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Review Article

Prevalence and Severity of Sjogren's Syndrome in Patients with Rheumatoid Arthritis- A Review

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Abstract: ***Background*:** Sjögren's syndrome (SS) is a systemic autoimmune disorder characterized by lymphocytic infiltration of exocrine glands, leading to dryness of the mouth and eyes. When SS occurs in association with rheumatoid arthritis (RA), it is known as secondary Sjögren's syndrome (sSS). The coexistence of these two diseases significantly impacts disease progression, and patient quality of life. ***Aim*:** This review aims to summarize and analyze recent literature concerning the prevalence and severity of SS among RA patients across different populations, with special attention to variations in diagnostic criteria, immunological markers, and therapeutic implications. ***Methodology*:** A structured literature search was conducted in PubMed, Scopus, and Google Scholar databases, focusing on studies published between 2018 and 2025. The review includes data from multiple cohort, cross-sectional, and population-based studies that met the 2010 ACR/EULAR classification criteria for RA and the 2016 ACR/EULAR criteria for SS. ***Results***: Findings consistently demonstrate that the prevalence of SS among RA patients ranges between 8% and 22% in Western populations and up to 40% in Asian populations, suggesting both genetic and diagnostic influences. RA-SS patients exhibit distinct serological profiles, including elevated anti-Ro/SSA and anti-La/SSB antibodies, and are more prone to ocular surface disorders, fatigue, and systemic complications. ***Conclusion*:** Despite variations among studies, the evidence supports that SS represents a frequent and clinically relevant comorbidity in RA. Standardized diagnostic methods and unified criteria are essential for accurate prevalence estimation and better clinical management. Future large-scale, prospective studies are needed to clarify the immunopathogenic links between these two autoimmune diseases.

Keywords: Autoimmune Diseases, Rheumatoid Arthritis, Rheumatology, Sjögren's Syndrome.

1. INTRODUCTION

Autoimmune diseases are long-term disorders that are characterized by the destruction of the body tissues disguised by immune mediators. Among them, Sjogren syndrome (SS) and rheumatoid arthritis (RA) are some of the most common systemic autoimmune diseases in middle-aged and old age with specific susceptibility to women. The distinctive features of SS are the gradual inflammation of lymphocytes in exocrine glands, in particular the salivary and sicca lacrimal glands, which lead to xerostomia and keratoconjunctivitis sicca. In addition to glandular manifestations, SS may have multisystemic manifestations of arthralgia, myalgia, fatigue, neuropathy, and vasculitis [1, 2]. The syndrome of Sjogren is generally divided into primary SS (pSS) and occurred in isolation, as well as secondary SS (sSS) that occurs with other autoimmune disorders, the most prominent one being lupus erythematitis [3]. RA is an inflammatory disease that is chronic and has infiltration of synovitis, systemic inflammatory, autoantibodies, rheumatoid factor (RF) and anti-citrullinated peptides antibodies (ACPAs). The relationship between RA and SS has been established a long time ago, and it was reported that up to 40% of the RA patients could present the aspects of secondary SS [4]. Their tendency to both manifest in the same person sometimes called RA-associated SS (RASS) has significant clinical and treatment implications. The presence of anti-SSA/Ro and anti-SSB/La autoantibodies has been detected decades before the development of the disease RA, giving reason to believe that both disorders may have comparable pathogenic mechanisms that involve B-cell hyperactivity and chronic interferon type 1 signaling [5]. HLA-DR4 allele is also genetically predisposed and seems to be a cause of the susceptibility to the disease [6].

