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ORIGINAL ARTICLE

Juvenile idiopathic arthritis and the temporomandibular joint

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KEYWORDS

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Abstract *Background:* The temporomandibular joint (TMJ) is one of the most underdiagnosed and undertreated conditions of juvenile idiopathic arthritis (JIA) because its involvement is often asymptomatic and the joint is difficult to examine.
Objectives: The aim of this study was to investigate clinical as well as magnetic resonance imaging findings of temporomandibular joint inflammation among juvenile idiopathic arthritis patients and to detect the correlation between them, moreover with different disease parameters.
Methods: Forty patients with JIA and 10 apparently healthy control subjects underwent clinical and post contrast magnetic resonance imaging (MRI) examinations for TMJs. MRI findings were scored. Clinical and laboratory disease parameters were recorded.
Results: The clinical symptoms and signs of TMJ arthritis were detected in 35% and 62.5% of JIA cases, respectively. While TMJ disease was observed in 80% of patients using contrast enhanced MRI. The mean total MRI score was significantly higher in patients with active disease compared

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to those without activity. Patients with systemic and polyarticular JIA showed significant increase in the mean of synovial enhancement, effusion and total MRI scores compared to those with the oligoarticular type. MRI abnormalities revealed significant association with clinical signs of TMJ examination but not with symptoms. Synovial enhancement score showed significant positive correlation with disease activity score and C-reactive protein as a marker of inflammation. A significant positive correlation was found between total MRI score and disease activity, functional and pain scores in patients with JIA.

Conclusions: TMJ arthritis is common among patients with JIA, therefore; examination of the TMJ is mandatory during the follow up of patients. Clinical signs of TMJ arthritis can be used as filter for MRI examination TMJ is an important joint which may be considered during categorizing JIA patients in different subtypes.

1. Introduction

Juvenile idiopathic arthritis (JIA) is the most common autoimmune autoinflammatory musculoskeletal disease in childhood worldwide, manifesting in girls more frequently.[1] It is defined as persistent arthritis for more than 6 weeks with an onset at younger than 16 years of age, after excluding other causes of joint inflammation.[2] The etiology is unclear but appears to be multifactorial and may be related to genetic factors associated with triggering events such as psychological stress, abnormal hormone levels, trauma, or infections.[3]

The International League of Associations for Rheumatology (ILAR) has concluded that the term "juvenile idiopathic arthritis" describes seven subtypes of arthritis according to the clinical features during the first 6 months of disease: oligoarticular JIA, polyarticular JIA, both rheumatoid factors positive and negative, systemic JIA, juvenile psoriatic arthritis, enthesitis-related arthritis, and undifferentiated arthritis.[3]

All joints can be affected in JIA including the temporomandibular (TMJ). Involvement of the TMJ was first reported in 1897 by Still when he described chronic arthritis in childhood. The reported frequency of TMJ affection varied in the literature depending on the population investigated, the subtypes of JIA represented and the method by which TMJ disease is diagnosed. In all subtypes of JIA, one or both TMJs can be affected and may even be the initial joint involved.[4]

Imaging remains an important tool in the assessment of juvenile arthritis patients. With improved treatment options, imaging must be very sensitive in detecting both inflammatory and destructive changes. Magnetic resonance imaging (MRI) in particular can detect synovitis and adds significant information to the clinical examination particularly in TMJ and foot joints.[5]

The aim of this study was to detect clinical as well as MRI findings of TMJ arthritis among JIA patients and to know the correlation between each of them moreover with different disease parameters.

2. Materials and methods

The present study included forty patients (26 girls and 14 boys) with JIA. Their age at the start of the study ranged from 8.5 to 17 years. Patients had either oligoarticular, polyarticular, or systemic-onset JIA according to the criteria of the International League of Associations for Rheumatology (ILAR).[6] They were attending the Pediatric immunology, Rheumatology and Rehabilitation outpatient clinics in Ain Shams University Hospitals. Ten age and sex matched apparently healthy subjects were enrolled in the study as the control group. Patients with cardiac pacemakers, metal implants or dental braces were excluded from the study. An informed consent was obtained from the control subjects, patients or their legal guardians.

