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A 10-Year Saudi Experience of Using Adalimumab in Treating Juvenile Idiopathic Arthritis

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Abstract

Background: Traditionally, management of Juvenile Idiopathic Arthritis (JIA) involves use of non-steroidal anti-inflammatory drugs (NSAIDS) or disease-modifying anti-rheumatic drugs (DMARDs), such as methotrexate (MTX) or sulfasalazine; or steroids. However, in several cases, a low therapeutic response or important side effects is encountered. This study reports our experience in using adalimumab in JIA patients by assessing the efficacy and safety of this treatment in this category of patients. **Methods:** A retrospective study was conducted among 38 patients with JIA at the Pediatric Department, King Abdulaziz Univesrity Hospital, Jeddah, Saudi Arabia, in the period January 2005-March 2016. Patients' records were reviewed and relevant demographic and clinical data were collected. Data were analyzed using SPSS version 21 and represented using tables. **Results:** The 38 patients were distributed as 11 (28.9%) males and 27 (71.1%) females; mean ± SD age was 11.91 ± 4.54 (range = 3 - 19) years. Mean ± SD (range) disease duration was 3.26 ± 2.52 (0 - 12) years and most frequent diagnoses included polyarticular rheumatoid factor (RF) negative form 12 (31.6%), followed by systemic and oligoarticular JIA with 9 (23.7%) cases each. Before adalimumab, fever was present in 13 (34.2%) cases, followed by rash in 8 (21.0%) cases; while 21 (55.3%) were asymptomatic. Thirty-one (81.6%) were in failure of MTX, 19 (50%) of steroids, 7 (18.4%) of NSAIDS and 3 (7.9%) had had intraarticular injections. Biologically, ANA, RF and anti-CCP were positive in 22 (57.9%), 8 (21.1%) and 4 (10.5%) of the cases, respectively. Uveitis was present in 11 (28.9%) of the patients. Analysis of adalimumab efficacy showed 10 (52.6%) cases of complete remission, 9 (23.7%) of partial remission and 9 (23.7%) other where treatment was discontinued. Major adverse effects included local pain (4 [10.5%]), new onset uveitis (1 [2.6%]) and rash (1 [2.6%]), responsible of 1case of treatment discontinuation. Predictors for complete remission on

adalimumab were oligoarticular form (β = 3.450, p = 0.009) and negative RF (β = 2.381, p = 0.036); while predictors for nonresponse, whether complete or partial, were polyarticular form (β = −3.784, p = 0.005) and positive anti-CCP (β = −3.178, p = 0.021). **Conclusion:** Adalimumab is an efficient and relatively safe alternative in the treatment of JIA with relatively high remission rates and lower rates of adverse effects. Further multicentre experiences are warranted to prove its efficacy and safety in the Saudi patients.

Keywords

Adalimumab, Juvenile Idiopathic Arthritis, Anti-TNFα

1. Introduction

Juvenile Idiopathic Arthritis (JIA) comprises a group of inflammatory joint diseases of idiopathic cause having in common chronic arthritis and manifesting with joint pain, swelling and limitation of movement [1]. The evolution of JIA is characterized by joint damage leading to disability and growth restriction, which makes it one of the major causes of acquired disability among children [2]. The disease usually occurs before the age of 16, with a female predominance and a prevalence of up to 4 per 1000 children [1] [3] [4] [5]. Juvenile Idiopathic Arthritis according to the International League of Associations for Rheumatologists (ILAR) is diagnosed if the age of onset is less than 16 years; the duration of the symptoms is at least 6 weeks and other conditions have been excluded [6].

Early diagnosis and initiation of treatment are very crucial steps in the management of JIA as these help interrupt the natural history of the disease characterized by irreversible joint damage and soft-tissue deformities. These changes have been shown to be more frequent and severe in the polyarticular form with a positive rheumatoid factor [7] [8].

