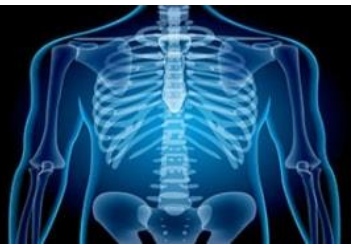
International Journal of Radiology and Diagnostic Imaging



**E-ISSN:** 2664-4444
**P-ISSN:** 2664-4436
www.radiologypaper.com
IJRDI 2023; 6(4): 24-28
Received: 03-07-2023
Accepted: 12-08-2023

**Dalia F Tahir**
Baghdad Health Directorate, Al-Karkh, Baghdad, Iraq

**Iman F Sardar**
Baghdad Health Directorate, Al-Karkh, Baghdad, Iraq

**Nagham Hussain Khalil**
Baghdad Health Directorate, Al-Karkh, Baghdad, Iraq

**Corresponding Author:**
**Dalia F Tahir**
Baghdad Health Directorate, Al-Karkh, Baghdad, Iraq

# The use of qualitative ultrasonic findings in the parotid gland to diagnose Sjogren's syndrome

**Dalia F Tahir, Iman F Sardar and Nagham Hussain Khalil**

**DOI:** https://doi.org/10.33545/26644436.2023.v6.i4a.357

**Abstract**
**Background:** Salivary gland ultrasound has emerged as a promising, non-invasive method for diagnosing Sjogren's syndrome, a condition characterized by changes in the morphology of salivary glands.
**Methods:** A study involving 66 Iraqi participants, including 33 diagnosed with Sjogren's syndrome and 33 controls, utilized ultrasound to examine the parotid glands. This technique evaluated five key parameters: echogenicity, inhomogeneity, presence of hypoechogenic areas, hyperechogenic reflections, and clarity.
**Results:** The study found that ultrasound was highly effective in diagnosing Sjogren's syndrome, with a diagnostic sensitivity of 81.8% and a specificity of 97.0%. Particularly noteworthy was the association of increased disease risk with specific ultrasound findings. A one-unit increase in the inhomogeneity score was linked to a 2.3-fold increase in the risk of Sjogren's syndrome, and a one-unit increase in the presence of hypoechogenic areas score led to a 3.5-fold increase in risk.
**Conclusion:** Drawn from the study highlights the utility of ultrasound in diagnosing Sjogren's syndrome. The presence of hypoechoic areas or parenchymal inhomogeneity on ultrasound proved to be highly accurate in distinguishing patients with Sjogren's syndrome from those without the condition. This demonstrates that salivary gland ultrasound is a valuable and non-invasive diagnostic tool for Sjogren's syndrome, offering a balance of ease, comfort, and accuracy.

**Keywords:** Sjogren's syndrome, salivary glands, ultrasound

## Introduction

Chronic and gradually progressing, Sjogren's syndrome (SS) is an autoimmune disorder distinguished by xerostomia and dry eyes, which are manifestations of lymphocytic infiltration of the exocrine glands. A minor yet noteworthy proportion of patients may develop malignant lymphoma; systemic manifestations affect approximately one-third of patients. The condition may manifest independently (primary SS) or in conjunction with other autoimmune rheumatic diseases such as vasculitis, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), mixed connective tissue disease, scleroderma, or primary biliary cirrhosis [1]. Distinguishing between the primary and secondary variants of the syndrome [2] is the second objective, in addition to subjective and objective evaluation of the ocular and sublingual components, which constitute the diagnostic approach to Sjogren's syndrome, which is quite complex. At present, complementary diagnostic techniques, including sialometry, sialoscintigraphy, and sialography, are utilized to evaluate the involvement of salivary glands in SS. These tests adhere to the classification criteria established by the American European Consensus Group (AECG). The utilization of these tests in conjunction with minor salivary gland (MSGB) biopsies may yield significant insights into the anatomical and functional impairments of these glands [3]. Nevertheless, their application in clinical settings is constrained by their inadequate specificity in diagnosing SS. Conversely, sialography and MSGB, while undeniably more specialized instruments, are invasive in nature and have the potential to induce distress in patients [4, 6]. Ultrasonography (US) has only lately been developed. Because it is non-invasive, does not utilize ionising radiation, can be repeated multiple times, and is available as an outpatient procedure, ultrasonography is more appealing. Excellent near field resolution is a result of the enhanced spatial resolution attained by the most recent iteration of machines and transducers. It is unsurprising that high resolution ultrasound (US) is becoming more prevalent in the field of head and neck imaging, given that the majority of structures and associated pathology in the

