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Evaluation of submandibular and parotid salivary glands by ultrasonography in patients with diabetes

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Abstract

Background: Microvascular complications of diabetes mellitus (DM) include oral manifestations and complications, including xerostomia, reduced salivary flow, susceptibility to infection, periodontal disease and salivary gland enlargement.

Objective: The present study aims to evaluate B-mode ultrasonography (USG) parameters such as size, volume and echogenicity of the submandibular and parotid salivary glands on both sides, shear-wave elastography (SWE) value and colour Doppler properties in patients with DM and healthy control groups.

Methods: In total, 160 right and left submandibular glands and 160 right and left parotid glands of 80 patients, 40 patients (20 type 1 DM, 20 type 2 DM) and 40 healthy control group, between the ages of 18–70 were examined by USG. Echogenicity, parenchyma internal structure, margin and dimensional measurements (antero-posterior length, supero-inferior length, medio-lateral length and volume) and colour Doppler with 'ML 6-15-D Matrix Array (4-15 MHz)' probe, shear-wave elastography '9L-D (2–8 MHz)' probe was investigated.

Result: Statistically significant difference was observed in echogenicity in the right submandibular gland, echogenicity in the right parotid gland, margin characteristics, parenchymal homogeneity and colour Doppler characteristics between the type 1 DM, type 2 DM and control groups ($p < .05$). It was observed that the size, volume and SWE values of both submandibular and parotid glands were higher in the DM patient group than in the control group. Higher values were observed in type 2 DM compared to type 1 DM in the patient group.

Conclusion: USG is an effective imaging technique in investigating the effects of diabetes on the submandibular and parotid salivary glands.

KEYWORDS
diabetes mellitus, parotid gland, shear-wave elastography, submandibular gland, ultrasonography

1 | INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder in which glucose, carbohydrate and fat metabolism are impaired due to an excessive increase in blood glucose level as a result of decreased ability of tissues to metabolise glucose. Various genetic and clinical factors play a role in its aetiology.[1,2] Type 1 DM, constituting 5%–10% of individuals with DM, is a condition that develops with the elimination of insulin secreted by the β cells in the islets of Langerhans in the pancreas, resulting in complete insulin deficiency.[3] Type 2 DM constitutes more than 90% of all diabetes cases and presents with increased plasma insulin levels due to decreased insulin sensitivity in the early stages.[3,4]

Acute and chronic complications occur as a result of changes in micro and macro circulation due to metabolic damages in DM.[2] Oral manifestations are among the microvascular complications encountered in diabetes. Oral manifestations and complications of DM include xerostomia, dental caries, salivary gland enlargement, decreased salivary flow, susceptibility to infection, delayed and abnormal wound healing, burning sensation and taste change, periapical lesions, periodontal disease, oral mucosal diseases, oral candidiasis, lichen planus, geographic and fissured tongue, and recurrent aphthous stomatitis.[5,6]

It is very important to image the salivary glands with appropriate imaging methods to detect any occurring changes. Ultrasonography (USG) is generally used in dentistry for various purposes such as salivary gland diseases, cervical lymphadenopathy, chewing, and the examination of neck muscles, thanks to its advantages such as being inexpensive, non-invasive, and radiation-free.[7–9] Colour Doppler USG is used to evaluate the vascularization of tissues such as blood flow velocity and resistance index and to distinguish between benign/malignant and between inflammatory/non-inflammatory lesions.[8,10] Ultrasound elastography is used to determine the resistance of tissues to the pressure of sound and to examine changes that occur in tissues as a result of this resistance. There are basically two different methods used today: strain elastography and shear-wave elastography (SWE).[11,12] SWE quantifies tissue stiffness by measuring the velocity of propagating shear waves following acoustic radiation force excitation. Here, user-related restraint is reduced, whereas repeatability and quantitative evaluation power increase since the compressing force is generated by a probe.[13,14]

There is a limited number of studies in the literature examining the effects of DM on the submandibular and parotid glands.[15–19] However, most of these studies included the parotid gland, and most of the examinations were cytological, with only two studies using computed tomography (CT) and one study using USG.

It has been suggested that enlargement of the salivary glands in diabetes occurs as an increase in the size of acinar cells, which causes the glands to appear densely on CT.[15] In a study examining the submandibular gland of patients with type 2 DM in the literature, impaired glandular function and enlargement of acinar cells were reported, and this is thought to be a compensatory mechanism against hyposalivation.[19] The lack of clarity on the pathological mechanisms of how DM contributes to these structural changes, and the scarcity of available studies on this subject demonstrate that this complication is not assessed or overlooked when the oral manifestations of diabetes are investigated.

The aim of this study is to evaluate B-mode USG parameters such as size, volume and echogenicity, SWE value and colour Doppler characteristics of bilateral submandibular and parotid salivary glands in patients with DM and healthy control groups. The null hypothesis was that there was no difference in the submandibular and parotid salivary glands of patients with DM and healthy control group patients.

2 | MATERIALS AND METHODS

Before starting the study, approval was obtained from the University Clinical Research Ethics Committee dated 30 April 2021 and numbered 2021/141.

