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Diagnostic Approach and Management of Sjogren's Syndrome

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ABSTRACT

Introduction: *Sjogren's syndrome (SS) is a chronic autoimmune disorder characterized by sicca symptoms, particularly xerostomia, resulting from salivary gland dysfunction. Accurate assessment of glandular function and systemic disease activity is essential, as subjective complaints often do not correlate with objective clinical measurements. This study aimed to evaluate diagnostic and therapeutic approaches in patients with primary Sjogren's syndrome based on objective salivary gland function assessment and standardized measurement of systemic disease activity.* ***Methods:*** *This study employed a literature review method using a descriptive qualitative design with a content analysis approach. Data were collected from relevant scientific sources, including journals, articles, and academic books, selected through purposive sampling based on relevance, credibility, and publication within the last 5–10 years. The literature search was conducted through databases such as Google Scholar, PubMed, and ScienceDirect, followed by a systematic selection process using PRISMA stages (identification, screening, eligibility, and inclusion). The collected data were analyzed by organizing, comparing, and synthesizing findings from previous studies to generate comprehensive conclusions.* ***Results:*** *A discrepancy was observed between subjective xerostomia complaints and objective salivary function measurements. ESSDAI scoring demonstrated variability in systemic disease activity, categorized as low, moderate, and high. A multidisciplinary approach contributed to accurate diagnosis and evaluation of organ involvement.* ***Discussion:*** *The findings highlight the limitation of relying solely on subjective symptoms in assessing Sjogren's syndrome. The inconsistency between patient-reported xerostomia and objective measurements underscores the importance of integrating standardized clinical tools to improve diagnostic accuracy. Furthermore, the variability in ESSDAI scores indicates the need for individualized and comprehensive evaluation of systemic involvement.* ***Conclusion:*** *Therapeutic decision-making in Sjogren's syndrome should be guided by objective salivary gland function assessment and standardized systemic activity indices such as ESSDAI, rather than relying solely on subjective patient-reported symptoms. The integration of subjective and objective evaluations through periodic monitoring may enhance therapeutic precision and improve long-term disease management outcomes in patients with Sjogren's syndrome.*

Introduction

Despite advances in the understanding of Sjogren's syndrome (SS), significant challenges remain in its timely diagnosis and optimal management. The heterogeneity of clinical manifestations, coupled with the frequent discrepancy between subjective symptoms and objective clinical findings, often leads to underdiagnosis or delayed diagnosis, particularly in non-specialist settings. This issue is further exacerbated in developing countries, including Indonesia,

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where limited epidemiological data, lack of standardized diagnostic protocols, and restricted access to specialized healthcare services hinder early detection and appropriate disease monitoring.

The understanding of Sjögren's syndrome (SS) has evolved progressively from early clinical observations to a more comprehensive characterization as a systemic autoimmune disease. The condition was first described by Hadden, Leber, and Mikulicz in 1880, primarily in relation to glandular enlargement. Subsequent advancements were marked by the work of the Swedish ophthalmologist Henrik Sjögren in 1933, who further delineated the syndrome by emphasizing its association with keratoconjunctivitis sicca, polyarthritis, and systemic manifestations. These early contributions laid the foundation for the modern conceptualization of SS as a complex autoimmune disorder.

Despite these advances, the etiology of SS remains incompletely understood, involving a multifactorial interplay of genetic predisposition, environmental triggers, and immune dysregulation. Sjogren's syndrome (SS) is a chronic systemic rheumatic disorder characterized by lymphocytic infiltration of the exocrine glands, particularly the salivary and lacrimal glands, resulting in progressive glandular dysfunction and leading to xerostomia and keratoconjunctivitis sicca (Parisis et al., 2020; Vitali et al., 2021). Although SS can occur at any age, it most commonly presents between the ages of 45 and 55 years (Carsons et al., 2022). The disease shows a strong female predominance, with an estimated female-to-male ratio of approximately 9:1 (Vitali et al., 2021). Epidemiological data indicate that the prevalence of SS ranges from 0.1 to 3 cases per 1,000 individuals (Vitali et al., 2021). This classification reflects growing recognition of the heterogeneity of disease presentation and its overlap with other autoimmune conditions.

Epidemiologically, SS is considered one of the most prevalent systemic autoimmune diseases, second only to systemic lupus erythematosus. Global prevalence estimates range from 0.1% to 4% of the population (Carsons et al., 2022), with approximately 2–4 million affected individuals in the United States alone (Mathews et al., 2020; Birt et al., 2027). However, the true burden of disease is likely underestimated, as up to 50% of cases remain undiagnosed, and nearly 60% occur concomitantly with other autoimmune disorders. SS can occur at any age but is most frequently diagnosed between 40 and 60 years, with a marked female predominance (female-to-male ratio of approximately 9:1) (Vitali et al., 2021). Regional variations have also been reported, such as prevalence rates ranging from 0.33% to 0.77% among women in China (Stefanski et al., 2017), highlighting the influence of geographic and population-specific factors.