neck are located within one to five centimetres beneath the skin surface and that it achieves a superior resolution [7]. Furthermore, the technique's accessibility and affordability contribute to its growing popularity in this domain. The utility of US in diagnosing Sjogren's syndrome and as a potential source of classification criteria for this disease has been recognized by both researchers and clinicians. In addition, the introduction of novel therapeutic approaches for Sjogren's syndrome has generated a demand for reliable and user-friendly imaging instruments that can track the progression of the disease [8, 13]. Since then, the number of studies evaluating the use of US in the diagnosis of SS has increased.

## Methods

66 Iraqi participants, ranging in age from 30 to 73 years, participated in the present investigation. The sample consisted of 33 adult volunteer subjects (4 males and 29 females), comprising the control group, and 33 patients diagnosed with Sjogren's syndrome (4 males and 29 females), comprising the Sjogren's syndrome cases group. These patients were selected in accordance with the American European Consensus Group's revised European criteria for Sjogren's syndrome [14]. Excludable were patients who had received radiation therapy for the head and neck, had a history of hepatitis C infection, had AIDS, had preexisting malignancy, sarcoidosis, graft-versus-host disease, or were prescribed anticholinergic medications. In order to facilitate access, each participant assumed the supine position, with the head turned counter-laterally and the neck hyperextended. Pupils were paired and five parameters were assessed using a semi-quantitative scoring system [15]. The initial parameter was parenchymal echogenicity, which was evaluated by comparing it to the thyroid gland or by examining the surrounding anatomical structures (muscular structures, subcutaneous fat) in cases of concurrent thyroid gland disease. We assigned a grade of 1 if the echogenicity was diminished to a level comparable to that of the thyroid. Graded from zero to three, homogeneity ranked second. A homogeneous gland received a grade of zero, distinct inhomogeneity received a grade of one, extensive inhomogeneity received a grade of three. The presence of hypoechogenic areas, which were rated on a scale of zero to three, constituted the third factor (grade zero: nonexistent; grade one: sporadic; grade two: multiple; grade three: copious). Fourth was the category of hyperechogenic reflections, which were assigned a grade between zero and three: zero (none), one (a few, dispersed), two (multiple), and three (many). The fifth grade, which ranged from 0 to 3, assigned the clarity of the borders of salivary glands as shown in Figures (1) and (2). Grade 0 corresponded to clearly defined, regularly spaced borders, grade 1 to partially defined borders, grade 2 to ill-defined borders, and grade 3 to invisible borders. The effectiveness of five US component scores in distinguishing cases with SS from controls was evaluated using discriminant analysis [16].