Prior to the study, power analysis was performed during the design phase. The patient and control groups were selected from patients aged 18 years and older who applied to our clinic for various reasons. USG was performed on patients who agreed to participate in the study. The patient group included 20 patients previously diagnosed with type 1 DM and 20 patients with type 2 DM, while the control group included 40 patients without any systemic disease. Those with a history of head and neck radiotherapy and chemotherapy, a history of salivary gland tumour, those who underwent surgical intervention on the salivary gland for any reason, cardiovascular diseases such as hypertension, angina, myocardial infarction, those who used drugs that would affect blood flow, smokers, blood disease and those with any endocrinopathy other than DM were excluded from the study.

2.1 | USG imaging procedures and measurements

Patients were examined with the GE LOGIQ S8 XDclear USG device, ML 6-15-D Matrix Array (4–15 MHz), and 9 L-D (2–8 MHz) linear probes in the Dentomaxillofacial Radiology department. All imaging procedures were performed by the same observer to eliminate differences emerging from inter-observer variability. Measurements were performed in the supine position and patients using removable or total dentures were asked to remove their prostheses.

The right and left sides of each patient were measured separately. To evaluate the repeatability and reliability of the measurements, the patients were rested for 5 min and USG images were recorded again after resting. The second measurement was performed in 2 weeks after resting. The dentomaxillofacial radiologist performing the USG examination was blinded to whether the patients had DM or were controls.

In the USG evaluation, real-time 2D display mode was used with the ML 6-15-D probe and extraoral and bilateral examinations were performed in B mode. The submandibular gland is positioned in two perpendicular planes (transversal and longitudinal) parallel to the lower edge of the mandible and vertical to the body of the mandible. For the parotid gland, it was positioned in two perpendicular planes (longitudinal and transversal planes) parallel to the mandible ramus and horizontal to the mandible ramus, and the probe was examined by the movement of the regions. Following the examination of echogenicity, parenchymal internal structure and margins in the obtained images, dimensional measurements were performed along the borders of the submandibular and parotid glands. For these measurements, the 'Measure' basic measurement mode key was pressed and the 'Volume' tab was selected from the touch panel. For the submandibular gland, antero-posterior and super-inferior lengths were measured while the probe was in the transversal position (Figure 1-1A), and medio-lateral length was measured while the probe was in the longitudinal position (Figure 1-1B) and automatic 'Volume' measurement was performed. For the parotid gland, the antero-posterior and super-inferior lengths were measured while the probe was in the longitudinal position (Figure 1-2A), and the mediolateral lengths were measured while the probe was in the transverse position (Figure 1-2B) and automatic 'Volume' measurement was performed.

Echogenicity was evaluated in terms of margin characteristics and parenchymal homogeneity over the existing B-mode image. The parenchyma of the submandibular and parotid glands was evaluated as hyperechoic, isoechoic, and hypoechoic in terms of echogenicity (Figure 2). The parenchyma of the submandibular and parotid glands was evaluated as homogeneous, minimally heterogeneous and distinctively heterogeneous (Figure 3). The margins of the submandibular and parotid glands were evaluated as regular, focal irregular and well-defined/irregular (Figure 4).

Then, to evaluate the blood supply of the glands via colour Doppler, 'ML 6-15-D Matrix Array (4-15 MHz)' probe and the region to be examined are selected, the probe for the submandibular gland is adjusted transversal, for the parotid gland the probe is adjusted longitudinally and 'Color Flow (CF)' mode was pressed and evaluations were made by adjusting the width of the area to be examined from the monitor. In the evaluation of the submandibular and parotid glands with colour Doppler USG, the vascularization of the glands was evaluated and vascularization was observed to be present/absent. If there was a result, the vascularization was evaluated as central/peripheral. Also, normal gland vascularization was classified as mild hypervascularization, hypervascularization and hypovascularization (Figure 5).

Finally, to evaluate the elastography of the glands with SWE, the probe was positioned transversally for the submandibular gland in B mode and longitudinally for the parotid gland using the '9L-D (2-8 MHz)' probe, and the 'Elasto' mode was switched by adjusting the width to be examined. After the SWE was activated, the patient was told to hold his/her breath and not to swallow for a while, thereby achieving complete immobility. During the examination, the USG probe was placed perpendicular to the desired area using adequate gel to avoid pressure. While determining the sampling area, the measurements were made by avoiding cystic

