Early diagnosis of temporomandibular joint arthritis in children with juvenile idiopathic arthritis. A systematic review



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Abstract

Aim Asymptomatic TMJ arthritis in juvenile idiopathic arthritis (JIA) patients may cause damage and deformity of the joint. The clinical manifestation of early-stage TMJ arthritis is not characteristic. Clinical findings commonly appear in a late stage of TMJ involvement, but they can also be masked by antirheumatic therapy. The absence of clinical symptoms, and the lack or insufficient clinical signs do not provide reliable information about the TMJ involvement. The aim of the study was to conduct a systematic review of the evidence for clinical symptoms and signs of early-stage TMJ arthritis, as well as for correlation between clinical parameters and TMJ abnormalities imaging in JIA patients.

Methods Study design: A systematic review of papers published from 1998 to 2019 regarding early clinical and imaging findings of TMJ arthritis in JIA patients.

Results The search resulted in 292 studies. Eleven publications were included in the review.

Conclusions Clinical signs and symptoms do not allow to detect the early stage of TMJ arthritis in JIA patients. To monitor individual orofacial development, periodic TMJ clinical examination should be a part of an evaluation of JIA children's growth. There is a need to develop clinical management guidelines, as well as diagnosis standards of clinical and imaging TMJ examination for JIA children, considering their developmental age.

KEYWORDS Temporomandibular joint; Juvenile idiopathic arthritis; Temporomandibular joint arthritis.

Introduction

Juvenile Idiopathic Arthritis (JIA) is the most common autoimmune systemic inflammatory disease of unknown aetiology affecting the connective tissue at the developmental age. The disease begins before the 16th birthday and persists for at least six weeks [Petty et al., 2004]. Depending on the clinical manifestation during the first six months, in accordance with the criteria of the International League of Associations for Rheumatology (ILAR), it can be classified as follows.

- Systemic arthritis: arthritis of one or more joints with fever, rash and frequent involvement of internal organs.
- Oligoarthritis: arthritis affecting ≤ 4 joints during the first six months of the disease:
  - persistent, affecting nor more than four joints throughout the whole course of the disease course;
  - extended, affecting more than four joints after the first six months of disease.
- Polyarthritis: arthritis affecting ≥ 5 joints during the first six months of the disease:
  - seronegative (polyarthritis RF-), negative rheumatoid factor (two or more tests for RF at least three months apart during the first six months of the disease);
  - seropositive (polyarthritis RF+), positive rheumatoid factor.
- Enthesitis related arthritis: arthritis and enthesitis.
- Psoriatic arthritis: arthritis and psoriasis.
- Undifferentiated arthritis: not meeting the criteria of any of the above types or more than one of the above types [Petty et al., 2004].

During this immune-mediated diseases, the synovial tissue of one or more joints is affected. The temporomandibular joint (TMJ) obeys the same biologic laws as do other synovial joints in the body. TMJ arthritis may accompany the involvement of other joints or be the first or only one [Martini et al., 2001; Scolozzi et al., 2005; Argyropoulou et al., 2009; Cedströmer et al., 2013]. The temporomandibular joint is surrounded by a thin, loose fibrous capsule, which attaches to the articular eminence, the articular disc and the neck of the mandibular condyle. The articular disc divides the joint into two compartments (synovial cavities). The articular capsule consists of two layers:

1) external, fibrous, composed of collagen fibers;
2) internal, synovial, which produces fat and mucin containing thick and sticky synovial fluid.

The fluid, filling the cavities, moisturises joint fibrocartilages and reduces friction thus facilitating joint mobility [Scolozzi et al., 2005; Cedströmer et al., 2013]. In the TMJ, similarly to other synovial joints, in the initial stage of the disease, the synovial membrane becomes inflamed, swollen and thickened. Continuous inflammation leads to the formation of pannus. It is suggested that pannus primarily, by isolation of the

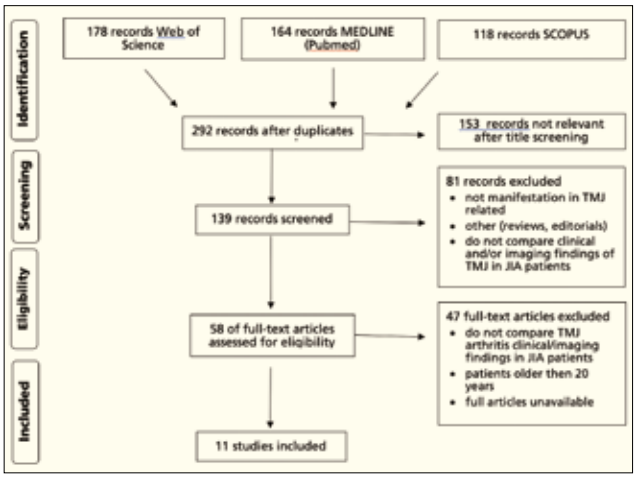


FIG. 1 PRISMA flowchart of the study selection process

articular cartilage from the synovial fluid, impairs nutrition and prevents the elimination of its metabolism products, contributing to an irreversible degeneration of non mineralised cartilage. Furthermore, pannus can accumulate osteoclast precursor cells, which can cause demineralisation and collagen matrix degradation of articular bone, leading to bone resorption and further to condylar destruction [Pedersen et al., 2001; Twilt et al., 2008].

