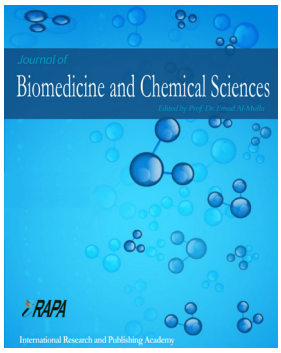
BIOMEDICINE AND CHEMICAL SCIENCES
Vol. 2 No. 4 | October, 2023 | 01-11
ISSN(e): 2790-296X | ISSN(p): 2957-5826
DOI: https://doi.org/10.5281/zenodo.15282922

01-BCS-2769-565



Juvenile Idiopathic Arthritis (JIA): Clinical Characteristics, Drugs, Assessment, and Disease Subtypes

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ARTICLE INFO

Article history:

Received on: August 19, 2023
Revised on: September 22, 2023
Accepted on: September 23, 2023
Published on: October 01, 2023

Keywords:

ANA
DMARDS
Juvenile idiopathic arthritis
Oligoarticular

ABSTRACT

Juvenile idiopathic arthritis (JIA) is a common type of arthritis in children and adolescents. This observational study was conducted in Baghdad (2019–2021). Records of JIA patients (n = 66) were documented from the teaching hospital in Al-Rusafa and Kadhimiya teaching hospital in Al-Karkh. JIA was categorised into 5 groups: Oligo JIA-Extended (OJIA-E) (n=16), OJIA-Persistence (OJIA-P) (n=15), Poly JIA (PJIA) (n=29), Systemic JIA (SJIA) (n=3), and Enthesitis-related Arthritis (ERA) (n=4). The Juvenile Arthritis Disease Activity Score-27 (JADAS 27) was used to measure disease activity for several months. JIA distribution in males and females (45.5% and 54.5%), respectively. The highest frequency of JIA type was observed in the age group 1-4 years with Oligo P (75%). Positive ANA test cases were found in 4 cases only. Four types of drugs and three types of biological drugs were found to be used to treat JIA. JADAS ranged from (8.1±5.7) to (19.4±8.6) with significant differences ($p<0.05$). Significant differences were noticed among the types of JIA in some blood tests and liver enzymes. The incidence of JIA decreased from 0.10/ 100000 to 0.005/ 100000. JIA with MTX, DMARDS duration, Steroid dosage, and JADAS all showed significant differences. There were no discernible differences in JIA with age, gender, disease duration, quantity of DMARDS, and blood tests.

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INTRODUCTION

The most typical type of arthritis in children and adolescents is juvenile idiopathic arthritis (JIA). All joint disorders that affect children and teenagers, including JIA, are collectively referred to as "juvenile arthritis" [1]. A child's type of arthritis may cause symptoms. Usually, it affects the hands, knees, ankles, elbows, and wrists, causing joint pain and inflammation. It can also infect other body parts. JIA can leave young people in excruciating pain and permanently disabled. According to Tupper (2012), pain has a detrimental effect on quality of life, participation in social activities, academic performance, and child development [2]. The biological, psychological, social, and environmental factors that affect JIA pain intensity may change throughout the day [3]. JIA pain intensity variability in children has not been well studied for potential contributing factors. Rheumatoid arthritis (RA) is characterized by morning pain, which can be distinguished from osteoarthritis (OA) pain, which

How to Cite:

Al-Obaidi, M. J., Samer, F. O., Mohammed, S. W., & Al-Malkey, M. K. (2023). Juvenile Idiopathic Arthritis (JIA): Clinical Characteristics, Drugs, Assessment, and Disease Subtypes. *Biomedicine and Chemical Sciences, 2*(4), 01–11.
https://doi.org/10.5281/zenodo.15282922

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peaked in the evening [4].

JIA is characterized as idiopathic (of unknown cause) arthritis that begins before the age of 16 and lasts for more than six weeks. The International League of Associations for Rheumatology (ILAR) distinguished six subgroups: psoriatic arthritis, systemic arthritis, oligoarticular arthritis, enthesitis-related arthritis (ERA), and polyarthritis with and without rheumatoid factor. Four or fewer joints, usually the larger ones (knees, ankles, and elbows), are affected by oligoarthritic. JIA's most prevalent subtype. Five or more joints are affected by polyarthritis, which frequently affects both sides of the body (both knees, both wrists, etc.). May impact both big and little joints. approximately 25% of kids with JIA are affected [5].

Affects all body parts, including the joints, skin, and internal organs. A rash and a high-spiking fever (103°F or higher) lasting at least two weeks are possible symptoms. 10% of children with JIA are affected. Joint symptoms and a scaly rash on the scalp, eyelids, elbows, knees, belly button, and/or behind the ears are signs of psoriatic arthritis (PsA). Skin symptoms can appear either prior to or following joint symptoms. may impact one or more joints, frequently the fingers, toes, ankles, wrists, and knees. Enthesitis-related: called spondylarthritis as well. affects the entheses, or points on the bone where the muscles, ligaments, or tendons attach. commonly impacts the knees, hips, and feet, but it can also impact the lower back, digestive tract, fingers, elbows, pelvis, chest, and digestive system (Crohn's disease or ulcerative colitis) [6].

The condition is more prevalent in boys and typically affects kids between the ages of 8 and 15. Undifferentiated: Inflammation is present in one or more joints but symptoms do not precisely match any of the subtypes. It is necessary to have knowledge of the epidemiology of JIA. Logic studies on the frequency of JIA have been carried out in Europe. the primary causes of variations in prevalence in the paediatric population [7]. A contemporary tool for measuring disease activity in children with juvenile idiopathic arthritis (JIA) is the Juvenile Arthritis Disease Activity Score (JADAS). The markers included in JADAS are joint count, doctor and patient's parent assessment, and erythrocyte sedimentation rate (ESR). It is advised to include a new marker, C-reactive protein (CRP), in JADAS [8].

JADAS10, JADAS27, and JADAS71 are the three versions of the JADAS that were created, each with a different active joint count included. The JADAS10 is based on the number of affected joints, regardless of their type, up to a maximum of ten joints; any number of joints above ten results in a score of 10. The cervical spine, elbows, wrists, first through third metacarpophalangeal joints, proximal interphalangeal joints, hips, knees, and ankles are among the joints that make up the JADAS27. This is based on prior research that revealed the 27-joint reduced count to be a reliable proxy for the total joint count in JIA [9]. Adding the scores in a final score that can range from 0 to 40 for the JADAS10, 0 to 57 for the JADAS27, and 0 to 101 for the JADAS71. Idiopathic arthritis in children (JIA) is one of the most common chronic, disabling diseases [10].