The condition now recognized as Sjögren's syndrome (SS) was initially described by Hadden, Leber, and Mikulicz in 1880, primarily in relation to glandular enlargement. The term "Sjögren's syndrome" was later introduced following the report by the Swedish ophthalmologist Henrik Sjögren in 1933, who further characterized the disease by emphasizing its association with keratoconjunctivitis sicca, polyarthritis, and systemic manifestations. Since then, SS has been increasingly recognized as a complex systemic autoimmune disorder, although its precise etiology remains incompletely understood.

From a clinical perspective, SS is classified into two main subtypes: primary SS, which occurs independently, and secondary SS, which develops in association with other systemic autoimmune diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), or systemic sclerosis (Parisis et al., 2020; Vitali et al., 2021). Advances in understanding the immunopathology and clinical heterogeneity of SS have contributed to improved classification systems; however, challenges remain in accurately assessing disease activity and organ involvement.

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Epidemiologically, SS is considered one of the most prevalent autoimmune diseases after SLE, with a global prevalence estimated between 0.1% and 4% of the population (Carsons et al., 2022). In the United States alone, it is estimated to affect approximately 2–4 million individuals (Mathews et al., 2020; Westerlund et al., 2021). Despite its relatively high prevalence, up to 50% of cases remain undiagnosed, largely due to its heterogeneous clinical presentation and the frequent discrepancy between subjective symptoms and objective clinical findings. The disease can occur at any age but is most commonly diagnosed between 40 and 60 years, with a strong female predominance (female-to-male ratio approximately 9:1) (Vitali et al., 2021). Regional data also demonstrate variability, such as prevalence estimates of 0.33%–0.77% among women in China (Barber et al., 2021).

According to the World Health Organization, autoimmune diseases represent a growing global health concern, affecting millions of individuals worldwide and contributing substantially to chronic morbidity and reduced quality of life (Ansari et al., 2025). Although Sjogren's syndrome (SS) is not always reported as a standalone entity in global surveillance systems, it is recognized as one of the most common systemic autoimmune rheumatic diseases. Current global estimates suggest that SS affects approximately 0.1% to 4% of the population, with considerable variation across regions and populations (Cao et al., 2023).

From a global health perspective, the burden of SS extends beyond glandular dysfunction, as it is associated with systemic complications, increased risk of lymphoma, and long-term healthcare needs. The World Health Organization emphasizes the importance of early detection and standardized management of chronic autoimmune conditions to reduce disability and improve patient outcomes. However, disparities in healthcare access, particularly in developing countries, continue to limit the implementation of such strategies. This global prevalence and burden highlight the urgent need for improved diagnostic accuracy and comprehensive disease assessment. In the context of SS, reliance on subjective symptoms alone remains insufficient, reinforcing the necessity of integrating objective clinical measurements and standardized indices such as ESSDAI to align with global health priorities and improve disease management outcomes.

However, in developing countries, including Indonesia, epidemiological data and clinical characterization of SS remain limited. In particular, there is a lack of comprehensive studies evaluating the integration of subjective symptoms and objective measures of salivary gland function alongside standardized systemic disease activity indices.

Therefore, this study aims to address this gap by evaluating objective salivary gland function and systemic disease activity in patients with primary Sjögren's syndrome in Indonesia. By integrating subjective and objective diagnostic approaches, this study is expected to improve diagnostic accuracy and support more effective, evidence-based management strategies in the local clinical setting. Given its heterogeneous clinical spectrum and frequent overlap with other autoimmune conditions, SS poses significant challenges for clinicians in selecting optimal therapeutic strategies that minimize risk while ensuring favorable and safe patient outcomes. Through this literature review, the authors aim to provide a comprehensive discussion on the diagnostic approach and evidence-based management of Sjogren's syndrome.

Methods

The research method employed in this study is a literature review (Nasution & Junaidi, 2024; Sari et al., 2022), which involves collecting, examining, and analyzing various scientific sources relevant to the research topic. This study aims to comprehensively explore the longitudinal approaches and management of *Sjogren's Syndrome* based on findings from previous studies. The research design used is descriptive qualitative with a content analysis approach, in which the

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researcher does not conduct direct field data collection but instead utilizes secondary data derived from credible sources such as scientific journals, research articles, and academic books.