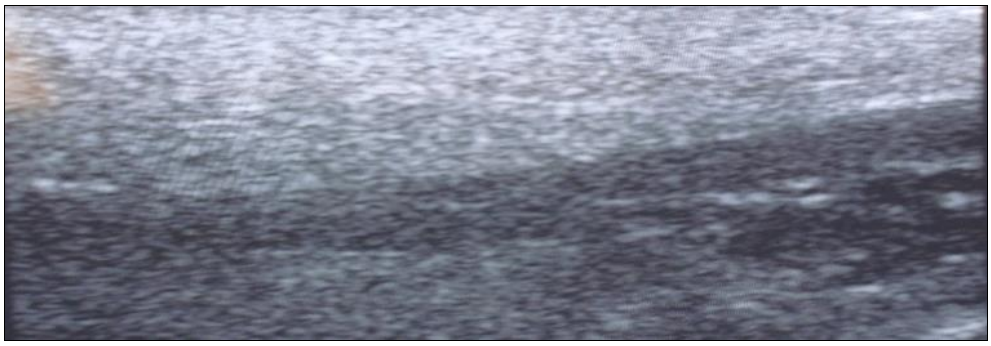


**Fig 1:** Normal parotid gland ultrasound

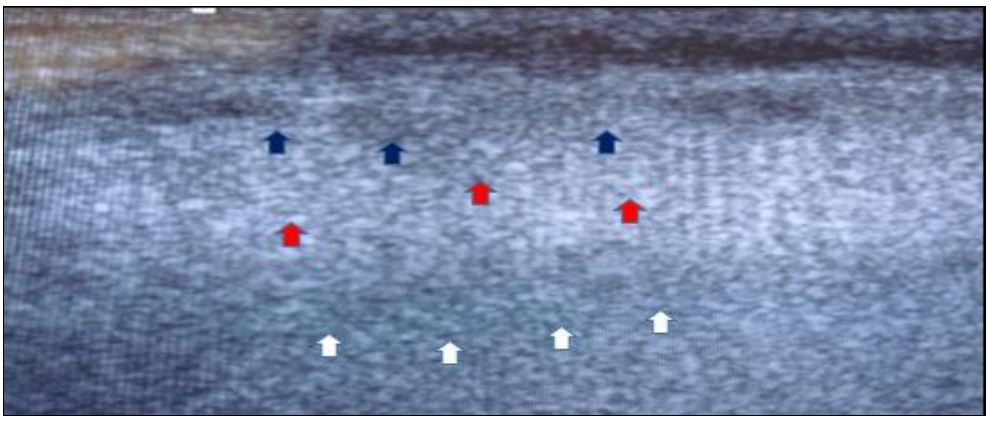


**Fig 2:** parotid gland of Sjogren's syndrome patient ultrasonograph; Black arrow (HPA), red arrow (HPR), white arrow (salivary gland border)

## Results

The frequency of US findings of SS study group SS in the parotid glands by mean of US grading to show the severity of the disease demonstrated that; it was highest for RPE with 60.6% then PHA in grade II-several with 42.4% then IH grade II evident IH with 40.9% then PHR in grade I-few (scattered) with 33.3% and finally clearness of salivary gland border with 33.3% for clear, regular defined borders, table (1).

**Table 1:** Frequency distribution of SS cases group by selected US features of disease severity in the parotid gland

| Parotid gland | N | % |
|---|---|---|
| **Reduced Parenchymal echogenicity** | | |
| Normal | 26 | 39.4 |
| Abnormal (Reduced) | 40 | 60.6 |
| **Inhomogeneity** | | |
| Grade 0-Homogenous | 4 | 6.1 |
| Grade I-Mild inhomogeneity | 25 | 37.9 |
| Grade II-Evident inhomogeneity | 27 | 40.9 |
| Grade III-Grossly in homogenous | 10 | 15.2 |
| **Presence of hypoechogenic areas** | | |
| Grade 0-Absent | 5 | 7.6 |
| Grade I-few (scattered) | 10 | 15.2 |
| Grade II-Several | 28 | 42.4 |
| Grade III-Numerous | 23 | 34.8 |
| **Presence of hyperechogenic reflections** | | |
| Grade 0-Absent | 12 | 18.2 |
| Grade I-few (scattered) | 22 | 33.3 |
| Grade II-Several | 20 | 30.3 |
| Grade III-Numerous | 12 | 18.2 |
| **Clearness of salivary gland borders** | | |
| clear, regular defined borders | 22 | 33.3 |
| Grade I-partly defined borders | 21 | 31.8 |
| Grade II-ill-defined borders | 18 | 27.3 |
| Grade III-borders not defined | 5 | 7.6 |
| Total | 66 | 100 |

As shown in table 2, by the ROC analysis all the previously mentioned scores had an almost perfect (ROC area almost equal to 1) diagnostic performance.

