Disease Characteristics Profile and Preferred drugs Treatment Outcomes of JIA Subtypes: A Tertiary Care Hospital Experience in Bangladesh

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Abstract

Background: Juvenile Idiopathic Arthritis (JIA) is a leading cause of chronic inflammatory joint disease in children. It has the potential to cause both short-term and long-term childhood morbidity and substantial disability which leave a long-lasting impact on the quality of life.

Aim: To evaluate disease characteristics profile in children with Juvenile Idiopathic Arthritis (JIA) subtypes, effective medication and their outcome.

Methods: This retrospective study was carried out using the medical records of follow-up center of the Rheumatology department of Bangladesh Shishu Hospital and Institute from January 2021 to December 2023.Ninety-five children who were diagnosed as JIA in this period were enrolled in this study. Data regarding clinical findings as articular, extra articular and systemic manifestations, biochemical profile, preferred drug, and remission or relapse rates of JIA subtypes were evaluated.

Results: Among 95 cases 68 were male and 27 were female. Male : Female ratio being 2.5:1. Age range of the patients was 1 year to 15 years. Maximum number of patients presented beyond 5 years of age (67%). Duration of illness was less than 6 months in the majority (61%). In terms of disease characteristics, enthesitis related arthritis (ERA) were the most frequent (34.74%) followed by systemic JIA (29.47%). Arthritis was found in 100% of JIA patients. Knee and ankle were the most frequently affected joints accounting for 80% of the cases in both poly and oligoarticular subtypes. In this study, fever was found in 37.89% and morning stiffness in 36.84% cases. Rash was detected 64% in Systemic Juvenile Idiopathic Arthritis (sJIA) patients. In this study 10.52% of JIA had joint contractures and/or deformities. Uveitis, hepatomegaly and or splenomegaly, pericarditis were relatively infrequent. A life-threatening complication of sJIA, macrophage activation syndrome (MAS) was present in 14% cases. At initial presentation, overall 36.84% in JIA cases were anemic. Leukocytosis was in 52.63% and 33% cases had thrombocytosis. ESR and CRP were raised 34.73% and 56.84% respectively of JIA patients. Both ESR and CRP elevation were in sJIA. Rheumatoid factor positivity was 8.42% of overall JIA, half of patients were polyarticular. ANA was positive 38% in oligoarticular, 23% in polyarticular. HLA-B27 was positive 79% in ERA. The overall response rate to therapy was 45%. 27% had clinical remission on medication and 18% had remission off medication while 52% still had the active disease and 3% expired.

Conclusion: The profile of JIA subtypes differ from each other. Used NSAID and steroids in the early period of disease was an effective treatment, especially addition of Methotrexate (MTX). Treatment with biologic agents in some of our patients flared after combination therapy with NSAID, steroids and MTX after 2 years became clinical remission.

Keywords: JIA subtypes, clinical and biochemical profile, preferred drug, outcome.

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Introduction

Juvenile Idiopathic Arthritis (JIA) is a heterogeneous group of childhood chronic arthritis with diverse clinical pattern. Various publications concerning JIA indicated that the clinical and biochemical presentation of the disease are variable. Different aspects of JIA has been extensively studied in developed countries. However, reports on JIA from developing countries are quite less.[1,2] JIA is an umbrella term, a group of subtypes having articular as well as extra-articular involvement are under this.[3,4] If the clinical picture is not fully established, differential diagnosis is difficult from other connective tissue disease. In the absence of definitive diagnostic criteria, many classification have been proposed according to number of joints involved, extra articular status and other associated clinical findings.[5]

According to International League against

Rheumatism (ILAR), JIA is defined as definite arthritis of unknown etiology begins before 16th birthday and persists for at least 6 weeks.[2] Three separate systems are used currently to classify JIA patients.[4] The American College of Rheumatology (ACR) defined 'juvenile rheumatoid arthritis' (JRA) as persistent arthritis in one or more joints for more than 6 weeks. They have classified JRA into three categories: systemic, polyarticular and pauci/oligoarticular. The European League against Rheumatism (EULAR) proposed the term 'juvenile chronic arthritis' (JCA) for the heterogeneous group of disorders that present as juvenile arthritis. The diagnosis of JCA required that arthritis begins before 16 years of age and lasts for at least 3 months.