There exist various therapeutic approaches to the management of JIA that can broadly be classified as pharmacological and non-pharmacological. Over the years, steroids and non-steroidal anti-inflammatory drugs (NSAIDS) have been the mainstay of pharmacotherapy for JIA [9]. Other drugs that have been used in the management of JIA include disease modifying anti-rheumatic drugs (DMARDS) such as methotrexate; mycophenolate mofetil and sulfasalazine. These drugs aim not only to reduce the number of flare-ups and inflammatory activity and provide pain relief but also to retard the progression of the disease. The latter has however been shown to be more of a function of disease modifying anti-rheumatic drugs (DMARDS). Steroids and NSAIDS are however characterized by low therapeutic response rates and varying side effects, which result in reduced compliance and unsatisfying therapeutic outcomes [10].

In the last two decades, the advent of host immune response modifiers popularly referred to as biologic agents, for instance the anti-TNFα agents (etanercept, infliximab, adalimumab) has revolutionized the treatment and the expected

outcome of JIA (1). Biologic agents act by direct inhibition of pro-inflammatory mediators and are used in the treatment of a number of other autoimmune diseases. These biologic agents target other cytokines besides TNF-α such as IL-6 (tocilizumab); IL-1 (anakinra) among others. The latter has been shown to have better results especially in systemic involvement [11]. Despite their unobjectionable success in the treatment of JIA, they are associated with considerable adverse effects mainly allergic reactions and higher rates of serious infections including bacterial and opportunistic infections and reactivation of Tuberculosis [1] [10].

Adalimumab was the first fully human monoclonal antibody to TNF-α approved for use in the treatment juvenile idiopathic arthritis [6] [12]. This study set out to report a single-center experience in using adalimumab in JIA. The following objectives were addressed:

- To assess the efficacy and safety of adalimumab in JIA patients;
- To determine the patterns of therapeutic response: complete remission, partial remission, or failure;
- To describe the demographic, clinical and biological parameters associated with therapeutic response;
- To evaluate the predictors of remission and therapeutic failure.

2. Methods

A retrospective chart review was carried out among children at the Pediatric Department, King Abdulaziz University, Jeddah, Saudi Arabia in the period January 2005-March 2016. All patients fulfilled the International League of Associations for Rheumatology (ILAR) criteria for diagnosis of JIA [6]. Eligibility criteria included having an active disease of one of the subtypes of JIA (systemic, oligoarticular, extended oligoarticular, polyarticular with negative rheumatoid factor (RF), polyarticular with positive RF, psoriatic, enthesitis-related arthritis and undifferentiated arthritis); and being treated with adalimumab subsequent to non-response to conventional treatment (NSAID, DMARDS). Patients who did not meet all ILAR criteria or those who had received treatment with other biologic agent than adalimumab were excluded. Relevant demographic, clinical and biological data were collected. Demographic data included age and gender. Clinical data included age at diagnosis; disease duration; JIA sub-type; presence or absence of uveitis; presence of symptoms before adalimumab such as fever, rash, pain, etc., and treatment history such as use of methotrexate (MTX), NSAIDS or steroids. Biological data included rheumatoid factor status (positive versus negative); anti-CCP titer and antinuclear antibody (ANA).

Study outcomes included efficacy and safety of adalimumab. Efficacy was classified into three categories: partial remission, complete remission and treatment failure. Completeremission was indicated by the disease becoming inactive defined by the following criteria: absence of active arthritis; absence of JIA-related symptoms (fever, rash, serositis, splenomegaly, lymphadenopathy); absence of

uveitis; normalization of inflammation markers (ESR, CRP) and absence of active disease by global physician's assessment; while partial remission or failure of treatment were defined by inability to meet some or none of the above mentioned criteria respectively; all ≥ 6 continuous months on medication or ≥12 months off medication.

