



Mini Review Article

Dentofacial Manifestations of Juvenile Idiopathic Arthritis - A Review

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ARTICLE INFO

A B S T R A C T

Received: 10 Jun 2020
Accepted: 27 Jun 2020

Juvenile Idiopathic Arthritis (JIA) is a chronic rheumatic condition that significantly impacts general well-being and stomatognathic system of children and young adolescent. Owing to the autoimmune nature towards the synovial membrane of joints, it results in a significant impact on the stomatognathic system. The pathogenesis mainly involves production of inflammatory mediators in the synovial membrane. As the inflammation and disease progress for longer time, many mediators such as Interleukins, tumor necrosis factor and fibroblast growth factor are directed towards the synovial membrane resulting in thickening and destruction of joints. When the disease activity involves Temporomandibular joint (TMJ), the signs and symptoms range from flattening of condyle to destruction of the joint. Major dentofacial problems are retrognathic mandible, short ramus height and length of mandible, class II malocclusion, convex profile and anterior open bite. Apart from this, there is increased prevalence of dental caries and periodontal health problems owing to the limited function of upper limb due to swelling and tenderness of joints and susceptibility to infections due to prolonged corticosteroid treatment. From a Pedodontist perspective, JIA children require early screening, close observation, and preventive treatment. Regular screening for upper limb disability, medication and their side effects, diet history, oral hygiene practices, and examination of TMJ for possible involvement is recommended as the disease can cause rapid destruction and it's difficult to predict. The present review aims to discuss the types of JIA, clinical features, oral health and TMJ related findings reported in some of the key studies and management of dentofacial changes in JIA children.

Key Words: Juvenile Idiopathic Arthritis, Temporomandibular Joint, dental caries, Occlusion, Magnetic Resonance Imaging, Panoramic Radiographs, macrophage activation syndrome.

1. INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a chronic joint disease most commonly seen in children and young adolescents. The incidence is reported as 2 -23 in 100,00 and prevalence is 4 -400 per 100,000 children [1]. Owing to its autoimmune

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pathogenesis the etiology is still not clear. Some of the factors discussed in studies to date include consanguinity, genetic factors, environmental factors, and viral infections [2].

According to the International League of Associations for Rheumatology (ILAR), JIA is classified into 7 types, discussed in Table 1 [3, 4].

Table 1: Classification of JIA

Types of JIA	CLINICAL FEATURES
Systemic arthritis	Mainly includes systemic illness such as Fever, lymphadenopathy and rash. Number of joints involved is variable.
Oligoarthritis	This is most common type of JIA. Number of joints affected is equal to or less than 4.
RF ⁺ -positive polyarthritis	Number of joints affected is greater than or equal to 5 joints. Most commonly involves small joints such as Metacarpophalangeal joints, wrist joints etc. Patients are Positive for Rheumatoid factor on serological test.
RF ⁻ -negative polyarthritis	Number of joints affected is greater than or equal to 5 joints. Most commonly involves small joints such as Metacarpophalangeal joints, wrist joints etc. Tests Negative for Rheumatoid factor on serological test.
Enthesitis-related arthritis	Most commonly known as Spondyloarthritis. Apart from joints, ligaments, muscles and tendons are affected. Number of joints affected is less than or equal to 4.
Psoriatic arthritis	The characteristic features include psoriatic rash behind ears, near eyes, knees, scalp and belly button. Number of joints affected are variable.
Undifferentiated arthritis	This is the last type classified when symptoms don't match with any type of JIA.

RF: Rheumatoid Factor

2. CLINICAL FEATURES

The onset of JIA can be seen from early childhood to adolescent age around 16yrs. There is more predilection for females than males with a ratio of 2.3:1 [4]. Depending on the type of JIA, the number of joints involved varies. In Oligoarthritis less than 4 joints are involved whereas in polyarthritis more than 5 joints are involved. The joint involvement varies in systemic, enthesitis-related, and psoriatic arthritis. Systemic arthritis includes a history of fever, rash, lymphadenopathy, and serositis [4]. Owing to the increase in ferritin, serum transaminases and decrease in platelet and fibrinogen level, there are very changes to develop Macrophage Activation syndrome. According to Ravelli A *et al*, recently a new classification criterion is developed [5, 6].