The EULAR classification subdivided JCA into systemic, poly articular, juvenile rheumatoid arthritis, pauci-articular and juvenile psoriatic arthritis. EULAR classifications have reversed the term JRA for children with arthritis and rheumatoid factor seropositivity. As definition and classification of their subgroups were different, the terms JCA (EULAR) and JRA (ACR) were not interchangeable.[2] Juvenile idiopathic arthritis (JIA) is the new term proposed by ILAR, in 1995 in Santiago and revised in 1997 in Durban. The ILAR classification subdivided JIA into seven categories: Systemic Juvenile Idiopathic Arthritis (sJIA), polyarticular RF negative, polyarticular RF positive, oligoarticular (persistent and extended), psoriatic, enthesitis-related, and undifferentiated arthritis (fits no category or fits more than one category). This classification system was developed to identify as far as possible clinically and biologically homogenous groups of children with chronic arthritis.

Criteria of sJIA: Fever of at least 2 weeks duration and arthritis in ≥1joint plus 1 or more of the following- erythematous rash, lymphadenopathy, serositis, hepatomegaly and/or splenomegaly. Life threatening complication of sJIA is macrophage activation syndrome (MAS). Features of MAS (e.g., non-remitting fever, cytopenia, liver and CNS dysfunction, lymphadenopathy, hepatospleenomegaly, hemorrhages, multiorgan failure).

Criteria of Oligoarthritis: Arthritis affecting ≤4joints during the first 6 months of disease either persistent (affect 4 or fewer joints throughout the disease course) or extended (affect more than 4 joints after the first 6 months of disease).

Criteria of Polyarthitis: Arthritis affecting ≥5joints during the first 6 months of disease, may be seropositive (RF- positive) or seronegative (RF- negative).

Criteria of Psoriatic arthritis: Arthritis and psoriasis, or arthritis and at least 2 of the following- dactylitis, nail pitting or onycholysis, psoriasis in a first-degree relative.

Criteria of Enthesitis related arthritis (ERA): Either arthritis and enthesitis, or arthritis or enthesitis with at least 2 of the following characteristics: onset of arthritis over 6 years of age and male child, the presence of or a history of sacroiliac joint tenderness and/or inflammatory of lumbosacral pain, the presence of HLA-B27 antigen, acute (symptomatic) anterior uveitis, history of ankylosing spondylitis, enthesitis related arthritis, a family history of an HLA-B27 associated disease as sacroilitis with inflammatory bowel disease, Reiter's syndrome, or acute anterior uveitis in a first-degree relative.

Criteria of Undifferentiated arthritis: Arthritis fulfills the criteria in no category or in 2 or more of the above categories.[6,7]

There is no definite test to confirm the diagnosis of JIA cases. Therefore, JIA is diagnosed through clinical profile on a combination of presenting signs and symptoms as well as biochemical tests and if necessary, medical imaging. A number of biochemical tests have been used to assist the diagnosis of JIA. Most commonly used to assess disease activity in JIA are C-reactive protein (CRP) and ESR. Both tests are non-specific measure of inflammation. Others that are useful to classify the subtypes of JIA include HLA-B27 and ANA.[8] The presence of HLA-B27 is an important part of the inclusion criteria used in the definition of enthesitis-related arthritis (ERA) based on the ILRA criteria. HLA-B27 has a strong association with ankylosing spondylitis (AS), which is notable considering that ERA is thought to be the pediatric counterpart of adult AS.[9] ANA positivity may represent a unique condition in JIA, frequently found in children with oligoarthritis. Rheumatoid factors (RFs) are most commonly detected in children at later age onset with polyarticular involvement.[10]

New advances in pharmacologic treatments have shown robust results. Even though none of the available drugs has a curative potential, prognosis of JIA has greatly improved as a result of use of these drugs over the years.[11] Early interventions with DMARDs (Disease Modifying Anti-rheumatic Drugs e.g.,MTX,Sulfasalazine) may help minimize joint damage[12] and increase remission rates.[13] However, use of such drugs can be complex particularly in terms of appropriate dosing and monitoring for possible adverse effects in children. Moreover, the long-term effects of these medications are still incomprehensive.[14]