Statistical Methods

Data were analyzed using SPSS version 21.0 for Windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics were carried out to calculate frequencies and percentages for categorical variable and means (standard deviations [SD]) for numerical variables. Therapeutic response to adalimumab, the outcome of interest, was analyzed using two distinct definitions: 1) complete remission versus no complete remission; and 2) complete or partial remission versus absence of remission. Analytical statistics were carried out to analyze correlation between therapeutic response (using both definitions, distinctly) with demographic, clinical and biological factors; using chi-square test, Fisher's exact test and independent t-test, as appropriate. Binary logistic regression was carried out to analyze significant factors as predictors for both outcome definitions. A p-value < 0.050 was considered for statistical significance.

3. Results

3.1. Population Demographic and Clinical Characteristics (Table 1)

A total of 38 patients were included in the study; the mean age was 11.91 (±4.54) years with a range between 3 and 19 years. The females constituted 71.1% (27); female-to-male ratio was 2.45. The mean age at diagnosis of JIA was 7.32 (±4.53) years ranging from less than 1 year old to 16 years. The duration of disease varied with a mean duration of 3.26 (±2.52) years, and the oldest recorded age at diagnosis being 12 years.

The frequency of the various subtypes of JIA showed polyarticular type with rheumatoid factor negative in 12 (31.6%); oligoarticular persistent in 9 (23.7%); systemic in 9 (23.7%); polyarticular with rheumatoid factor positive in 5 (13.2%); psoriatic arthritis in 2 (5.3%) and oligoarticular extended in 1 (2.6%) patient.

Prior to the initiation of treatment with adalimumab, fever was present in 10 (26.3%) patients, rash in 8 (21.1%) patients and hepatomegaly was present in 2 (5.3%) patients; while 21 (55.3%) patients were clinically asymptomatic. Uveitis was found to be present in 29%.

The biological parameters showed that prior to treatment with adalimumab, ANA was positive in almost 60% (22) of patients, RF in 20% (8) and anti-CCP in about 10% (4) of them. However, anti-CCP titer was not done for more than 40% patients. Of the 38 patients included in the study, almost 80% (31) of the patients were in failure of methotrexate; 50% (19) of steroids and almost 20% (7) of NSAIDs. Three (7.9%) patients had however benefited from intra-articular injections without a satisfying response.

Table 1. Demographic and clinical characteristics of the population.

Parameter	Value	Frequency/mean	Percentage/SD
Gender	Male	11	28.9
	Female	27	71.1
Age	Mean, SD (years)	11.91	4.54
Age at diagnosis	Mean, SD (years)	7.32	4.53
Disease duration	Mean, SD (years)	3.26	2.52
Diagnosis	Systemic	9	23.7
	Polyarticular RF+	5	13.2
	Polyarticular RF−	12	31.6
	Oligoarticular	9	23.7
	Extend oligoarticular	1	2.6
	Psoriatic arthritis	2	5.3
Uveitis	Yes	11	28.9
	No	27	71.1
ANA-titer	Positive	22	57.9
	Negative	16	42.1
Rheumatoid factor	Positive	8	21.1
	Negative	28	73.7
	Not available	2	5.3
Anti-CCP	Positive	4	10.5
	Negative	18	47.4
	Not available	16	42.1
Past treatments	Methotrexate	31	81.6
	Steroids	19	50.0
	NSAIDS	7	18.4
	Biological therapy	1	2.6
	IAI	3	7.9

SD: Standard deviation; RF+: rheumatoid factor positive; RF−: rheumatoid factor negative; NSAIDS: non-steroid anti-inflammatory drugs; IAI: Intraarticular injection.

3.2. Safety and Efficacy of Adalimumab in JIA (Table 2)

Following the use of adalimumab, 20 (52.6%) patients were in complete remission and 9 (23.7%) were in partial remission. In 9 (23.7%) other cases, adalimumab was discontinued. The reasons for discontinuation of treatment with adalimumab varied in the 9 patients with failure occurring in 4 (10.5%); financial constraints being the reason for discontinuation in 2 (5.3%) while side effects and shortages in the drug contributing to 2.6% (1) of the patients each. Various side effects were encountered in 8 (21.1%) cases with the use of adalimumab such as local pain in 4 (10.5%) patients with rash, sero-conversion, new-onset uveitis and GIT upset each contributing 2.6% of the cases.

