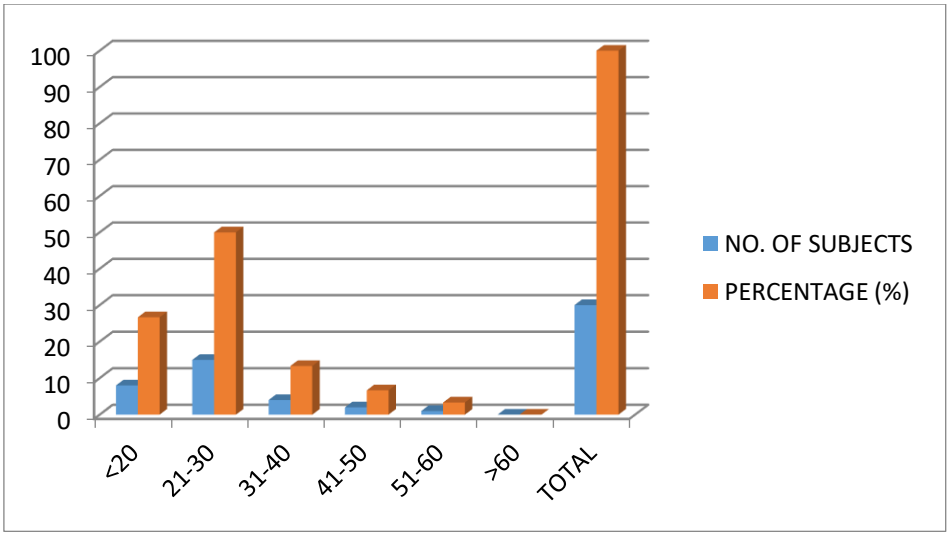
Arthritis from tubercular and non-tubercular mycobacteria as well as septic arthritis was diagnosed based on the clinical and radiological features with or without microbiological confirmation. Brucella arthritis was diagnosed based on a positive IgM/IgG ELISA or standard agglutination test.

After assignment of the final diagnosis, all the recruited patients were categorized into two groups of infectious and non-infectious arthritis. Both groups were then compared for the distribution of various clinical parameters. The radiological features compared were the presence of radiographic findings on the chest x-ray, the number of joints affected, involvement of axial skeleton and presence of erosive arthritis. Among the lab parameters, ESR and CRP were compared between the two groups. The subjectswho appeared ambiguous while assigning them to a particular group were excluded.

OBSERVATIONS & RESULTS

Table no. 1: Distribution of study subjects according to age groups

Age Groups	No. of Subjects	Percentage (%)
<20	8	26.67
21-30	15	50
31-40	4	13.33
41-50	2	6.67
51-60	1	3.33
>60	0	0
TOTAL	30	100.0



Mean age

Mean	Std. Deviation
25.5333	10.71491

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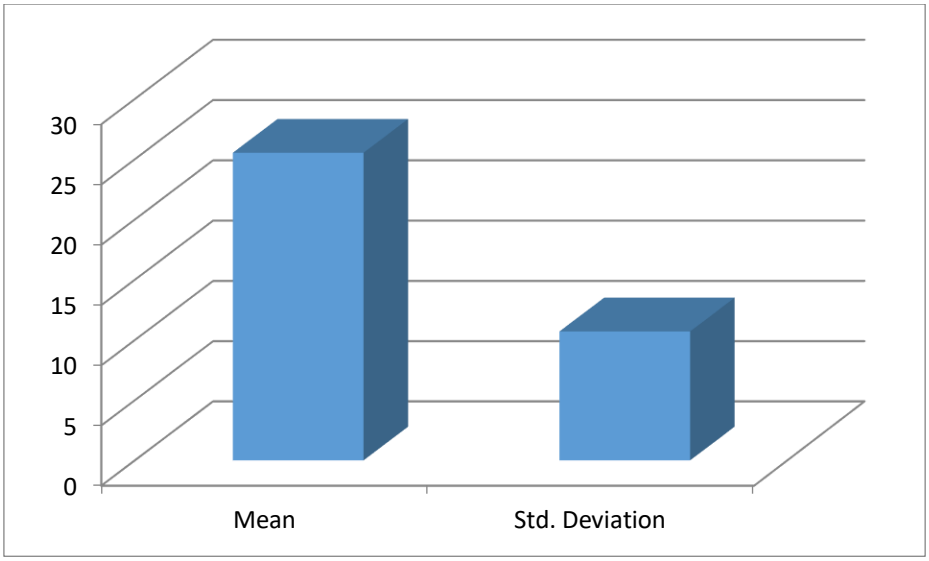