A clinical activity score was assigned based on the presence of joint swelling, warmth, redness, range of motion, pain, morning stiffness, and the use of anti-inflammatory medications. The score ranged from 0 to 5 with 0 representing no complaints or physical findings of active disease and no use of anti-inflammatory medications, and 5 representing very active clinical disease and the use of anti-inflammatory medication. The disease was defined as active if the score was $\geqslant 3$ and inactive if the score was $\leqslant 2$.[7]

Functional ability was assessed using childhood health assessment questionnaire (C-HAQ): which describes the child's usual activities in 8 domains over the past week. It includes dressing and grooming, arising, eating, walking, with or without aids or assistive devices, hygiene, reach, grip, and activities. Each question is scored from 0 to 3 (0 = no difficulty, 1 = some difficulty, 2 = much difficulty, 3 = unable to do). The score for each of the 8 functional areas was averaged to calculate the Disability Index. Patients were classified as mildly disabled (score < 1), moderately disabled (score 1–2) or severely disabled (score > 2).[8] Visual analogue scale was used for the assessment of pain severity.[9]

Clinical evaluation of TMJ: Patients were asked about the history of TMJ pain at rest or on movement (eg: opening or chewing), morning stiffness longer than 15 min and crepitations. Clinical examination included: detection of joint tenderness (by palpation on the area in front of ear trigs and external acoustic meatus,[10] crepitations (by using a stethoscope while the patient is asked to perform movement of the TMJ).[10] The maximal jaw mobility was assessed by maximal interincisal mouth opening (MIO): upon maximal mouth opening, a millimeter ruler was used to measure the vertical distance from the incisal edge of the upper maxillary incisor to the opposing mandibular incisor adding the vertical overbite. MIO was considered to be restricted when $\leqslant 40$ mm.[11]

Laboratory investigations including: Erythrocyte sedimentation rate (ESR) using Westergreen method. C-reactive protein (CRP) quantitative determination (Gmbh, Hannover, Germany).

Imaging study of TMJ by MRI: The MRI was carried out using a 1.5 T Signa Horizon magnet. The examination which was performed with a TMJ coil included coronal T_1, T_2

weighted images and sagittal T_1, T_2 weighted images. After injection of gadolinium-based contrast medium, sagittal and coronal fat saturated T_1 weighted images were performed. The variables evaluated were enhancement of the synovial membrane, condylar morphology, presence of pannus, and intraarticular fluid. Enhancement of the synovial membrane which indicates synovial hyperplasia was defined as an increase in signal intensity of the synovium comparing the precontrast image with the post-contrast image. Pannus was defined as an intermediate signal of intraarticular mass on the precontrast T_1 weighted images. Intraarticular fluid (effusion) was defined as low signal intensity mass within the joint cavity. The MRI variables were scored as follows for each joint: enhancement (0 = no enhancement, 1 = slight enhancement, 2 = strong enhancement), condylar morphology (0 = no erosions, 1 = mild erosions, 2 = severe erosions), pannus (0 = no visible pannus, 1 = small amount of pannus, 2 = large amount of pannus), and intraarticular fluid (0 = no fluid, 1 = small amount of fluid, 2 = large amount of fluid). The maximum total MRI score could therefore be 8 per joint or 16 per patient.[12] The control group was subjected to MRI of TMJs without contrast.

2.1. Statistical analysis

This was done using SPSS 10 for Windows (Statistical Package for the Social Sciences). Descriptive statistics: mean, standard deviation, minimum, maximum and range of numerical data. Frequency and percentage of non-numerical data. Independent sample Student's *t*-test was used to test the difference between two groups (for continuous variables).Chi square test to compare between groups regarding non numerical variables. Correlation studies were done by Pearson correlation coefficient (r) to assess strength and direction of the linear relationship between two variables. One way analysis of variance (ANOVA) test (F) was used to test the difference between more than two means. $p > 0.05$ is considered significant and $p < 0.001$ indicates high significance while $p > 0.05$ denotes non-significant.

3. Results

This study was conducted on 40 patients with JIA. 10 apparently healthy subjects with matched age and sex have constituted the control group.