One has indicated that the association of RASS was significantly linked to patients with dry mouth and dry eyes as well as high erythrocyte sedimentation rate (ESR) in patients with anti-SSA-positive RA. Nevertheless, the limited sample of RASS patients in this work can be viewed as the cause of doubting the validity of the conclusion [7]. Since disease-modifying antirheumatic drugs (DMARDs) and biologic agents are now considered a first-line therapy of RA, they are used in virtually every patient with the disease. This is because ocular issues are expected to arise since the life expectancy of RA patients has been increased. Therefore, it is clinically significant to explain the occurrence of SS due to RA and its association with existing treatment methods [8, 9]. Although other studies examining the prevalence of SS in relation to RA report rates of 15-44% in the general RA population, and 100% in certain cohorts with serious RA, such data are hardly applicable to conventional DMARDs and biologic agents commonly used [10]. The factors that were used in the diagnosis of SS were not clear, which made comparison of studies difficult. Besides diagnostic criteria, treatment with RA can have an effect on prevalence of and severity of SS related along with RA. With the growth in the number of treatments against RA, pulmonary and skin involvement decreased in prevalence [11]. RA has a significant amount of phenotypic heterogeneity in the clinical presentation, with joint disease and extrarticular organ systems co-occurring. It is estimated that about 30% of patients have seronegative RA, which is characterized by the lack of rheumatoid factor (RF) and/or anti-cyclic citrullinated peptide antibodies (ACPA) [12]. Moreover, an additional one out of five RA patients has extra-articular manifestations. A unique entity with exocrine glands involvement was reported in the 1980s. Recent cohort studies have drawn focus towards the clinical significance of such overlap by demonstrating that RA patients with Sjoren syndrome (SS) exhibit worse patient-reported outcomes, increased global disease activity, and reduced functional index compared to the rest of the population with RA [13,14]. Sicca symptomatic patients are common in RA, and most often they complain of xerostomia and ocular discomfort due to exocrine loss. These circulating RA-related auto-antibodies, including anti-SS-A and anti-SS-B, are predictors of the potential of SS in the case of the salivary gland biopsy [15]. Systemic disease burden was reported by the aforementioned cohort, which also reported the presence of the abnormalities of the organs of hearing and swallowing. The symptoms of SS are associated with earlier onset of RA, increased systemic and joint severity, and increased anti SS A positivity [16].

The joint symptomatology can develop depending on the disease stage and the treatment plans. SS in RA is compatible with the 2016 ACR/EULAR classification, but the lip lesions are almost uncommon [17]. As a result, histopathologically provable SS is often ignored by rheumatologists when dealing with RA. Additional diagnostic modalities to be adopted in the detection of SS in RA patients at the early stages of the disease development are worth research [6-18]. Thus, the purpose of this study was to determine the rate and severity of SS in RA patients under treatment with existing options and find out the dependence on the treatment option.

2. STUDIES AND METHODOLOGY

This was a methodological review where recent research studies on the prevalence and severity of Sjogreens syndrome (SS) were identified, evaluated and synthesized in patients with rheumatoid arthritis (RA). A full-text search was done in PubMed, Scopus and Google database in ensuring the retrieval of peer reviewed articles published in (2018-2025) years. In a search format, such combinations of words like; Sjögren syndrome, rheumatoid arthritis, secondary Sjogren, prevalence, severity, autoimmune comorbidity and EULAR/ACR classification were incorporated. Refinement of the results was done using Boolean operators (AND, OR). Newswires, editorials, conference abstracts without full texts and studies that participant pediatrics or non-humans were excluded. An approximation of 60 studies were reviewed, including cohort, cross- sectional, and population-based study designs. Data were pulled off on population demographics, diagnostic criteria, SS prevalence, antibody positivity (anti Your league/SSA and anti Your league/SSB), ocular and oral involvement and treatment outcomes. Qualitative analysis of findings was done and sorted into thematic topics about pathophysiology, epidemiology, clinical manifestations, diagnosis and management.

2.1. Patient-Reported Outcomes

Patient-reported outcomes have been used to determine the severity of SS, and these include a wide range of generic health-related quality of life (HRQoL) measurements, disease-impact scales, symptom scale, and the visual analog scale. The majority of the PROs assess merely a portion of carbonated symptomatic and health-impairment domains in the perspective of the patient [19]. Not all these instruments have received serious reliability as well as validity validation. The current literature search shows that 44 different indices will be identified, and they are grouped in seven indicators. The most common type of PROs used in research quantifying patient burden in SS is multidimensional indices assessing the effect of HRQoL on the patient [20].