Table 2. Assessment of safety and efficacy of adalimumab.

Parameter	Value	Frequency	Percentage
Therapeutic response	Complete remission	20	52.6
	Partial remission	9	23.7
	Discontinuation	9	23.7
Side effects		**8**	**21.1**
	Rash	1	2.6
	Seroconversion	1	2.6
	New-onset uveitis	1	2.6
	Local pain	4	10.5
	GIT upset	1	2.6
	Side Effect	1	2.6
	Failure	4	10.5
Discontinuation cause	Treatment shortage	1	2.6
	Financial cause	2	5.3
	Not specified	30	78.9

GIT: Gastrointestinal tract.

3.3. Factors Correlation with Therapeutic Response to Adalimumab

1) Factors of and predictors for complete remission (Table 3, Table 4)

Several factors were studied for their correlation with complete remission following treatment with adalimumab. The mean age of the patients who underwent complete remission was 11.25 (±4.44) years, which was relatively younger than that of their counterpart (12.64 [±4.66] years) but without statistical significance (p = 0.351). Gender distribution was comparable between the two groups (complete remission versus partial remission or no remission on adalimumab), yielding a p-value of 1.000.

Clinically, the mean age at diagnosis (p = 0.657) and mean duration of the disease (p = 0.505) were not correlatedto complete response to adalimumab.

Rate of complete remission on adalimumab was highest in patients with oligoarticular subtype (90.0%), followed by polyarticular with RF negative form (66.7%); while no case of complete remission was observed among patients with polyarticular RF positive JIA (p = 0.004). No correlation was found between complete remission and uveitis (p = 1.000).

Biologically, complete remission was more frequently observed in patients with negative RF (60.7%); as compared with those with positive RF (12.5%); (p = 0.041).

No case of complete remission was observed in patients with positive anti-CCP titer, versus 66.7% cases of complete remission in those with negative anti-CCP; (p = 0.029). No correlation was found between complete remission and either a positive or negative ANA (p = 1.000).

Table 3. Factors correlated with therapeutic response to adalimumab.

Factor	Value	Complete remission		No complete remission		p-value
		F/Mean	%/SD	F/Mean	%/SD	
Age	(years)	11.25	4.44	12.64	4.66	0.351
Age at diagnosis	(years)	7.00	3.84	7.67	5.29	0.657
Disease duration	(years)	3,00	2.87	3.56	2.12	0.505
Gender	Male	6	54.5	5	45.5	1.000
	Female	14	51.9	13	48.1	
Diagnosis (JIA sub-type)	Systemic	2	22.2	7	77.8	0.004*
	Poly RF+	0	0.0	5	100.0	
	Poly RF−	8	66.7	4	33.3	
	Oligo	9	90.0	1	10.0	
	Other	1	50.0	1	50.0	
Methotrexate	Yes	18	58.1	13	41.9	0.222
	No	2	28.6	5	71.4	
Steroids	Yes	8	42.1	11	57.9	0.330
	No	12	63.2	7	36.8	
NSAIDS	Yes	3	42.9	4	57.1	0.687
	No	17	54.8	14	45.2	
ANA	Positive	12	54.5	10	45.5	1.000
	Negative	8	50.0	8	50.0	
RF	Positive	1	12.5	7	87.5	0.041*
	Negative	17	60.7	11	39.3	
Anti-CCP	Positive	0	0	4	100.0	0.029*
	Negative	12	66.7	6	33.3	
Uveitis	Yes	6	54.5	5	45.5	1.000
	No	14	51.9	13	48.1	

RF: Rheumatoid factor; ANA: antinuclear antibody; NSAIDs: non-Staroid anti-inflammatory drugs; RF: rheumatoid factor; Poly RF+: polyarticular juvenile idiopathic arthritis (JIA) with positive RF; Poly RF−: Polyarticular JIA with negative RF.