The clinical manifestation of early-stage of TMJ arthritis is not characteristic. The absence of clinical symptoms, and the lack or insufficient clinical signs do not provide reliable information about the TMJ involvement [Weiss et al., 2008; Argyropoulou et al., 2009; Hu et al., 2009; Müller et al., 2009; Mohammed et al., 2012; Cedströmer et al., 2013; Keller et al., 2015; Zwir et al., 2015; Kirkhus et al., 2016]. Asymptomatic in the initial stage, TMJ inflammation may cause damage and deformity of the joint, leading to impaired function and mobility. In addition, the involvement of the mandibular growth zone located below the fibrocartilage, leads to mandibular growth disturbances.

Condylar damage may be present early in the disease course and may progress without clinically detectable symptoms or signs [Twilt et al., 2008; Stoll et al., 2018]. Clinical findings commonly appear in a late stage of TMJ involvement [Cedströmer et al., 2013; Kirkhus et al., 2016; Tolend et al., 2018], but they can also be masked by antirheumatic therapy [Keller et al., 2015; Tolend et al., 2018]. Chronic inflammation of the temporomandibular joint results in a degenerative alteration of the joint and the presence of subjective symptoms and clinical signs, such as pain upon palpation, sounds upon mouth opening like cracks and crepitations, reduced maximum interincisal opening (MIO), limited movements and jaw deviation. Moreover, the involvement of the mandibular growth zone may affect the mandibular development and thus cause irreversible morphological disturbances [Cedströmer et al., 2013; Kuseler et al., 2005]. The degree of such changes is closely related to the potential growth of the mandible and depends on the child's age at onset of the disease, disease duration, JIA category and course [Assaf et al., 2013; Cedströmer et al., 2013]. The most intense mandible growth occurs in the first 6 years of age and, in its later development, physiologically lasting until 21 years of age, the mandible growth potential drops to 15%. Thus, the younger the child, the greater the morphological disturbances can be present [Kuseler et al., 2005]. If the process is unilateral or the disease is more severe in one of the joint, facial asymmetries and jaw deviation can be present [Twilt et al., 2008; Hu et al., 2009; Ringold and Cron, 2009; Arvidsson et al., 2010; Assaf et al., 2013; Cedströmer et al., 2013; Koos et al., 2014; Keller et al., 2015; Stoll et al., 2018]. Bilateral long-lasting TMJ arthritis negatively affects the growth and development of the mandible results in the following types of malocclusion: mandibular micrognathia, retrognathia, posterior rotation, open skeletal bite and bite disorders [Arvidsson et al., 2010; Koos et al., 2014; Keller et al., 2015]. The incidence of TMJ involvement in JIA patients is often underestimated. According to the literature, the prevalence of TMJ arthritis in those patients varies from 17 to 87% [Pedersen et al., 2001; Arabshahi and Cron, 2006; Twilt et al., 2008; Weiss et al., 2008; Arvidsson et al., 2010; Abramowicz et al., 2013; Stoll et al., 2018]. More common is the bilateral TMJ involvement, but in 27–50% of patients is unilateral [Huntjens et al., 2008; Twilt et al., 2008]. Probably TMJ arthritis starts as an asymmetric feature and becomes increasingly symmetric in the later stages [Hu et al., 2009]. The wide range of TMJ arthritis prevalence can be explained by many factors, e.g. the use of different diagnostic methods, non-standardised diagnostic criteria, difficulties in TMJ examination in paediatric patients (mainly due to lack of cooperation), diseases duration, JIA type and activity (periods of remission and exacerbation), and also absence of clinically detectable symptoms or signs in the early stage of the disease [Cedströmer et al., 2013; Zwir et al., 2015; Kirkhus et al., 2016]. Among JIA children, females dominate, with distribution 3:2 [Arabshahi and Cron, 2006; Twilt et al., 2008]. Imaging diagnosis of TMJ involvement is an important tool in the assessment of TMJ arthritis in JIA patients. Currently, magnetic resonance imaging (MRI) is the gold standard in the diagnosis of TMJ arthritis in this group of patients and enables to detect both early, acute, inflammatory as well as long-lasting, chronic, destructive changes [Weiss et al., 2008; Abramowicz et al., 2011; Meyers and Laor, 2013; Koos et al., 2014; Zwir et al., 2015; Stoustrup et al., 2017]. But, for MRI examination, especially in small or uncooperative children, general anaesthesia or conscious sedation is required [Weiss et al., 2008; Abramowicz et al., 2011]. Due to the risk of irreversible and unfavourable morphological and functional changes, special attention should be paid to TMJ in JIA children [Cedströmer et al., 2013; Stoustrup et al., 2017]. In an early stage of the disease, the diagnosis of TMJ inflammation may be difficult, as the patients usually do not complain about pain, and there is a lack of clinical signs of TMJ involvement [Hu et al., 2009].