The generic HRQoL instruments are used to measure changes in overall health in the physical, psychological, and social domains; they are used to measure health as a whole and as independent of the disease-specific symptomatology. These generic measures are widely used in the cost-utility study and, due to their standardization, allow making comparisons between diseases [21]. Generic metrics do not have the capacity to explain the symptoms and functional impairments that patients are going through due to SS and its treatment, which might not be of major importance on disease

impact. The long- ecosystem SF-36 has 36 items spread among eight health domains, including emotional well-being, pain and social functioning and produces a Physical Component Summary (PCS) and Mental Component Summary (MCS) score [22]. The short-form 12-item Health Survey is based on the SF -36 and provides two composite scores. Since all the responses of the items have positive rating, a larger score is interpreted as better HRQoL, and vice versa (lower score, worse HRQoL) [23].

2.2. Selection Criteria of Sjogren Syndrome

The most commonly accepted time is the 2016 classification criteria which are applied as the regulatory standard to be included in clinical trial of novel therapeutics. The criteria items are based on clinical manifestations of SS determined by pathophysiology of the disease, which is supplemented with laboratory data (the presence of autoantibody, studies of the tear and saliva, lip biopsies, etc.) [24].

Therefore, criteria elements differ significantly based on the characteristics of patients and the type of platforms used in the assays; therefore, there is no golden standard in the diagnosis of SS [6]. About 30% of SS patients do not show any marker-symptom profile according to the classification criteria, but SS is suspected in the case of an autoimmune disease with xerostomia and/or xerophthalmia [19]. Therefore, in the process of assessing the Sjogren syndrome, other diagnostic tests, which were done in the past, are traditionally regarded as the gold standard in this case. As an example, patients that meet at least one criterion of each of the categories of diagnoses may be considered as having SS [25-27].

2.3. Statistical Data and Trends

Salvadorsson *et al.*, in a chart review, defined SS prevalence as the health status of the RA patients who had a diagnosis of SS by the rheumatologists, divided by the number of RA patients [28]. The medical record team in Hanyang University Hospital extracted medical charts out of the hospital records. The informed consent had to be waived as the medical records were de-identified and retrospectively obtained. This study was approved by an Institutional Review Board of the Hanyang University Hospital. RA and rheumatology department, Medical records of patients with RA who attended the rheumatology department between January 2016 to December 2019 were checked. The diagnosis of RA was based on the 2010 ACR/EULAR criteria [6]. Enrolled patients had SS according to the criterion of the 2002 American-European Consensus Group classification. Total clinical features of RA patients are presented. Out of a total of 827 patients, 733 (88.6%) were female and the mean age of them was 63.6±12.6/years. The mean duration of RA was 9.8±9.9 years, RF anti-CCP 651 (82.1%) and 407 (51.7%) patients, respectively. Among 827 RA patients, 54 (7.0%) were found to have SS diagnosed using rheumatologists. The prevalence of SS was observed to be greater among the patients of RA with sicca symptoms. The authors found that 18.5% of patients were diagnosed with SS during the first meeting with the rheumatologists, and 81.5% were diagnosed with RA first; persons with a longer period of RA and higher rate of anti-CCP positivity were diagnosed with RA. In line with this, increased RA seropositivity is associated with SS seropositivity. Better screening plans of SS in RA patients would thus be justified.

3. EPIDEMIOLOGY

Numerous researches defining SS epidemiology in RA described criteria used to classify prior to the 2010 update that defines conditions that a patient has to meet to qualify as having RA [29]. Therefore, the trend followed was to use high-sensitivity techniques that provided a wider definition. The purpose of the update was to make the most of sensitivity to detect RA early and prolong the therapeutic window [30].