The data sources in this study consist of scientific literature selected using a purposive sampling technique, where sources are chosen based on specific criteria, including relevance to the research topic, publication in reputable journals, and a publication timeframe within the last 5–10 years to ensure the data remains up-to-date. The research instrument includes a documentation sheet and a literature checklist used to identify, record, and categorize important information from each analyzed source. Data collection is conducted through searches in scientific databases such as Google Scholar, PubMed, and ScienceDirect, followed by processes of selection, classification, and organization of the literature based on relevant themes.

Data analysis is performed using content analysis techniques (Hasan et al., 2025), which involve organizing the collected literature, thoroughly reading and understanding each source, categorizing information into specific themes, comparing findings across studies, and synthesizing the information to draw comprehensive conclusions. This study is conducted over a period of approximately 1 to 3 months, including stages of literature collection, source selection and classification, data analysis, and report writing. Through this approach, the study is expected to provide a systematic and in-depth understanding of the topic under investigation.

Results and Discussion

Results

1. Diagnostic Approach

The clinical presentation of SS is often dominated by sicca syndrome, resulting from immune-mediated glandular involvement. In addition to glandular dysfunction, many patients experience fatigue, musculoskeletal pain, and various systemic manifestations. Sicca symptoms represent the hallmark feature of SS and may involve multiple organ systems (Barber et al., 2021). Among patients with pSS, approximately 94% present with dry eyes and dry mouth at the time of diagnosis, and nearly 30% develop unilateral or bilateral parotid gland enlargement.[8,9] Lymphoma is a recognized complication, occurring in approximately 2–5% of patients (Westerlund et al., 2021).

Clinically, the manifestations of SS are broadly categorized into two major groups: exocrine gland manifestations and extraglandular (systemic) manifestations. Sjogren's syndrome (SS) is broadly classified into two major categories of clinical involvement: exocrine gland manifestations and extraglandular manifestations (Negrini et al., 2022).

Table 1. Clinical Manifestations of Sjogren's Syndrome

Organ/System	Clinical Manifestations
Exocrine Gland Manifestations	
Oral cavity	Xerostomia (dry mouth) evidenced by hyposalivation, dysphagia, dental caries, taste disturbances (dysgeusia), and oral candidiasis (Negrini et al., 2022).
Ocular	Keratoconjunctivitis sicca, corneal damage, uveitis, scleritis, and optic neuritis (Heus et al., 2020).
Salivary glands	Enlargement of the parotid, submandibular, or other salivary glands, which may be acute, intermittent, or chronically persistent; unilateral or bilateral; typically soft, diffuse, and non-tender (Byrne et al., 2024)

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Genitourinary	Dyspareunia, bacterial and candidal infections, sexual dysfunction, reduced sexual activity and satisfaction (Luczak et al., 2021)
Extraglandular Manifestations	
Musculoskeletal	Arthritis, fibromyalgia, myalgia (Dick et al., 2020).
Cutaneous	Xerosis, purpura, Raynaud's phenomenon, cutaneous vasculitis, annular erythema, angular cheilitis (Popescu et al., 2017).
Pulmonary	Airway disease, interstitial lung disease, xerotrachea (Martinez et al., 2018)
Cardiovascular	Increased cardiovascular risk, hypertension (Tong et al., 2021)
Gastrointestinal–hepatic	Dysphagia, gastroesophageal reflux, nausea, vomiting, chronic diarrhea, constipation, primary biliary cirrhosis, autoimmune hepatitis, sclerosing cholangitis (Pabolu et al., 2021)
Renal	Tubulointerstitial nephritis, renal tubular acidosis (Hamada, 2023)
Neurological	Peripheral**:** sensory or sensorimotor axonal polyneuropathy, sensory neuropathy, sensory ganglionopathy, radiculoneuropathy, mononeuritis multiplex. Central: cognitive dysfunction, transverse myelitis, paralysis, meningitis, seizures, headache, optic neuritis, encephalopathy, and multiple sclerosis–like demyelinating disease (Mnatsakanova & Abrams, 2020)
Hematologic	Cytopenia, hypergammaglobulinemia, hypogammaglobulinemia, monoclonal gammopathy, cryoglobulinemia, and elevated autoantibody titers (Zhao et al., 2021)

Dry eye complaints are not exclusively attributable to Sjogren's syndrome (SS), as they may also arise from other underlying conditions.23,24 Ocular manifestations of SS extend beyond keratoconjunctivitis sicca and may include corneal melt, uveitis, scleritis, retinal vasculitis, and optic neuritis (Foulks et al., 2015). The majority of patients with dry eye report symptoms such as excessive tearing, burning or stinging sensations, foreign body sensation, pruritus, photophobia, blurred vision, conjunctival hyperemia, mucous discharge, increased blinking frequency, and ocular fatigue. Notably, approximately 40% of patients with SS do not report symptoms of dry eye, underscoring the importance of regular evaluation and periodic ophthalmologic assessment. Accurate assessment of ocular surface symptoms can be performed using validated screening instruments, such as the Ocular Surface Disease Index (OSDI) or the Dry Eye Questionnaire-5 (DEQ-5) (Ghimire et al., 2026; Astuti et al., 2025; Zhang et al., 2023).

