

Oral Findings in Rheumatoid Arthritis Patients

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Abstract

Background: Rheumatoid arthritis affects women more than men 3:1. Rheumatoid arthritis can start at any age but most commonly occurs in the 30 – 50 age groups. Rheumatoid arthritis also has oral, ocular manifestations, dryness, swelling of salivary glands, xerostomia, oral and mucosal ulcerations. The aims of this study were to determine the oral manifestations in newly and old (previously) diagnosed Rheumatoid arthritis patients and compare it with healthy controls (without systemic diseases) and finally to find the accurate prevalence of these manifestations in rheumatoid arthritis patients.

Materials and methods: Seventy two (72) subjects were incorporated in this study, they were divided into 2 groups, Rheumatoid arthritis patients group: fifty – two (52) patients with rheumatoid arthritis, they were (11) males and (41) females, Seventeen newly diagnosed rheumatoid arthritis untreated patients. Thirty five rheumatoid arthritis patients were on methotrexate treatment. All rheumatoid arthritis patients were without any other systemic disease. Healthy control group: - twenty healthy control subjects with no signs and symptoms of any systemic disease. They were sex and age matched to rheumatoid arthritis patients.

Results: The results revealed that the main oral manifestations of Rheumatoid arthritis patients were angular cheilitis, candidial infection, tempromandibular joint disorder, oral ulceration, and xerostomia. In old diagnosed rheumatoid arthritis patients, the percentages of oral ulcerations, tempromandibular joints, and xerostomia was significantly higher than in newly diagnosed rheumatoid arthritis patients. While the percentage of angular chilitis and candidial infections in newly diagnosed rheumatoid arthritis patients was significantly higher than in old (previously) diagnosed patients.

Conclusion: Rheumatoid arthritis is a chronic disease in which Saliva is a good recommended sample for evaluation and estimation of the severity of disease as well as treatment follow up. Oral ulceration and xerostomia are the most prominent oral manifestations coincide with the progress of the disease and treatment.

Keywords: Rheumatoid arthritis, Oral manifestations, Saliva.

المخلص

اهداف الدراسة: التهاب المفاصل الروماتويدي أو الرثوي يؤثر على النساء أكثر من الرجال. يمكن أن يبدأ التهاب المفاصل الروماتويدي أو الرثوي في أي عمر لكنه يحدث غالباً في الفئات العمرية من 30-50 سنة. التهاب المفاصل الرثوي له أعراض ظاهرية فموية منها الانتفاخ في الغدد اللعابية، جفاف الفم، تقرحات فموية ومخاطية. إن الهدف من الدراسة هو تحديد الظواهر الفموية في مرضى التهاب المفاصل الرثوي أو الروماتويدي المشخصين حديثاً وكذلك المشخصين قديماً ومقارنتهم بالأشخاص الأصحاء (المجموعه الظابطه). (بدون اي اعراض لاي امراض اخرى تذكر) وتحديد النسبه للظواهر الفمويه لهؤلاء المرضى.

المواد وطرق العمل: شملت هذه الدراسة اثنان وخمسون شخصاً (52) ؛ سبعة عشرة (17) منهم شخّصوا حديثو الاصابه بالتهاب المفاصل الروماتويدي أو الرثوي ؛ خمسة و ثلاثون (35) منهم شخّصوا كالتهابات قديمه بالتهاب المفاصل الروماتويدي أو الرثوي وكانوا أساساً تحت تأثير العلاج بالميثوتريكسيت طوال فتره المرض. هؤلاء المرضى تطابقوا في العمر و الجنس مع عشرين (20) من الأشخاص الأصحاء (المجموعه الظابطه). فحص كل مريض فمويًا من الداخل والخارج لإيجاد أي عوارض فموية أو اضطراب في (مفصل الفك الصدغي) .