Although the course of JIA in an individual child is unpredictable, some prognostic criteria can be made on the basis of disease subtype and course. Children with persistent oligoarticular subtype flare but a majority achieving disease remission. Those with extended oligoarticular, polyarticular subtypes, specially QRA (Quantitive Rheumatoid arthritis) factor positive and sJIA subtype have poorer prognosis. Extended oligoarticular subtype is treated as polyarticular subtype. Prognosis can be averted with early diagnosis and implementation of systemic therapy. The child with polyarticular JIA often has a more prolonged course of arthritis and requires early and aggressive therapy. Predictors of severe and persistent disease include young at onset, RF

seropositivity, and involving the hip and hand/wrist associated with a poorer prognosis and may lead to significant functional impairment. sJIA is often the most difficult to control in terms of both articular inflammation and systemic manifestations. Poorer prognosis is related to poly articular distribution of arthritis, fever lasting >6 months and increased inflammatory markers, such as platelet count, CRP, ESR.[15]

Still very few analyses have been reported about the characteristics of different JIA subtypes and preferred drugs and their efficacy and outcome in Bangladesh. So, this study was carried out to evaluate the disease characteristics profile of JIA subtypes, effective medication and their outcome.

Methods

This retrospective study using the medical records of 95 JIA children diagnosed according to ILAR at follow-up center by Rheumatology department of Bangladesh Shishu Hospital and Institute from January 2021 to December 2023. Data regarding clinical profile as articular, extra-articular manifestations, ophthalmologic and biochemical profile as well as effective medication and prognosis of affected children were evaluated. All patients were evaluated by an ophthalmologist for any evidence of uveitis with slit lamp examination. Necessary investigations were done including hemoglobin estimation, total and differential count of WBC, ESR, CRP, rheumatoid factor (RF) positivity or not, antinuclear antibody (ANA), HLA B-27 and radiological findings (narrowing or erosion of joint space, polyarticular synovitis, articular surface erosion, ankylosis and fusion formation).

At initial presentation, patients were anemic (hemoglobin<10 g/dl), WBC counts >11,000/cu mm and Platelet>450,000/cu mm were considered as significant. The rate of erythrocyte sedimentation (ESR) >20 mm/hr. and C reactive protein (CRP) is considered to be higher both boys and girls than 5 mg/L. Ferritin was accepted as normal between 7-140ng/ml. Rheumatoid factor (RF) was determined by latex agglutination method.[16] MAS was diagnostic when features with nonremitting fever, hepatomegaly, splenomegaly, liver dysfunction, CNS manifestation, cytopenia, serum ferritin >684ng/mL present in a sJIA patient.[16,15]

Patients in this study were evaluated according to the presence or absence of poor prognostic criteria (e.g., RF positivity, radiological narrowing or erosion of joint space, polyarticular synovitis, nonsteroidal treatment for one year and dramatic improvement in combination with MTX, Intraarticular steroid or slow acting anti-rheumatic drugs, HLA B27 positivity in patients with polyarticular arthritis.

The prognosis was considered to be poor- when there is presence of polyarthritic JIA, sJIA with polyarticular involvement, accompanied with severe anemia, presence of hyperferritinemia, and very high ESR.[17] Clinical remission is accepted as our patient hadn't morning stiffness last no longer than 15 minutes, fatigue and absence of soft tissue swelling, absence of pain and limitation of movement.[17] The Carol Wallace criterion were applied which defined 3 stages of disease: clinical remission off medication, clinical remission on medication, active disease.[18]

In JIA, clinical "remission on treatment" is defined as a period of at least 6 continues months where the disease is inactive. This state signifies disease control and reduced inflammation, but continues medication to maintain this inactive state and prevent disease flares or long-term joint damage. This process is a necessary step before a child can be considered for clinical remission off medication. Clinical "remission off treatment" is a process that aims to discontinue medication when a patient achieves sustained remission, meaning the disease is inactive for at least 12 continuous months without medication.

Data was analyzed and tabulated manually. This study was used to evaluate clinical characteristics of children with JIA subtypes, response to therapy and their outcome over a period of about 3-years' experience.