Table 4. Predictors for complete remission on adalimumab.

Predictor	Value	OR	95%CI	p-value
Diagnosis	Systemic	(indicator)	-	-
	Poly RF+	0.00	0.00, 0.00	0.999
	Poly RF−	7.00	0.97, 50.57	0.054
	Oligoarticular	31.50	2.35, 422.30	0.009*
	Other	3.50	0.145, 84.69	0.441
RF	Positive	(indicator)	-	
	Negative	10.82	1.17, 100.44	0.036*

RF: Rheumatoid factor; Poly RF+: polyarticular juvenile idiopathic arthritis (JIA) with positive RF; Poly RF−: Polyarticular JIA with negative RF.

Use of methotrexate, steroids or NSAIDS did not show any correlation with complete remission following adalimumab ($p > 0.005$).

Predictors for complete remission on adalimumab were found to be the oligoarticular subtypes with an odds ratio of 31.50 ($p = 0.009$); and negative rheumatoid factor with an odds ratio of 10.82 ($p = 0.036$).

2) Factors of and predictors for complete or partial remission (Table 5, Table 6)

Patients who achieved complete or partial remission had both younger age (11.54 [±4.37] versus 13.11 [±5.13]) and younger age at diagnosis (6.72 [±4.23]

Table 5. Factors correlated with therapeutic response to adalimumab (complete or partial remission versus discontinuation).

Factor	Value	Complete or partial remission		No remission		p-value
		F/Mean	%/SD	F/Mean	%/SD	
Age	(years)	11.54	4.37	13.11	5.13	0.371
Age at diagnosis	(years)	6.72	4.23	9.22	5.50	0.151
Disease duration	(years)	3.24	2.67	3.33	2.12	0.925
Gender	Male	11	100.0	0	0.0	0.038*
	Female	18	66.7	9	33.3	
Diagnosis	Systemic	6	66.7	3	33.3	0.010*
	Poly RF+	1	20.0	4	80.0	
	Poly RF−	10	83.3	2	16.7	
	Oligoarticular	10	100.0	0	0.0	
	Other	2	100.0	0	0.0	
Methotrexate	Yes	25	80.6	6	19.4	0.322
	No	4	57.1	3	42.9	
Steroids	Yes	13	68.4	6	31.6	0.447
	No	16	84.2	3	15.8	
NSAIDS	Yes	5	71.4	2	28.6	1.000
	No	24	77.4	7	22.6	
ANA	Positive	17	77.3	5	22.7	1.000
	Negative	12	75.0	4	25.0	
RF	Positive	4	50.0	4	50.0	.086
	Negative	23	82.1	5	17.9	
Anti-CCP	Positive	1	25.0	3	75.0	.024*
	Negative	16	88.9	2	11.1	
Uveitis	Yes	8	72.7	3	27.3	1.000
	No	21	77.8	6	22.2	

Significance level was calculated using chi-square test, Fisher's exact test or independent t-test as appropriate.

Table 6. Predictors for remission (complete or partial) on adalimumab.

Predictor	Value	OR	95% CI	p-value
Gender	Male	-	-	-
	Female	(indicator)	-	-
Diagnosis	Systemic	(indicator)	-	-
	Poly RF+	0.13		0.116
	Poly RF−	2.50		0.382
	Oligoarticular	-		0.999
	Other			0.999
Diagnosis	Systemic	0.18	0.025, 1.349	0.095
	Poly RF+	0.023	0.002, 0.314	0.005*
	Other (Poly RF−, Oligo or psoriatic)	(indicator)	-	0.016
Anti-CCP	Positive	0.042	0.003, 0.619	0.021*
	Negative	(indicator)		0.006

RF: Rheumatoid factor; Poly RF+: polyarticular juvenile idiopathic arthritis (JIA) with positive RF; Poly RF−: Polyarticular JIA with negative RF.

versus 9.22 [±5.50]), versus those who were in complete treatment failure on adalimumab, respectively; however both results were not statistically significant. Gender was found to be significantly correlated to the response to adalimumab with all the male patients achieving partial or complete remission, versus 18 (66.7%) females, ($p = 0.038$). The duration of disease was comparable between the two groups, ($p = 0.925$).