The aim of the study was to conduct a systematic review of the evidence for early-stage of TMJ arthritis clinical symptoms and signs, as well as for correlation between clinical parameters and TMJ abnormalities imaging in JIA patients.

Materials and methods

Search strategy

According to inclusion criteria, selection method and planned methodology of data analysis and synthesis [Higgins et al., 2011], publication search strategy was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Fig. 1) [Moher et al., 2009].

The following electronic medical databases were searched: MEDLINE (by PubMed), SCOPUS and Web of Sciences. The

Reference	Country	# of patients age at examination	Females	JIA duration	Age at diagnosis (years)	Type of JIA (% of patients)
Savioli et al. (2004)	Brazil	36 10.8 y (4.7 – 20)	72.2%	7 (1 – 16) years	4.6 y	Systemic 62% - Oligoarticular extended 19% - Polyarticular RF neg 19%
Jank et al. (2007)	Germany/ Austria	48 female 10.2 y male 11.5 y	60.4%	5.17 years	Unknown	Systemic 8.3% - Oligoarticular 39.6% Enthesitis-related arthritis (ERA) 14.6% Polyarticular - 22.9% - Psoriatic arthritis 2.1% - Unclassified 12.5%
Weiss et al. (2008)	USA	32 female 8.4 y (1.9-17.2) male 9.9 y (1.5-13.8)	78%	3 (0.5-18) months	Male 9.9 y (1.5-13.8) Female 8.4 y (1.9-17.2)	Systemic 3% - Oligoarticular 34% Enthesitis-related arthritis (ERA) 16% Polyarticular RF neg 22% - Polyarticular RF pos 9% - Psoriatic arthritis 13% Unclassified 3%
Müller et al. (2009)	Switzerland	30 9.8 y (2.8-16.9)	53%	2.4 (0.1-12.3) years	5.5 y (1.1 – 14.9)	Oligoarticular persistent 33% - Oligoarticular extended 7%- Enthesitis-related arthritis (ERA) 13% - Polyarticular RF neg 43% - Psoriatic arthritis 3%
Hu et al. (2009)	Belgium	100 10.5 y (1.7 – 19.4)	65%	2.96 (0.2-15) years	Unknown	Systemic 12% - Oligoarticular 39% Enthesitis-related arthritis (ERA) 22% Polyarticular RF neg 24% - Polyarticular RF pos 1% - Psoriatic arthritis 2%
Leksell et al. (2008)	Sweden	41 13.6 y	70.7%	7.7 (0-15) years	5.11 y (1-15)	Systemic 12% Oligoarticular 22% Enthesitis-related arthritis (ERA) 2% Polyarticular 37% - Psoriatic arthritis 17% - Unclassified 15%
Mohammed et al. (2012)	Egypt	40 14.1 y (8.5 – 17)	65%	4.8±2.4 years	9.3±2.8 y	Systemic 15% - Oligoarticular 17.5% Polyarticular 67.5%
Cedstrőmer et al. (2013)	Sweden	266 10.0 y	76%	2.9 years	7.1 y	Systemic 2% - Oligoarticular persistent 36% - Oligoarticular extended 14% Enthesitis-related arthritis (ERA) 2% Polyarticular RF neg 26% - Polyarticular RF pos 6% - Psoriatic arthritis 9% Unclassified 5%
Assaf et al. (2013)	Germany	20 Female 10.9 y Male 12.0 y	85%	Female 4.4 years Male 3.0 years	Female 6.5 y Male 9 y	Systemic 5% - Oligoarticular 50% Enthesitis-related arthritis (ERA) 10% Polyarticular10% - Psoriatic arthritis 25%
Keller et al. (2015)	Switzerland	76 9.7 y (1.9-18.6)	55%	2.4 (0-15.7) years	5.5 y (1-14.9)	Systemic 1% - Oligoarticular persistent 32% - Oligoarticular extended 15% Enthesitis-related arthritis (ERA) 12% Polyarticular RF neg – 33 Psoriatic arthritis 3% Unclassified 5%
Zwir et al. (2015)	Brazil	75 - 12.4 y (5-19)	66.7%	6 (1-16) years	5.8 y (0.6-17)	Oligoarticular 52% Polyarticular 48%

TABLE 1
Studies included in the present systematic review.

search strategy was carried out using the indexation of MeSH (Medical Subject Headings) synonyms and using Boole logical operators. The search engines used the following terms: ("juvenile idiopathic arthritis" OR "JIA") AND ("temporomandibular joint" OR "temporomandibular disorder" OR "TMJ" OR "TMD") AND ("radiographic examination" OR "orthopantomogram" OR "OPG" OR "ultrasonography" OR "US" OR "magnetic resonance imaging" OR "MRI" OR "computed tomography" OR "CT" OR "conical tomography" OR "cone-beam computed tomography" OR "CBCT"). The last search was made on June 5th, 2019. To identify further research related to the discussed issue, the references of previously found articles were also checked.