TABLE NO. 1 shows distribution of study subjects according to age groups. 50% were aged 21-30yrs, followed by 26.67% less than 20yrs, and minimum being 3.3% were 51-60yrs. Mean age being 25.533±10.71yrs.

Table no. 2: Distribution of study subjects according to gender

Gender	No. of Subjects	Percentage (%)
Female	11/30	36.67
Male	19/30	63.33

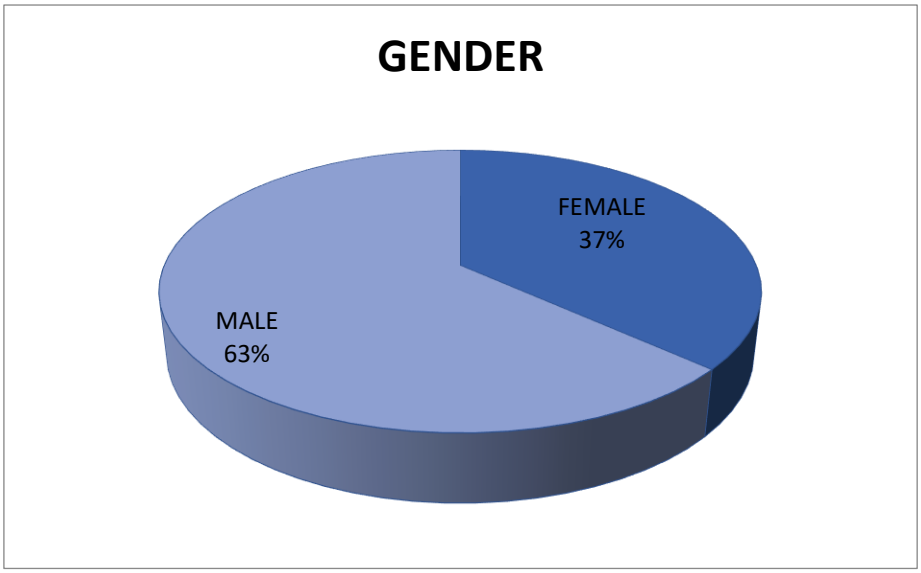

TABLE NO. 2 shows distribution of study subjects according to gender. 63.33% were males and 36.67% were females.

Table no. 3: Distribution of study subjects according to fever

Fever	No. of Subjects	Percentage (%)
YES	17/30	56.7

TABLE NO. 3 Shows 56.7 % subjects in study were having fever, it includes 3 patients of JIA, 1 patient of Gout arthritis, 2 patient of septic arthritis, 1 of TB hip joint, 2 patients of SLE, 4 of reactive arthritis, and 4 patients of spondyloarthritis presents with the fever.

Table no. 4: Distribution of study subjects according to weight loss

Weight Loss	No. of Subjects	Percentage (%)
YES	8/30	26.67

TABLE NO. 4 shows distribution of study subjects according to weight loss. 26.67% were having weight loss. Most patients with long standing rheumatological complaints presented with weight loss.

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5 patients of spondyloarthritis, 1 of JIA, 1 of Rheumatoid arthritis and 1 patients of Tubercular hip joint presented with weight loss.