Situational and behavioral influences may lead to non-repeating changes in pain that last only one day. For people with arthritis and other inflammatory musculoskeletal pain issues, physical activity causes discomfort [2]. The aim of current work is to observe the clinical characteristics, drugs, assessment, and disease subtypes of JIA.

MATERIALS & METHODS

Studied Population

Baghdad is a capital of the Iraq with population of 7 134 697 inhabitants. It comprises two sides Al-Kark and Al-Rusafa have widely differing population densities, ranging from 55.5/km2 and 1473.3/km2. The population at risk may be 2 million children under the age of 20 years. The study was conducted through the period (2019-2021), the patients were recruited from Teaching Hospital in Al-Rusafa and Kadhimiya Teaching Hospital in Al-Kark data set were evaluated. The ethical approval was taken from College of Science, University of Baghdad.

Inclusion and Exclusion Criteria

Only JIA patients were included. A patient had to exhibit one or more joints that were swollen, or have a restricted range of motion with pain or tenderness, according to the current definition of arthritis in children. The symptoms needed to be present for at least 6 weeks in order to be diagnosed with JIA, and mechanical disorders or other clearly recognizable causes needed to be eliminated. Additionally, a paediatric rheumatologist had to confirm the JIA diagnosis for the study's purposes.

Classification Criteria

In this study, the Edmonton revision of the 2001 ILAR classification criteria for JIA was applied. Systemic arthritis, oligoarthritic (persistent or

extended), polyarthritis (RF-negative), polyarthritis (RF-positive), psoriatic arthritis, enteritis-related arthritis, and undifferentiated arthritis are the seven categories into which JIA patients can be divided based on the strict definition and exclusion of these criteria. The JIA categories are all exclusive of one another. Laboratory data are only used as "descriptors," with clinical features serving as the primary basis for classification by standardization of uveitis [11].

Laboratory Investigations

Semi-quantitative latex testing was used to assess RF; titres greater than 30 IU/mL were regarded as positive. On Hep-2 cells, antinuclear antibodies (ANA) were found using indirect immunofluorescence, with positive titres starting at 1/40. According to the ILAR criteria, at least two RF and ANA determinations that were made during the first six months of the disease had to be positive and be spaced out by three months.

Statistical Analysis

The mean, range, and standard deviation (SD) are used to express the results for the continuous variables. Case and percentage counts are used to report categorical variables. Using of Fisher's exact test among categorical variables were investigated. A p-value of 0.05 or lower was regarded as significant. SPSS Inc., Chicago, IL, USA, released SPSS for Windows version 25 for the analyses.

RESULTS

Gender of JIA Patients

JIA distribution in both male and female in nearest ratios (30 males and 36 females) (45.5% and 54.5%) (Figure 1) (Table 1).

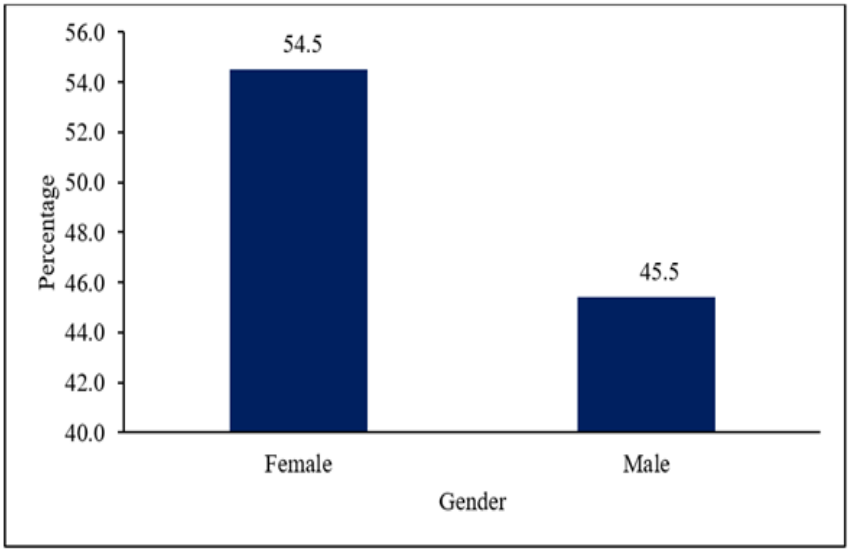

Fig. 1. Percentages of male and female infected with JIA disease.

Table1
Baseline clinical and inflammatory parameters in different groups of JIA

Variables	JIA subtypes (n=66)							
	Oligo-E (n=16)	Oligo-P (n=15)	Poly (n=29)			SJIA (n=3)	ERA (n=4)	Total (n=66)
			(RF-) (n=13)	(RF+) (n=6)	Un-differentiated (n=9)			
Gender n (%)								
Male	4 (13.3)	9 (30)	8 (26.7)	2 (6.7)	4 (13.3)	1 (3.3)	2 (6.7)	30 (100)
Female	12 (33.3)	6 (16.7)	5 (13.9)	4 (11.1)	5 (13.9)	2 (5.6)	2 (5.6)	36 (100)
Age (year) n (%)								
1-4 Y	0 (0.0)	3 (75)	1 (25)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100)
5-10 Y	9 (36)	5 (20)	5 (20)	1 (4)	3 (12)	2(8)	0 (0.0)	25 (100)
>10 Y	7 (18.9)	7 (18.9)	7 (18.9)	5 (13.5)	6 (16.2)	1(2.7)	4 (10.9)	37 (100)
ANA test								
Positive (n=4)	3 (75)	0 (0.0)	1(25)	0 (0.0)	No record	0 (0.0)	0 (0.0)	4 (100)
Negative (n=53)	13 (24.5)	15 (28.3)	12 (22.6)	6 (11.3)	No record	3 (5.7)	4 (7.5)	53 (100)

