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ASSOCIATION OF C-REACTIVE PROTEINS AND ERYTHROCYTE SEDIMENTATION RATE WITH DISEASE ONSET AMONG PATIENTS WITH JUVENILE RHEUMATOID ARTHRITIS

Dr Syeda Malalay[1], Dr Umm E Kalsoom[2] , Dr Madiha Nawaz[3] , Dr Parsa Ali[4]

[1, 2] Pediatric Resident, Lady Reading Hospital, Peshawar., [3,4] Gomal Medical College, Dera Ismail Khan.

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Abstract:

Aim: *To determine the relationship between serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and active disease in patients with juvenile rheumatoid arthritis (JRA).*

Methods: *This is a cross-sectional analytical study conducted over a year from October 2020 to October 2021 at Lady Reading Hospital, Peshawar Rheumatology and Pediatrics Unit. All MJA patients who met the criteria of the American College of Rheumatology (ACR) were enrolled in the study. The ACR 20 recovery criteria were used to define disease forgiveness, and those meeting the ACR 20 recovery criteria were included in the remission group. Laboratory tests such as PCR and ESR were done. Statistical analysis was performed using SAS software (version 10.3).*

Results: *90 patients were enrolled in the study, 28 (31.2%) in the remission group and 62 (68.88%) in the active disease group. There were 61.11% (n = 55) of women, and the ratio of men to women was 3: 4. The mean age of the subjects was 10.12 ± 3.39 years (4-17 years). Age distribution at reporting by different subgroups, 13 patients (14.44%) 1-5 years old, 31 patients (34.44%) 5-10 years old, 40 patients 10-15 years old (44.44 %), and 6 patients (6.66) were over 15 years of age. The mean disease duration was 2.40 + 2.11 years (range = 0.3 to 7 years). The onset of the disease in 21 patients (23.33%) was after one year (22.9%), in 48 patients (53.33%) between years and 5 years from the onset of the disease, in 21 patients (23.33%) five years. The most common type of arthritis was polyarthritis in 43 patients (47.77%), followed by polyarthritis in 31 patients (34.44%), and systemic onset in 12 patients (13.33%). The mean ESR was 41.03 + 27.80 mm / h 1 (range = 07-128 mm / h 1) and the mean CRP was 16.1 + 13.80 mg / L (range = 6-47 mg / L). ESR was> 30 mm / 1 hour. in 50 (55.55%) of 90 patients, while 43 (86%) of these 50 patients were in the active disease group. Similarly positive CRP was detected in 58 (64.44%) patients, of which 52 (89.7%) belonged to the group with active disease. Compared to the remission and active disease groups, 33 of the patients with active disease were female. In the active disease group, the mean age was 11.01 + 3.30 years, and the duration of the disease in patients started after one year. Polyarthritis was detected in 26/62 (41.9%) of patients from the active group of the disease.*

Conclusions: *High CRP and ESR parameters are good in predicting active disease in JRA patients.*

Key words: *C-reactive protein, juvenile rheumatoid arthritis, JRA and erythrocyte activity.*

Corresponding author:

Dr Syeda Malalay

Pediatric Resident, Lady Reading Hospital, Peshawar

Smalalay55@gmail.com

QR code

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INTRODUCTION:

Juvenile rheumatoid arthritis (JRA) is a chronic inflammatory disease with varying frequencies of racial and ethnic subtypes [1-2]. The incidence of JRA in the 15-year-old white population is 13.9 / 100,000. Although some patients may experience mild remission, JRA is a possible cause of disability, discomfort and long-term disability [3]. Recent advances in treatment seem promising and early treatment, coupled with timely rehabilitation, can optimize outcomes. Therefore, identifying patients with JRA at high risk of developing adverse events helps in selecting patients for aggressive early treatment. Many advertisers score, but only a few identify themselves as first-time advertisers [4]. JRA laboratory studies can be used to provide evidence of inflammation, monitor treatment toxicity, and better understand disease pathogenesis [5]. Useful laboratory tests for JRAs include blood count (CBC), rheumatoid factor (RF), and inflammatory markers such as red blood cell sedimentation rate (ESR) and C-reactive protein (CRP). Westergren's ESR is the rate at which red blood cells decline over a period of 1 hour [5]. This is a useful but surprising measure of active disease both at the beginning and during the follow-up of a child with arthritis. Acute phase proteins (APP) are proteins that increase plasma levels during acute phase reactions such as trauma, infection, cancer, overexertion, and rheumatic diseases [6]. The application includes certain protein supplements, CRP and fibrinogen to help protect and maintain osteosis. C-reactive protein is an acute-phase protein found in the blood, and its levels increase with any inflammation in the body. During the acute phase of the response, CRP levels increase significantly and peak at 2 and 48 hours after acute trauma. As the acute phase response decreases, CRP decreases with a relatively short half-life of 18 hours [7-8]. CRP is a more sensitive and accurate reflection of the acute phase response than ESR. During the first 24 hours of the acute phase, ESR may be normal, but as CRP levels rise before treatment, CRP tends to return to normal rather than ESR [9]. The present study was conducted to determine the relationship between C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) and active disease in patients with juvenile rheumatoid arthritis.

METHODS:

It is a cross-sectional analytical study conducted for a year from October 2020 to October 2021 at Lady Reading Hospital, Peshawar Rheumatology and Pediatrics Unit. Official approval was obtained from the local ethics committee and informed consent from all patients were taken. All male and female patients who met the American College of Rheumatology (ACR) JRA criteria were enrolled in the study. ACR criteria include: one or more arthritis symptoms under 16 years of age, disease duration of at least 6 weeks, type of disease as defined in the first 6 months: Polyarthritis: When 5 or more joints are inflamed ii. Polyarthritis: less than 5 swollen joints, iii. Systemic onset: characteristic of febrile arthritis) Except for other forms of juvenile arthritis. Data collected at the first visit to the clinic included demographics, time of onset, and type of arthritis in a pre-designed format. ACR 20 treatment criteria were used to define disease remission. The ACR 20 improvement criteria showed a 20% improvement in the number of swollen joints, and 28 or more joints were assessed in the painful joint. In addition, 3 out of 5 measures improved by 20%: patient pain assessment, patient overall assessment, GP assessment, patient self-assessment of disability, and acute phase reagent (CRP or ESR). A horizontal visual analog scale (typically 10 cm) representing the patient's current pain status and the physician's and patient's overall assessment. Patients who met the ACR20 improvement criteria were in the remission group and the rest of the patients had active disease. Laboratory parameters such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were required. A quantitative agglutination method (Human Tex CRP, Wiesbaden, Germany) was used to analyze serum CRP concentrations and Westergren ESR for ESR levels. Samples were considered "positive" if CRP was present at a concentration of 6 mg / L or higher. The increase in KSS in the first hour was over 30 mm. The analysis of the statistical data was performed using the statistical analysis system (SAS) version 10.3. The mean, standard deviation, and range were determined for all quantitative variables. Baseline rates and percentages, age and sex distribution, and disease duration were used to identify and identify active disease groups and types of arthritis. Binary logistic regression was used to determine the age and time of onset as well as the active disease group and the relationship between ESR and CRP. A p value <0.05 was considered statistically significant.

RESULTS:

The study included 90 patients, 28 (31.2%) in the remission group and 62 (68.88%) in the active disease group. There were 61.11% (n = 55) of women, and the ratio of men to women was 3: 4. The mean age of the subjects was 10.12 ± 3.39 years (4-17 years). Age distribution at reporting by different subgroups, 13 patients (14.44%) 1-5 years old, 31 patients (34.44%) 5-10 years old, 40 patients 10-15 years old (44.44 %), and 6 patients (6.66) were over

15 years of age. The mean disease duration was 2.40 + 2.11 years (range = 0.3 to 7 years).