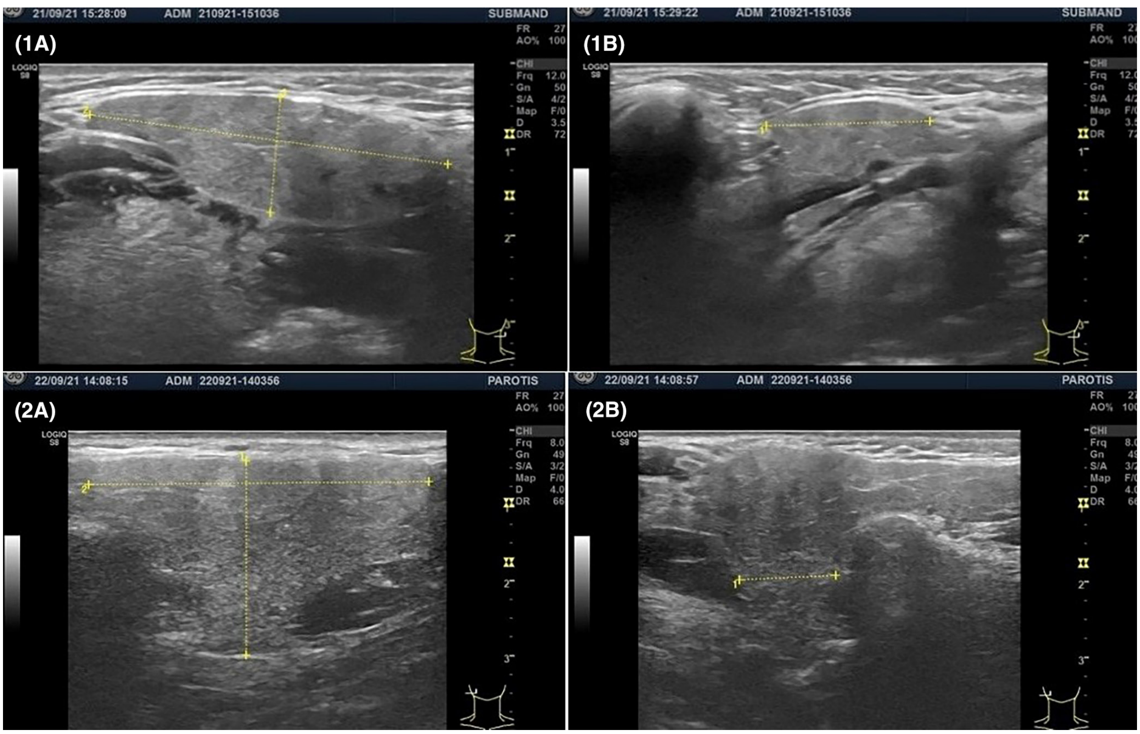

FIGURE 1 B mode ultrasonography images: submandibular gland, (1A) antero-posterior and super-inferior measurement with the prop in the transversal position, (1B) medio-lateral measurement with the prop in the longitudinal position. Parotid gland, (2A) antero-posterior and super-inferior measurement with the probe in the longitudinal position and (2B) medio-lateral measurement with the probe in the transversal position.

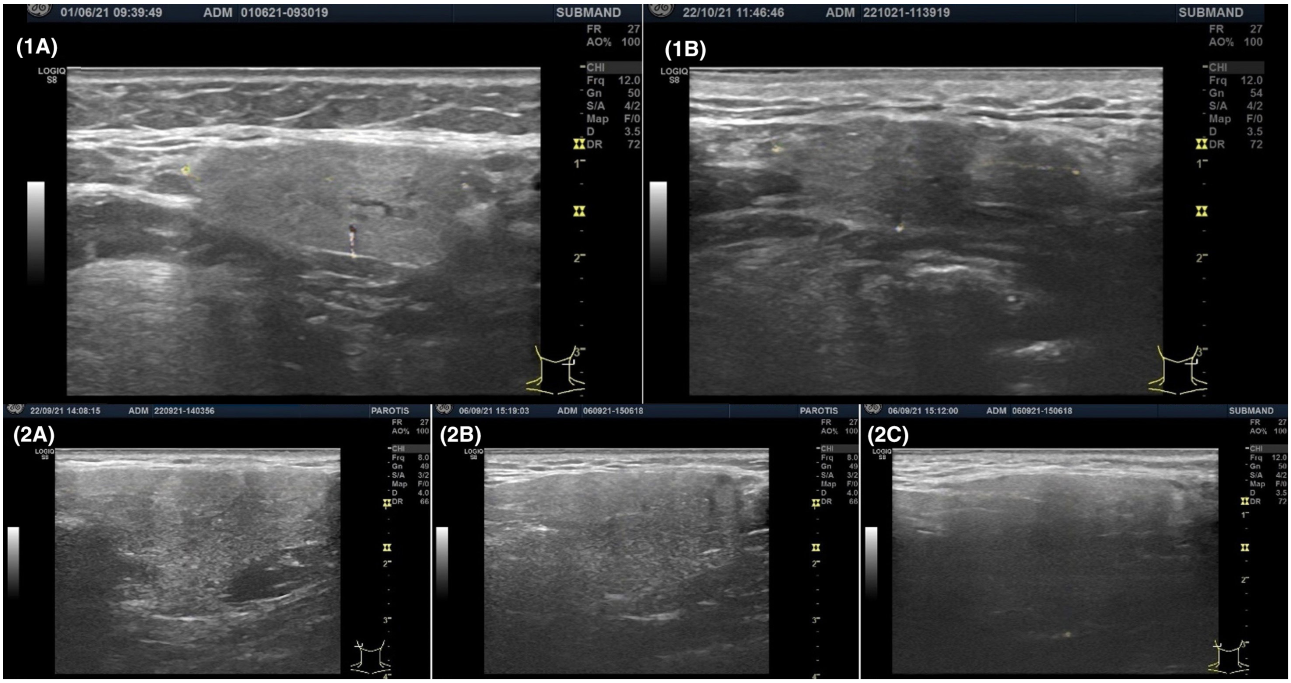

FIGURE 2 Ultrasonography images: (1A) submandibular gland with isoechoic echogenicity, (1B) submandibular gland with hypoechoic echogenicity; (2A) parotid gland with hyperechoic echogenicity, (2B) parotid gland with isoechoic echogenicity, (2C) Parotid gland with hypoechoic echogenicity.