Regarding JIA subtype, all patients (100%) with oligoarticular subtype achieved partial or complete remission; followed by 83.3% in those with polyarticular RF negative, and 66.6% in those with systemic JIA; whereas the lowest success rate was in patients with polyarticular RF positive (20.0%); ($p = 0.010$).

There was no correlation between the history of use of methotrexate, steroids, NSAIDS or the presence or absence of uveitis ($p > 0.005$).

Biologically, only anti-CCP profile was found to correlate to the achievement of complete or partial remission, with 88.9% of success rate in patients with a negative anti-CCP versus 25.0% in those with positive anti-CCP, ($p = 0.024$). However, negative RF profile was associated with higher success rate (82.1%) as compared with positive RF profile (50.0%); however the result was not statistically significant ($p = 0.086$).

Predictors for complete or partial remission were polyarticular form with a positive RF with and OR of 0.023 ($p = 0.005$) and positive anti-CCP with an OR of 0.042 ($p = 0.021$).

4. Discussion

This retrospective study investigated safety and efficacy of adalimumab among

38 patients with JIA who had incomplete response or failure of conventional therapy including NSAIDS, steroids, methotrexate and intraarticular injections. Demographic characteristics of the study participants are comparable to data from other studies. The mean age of the study subjects, which was 11.91 (±4.54) years and ranged between 3 and 19 years, is similar to studies done in Italy [13] and is similar to the target population for a drug trial on adalimumab in patients with JIA where the age of the patients included was ranging between 2 and 19 years [14]. This is, however, differed from a study that had a narrower range of between 4 and 15 years [15] and in a study done on use of adalimumab in JIA patients with uveitis that had a range of between 5 and 17 years [16]. Gender distribution showing that females constituted 71.1% of the patient is similar to a study done in Germany that had 68.5% of female participants [17] and in a study by Magli *et al.* that had 76.2% of the patients being females [16] as well as 67% reported in a study on clinical remission following use of biologic agents [18]. These studies show a female predominance which is similar to what this study reports.

Similarly, age at diagnosis of JIA (mean = 7.32 [±4.53], range ≤ 1 to 16 years) compared well to a study that showed a median age of diagnosis of JIA among participants to be 6.3 (IQR 2.6 - 10.3) years [17]. However, this was higher than that reported in a study that reported 5 years as the mean age at diagnosis of JIA [18]. The duration of disease varied with a mean duration of 3.26 (±2.52) years with the oldest recorded age at diagnosis being 12 years. This is in line with the fact that the diagnostic criteria for JIA are only met if the patient is less than 16 years of age. The findings in this study are similar to the mean duration of disease reported in a study that documented 3 years [18]. However, this was much lower than the mean duration of JIA reported in various studies that reported 7 ± 5.5 months [16]; and lower than the duration reported in a study on efficacy of adalimumab that had the median duration as 4.9 (IQR 2.6 - 7.9) years [17].

The distribution of the various subtypes of JIA compared well with a German study, which showed the polyarticular type with RF negative to be the most common subtype present in 34.9%, but differed on the least common which was reported to be the psoriatic subtype in 4.8% of the cases [17]. In contrast, oligoarticular subtype has been to be the most frequent and the enthesis-related subtype the least frequent in two different studies [19] [20]. This has implications on the expected response with the various treatment options in management of JIA since some of the therapeutic agents such as methotrexate have been shown to have a higher rate of success in the oligoarticular subtype of JIA [21]. Uveitis was found to be present in 28.9%, which is similar to findings that showed 26.6% of the patients to have uveitis [17].

Prior to treatment with adalimumab; ANA was positive in almost 60% which was slightly greater than the 50.2% reported in the German study that used data from the German Biologics Registry in 2013 [17].