Disease duration							
	6.8 ± 3.6	5.9 ± 5.9	7.5 ± 6.7	10.4 ± 4.8	8.2 ± 6.5	9 ± 4	7.5 ± 7.2
MTX treatment							
Amount (mg)	11.25 ± 3.5	7.38 ± 2.4	10.96 ±3.8	12 ±1.8	11 ±2.9	10 ± 4	14.1±1.2
Duration (year)	2.7 ± 2.2	1.7 ± 1.6	1.06 ±1	2.52 ± 2.2	3.7 ± 4.9	3.17 ± 0.8	2.25±1.25
DMARDS treatment							
Type	SSZ IMMURAN	SSZ IMMURAN CQ	SSZ LEFLUNOMIDE	SSZ IMMURAN CQ	SSZ IMMURAN CQ	SSZ	SSZ IMMURAN
Amount (mg)	210 ±156	61.3± 133	532±317	369±294	343±346	300±200	87.5±12.5
Duration (month)	1.2±1.06	0.2±0.5	0.41±1.5	0.5±1.07	1.4±1.1	No record	1±1
Steroid treatment							
Type	PND MG	PND	PND MG	PND	PND MG	PND MG	MG
Amount (mg)	7.9±4.6	5±4.1	4.8±11.3	10.7±3.7	12±9.2	9.1±1.1	5±0.0
Duration (year)	4.6±2.7	4.8±3.5	1±0.7	0.7±0.3	1.7±2.2	3.4±3.9	0.6±0.3
Biological treatment							
Type	INF ENBREL	ENBREL	ENBREL	ENBREL	ENBREL PND	ENBREL	No record
Amount (mg)	25±0.0	25±0.0	37.5±12.5	25±0.0	25±0.0	25±0.0	No record
Duration (month)	2.1±1.5	7.1±8.3	No record	No record	No record	0.7±0.5	No record
Hands X-Ray Monitoring							
Baseline	1.wrists erosions 2.Crowdness of carpus	Crowdness of carpus	1.Avascular Necrosis of Carpal bones 2.StageIII	1.No erosions, stage I 2. stage III	At beginning 5 joints	1.Wrists and carpus erosions 2. Rt. Wrist stage 4, 3. Lt. wrist stage 3	

ERA=Enthesitis-related arthritis, PJIA= polyarticular JIA, SoJIA =Systemic-onset juvenile idiopathic, arthritis. disease modifying antirheumatic drugs (DMARDs), Demographic and clinic data for all patients requiring treatment with intraarticular steroids (INF) or systemic treatment.

Age of JIA patients

JIA was recorded in maximum age at >10 years group (56.1%) and in minimum age at 1-4 years group (6.1%). Highest frequency of JIA type was observed in age group 1-4 years with Oligo P (75%). Highest frequency of JIA type was observed in age group 5-10 years with Oligo E (36%). Highest frequency of JIA type was observed in age group >10 years with Oligo E, Oligo P, and Poly (RF negative) (18.9%) (Figure 2) (Table 1).

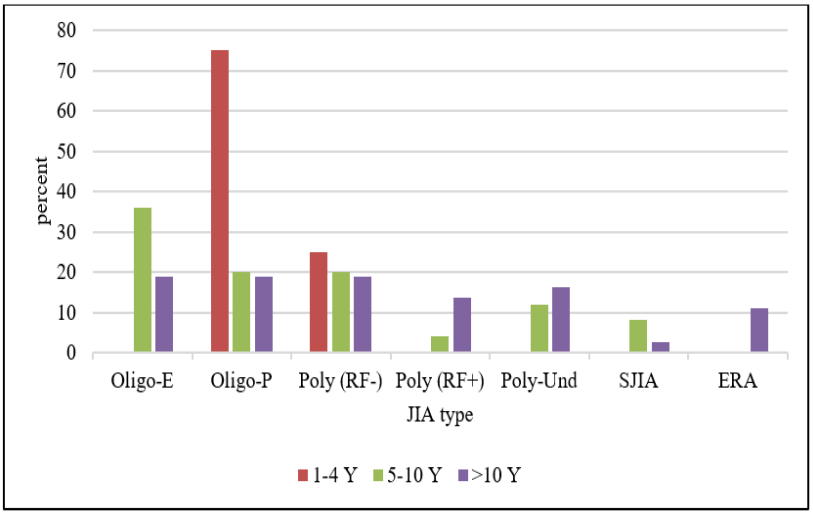

Fig. 2. Distribution of JIA types in age groups.

Antinuclear Antibody (ANA) test

Positive ANA test cases were found in 4 cases only while the negative results of the test were found in 53 cases, residual cases were not recorded. Highest frequency of positive test was observed in Oligo-E (75%) (Table 1).

Disease Duration

JIA duration was ranged from 5.9 years to 10 years. Highest duration of disease was observed in Poly (RF+) type (10.4 ± 4.8) years (Table 1).

Methotrexate Drug (MTX),Amount and Duration

Amount of MTX drug that used to treat JIA was ranged from 7.38 mg to 14.1 mg for period ranged from 1.06 year to 3.7 years. Highest dose of MTX was found to be gives to the patients with Poly (RF+) type (12 ± 1.8 mg). Highest duration of treatment was observed in patients with Poly undifferentiated type of JIA (Table 1).

Disease-modifying Antirheumatic Drugs (DMARDS) Types, Amounts,and Duration

Four types of drugs found to be used to treat JIA including Sulfasalazine (SSZ), chloroquine (CQ), Azathioprine (IMMURAN), and Leflunomide. Amount of DMARDS drug that used to treat JIA was ranged as (61.3± 133)/ mg to (532±317)/ mg. Period of using DMARDS drugs to treat JIA was ranged as (0.2±0.5)/ months to (1.4±1.1)/ months. Three types of DMARDS treatment were found to be used for Oligo and Poly (RF+) JIA types, while the other types of JIA used ether one or two DMARDS drugs. Highest dose of DMARDS drug was found to be used in patients with Poly (RF-) as 532±317. Longest period of treat with DMARDS was found in patients with Poly undifferentiated RF as 1.4±1.1 month (Table 1).

Steroid Treatment, Type, Amount, and Duration

Corticosteroid's type was used to treat JIA as PND and MG. Amount of corticosteroid drug that used to treat JIA was ranged as 4.8 mg to 12 mg. Period of using corticosteroids drug to treat JIA was ranged as 0.6 months to 4.8 months (Table 1).

Biological Treatment

Three types of biological drugs were used to treat JIA including Infliximab (INF), Etanercept (ENBREL), and PND (Table 1).