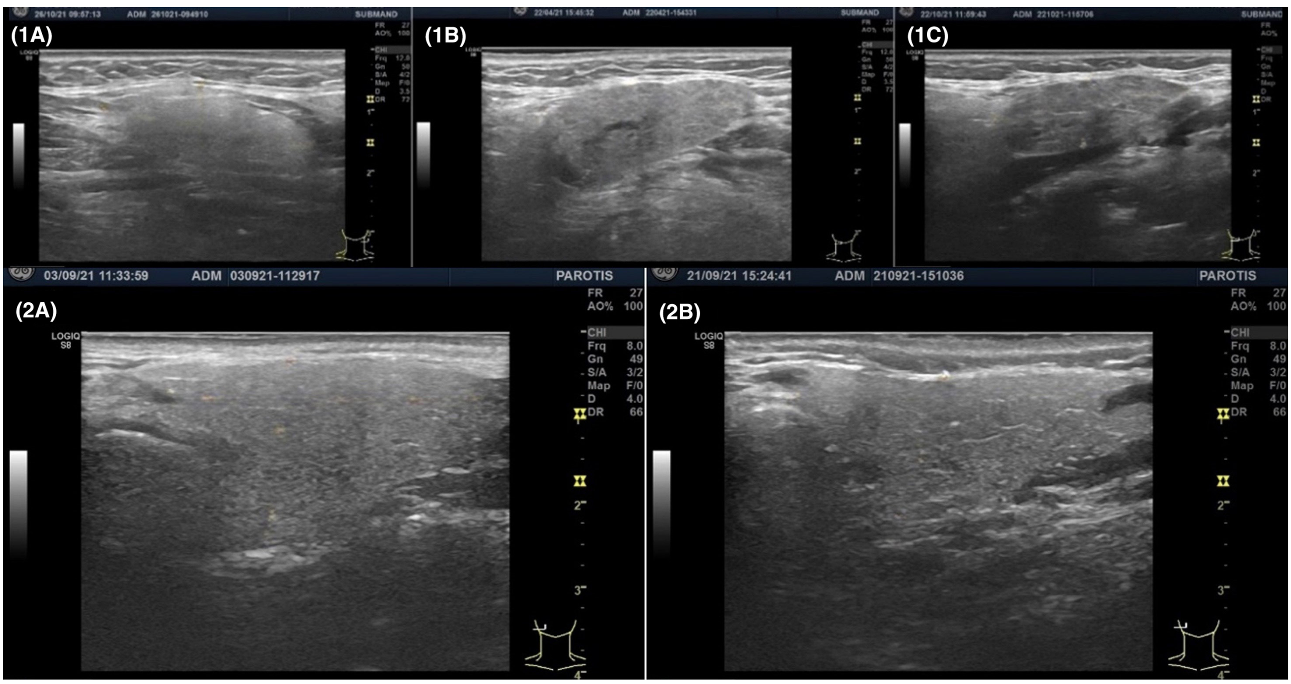

FIGURE 3 Ultrasonography images: (1A) submandibular gland with homogeneous internal structure, (1B) submandibular gland with minimal heterogeneous internal structure, (1C) submandibular gland with distinctive heterogeneous internal structure, (2A) parotid gland with minimal heterogeneous internal structure, (2B) parotid gland with distinctive heterogeneous internal structure.

areas and vascular structures as much as possible and without going within the borders of the salivary gland. Circular regions of interest (ROI) were placed by the same observer to cover as much salivary gland area as possible. A total of three measurements were made at each cine cycle from the measurement point in each salivary gland, one for each square recorded. The circular ROI diameter was determined as 0.75 cm and the average kiloPascal (kPa) value was used for statistics (Figure 6).