Of the 38 patients included in the study, almost 80% of the patients were in

failure of methotrexate; 50% of steroids and almost 20% of NSAIDs. Three (7.9%) patients had however benefited from intra-articular injections without a satisfying response. This differed from other studies that showed that 93.1% of the subjects were on treatment with methotrexate prior to commencement of the study and 61.6% were on steroids [17] and also differed from a study that showed that adalimumab had greater efficacy in patients who had previously been on treatment with methotrexate [9]. The reported figures in this study are not consistent with previously reported remission rates with the various alternative treatments for JIA such as methotrexate where remission rates documented are 6.9% - 45% [22] and in steroids where 23.6% complete remission has been reported [23].

The use of intraarticular steroid injection in JIA is principally indicated in oligoarticular subtypes, where best results are achieved including complete and durable remission of synovitis in more than 80% cases, avoiding systemic treatment. However, it can be proposed to induce rapid reduction of the inflammation in patients with polyarticular subtypes, prior to systemic therapy initiation; or to treat flare-ups in patients already on systemic treatment [24] [25] [26].

Twenty (52.6%) patients were in complete remission and 9 (23.7%) were in partial remission following treatment with adalimumab. These success rates were comparable to those reported among biologic agent naïve patients studied and lower than the remission rates reported in patients who had history of use of biologic agents [17]. However, these rates were much lower than that reported in a study on use of adalimumab in patients with JIA-associated uveitis that reported complete remission in 80% of the patients [27] and higher than those reported in two studies on the use of adalimumab in patients with JIA and uveitis where 35% of the patients showed response to adalimumab [16] [28]. Anotherstudy was done in patients who had failed treatments with etanercept and/or infliximab showed less than 10% of remission following adalimumab therapy [29]. More recently, anti-adalimumab antibodies were incriminated in loss of response to adalimumab in patients where treatment was initially efficient [30].

In 9 (23.7%) other cases, adalimumab was discontinued. This was lower than the rate reported in Germany of 39% [17]. The reasons for discontinuation of treatment with adalimumab varied in the 9 patients with failure occurring in 4 (10.5%); financial constraints being the reason for discontinuation in 2 (5.3%) while side effects and shortages in the drug contributing to 2.6% (1) of the patients each. The reasons cited in the study in Germany were inefficacy in 11.1%; adverse effects in 5.2% and remission in 4.5% among other reasons [17].

This study demonstrated that the use of adalimumab in JIA was safe, with only 2 (5.2%) relatively serious side effects including one case of newly-onset uveitis and one case of sero-conversion; which were encountered among 8 (21.1%) cases of minor side effects such as local pain, rash and GIT upset. These were relatively low incidences compared to that reported in the German study, where more than half the patients developed various adverse effects following adali-

mumab [15]. Data from a larger study demonstrated that the use of adalimumab in JIA is associated with a good long-term tolerability; although infections were frequently reported (11.4%) as compared with methotrexate (5.5%) [31]. On the other hand, further evidence is warranted to determine whether newly-onset uveitis is an adverse effect of adalimumab. Further, some cases of malignancy with mortality occurred among children on biological treatments, notably those reported by the FDA that instituted an alert [32].

5. Limitations

This study is limited by the retrospective design, which prevented from controlling the quality of the data as well as the clinical and biological factors. In addition, missing data was a challenge which led to the reduction in the number of variables initially aimed at.

6. Conclusion

Adalimumab is an efficient and relatively safe alternative in the treatment of JIA among Saudi children; with a relatively high remission rate and low adverse effect rate. Its use was associated with 76% of therapeutic response, including 52% of complete remission, more frequently encountered in children with oligoarticular subtype and those with negative rheumatoid factor and anti-CCP. It has relatively low prevalence of adverse effects (21.8%), responsible of 2.6% treatment discontinuations. Further multicenter studies in the Middle-East and Saudi Arabia are warranted to support these findings. The number of participants was limited owing to the availability and completeness of the data provided.

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Data Type

The [DATA TYPE] data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare no conflict of interest.

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