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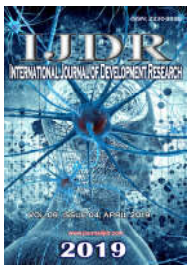

RESEARCH ARTICLE OPEN ACCESS

ANALYSIS OF CASE REPORTS ON SJOGREN'S SYNDROME ASSOCIATED TO RHEUMATOID ARTHRITIS

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ABSTRACT

Purpose: This paper aimsis to conduct a systematic and critical review of case reports in individuals with a diagnosis of Sjogren's syndrome associated with rheumatoid arthritis, emphasizing the epidemiological profile, clinical manifestations, diagnosis and proposed treatments. **Materials and methods:** A critical literature review of the clinical cases published by a single researcher on the Bireme and PubMed websites using combined key words such as Rheumatoid Arthritis and Sjogren's syndrome. These cases are in English, Portuguese and Spanish. For ease of evaluation of the articles, the study observed the epidemiological profile, the clinical manifestations, diagnosis and the proposed treatments. Finally, the data obtained were tabulated and analyzed. **Results:** An analysis of 11 articles was carried out at the end, observing that there is a positive relation between rheumatoid arthritis and Sjogren's syndrome and the literature does not show much concern with oral evaluation. However, there is a deficiency in patients' oral health due to lack of salivation and alveolar bone loss. **Conclusion:** Although these diseases are interrelated, the signs and symptoms are different, as is the form of treatment and diagnosis.

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INTRODUCTION

Sjögren's syndrome (SS) is a chronic autoimmune inflammatory disease, which mainly involves the lacrimal and salivary glands causing functional impairment in its secretory performance. The clinical presentations of SS are dry keratoconjugitis and xerostomia (FREITAS *ET AL*., 2004). There are also other systemic manifestations such as cutaneous vasculitis, cryoglobulinemia, autoimmune hepatitis, pulmonary fibrosis and involvement of the central nervous system (LIQUIDATO AND BUSSOLOTI FILHO, 2005). The etiology of SS is still uncertainand has been reported since alteration of autoimmune system regulators with differentiation of lymphocytes in autoantibodies and hypergammaglobulinemia, abnormality in the patient's immunity with presence of factors such as genetic and environmental predisposition, and infectious etiology of Epstein-Barr virus (FREITAS *et al*., 2004).

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It has a predilection for women in the ratio of 9: 1, between the fourth and fifth decades of life, however due to the difficulty in diagnosing SS the exact establishment of this prevalence may be erroneous (LIQUIDATO and BUSSOLOTI FILHO, 2005). This syndrome has two forms of clinical presentation. The primary one in which the implication is systemic, being isolated without association with any autoimmune disease. The secondary one is concomitant with autoimmune diseases such as rheumatoid arthritis (RA), lupus, primary biliary cirrhosis, systemic sclerosis, among others, however, the most common is RA (COSTA *ET AL*., 2014). RA is a progressive autoimmune, chronic disease that affects the joints by deforming or destroying them with bone and cartilage erosions. This disease affects more women than men. Between the fourth and fifth decade of life and it may cause work incapacity with its advancement in women (COSTA *ET AL*., 2014). Environmental, hormonal and immunological factors influence the evolution of autoimmune diseases that will affect patients who are genetically susceptible (GOELDNER *ET AL*., 2011).

Table 1. Description of case reports and Rheumatoid Arthritis

Articles	Nº of cases	Sex / age / skin color	Diagnosis	Clinical manifestations	Treatment
Lawall *et al.*	01	Female / 32 years old / leucoderma	RA	Fatigue, pain in the joints of the hands, wrists and elbows	Not informed
Freitas *et al.* (2004)	01	Female / 63 years old / leucoderma	RA	Not informed	Use of corticosteroids
Bezerra *et al*. (2010)	01	Female / 49 years old / leucoderma	RA, fibromyalgia, myositis	knees in a degenerative situation, ankles and hands associated with fibromyalgia, muscle and facial pain and fatigue	Non-steroidal anti-inflammatory drugs for joint problems and when necessary, anti-depressant medication to relieve the discomfort caused by fibromyalgia.
Gehlen*etal*. (2012)	82	72 women and 10 men / mean of 51 years / not informed	RA	Not informed	Not informed
Ladino *et al.* (2015)	01	Male / 12 years old / Not informed	There were no signs of RA	Arthralgia on the shoulders and left knee.	Prednisone and hydroxychloroquine
Taneichi *et al.* (1993)	01	Female / 24 years old / not informed	RA	Morning stiffness, pain and swelling of the proximal bilateral interphalangeal joint and pain in the knee joints.	Loxoprofeno auranofina
Turkcapar *et al.* (2006)	01	Female / 45 years old / Caucasian	RA and proximal scleroderma	Fatigue, dyspnoea, chest pain and arthralgia, involvement of the joints of the hands, elbows and ankles, morning stiffness, sclerosis on the face and fingers.	Low doses of methotrexate, and prednisolone
Edvard S. Falk (1979)	01	Male / 74 years old / not informed	RA	Shoulder, elbow, hand, ankle, and knee pains, moderate swelling in small and medium joints, bullous eruption with crusts and lightly encrusted, involvement of the thorax and abdômen.	Triamcinolone phenylbutazone, indomethacin and, subsequently, salicylates, chloroquine and aurotiomal sodium
Calabrese *et al.* (1989)	01	Female / 64 years / no informed	RA, human immunodeficiency virus	Systemic polyarthritis of the small joints of the hands and wrists, morning stiffness, fatigue and subcutaneous nodules, synovitis of the fingers and cortical erosions of several metacarpophalangeal.	Aspirin and Intermittent injections of adrenocorticotrophic hormone Hydroxychloroquine
Miyagawa *et al.* (1989)	01	Female / 49 years old / not informed	RA, scleredema	Pain and deformities involving hands, ankles and feet.	Auranofine, loxoprofen and disodium lobenzarit
Young *et al.* (2018)	01	Female / 18 years old / not informed	RA	Not informed	Benlysta, glaxosmithkline, zoloft pfizer, aspirin, ibuprofen, prednisone, cevimeline,