Inclusion/exclusion criteria

The analysis included publications that met the following criteria: concerned clinical and control studies, and correlation of clinical findings with TMJ imaging results (radiographic examination; orthopantomogram, OPG; ultrasonography, US; MRI; computed tomography, CT; cone-beam computed tomography, CBCT) of the temporomandibular joint in juvenile idiopathic arthritis patients. The studied publications covered the last 20 years, i.e., January 1998 – May 2019. Editorials, commentaries, letters to editors and non-human studies, reviews, studies on patients over 20 years old and duplicates were excluded from the study. The language of publication was not an exclusion criterion.

Study selection

PICO (Patient/Population, Intervention, Comparison group and Outcome(s)) Criteria were used to screen the studies by title and abstract [Moher et al., 2009]. In addition, to identify additional publications not found in the databases the

Reference	JIA patients		Control group	
	# of patients age (years) % of female	Clinical symptoms and signs OR imaging findings	# of patients age (years) % of female	Clinical symptoms and signs OR imaging findings
Savioli et al. (2004)	36 10.8 (4.7 – 20) 72.2	Helkimo index clinical dysfunction 94% mild 50% moderate 13% severe 30%	13 9.4 (5.4 – 14) 69.2	Helkimo index clinical dysfunction 30% mild 23% moderate 7% severe 0%
Mohammed et al. (2012)	40 14.1±2.3 65	Symptoms: 35% TMJ pain 17.5% TMJ crepitation 7.5% Signs 62.5% TMJ tenderness on palpation 25% TMJ crepitation on movement 20% decreased MIO 25% MIO = 43.3±5.0 5mm	10 14.5±2.8 60	Symptoms 0% Signs 0% MIO = 53.4±1.1 mm
Leksell et al. (2008)	41 13.6 70.7	Symptoms: TMJ pain at rest 22% TMJ pain at chewing 71% TMJ pain at jaw opening 68% Signs: MIO <40 mm 32% TMJ sounds 78% TMJ palpation pain 72% muscle palpation pain6 0%	41 31.1 70.7	Symptoms: TMJ pain at rest 0% TMJ pain at chewing 0% TMJ pain at jaw opening 0% Signs: MIO <40 mm 0% TMJ sounds17% TMJ palpation pain 2% muscle palpation pain 12%
Hu et al. (2009)	32 11.1 (3.3 – 19.4) 62.5	condylar damage 75%	32 11.1 (3.3 – 19.4) 62.5	condylar damage 15.6%

TABLE 2 Clinical findings of TMJ inflammation among JIA patients and healthy controls-data abstracted from studies included in the systematic review.

reference section of each study was hand-searched. The first step of study selection was to analyse only the titles obtained from databases, and the next one to read the abstracts of selected publications [Moher et al., 2009]. The final decision to include or exclude the publication for further analysis was based on the analysis of full texts of the selected papers. Study selection was performed independently by two researchers (T. P-K, E. P-W), who earlier, based on 20% of publications, were calibrated regarding the application of inclusion criteria for further analysis. The agreements between reviewers were found to be good (k = 0.85).

Data extraction

One reviewer (T. P-K) extracted the data from the included studies. To eliminate bias, the reviewer (E. P-W) was responsible for checking the extracted data.

Additional information

The heterogeneity between studies made it impossible to carry out a meta-analysis.

Results

Study selection

The systematic search of medical databases, after eliminating repetitions, resulted in 292 publications, which corresponded to the assumed search criteria. Based on information provided in the study titles and abstracts, an initial selection of reports was carried out. A total of 234 articles were excluded for various reasons, including articles focused on topics other than TMJ arthritis in JIA patients; articles did not relate to clinical and/or imaging findings of TMJ arthritis; review articles and; editorial papers. The remaining 58 were screened on reading the full-text. Another 47 articles were excluded, because: they did not compare TMJ arthritis clinical/imaging findings in JIA patients; examined patients were older than 20 years; full articles were unavailable. None of the articles was included from hand searched bibliographic references. Eleven publications were qualified for further analysis [Savioli et al., 2004; Jank et al., 2007; Leksell et al., 2008; Weiss et al., 2008; Hu et al., 2009; Müller et al., 2009; Mohammed et al., 2012; Cedströmer et al., 2013; Assaf et al., 2013; Keller et al., 2015; Zwir et al., 2015] (Fig. 1).