Results

Among 95 JIA patient, 68 were male and 27 were female (M: F=2.5:1) and hailing more from urban area than rural (1.5:1) (Fig.1and Fig.2).

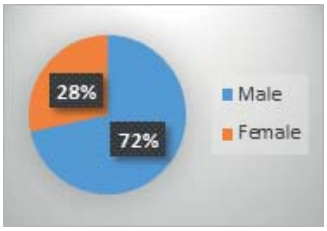

Fig 1. Gender distribution

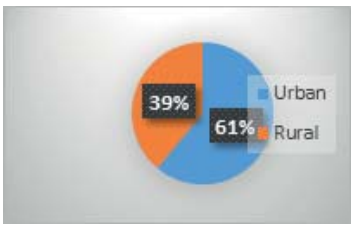

Fig 2. Residing status

Patients were mostly aged beyond 5 years of age (67%) and duration of illness was less than 6 months in the majority (61%) of JIA patients (Table I and Table II).

Table I: Age of initial presentation of study patient (n=95)

Age	Number	Percentage
>12 m-<3yr	14	14.74
3yr-5yr	17	17.89
>5yr-16yr	64	67.37
Total	**95**	**100.00**

Table II: Duration of illness (n=95)

Duration	Number	Percentage
<6m	58	61.05
6m-12m	14	14.74
>12 m	23	4.21
Total	**95**	**100.00**

In terms of disease characteristics, ERA patients were most frequent (34.74%) followed by sJIA (29.47%) and poly articular rheumatoid factor negative (24.21%) (Table III).

Table III: Subtypes of Juvenile Idiopathic Arthritis (JIA) (n=95)

Types	Number	Percentage
Poly articular (RF-positive)	3	3.16
Poly articular (RF-negative)	23	24.21
Oligoarticular (Persistent)	7	7.37
Oligo articular (Extended)	1	1.05
Systemic JIA	28	29.47
Enthesitis related arthritis	33	34.74
Total	**95**	**100.00**

All JIA patients presented with arthritis. Knee and ankle were the most frequently affected joints accounting for an 80% of the cases in both poly and oligoarticular subtypes. Other joints that were involved wrist, elbow, shoulder, metacarpo-phalangeal, inter-phalangeal and hip joints. In this study, fever was found in 37.89% and morning stiffness in 36.84% of cases. Fever in polyarticular group was 31% and 100% in sJIA. Rash was 64% and lymphadenopathy was 36% in sJIA. Hepato and/or splenomegaly was 18% in sJIA. Pericarditis was 10.71% in sJIA. Rash, lymphadenopathy, hepato and/or splenomegaly, pericarditis and life threatening complication as MAS were found only in sJIA. In this study, MAS was 4.21% in sJIA. Uveitis was relatively infrequent. Uveitis was found 3% in ERA and 11.53% in Poly JIA. 10.52% of JIA had joint deformities, 30.77% in Poly JIA and 6.06% in ERA (Table-IV and Fig.3).

Table IV: Pattern of clinical profile in different subtypes of JIA (n=95)

Features	Number	Percentage
Arthritis [All JIA cases]	95	100.00
Fever [*sJIA 28(100%), PolyJIA 8(30.76%)]	36	37.89
Morning Stiffness [**ERA 13(39.39%), sJIA 9(32.14%), Poly JIA 8(30.76%), Oligo JIA 5(62.5%)]	35	36.84
Rash [64.28% in sJIA]	18	18.94
Lymphadenopathy [36% in sJIA]	10	10.52
Hepato and/or splenomegaly [18% in sJIA]	5	5.26
Uveitis [ERA 1(3.03%), Poly JIA 3(11.53%)]	4	4.21
***MAS [14.24% in sJIA]	4	4.21
Pericardits [10.71% in sJIA]	3	3.15
Joint Contractures &/ or deformities [Poly JIA 8(30.77%), ERA 2(6.06%)]	10	10.52

*sJIA (Systemic Juvenile Idiopathic Arthritis) **ERA (Enthesitis Related Arthritis)