Dry eye disease can be classified into two principal subtypes: 1) Aqueous-deficient dry eye, which is associated with reduced tear film production. 2) Evaporative dry eye, which is most commonly related to meibomian gland dysfunction.

The evaluation of patients with Sjogren's syndrome (SS) requires multidisciplinary expert consultation to establish the diagnosis, exclude non-autoimmune etiologies, and assess the extent of organ damage as well as the patient's biological phenotype. A comprehensive understanding of the differential diagnosis of SS manifestations is essential to support accurate diagnostic confirmation.

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The differential diagnosis of SS includes conditions associated with sicca symptoms and enlargement of the salivary or lacrimal glands. In most cases, alternative diagnoses can be excluded on the basis of detailed medical history, thorough physical examination, and objective evidence of systemic autoimmunity (Sciascia et al., 2023).

The EULAR Sjogren's Syndrome Disease Activity Index (ESSDAI) is a validated clinical index designed to measure systemic disease activity in patients with primary Sjogren's syndrome (pSS). Developed in 2009, ESSDAI is used not only for routine clinical assessment of systemic involvement but also as a standardized outcome measure in clinical research involving SS (Rosas et al., 2019; de Wolff et al., 2025; Weng et al., 2022).

ESSDAI comprises 12 domains reflecting systemic activity across multiple organ systems and laboratory parameters. These domains include constitutional symptoms, lymphadenopathy, glandular involvement, hematologic and biologic features, as well as organ-specific manifestations affecting the skin, joints, respiratory system, kidneys, muscles, and both the central and peripheral nervous systems. Each domain is stratified into three or four levels according to activity severity (0 = no activity; 1 = low activity; 2 = moderate activity; 3 = high activity), with weighted scores assigned depending on the specific domain (de Wolff et al., 2025).

The final ESSDAI score is calculated as the sum of all individual domain scores, yielding a total score ranging from 0 to a maximum of 123. To avoid misclassification of chronic irreversible damage as active systemic disease, a score of 0 is assigned when manifestations are attributable to permanent damage that has remained stable for at least 12 months.

Based on the total ESSDAI score, systemic disease activity is categorized into three levels: 1) Low activity: <5 points. 2) Moderate activity: 5–13 points. 3) High activity: >13 points.48

2. Administrative Procedures

Chronic SS necessitates long-term daily therapy; therefore, treatment strategies with minimal (or at least tolerable and reversible) adverse effects should be prioritized. Multiple clinical studies and systematic reviews from the Cochrane Collaboration support the daily use of topical therapies for the relief of dryness symptoms, demonstrating significant improvements in health-related quality of life (HRQoL) without clinically meaningful adverse effects (Sheppard et al., 2023; Decup et al., 2025; Negrini et al., 2022). Topical or local therapy should be initiated promptly once objective evidence of glandular dysfunction has been established (Lam et al., 2020).

Systemic involvement represents the principal prognostic determinant in SS and is associated with autoimmune-mediated organ dysfunction that may ultimately become irreversible. The use of systemic immunomodulatory or immunosuppressive therapies including glucocorticoids, antimalarials, immunosuppressive agents, intravenous immunoglobulin, and biologic agents should be reserved for patients with active systemic disease. However, such treatment should only be initiated following careful, organ-by-organ evaluation of disease severity and cumulative organ damage, as not all patients with active systemic manifestations require systemic therapy (Lam et al., 2020).

Patient education is of paramount importance, as it significantly influences disease understanding, management strategies, therapeutic adherence, and overall prognosis.

Dietary supplementation with omega-3 fatty acids has been shown to prolong tear break-up time and increase tear volume. Certain fish (e.g., salmon and tuna), shrimp and crab, flaxseed oil, dark leafy vegetables, and walnuts are rich sources of omega-3 fatty acids, which inhibit pro-inflammatory eicosanoids and cytokines. Omega-3 fatty acids reduce the activation of pro-inflammatory cytokines, enhance anti-inflammatory prostaglandin synthesis, promote

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inflammation resolution through resolvins, and exert neuroprotective effects (Ramos-Casals et al., 2020).