Table no. 5: Distribution of study subjects according to joint involved

Joint Involved	No. of Subjects	Percentage (%)
Ankle	8	26.67
Back pain	6	20
Shoulder	3	10
Great toe	1	3.33
Hip	2	6.67
Elbow	2	6.67
PIP	3	10
Wrist	5	16.67
Low back	1	3.33
Knee	18	60
MCP	4	13.33
Total	30	100

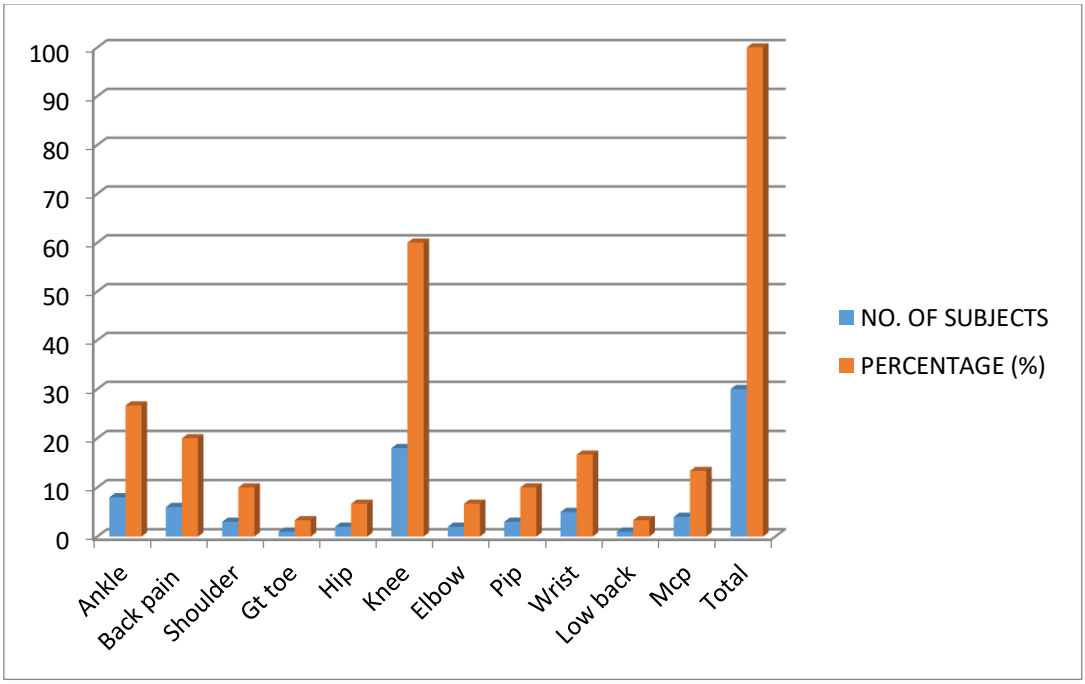

TABLE NO. 5 shows distribution of study subjects according to joint involved. 60% were having knee joint involvement, 26.67% were having ankle involvement followed by back pain, wrist involvement, MCP; and minimum 3.33% had involvement of great toe and low back.

In this study 3 patients were diagnosed as Oligoarthritis associated with SLE, all 3 patient diagnosed according to new ACR-EULAR Criteria. All of the three were meeting the minimum 10 points according to ACR-EULAR criteria for SLE.

Table no. 6: Distribution of study subjects according to HLAB27

HLAB27	No. of Subjects	Percentage (%)
POSITIVE	15/30	50.0

TABLE NO. 6 shows distribution of study subjects according to HLAB27. 50% had positive HLAB27.

HLAB27 came out to be positive in patients diagnosed with Juvenile Idiopathic arthritis, Spondyloarthritis(axial and peripheral) and Reactive arthritis.

Table no. 7: Distribution of study subjects according to RA factor

RA Factor	No. of Subjects	Percentage (%)
POSITIVE	6/30	20.0

TABLE NO. 7: shows distribution of study subjects according to RA-factor. 40% were having negative and 20% had positive RA-factor. Out of 6 patient came RA -factor positive, four patients were diagnosed with

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Rheumatoid arthritis with oligoarthritis. One patient of SLE with oligoarthritis also came positive for RA factor and 1 patient of Juvenile idiopathic arthritis came out to be RA factor positive.