*** MAS (Macrophage Activation Syndrome)

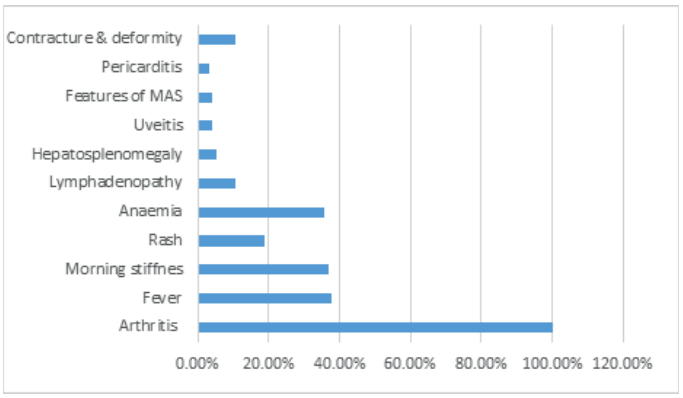

Fig 3. Frequency distribution of clinical presentation among study patients

At initial presentation anemia in 36.84%. Among anemic cases, the majority (50%) was in sJIA and 39% in ERA. Leukocytosis was 52.63% and thrombocytosis was 32.68% of overall JIA cases. Other acute phase reactants, ESR and CRP were raised in 34.73% and 56.84% JIA patient respectively. It was observed that sJIA had high both ESR and CRP (Table V). Overall rheumatoid factor positivity was 8(8.42%), half of patients were polyarticular. ANA was positive 38% in oligoarticular and 23% in polyarticular. HLA-B27 was positive 79% in enthesitis related arthritis (ERA), 7.69% in polyarticular and only 3.57% in sJIA patient (Table V).

Table V: Pattern of biochemical profile in different subtypes of JIA (n=95)

Biochemical profile	Subtype				Overall
	Oligoarticular (n=8)(overall%)	Polyarticular (n=26) (overall%)	sJIA(n=28) (overall%)	ERA(n=33) (overall%)	n=95(%)
Hb <10 g/dl	3(37.5%)	5(19.23%)	14(50%)	13(39.39%)	35(36.84%)
WBC counts >11,000/cu mm	3(37.5%)	13(50%)	20(71.43%)	14(42.42%)	50(52.63%)
Platelet>450,000/cumm	2(25%)	9(34.61%)	10(35.71%)	11(33.33%)	32(32.68%)
ESR>20 mm/hr	3(37.5%)	10(38.46%)	11(39.28%)	9(27.27%)	33(34.73%)
CRP (>5 mg/L)	5(62.5%)	9(34.61%)	22(78.57%)	18(54.54%)	54(56.84%)
QRA +ve	0(00%)	4(15.38%)	2(7.14%)	2(6.06%)	8(8.42%)
ANA +ve	3(37.5%)	6(23.08%)	2(7.14%)	2(6.06%)	13(13.68%)
HLA-B27	0(00%)	2(7.69%)	1(3.57%)	26(78.78%)	29(30.53%)

Prognosis was analyzed as response to therapy at the time of last follow-up. The overall response rate to therapy was 45% (n=40). Out of 88 patients who continued to follow in the clinic. Among those, 24(27.27%) had clinical remission on medication and 16 (18.18 %) had clinical remission off medication while 46(52.27%) still had the active disease in their last follow-up and 3% had expired. Best response was seen in oligoarticular persistent subtype while worse in oligoarticular extended subtype, polyarticular subtype specially QRA positive and sJIA subtype. In ERA, inflammation of the small joints of the foot, or tarsitis, was highly suggestive and upto 40% of children develop clinical or radiographic evidence of sacroiliac joint arthritis as part of their disease; approximately 20% had evidence of sacroiliac joint arthritis at diagnosis.7(7.36%) patients were lost to follow-up due

to accessibility, as they were from remote areas of the country. 2(2.27%) patients died, 1 with sJIA who subsequently developed Macrophage Activation Syndrome (MAS) and 1 sJIA patient with septicemia. (Table VI). None of our patients developed amyloidosis.