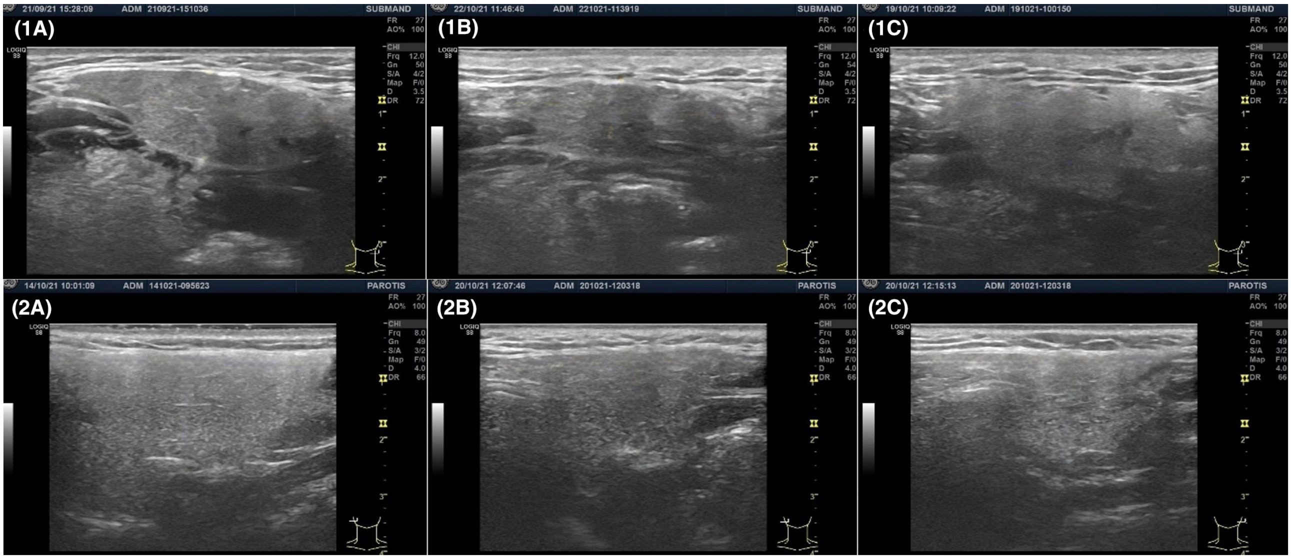

FIGURE 4 Ultrasonography images: (1A) submandibular gland with regular margin, (1B) submandibular gland with focal irregular margin, (1C) submandibular gland with well-defined irregular margin, (2A) parotid gland with regular margin, (2B) parotid gland with focal irregular margin, (2C) parotid gland with ill-defined irregular margin.

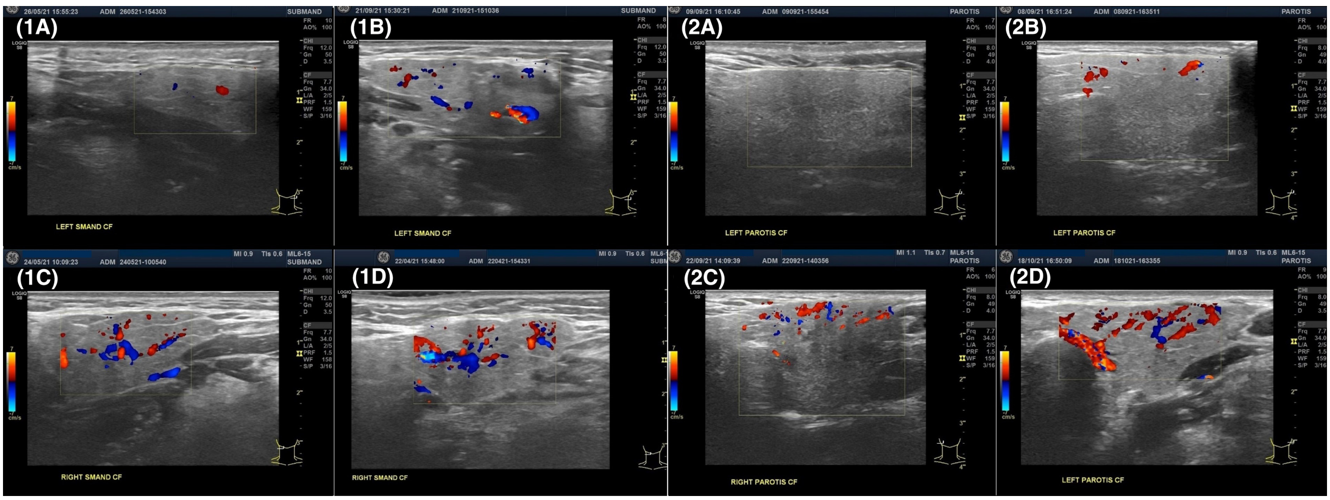

FIGURE 5 Colour Doppler ultrasonography images: (1A) submandibular gland with central blood flow and hypovascularization, (1B) submandibular gland with peripheral blood flow and normal vascularization, (1C) submandibular gland with central + peripheral blood flow and mild hypervascularization, (1D) submandibular gland with central + peripheral blood flow and hypervascularization. (2A) Parotid gland without vascularization, (2B) parotid gland with peripheral blood flow and normal vascularization, (2C) parotid gland with central + peripheral blood flow and mild hypervascularization, (2D) parotid gland with central + peripheral blood flow and hypervascularization.

2.2 | Statistical analysis

Kappa statistics were applied to evaluate intra-observer compliance. The conformity of the data to normal distribution was tested with the Shapiro Wilk and Kolmogorov Smirnow tests, while an 'Independent Two-Sample T-test' was used to compare normally distributed variables in two independent groups, and One-Way Analysis of Variance (ANOVA) was used to compare more than two independent groups. 'The Mann-Whitney U test' was used to compare non-normally distributed variables in two independent groups, and 'The Kruskal Wallis H test' was used to compare more than two independent groups. The Pearson Chi-square and Yates correction were used to test the relationship between categorical variables. Descriptive statistics are expressed as mean ± standard deviation and median (minimum-maximum) for numerical variables, and number and percentage for categorical variables. Statistical analyses were performed using SPSS for Windows version 22.0 (Armonk, NY, IBM) package program, and $p < .05$ was considered statistically significant.