Clinical manifestations of RA involve the joints of the hands and wrists. However, it may involve the knees, hips, shoulders, elbows, temporomandibular and synovial joints of the spine. The manifestations can be of varied forms from the moderate one until a progressive and destructive polyarthritis, presenting clinically pain, edema and local heat. According to GOELDNER *et al*. (2011), extra-articular manifestations are observed in approximately 50% of patients, with SS being the most common. Literatures already report the association of RA with secondary SS. Nevertheless, the fact this syndrome has several etiologies generates difficulty in diagnosis. Although they present several diagnostic criteria, literatures do not use them in isolation to define SS. Therefore, there is a need for multidisciplinary team evaluation. Another controversial factor in the literature is the clinical manifestation of SS associated with RA in addition to the types of treatments proposed (FELBERG and DANTAS, 2006). For all the above, it is important to note the importance of this paper. In this context, the objective of the present study is systematically and critically review the case reports in individuals with RA associated with RA, emphasizing the epidemiological profile, clinical manifestations, diagnoses and proposed treatments.

MATERIALS AND METHODS

A literature review of the clinical cases published by a researcher on the Bireme and PubMed websites, using keywords such as Rheumatoid Arthritis and Sjogren's syndrome, was searched in a search for articles available online in English, Portuguese and Spanish, published in the period of 2011 to 2018, besides the integration of classic articles between the years 1979 and 1989.The inclusion criteria adopted for the research were articles involving the themes Sjogren's syndrome and rheumatoid arthritis, description of case reports, in the periods already mentioned. It was initially performed the analysis by title of the periodicals, with the subsequent evaluation of the abstracts in order to use them in the present research, ending with observation of the complete article.

RESULTS

The tables 01 and 02 present the data described in each article studied. This present study observed that the most frequent autoimmune disease associated with Sjogren's syndrome is rheumatoid arthritis. Through analysis, the greatest predilection for women over 35 years old is evident, since among the articles only 03 patients were younger than 35 years (LAWALL *et al*., 2006), (LADINO *et al*., 2015) and (YOUNG *et al*., 2018). The most common symptoms found in almost all articles are mouth and dry eye symptoms (CALABRESE *et al*., 1989), (FALK 1979), (LADINO *et al*., 2015), (LAWALL *et al*., 2006), (CALABRESE *et al*., 1989), (FALK *et al*., 1989). Moreover, pains in the joints, especially of the hands, elbows, knees and wrists (MIYAGAWA *et al*. (TANEICHI *et al*., 1993) and (TURKALLAPAR *et al*., 2004), (GEHLEN *et al*., 2012), (LADINO *et al*. *et al*., 2006). Analyzing the two tables and the types of treatments proposed for RA and SS, it is noted that some articles did not inform the type of treatment for SS, and those who presented, quoted artificial tears and saliva (BEZERRA *et al*. , 2010), (FREITAS *et al*., 2004) and (LADINO *et al*., 2015).