Hands X-Ray Monitoring

Monitoring of JIA by hands x-ray was included wrists erosions and overcrowding of carpus in oligo-E type, crowdness of carpus in oligo- P type, Avascular Necrosis of Carpal bones and Stage III in poly (RF-), No erosions, stage I, stage III in poly (RF+), and Wrists and carpus erosions, Rt.Wrist stage 4, Lt. wrist stage 3 in SJIA (Table 1).

Juvenile Arthritis Disease Activity Score27 (JADAS27) assessment

The score of JADAS27 was calculated at baseline, after one month, after three months, after 6 months, and after 9 months for all types of JIA (OJIA-E, OJIA-P, PJIA/RF+, PJIA/RF-, PJIA/RF undifferentiated, SJIA, and ERA). Baseline assessment profile showed that the score was ranged from 12.2 ± 6.3 in OJIA-P subtype to 31.5 ± 1.6 in SJIA subtype. High significant differences among the types of JIA in this stage of assessment ($p<0.05$). One month assessment profile showed that the score was ranged from 5.3 ± 2.2 in ERA subtype to 19.3 ± 5.5 in SJIA subtype. High significant differences among the types of JIA in this stage of assessment ($p<0.05$).

Three months assessment profile showed that the score was ranged from 6.2 ± 2.2 in ERA subtype to 28.1 ±20 in SJIA subtype. High significant differences among the types of PJIA/RF+ in this stage of assessment ($p<0.05$). Six months assessment profile showed that the score was ranged from 4.6 ± 4.1 in OJIA-P subtype to 11.5 ± 0.9 in SJIA subtype. No significant differences among the types of PJIA/RF+ in this stage of assessment ($p<0.05$). Nine months assessment profile showed that the score was ranged from 0.0 in PJIA/RF undifferentiated subtype to 16 ±2.4 in SJIA subtype. No significant differences among the types of PJIA/RF+ in this stage of assessment ($p<0.05$) (Table 2).

Table 2

Changes in disease activity over time in different subsets of JIA with intra-group comparison

JADAS27	OJIA-E (n=16)	OJIA-P (n=15)	PJIA			SJIA (n=3)	ERA (n=4)	p-value
			(RF-) (n=13)	(RF+) (n=6)	Un-differentiated (n=9)			
Baseline assessment								
Sw Jt.	10.3±10.2	2.06±1.3	11.1±6.34	5.3±3.14	13.1±10.4	10.3±1.4	3.2±1.2	0.0001*
Pt. VAS	6.3±2.05	4.1±2.03	6±1.79	5±2.23	6±1.69	8±1.2	5.7±2.2	0.054*
Phy. VAS	5.9±1.7	3.9±2.01	5.9±1.81	4.8±1.77	5.5±2.11	8.3±0.8	4±1.5	0.010*
ESR	57.3±34.5	43.9±32.7	73.5±45.7	55.8±22.5	62±29.2	69±36.1	30.7±30.7	0.399
Score	26.3±13.9	12.2±6.3	27.3±12.02	17.8±6.08	28.2±11.5	31.5±1.6	14±5.5	0.001*
One month assessment								

JADAS								
Sw Jt.	4.8±4.8	1.6±1.6	7.7±4.2	4.5±1.7	8.5±10.5	9.5±1.5	0.0	0.001*
Pt. VAS	4.5±2.3	3.3±3.2	4.6±1.7	4.6±2.2	5.3±1.7	5.6±2.4	3.3±1.8	0.396
Phy. VAS	4.1±1.9	3.2±2.1	3.9±1.6	4.1±1.7	4.5±2.1	4.6±1.6	2.3±1.2	0.565
ESR	42.9±35.3	29.3±25.4	60.6±36.1	44.1±26.1	57.5±33	46.3±23.9	16.3±8.9	0.184
Score	15.4±10.4	8.3±7.4	19.06±9.7	15.7±4.7	17.5±12.5	19.3±5.5	5.3±2.2	0.024*
Three-month assessment								
JADAS								
Sw Jt.	3.7±5.2	1.09±1.5	6±5.5	11.5±11	9.5±9.7	5.5±1.5	0.0	0.020*
Pt. VAS	3.9±2.1	2.8±2.3	4.3±2.05	5.25±2.4	4.3±1.7	4.6±2.8	3±0.8	0.495
Phy. VAS	3.3±1.9	2.1±1.7	4.1±1.7	4.7±2.1	4.1±2.2	4.6±2.8	2.3±1.2	0.173
ESR	30.9±27.3	36.9±38	61.9±29.7	50±26.6	56.8±35.8	38.3±6.2	29.3±35.8	0.180
Score	9.2±8.3	7.7±8.2	18.1±10.5	28.1±20	19.3±11.4	14.8±8.3	6.2±2.2	0.021*
Six-month assessment								
JADAS								
Sw Jt.	2.5±2.7	0.25±0.7	3.5±3.8	2±2	0.0	3±1	2 ±1	0.137
Pt. VAS	3.6±2.1	1.6±1.3	3.6±2.1	3±1	2±0.8	5±1	3.5±1.5	0.179
Phy. VAS	3.2±1.8	1.5±1.06	3±2	2±1	2±0.8	3.5±0.5	3.5±1.5	0.292
ESR	35.7±29.9	36.6±30.7	46.6±34.9	42.5±27.5	55±21.6	20.5±4.5	23.5±16.52	0.930
Score	10.8±8.9	4.6±4.1	11.4±10.4	9.2±1.2	7.5±3.5	11.5±0.9	9.3±3.6	0.588
Nine-month assessment								
JADAS								
Sw Jt.	1.2±1.7	0.0	2.2±2.03	1.5±1.5	0	5.0±0.0	0.0	0.128
Pt. VAS	2.2±1.8	2.5±1.7	3.4±2.6	3.5±0.5	0	5.5±1.5	3±3	0.528
Phy. VAS	1.8±1.4	2±0.8	2.6±2.1	2.5±0.5	0	4.5±0.5	0.5±0.5	0.245
ESR	34.7±32.7	38.5±31.9	46.6±30.5	47.5±22.5	0	30.5±4.5	4.5±1.5	0.391
Score	6.8±7.7	6.3±3.7	10.8±7.3	10.2±0.2	0.0	16±2.4	1.9±3.3	0.214

*Significant differences

The results of current study showed significant differences among the periods of assessment (Initial, 1 month, 3 months, 6 months, and 9 months) in subtypes (OJIA-E, PJIA RF negative, and PJIA RF undifferentiated). No significant differences recorded among the periods of assessment in subtypes (OJIA-P, PJIA RF positive, SJIA, and ERA) (Table 3).