النتائج: ان نتائج البحث وجدت الأعراض الفموية المهمة لدى مرضى التهاب المفاصل الروماتويدي أو الرثوي كانت جفاف الفم ، اختلال المفصل الفكي الصدغي ، التهاب الشفة الزاوي ، التقرح الفموي و خمج المبيضة البيضاء الفموية الفطريات. أظهرت النتائج أن نسبة عوارض التقرح الفموي و عوارض الجفاف الفموي لدى مرضى التهاب المفاصل الروماتويدي أو الرثوي المشخصين قديما كانت أعلى بشكل واضح معنوي من المشخصين حديثا. بالنسبة للمرضى المشخصين قديما ، كانت نسبة التقرح الفموي واختلال المفصل الفكي الصدغي وجفاف الفم اعلى منها في المرضى المشخصين حديثا، بينما كانت نسبة التهاب الشفة الزاوي خمج المبيضة البيضاء الفمويه الفطريات في مرضى المفاصل الرثوي او الروماتيدي في المرضى المشخصين حديثا اعلى المرضى المشخصين قديما.

الاستنتاج: التهاب المفاصل الروماتويدي أو الرثوي هو مرض مزمن يمكن اعتبار اللعاب نموذجا جيدا يوصى باستخدامه لتقييم وتقدير شدة المرض ومتابعه تأثير العلاج. تزداد النسبة المئوية للعوارض الفموية متمثلة بتقرح الفم وجفاف الفم بتقدم المرض وزيادة فتره العلاج.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disorder with systemic features and joint involvement, resulting in an erosive synovitis, cartilage degradation, and joint destruction⁽¹⁾. Its incidence is two to three times greater in women⁽²⁾, Rheumatoid arthritis affects about 1% of the world's Population, when defined by either the presence of serum Rheumatoid Factor (RF) or erosive changes on radiographs in a patient with a compatible clinical presentation⁽³⁾. The etiology of rheumatoid arthritis is not fully understood. Evidence points to a complex interplay between environmental and genetic factors⁽⁴⁾. No single diagnostic test definitively confirms the diagnosis of rheumatoid arthritis. However, several tests can provide objective data that increase diagnostic certainty and allow disease progression to be followed. The American College of Rheumatology Subcommittee on Rheumatoid Arthritis (ACRSRA) recommends that base line laboratory evaluations include a complete blood count with differential, rheumatoid factor, and Erythrocyte Sedimentation Rate (ESR) or C - reactive protein (CRP). Therapeutic goals include preservation of function and quality of life, minimization of pain and inflammation, joint protection, and control of systemic complications⁽⁵⁾. Low dose methotrexate is used extensively as a second line therapy in the treatment of RA, but few clinical trials have reported oral mucosal impairments in patients taking low dose of methotrexate⁽⁶⁾. The

Tempromandibular Joint (TMJ) is often involved in rheumatoid arthritis. This is usually characterized by erosion in the condyle leading to a decreased range of motion of the mandible with pain upon movement⁽⁷⁾. Xerostomia is often defined as a subjective complaint of dry mouth that may result from deficient production of saliva. Woman suffering from rheumatic diseases in advanced age should be warned about high probability of developing symptoms of oral and ocular dryness with all the ensuring complications⁽⁸⁾. Rheumatoid factor, an IgM anti globulin against the Fc portion of human IgG, is detected in about 70% of patients with RA. Evidence suggests its participation in disease pathogenesis. The presence of RF in RA is associated with extra – articular manifestations of disease, and its absence is generally associated with milder disease⁽⁹⁾. The measurement of RF is an important marker for assessing and monitoring this immunologic response. Many rheumatic conditions and other chronic inflammatory processes may produce rheumatoid factor⁽¹⁰⁾. The tempromandibular joint (TMJ) is the most active joint in the body as it needs to open and close up to 2000 times per day to account for a full day's worth of chewing, Talking, breathing, swallowing, yawning, and snoring⁽¹¹⁾. The jaw, cervical spine, and alignment of the teeth are integrally related, and dysfunction in one of these regions may lead to a tempromandibular joint (TMJ) disorder, which is a term used to describe a variety of clinical disorders resulting in jaw pain or dysfunction. The etiology of TMJ disorder is often multifactorial and may be