Among patients of this study; 26 were girls (65%) and 14 were boys (35%), 6 patients (15%) were diagnosed as systemic onset JIA, 7 patients (17.5%) with the oligoarticular type and 27 patients (67.5%) with polyarticular disease. The control group was composed of 6 females (60%) and 4 males (40%), their mean age was 14.5 ± 2.8 years .The demographic, clinical and laboratory characteristics of patients are shown in Table 1.

Temporomandibular joint clinical parameters showed that symptoms were present among 14 JIA patients (35%): 7 patients (17.5%), 3 patients (7.5%) complained of TMJ pain at rest and crepitations, respectively. While pain on jaw movement and morning stiffness > 15 min were the symptoms in 8 patients (20%) for each of them. Moreover clinical examination revealed signs of TMJ involvement in 25 patients (62.5%); manifested by tenderness on joint palpation in 10 patients (25%), crepitations on movement in 8 patients (20%) and decreased maximal interincisal opening (MIO) in 10 patients (25%). The mean value of MIO among JIA patients was 43.3 ± 5.1 mm which was significantly decreased in comparison to control subjects (53.4 ± 1.1 mm), $t = 6.2$, $p < 0.001$. No clinical symptoms or signs of TMJ disease could be detected in the control group.

Table 1 Demographic, clinical and laboratory characteristics of juvenile idiopathic arthritis patients.

Age (years)	14.1 ± 2.3
Age at disease onset (years)	9.3 ± 2.8
Disease duration (years)	4.8 ± 2.4
Disease activity score	3.3 ± 1.1
Child health assessment questionnaire	0.92 ± 0.45
Pain score	1.4 ± 0.59
Maximal interincisal opening (mm)	43.3 ± 5.05
C-reactive protein (mg/ml)	21.4 ± 11.2
Erythrocyte sedimentation rate (mm/h)	62.9 ± 37.6

Values are in mean ± SD.

Contrast enhanced MRI was done for 40 patients (80 TMJs): 32 patients (80%) showed MRI abnormalities while 8 patients had no MRI findings. The mean total score for MRI among JIA patients was 5.1 ± 4.1.

Synovial enhancement showed the highest frequency among the findings of contrast enhanced MRI, it was detected in 32 patients (80%), 62 TMJs (77.5%) with a mean score 2.6 ± 1.5. While joint effusion was present in 26 patients (65%), 38 TMJs (47.5%) with a mean score 1.4 ± 1.4. Whereas, pannus and erosions were found in 10 patients (25%) for each but in 18 joints (22.5%), 14 joints (17.5%), respectively with a mean score of pannus 0.60 ± 1.1 and erosions 0.47 ± 0.93. Among JIA patients, there were 7 patients without clinical signs on TMJ examination but MRI abnormalities were detected in them. Regarding the control group, no TMJ abnormalities were found by MRI examination.

When disease activity was considered; age, age at disease onset and disease duration showed no statistically significant difference between active JIA patients and those without activity ($p > 0.05$), while the difference between both groups regarding other clinical, laboratory and MRI parameters are demonstrated in Table 2.

Using the analysis of variance test; patients with systemic onset JIA showed the worst results regarding clinical disease parameters, markers of inflammation and MRI scores followed by the polyarticular type in comparison to patients with oligoarticular disease (Table 3).

A significant decrease in MIO has been detected among JIA patients with pain of TMJ whether at rest or on jaw movement ($t = 4.2$, $p < 0.001$, $t = 4.4$, $p < 0.001$), respectively when compared with patients who did not complain of TMJ pain.

Using Chi-square test: A significant association has been found between clinical signs of TMJ affection and contrast enhanced MRI TMJ abnormalities (25 patients have shown signs of TMJ affection by both clinical and contrast enhanced MRI examinations ($X^2 = 16.6$, $p < 0.001$), while this association was not detected regarding symptoms ($X^2 = 5.3$, $p > 0.05$) among JIA patients.

Pearson correlation coefficient test resulted in a significant negative correlation between MIO and clinical, functional as

Table 2 Comparison between JIA patients with active and inactive disease regarding clinical, laboratory and MRI scores.