Table 3
Changes in disease activity over time in different subsets of JIA with period of assessment comparison

JADAS score	OJIA-E (n=16)	OJIA-P (n=15)	PJIA			SJIA (n=3)	ERA (n=4)
			(RF-) (n=13)	(RF+) (n=6)	Un-differentiated (n=9)		
Initial	26.3±13.9	12.2±6.3	27.3±12.02	17.8±6.08	28.2±11.5	31.5±1.6	14±5.5
1 mo.	15.4±10.4	8.3±7.4	19.06±9.7	15.7±4.7	17.5±12.5	19.3±5.5	5.3±2.2
3 mon.	9.2±8.3	7.7±8.2	18.1±10.5	28.1±20	19.3±11.4	14.8±8.3	6.2±2.2
6 mon.	10.8±8.9	4.6±4.1	11.4±10.4	9.2±1.2	7.5±3.5	11.5±0.9	9.3±3.6
9 mon.	6.8±7.7	6.3±3.7	10.8±7.3	10.2±0.2	0.0	16±2.4	1.9±3.3
p-value	<0.05	>0.05	<0.05	>0.05	<0.05	>0.05	>0.05

Yellow highlight refers to significant differences

Blood test

The results of current work showed that no significant differences among sub types of JIA in blood tests (Hb, WBC, AST, ALT, Urea, and Creatinine) at baseline. Significant differences were noticed among the types of JIA in AST, ALT, and Creatinine after one month assessment. Also, significant differences were

noticed among the types of JIA in WBC and Creatinine after three months assessment. Furthermore, significant differences were noticed among the types of JIA in Hb, WBC, AST, ALT, Urea, and Creatinine after six- and nine-months assessment (Table 4).

Table 4
Baseline, one month, three months, six months, and nine months blood tests in different sub groups of JIA.

Parameters	JIA subtypes Total (n=66)							
Variables	Oligo E (n=16)	Oligo P (n=15)	Poly (n=29)			SJIA (n=3)	ERA (n=4)	p-value
			(RF-) (n=13)	(RF+) (n=6)	Un-differentiated (n=9)			
Blood tests at Baseline								
Hb (g/dl)	11.1±2.1	10.9±1.5	9.8±1.9	11.4±1.9	11.5±1.3	8.9±1.2	11.3±1.8	0.53
WBC (x10³/ mm³)	11.09±4.6	10.7±5.4	9.4±4.1	10.2±8.2	8.2±2.4	22±4.2	8.8±2	0.07
AST (U/L)	16.7±7.7	21.1±15.9	20.7±9.2	18.8±7.6	17.4±4.9	9.6±2.05	16.7±3.8	0.16
ALT (U/L)	13.4±7.01	14±8.2	16.2±8.1	10.2±4.6	11.1±2.2	6.3±0.4	13.7±3.4	0.60
U (mg/dl)	18.8±9.8	23.05±7.2	19.2±17.9	19±12.3	24.7±9.5	22±6.9	23±0.0	0.29
C (mg/dl)	0.51±0.12	0.52±0.17	0.58±0.27	0.6±0.2	0.6±0.09	0.4±0.06	0.57±0.0	0.14
Blood tests after one month								
Hb (g/dl)	11.6±1.6	11.4±1.5	10.1±2.1	11.5±2.5	11.6±1.8	10±0.2	12.7±1.4	0.29
WBC (x10³/ mm³)	10±4.1	9.1±3.8	9.1±5.1	10.5±3.8	8.4±3.2	15.9±2.2	7.9±0.9	0.25
AST (U/L)	18.4±11	20.1±17.5	24.9±11.2	23±17	14.6±3.2	17.6±10	11.6±7.4	0.05
ALT (U/L)	18.6±10.5	12.9±7.6	16.5±10.1	24.6±30	12.2±3.1	17.3±12	11±5.7	0.04
U (mg/dl)	16.1±5.8	25.5±8.3	22.1±16	18.7±8.7	17.6±10.7	22.5±7.5	16.6±9.1	0.30
C (mg/dl)	0.53±0.14	0.55±0.17	0.47±0.20	0.47±0.22	0.68±0.15	0.5±0.0	0.62±0.06	0.02
Blood tests after three months								
Hb (g/dl)	11.6±1.4	11.6±2.09	9.5±2.1	11.7±2.1	11.2±1.8	10.3±1.06	12.3±2.5	0.31
WBC (x10³/ mm³)	8.4±2.8	11.08±3.8	10.3±4.4	12.1±4.1	7.3±2.2	17.3±2.2	8.2±2.2	0.02
AST (U/L)	18.9±14	20±11.4	21.5±9.1	19.2±8.1	17.6±7.3	11.3±3.09	24.5±17.5	0.21
ALT (U/L)	14.1±11.8	16.3±11.2	15.8±8.4	10.2±3.7	15±4.5	6.3±1.6	29±21	0.15
U (mg/dl)	23.7±18.8	20.9±12.1	20.4±13.1	11.1±6.8	18.9±14.8	7.8±5.7	17.8±11.2	0.83
C (mg/dl)	0.53±0.12	0.48±0.16	0.70±0.17	0.68±0.09	0.61±0.13	0.4±0.0	0.44±0.04	0.001
Blood tests after six months								
Hb (g/dl)	11.6±1.8	11.2±2.09	10.9±1.6	12.9±1.1	10.4±0.8	9.8±0.09	13.9±0.3	0.1
WBC (x10³/ mm³)	8.7±3.1	11.3±5.5	10.9±4.4	8±3.8	7.8±0.3	16.8±1.9	7.8±1.1	0.28
AST (U/L)	19.3±9.3	23.8±9.09	18.6±8.4	17±10	10.6±5.4	17±0.0	16.5±10.5	0.01
ALT (U/L)	14.7±7.9	24.2±15	13.3±5.3	6±2	7.3±2.8	8±0.0	18±10	0.01
U (mg/dl)	27.1±6.7	25.7±8.7	28.7±24.2	11.1±7.8	10.5±8.1	30±9.5	27±1	0.01
C (mg/dl)	0.52±0.13	0.56±0.29	0.55±0.19	0.63±0.20	0.84±0.04	0.56±0.23	0.61±0.09	0.002
Blood tests after nine months								
Hb (g/dl)	11.2±2.5	12.3±1.5	9.9±2.6	12.5±0.25	No record	9.9±0.5	14.3±1.1	0.001
WBC (x10³/ mm³)	7.7±2.6	9.5±5.6	11±4.5	8.5±3.8	No record	14.3±2.4	7.9±0.5	0.001
AST (U/L)	19.8±8.4	20.6±9.7	17.2±10.6	12.5±9.5	No record	13±0.0	17±8	0.001
ALT (U/L)	22.3±10.6	16.3±9.07	14.9±6.6	5±1	No record	21±0.0	12±6	0.001
U (mg/dl)	26.1±10.1	26.5±15.2	19.2±13.9	27.5±12.5	No record	29±0.0	28±0.0	0.001
C (mg/dl)	0.62±0.08	0.54±0.36	0.59±0.08	0.58±0.12	No record	0.8±0.0	0.62±0.08	0.04