Table 2. Description of the diagnosis and oral manifestations of Sjogren's syndrome

Articles	Diagnosis / Diagnostic methods	Clinical manifestations	Oral Manifestations	Treatment
Lawall *et al.* (2006)	SS secundária, sialectasia puntiforme/ not informed	Bilateral swelling in the parotid region, pain after meals, dry mouth, pruritus, eye burning, dryness, small fissures, dry mouth.	Dental calculus on most teeth, some carious lesions and halitosis.	Tartarectomy, dental polishing, topical application of fluoride; rifampicin; for left parotid infection, salivary secretion was stimulated with intrabucal lemon drops and manual massage of the parotid gland; water intake (two liters / day) and use of oral lubricant ointment.
Freitas *et al.* (2004)	SS secondary, erythematous candidiasis of the mucosa palatine / not informed	Sensation of dryness and burning of the mouth, difficulty in chewing and swallowing of food, rough sensation in the eyes, vaginal dryness, dryness of the buccal mucosa, and lingual surface fissured and despapilada.	Erythematous candidiasis in the palatal mucosa, periodontal disease and presence of gingival bleeding.	Use of artificial saliva and tear, vaginal lubricant, antifungal and oral hygiene instruction.
Bezerra *et al.* (2010)	RA, secondary SS / Schirmer and Rose Bengal tests, conclusive submandibular ultrasonography for nonspecific sialodenitis and scintigraphy	Pain in the submandibular glands, fissure in the labial commissures, pharyngeal dryness causing pain in the vocal cords and difficulty of breathing, sensation of presence of sand grains in the eyes and burning.	Class V caries lesions, bacterial plaque deposits, chronic atrophic candidiasis associated with the use of removable partial dentures and irritation of the gingival mucosa.	Artificial tears and ocular ointments for ocular involvement, artificial saliva, Class V restorations, antifungal medication, periodontal therapy, topical application of fluoride and fluoride-rich mouthwash solutions.
Gehlen*et al.* (2012)	Secondary SS / Schirmer's test, biopsy of the minor salivary gland.	Dry eyes	Dry mouth	Not informed
Ladino *et al.* (2015)	He/she presented xerophylia, primary SS / Shirmer's test, minor salivary gland biopsy for diagnosis confirmation, scintigraphy resulting in severe dysfunction of the salivary glands and moderate parotid dysfunction.	Dry eyes, pain in the parotid region, dry oral mucosa, thick saliva and changes in the salivary glands.	Presence of multiple dental caries.	Use of artificial tears and treatment with prednisone and hydroxychloroquine.
Taneichi *et al.* (1993)	Secondary SS and punctate sialectasis / lip biopsy revealed slight lymphocyte infiltrates, Shirmer's test and pink-bengal staining were not normal.	Dry eyes, pyrexia and swelling of the cervical and auxiliary lymph nodes	Dry mouth	Não informou
Turkcapar *etal*. (2006)	SS secondary/ Not informed.	Photosensitivity, difficulty swallowing, reflux and pruritus in the eyes.	Dry mouth	Prednisolone
Edvard S. Falk (1979)	SS, chronic sialoadenitis, parotid gland atrophy bilateral conjunctivitis with lack of tear production / Not informed.	Dry throat and eyes	Dry mouth	Not informed
Calabrese *et al.* (1989)	SS, human immunodeficiency virus / Not informed.	Dryness of the eyes and diffuse lymphadenopathy	Dry mouth	Not informed
Miyagawa *et al.*(1989)	SS and Scleredema / sialography and salivary gland scanning	Dry eyes and tightening of the skin.	Dry mouth and difficulty opening the mouth	Not informed
Young *et al* (2018)	SS and systemic lupus erythematosus /Not informed.	Not informed	Symptoms of dry mouth, hyposalivation, considerable sensitivity, plaque, calculus, severe generalized chronic gingivitis with bleeding and carious lesions	Oral hygiene instructions, caries treatment, oral pH neutralizing lubricant spray containing xylitol and xylitol gum, calcium phosphate paste and casein phosphate

The most common diagnostic methods presented in Table 2 were Schirmer's test and biopsy (BEZERRA *et al*., 2010), (GEHLEN *et al*., 2012), (LADINO *et al*., 2015) and (TANEICHI *et al*., 1993). The articles showed that the drugs for treatment of RA are varied, containing corticosteroids, analgesics and anti-inflammatories (BEZERRA *et al*., 2010), (CALABRESE *et al*., 1989), (LADINO *et al*., 2015), (LAWALL *et al*., 2006), (MIYAGAWA *et al*., 1989), (TANEICHI *et al*., 1993), (TURKCAPAR *et al*., 2006) e (YOUNG *et al*., 2018). This indicates that there is no drug standardization to treat RA, but drugs to control or reduce the symptoms. Not all the articles studied do not cite the oral manifestations even if important. They mention calculi, carious lesions, periodontal diseases, gingival bleeding. These oral manifestations were treated through prophylaxis, restoration, supragingival scaling, fluoride application, oral hygiene instruction and mouthwash solutions (BEZERRA *et al*., 2010) (FREITAS *et al*., 2004) (LADINO *et al*. 2015) and (LAWALL *et al*., 2006).