Table VI: Outcome of different subtypes of JIA

	sJIA (n=28)	PolyJIA (n=26)	Oligo (n=8)	ERA (n=33)	Overall (%) (n=95)
Clinical "remission on medication"	4	5	2	13	24(25.26%)
Clinical "remission off medication"	3	1	5	7	16(16.84%)
Active disease	16	19	1	10	46(48.42%)
Expired	2	-	-	-	2(2.10%)
Lost to follow-up	3	1	-	3	7(7.36%)

Discussion

This retrospective study was carried out in a tertiary care hospital, Bangladesh. Thereby, those profile may not represent the findings in the community. It is well established females always outnumber males among JIA patients.[19,20] However, the reverse was found in this study where males preponderance (M: F=2.5:1) present. This was consistent with some other studies.[21,22] Urban versus rural area ratio was 1.5:1.

In this study, age of initial presentation was mostly beyond 5 years of age (67%). The age at onset in other studies 6.9 years in Turkish children, 10.7 years as described by Nighat et al and 11.8 years in African children.[23-25] Duration of illness in majority of cases was less than 6 months (61%). In another study it was 1.15 years.[26] In our series about 35% of children had ERA, 30% sJIA, 25% poly articular rheumatoid factor negative JIA and 7% had persistent oligoarthritis. Most of the literature show that oligoarticular JIA is the most frequent subtype (50%-60%).[19,20,27] A higher frequency of enthesitis related JIA was observed among patients of Asian origin, while those of Black origin or native North American origin were more likely to develop polyarticular RF positive JIA.[28] In their series, Schaller and Wedgwood detected 37% of polyarticular and oligoarticular types and 26% of sJIA type.[29] The presentation of our JIA cases was consistent with Davidson J et,al.[30]

All patients (95) presented to us with arthritis (100%). Similar result was found in Rahman SA.[31] Knee and ankle were the most frequently affected joints accounting for an 80% of the cases in both poly and oligoarticular subtypes. Other joints that were involved wrist, elbow, shoulder, metacarpo-phalangeal, inter-phalangeal and hip joints. This is comparable to data reported in other studies by Seth et al., Aggarval et al. and Singh et al.[32-34]

In our study, fever was 37.89% and morning stiffness was 36.84% of JIA cases in this study. Fever was 100% in sJIA and 31% in poly JIA. Patients with oligoarticular and ERA had no fever. Rheumatoid rash is one of the classic findings in sJIA. The rate of rash was 42.6% in Petty's study.[35] In our study, rash was detected 64.28% in sJIA. Lymphadenopathy 70% in sJIA and 5% in polyarticular is reported. In this study, 10.52% of JIA patients with lymphadenopathy, all was in sJIA (36%). Hepatomegaly and/or splenomegaly most commonly occurs in the sJIA. In other study, hepatomegaly and/or splenomegaly was 90% of sJIA, 10% of polyarticular JIA, and 0% of oligoarticular JIA reported.[20] In our study where hepato and/or splenomegaly was 18% in sJIA.

Life-threatening complication of sJIA as macrophage activation syndrome (MAS) is rarely seen. Fourteen percent (14%) sJIA had been suffering from MAS in this study. This is rarely seen in 5%-8% of sJIA in Ravelli A study.[36] Joint deformities developed in 14.7% of overall JIA cases. 20.5% in polyarticular and 10% in sJIA. There was no deformity in oligoarticular in Tekeli AA study.[37] In this study, joint deformities were 10.52% in overall JIA cases (30.77% in poly JIA, 6% in ERA and no in oligoarticular). In our study, uveitis was relatively infrequent (3.03% in ERA and 11.53% in poly JIA). Only 3% JIA cases having uveitis in another study.[38] Pericarditis is infrequent in JIA, found only in sJIA patient. It is usually asymptomatic, and some children may have dyspnea or precordial pain. In this study, pericarditis was infrequent 3% in overall JIA patients. Lietman and colleagues found pericarditis 7%.[39]

Among biochemical profile, CBC (complete blood count) showed that overall 36.84% JIA patients were anemic at initial presentation, among them majority (50%) was in sJIA and 39% in ERA. White cell counts were raised in overall 52.63% of JIA patients. 71% in sJIA. 34.77% had thrombocytosis with overall JIA cases. 36% in sJIA. In another study Tekeli AA showed anemia was found in 76.9%, leukocytosis in 38.5% and thrombocytosis in 76.9% of JIA patients.[37]