due to stress, jaw malocclusion, habitual activities including bruxism, postural dysfunction, inflammatory conditions and trauma⁽¹²⁾. TMJ disorders are more commonly seen in females as compared to males and usually in the age range from 20-40 years. Arthritis / arthralgias that affect the TMJ include osteoarthritis (OA), rheumatoid arthritis (RA), juvenile rheumatoid arthritis (JRA), and ankylosis. Up to 50% of patients with RA or JRA develop symptoms in the TMJ, and women tend to be more affected than men. Additionally, patients with (RA) or (JRA) have high incidence of cervical spine involvement, and this, in turn, increases their risk of TMJ disorders⁽¹³⁾. The TMJ and most of the muscles of mastication are innervated by the mandibular branch of the trigeminal Nerve⁽¹³⁾. The temporomandibular joint (TMJ) is often involved in rheumatoid arthritis. This is usually characterized by erosion in the condyle leading to a decreased range of motion of the mandible with pain upon movement⁽¹⁴⁾. Xerostomia is often defined as a subjective complaint of dry mouth that may result from deficient production of saliva. Most of xerostomia patient's complaints are oral dryness, burning mouth, increased thirst, loss of taste, difficulty swallowing, chewing, speaking, oral breathing, unpleasant taste and odor, sensitive teeth, gastroesophageal reflux, and malfunction of removable prosthesis⁽¹⁵⁾. Oral dryness and salivary gland swelling can also be found in patients with rheumatoid arthritis. These patients can also develop secondary sjögren's syndrome⁽¹⁶⁾. Xerostomia can be associated with fissured tongue, depapillation and redness of the tongue, cheilitis, and candidiasis. Swallowing and speaking may become difficult due to persistent xerostomia. Bacterial parotitis, which is usually accompanied by fever and purulent discharge from the gland, may also occur. There is an increase in dental caries, especially around the cervical region of the teeth⁽¹⁷⁾.

Table 1. Causes of Xerostomia in RA patients (Moore et al., 2008).

CAUSES OF XEROSTOMIA.	
SELECTIVE SEROTONIN REUPTAKE INHIBITORS	
MEDICATIONS	
Primary Sjögren's Syndrome	
Secondary Sjögren's Syndrome	
—	Connective Tissue Disease
—	Rheumatoid arthritis
—	Systemic lupus erythematosus
—	Systemic sclerosis
—	Mixed connective tissue disease
OTHER CONDITIONS	
—	Radiation Therapy
—	Primary Biliary Cirrhosis
—	Vasculitis
—	Chronic Active Hepatitis
—	HIV
—	AIDS
—	Bone Marrow Transplantation
—	Graft-vs.-Host Disease
—	Renal Dialysis
—	Anxiety or Depression
—	Diabetes, Type 1 or 2

Angular cheilitis, this term refers to inflammation at the corners of the mouth. The clinical signs and symptoms include redness and soreness, with possible formation of fissures and crusting ulcers. A mixed infection of candidial plus certain bacteria is responsible for the infection. Angular cheilitis is pronounced in individuals who have deep skin folds at the angles of the month. This occurs in individuals with over closed vertical dimension. Presumably the fold of skin provides an ideal environment for the microorganisms to proliferate⁽¹⁸⁾. Oral Candidiasis (candidosis) is an infection with multiple manifestations. The underlying causes of oral candidiasis include antibiotic therapy, poor denture hygiene, xerostomia, immune deficiencies, and diabetes. Candidial infection may be superimposed on other mucosal and may disguise the underlying disease. The diagnosis is established using clinical appearance and patient history, and it may require diagnostic tests. A significant segment of the population carries candida, without any symptoms of infection, complicating the use of diagnostic tests⁽¹⁹⁾. Oral ulceration is a breakdown of mucosal layer and leaving this area more painful