**Table 2:** ROC area for selected US scores when used to predict a diagnosis of SS differentiating it from controls

| | ROC area | P |
|---|---|---|
| Presence of hypoechogenic areas score | 0.978 | <0.001 |
| Inhomogeneity score | 0.971 | <0.001 |
| Total score for submandibular glands | 0.942 | <0.001 |
| Presence of hyperechogenic reflections score | 0.916 | <0.001 |
| Reduced Parenchymal echogenicity score | 0.893 | <0.001 |
| Clearness of salivary gland borders score | 0.807 | <0.001 |

The multivariate models include the multiple logistic regression model and discriminant analysis. As shown in table 3, a multiple logistic regression model with the 5 US component scores as the independent (explanatory variables) was used to assess the net and independent effect of each of these variables on the risk of having SS as the dependent variable. The backward selection method resulted in a model containing only 2US component scores that significantly contribute to the risk of having the disease. These components are IH and PHA score. For each one-unit increase of IH score significantly increase the risk of having the disease by 2.3 times after adjusting for the other independent variable included in the model. For each one-unit increase of PHA significantly increases the risk of having the disease by 3.5 times after adjusting for the other independent variable included in the model. The model containing only 2 out of 5 component US cores was statistically significant and able to classify the study subjects with an overall accuracy of 93.9%.

**Table 3:** Multiple logistic regression model with the risk of having SS as the dependent variable and selected US component scores as the independent (explanatory variables). The backward selection method is used

| | Partial OR | P |
|---|---|---|
| Inhomogeneity score | 2.3 | 0.031 |
| Presence of hypoechogenic areas score | 3.5 | 0.024 |

Overall model predictive accuracy = 93.9%. P (Model) < 0.001

Also discriminant analysis was used to assess the relative importance of 5 US component scores in differentiating cases with SS from controls. The first two components, PHA and IH score were the strongest discriminating components between cases and controls, since they had the highest standardized discriminant coefficients. RPE score, PHR score ranked second in its discriminating ability. The Clearness of salivary gland borders score had the lowest value. The model was statistically significant and able to classify the study subjects with an overall accuracy of 93.9%, table (4).

**Table 4:** Discriminant analysis showing the relative importance of 5 US component scores in the context of case-control differentiation

| | Standardized discriminant function |
|---|---|
| Presence of hypoechogenic areas score | 0.89 |
| Inhomogeneity score | 0.862 |
| Reduced Parenchymal echogenicity score | 0.659 |
| Presence of hyperechogenic reflections score | 0.617 |
| Clearness of salivary gland borders score | 0.448 |

Overall model predictive accuracy = 93.9%. Wilks' Lambda = 0.27. P (Model) < 0.001

## Discussion

In the present study, sonographic grading was based on the qualititative US findings; and they were RPE, IH, PHA, PHR and clearness of gland border diagnostic of SS, these findings were reported in many studies like Mandel and Orchowski [17], Makula *et al.* [18] and Shimizu *et al.* [19]. The results of the study were slightly higher than a study made by Makula *et al.* [18] where RPE was detected in 66 parotids of the 124 parotids examined in about 53.2% and evident IH detected in 40 parotids, about 32.2%, while PHA was in agreement with a study made by Chikui *et al.* [20] as it was detected in 78 parotids of 182 parotids in about 42.8% but the PHR was detected in 46 parotids in about 25.2% which was lower than the present study, such variation could be due to different methodology. The ROC analysis showed that the performance of "IH" was (0.971 by ROC area with P <0.001) and "PHA" was (0.978 by ROC area with P <0.001) had an almost perfect diagnostic performance (ROC area almost equal to 1). Milic *et al.* [21] evaluated the diagnostic performance of US and scintigraphy in SS. Through ROC curves, US arose as the best performer (0.95 ± 0.01), followed by scintigraphy (0.86 ± 0.31). This finding is close to present study finding, the variation could be due to the sample size difference. On the other hand, Salaffi *et al.* [22] studied US findings in SS and evaluated them with a scoring system of 0-16 range, and the results were compared with minor salivary gland biopsy. Through ROC curve salivary US was the best performer (0.859±0.049) followed