Yellow highlight refers to significant differences

Incidence Rate

The incidence rate per 100000 individual of the disease was decreased from 0.10/ 100000 to 0.005/ 100000 through the period of the research (2019-2021) generally (Figure 3). Our result of incidence rate was less than the results of another study which found that the mean annual incidence rate for JIA was

estimated to be 12.8/100,000 children <16 years, with the highest age-specific annual incidence at the age of 2 years (36/100,000) (Berthold et al., 2019).

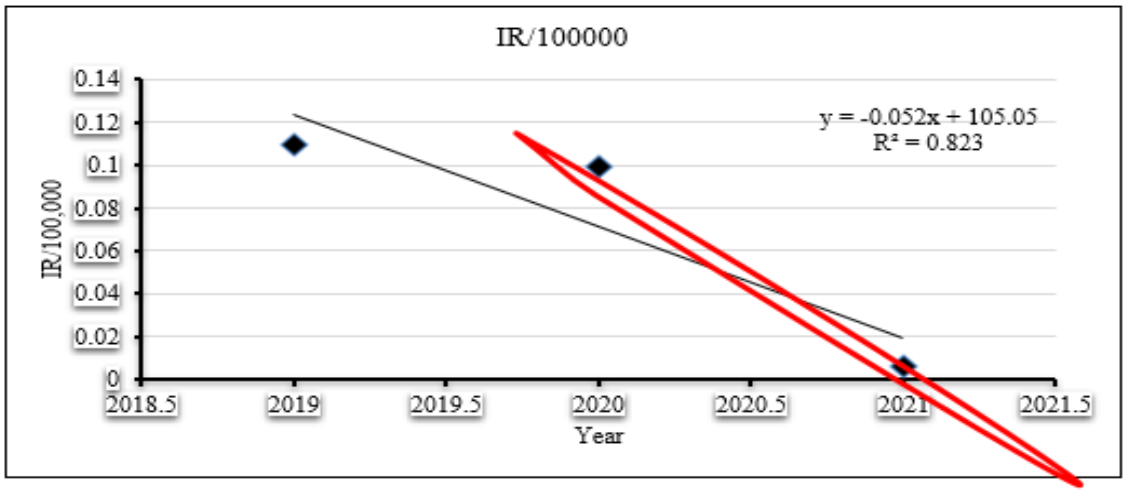

Fig.3. The incidence rate per 100000 for JIA disease through the period (2019-2021).

Discussion

In (Table 1) and (Figure 1) we see the JIA distribution in both male and female in nearest ratios (30 males and 36 females) (45.5% and 54.5%). This finding was supported by a study that discovered that 12.4% of the cases from the region with oligoarticular sub-type were females predominating (61.6%). In accordance with a review of Consolaro et al., (2019), girls in the area are more likely than boys to develop JIA [12, 13]. The ratios do, however, vary noticeably between the various nations in the region. In the majority of studies carried out in distinct African and Middle Eastern nations, they found a higher female to male ratio [14]. It is apparent that many autoimmune diseases are more common in women, but referral INF, study methodologies, case ascertainment, and geography can all affect the gender ratios in different ways [15, 16].

In (Table 1) and (Figure 2), JIA was recorded in maximum age at >10 years group (56.1%) and in minimum age at 1-4 years group (6.1%). Highest frequency of JIA type was observed in age group 1-4 years with Oligo P (75%). Highest frequency of JIA type was observed in age group 5-10 years with Oligo E (36%). Highest frequency of JIA type was observed in age group >10 years with Oligo E, Oligo P, and Poly (RF negative) (18.9%). These finding were supported with a study in Saudi Arabia which found that the mean age of onset of JIA symptoms was 7.11 ± 3.65 years [17].

From the results documented in (Table 1), the study found that the positive ANA test cases were found in 4 cases only while the negative results of the test were found in 53 cases, residual cases were not recorded. Highest frequency of positive test was observed in Oligo-E (75%). This outcome was consistent with a study that found that 12/23 patients with oligoarticular JIA (52.17%) had the majority of positive ANA results [17].

Frome the finding tabulated in (Table 1), JIA duration was ranged from 5.9 years to 10 years. Highest duration of disease was observed in Poly (RF+) type (10.4 ± 4.8) years. This finding was in lined with the finding of a study which found that the average duration of symptoms is six weeks or longer, and they frequently last for months or years. The illness can persist into adulthood in some kids. The length of JIA varies according to its type [18].

About the amount of MTX drug that used to treat JIA, it was ranged from 7.38 mg to 14.1 mg for period ranged from 1.06 year to 3.7 years. Highest dose of MTX was found to be gives to the patients with Poly (RF+) type (12 ± 1.8 mg). Highest duration of treatment was observed in patients with Poly undifferentiated type of JIA (Table 1). The findings of a study that showed that the amount of methotrexate (MTX) prescribed for juvenile idiopathic arthritis (JIA) can vary depending on factors like the child's weight and the severity of the condition supported these findings. The dosage of MTX is typically 10 mg/m2 to 30 mg/m2 of body surface area, or up to 0.6 mg/kg of the child's weight, given once a week. Depending on how well the child responds to the medication, the dose may need to be changed over time [18].