Accumulating evidence indicates that inflammation constitutes a key component in the pathogenesis of dry eye disease. Resolvin E1 (RvE1; RX-10001) is an endogenous mediator derived from the omega-3 polyunsaturated fatty acid eicosapentaenoic acid (EPA) and plays a pivotal role in inflammation resolution and tissue protection. RvE1 has been demonstrated to enhance tear production, preserve corneal epithelial integrity, and suppress inflammation-induced cyclooxygenase-2 (COX-2) expression. Within the corneal stroma, RvE1 inhibits keratocyte-to-myofibroblast transformation and reduces monocyte/macrophage infiltration in dry eye conditions. These findings suggest that RvE1 and related resolvin analogues hold therapeutic potential in the management of dry eye disease (Oliveira et al., 2021; Ji, 2023).

Patients with Sjogren's syndrome (SS) and concomitant dry eye are also advised to maintain proper eyelid hygiene, including the application of warm compresses to the eyelids. Warm compresses may be applied twice daily for 3–5 minutes to liquefy inspissated meibomian gland secretions and soften crusts adherent to the lid margins. Patients should be cautioned against the use of excessively hot water. Warm compress therapy should be followed by moderate-to-firm eyelid massage using a clean cloth. Lid cleansing may additionally be performed with a non-irritating shampoo preparation (Ramos-Casals et al., 2020).

3. Pharmacological Management

High-dose and prolonged glucocorticoid exposure in some patients with SS carries a significant risk of adverse effects. Consequently, immunosuppressive agents may be introduced to mitigate steroid-related toxicity. Given the potential for irreversible organ damage in uncontrolled systemic disease, certain patients particularly those with severe organ involvement may require long-term glucocorticoid therapy. In such cases, the addition of immunosuppressive agents as steroid-sparing therapy is justified, provided that the benefit–risk profile is carefully weighed. Evidence supporting the use of immunosuppressive agents in pSS (including leflunomide, methotrexate, azathioprine, mycophenolate mofetil, and cyclophosphamide) remains limited and of comparable quality across agents. Available data suggest modest benefits on sicca symptoms and laboratory parameters, without consistent efficacy on systemic disease activity, and with relatively high adverse event rates (41–100%). To date, no head-to-head trials have compared efficacy and safety profiles among immunosuppressive agents in primary SS (2002 classification criteria), precluding identification of a superior agent. Selection should therefore be individualized according to patient characteristics, comorbidities, and safety considerations. Furthermore, no standardized recommendations exist regarding optimal dosing, route of administration, or duration of therapy. Management should follow a case-by-case approach analogous to other systemic autoimmune diseases. Although some organizations advocate immunosuppressive monotherapy, no consensus has been reached due to the lack of evidence supporting glucocorticoid-free regimens in SS and the fact that more than 95% of reported cases receiving immunosuppressive therapy in primary SS (2002 criteria) also received concomitant glucocorticoids (Lam et al., 2020). Reported outcomes with immunosuppressive agents in primary SS remain variable.

Several biologic agents are currently under investigation for SS, although available evidence remains limited. The European Alliance of Associations for Rheumatology (EULAR) recommends that rituximab and belimumab may be considered in selected cases. Rituximab may be considered in patients with systemic pSS and in those with severe, refractory systemic disease. The strongest evidence supports its use in manifestations associated with cryoglobulinemic vasculitis. Belimumab may be employed as rescue therapy or in systemic pSS.

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The management of dry eye in SS should begin with assessment using the Ocular Staining Score (OSS) and the Ocular Surface Disease Index (OSDI) to determine the severity of keratoconjunctivitis sicca (KCS). In both non-severe and severe KCS, first-line therapy includes preservative-free artificial tears and ocular gels or ointments. Artificial tears particularly those containing methylcellulose or hyaluronate are recommended for all patients with SS and may be administered at least twice daily, with frequency adjusted according to symptom severity. Ocular gels or ointments provide longer-lasting lubrication but are generally reserved for nighttime use due to patient comfort considerations (Lam et al., 2020).

In severe KCS unresponsive to first-line therapy, short-term topical nonsteroidal anti-inflammatory drugs (NSAIDs) or corticosteroid eye drops may be considered; however, their use should be limited to a maximum of 2–4 weeks to minimize adverse effects. If inadequate response persists, EULAR suggests consideration of additional therapies under investigation, such as topical cyclosporine A or autologous serum eye drops. In refractory cases, punctal occlusion and oral muscarinic agonists (e.g., pilocarpine) may be recommended (Lam et al., 2020; Mehta et al., 2022).