by the minor salivary gland biopsy (0.698±0.068). The variation from the present study is due to different methodology used (different scoring system), also Salaffi et [23] found that the performance of US by ROC curves was 0.89 which was the best performer than sialography (0.8) and scintigraphy 0.78, these results varies from our study in the difference in sample size as they examined 77 SS patients and 79 controls. Milic *et al.* [24] made a study to evaluate the diagnostic value of a novel US scoring system for parenchymal inhomogeneity ranging (0-12), as a useful single US criterion in the evaluation of salivary gland involvement in SS. Through ROC curves, US IH score was highly significant (0.96 ± 0.01). This result is in agreement with the result of the present study, the slight variation could be due to different sample size since they included in their study 159 SS patients (primary and secondary) with 36 subjects served as controls. The multiple logistic regression model showed that only 2 out of 5 US component scores (IH and PHA score) that was statistically significant and able to classify the study subjects with an overall accuracy of 93.9%. In Shimizu *et al.* [25] study the PHA was with accuracy of 84.8% and PHR with accuracy of 93.7% making them the 2 US findings out of 4 components that can differentiate SS patients with high accuracy, in the present study PHA and IH were the 2 US findings that can differentiate SS patients, this variation from our study is due to different scoring system used. Discriminant analysis that was used in the present study stated that PHA score and IH score were the strongest discriminating components between cases and controls, since they had the highest standardized discriminant coefficients, and they were statistically significant and able to classify the study subjects with an overall predictive accuracy of 93.9%, and this agrees with Makula *et al.* [26] study where IH and PHA showed the most important structural changes the salivary glands of SS patients. On the other hand, Ariji *et al.* [27] found that by discriminant analysis, PHA and HPR were the strongest components for differentiating SS patients from controls; this result is close to the present study with a slight variation that was due to different methodology used (quantitative scoring system). While Chikui *et al.* 2009 [20] found that by multivariate analysis, the finding of PHA was useful in predicting SS while PHR was not useful and these results are close to the present study, the slight difference is due to different methodology used.

## Conclusion

This study leads us to believe that salivary gland ultrasound is a useful method in visualizing glandular structural changes in patients suspected of having Sjogrens syndrome which leads to the opportunity of including it among the tests for the diagnosis and the classification of the disease.

## Conflict of Interest

Not available

## Financial Support

Not available

## References

1. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, *et al.* Harrison's Principle of Internal Medicine, 17th edition. New York: McGraw-Hill companies; c2008. p. 2107-2112.
2. Jonsson R, Bowman SJ, Gordon TP. Sjogren's syndrome in arthritis and allied conditions. In: Koopman WJ, Moreland LW, editors. A textbook of rheumatology. 15th ed. Philadelphia: Lippincott, Williams and Wilkins; c2005. p. 1681-705.
3. Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE, *et al.* Classification criteria for Sjogren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis. 2002;61:554-8.
4. Jensen SB, Vissink A. Salivary Gland Dysfunction and Xerostomia in Sjogren's Syndrome. Oral Maxillofac Surg Clin North Am. 2014;26:35-53.
5. Kalk WW, Vissink A, Spijkervet FK, Bootsma H, Kallenberg CG, Nieuw Amerongen AV, *et al.* Sialometry and sialochemistry: Diagnostic tools for Sjogren's syndrome. Ann Rheum Dis. 2001;60:1110-6.
6. Baldini C, Gallo A, Perez P, Mosca M, Alevizos I, Bombardieri S, *et al.* Saliva as an ideal milieu for emerging diagnostic approaches in primary Sjogren's syndrome. Clin Exp Rheumatol. 2012;30:785-90.
7. Ahuja AT, Evans RM. Practical Head & Neck Ultrasound. London: Greenwich Medical Media Limited; c2000. p. 3-27.
8. Delli K. Diagnostic properties of ultrasound of major salivary glands in Sjogren's syndrome: a meta-analysis. Oral Dis. 2015;21(6):792-800.
9. Zhou M. Diagnostic accuracy of salivary gland ultrasonography with different scoring systems in Sjogren's syndrome: A systematic review and meta-analysis. Sci. Rep. 2018;8(1):17128.
10. Jousse-Joulin S. Salivary gland ultrasound abnormalities in primary Sjogren's syndrome: Consensus US-SG core items definition and reliability. MD Open. 2017;3(1):e000364.
11. Jousse-Joulin S. Video clip assessment of a salivary gland ultrasound scoring system in Sjogren's syndrome using consensual definitions: An OMERACT Ultrasound Working Group reliability exercise. Ann Rheum Dis. 2019;78:967-73.
12. Geng Y. Salivary gland ultrasound integrated with 2016 ACR/EULAR classification criteria improves the diagnosis of primary Sjogren's syndrome. Clin. Exp. Rheumato. 2020;38(2):322-8.
13. Jousse-Joulin S. Weight of salivary gland ultrasound compared to other items of the 2016 ACR/EULAR classification criteria for primary Sjogren's syndrome. J Intern Med. 2020:287(2):180-8.
14. Vitali C, Bombardieri S, Jonsson R. Classification criteria for Sjogren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis. 2002; 61:554-8.
15. Hocevar A, Ambrozic A, Rozman B, Kveder T, Tomsic M. Ultrasonographic changes of major salivary glands in primary Sjogren's syndrome: Diagnostic value of a novel scoring system. Rheumatology. 2005;44:768-72.
16. Biao ZA. Semiparametric hypothesis testing procedure for the ROC curve area under a density ratio model. Computational statistics and data analysis. 2006;50(7):1855-1876.
17. Mandel L, Orchowski Y. Using ultrasonography to diagnose Sjogren's syndrome. JADA. 1998;129:1129-1133.
18. Makula E, Pokorny C, Rajtar M, Kiss I, Kovacs A.