Table no. 8: Distribution of study subjects according to anti-CCP2 Ab

ANTI-CCP2	No. of subjects	Percentage (%)
POSITIVE	3/30	10.0

TABLE NO. 8: shows distribution of study subjects according to Anti-CCP2. 16.7% were having negative and 10% had positive Anti-CCP2

Table no. 9: Distribution of study subjects according to TB-PCR

TB-PCR	No. of subjects	Percentage (%)
POSITIVE	1/30	3.3

TABLE NO. 9: shows distribution of study subjects according to TB-PCR. 3.3% had positive TB-PCR.

Table no.10: Distribution of study subjects according to finding in synovial fluid

Synovial finding	No. of subjects	Percentage (%)
AFB seen	1/30	3.3
Crystal	1/30	3.3
Neutrophilic	2/30	6.7

TABLE NO. 10: shows distribution of study subjects according to Synovial. 3.3% had AFB seen in TB hip, and crystals seen in synovial aspirate from great toe of patient diagnosed with Gout; 6.7% were having neutrophilic synovial fluid among two patients of Septic arthritis.

Table no. 11: Distribution of study subjects according to finding on MRI-Pelvis

MRI-Pelvis	No. of subjects	Percentage (%)
Sacroilitis	5/30	16.6
TB hip joint	1/30	3.3

TABLE NO. 11 shows distribution of study subjects according to MRI-Pelvis. 16.6 % patients had sarcoilitis; 3.3% TB hip joint.TB Hip typically showed synovial effusion with thickening, bone edema and areas of bony destruction.

Table no. 12: Distribution of study subjects according to diagnosis

Diagnosis	No. of subjects	Percentage (%)
Axial spondyloarthritis	6/30	20.0
TB hip joint	1/30	3.3
Gout	1/30	3.3
Juvenile idiopathic arthritis	5/30	16.7
Peripheral spondyloarthritis	4/30	13.3
Rheumatoid arthritis	4/30	13.3
Reactive arthritis	4/30	13.3
Septic arthritis	2/30	6.7
Systemic lupus erythematous	3/30	10.0

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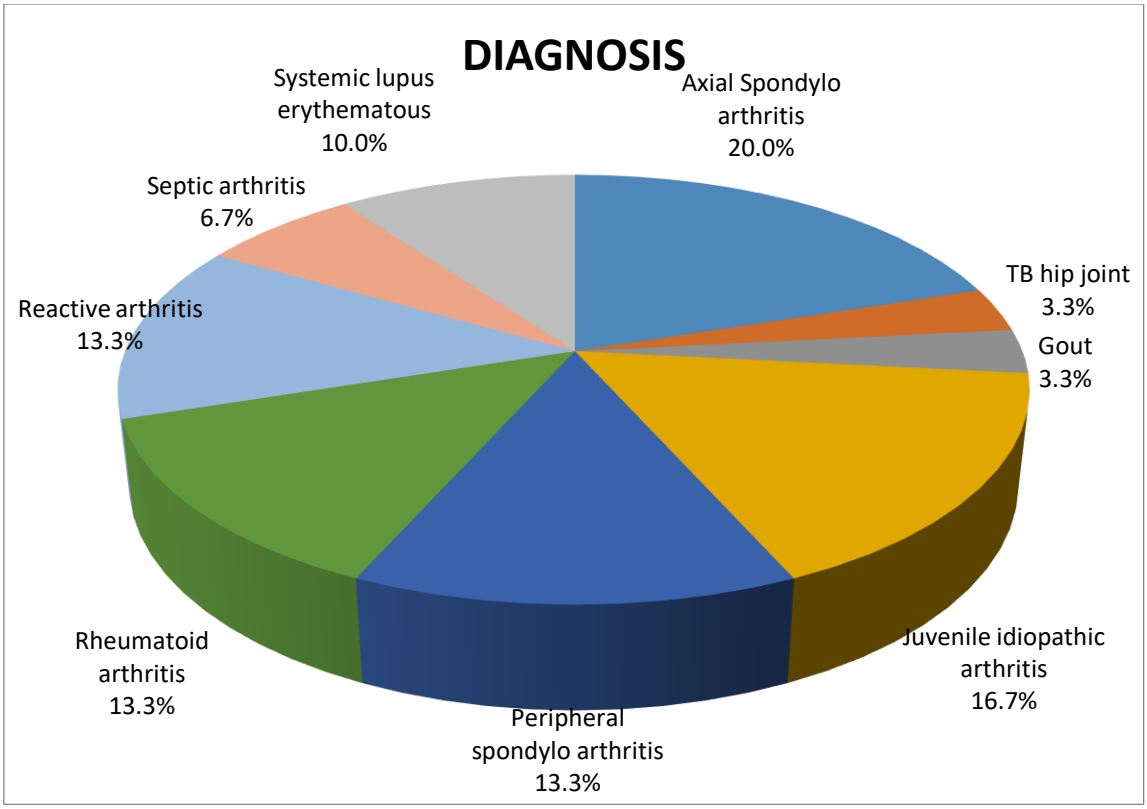