Distribution of Patients given in Table-I

Males	35(38.9%)
Females	55 61.11%
Total	90(100%)
Active disease patients' group	62(68.88%)
remission group	28 (31.2%)
Mean age	10.12 ± 3.39 years (4–17 years)
Age group	
1-5 years	13 (14.44%)
5-10 years	31 (34.44%)
10-15 years	40 (44.44%)
over 15 years	6 (6.66%)
Mean duration of the disease	2.40 + 2.11 years (range= 0.3–7 years).`
Type of arthritis	
polyarthritis	43 (47.77%)
oligo-arthritis	31 (34.44%)
systemic onset	12 (13.33%)

The onset of the disease in 21 patients (23.33%) was one year (22.9%) after it starts, in 48 patients (53.33%) between years and 5 years from the onset of the disease, in 21 patients (23.33%) five years . The most common type of arthritis was polyarthritis in 43 patients (47.77%), followed by polyarthritis in 31 patients (34.44%), and systemic onset in 12 patients (13.33%). The mean ESR was 41.03 + 27.80 mm / h 1 (range = 07-128 mm / h 1) and the mean CRP was 16.1 + 13.80 mg / L (range = 6-47 mg / L). ESR was> 30 mm / 1 hour. in 50 (55.55%) of 90 patients, while 43 (86%) of these 50 patients were in the active disease group. Similarly positive CRP was detected in 58 (64.44%) patients, of which 52 (89.7%) belonged to the group with active disease. Compared to the remission and active disease groups, 33 of the patients with active disease were female. In the active disease group, the mean age was 11.01 + 3.30 years, and the duration of the disease in patients started after one year. Polyarthritis was detected in 26/62 (41.9%) of patients from the active group of the disease.

ACR 20 Improvement Criteria in Active Disease Group and Remission Group shown in Table-II

ACR20 Improvement Criteria	**Active Disease Group n=62 (Percentage)**	**Remission Group n=28) (Percentage)**	**Total n=90 (Percentage)**
Swollen joint count		17 (67.7)	59 (65.5)
0-4 joints	42 (67.7)		
4-8 joints	12 (19.3)	8 (28.6)	20 (22.2)
>8 joints	08 (12.9)	3 (10.7)	11 (12.2)
Tender joint count		20 (71.4)	52 (57.8)
0-4 joints	32(51.6)		
4-8 joints	16 (25.8)	4 (14.3)	20 (22.2)
>8 joints	14 (22.5)	4 (14.3)	18 (20)

Pain visual analogue scale		25 (89.3)	55 (61.1)
Mild pain (0-3)	30 (48.4)		
Moderate pain (4-6)	24 (38.7)	1 (3.6)	25(28.9)
Severe pain (> 6)	09 (14.5)	1 (3.6)	10 (10.0)
Physician's global assessment		23 (82.1)	31 (34.4)
Mild	08 (12.9)		
Moderate	17 (27.4)	02 (7.1)	19 (21.1)
Severe	37 (59.7)	03 (10.8)	40 (44.4)
Patient's global assessment		26 (92.8)	34 (37.8)
Mild	08 (12.9)		
Moderate	31 (50.0)	00 (0)	31 (34.4)
Severe	23 (37.1)	1(3.6)	24 (26.7)
***ESR > 30mm in 1st hour**	43 (86)	06 (21.4)	49 (54.4)
****CRP > 06 mg/l**	52 (89.7)	05 (17.9)	57 (63.3)

The comparison of the two groups (Table 2) showed an improvement in all segments of the remission group compared to the group with active disease according to the ACR 20 criteria. Binary logistic regression was used to determine their relationship with the active disease group CRP and ESR. The regression model also initially considered remission, early age, and other quantitative parameters that affect disease duration. Duration of disease at presentation ($p = 0.042$), higher ESR ($p = 0.0022$), and positive CRP ($p = 0.0013$) were associated with active disease on presentation. In this study, the age of presentation was not related to the active disease group (Table 3).