Study characteristics

A summary of the characteristics of the selected studies is listed in Table 1. In the publications included in the hybrid narrative review, girls account for about 68% of examined JIA patients. TMJ clinical parameters showed that the frequency of subjective symptoms, signs of TMJ involvement, as well as imaging TMJ abnormalities are very diversified in the considered publications. In most of the studies, the JIA duration was not relevant in the patient's selection to the study group, but Weiss et al. [2008] included newly diagnosed patients only, whose JIA duration did not exceed 18 months. In others JIA duration varies from 0 to 16 years. Except for the studies of Jank et al. [2007] and Hu et al. [2009] all others studies gave the information about child's age at JIA diagnosis.

Clinical findings of TMJ inflammation among JIA patients and healthy controls

Savioli et al. [2004] for the assessment of TMJ dysfunction used the Helkimo index [Helkimo, 1974], which consists of an anamnestic index (Ai) and a clinical dysfunction index (Di). Anamnestic information related to patient-reported symptoms is collected with standardised questions to the patients and/or parents. Clinical dysfunction index evaluates TMJ pain and pain on movement of the mandible, mandibular mobility, TMJ function, muscle pain on a three-point scale of increasing severity. By the anamnestic and clinical data, the index value

is calculated. Mohammed et al. [2012] and Leksell et al. [2008] did not use any validated measure but noted the presence or absence of signs and symptoms only. In all three publications, subjective symptoms and clinical signs of TMJ arthritis were significantly more frequent in JIA patients compared to healthy controls. Furthermore, Mohammed et al. [2012] reported

Reference	Subjective symptoms	Clinical signs		Medical imaging	
				Imaging meth.	TMJ involvement *(% of TMJs)
Jank et al. (2007)	TMJ pain on palpation 22.9% - TMJ crepitation 22.9% TMJ clicking 14.5% - History of closed lock of the TMJ 27.1% - Pain on palpation (masseter muscle) 20.8% - Pain on palpation (temporal muscle) 4.2% - Deviation of mouth-opening movement 20.8%			US	Disc dislocation 55.5% (% of TMJs)*
Weiss et al. (2008)	Abnormal: 19 TMJ pain at rest – 0 TMJ pain with chewing – 16 TMJ clicking – 13 TMJ locking – 3	Abnormal: 41% Decreased MIO 22% - TMJ clicking 6% - TMJ tenderness to palpation 13% - TMJ tenderness with opening 13% - Absent translation 6% Asymmetric opening 19% - Micrognathia 0%		MRI US	MRI: Acute arthritis 75% bilateral 83% unilateral 17% Chronic arthritis 69% bilateral 68% unilateral 32% US: Acute arthritis 0% Chronic arthritis 28% bilateral 44% unilateral 56%
Hu et al. (2009)	Abnormal: 55% - Decreased MIO 28% - Muscle tenderness 22% - Deviation of mouth-opening movement 21% - TMJ tenderness 14% TMJ sounds 10%			DPT in 32% of patients	Condylar damage 75% bilateral 74% unilateral 26%
Müller et al. (2009)	Rheumatologic Active arthritis 43% 50% unilateral Chronic arthritis 50%	Orthodontic Active arthritis 53% 24% unilateral Chronic arthritis 47%		MRI US	MRI: Active arthritis 63% bilateral 68% unilateral 32% Chronic arthritis 30% US Active arthritis 28% bilateral 50% unilateral 50% Chronic arthritis 24%
Mohammed et al. (2012)	Abnormal: 62.5% - TMJ tenderness on palpation 25% - TMJ crepitation on movement 20% - Decreased MIO 25%			MRI	Arthritis 80% - Synovial enhancement 80% Joint effusion 65% - Pannus & erosion 25%
Cedstrőmer et al. (2013)	Abnormal 32% – 76% in different categories JIA	Abnormal 57.7% – 92% in different categories JIA		OPT	OPT in half of patients (n=130) Condylar alternation 37%
Assaf et al. (2013)	Deviation of the chin to the middle of the face 75% - Deviation in mouth opening 70% - Reduced MIO of less than 30 mm 40% - Reduced protrusion 5% Reduced laterotrusion 0% - TMJ clicking during mouth opening 35% TMJ crepitation 5% - TMJ pain on palpation 10%			HR-US	Arthritis 77.5% - Synovial width 34.4% - Effusion int he join space 12.5% - Width of the articular disc 30% - Condylar erosion 77.5% - Irregularities on bone surface 25%
Keller et al. (2015)	Pain 37%	Rheumatologic TMJ pain 29% MIO 44.8 mm (32-59%) MIO smaller then 10th percentile 17% Mandibular retrognathism 16% Mandibular asymmetry 37%	Orthodontic TMJ pain 46% - Muscles pain 47% - TMJ clicking 20% TMJ crepitation 21% MOC 44.6 mm (29-59%) MOC smaller then 10th percentile 18% - Mandibular retrognathism 17% - Mandibular asymmetry 41%	MRI	Arthritis 71% bilateral 70% unilateral 30% Active arthritis 68% Condylar deformity 33%
Zwir et al. (2015)	Abnormal: 1st evaluation 37%- 2nd evaluation after one year 14.6% TMJ pain at rest 13.3 %; 5.33% TMJ pain at function – 26.6; 13.33 TMJ sounds 25.3%; 6.6% Decreased MIO 6.6%; 2.66%	Abnormal: 1st - 46.5% 2nd - 38.6% Pain on TMJ palpation 33.3%; 5.3% - Decreased MIO 33.3%; 13.33% TMJ crepitus 9.33%; 8.0% MIO = 21 – 58 mm; 30– 61 mm MIO < 4mm – 25; 13.3%		MRI	Synovial enhancement 93.7%; 86.7% bilateral 89.3%; 77.3% Erosion 19.3%; 20%