TABLE NO. 12 shows distribution of study subjects according to diagnosis. 20% had Axial Spondyloarthritis; 16.7% were Juvenile idiopathic arthritis and minimum being 3.3% TB hip joint and gout. In this study 13.3% of RA and 10% of SLE patient presented as oligoarthritis.These subsets of patients may later progress to polyarticular arthritis.

Table no. 13: Mean of various laboratory investigations

	Mean	Std. Deviation
DURATION (months)	22.0940	28.33151
Hb (g/dl)	11.8700	1.36259
TLC (per microliter)	10951.6667	4385.80868
Platelet (lakh/microliter)	2.8233	1.02778
Ser. Total Protein (g/dl)	7.2034	.77482
Albumin (g/dl)	3.5759	.53895
Cr (mg/dl)	0.827	0.221
Urea (mg/dl)	27.5	12.98
CRP (mg/dl)	29.0148	16.29836
ESR (mm)	26.1391	10.29076

TABLE NO. 13 shows mean values of various parameters. Duration was 22.0940±28.33151 months, Hb was 11.8700±1.36259 g/dl, TLC was 10951.6667±4385.80868 per microliter, Platelets were 2.8233±1.02778 lakh/microliter, Ser. Total Proteinwas 7.2034±.77482 g/dl, Albumin was 3.5759±.53895 g/dl, Creatinine was 0.827±0.221 mf/dl, Urea was 27.5±12.98 mg/dl, CRP was 29.0148±16.29836 mg/l and ESR was 26.1391±10.29076 mm.

DISCUSSION

In light of the higher prevalence of tuberculosis and other infectious diseases,[1]it is possible that the clinical profile of Indian patients with oligoarthritis could be different from those of the developed countries. Due to ambiguity in the initial presentation of infectious and non-infectious causes, it is important to explore the differences which could help in the early identification of infectious arthritis. Thus, it is important to assess the clinico-pathological features of the disease and identify the various etiological factors which leads to oligoarticular inflammatory arthritis. The present study was conducted with an aim to study the etiological profile of the patients diagnosed with oligoarticular inflammatory arthritis, reporting at a tertiary care center of north India. It was conducted at the Departments of Internal Medicine and Orthopedics, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

Oligoarticular juvenile idiopathic arthritis (Oligo-JIA) is the most frequently diagnosed chronic arthritis in children of Europe and North America. It accounts for

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50-80% of all children with chronic arthritis[2]. Oligo-JIA is defined as an inflammatory arthritis of unknown origin starting before the age of 16 years and persisting for more than 6-week duration.

In the present study, 50% were aged 21-30yrs, followed by 26.67% belonging to less than 20yrs, and minimum being 3.3% were in the group 51-60yrs. Mean age of subjects was 25.533±10.71yrs. We also observed a male predominance with 63.33% males and 36.67% were females. In contrast to our study, Raab, A et al.[3] found that the mean age of patients suffering with Oligo-JIA was 5.2±3.7yrs. Contrasting results were observed in a study by Macaubas C et al. who also found that incidence of Oligo-JIA at age 2-4 years, with female:male ratio being 3:1. Barut K, et al.[4], also stated that Oligo-JIA is common among young female patients and usually accompanied by anti-nuclear antibodies positivity and anterior uveitis. The results of our study are contrasting. This might be because of the reason that our sample size was short and results are based only on the subjects who reported to us.