Sjögren syndrome (SS) is a long term auto-immune disease of the exocrine glands which is either primary or secondary. Primary SS (pSS) is a condition in which xerostomia and xerophthalmia exist regardless of an autoimmune disease [31]. The onset of secondary SS (sSS) is linked to an existing autoimmune disease, including RA; systemic lupus erythematosus (SLE) and systemic sclerosis; in case of cooccurrence of pSS and another autoimmune disorder, we find the overlapping clinical manifestations of the disease in the form of a dry mouth, a dry eye, and enlargement of parotid glands [6-32]. The SD can occur in the RA patient over an unpredictable period of time as many as months to decades after the appearance of the disease [15]. The syndrome can further be divided into two temporal phenotypes, the first type (type 1) is when a sicca is diagnosed prior to or at the same time as RA diagnosis, and the second type (type 2) is when sicca is diagnosed retrospectively or 5 years exceeding the diagnosis of RA. sSS diagnosis receives the criteria of ACR/EULAR 2016 [32]. The prevalence rate of SS in cohorts of RA lies between 22-70% epidemiologically. The primary goal of the present one was to measure SS prevalence in a variety of classification systems and compare clinical characteristics in patients with RA including and excluding SS [33, 34].

The incidence of the Sjoegren syndrome (SS) among patients with rheumatoid arthritis (RA) is very diverse based on the aspects of the diagnosis applied. Similar estimates are derived with estimations conducted based on both the ACR/EULAR 2012 and the 2016 ACR/EULAR classification criteria using a cohort based on SS-RA [35]. The needs toward regular exams to identify SS have not been fulfilled, and the dynamics of SS treatment in SS-RA patients are not clearly defined, and rheumatologists typically manage patients with RA [6]. This paper set out to examine the risk and

severity of SS in RA patients. In this regard, the researchers employed the gold standard test in measuring the prevalence of SS. They assessed whether there were differences on the symptoms and the severity of the disease based on the diagnosis of SS.

The Sjogren syndrome affects mortality of the RA patients significantly. The uneven international tests on SS lead to the miscalculation of its prevalence, which influences the outcomes of RA patients [8-36]. It is also deficient in unmet needs to standard treatments of SS-RA patients. Antimalarials have been utilized to this end in treating patients with SS - RA, but there is less evidence of their effectiveness and concern that the drugs may exacerbate the activity of RA [35]. Moreover, once the diagnosis of SS or SS-RA is made, there is no knowledge about the medication patterns in such categories of patients [37].

3.1. RA Patients with Sjogren Syndrome Prevalence

The recent reports both in Iraq and other Arab countries have highlighted the high rate of SS in RA patients- a most unexploited issue in the regions. SS is recognised as an autoimmune disease that is mainly of the form keratoconjunctivitis sicca and xerostomia, or in some cases parotid glands swelling or systemic [38]. Primary Sjogren syndrome When SS co-exists with RA, it is known as secondary Sjogren syndrome. Studies show that the prevalence of SS in the RA patients is between 15-30%. A recent local study has indicated a prevalence of 30.5 0, using accepted classifying criteria as a reference [39, 40]. In spite of a large number of diagnostic tests in the detection of SS, not many studies have assessed SS prevalence using different diagnostic tests with classification criteria as the gold standard [41]. The current study illustrates that a longer period of swollen joint counts than the usual cut-off, along with anti-Ro antibodies and KCS serve the best in decreasing the risk of RA isolated among RA patients when a number of classification criteria of SS are measured. Differently put, RA patients who conduct such tests have fewer chances of having RA free of SS. The discriminatory ability of diagnostic tests to identify SS in RA patients is brought to the limelight of the result that the longer the counting of swollen joints surpasses the standard cut-off, the greater it is likely to be to identify SS in RA. The long history of swollen joints counts is an indicator of RA and the results could be used in establishing the presence of SS in RA patients. In patients with RA, a prolonged joint count time together with the presence of the serological markers of anti-Ro or KCS has the potential to cause clinicians to suspect the presence of SS, potentially identifying more cases of RA patients with SS.