TABLE 3 Correlation between clinical parameters and imaging examinations-data abstracted from studies included in the systematic review.

significantly lower maximum interincisal opening (MIO) in JIA patients comparing to healthy controls and a significant negative correlation between MIO and clinical and functional parameters among JIA patients (Table 2).

Clinical findings of TMJ inflammation among patients with different JIA type

Taking account the JIA category, Mohammed et al. [2012] showed that patients with systemic diseases onset JIA had the worst results regarding clinical diseases parameters followed by the polyarticular type in comparison to patients with oligoarticular diseases. MIO was significantly lower among patients with systemic diseases than the polyarticular type, and it was the highest among patients with oligoarticular JIA. Also, higher frequency of TMJ dysfunction in systemic JIA type was noted Savioli et al. [2004] . It must be stressed that in those two publications [Savioli et al., 2004; Mohammed et al., 2012] the patients were diagnosed with systemic, polyarticular and oligoarticular JIA type only. Cedstrőmer et al. [2013], using the Helkimo index [Helkimo, 1974] to assess TMJ dysfunction, also compared clinical findings between patients with different JIA type. Patients diagnosed with psoriatic arthritis had significantly more and the most advanced subjective symptoms and clinical signs, while patients with persistent oligoarthritis had the fewest. Moreover, Cedstrőmer et al. [2013] OPGs did not confirm the relationship between the degree of condylar alternation and the JIA type. The different result was obtained by Mohammed et al. [2012], who noted the positive correlation between the advancement of clinical signs and TMJ abnormalities found by MRI examination.

Imaging findings of TMJ inflammation among JIA patients and healthy controls

Reports regarding TMJ imaging between JIA patients and healthy children are rare, and only one such publication was included in this systematic review. Hu et al. [2009] conducted the radiographic investigation (dental pantomogram) among 32 JIA patients with TMJ involvement (at least one symptom compatible with TMJ arthritis was present) and 32 healthy age- and gender-related children, in whom X-rays were taken as a part of orthodontic treatment. The study showed that condylar lesions were significantly more prevalent in JIA patients (Table 2).

Correlation between clinical parameters and pathologic imaging findings

The pain of TMJ and/or masticatory muscles is one of the symptoms of TMJ involvement in JIA patients. In seven analysed publications [Jank et al., 2007; Weiss et al., 2008; Müller et al., 2009; Assaf et al., 2013; Cedströmer et al., 2013; Keller et al., 2015; Zwir et al., 2015] authors did not note a statistical relationship between pain and TMJ abnormalities imaging. According to these authors, pain is not conclusive exponents of an ongoing TMJ arthritis in JIA patients. Different results were obtained by Mohammed et al. [2012], who noted a significant association between pain on palpation of TMJ and contrast-enhanced MRI TMJ abnormalities (Table 3).

The reviewed publications show that of all clinical parameters the maximal interincisal mouth opening (MIO) and jaw deviation are of most importance. Other symptoms do not seem characteristic of TMJ arthritis in JIA patients. Müller et al. [2009] and Mohammed et al. [2012] showed a significant negative correlation between the MIO and clinical, functional, as well as different MRI scores among JIA patients. Zwir et al. [2015] and Keller et al. [2015], using MRI technique, did not show such relationship. Also, Cedstrőmer et al. [2013] did not show it with the OPG imaging. Also, Mohammed et al. [2012] reported significantly decreased MIO among JIA patients with TMJ pain in comparison to patients without pain, and a significant negative correlation between reduced MIO and pain score.

Weiss et al. [2008], conducting their research among 32 newly-diagnosed children showed that both the subjective symptoms reported by patients and the results of the physical examination are not conclusive of TMJ arthritis. In 68% of examined children no jaw deviations was present, and in 71% of those in whom MRI showed acute TMJ inflammation no subjective complaints were noted.