We found that 43.33% were not having fever while 56.7% were having fever. 26.67% were having weight loss. In accordance with our study,Richie AM et al.[5] observed that patients with an inflammatory arthritis are more likely to have palpable synovitis and morning stiffness. Fatigue, fever and weight loss are seen in severe form of the disease. Oligoarticular JIA is a benign form of the disease, involving up to four joints of lower limbs in an asymmetric pattern. Around 80% of patients have a single or both knee involved; hip or ankle joints are less often affected, and other peripheral joints have also been found to be affected.

In our study, we observed that 26.67% were having ankle involvement, followed by back pain, wrist involvement, MCP joint and minimum 3.33% had involvement of great toe and low back.

Cassidy JT, et al.[6]and Ravelli A et al.[7]found a contrasting result and revealed that commonly affected joint is the knee, with the leg on the affected side becoming longer. Musculoskeletal abnormalities like flexion contractures and atrophic muscles around the inflamed joint has also been found to be involved.

In accordance with our study, Weiss JE et al.[8] found that Oligoarticular JIA predominantly involves lower-extremity joints, such as the knee and ankle joint. The hip joint is rarely affected. Small-joint involvement is pretty rare in this entity.

In present study, 36.67% were having negative ASO titre. 16.7% were having negative ANA, and 10% had positive ANA. 10% were having negative and 10% had positive Anti-dsDNA Ab.

Over the last two decades,resurgence of tuberculosis is being observed worldwide. Patients with extra-articular TB may present with a variety of rheumatic symptoms and signs. Tubercular arthritis usually manifests as monoarthritis of hip, knee or ankle, but its oligoarticular and polyarticular forms are not very rare, in which case it can mimic inflammatory diseases such as spondyloarthropathiesor rheumatoid arthritis. Antibodies likeanti-cyclic citrullinated peptides(Anti-CCP) are highly specific for RA.Its specificity is up to 98% in comparison with 0-1% of healthy controls and 2-5% of diseased controls. Anti-cyclic citrullinated peptides are present early in the disease process and may even pre-date the onset of RA by many years. In our study, we found that 16.7% were having negative and 10% had positive Anti-CCP2 Ab in patients with Oligo-JIA. 40% were having negative and 20% had positive RA factor.

HLA-B27 comprises of 25 glycoproteins (HLA-B*2701 to HLA-B*2725) that are known as subtypes of HLA-B27. The association of reactive arthritis with HLB27 issubstantiatedby the fact that the prevalence of disease in HLB27-positive subjects is five-fold higherthan in the general population. Human leucocyte antigen class I allele HLA-B27 is linked with ankylosing spondylitis, a chronic inflammatory disease. More than 90 % of patients with ankylosing spondylitis possess the HLA-B27 allele, but only 1 % of people with HLA-B27 develop the disease.We also observed HLA-B27 levels in our study in patients with OJIA. We found that 13.3% were having negative and 50% had positive HLAB27. 3.3% had positive TB-PCR.

Synovial fluid analysis is crucial in the evaluation of inflammatory arthritis. Synovial fluid was analysed in our study for total and differential count, polarized light microscopy, Grams stain and culture including fungal. Mycobacteriology was done as was appropriate.

Earlier, it was thought that the immunopathogenesis of oligoarticular JIA is driven primarily by adaptive immune responses, since the disease is associated with HLA class II genetic variants and the presence of auto antibodies. However, abnormalities in the adaptive immune system cannot fully explain the pathology of JIA, and the importance of the innate immune system in oligoarticular JIA is increasingly being recognized.

The synovial fluid in patients with JIA contains high levels of monocyte-derived cytokines. The synovial monocytes are polarized with impaired phagocytic ability. The role of innate immune response is also emphasised by the fact that in the treatment of oligoarticular JIA, the most commonly used drugs are either non-specific or target important components of the innate immune system such as tumor necrosis factor alpha (TNFα) and interleukin 6 (IL-6), while therapies targeting T and B cells in the adaptive immune system are seldom used.