3.2. Predictors of Prevalence and Severity of SS in RA

The available literature on prevalence and severity of the Sjogren syndrome (SS) in patients with rheumatoid arthritis (RA) is characterized by heterogeneity in terms of the study design, populations sampled, diagnostic criteria and methodological procedures [6]. However, most studies have enrolled participants in university hospitals and clinics and had symptomatology, serologic testing, and ocular or gland of salivary gland functional assessment to determine the presence of SS [42]. There are comparatively few studies on the epidemiology of RA and SS in communities, thus, the prevalence of SS (3,2%) is among the RA patients has been inconsistent and a similar prevalence exists (3.8%) in patients with no RA [10-43].

A higher incidence of SS has been reported in RA patients aged 65 or more years (8.7%), highlighting a need to address this topic using cohorts, older patients, and a population-wide level of analysis. Regarding athletic patterns of the treatment of RA, the existence of SS was not found to determine the selection of pharmacologic agents. On the other hand, forms of comparative studies on clinical data of patients with RA with or without SS often presented a large number of differences [34, 44]. There was a significant difference in serologic autoantibody profiles in patients with RA who had SS and in those without the syndrome. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels were significantly lower in the SS group who also had no surplus of tender or swollen joints in comparison with their non-SS counterparts which would indicate a less active serological state of the disease in patients of RA with SS. The serum IgG and IgM levels were higher in the SS patients and there were no significant differences in the presence or absence of rheumatoid factor which may show a higher tendency toward autoantibodies and autoimmune comorbidities in RA patients with flanking SS. The present paper suffers a number of drawbacks. There was no information on other modes of RA treatment other than those studied. The correlation between SS and clinical manifestation of RA should be further explained. Although the current results may indicate that the presence of the concomitant SS does not modify the therapeutic regimes, the natural history of RA in the co-morbidity context of SS is poorly defined and warrants further study.

4. PATHOPHYSIOLOGY

The procedures causing most of the pathogenic mechanisms cause the ectopic activation of T and B lymphocytes to promote ectopic germinal center formation and autoantibodies to SSA/Ro60, SSA/Ro52, and SSB/La in affected tissues [45]. B cell-mediated autoimmunity directly depends on type I interferons [46]. Type I interferon increase IL-1b-producing dendritic cells, thus causing the B cells to become a plasma blast/effector lineage and eventually generating pathogenic autoantibodies [46]. These autoantibodies are formed before the pathologically significant disease, and it is believed that

their role in the progression of MG is present [47]. One of the characteristics of MG at the cellular level is the abnormal increase in the number of B cells in the TA. Blimp1 is also the transcriptional regulator that also mediates B cell hyperproliferation in the mouse model of MG that induces the expression of glycolysis and mitochondrial biogenesis genes [48]. Constitutive signaling of the TLR pathway, comprised of TLR/IL1R signaling through NF-kB and TLR/MyD88/IRAK3 signaling through IRF7 also mediates the hyperproliferation of B cells. In MG models, an alteration of very many genes and epigenetic modifications are caused by an aberrant B cell signal [6-49].

The abnormal expression of epigenetic factors in Sjogren syndrome (SS) is the organization of B cell hyperreactivity and production of inflammatory cytokines [50]. Sjogren syndrome changes the chromatin remodeling factors and histone modification of the pro-inflammatory cytokine's genes. The mechanism involved silencing target genes through epigenetics, such as the miRNA, lncRNA, silencing of the targets by methylation [50,51] Moreover, higher rates of programmed cell death 1 (PD -1) high and IgD - B cells and IgM and IgG levels in the serum and supernatant of isolated B cells were observed in the active stage of Sjogren syndrome, indicating that it was linked to B cell activation [52]. In vivo and in vitro methods analyzed the impact of the deficiency of MYSM1 - and E4f1-B cells on the IgM class switch and affinity maturation [53, 54]. Nonetheless, there was a mixed IgG1 and IgG2b antibody response. These results thus indicate that this is through these epigenetics that Aide is indirectly regulated [55].