Discussion

Early clinical symptoms of TMJ involvement in JIA patients are not characteristic. The five classical signs of inflammation, such as rubor, calor, dolor, rubor, tumor, and functio laesa (redness, temperature, pain, swelling, loss of function), are rarely associated with TMJ synovitis in JIA patients [Cedströmer et al., 2013; Koos et al., 2014]. Usually, patients do not complain about pain, there is no swelling, and a slight limitation of MIO and/or jaw mobility may not be noticeable. Unfortunately, due to the asymptomatic course, in approximately 2/3 of patients TMJ involvement is detected very late [Assaf et al., 2013; Tzaribachev et al., 2010], but the progressive character of the disease may lead to the permanent and irreversible joint destruction [Arabshahi and Cron, 2006; Argyropoulou et al., 2009].

The TMJ arthritis prevalence indicates the need to implement clinical trials considering patients' complaints, clinical and imaging findings not only to diagnose the early stage of TMJ arthritis but also to periodically monitor the TMJ function as well as mandible growth and development in JIA patients [Stoustrup et al., 2017; Tzaribachev et al., 2010]. As shown in the reviewed publications, TMJ pain is not a specific and characteristic feature of TMJ synovitis [Weiss et al., 2008; Abramowicz et al., 2013; Cedströmer et al., 2013]. Spontaneous pain of this joint is rare, and the majority of patients reported pain only during mouth movements and/or chewing. Usually, the TMJ pain is a late symptom of an ongoing chronic TMJ arthritis [Stoustrup et al., 2017]. As in the case of pain, available literature presents various views on characteristic clinical signs of the early stage of TMJ arthritis [Müller et al., 2009; Tzaribachev et al., 2010; Assaf et al., 2013; Cedströmer et al., 2013; Keller et al., 2015]. Some authors have shown that limited maximum interincisal opening (MIO) and jaw deviation may be highly sensitive and characteristic markers of TMJ synovitis [Abramowicz et al., 2013; Keller et al., 2015; Stoll et al., 2018]. Others argue that although these signs are often present in JIA patients, they cannot be considered a marker of early TMJ arthritis [Pedersen et al., 2001; Twilt et al., 2008; Müller et al., 2009; Abramowicz et al., 2011; Assaf et al., 2013; Cedströmer et al., 2013; Stoustrup et al., 2017]. Limited MIO, just as pain, is more frequent among JIA patients with long-standing and active diseases [Mohammed et al., 2012]. Despite extreme views, the researchers agree that pain or limited MIO noting clinically should prompt the physician to undertake further detailed

TMJ diagnosis, including imaging investigation. Primarily that, this clinical findings already present at an early stage of the disease increases the risk of chronic TMJ arthritis, permanent joint deformities, and, as mentioned before, if it is present during developmental age, inhibition of mandibular growth and development [Müller et al., 2009; Cedströmer et al., 2013; Keller et al., 2015; Stoll et al., 2018]. Clinical symptoms, such as reduced translation, reduced protrusion/laterotrusion, asymmetric protrusion, TMJ crepitation or reduced bite force are not considered to be characteristic markers of the early stage of TMJ arthritis in JIA patients [Twilt et al., 2008].

On the basis of the systematic review, it seems that it is necessary to use in TMJ examination of paediatric patients the pediatric MIO norms, correlated to their age [Keller et al., 2015; Stoustrup et al., 2017]. Within the reviewed publications some authors [Weiss et al., 2008; Hu et al., 2009; Assaf et al., 2013; Keller et al., 2015] referred the MIO of the JIA children to the results of healthy age-related children, but others considered MIO as limited when ≤ 40mm (as for adults) [Savioli et al., 2004; Leksell et al., 2008; Müller et al., 2009; Mohammed et al., 2012; Cedströmer et al., 2013]. Moreover, it should be emphasised that the results of a clinical examination do not always provide precise information. Some symptoms, such as pain, especially in small children can be evaluated indirectly by asking their parents. Moreover, the success of a physical examination largely dependents on the little patient cooperation and may have a significant impact on the results [Kirkhus et al., 2016].

Clinical symptoms and signs are usually markers of chronic TMJ arthritis. Jank et al. [2007] and Cedstrőmer et al. [2013] noted the positive correlation between the frequency and severity of clinical signs and the JIA duration. But the lack of symptoms and signs on an early stage of the TMJ involvement does not exclude the TMJ arthritis [Mohammed et al., 2012]. Therefore, early imaging investigation of this joint is necessary. Currently, the MRI is the gold standard for the diagnosis of TMJ arthritis [Huntjens et al., 2008; Jank et al., 2007; Abramowicz et al., 2011; Keller et al., 2015; Tolend et al., 2018]. This method allows the diagnosis of 63–91% of TMJ inflammatory changes [Pedersen et al., 2001; Twilt et al., 2008; Weiss et al., 2008; Arvidsson et al., 2010; Stoll et al., 2018], both active lesions (effusion or synovial thickening) and degeneration changes indicative of an ongoing process. Although this imaging tool enables to diagnose early changes that cannot be noticed clinically, its availability, high cost and sometimes the necessity of anaesthetising children for the examination does not allow the use of MRI as a screening method in JIA patients [Jank et al., 2007; Tolend et al., 2018].