	Active disease no.[a] (28)	Inactive disease no.[a] (12)	*p*
C-HAQ[b]	1.1 ± 0.35	0.44 ± 0.20	0.000*
Pain score	1.6 ± 0.52	0.85 ± 0.21	0.000*
MIO[c] (mm)	40.8 ± 3.4	49.0 ± 3.1	0.000*
CRP[d] (mg/ml)	27.7 ± 6.4	6.5 ± 0.66	0.000*
ESR[e] (mm/h)	82.8 ± 25.9	16.4 ± 3.1	0.000*
Synovial enhancement score	3.2 ± 0.92	0.66 ± 0.98	0.000*
Effusion score	2.0 ± 1.3	0.0 ± 0.0	0.000*
Pannus score	0.85 ± 1.3	0.0 ± 0.0	0.032**
Erosion score	0.67 ± 1.1	0.0 ± 0.0	0.033**
Total MRI[f] score	7.0 ± 3.4	0.66 ± 0.98	0.000*

[a] Number.
[b] Child health assessment questionnaire.
[c] Maximal interincisal opening.
[d] C-reactive protein.
[e] Erythrocyte sedimentation rate.
[f] Magnetic resonance imaging.
* Highly significant.
** Significant, values are in mean ± SD.

Table 3 Clinical, laboratory and MRI parameters in different subtypes of JIA patients.

	Systemic JIA[a] no.[d] (6)	Polyart[b] JIA no. (27)	Oligoart[c] JIA no. (7)	*p*
Disease activity score	4.3 ± 0.51	3.4 ± 0.97	2.0 ± 0.0	0.000*
C-HAQ[e]	1.3 ± 0.25	0.96 ± 0.41	0.42 ± 0.26	0.000*
Pain score	1.8 ± 0.65	1.5 ± 0.51	0.72 ± 0.16	0.000*
MIO[f] (mm)	37.3 ± 0.51	42.9 ± 4.0	49.8 ± 2.9	0.000*
CRP[g] (mg/ml)	35.0 ± 1.7	22.1 ± 9.2	6.7 ± 0.48	0.000*
ESR[h] (mm/h)	106.3 ± 32.1	65.4 ± 29.8	16.0 ± 3.8	0.000*
Synovial enhancement score	4.0 ± 0.0	2.6 ± 1.5	1.1 ± 1.1	0.003**
Effusion score	3.3 ± 0.51	1.3 ± 1.3	0.0 ± 0.0	0.000*
Pannus score	2.6 ± 1.3	0.29 ± 0.72	0.0 ± 0.0	0.000*
Erosion score	2.3 ± 1.0	0.18 ± 0.39	0.0 ± 0.0	0.000*
Total MRI[i] score	12.3 ± 1.8	4.5 ± 2.9	1.1 ± 1.1	0.000*

[a] Juvenile idiopathic arthritis.
[b] Polyarticular.
[c] Oligoarticular.
[d] Number.
[e] Child health assessment questionnaire.
[f] Maximal interincisal opening.
[g] C-reactive protein.
[h] Erythrocyte sedimentation rate.
[i] Magnetic resonance imaging.
* Highly significant.
** Significant, values are in mean ± SD.

well as different MRI scores among patients with JIA which are mentioned in Table 4.

Synovial enhancement score which is a reflection of synovial inflammation as well as the effusion score showed statistically significant positive correlations with disease activity score; $r = 0.83$, $p < 0.001$, $r = 0.79$ $p < 0.001$ and the marker of inflammation; CRP, $r = 0.86$, $p < 0.001$, $r = 0.82$, $p < 0.001$, respectively. In addition pannus and erosion scores were positively correlated to C-HAQ; $r = 0.33$, $p < 0.05$ for pannus, $r = 0.39$, $p < 0.05$ for erosions.

A negative correlation was observed between total MRI score on one hand and age, age at disease onset and disease duration, although it failed to reach statistical significance ($p > 0.05$), while this correlation was significantly positive with disease activity score, C-HAQ, pain score and CRP (Table 5).