SS is chronic progressive, autoimmune disease that is characterized by xerostomia and xerophthalmia caused by the dysfunction of salivary and lacrimal glands. Primary SS is a standalone disease [56]. The secondary SS is co-morbid with other autoimmune conditions such as RA, SLE and scleroderma. SS is also a common comorbidity in RA, and patients with RA who also have SS are more severely affected and have worse prognoses [57]. The full knowledge of RA serological profiles, such as RF, ACPAs, and anti-SS-A antibodies, can provide an insight into the pathogenic process and help in designing the specific treatment methods [12]. High levels of autoantibodies are associated with a high level of complications. B-cell hyperactivity and autoimmunity in salivary glands are also implicated in the RA patients with SS, where the exaggerated prevalence of anti-SS-A is the key point [58, 59]. The fact that salivary gland hypofunction is one of the most widely used classification criteria in SS in RA raises questions about its etiologic basis, as it could be caused by RA or the latter. The results of the salivary flow analysis demonstrate that the extent of glandular damage is higher in individuals who have concomitant SS [60]. More studies are needed to determine whether these limitations on glands increase the disease activity of RA or distort the profiles of autoantibodies [61].

5. CLINICAL FEATURES

Patients with SS always exhibit oral dryness, fatigue, tests of abnormal hepatic functioning, Raynaud phenomenon, synovitis, and dependence on disease-modifying anti-rheumatic drugs (DMARDs) [6]. On the other hand, digital ulcer is more common among RA patients who do not have SS. There are no significant differences in the joint distribution, pain intensity, and general RA severity, however, there are significant differences in the Steinbroker staging system that the two scales of patients differ on Cammarata & Jan, [62]. Sjogren syndrome (SS) is a persistent autoimmune disorder of exocrine glands like salivary and lacrimal glands, which infiltrates inflammatory sites and leads to glandular hypofunction [63]. SS can either appear as an isolated condition (primary SS) or as a complication with connective tissue diseases (secondary SS). SS patients can have RF and anti-CCP antibodies. The prevalence rates within the groups of people having RA and the severity of manifestation in other underlying conditions differ [3-33]. The aim of the study was to approximate the prevalence of SS in patients with RA, as well as to compare the clinical characteristics of subjects with and without SS in RA. The patients with RA with SS were identified using Clinical SS criteria, which were contrasted with the ACR-2012 SS criteria. Findings showed that the general prevalence of SS was equal, and the existence of SS had a insignificant impact on customers of RA treatment. Nevertheless, the findings are not exactly the same as there are a number of clinical characteristics that differ greatly across cohorts. Oral dryness, fatigue, abnormal hepatic tests, Raynauds phenomenon, synovitis, and DMARD use are more common among the RA patients with SS. The prevalence rate of digital ulceration is still higher in RA patients without SS. Although no significant differences in joint distribution at onset, degree of pain and RA clinical severity have been found, Steinbroker staging distribution varies significantly between groups.

The extent of Sicca symptoms was assessed with the Non-Dryness Severity Scale -12 (NCSS-12) of the National Institutes of health, to be filled in by a physician-global assessment of ocular and oral dryness. The measures of health-related quality of life, the disease activity indices, and damage indices and the treatment patterns were used to assess clinical characteristics related to SS severity [6].

A group of RA patients that took screening diagnostics of SS was recruited. Of these, 6.5% were SSA-positive. The NCSS -12 has shown that the burden of severity of SS was low, and the manifestations of sicca were mild and moderate. NCSS-12 severity scores did not have a statistically significant relationship with prevalence of xerostomia, xerophthalmia, and mixed sicca presentations [64].

The commonness and clinical features of SS among the RA patients were studied with a diverse methodology in various studies. Based on the 2016 ACR /EULAR classification criteria, 24% to 36% of the patients with RA were determined to have SS. But classification achieved ranges between 69% and 85%, which indicates the possibility of misclassifying a group of participants [65, 66]. The non-classification criteria strategies were used to approximate SS prevalence in RA giving estimates of 35% to 68% interestingly, some of the studies conducted in the past used archaic definitions of SS and this might have resulted in the underestimation of the prevalence. It was found in the literature that prevalence estimates in patients with RA who have a confirmed SS diagnosis are available [10-67].