during the irritation by irritant to subjects. In rheumatoid arthritis patients, they prone to infection in which mucositis causes oral complications due to administration of methotrexate (MTX). The healing time for mucositis is typically 12 – 16 days, but it depends on the proliferation rate of the mucosa, the reestablishment of the local flora in the oral cavity, and other extraneous factors. The areas of erythema can develop into raised white desquamative patches that become painful ulcerations⁽²⁰⁾. Mucositis also compromises the body's defenses against the invasions of microorganisms from the oral cavity into the blood stream thus, increasing the risk of systemic infection. This situation can potentially lead to a cascade of events altering the patients over all health⁽²¹⁾. Painful ulceration in the oral cavity render patients with the inability to eat, drinks, or swallow⁽²²⁾.

Materials and methods

Patients were selected from the rheumatology department of Merjan teaching hospital in Babil – Hilla during the period from October 2012 to February 2013. Seventy two (72) subjects were incorporated in this study, Informed consent and ethical approval was obtained. For each individual a questionnaire case sheet was filled out. Each patient was examined extra and intra orally to detect any oral lesions and TMJ disorder, they were divided into 2 groups: arthritis patients group: fifty – two(52) patients with rheumatoid arthritis, they were (11) males and (41) females already diagnosed by a rheumatology specialist, depending on the criteria of the American College of Rheumatology (ACR) (Arnett *et al.*, 1988) They were subdivided into 2 sub- groups: Seventeen newly diagnosed rheumatoid arthritis patients without any treatment. Thirty five rheumatoid arthritis patients on methotrexate treatment. All RA patients were without any other systemic diseases. Healthy control group:- twenty healthy

control subjects with no signs and symptoms of any systemic disease. They were sex and age matched to rheumatoid arthritis patients . All control and patient groups were with no periodontal disease.

Results

The results showed that only 14 (26.9%) of rheumatoid arthritis patients had angular cheilitis, 7 (41.1 %) were of newly diagnosed patients and 7 (20.0 %) were of old diagnosed patients. These results are shown in (Table 1).The results showed that only 29 patients (55.7 %) with rheumatoid arthritis had oral ulceration, 7 (41.1 %) were of newly diagnosed RA patients and 22 (62.8%) were of old diagnosed RA patients as shown in 33 (63.4 %) of rheumatoid arthritis patients had (candidial infection), 13 (76.4 %) were of newly diagnosed patients and 20 (57.1 %) were of old diagnosed patients, those results were shown in (Table 1). The results showed that 32 (61.5 %) of patients with rheumatoid arthritis had xerostomia, 4 (23.5 %) patients were of newly diagnosed patients and 28 (80.0 %) patients were of old diagnosed patients .In Tempromandibular Joint (T.M.J) involvement of rheumatoid arthritis patients, 13 (76.4 %) patients were of newly diagnosis patients and 27 (77.1 %) patients were of old diagnosed RA patients.

Discussion

Rheumatoid arthritis is a chronic progressive multi systemic inflammatory disease .It usually involves middle aged adults with a female being affected more than males⁽²³⁾. It has been reported that women mount more robust immune responses, and these responses tend to be more Th1-like response. Since this type of immune response is pro-inflammatory, it may enhance the development of autoimmunity.