Other acute phase reactants, ESR and CRP were also raised with frequency of 34.73% and 56.84% respectively. It was observed that almost all patients with sJIA had high ESR and CRP. In this study overall positivity of rheumatoid factor was 8.42% in JIA. Among them half of the cases were polyarticular.The presence of HLA-B27 is an important of the inclusion criteria used in the definition of enthesitis-related arthritis (ERA) based on ILRA criteria. Approximately 60%-80% of children with ERA represent positive for HLA-B27.[9] Although HLA-B27 is frequently present in these children, the presence or absence of HLA-B-27 cannot be relied upon to confirm or exclude the diagnosis of JIA. This is an indicator of risk factor rather than a diagnostic test. HLA-B-27 also has a strong association with ankylosing spondylitis (AS), which is notable considering that ERA is thought to be the pediatric counterpart of adult AS. In our study, HLA-B27 was 79% in ERA, 7.69% in polyarticular, 3.57% in sJIA and no in

oligoarticular. ANAs are most frequently found in 65%-85% of children with oligoarthritis.[40] In this study, ANA was positive 37.5% in oligoarticular JIA.

NSAIDs (e.g., naproxen, indomethacin) were used as the most commonly prescribed drugs as first line agent in this study patients. Corticosteroids were used to sJIA patients, polyarticular and extended oligoarticular subtypes who showed less satisfactory or no response to NSAIDs in period of 4-6weeks' time. Methotrexate (MTX) was the preferred agent used mostly in polyarticular subtype and in few case of oligoarticular extended and systemic JIA subtypes. Combination therapy of two or more drugs such as NSAID with steroid, NSAID with MTX and NSAIDs and steroids and MTX was required in selected cases of sJIA, polyarticular QRA positive and extended oligoarticular subtypes. In our study, clinical remission was seen in 40.54% of our MTX-treated patients. Remission was observed with MTX in 31.5% poly JIA and 43.75% sJIA. Among 8 oligo JIA patients, 5 patients successfully became clinical remission with NSAID and oral opr intraarticular steroid, 2 with MTX and 1 patient persist active state even combination with NSAID, steroid and MTX. Sulfasolazine was used mostly in patients with QRA positive as an adjunctive therapy with NSAIDs and MTX. Sulfasolazine was given to ERA patient, 20 (67%) patients became clinical remission. The frequency of recurrence or active state of ERA was high 10(33%) especially central axial joints. We did not observe any major side effects that would require discontinuation of the medicines. Most patients experienced mild to moderate gastrointestinal discomfort with nausea and vomiting mainly with MTX and sulfasolazine. These symptoms were successfully managed with gastro-protective agents in the form of antacids and proton pump inhibitors. Folic acid supplements were used in all patients requiring MTX. Introduction of biologic agents in the management of JIA (e.g., Tocilizamb especially for sJIA and Eternacept for central axial arthritis of ERA) opens a new era in the prognosis and long-term outcome of the disease and the better future prospects.[41-43]

The frequency of relapses after remitting or active arthritis recurrence in JIA is quite high. In our study, the relapse rate was 53.4%. The most frequent relapse was seen in 76% of polyarticular followed by 70% in sJIA, 33.3% in ERA and 12.5% in oligoarticular subtype. In other study, relapse rate in JIA patient was 40.4%. 87.5% in sJIA, 37.5% in polyarticular and 18.2% in oligoarticular subtype.[37] Few patients who had active disease after getting DMARD for 2 years, aggressive management with biologic therapy was given. Three patient in sJIA, after combination therapy with Naproxen, MTX and steroids had flare-then they were treated with biologic agent Tocilizumab and get clinical remission.

Conclusion

The clinical and biochemical profile of Juvenile Idiopathic Arthritis (JIA) cases differ from each other mainly in terms of subtypes of the disease. Use of NSAID and steroids in the early period or addition of MTX was an effective treatment. Treatment with biologic agents in some of our patients who had flare after combination therapy with NSAID, steroids and MTX for 2 years got the clinical remission.

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