We also observed synovial fluid and found that 3.3% had AFB, and crystals; 6.7% were neutrophilic. In accordance with our study, Wirestam L et al.[9] also supported that neutrophils represent a major part of the innate immune system, and the dysfunctional

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neutrophils at least partlydrive the pathology of autoimmune rheumatic diseases.

Poudel P et al.[10] mentioned that septic arthritis and crystalline arthropathies usually have neutrophilic predominance, while rheumatoid arthritis usually has lymphocytic predominance in the synovial fluid. Monosodium urate crystals on polarized light microscopy are needle-shaped and strongly negatively birefringent while weak positive birefringence and rhomboid shape on polarized microscopy is exhibited by calcium pyrophosphate crystals. Basic calcium phosphate crystals are not visible on polarized light microscopy and need special staining for visualization.

Contrast-enhanced MRI is the most sensitive method for detection of synovitis and is the only modality to detect bone marrow edema, both of which indicate active inflammation. Iridocyclitis is seen in almost 30% of the patients of oligoarthritis, necessitating its routine ophthalmologic screening. In our study, 16.6% patients had sacroilitis and 3.3% had TB of hip joint on MRI.

Diagnostic problems with JIA are common. While this is an obvious truth for rheumatologists, physicians of other specialties are often misled by the fact that in JIA basic biochemical test results may stay within the normal range. This phenomenon seems to contradict the fact that JIA is merely an inflammatory process.

We observed that the mean duration of disease at presentation was 22.0940±28.33151 months, Hb was 11.8700±1.36259, TLC was 10951.6667±4385.80868, platelet counts were 2.8233±1.02778 lakh/ml, serum total proteins were 7.2034±.77482 g/dl, albumin was 3.5759±.53895 g/dl, creatinine was 0.827±0.221 mg/dl, urea was 27.5±12.98 mg/dl, CRP(q) was 29.0148±16.29836 mg/L and ESR was 26.1391±10.29076 mm.

Similar to our study Packham JC et al.[11] found that mean duration of OJIA was around 16yrs. Peterson et al.[12] performed the only population-based long-term outcome study, on 44 patients with a mean duration of disease of 24.7 yrs. Because it was a population-based study, a high proportion of oligoarticular arthritis (73%) was found in the study group. Zak and Pedersen[13] reviewed a group of 65 patients with an average 26.4 year of disease.

Guillaume S et al.,[14] and Al-Matar MJ, et al.[15]revealed that laboratory indicators of inflammation may be normal, although mild to moderate elevation of the ESR and CRP levels may occur during the acute phase of the disease. High ESR and upper extremity arthritis are more common in patients with extended oligoarticular JIA. Mild anaemia and leucocytosis could be seen in patients with acute arthritis.

We observed that 20% had Axial Spondyloarthritis; 16.7% were Juvenile idiopathic arthritis and minimum being 3.3% TB hip joint and gout. Zuber Z et al.[16] stated that treatment with b-DMARDs depends on the form of o-JIA and whether the disease is expected to evolve in the future towards RA, psoriatic arthritis (PsA), ankylosing spondylitis (AS) or spondyloarthropathy (SpA).

Oligoarticular JIA is a seemingly benign form of the disease. At the age of 12–16 years, Oligo-JIA accounts for less than 40% of all new JIA cases. Oligo-JIA is a systemic disease in which child's normal development, growth, mass and body-proportions are affected. Growth impairments become a significant emotional burden for the patients, worsening the social functioning and lowering the quality of life. The child's development should be assessed systematically by keeping a watch on his body weight and height. These measurements need to be plotted on a centile grid. Unexplained lag in growth from the population age norm on centile grids warrant a thorough assessment of the musculoskeletal system. The inflammatory process, disturbances ingait and developmental delays that continue may remain unnoticeable, even by the patient's close family.

CONCLUSION

In this study, maximum cases accounting to 20.0% had axial spondyloarthritis and the minimum wereTB of hip joint and gout, each accounting to 3.3% of the whole. Juvenile idiopathic arthritis accounted for 16.7%. Peripheral spondyloarthritis, RA and ReA, each of the three accounted for 13.3% of the cases and 10% subjects with SLE presented as oligoarthritis. The cases with septic arthritis constituted 6.7% of the whole chunk.

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