About the drugs used to treat the JIA, in (Table 1) the results noticed 3 types of DMARDS treatment were used for Oligo and Poly (RF+) JIA types, while the other

types of JIA used ether one or two DMARDS drugs. Highest dose of DMARDS drug was found to be used in patients with Poly (RF-) as 532±317. Longest period of treat with DMARDS was found in patients with Poly undifferentiated RF as 1.4±1.1 month. Sulfasalazine (SSZ) is a type of antibiotic has long been used as a JIA treatment. A randomized controlled trial of children with oligoarticular and polyarticular arthritis found it to be superior to placebo, and long-term follow-up revealed that the children who were initially treated with SSZ fared better than those who were initially treated with placebo at a median of 9 years after the study. The maximum safe dose of CQ phosphate is considered to be 4 mg/kg/day or 100 mg/m2/day [26].

Azathioprine (IMMURAN) Azathioprine has been used for the treatment of JIA and occasionally achieved JIAU inactivity and spared corticosteroids [19]. The use of leflunomide can be justified with the evidence level 2 because of a double-blind, controlled study with inconclusive results in polyarticular juvenile arthritis [20]. Not approved for treatment of JIA, therefore not recommended for therapy. Dosage in children up to 20 kg body weight 10 mg daily, 20 mg kg body weight 15 mg daily and 20 mg in over 40 kg body weight [21].

Corticosteroid's type was used to treat JIA as PND and MG. Amount of corticosteroid drug that used to treat JIA was ranged as 4.8 mg to 12 mg. Period of using corticosteroids drug to treat JIA was ranged as 0.6 months to 4.8 months (Table 1). All algorithms have in common to treat all patients with active polyarticular JIA with Methotrexate and to provide concomitant treatment with NSAIDs, oral prednisolone (equivalent of 0.2 mg/kg/day) and intraarticular corticosteroids optionally. Algorithm No. 1 is characterized by an add-on therapy of Methotrexate with a biologic starting at month 3. Algorithm 2 is characterized by switching to a monotherapy with a biologic. Algorithm 3 is characterized by an initial intravenous steroid pulse therapy and algorithm 4 is characterized by an initial intraarticular steroid therapy into numerous, at least more than 4 active joints [22].

Three types of biological drugs were used to treat JIA including Infliximab (INF), Etanercept (ENBREL), and PND (Table 1). Etanercept is very effective for the treatment of JIA. Data from clinical trials and open-label studies support its clinical efficacy in 80% of patients which appears to be sustained over several years for the majority of treated patients. The safety profile is also acceptable with a serious adverse event rate of 0.03 - 0.12 per patient-year. Mechanism of action TNF inhibitor Usual dosing 0.4 mg/m2 (max 25 mg) FDA-approved uses [23].

The score of JADAS27 was calculated at baseline, after one month, after three months, after 6 months, and after 9 months for all types of JIA (OJIA-E, OJIA-P, PJIA/RF+, PJIA/RF-, PJIA/RF undifferentiated, SJIA, and ERA). JADAS27 is an absolute disease activity measure that can be used to determine and evaluate disease activity status and course in individual patients. It consists of the following measures: physician's global assessment (score 0-10), parent's global assessment (0-10), active joint count (assessed in score of 27), and ESR (normalized to score 0-10) [24].

The incidence rate per 100000 individual of the disease was decreased from 0.10/ 100000 to 0.005/ 100000 through the period of the research (2019-2021) generally (Figure 3). Our result of incidence rate was less than the results of another study which found that the mean annual incidence rate for JIA was estimated to be 12.8/100,000 children < 16 years, with the highest age-specific annual incidence at the age of 2 years (36/100,000) [25].

CONCLUSION

JIA with MTX, DMARDS duration, Steroid dosage, and JADAS all showed significant differences. There were no discernible differences in JIA with regard to age, gender, the length of the disease, the use of MTX, the quantity of DMARDS, the use of steroids, and blood tests. The disease's incidence rate was declined from 2019 to 2021.

Competing Interest

The authors had no competing interests.

References

[1] Martini, A., Lovell, D. J., Albani, S., Brunner, H. I., Hyrich, K. L., Thompson, S. D., & Ruperto, N. (2022). Juvenile idiopathic arthritis. *Nature Reviews Disease Primers, 8*(1), 5. https://doi.org/10.1038/s41572-021-00332-8

[2] Tupper, S. (2012). *Within-day variability of pain in youth with juvenile idiopathic arthritis and non-arthritic pain conditions* (Doctoral dissertation, University of Saskatchewan).

[3] Stinson, J., Connelly, M., Kamper, S. J., Herlin, T., & April, K. T. (2016). Models of care for addressing chronic musculoskeletal pain and health in children and adolescents. *Best Practice & Research Clinical*

Rheumatology, 30(3), 468-482.
https://doi.org/10.1016/j.berh.2016.08.005

[4] Stinson, J. N., Luca, N. J., & Jibb, L. A. (2012). Assessment and management of pain in juvenile idiopathic arthritis. *Pain Research and Management, 17*(6), 391-396.
https://doi.org/10.1155/2012/237258

[5] Fadl, A. A., Alsuwaidani, S. A. H., Batti, S. M. A., Saleh, Z. H. S. A., Ghareeb, F. A. A., Alrebh, Z. H. A., Omran, L. A. A., ALRadhwan, M. S., Almarhoon, F. H. A., Almutlaq, Z. A. S. and Aysh, H. T. A. (2022) Overview on juvenile psoriatic arthritis: A Review, *Journal of Pharmaceutical Research International*, 34(61), pp. 1–7.
https://doi.org/10.9734/jpri/2022/v34i617274

[6] Zaripova, L. N., Midgley, A., Christmas, S. E., Beresford, M. W., Baildam, E. M., & Oldershaw, R. A. (2021). Juvenile idiopathic arthritis: from aetiopathogenesis to therapeutic approaches. *Pediatric Rheumatology, 19,* 1-14.
https://doi.org/10.1186/s12969-021-00629-8

[7] Rosenberg, A. M. (2020). Do we need a new classification of juvenile idiopathic arthritis? *Clinical Immunology,* 211.
https://doi.org/10.1016/j.clim.2019.108298

[8] Consolaro, A., Giancane, G., Schiappapietra, B., Davì, S., Calandra, S., Lanni, S., & Ravelli, A. (2016). Clinical outcome measures in juvenile idiopathic arthritis. In *Pediatric Rheumatology* (Vol. 14, Issue 1). BioMed Central Ltd.
https://doi.org/10.1186/S12969-016-0085-5