The criteria include, Ferritin > 684ng/ml and any of the 2 from the below [5, 6]:

- Platelet count 181 × 109/l
- Aspartate aminotransferase > 48 units/l
- Triglycerides > 156 mg/dl
- Fibrinogen 360 mg/dl

Children with JIA report general disabilities in performing daily routine works. Owing to swelling and tenderness of major joints in the body, osteoporosis and long-term treatment with Corticosteroids, disease modifying anti -

rheumatic agents, intra articular injections the activity and growth of these children is significantly affected compared with healthy children of similar age and gender [7]. Due to prolonged use of steroids, these children are more prone to infections. Other systemic problems include chronic anterior uveitis, fever, anemia, malnutrition and amyloidosis [7].

When the arthritis involves temporomandibular joint (TMJ) and joints of upper limb, there is an impact on dentofacial growth and oral hygiene respectively. Poor oral hygiene indicates increased dental caries and periodontal problems [7]. TMJ arthritis leads to reduced growth of mandible compared to maxilla, resulting in Angle's Class 2 malocclusion, vertical growth pattern and anterior open bite tendency. The involvement of condyle may vary from erosion of the articular surface to severe destruction resulting in facial asymmetry [7].

The present review aims to discuss the types of JIA, clinical features, oral health and TMJ related findings reported in some of the key studies and management of dentofacial changes in JIA children. This article serves as single point of source for studies reporting oral health status, TMJ dysfunction, imaging modalities carried out so far and progress in the management of JIA patients with TMJ arthritis and dentofacial deformities.

3. DENTAL IMPLICATIONS

Oral Health: The etiology of dental caries in JIA children is multifactorial. The prevalence of dental caries is reported to be higher in JIA patients owing to difficulty in brushing due to the involvement of the upper limb. According to Walton AG *et al* [7], especially in polyarthritis JIA, the involvement of small joints such as wrist and metacarpophalangeal joints result in inability to brush, functional failure, inability to walk, and social isolation. Walton AG *et al* [8], reported that chronic anterior uveitis in children with JIA is a complication due to corticosteroid treatment. JIA patients are on chronic use of sugar containing medications which might be the factor for caries. The quality of saliva is low due to lower concentrations of Calcium, phosphorous, potassium, lysozyme, and Immunoglobulin [8]. Ahmed N *et al* [9] reported an increased prevalence of dental caries, periodontal diseases due to 50% of children had upper limb disability and limited manual dexterity. JIA children tend to have more gingival diseases due to different microbiological spectrum. According to Nibbo *et al*, [10] JIA children have high prevalence of bacteria such as Hemophilus, Kingella, Porphyromonas compared to the healthycontrol groups. In the Polyarthritis group, porphyromonas and Rothia were more abundant whereas in the control group Prevotella group bacteria were more abundant. Various studies that have reported the increased prevalence of dental caries and poor oral hygiene are discussed in Table 2.