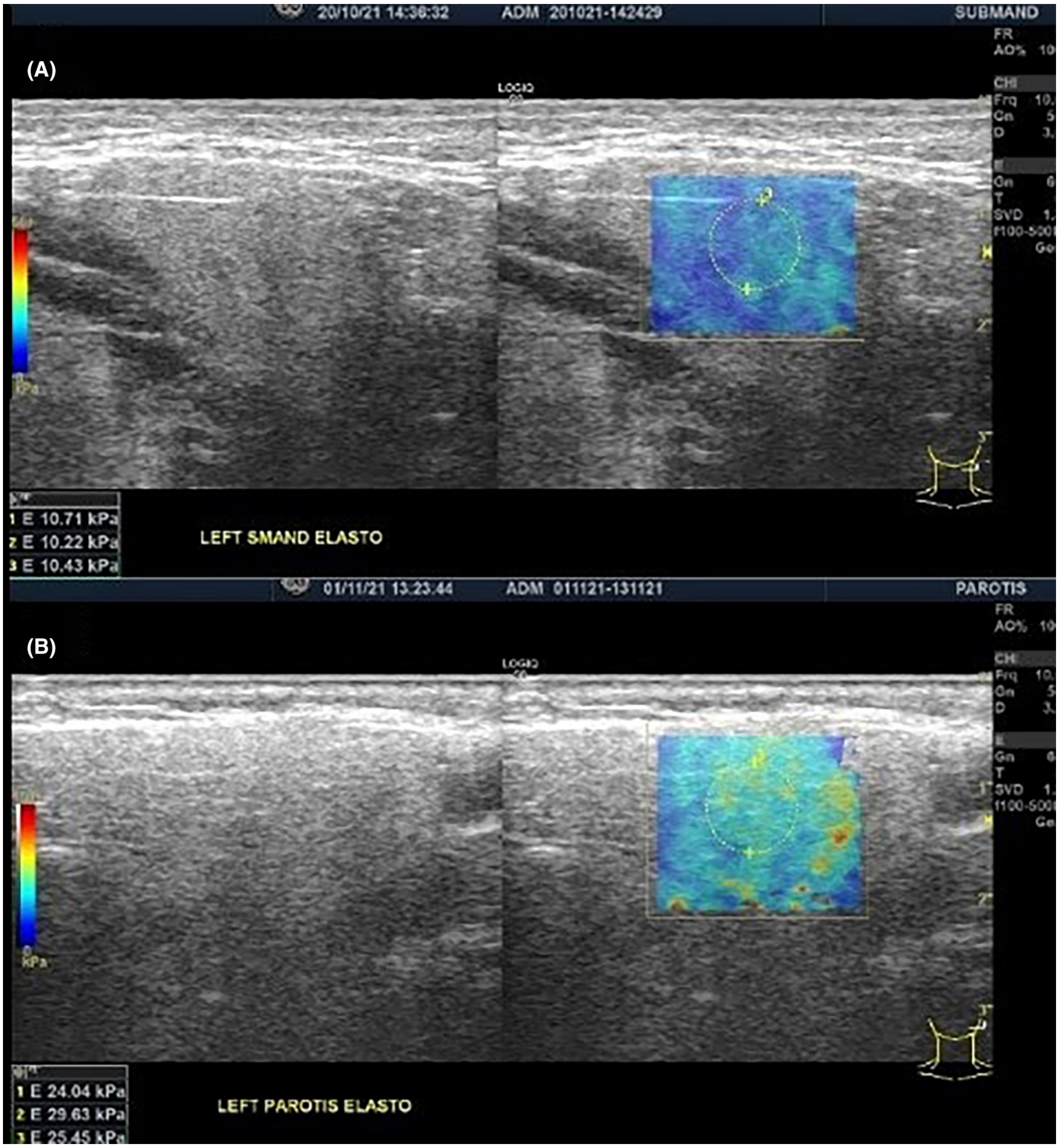

FIGURE 6 Shear-wave elastography (SWE) images: (A) transversal submandibular gland, (B) longitudinal parotid gland.

3 | RESULTS

Intra-observer reliability was determined to be excellent for evaluations and measurements (κ: 0.93). One hundred sixty submandibular and 160 parotid salivary glands on both sides of a total of 80 patients (43 females and 37 males), 40 patients in each group (type 1 DM 20 cases and type 2 DM 20 cases), including the patient group and the control group, were evaluated, respectively. The mean age of the cases in the patient group aged between 18 and 66 (23 females and 17 males) was 45.17 ± 12.52 in females and 41.35 ± 15.37 in males. The mean age of the cases in the control group aged between 18 and 70 (20 females and 20 males) was 41.1 ± 11.69 in females and 35.6 ± 14.48 in males. A statistically significant difference was found in the mean age between the patient group and the control group ($p < .05$). The mean age was 37.6 for type 1 DM, 49.5 for type 2 DM, and 38.32 for the control group. While there was no significant difference in the mean age between the type 1 DM and control groups, the mean age was observed to be higher in the type 2 DM group than in the other groups. There was no statistically significant difference in gender between the patient group and the control group ($p > .05$).