4. Discussion

Patients with JIA are at high risk of developing arthritis of the TMJ.[13] Arthritis of TMJ is a concern, particularly in patients who are growing, because the mandibular growth plate is located below the fibrocartilage and therefore is susceptible to damage from inflammation.[14]

It has been demonstrated that clinical manifestations such as pain at rest, local morning stiffness, decreased mouth

Table 4 The correlation between MIO and different disease parameters in patients with JIA.

	MIO[a,*]	
Disease activity score	*r*	−0.85
C-HAQ[b]	*r*	−0.84
Pain score	*r*	−0.72
C-reactive protein	*r*	−0.87
Synovial enhancement score	*r*	−0.74
Total MRI[c] score	*r*	−0.80

[a] MIO: maximal interincisal opening.
[b] C-HAQ: child health assessment questionnaire.
[c] MRI: magnetic resonance imaging.
[*] Highly significant.

Table 5 The correlation between total MRI score and disease variables in patients with JIA.

	Total MRI score[a,*]	
Disease activity score	*r*	0.81
C-HAQ[b]	*r*	0.74
Pain score	*r*	0.72
C-reactive protein	*r*	0.88

[a] MRI: magnetic resonance imaging.
[b] C-HAQ: child health assessment questionnaire.
[*] Highly significant.

opening, pain during joint movement may point at TMJ involvement among patients with JIA.[4] Our study showed that TMJ pain at rest, pain on jaw movement, tenderness on palpation and crepitations were present in 17.5%, 20%, 25% and 20% of JIA patients, respectively. These findings are supported by several authors[15–17] except for the frequency of crepitations which was contradicted by one study as they have detected some kind of joint noise in 49% of JIA patients.[18]

Limited MIO has been recorded in 23.3% of JIA patients,[19] our results were nearly the same (25%). One other study had revealed that the maximal opening capacity of patients was at the lower range of normal but it was significantly decreased in JIA patients compared to controls.[20] Our findings are consistent with them. In addition; MIO was significantly lower among patients with systemic JIA than the polyarticular type and it was the highest among patients with oligoarticular disease. A result that was confirmed by a report which noted a better MIO among oligoarticular JIA patients than the polyarticular type.[21]

A former study had concluded that restricted MIO was the most frequent clinical finding occurring in nearly one third of patients (33.3%) and it was more frequent among JIA patients with long standing and active disease, they suggested that impaired function of the TMJ and surrounding muscles during activity explains the association with disease activity and possibly with severity.[10] This research is ongoing with them as decreased MIO was one of the most frequent signs of TMJ involvement in patients with JIA (25% of cases) and it was significantly decreased for patients with active disease compared to those with no activity. Reduced MIO also showed high significant negative correlations with disease activity score and child health assessment questionnaire.

The mean MIO was significantly decreased among JIA patients with TMJ pain in comparison to patients without pain in this work. Moreover, there was a significant negative correlation between reduced MIO and pain score. This may reflect pain limited movement.[21]

The lack of symptoms and abnormalities on TMJ examination does not exclude the presence of TMJ disease, so radiological examination on regular basis is necessary.[14,22] MRI is considered the gold standard for the study of TMJ disease because it evaluates bone and depicts intraarticular fluid. Contrast enhanced MRI after injection of gadolinium demonstrates an inflammatory state in the joint.[20,23]

In this study 80% of JIA cases showed TMJ affection using post-contrast MRI. A recent report has supported our results as they have recorded a frequency (75%) of TMJ arthritis using gadolinium enhanced MRI among their patients.[14] They mentioned that it is at the higher end of previously reported ranges 17–87%[13,24] which indicates that TMJ is one of the most commonly involved joints in patients with JIA. While a former study had detected TMJ abnormalities among 45% of patients with JIA diagnosed by orthopantogram.[16] They said that the frequency of TMJ involvement depends on the radiographic tool used to find out TMJ disease. Contrast enhanced MRI may be an efficient method in diagnosing inflammatory changes in TMJ.[12]

Several authors have reported that patients in their study were diagnosed to have JIA due to arthritis in joints other than the TMJ and they were surprised to see that the majority already had the signs of TMJ involvement on MRI examinations. They detected synovial enhancement in 93%, erosions in 71% and pannus in 26% of TMJs.[12] This study is ongoing with them regarding the high frequency of temporomandibular joints with synovial enhancement (77.5%) but it detected lower frequencies of erosions (17.5%) and pannus (22.5%). Synovial enhancement was visualized in 72% of patients with JIA in a more recent report[25] which also confirms our results that had included 80% of cases.