DISCUSSION

The present results show that the association of RA with SS is a proven factor in which corroborates with the literature studied (LAWALL *et al*., 2006).

As observed, the most common symptoms among patients with SS are the sensation of dryness in the eyes and mouth (CALABRESE *et al*., 1989), (FALK 1979), (LADINO *et al*., 2015), (LAWALL *et al*., 2006), (MIYAGAWA *et al*., 1989), (TANEICHI *et al*., 1993) and (TURKCAPAR *et al*., 2006). Also in RA, joint pains mainly from the hands, elbows, knees and wrists. (LADINO *et al*., 2006), (LAWALL *et al*., 2006), (CALABRESE *et al*., 1989), (FALK 1979), (FREITAS *et al*. (TANEICHI *et al*., 1993) and (TURKCAPAR *et al*., 2006). According to GEHLEN *et al*. (2012) and BEZERRA *et al*. (2010), the confirmation of the dry eye symptom is confirmed through the result of Schimer's positive test, added to the complaints presented by the patients GEHLEN *et al*. (2012). In addition, states that the onset of eye diseases is not associated with the duration of RA.

This test was described in the present study in the studies analyzed (BEZERRA *et al*., 2010), (GEHLEN *et al*., 2012), (LADINO *et al*., 2015) and (TANEICHI *et al*., 1993). As regards SS diagnosis, its establishment is still uncertain, because the symptoms are not specific, standardized and because of the diversity of diagnostic methods (FELBERG and DANTAS, 2006), (LAWS *et al*., 2004) *et al*., 2006) and (LIQUIDATO and BUSSOLOTI FILHO, 2005), corroborating with the study by BEZERRA *et al*. (2010). In the literature the most common symptoms of RA are pains in the hands, elbows, knees and wrists (Calabrese *et al*., 1989) (FALK, 1979), (FREITAS *et al*., 2004), (GEHLEN *ET AL*., 2012), (TANEICHI *et al*., 1993) and (TURKCAPAR *et al*., 2006). The diagnosis must be made precisely because the symptoms of the disease are not exclusive and simultaneous, therefore laboratory, radiographic and clinical findings are necessary to diagnose at an earlier stage due to its aggressive nature(GOELDNER *et al*. (2011) and(TURKCAPAR *et al*., 2006).GOELDNER *et al*. (2011) report that magnetic resonance imaging has been the most effective imaging technique for the early diagnosis of RA, since it points to changes in both soft tissue and cartilage and bone. The most frequent oral manifestations were calculations, carious lesions, periodontal diseases and gingival bleeding (BEZERRA *et al*., 2010), (FREITAS *et al*., 2004), (LADINO *et al*., 2015), (LAWALL *et al*., 2006) and (YOUNG *et al*., 2018).FREITAS *et al*. (2004) showed that SS patients have a high prevalence of dental cavities usually in the cervical region of the teeth and presence of periodontal disease.

PORTER *et al*. (2004) and RADFAR *et al*. (2003) describe that infections and carious lesions occur due to decreased salivary flow. Also for this reason, Al-Hashimi (2001) points out patients with SS present higher rates of alveolar bone loss and dental plaque. LAWALL *et al*. (2006) explain that quality of life and basic daily activities can be interfered by oral changes presented by the patient. However, HAY *et al*. (2001) point out that xerostomia does not affect the quality of life and nutrition of the syndromic patients. Treatment of RA is based on medications to control symptoms through analgesics, corticosteroids and anti-inflammatories (BEZERRA *et al*., 2010), (CALABRESE *et al*., 1989), (LADINO *et al*., 2015), (LAWALL *et al*., 2006), (MIYAGAWA *et al*., 1989), (PORTER *et al*., 2004) and (TANEICHI *et al*., 1993), (TURKCAPAR *et al*., 2006). Currently for the treatment of RA are applied medication, educational measures and psycho-occupational therapies (GEHLEN *et al*., 2012). For the treatment of SS symptoms, the most common in the literature were saliva and artificial tears (BEZERRA *et al*., 2010), (FREITAS *et al*., 2004) and (LADINO *et al*., 2015). FREITAS *et al*. (2004) mention that the therapy aims to alleviate ocular and oral symptoms improving the quality of life of patients with syndromes. In the present study, it was found that the use of fluoride in the treatment of oral hygiene, as well as in oral hygiene and oral hygiene, and (LAWALL *et al*., 2006).

Conclusion

This work concludes that the confirmation of the positive relationship between SS and RA, in which, despite interrelating the signs and symptoms of diseases are different. The most prevalent form of SS treatment was the use of saliva and artificial tears. However, the way of treating RA did not follow a predominant pattern of medications. The study verified that there is a relationship between SS with the oral health deficiency of patients due to lack and salivation and alveolar bone loss. This paper ends with the observation of the literary shortage of case reports on the theme proposed in the present study.

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