When the correlation of the right–left submandibular gland and parotid glands with respect to age was examined, it was found that there was a weak negative correlation between age and the supero-inferior dimension value of the right submandibular gland ($r = -0.273$; $p = .014$), and a weak positive correlation between age and the supero-inferior value of the right parotid gland ($r = 0.281$; $p = .012$). There was no statistically significant relationship between age and other variables ($p > .05$).

The size, volume and SWE values of the right and left submandibular and parotid glands are illustrated in the graph in Figure 7. It was observed that the size, volume and SWE measurements of the right and left parotid glands were higher than those of the right and

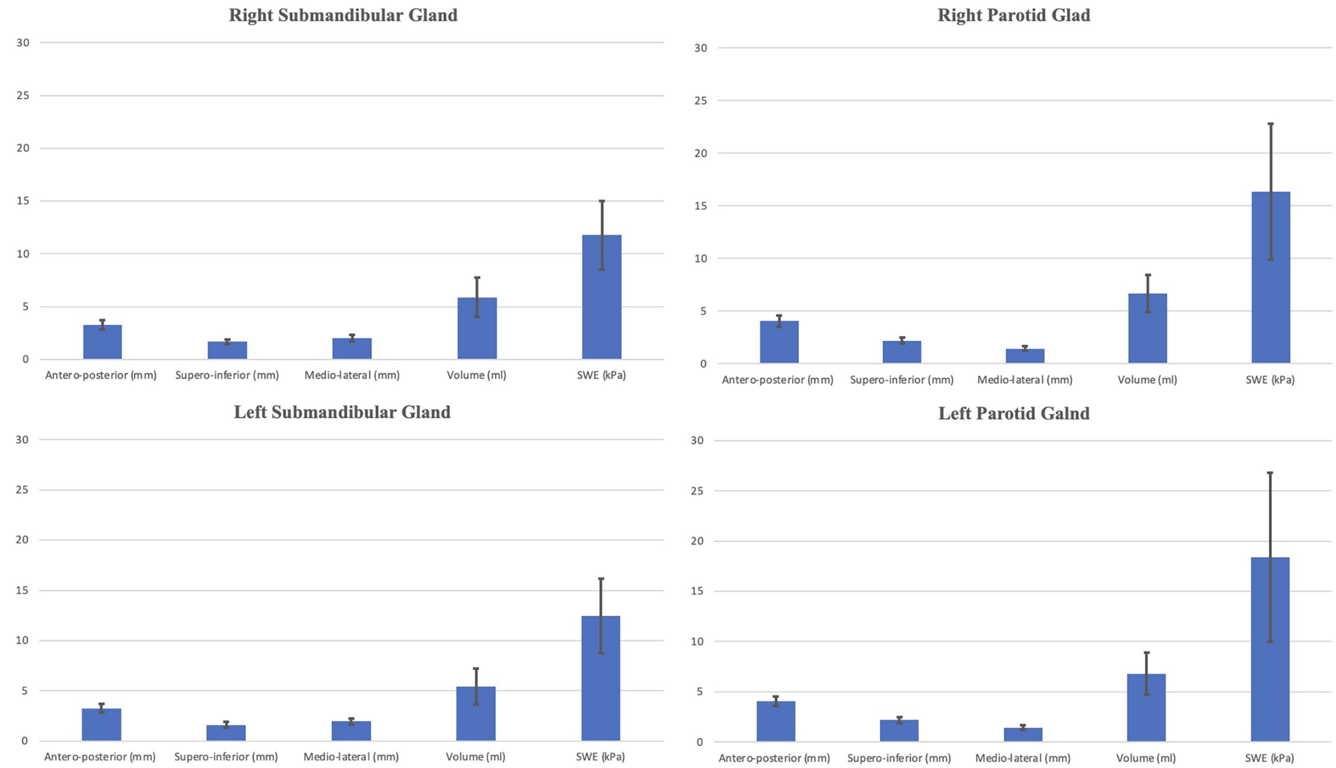

FIGURE 7 Graphing the mean and standard deviation of descriptive statistics of size, volume and shear-wave elastography (SWE) variables in right and left submandibular and parotid glands.

left submandibular glands, but there was no statistically significant difference between the values.

Echogenicity, margin characteristics, parenchymal homogeneity, vascularization, and colour Doppler characteristics of the bilateral submandibular and parotid glands by the patient and control groups are shown in Tables 1 and 2. While a statistically significant difference was found between the patient and the control groups in echogenicity and colour Doppler characteristics of the right submandibular gland ($p<.05$), there was no statistically significant difference in echogenicity, margin characteristics, parenchymal homogeneity and colour Doppler variables of the left submandibular gland ($p>.05$). In the right submandibular gland, 90% of patients with type 1 DM, 100% of patients with type 2 DM, and 65% of the control group displayed isoechoic echogenicity, with the echogenicity characteristics showing a statistically significant difference between the type 1 DM, type 2 DM and control groups ($p<.05$).