Parotid gland ultrasonography as a diagnostic tool in primary Sjogren's syndrome. British Journal of Rheumatology. 1996;35:972-977.
19. Shimizu M, Ussmuller J, Hartwein J. Statistical study for sonographic differential diagnosis of tumorous lesions in the parotid gland. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1999;88:226-33.
20. Chikui T, Okamura K, Tokumori K, Nakamura S, Shimizu M, Koga M, *et al.* Quantitative analysis of sonographic images of the parotid gland in patients with Sjogren's syndrome. Ultrasound in Med. & Boil. 2006;32:617-622.
21. Milic V, Petrovic R, Boricic IV, Marinkovic-Eric J, Radunovic GL, Jeremic PD, *et al.* Diagnostic Value of Salivary Gland Ultrasonographic Scoring System in Primary Sjogren's Syndrome: A Comparison with Scintigraphy and Biopsy. J Rheumatol. 2009;36:1495-500.
22. Salaffi F, Argalia G, Carotti M, Giannini FB, Palombi C. Salivary gland ultrasonography in the evaluation of primary Sjogren's syndrome. Comparison with minor salivary gland biopsy. J Rheumatol. 2000;27:1229-3.
23. Salaffi F, Carotti M, Iagnocco A, Luccioli F, Ramonda R, Sabatini E, *et al.* Ultrasonography of salivary glands in primary Sjogren's syndrome: A comparison with contrast sialography and scintigraphy. Rheumatology. 2008;47:1244-1249.
24. Milic VD, Petrovic RR, Boricic IV, Radunovic GL, Pejnovic N, Soldatovic I, *et al.* Major salivary gland sonography in Sjogren's syndrome: diagnostic value of a novel ultrasonography score (0-12) for parenchymal inhomogeneity. Scand J Rheumatol. Early Online; c2010. p. 000-000.
25. Shimizu M, Okamura K, Yoshiura K, Ohyama Y, Nakamura S, Kinukawa N, *et al.* Sonographic diagnostic criteria for screening Sjögren's syndrome. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;102:85-93.
26. Makula E, Pokorny G, Kiss M, Voros E, Kovacs L, Kovacs A, *et al.* The place of magnetic resonance and ultrasonographic examinations of the parotid gland in the diagnosis and follow-up of primary Sjogren's syndrome. Rheumatology. 2000;39:97-104.
27. Ariji Y, Ohki M, Eguchi K, Izumi M, Ariji E, Mizokami A, *et al.* Texture Analysis of Sonographic Features of the Parotid Gland in Sjögren's Syndrome. AJR Am J Roentgenol. 1996;166(4):935-41.

**How to Cite This Article**
Tahir DF, Sardar IF, Khalil NH. The use of qualitative ultrasonic findings in the parotid gland to diagnose Sjogren's syndrome. International Journal of Radiology and Diagnostic Imaging 2023; 6(4): 24-28.