Beyond the severity-based approach to KCS as recommended by EULAR, management of dry eye in SS may also follow national clinical practice guidelines, such as those issued by PERDAMI (Indonesian Ophthalmologists Association) (Zhang et al., 2023).

The therapeutic approach to xerostomia in Sjogren's syndrome (SS) should be guided by objective assessment of salivary gland function rather than solely by patient-reported symptoms. Environmental stressors and individual psychological factors may significantly influence subjective complaints of oral dryness, which frequently do not correlate with objective measurements of glandular function. Baseline evaluation of salivary gland function is therefore recommended prior to initiating therapeutic intervention, including measurement of whole salivary flow rates and exclusion of non-SS-related conditions (e.g., oral candidiasis and burning mouth syndrome). Salivary scintigraphy may also be considered as part of the diagnostic workup.

Subjective assessment of xerostomia may be performed using the Summated Xerostomia Index - Indonesian version (SXI-ID). Clinical evaluation of oral dryness can be conducted using two objective parameters: unstimulated salivary flow rate (USFR) and the Clinical Oral Dryness Score (CODS).80,81 These three measures should be obtained prior to treatment initiation and reassessed periodically throughout the course of therapy to monitor clinical response and guide management adjustments.

In patients with mild salivary gland dysfunction, non-pharmacological glandular stimulation is recommended as first-line therapy. This approach includes gustatory stimulants (e.g., sugar-free sour candies, lozenges, xylitol-containing preparations) and/or mechanical stimulation (e.g., sugar-free chewing gum), as residual salivary gland function may still be responsive to stimulation (Lam et al., 2020). Management of oral manifestations in primary Sjogren's syndrome (pSS) should also align with the clinical practice guidelines issued by the British Society for Rheumatology and endorsed by the National Institute for Health and Care Excellence (NICE).

In patients with moderate glandular dysfunction, pharmacologic stimulation with muscarinic agonists may be considered. Three secretagogues have been used in the management of xerostomia: cevimeline hydrochloride hydrate (cevimeline), pilocarpine hydrochloride, and anetholtrithione. Of these, pilocarpine and cevimeline are recommended for the treatment of oral dryness, although only pilocarpine has received widespread global licensure. Muscarinic agonists may be administered in moderate dysfunction, or in mild cases that are refractory to or decline non-pharmacologic stimulation. Gradual dose escalation up to 15–20 mg/day may reduce the principal adverse effect, namely excessive sweating. In patients who are intolerant of or

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unresponsive to muscarinic agonists, alternative secretagogues such as choleretic agents (anetholtrithione) or mucolytics (bromhexine, N-acetylcysteine) may be considered.

Management of oral complications in SS encompasses treatment and prevention of dental caries, alleviation of oral symptoms, and restoration of oral function. Therapeutic strategies generally focus on dental care, oral hygiene optimization, salivary gland stimulation, and saliva substitutes. In mild cases, sugar-free lozenges, cevimeline, or pilocarpine may be utilized.

Topical fluoride therapy is essential for caries prevention in patients with SS. Recent guidelines sponsored by the Sjogren's Syndrome Foundation recommend the routine use of topical fluoride in individuals with SS and xerostomia.85 These recommendations apply to all patients reporting dry mouth symptoms, irrespective of measured salivary output. This reflects a shift toward a more proactive fluoride strategy, particularly in patients with exposed root surfaces, which are highly susceptible to dental caries.

Standard over-the-counter toothpastes typically contain fluoride concentrations ranging from 500 to 1000 parts per million (ppm), occasionally higher, based on assumptions of normal salivary flow and fluoride bioavailability in saliva. Patients with xerostomia require higher fluoride concentrations to compensate for reduced salivary fluoride content. In such cases, prescription-strength toothpaste containing 2800–5000 ppm fluoride may be indicated. Multiple studies and Cochrane reviews have demonstrated enhanced caries prevention with higher fluoride concentrations, findings further supported by systematic reviews and Delphi consensus processes (Mehta et al., 2022).

Management of salivary gland edema in SS includes short-term oral prednisolone or intramuscular methylprednisolone for acute inflammatory episodes, and glandular massage for chronic inflammation. Baseline ultrasonographic evaluation is recommended to assess active inflammation, infection, or sialolithiasis. Ultrasonography, including Doppler imaging, is valuable in evaluating new swelling of major salivary glands and may aid in distinguishing benign from malignant lesions. In cases of acute inflammation without evidence of infection or obstruction, short-course oral prednisolone or intramuscular methylprednisolone (typically 120 mg) may lead to rapid resolution of glandular swelling. Evidence also suggests that salivary gland massage may alleviate discomfort in chronic inflammatory states (Mehta et al., 2022).