Table 2: Illustration of studies in JIA children

Studies	Parameters	Major Outcome
Lehtinen A <i>et al.</i> , (2000) [11]	Dental Maturity in Juvenile Rheumatoid Arthritis (JRA) children (Age: 6.3 – 14.4yr) on Cortisone treatment compared to healthy controls.	Cortisone reportedly caused early eruption of incisors, increased root formation and cell division, affected cartilage mediated skeletal growth. There is advanced dental maturity and increase in plasma IGF -1 Concentration that enhances dentinogenesis in JRA children
Sidiropoulou-Chatziagianni S <i>et al.</i> , (2001) [12]	Dentoskeletal growth in JIA children (Age: 6-9yrs) compared with healthy children. Analysis was performed using lateral Cephalograms and panoramic radiographs.	Mandibular retro position and short ramus height and length more in females, condylar lesions in Polyarticular type of JIA.
Olson JC, (2003) [13]	Meta-Analysis of 34 epidemiological studies.	Incidence 0.008 to 0.226/1000 children per year, Prevalence 0.07 to 4.01/1000 children. Oligoarthritis is most common type of JIA with predominance in females. Growth disturbances include micrognathia.
Welbury RR <i>et al.</i> , (2003) [14]	Gingival index, plaque index, oral cleanliness index and dental caries DMFT (Decayed, missed, filled teeth) index in JIA children (Age: 0 – 11yrs) with healthy controls.	Increased levels of dental caries and poor oral hygiene in JIA children. High levels of untreated dental caries.
Ahmed N <i>et al.</i> , (2004) [9]	TMJ dysfunction, dental caries, bacterial dental plaque, gingival inflammation in JIA children (4 – 16yrs).	No significant difference in dental caries and plaque score. However, Gingival score and TMJ dysfunction were high in JIA children.
Savioli C <i>et al.</i> , (2004)[15]	DMFT index, plaque and gingival bleeding index, dental relationship, facial profile, and Helkimo's index. Mean age of JIA group 10.8 yrs compared with healthy control group.	Convex facial profile and class 2 malocclusion in 12 children, Plaque and gingival indices high in JIA children. TMJ dysfunction, decreased mandibular opening, mandibular mobility was seen in 94%, 80% and 33% of JIA group.
Engstrom AL <i>et al.</i> (2007)[16]	Follow up study of 40 JIA patients (18 ± 4.5years). Initially screened in 1986 and followed up for 15yrs and rescreened in 2001.	Pain in cervical region, jaw muscles, TMJ, neck and shoulders.
Ringold S and Cron R Q (2009) [17]	Magnetic resonance imaging (MRI), Panoramic radiographs and computed tomography (CT) examination of TMJ arthritis in JIA children.	75% of children with JIA showed active TMJ arthritis. MRI with gadolinium enhancement was very effective in detecting TMJ arthritis.
Cedstromer A <i>et al.</i> (2013) [18]	Orofacial signs, TMJ disease activity, and condylar alterations using panoramic radiographs in JIA patients with mean age of 2.9yrs from the onset of JIA.	Clinical signs of TMJ dysfunction were seen in 57.7% - 92% and subjective symptoms in 32-76%. Psoriatic arthritis group presented with more symptoms compared to oligoarthritic group.

Pugliese C <i>et al.</i> (2016) [19]	Periodontal evaluation, fasting lipoproteins, and anti-lipoprotein lipase antibodies in JIA females (11.90 ± 2.0 vs. 12.50 ± 3.0 years) compared to healthy control group.	Similar scores for gingival index, dental plaque, gingival bleeding, and clinical dental attachment indices in JIA patients and controls were reported. Cyclosporine was mainly found in JIA group. There was positive correlation between dental caries and JIA activity.
Frid P <i>et al.</i> , (2017) [20]	Demographic, disease activity, disability, and health-related quality of life (HRQOL) of JIA compared with healthy peers.	The Polyarticular group of JIA showed higher TMJ disease activity, disability and low HRQOL.
Hugle B <i>et al.</i> , (2017) [21]	JIA patient with TMJ arthritis were screened for clinical, laboratory, imaging and medication history.	Oligoarthritis was the most common type of JIA. 40% were on Nonsteroidal anti-inflammatory medications, 33% were on Methotrexate and/or leflunomide, 35% were on Intraarticular TMJ steroid joint injections. Bilateral TMJ involvement was seen in 65.5% of JIA patients.
Menon NVB <i>et al.</i> (2018) [22]	Overall profile of JIA patients (mean age 8.9 ± 3.8 years) using juvenile arthritis damage index (JADI) score.	Most common type of JIA was Polyarticular followed by systemic arthritis. Knee and ankle joints were more commonly involved. Articular and extra articular involvement was more in systemic type of JIA and showed positive correlation with duration of illness. Macrophage activation syndrome was reported in 50% of patients with systemic arthritis.
Merle CL <i>et al.</i> , (2020) [23]	DMFT/dmft Index, gingival inflammation (papilla-bleeding-index(PBI) and periodontal screening index (PSI). Functional examination of TMJ with modified Helkimo's Clinical Dysfunction Index and radiographic scoring in JIA children.	Functional examination revealed Osteoarthritis of TMJ. Periodontal screening index was high in 57.6% of JIA patients. The radiographic features and PSI findings were positively correlated with increased C- reactive protein levels in serum.

Dentofacial Manifestations: The immune response is directed towards the synovial membrane of Temporomandibular Joint (TMJ). This response in turn activates the serum cascade system, leading to edema, vasodilatation, and T-cells infiltration [3]. The synovium of patients with TMJ arthritis has mediators of inflammation such as tumor necrosis factor, interleukins, platelet derived growth factor, and Interleukins such as IL-1, IL-6, IL-8 and IL-15. When the inflammation lasts for longer time as in cases of active disease activity, the synovium thickens, and destruction of joint begins [3]. Kjellberg H [24] reported reduced overbite, general and local crowding, labial inclination of lower incisors, and a tendency of occlusion to change from class I to class II. When the arthritis involves

TMJ, the signs and symptoms include flattening of condyle, narrowing of joint spaces, osteophyte formation, restricted movement of condyle and subchondral and osteophyte formation. According to Sidiropoulou-Chatzigianni S *et al*, [12] children with JIA have retrognathic mandible when compared to healthy children. There is more tendency for vertical growth pattern and posterior rotation of mandible and in most severe cases ‘Bird Face’ deformity is seen. There is an increase in anterior facial height and open bite.