The present work had observed effusion in 47.5% of TMJs among patients with JIA. On the contrary a previous study, showed a higher frequency (57%) for TMJ effusion using MRI.[21] This may be due to that their patients were younger at disease onset than JIA patients in this study. Young age at disease onset is considered one of the causes of bad prognosis regarding TMJ.[26] While a single report had found that by MRI, effusion was present in only 10% of TMJs.[23]

Our results had demonstrated symptoms and signs of TMJ involvement in 35% and 62.5% of JIA patients, respectively. A finding that is supported by a previous study which stated that TMJ disease may occur in many JIA cases with activity continuing for many years without presenting symptoms.[12] Other reports had noted that despite increased TMJ changes by MRI, little symptoms could be detected; they suggested that symptoms under estimate the inflammatory state of TMJ among patients with JIA.[16,20] Recently several authors discovered that all patients with clinical signs on TMJ examination had TMJ disease on post contrast MRI assessment.[23] This study is consistent with them as we have detected a significant association between MRI findings and signs of TMJ involvement while this association was not significant regarding symptoms. Our results are in accordance with a previous study which had proposed that clinical examination seems to be more reliable than asking for symptoms of TMJ affection, since all patients show-

ing findings by clinical examination also had pathological signs on post contrast MRI. So it seems more reasonable to select patients without clinical findings for MRI examination.[12]

Several studies had concluded that JIA disease activity and severity could be reflected in TMJ involvement. They reported that inactive disease state prevents TMJ abnormalities among patients with JIA and this needs institution of more aggressive therapy that will decrease disease activity. Moreover, they recorded a significant association between abnormal MRI findings of TMJs and disease activity among patients with JIA.[23,27,28] The present study had pointed to a significant increase in the mean of synovial enhancement, effusion and total MRI scores in JIA patients with active disease compared to those who were not in the active phase of the disease .Our results have also showed a significant positive correlation between synovial enhancement, effusion and total MRI scores on one hand with disease activity score on the other hand. Moreover C-HAQ was positively correlated with both pannus and erosion scores. On the contrary, a former study found no correlation between disease characteristics such as disease activity, disease duration and radiological manifestations of TMJ abnormalities in patients with JIA.[10] This difference with our results may be due to that they have examined TMJs by orthopantogram while contrast enhanced MRI was the tool used to diagnose TMJ disease in this study.

Some reports had noted that the severity of TMJ involvement was more pronounced in systemic as well as polyarticular JIA and that the worst out come for TMJ affection was detected in patients with systemic or polyarticular disease.[13,26] The results of this study are ongoing with them as the total MRI score of TMJ abnormalities was significantly higher among patients with systemic followed by polyarticular then oligoarticular JIA. This may be explained by an opinion which states that patients with oligoarticular arthritis are more likely to have longer periods of inactive disease compared to the polyarticular type.[29] Our results are in accordance with this opinion as disease activity score was significantly higher for patients with systemic followed by polyarticular JIA while those with oligoarticular type showed inactive disease.

It had been reported that studies correlating changes of MRI results in joints other than the TMJ with histological findings have shown that enhancement of synovial membrane on using gadolinium enhanced MRI is related to synovial inflammation, animal studies of TMJ arthritis comparing histological findings with MRI support this conclusion.[12,30] Our study had pointed to a high significant positive correlation between synovial enhancement score and CRP levels as a marker of inflammation.

5. Conclusions

TMJ arthritis could be detected in most cases of JIA using contrast enhanced MRI. Systemic and polyarticular JIA subtypes showed the worst results regarding MRI scores. Contrast enhanced MRI may be recommended in JIA patients especially those with no clinical signs of TMJ disease. TMJ examination must be considered during follow up of patients with JIA. Once TMJ arthritis is discovered; synovitis is in need to be controlled to avoid progressive joint damage. TMJ may have to be kept in consideration during categorizing patients with JIA.

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