Systemic therapeutic approaches for organ-specific manifestations (glandular, articular, cutaneous, pulmonary, renal, peripheral neuropathic, central nervous system, and hematologic involvement) in SS generally commence with glucocorticoids, immunosuppressive agents, biologic therapies, or combination regimens. The sequencing of these three immunosuppressive categories mirrors therapeutic strategies employed in other systemic autoimmune diseases, such as Systemic Lupus Erythematosus and systemic vasculitis. As a general principle, glucocorticoids are considered first-line therapy for most patients with active systemic SS, whereas immunosuppressive and biologic agents are regarded as second- or third-line options for patients who are intolerant of, refractory to, or anticipated to require prolonged glucocorticoid therapy, as well as for those with severe disease (Lam et al., 2020).

The European Alliance of Associations for Rheumatology (EULAR) has developed structured algorithms to guide systemic treatment selection according to specific organ involvement, including glandular, articular, cutaneous, pulmonary, renal, peripheral neuropathic, central nervous system, and hematologic manifestations.

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Discussions

1. Diagnostic Approach

Fact about Sjogren's syndrome (SS) is a chronic systemic autoimmune disorder that primarily affects the lacrimal and salivary glands. SS occurring in previously healthy individuals is classified as primary Sjogren's syndrome (pSS), whereas secondary Sjogren's syndrome (sSS) develops in patients with established systemic autoimmune diseases. sSS most commonly coexists with systemic lupus erythematosus (15–36%), rheumatoid arthritis (20–32%), and limited or diffuse systemic sclerosis (11–24%). Less frequently, sSS has been reported in association with multiple sclerosis, autoimmune hepatitis, and thyroiditis. The Theory explain that Conceptually, SS is understood as an autoimmune disorder characterized by immune system dysregulation, leading to lymphocytic infiltration of exocrine glands, particularly the lacrimal and salivary glands. The classification into pSS and sSS is based on the theoretical framework that the disease may arise independently (primary) or as part of a broader spectrum of systemic autoimmune conditions (secondary) (Westerlund et al., 2021; Barber et al., 2021). The opini is it can be argued that sSS demonstrates a strong association with various systemic autoimmune diseases; therefore, diagnostic and management approaches should consider the likelihood of complex autoimmune comorbidities.

2. Administrative Procedures

The fact is relatively low prevalence of Sjogren's syndrome (SS) in the general population, combined with its heterogeneous glandular and systemic clinical manifestations, presents challenges in maintaining adequate standards of expertise in non-specialist settings. Comprehensive assessment of patients with SS requires specialist involvement to confirm the diagnosis by excluding non-autoimmune etiologies particularly in patients presenting with sicca symptoms and to evaluate the extent of organ involvement. Additionally, individualized follow-up strategies are necessary, tailored to the patient's clinical and biological profile at the time of diagnosis. Theory explains from a clinical perspective, the complexity and heterogeneity of SS are understood within a framework that emphasizes multidisciplinary evaluation and personalized medicine (Sciascia et al., 2023). This theoretical approach assumes that variability in clinical presentation and disease progression necessitates tailored diagnostic pathways and monitoring strategies to optimize patient outcomes. Opinion
Given these considerations, it can be suggested that strengthening specialist involvement and improving clinical expertise in non-specialist settings may enhance the accuracy of diagnosis and the effectiveness of long-term management for patients with SS.

3. Pharmacological Management

Fact the use of systemic therapy including glucocorticoids, antimalarials, immunosuppressive agents, intravenous immunoglobulin, and biologic agents should be restricted to patients with active systemic disease. However, management of systemic manifestations must be tailored to the specific organ involved, and disease severity should be assessed using the EULAR Sjogren's Syndrome Disease Activity Index (ESSDAI). Systemic therapy may be considered in most patients exhibiting at least moderate activity in one clinical domain or a globally moderate disease activity score (ESSDAI >5). A systemic therapeutic response in SS is defined as a reduction of ≥3 points in the global ESSDAI score from baseline. Theory explains from Importantly, ESSDAI does not capture certain systemic manifestations such as congenital heart