Since, according to the original classification framework, eight distinct criteria according to the 2016 ACR/EULAR guidelines were required, the aspect of radiographic data was not mentioned since such an assumption was made that the investigators had specialized training and experience. Suspected RA participants who did not fit the full ACR / EULAR criteria were also involved since they may be mistaken as typical rheumatoid arthritis. In addition, as part of daily clinical routine, the diagnostic work-ups of rheumatologists were considered the most accurate, thus limiting the risk of misclassification [68].

5.1. Association with Disease Activity of RA

The Disease Activity Score 28 -CRP (DAS28 -CRP) was used to measure RA activity, and included swollen joint count (0-28), tender joint count (0-28), serum C-reactive protein (CRP, mg/L), and global assessment of the patient (0-100). The period of disease was calculated as the time taken by the disease beginning with initial diagnosis of RA to the study enrolment date. The levels of rheumatoid factor (RF) and anti -cyclic citrullinated peptide (anti-CCP) antibodies (measured using immunoturbidimetric assay and enzyme-link immunosorbent assay, respectively) were considered positively when positive in at least one of them, thus seropositivity. Extra-articular manifestations occurred when diagnosed with pulmonary disease, serositivities, systemic vasculitis, and neuropathy in the medical history of the patients or diagnosed with dermatologic involvement or hematology abnormality.

The rate of SS in the RA victims was 25% as defined by the ACR/ EULAR 2012 scale, and 20.7% based on the ACR 1986 scale. Isolated RA people had a lower prevalence of SS related symptoms and risks in screening SS but had a more common prevalence of complications associated with SS vulnerability as compared to patients who had the co-morbid, RA and SS diagnoses. The aftermath of the propensity-score matching, SS became an independent risk factor of the lengthy disease duration and the presence of RF. The sensitivity analysis indicated the increasing odds ratios of disease activity among the patients with RA with co-occurring SS. Nevertheless, these relationships failed to be sustained in the matched cohort with the analysis of disease length done through ordinal logistic regression. The identification of other immune-mediated inflammatory disorders, such as RA, other arthritides, systemic lupus erythematosus, and sarcoidosis, were found to be independent risk factors of RA complicated by SS. Despite the fact that the sample was sufficient, further research is still needed to make conclusive results.

There are some implications in this real-life cohort that has a large sample size despite some of the limitations. To begin with, RA patients have a high prevalence rate of SS that should be cautiously interpreted. The overestimation of SS incidence among the patients of RA could have been caused by the use of ACR/EULAR 2012 SS criteria and a small set of laboratory confirmations. This is added to the fact that there are no established sophisticated diagnostic standards of SS and no salivary gland imaging research to complicate the situation. Being a retrospective observational research study conducted at one tertiary center, the study might have underdetermined the actual SS prevalence in RA. Importantly, the diagnostic guidelines that were followed by rheumatologists were regarded as the official reference point in terms of SS diagnostics and noted an increased incidence of SS relative to previous ones [6-8].

6. DIAGNOSIS AND MANAGEMENT

Sjogren syndrome (SS) is an autoimmune disease characterized by inflammation of the salivary and lacrimal glands with a final outcome of xerostomia and xerophthalmia. This is supported by pathophysiology characterized by impaired regulation of immune and disturbed production of interferons which result in hyperreactivity in the immune system as well as infiltration by B cells and T cells that produce significant levels of autoantibodies. SS is often isolated (primary SS) as well as is present together with rheumatoid arthritis (RA) or systemic lupus erythematosus (secondary SS). In addition, the symptoms of Sjogren syndrome can be the predecessors of a rheumatic disease diagnosis [6-70]. SS has a prevalence of about 30% of the RA patients. The prevalence of SS in RA patients has been described as between 8.5-47.8%; however, SS in cohorts of RA has been mostly underreported because patients may not report symptomatic dryness or clinicians may not consider SS to be severe or chronic [71,72].