In a study by Leksell E *et al* [25] a panoramic radiograph was analyzed for deviations in TMJ structure ranging from a small abnormality of the condyle deviating slightly from the convex shape (usually flattened) to a completely absent or short flat condyle and found out that 77% of JIA children have shown structural condylar changes on orthopantomogram (OPG). With the advent and usage of cone-beam computed tomography (CBCT) to evaluate TMJ arthritis in a study by Al shwaikh H *et al* [26] evaluated the morphological changes in the structure of the TMJ in JIA patients using CBCT and concluded that the most prevalent feature in the JIA group is condyle surface flattening on both sides. Condyle surface erosion and osteophyte were also frequent and occurred with high statistical significance in both males and females [26].

In a study using magnetic resonance imaging (MRI) scans for the affected TMJ in JIA cases, Mohammed Y *et al* [27] reported a significant positive correlation was found between total MRI score and disease activity, functional and pain scores in 80% of patients with JIA as C reactive protein scores were increased significantly. A similar study by Abdul-Aziez OA *et al* [28] serum levels of the pro-inflammatory protein S100A12, was measured to investigate clinical as well as contrast-enhanced magnetic resonance imaging findings of TMJ inflammation among JIA patients and concluded that, Serum S100A12 levels showed a significant positive correlation with synovial enhancement score. Thus, TMJ arthritis was detected in 80% of JIA patients using MRI [28].

Concerning TMJ arthritis, the various radiographic and MRI investigational studies regarding the anatomy of the glenoid fossa and the condylar head have reported a higher frequency of surface flattening of the condylar head in children and young adolescents [29] Development of malocclusion and facial deformities such as micro- or retrognathia, are later scenarios associated with established permanent sequelae in the TMJ [30 -33].

Various studies performed by using advanced diagnostic aids such as panoramic radiographs, cone-beam computed tomography (CBCT), MRI scans of TMJ, and serological tests have suggested similar views related to occlusal changes and TMJ arthritis as seen in Table 2.

4. MANAGEMENT

Isola G *et al*, [34] reported a treatment with functional appliances for JIA patients had significant improvement in

occlusal abnormalities, mouth opening, and TMJ arthritis. In cases with active JIA, where skeletal maturity is reached, the best approach is to defer the treatment until the arthritis is under control. In severe cases of facial asymmetry, mandibular advancement and bilateral sagittal split osteotomy with genioplasty is recommended [35]. For mandibular condyle erosion cases and synovitis, orthognathic surgery along with TMJ surgeries have been proven to be successful. TMJ surgeries include synovectomy, meniscectomy, and reconstruction with costochondral grafts. The disadvantages of costochondral grafts are resorption, overgrowth, and ankylosis of joint. However, surgeons have reported positive outcomes with close post-operative follow-ups [35].

For upper limb dysfunction, brushing with electric toothbrushes is recommended. To prevent caries and gingival health issues, fluoride varnishes, pit and fissure sealants and sugar free medications are suggested. Radiographic examination of early cases of TMJ can prevent and intercept the developing malocclusion and TMJ arthritis.

5. CONCLUSION

JIA has a significant impact on oral health and TMJ. Owing to its autoimmune and chronic nature, the treatment regimen is long term and is based on steroids. It's imperative to understand the dentofacial growth and function of stomatognathic system. The major aspect to understand is not all children with JIA will have TMJ involved. Its highly unpredictable which child will show TMJ dysfunction. All children and young adolescents should be followed up for long term period as there are chances of active disease to relapse. From a pedodontist perspective, these patients require early screening, close observation, and preventive treatment. Regular screening for upper limb disability, medication and their side effects, diet history, oral hygiene practices, and possible involvement of TMJ is recommended as the disease can cause rapid destruction and it's difficult to predict. In severe cases, orthodontic intervention and orthognathic surgery are recommended.

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Conflict of Interest: None

Source of Funding: Nil