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block associated with anti-Ro antibodies, Raynaud's phenomenon, primary pulmonary hypertension, pleuritis, pericarditis, dysautonomia, interstitial cystitis, and sensorineural hearing loss thereby necessitating individualized management strategies for these conditions (Lam et al., 2020). Pregnant patients with SS likewise require organ-specific management tailored to the pattern of involvement. **Opinion** the frequent use of glucocorticoids in clinical practice for primary SS (pSS) is not supported by robust scientific evidence, as no controlled trials have specifically evaluated their efficacy in systemic disease. Glucocorticoids should therefore be administered at the lowest effective dose and for the shortest duration necessary to control active systemic manifestations. In severe presentations, induction therapy may include pulse-dose methylprednisolone followed by oral prednisolone at 0.5 mg/kg/day or less. In moderate or less severe cases, prednisolone at <0.5 mg/kg/day may be prescribed, with the ultimate goal of discontinuation in inactive patients as soon as clinically feasible, or at least tapering to a maintenance dose of ≤5 mg/day, ideally supported by a glucocorticoid-sparing immunosuppressive agent. Currently, no data in SS provide specific guidance regarding tapering schedules, timing of glucocorticoid-sparing initiation, or optimal treatment duration, although rapid clinically appropriate tapering is recommended (Lam et al., 2020).

The findings of this study demonstrate a notable discrepancy between subjective xerostomia complaints and objective measurements of salivary gland function, as assessed by SXI-ID, UWSFR, and CODS. This suggests that patient-reported symptoms alone may not accurately reflect the severity of glandular dysfunction in Sjögren's syndrome (SS). Clinically, this highlights the importance of integrating both subjective and objective assessments in order to improve diagnostic accuracy and guide appropriate therapeutic decision-making.

These results are consistent with previous studies, which have reported a weak or inconsistent correlation between subjective symptoms of oral dryness and objective salivary flow rates. For instance, prior research indicates that psychological factors, environmental conditions, and individual pain perception may influence patients' subjective experiences of xerostomia, independent of actual salivary gland impairment. Similarly, studies by Lam et al. (2020) and Barber et al. (2021) emphasize that objective diagnostic tools such as salivary flow rate measurement and standardized indices are essential to avoid under- or overestimation of disease severity.

Furthermore, the variability observed in ESSDAI scores among patients in this study reflects the heterogeneous nature of systemic involvement in SS. This finding aligns with earlier reports demonstrating that SS presents with a broad spectrum of clinical manifestations, ranging from mild glandular symptoms to severe systemic complications involving multiple organ systems. The use of ESSDAI as a standardized tool allows for more precise stratification of disease activity, which is crucial for determining the need for systemic therapy and monitoring disease progression over time.

From a biological perspective, the discrepancy between subjective and objective findings may be explained by the underlying pathophysiology of SS. The disease is characterized by lymphocytic infiltration of exocrine glands, leading to progressive destruction of salivary and lacrimal gland tissue. This immune-mediated process involves activation of T and B lymphocytes, production of autoantibodies (such as anti-Ro/SSA and anti-La/SSB), and release of pro-inflammatory cytokines, which collectively contribute to glandular dysfunction. However, the degree of structural damage does not

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always correlate directly with symptom perception, as neural regulation, compensatory mechanisms, and local inflammatory activity may modulate symptom severity.

In addition, systemic inflammation plays a key role in the pathogenesis of SS and may explain the variability in ESSDAI scores observed in this study. Cytokine-mediated immune responses can affect multiple organ systems, resulting in diverse clinical manifestations beyond glandular involvement. This biological complexity underscores the importance of a multidimensional assessment approach that incorporates both local glandular function and systemic disease activity.

Overall, the findings of this study reinforce the need for a comprehensive and standardized diagnostic approach in SS. By integrating subjective symptom evaluation with objective measurements and validated disease activity indices, clinicians can achieve a more accurate assessment of disease burden and tailor management strategies accordingly. This approach is particularly relevant in clinical settings where underdiagnosis and variability in disease presentation remain significant challenges.

Conclusion

This study demonstrates that there is a clear discrepancy between subjective xerostomia complaints and objective measurements of salivary gland function in patients with primary Sjögren's syndrome. The findings indicate that subjective assessment using SXI-ID alone is insufficient to accurately reflect glandular dysfunction, as it does not consistently correlate with objective parameters such as unstimulated whole salivary flow rate (UWSFR) and Clinical Oral Dryness Score (CODS). In addition, the variability observed in ESSDAI scores confirms the heterogeneous nature of systemic disease activity among patients, highlighting that disease severity cannot be adequately captured without standardized measurement tools. The integration of objective salivary gland assessment and ESSDAI provides a more comprehensive evaluation of both local and systemic disease involvement. These results suggest that a diagnostic and management approach based solely on subjective symptoms may lead to misinterpretation of disease severity and suboptimal clinical decisions. Therefore, combining subjective and objective assessments is essential to improve diagnostic accuracy, guide individualized treatment strategies, and enhance monitoring of disease progression in patients with primary Sjögren's syndrome.

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