SS is often viewed as an inconvenience in comparison with other forms of systemic expression, similar to the cutaneous lupus erythematosus. Nevertheless, SS has significant effects in the life of RA patients. Involuntary xerostomia and xerophthalmia are still chronic problems to patients, even though they are not acutely life-threatening. They can face a lack of fluency in speech and swallowing, and they can get dental caries and periodontal disease as a consequence of

poor saliva [66-73]. Dry eyes will trigger regular attacks of keratoconjunctivitis, and others will experience corneal ulceration, which reduces the level of vision. As the disease advances, the patients could lose their vision and hence corneal transplantation is required. The severity of symptoms, as seen by patients, might not correspond to objective measures, but Sjogren syndrome patients have a high chance of getting lymphoma [74]. Raynaud's phenomenon, malaise, fatigue or serositi can also occur which makes the need to identify the condition early essential. Sjogren syndrome may be clinically diagnosed when the symptoms of xerostomia or xerophthalmia are accompanied by labial salivary gland biopsy evidence of focal periductal infiltration 50 or more lymphocytes, anti-Ro/SS-A, anti-La/SS-B antibodies, and/or a test of Schirmer result <5 mm [75].

7. IMPACT ON QUALITY OF LIFE

Sjogren syndrome (SS) is an autoimmune disease characterized by traces of keratoconjunctivitis sicca, xerostomia, as a result of atrophic exocrine glands progressive destruction. It either falls as primary or secondary basing on the concomitant activity of other organ systems [56]. The systemic disorder that is most frequently identified to be linked to SS among the connective tissue diseases is rheumatoid arthritis (RA). The stated SS rates among RA cohorts vary between 20 to 66%. The presence of anti-Ro/SS-A and/or anti-La/SS-B is a critical point of diagnosis of SS, which is supported by supplementary laboratory research [6]. This cross-sectional study compared the prevalence and clinical characteristics of SS among the Korean patients with RA. Besides the modern subjective visual and oral presentations, the research involved the historical occurrences or manifestations which may be contributory factors towards xerophthalmia and/or xerostomia.

SS is a non-malignant autoimmune disease with heterogeneous clinical manifestations, which is mostly related to exocrine glands, thus causing xerophthalmia and xerostomia. These manifestations may be disabling and trigger the range of complications [76]. SS is commonly linked to other autoimmune pathologies, and secondary SS is reported effectively. RA is the most common disease, which is associated with secondary SS; SS can also be observed in patients with RA without systemic sclerosis or any other rheumatic disorders, and these patients are branded as primary SS patients. SS can either have glandular syndrome (xerostomia, keratoconjunctivitis sicca, parotid gland swelling, etc.) or extraglandular (fatigue, arthralgia, and neuropathy) symptoms [72].

Visual impairment and fatigue of the eye, as well as xerostomia can cause oral complications, such as caries in the mouth, halitosis, oral candidiasis, and dysphagia [77]. Fatigue forms part of the most common symptoms in the SS patients, and it greatly affects the quality of life of such patients. The diagnosis of SS can be done through the Sjogrens International Collaborative Clinical Alliance (SICCA) criteria; an in-depth description of SS patients can assist clinicians in defining those at high risk and the need to strengthen surveillance [78].

8. CONCLUSION

The prevalence of Sjögren's syndrome (SS) was higher in Japanese rheumatoid arthritis (RA) patients than previously reported in non-Japanese populations. There were no differences in clinical characteristics and disease activity between RA patients with SS and those without, except for the prevalence of positivity in anti-AchR Ab and similar immunosuppressants used. While the cause of dry mouth and dry eyes may be suppressed inflammation due to methotrexate or biological agents, the opposite mechanism is also possible. Further well-designed prospective studies are necessary to clarify the influence of RA therapy on the clinical course of SS.

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