[9] Bazso, A., Consolaro, A., Ruperto, N., Pistorio, A., Viola, S., Magni-Manzoni, S., Malattia, C., Buoncompagni, A., Loy, A., Martini, A., & Ravelli, A. (2009). Development and testing of reduced joint counts in juvenile idiopathic arthritis. *Journal of Rheumatology, 36*(1), 183–190.
https://doi.org/10.3899/jrheum.080432

[10] Giancane, G., Rosina, S., Consolaro, A., & Ruperto, N. (1926). Outcome Scores in Pediatric *Rheumatology.*
https://doi.org/10.1007/s11926-021-00988-x/Published

[11] Standardization of Uveitis Nomenclature (SUN) Working Group. (2021). Classification criteria for juvenile idiopathic arthritis–associated chronic anterior uveitis. *American Journal of Ophthalmology, 228*, 192-197.
https://doi.org/10.1016/j.ajo.2021.03.055

[12] Prakken, B., Albani, S., & Martini, A. (2011). Juvenile idiopathic arthritis. *The Lancet, 377*(9783), 2138-2149.
https://doi.org/10.1016/S0140-6736(11)60244-4

[13] Consolaro, A., Giancane, G., Alongi, A., van Dijkhuizen, E. H. P., Aggarwal, A., Al-Mayouf, S. M., Bovis, F., De Inocencio, J., Demirkaya, E., Flato, B., Foell, D., Garay, S. M., Lazăr, C., Lovell, D. J., Montobbio, C., Miettunen, P., Mihaylova, D., Nielsen, S., Orban, I., … Wouters, C. (2019). Phenotypic variability and disparities in treatment and outcomes of childhood arthritis throughout the world: an observational cohort study. *The Lancet Child and Adolescent Health, 3*(4), 255–263.
https://doi.org/10.1016/S2352-4642(19)30027-6

[14] Abou El-Soud, A. M., El-Najjar, A. R., El-Shahawy, E. E., Amar, H. A., Hassan, T. H., Abd-Allaha, S. H., & Ragab, H. M. (2013). Prevalence of juvenile idiopathic arthritis in Sharkia Governorate, Egypt: Epidemiological study. *Rheumatology International, 33*(9), 2315–2322.
https://doi.org/10.1007/s00296-013-2707-2

[15] Kronzer, V. L., Bridges, S. L., & Davis, J. M. (2021). Why women have more autoimmune diseases than men: An evolutionary perspective. *Evolutionary Applications, 14*(3), 629–633.
https://doi.org/10.1111/eva.13167

[16] Tincani, A., Gerardi, M. C., Fredi, M., & Andreoli, L. (2018). Gender differences in rheumatology and the point of view of the Italian Society for Rheumatology (SIR). *Journal of Sex-and Gender-Specific Medicine, 4*(2), 79.

[17] Al-Hemairi, M. H., Albokhari, S. M., & Muzaffer, M. A. (2016). The pattern of juvenile idiopathic arthritis in a single tertiary center in Saudi Arabia. *International Journal of Inflammation,* 2016.
https://doi.org/10.1155/2016/7802957

[18] Al-Mayouf, S. M., Al Mutairi, M., Bouayed, K., Habjoka, S., Hadef, D., Lotfy, H. M., Scott, C., Sharif, E. M., & Tahoun, N. (2021). Epidemiology and demographics of juvenile idiopathic arthritis in Africa and Middle East. In *Pediatric Rheumatology* (Vol. 19, Issue 1). BioMed Central Ltd.
https://doi.org/10.1186/s12969-021-00650-x

[19] Goebel, J. C., Roesel, M., Heinz, C., Michels, H., Ganser, G., & Heiligenhaus, A. (2011). Azathioprine as a treatment option for uveitis in patients with juvenile idiopathic arthritis. *British Journal of Ophthalmology, 95*(2), 209–213.
https://doi.org/10.1136/bjo.2009.173542

[20] Brunner, H. I., Ruperto, N., Zuber, Z., Keane, C., Harari, O., Kenwright, A., Lu, P., Cuttica, R., Keltsev, V., Xavier, R. M., Calvo, I., Nikishina, I., Rubio-Pérez, N., Alexeeva, E., Chasnyk, V., Horneff, G., Opoka-Winiarska, V., Quartier, P., Silva, C. A., … Schikler, K. (2015). Efficacy and safety of tocilizumab in patients with polyarticular-course juvenile idiopathic arthritis: Results from a phase 3, randomised, double-blind withdrawal trial. *Annals of the Rheumatic Diseases, 74*(6), 1110–1117.
https://doi.org/10.1136/annrheumdis-2014-205351

[21] Burns, P. B., Rohrich, R. J., & Chung, K. C. (2011). The levels of evidence and their role in evidence-based medicine. *Plastic and Reconstructive Surgery, 128*(1), 305–310.
https://doi.org/10.1097/PRS.0b013e318219c171

[22] Horneff, G., Klein, A., Ganser, G., Sailer-Höck, M., Günther, A., Foeldvari, I., & Weller-Heinemann, F. (2017). Protocols on classification, monitoring and therapy in children's rheumatology (PRO-KIND): Results of the working group Polyarticular juvenile idiopathic arthritis. In *Pediatric Rheumatology* (Vol. 15, Issue 1). BioMed Central Ltd.
https://doi.org/10.1186/s12969-017-0206-9

[23] Berard, R. A., & Laxer, R. M. (2013). Etanercept (Enbrel) in the treatment of juvenile idiopathic arthritis. *Expert Opinion on Biological Therapy, 13*(11), 1623–1630.
https://doi.org/10.1517/14712598.2013.840580

[24] Al-Bassam, W. W., Ad'hiah, A. H., & Mayouf, K. Z. (2020). Biomarker significance of interleukin-18 in juvenile idiopathic arthritis. *Iraqi Journal of Science, 61*(12), 3200–3207.
https://doi.org/10.24996/ijs.2020.61.12.7

[25] Berthold, E., Månsson, B., & Kahn, R. (2019). Outcome in juvenile idiopathic arthritis: A population-based study from Sweden. *Arthritis Research and Therapy, 21*(1).
https://doi.org/10.1186/s13075-019-1994-8

[26] Laaksonen, A. L., Koskiahde, V., & Juva, K. (1974). Dosage of antimalarial drugs for children with juvenile rheumatoid arthritis and systemic lupus erythematosus: a clinical study with determination of serum concentrations of chloroquine and hydroxychloroquine. *Scandinavian Journal of Rheumatology, 3*(2), 103-108.
https://doi.org/10.3109/03009747409115809