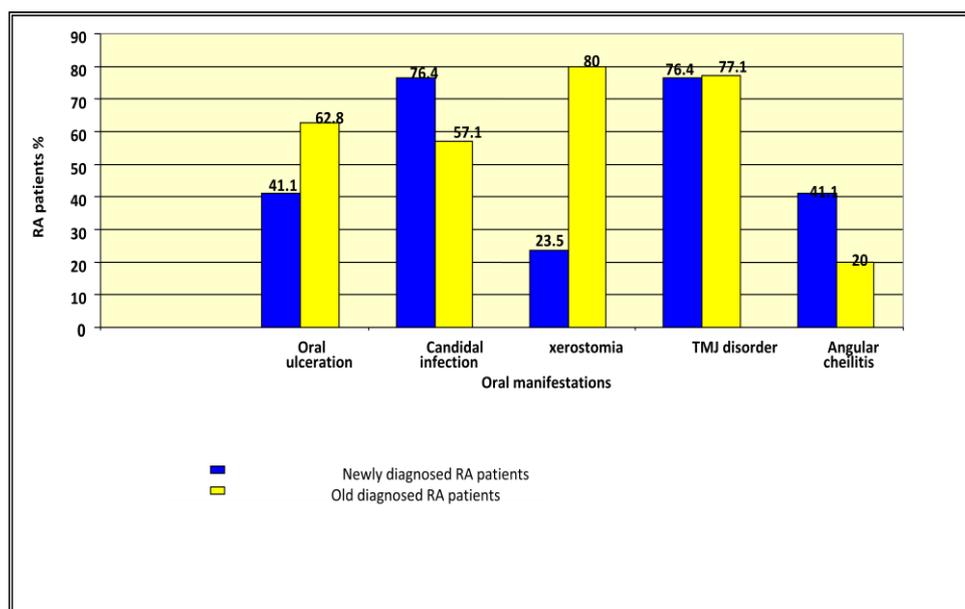


Figure1: Oral manifestations in RA patient

Whether the bias toward a Th1 response is due to differences in sex steroid between males and females is less certain and need confirmations⁽²⁴⁾. From the best of our knowledge was it the first study that deals with angular cheilitis in RA patients. Studies analyzing oral lesions, related to different doses and routes of administration of methotrexate (MTX) must be performed in order to understand the natural

history of the oral manifestations related to the use of MTX. Oral candidiasis was one of the oral manifestations found in this study, the number of RA patients on MTX treatment with oral candidiasis were higher than those RA patients without MTX therapy. These candidiasis were presented in this group may be due to the use of immunosuppressive drugs or to lower salivary flow rates that usually affect RA patients, these results matched with Russel and Reisine, 1998. In the present study the percentage of patients with oral ulceration was higher in R.A patient on low dose MTX therapy than in RA without any treatment. The appearance of oral lesion (oral ulceration) related to MTX use. The mechanism by which the MTX causes oral events are due to inhibition of

inflammatory markers, also in an increase of adenosine, which is associated with several anti inflammatory and immunosuppressive effects. This study revealed that xerostomia was an important oral manifestation of RA patients. This results were matched with other studies⁽²⁵⁾ who stated that sjögren's syndrome is a common autoimmune rheumatic disease, secondary to rheumatoid arthritis affected more commonly middle-aged women than men, the most common symptoms in sjögren's syndrome are dry mouth (xerostomia), dry eyes (kerato conjunctivitis sicca syndrome), these symptoms associated with swelling of the salivary glands, xerostomia, the primary symptom of sjögren's syndrome, can affect oral mucosa. Xerostomia occurs only when the rate of salivary flow is reduced. The results also showed that the percentage of patients with xerostomia was significantly higher in old diagnosed RA patients (on MTX) than in newly diagnosed RA patients, this may be due to the effect of drug it 'self. A main problem in evaluations of the impact of disease on salivary gland performance is the difficulty of discriminating between effect of the disease and it's pharmacologic treatment. The main reason for decreased

saliva flow has been reported to be medication. The results revealed that main the oral manifestations of RA patients was T.M.J disorder, it affects about 76.9% of RA patients, which was agreed with other studies⁽²⁶⁾. Involvement of T.M.J results from granulomatous involvement of articular surface of the synovial membrane, which leads to destruction of the underlying bone. Symptoms are characteristic of T.M.J dysfunction⁽²⁷⁾.

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