Relation of Active disease with various parameters in Juvenile Rheumatoid Arthritis patients shown in Table-III

Variable	df	Estimated value	t-value	p-value
Age at presentation	1	-0.00249	-0.18	0.85
Duration of disease at presentation	1	-0.04461	-2.1	0.042
*ESR	1	-0.00512	-3.12	0.0022
**CRP	1	-0.01078	-3.29	0.0013

DISCUSSION:

Juvenile rheumatoid arthritis (JRA) is the utmost communal rheumatic disease in children. It has been disputed in the last decade that JRA is a disease that usually resolves in childhood [10]. Remission usually occurs within the first five years after onset and is less common in patients with systemic symptoms and polyarticular JRA [11]. Therefore, JRA is a disease that usually develops into adulthood [12]. Compared to the previous decades, functional outcomes have improved, but the estimated rate of arthroplasty is still very high. This study found that the age and gender of the women of late admission were dominant. This is in line with another study by Lahore. The age of old age was also evident in the presentations in India. This may be due to the ethnic and geographic similarity of both populations or to the biological characteristics of the disease in this

subcontinent. The gender predominance of women in the JRA has been described in Western literature and has been reported in many studies in Sri Lanka and Bangladesh. It is well known that female gender is associated with active disease. In this cross-sectional study, 68.8% of patients had active disease [12]. Boucher et al. More than 80% of patients had active disease in adulthood. Research in India showed similar results. The most common type of JRA in this study was polyarticular JRA. Multiple studies in Lahore, Sri Lanka and India have produced similar results. This is different from the West, where polyarthritis and systemic disease are more common than polyarthritis. Moreover, while all studies in Pakistan, India and Sri Lanka are hospitalized, comparisons are difficult as studies in Western countries are population studies18. When comparing the different subtypes of the active disease group and the remission group, it was found that only one disease type was not negative in our study. This is because different variables influence different types of outcomes, such as gender, duration of the underlying disease, and seropositivity [13-14]. This is in line with another work by Oen et al. The different subtypes have been replaced by different variants. Guillaume et al. reported that the arthritis group was in remission more often than the other types. Similarly, Aggarwal et al. Found that 45% of patients in the non-linear group and 20% of patients in the polyarticular group were in remission. All subtypes could be due to the fact that most of the population suffered from late-stage disease in our study [15-16]. This is consistent with research in India that long disease duration is associated with persistent active disease. Zak et al. Disease duration was also found to be the strongest predictor of adverse disease outcomes at baseline [17]. Two known acute phase reagents, CRP and ESR, are used clinically in the follow-up of JRA patients. In this study and in parallel with other studies, these parameters increased in patients with active disease and were found to be normal in patients in remission. Al-Matar et al. They concluded that the highest ESR in the first six months in the group with polyarthritis is one of the risk factors in patients without linear JRA [16-17]. Flato et al. High CSR values had little or no effect on the prognosis on admission. They also showed that increasing the duration of ESR in the first six months is a risk factor for poor performance. Several studies have shown that ESR may be a better parameter than CRP levels, but a high baseline CRP level may strongly predict failure of initial remission therapy. Zak et al. The diagnosis showed a marked increase in CRP in people with active disease. In another study, increased markers of inflammation, including ESR and CRP, along with other factors such as female gender, polyarthritis, and seropositivity, were consistent predictors of poor prognosis.

CONCLUSION:

Juvenile rheumatoid arthritis is a chronic disease that causes long-term disability. Positive CRP and increased ESR are strongly associated with active disease in JRA patients. Late referrals to a pediatric rheumatologist have a poor prognosis for disease remission. Early recommendations and strict disease control help to alter the course of the disease in line with clinical and laboratory parameters.

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