In recent years, many diagnostic imaging tools for early detection of inflammatory changes of TMJ in JIA children were proposed, but visualisation of TMJ is difficult due to its location, small size, limited access, and bone anatomy [Cedströmer et al., 2013; Kirkhus et al., 2016]. Conventional radiographs, such as orthopantomogram (OPG), due to the overlapping of anatomical structures and numerous possible artifacts is of little diagnostic significance in JIA patients [Cedströmer et al., 2013]. It allows detection of condylar asymmetry and chronic condylar destructive changes, such as erosion, osteophytes and surface flattening [Huntjens et al., 2008; Cedströmer et al., 2013]. It should be added that the TMJ involvement in JIA patients can also be seen by shortening of the mandibular ramus, which is a result of the damage of the growth zone [Koos et al., 2014]. However, slight bony lesions and acute inflammatory pathologies, such as effusion or synovial thickening cannot be visualised by OPG [Huntjens et al., 2008; Cedströmer et al., 2013]. However, it is a relatively inexpensive examination and easy to perform. More anatomical details, comparing to OPG, are provided by computed tomography (CT). However, as it cannot depict an active TMJ arthritis, similarly to OPG, it was not applied to diagnose the TMJ in JIA patients [Huntjens et al., 2008; Kirkhus et al., 2016; Tolend et al., 2018].

Cone beam computed tomography (CBCT) introduced in recent years allows an accurate assessment of osseous structures in the TMJ. With lower radiation dose compared to OPG or classic CT, the study allows obtaining the high-resolution 3D image of high diagnostic value [Huntjens et al., 2008]. Unfortunately, it allows the visualisation of bone lesions only, resulting from chronic inflammation, but offer less assistance in the analysis of soft tissue structures, such as inflamed synovium, articular disc or cartilage [Huntjens et al., 2008; Koos et al., 2014].

Recently high-resolution ultrasonography (HR-US) was shown to be an alternative method in the imaging diagnosis of TMJ [Jank et al., 2007; Weiss et al., 2008; Müller et al., 2009; Assaf et al., 2013; Kirkhus et al., 2016]. Jank et al. [2007] showed that HR-US could be used to visualize destructive changes, disc dislocation, and effusion. Moreover, the authors noted a significant correlation between the duration of the disease and the destructive changes of the TMJ and disc dislocation in the maximum open-mouth position. However, these pathological changes by many researchers [Weiss et al., 2008; Müller et al., 2009] are considered a late manifestation of TMJ arthritis. Weiss et al. [2008] and Müller et al. [2009] demonstrated lower efficacy of the US compared to MRI in the diagnosis of early changes of TMJ arthritis in JIA patients. In Weiss et al. [2008], in 75% of all JIA patients, MRI showed acute TMJ inflammation, which, however, was not confirmed in the US. MRI compared to the US was also more likely to diagnose chronic inflammation in 69% and 28% of patients, respectively. A different result was obtained by Assaf et al. [2013], who established using HR-US the presence or absence of TMJ involvement in 20 JIA children, in whom TMJ arthritis was confirmed before by MRI. The authors showed a 91% compliance of HR-US results with the MRI. According to Assaf et al. [2013] HR-US enables to penetrate deeper into soft tissues and allows the detection of skeletal and synovial changes, joint effusion and cartilage thickening, and therefore could be one of the diagnostic tools for evaluation of TMJ involvement in JIA children [Jank et al., 2007; Assaf et al., 2013].

Currently, there are no clinical guidelines and diagnostic norms for evaluation of TMJ involvement for JIA patients [Jank et al., 2007; Cedströmer et al., 2013; Kirkhus et al., 2016; Stoustrup et al., 2017]. It seems that absence of characteristic clinical symptoms of the TMJ synovitis and low usefulness of conventional radiological investigations (OPG) in an initial stage of the disease may inhibit the diagnosis of active synovitis and result in an underestimation of the TMJ arthritis prevalence in JIA patients [Abramowicz et al., 2011; Abramowicz et al., 2013]. Moreover, to establish a correct diagnosis it is necessary to exclude Myofascial Pain Dysfunction Syndrome (MPDS) [Abramowicz et al., 2013] or other temporomandibular dysfunctions (TMD) [Abramowicz et al., 2013; Stoustrup et al., 2017]. It should also be remembered that pain and other clinical symptoms and signs may also occur in generally healthy children [Abramowicz et al., 2013].

Conclusions

Clinical signs and symptoms do not allow to detect the early stage of TMJ arthritis in JIA patients.

To monitor individual orofacial development, periodic TMJ clinical examination should be a part of an evaluation of JIA children's growth. There is a need to develop clinical management guidelines, as well as diagnosis standards of clinical and imaging TMJ examination for JIA children, considering their developmental age.

Conflict of interests

The authors declare that they have no conflict of interest.

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