A statistically significant difference was noted in the echogenicity and colour Doppler characteristics of the right parotid gland and the echogenicity, margin characteristics, parenchymal homogeneity, and colour Doppler variables of the left parotid gland between the patient and control groups ($p<.05$). A statistically significant difference was observed in the right parotid gland in terms of echogenicity, margin features, parenchymal homogeneity and coloured Doppler characteristics compared to type 1 DM, type 2 DM, and control groups ($p<.05$). It was determined that 75% of the right parotid glands displayed isoechoic echogenicity in the type 1 DM group, while 50% displayed focal irregular margins, 75% showed distinctively heterogeneous parenchyma heterogeneity and 60% demonstrated no bleeding. Isoechoic echogenicity was observed in 90% of the type 2 DM group, focal irregular border in 65%, minimal heterogeneous parenchymal heterogeneity in 65% and peripheral vascularization in 55% of the cases. In the control group, isoechoic echogenicity was observed in 100% of the right parotid glands, focal irregular border in 70%, minimal heterogeneous parenchymal heterogeneity in 60% and peripheral vascularization in 80% of the cases. A statistically significant difference was found in the left parotid gland in terms of echogenicity, parenchymal homogeneity and colour Doppler characteristics compared to type 1 DM, type 2 DM, and control groups ($p<.05$). In the type 1 DM group, it was determined that the left parotid glands showed isoechoic echogenicity in 75%, focal irregular borders in 50%, significant heterogeneous parenchymal heterogeneity in 65% and no vascularization in 60% of the cases. Isoechoic echogenicity was observed in 95% of the type 2 DM group, focal irregular border in 55%, marked heterogeneous parenchymal heterogeneity in 55% and peripheral vascularization in 55% of the cases. It was determined that 100% of the right parotid glands displayed isoechoic echogenicity in the control group, 80% had focal irregular margins, 72.5% had minimal heterogeneous parenchyma heterogeneity, and 67.5% displayed peripheral vascularization.

Size (antero-posterior, super-inferior, medio-lateral), volume and SWE values of the right and left submandibular glands and

TABLE 1 Comparison of right–left submandibular gland echogenicity, margin properties, parenchymal homogeneity, vascularization and colour Doppler variables according to patient and control groups.

	Right submandibular gland			Left submandibular gland		
	Group			Group		
	Patient	Control		Patient	Control	
Values	*N* (%)	*N* (%)	*p*-value	*N* (%)	*N* (%)	*p*-value
Echogenicity						
Hyperechoic	0 (0.0)	0 (0.0)	.003*	0 (0.0)	0 (0.0)	.181
Hypoechoic	2 (5.0)	14 (35.0)		6 (15.0)	12 (30.0)	
Isoechoic	38 (95.0)	26 (65.0)		34 (85.0)	28 (70.0)	
Margin properties						
Regular	17 (42.5)	12 (30.0)	.504	15 (37.5)	15 (37.5)	1.000
Focal irregular	22 (55.0)	27 (67.5)		21 (52.5)	21 (52.5)	
Significantly irregular	1 (2.5)	1 (2.5)		4 (10.0)	4 (10.0)	
Parenchyma homogeneity						
Homogeneous	8 (20.0)	17 (42.5)	.086	13 (32.5)	20 (50.0)	.113
Minimally heterogeneous	28 (70.0)	21 (52.5)		26 (65.0)	17 (42.5)	
Significantly heterogeneous	4 (10.0)	2 (5.0)		1 (2.5)	3 (7.5)	
Vascularization						
Peripheral	21 (52.5)	14 (35.0)	.035*	18 (45.0)	17 (42.5)	.635
Central	10 (25.0)	6 (15.0)		8 (20.0)	7 (17.5)	
Central + peripheral	9 (22.5)	20 (50.0)		11 (27.5)	15 (37.5)	
None	0 (0.0)	0 (0.0)		3 (7.5)	1 (2.5)	
Colour Doppler						
Hypovascularization	2 (5.0)	2 (5.0)	.995	8 (20.0)	7 (17.5)	.616
Mild hypervascularization	11 (27.5)	12 (30.0)		9 (22.5)	13 (32.5)	
Hypervascularization	6 (15.0)	6 (15.0)		6 (15.0)	3 (7.5)	
Normal	21 (52.5)	20 (50.0)		17 (42.5)	17 (42.5)	

Note: Pearson Chi-square test, Yates correction, *$p < .05$.

right and left parotid glands are shown in Table 3 by the patient and the control groups. All values were observed to be higher in the submandibular and parotid glands on both sides in the patient group compared to the control group. In addition, a statistically significant difference was found in the mean anterior–posterior and volume of the right submandibular gland, the mean medio-lateral and volume values of the right parotid gland, and the median SWE values of the left parotid gland between the patient and the control groups ($p < .05$).

The size (antero-posterior, super-inferior and media-lateral), volume and SWE values of the right and left submandibular gland and parotid glands of the type 1 DM, type 2 DM, and control groups are shown in Table 4. All parameters were observed to be higher in the submandibular and parotid gland in the type 2 DM patient group on both sides compared to the type 1 DM patient group and the control group. However, a statistically significant difference was found in the median right submandibular gland volume, the mean right parotid gland super-inferior, the medio-lateral and volume, and the median left parotid gland SWE values between the type 1 DM and type 2 DM groups ($p < .05$).

4 | DISCUSSION

There are studies reporting structural changes in the salivary glands of patients with DM, especially in the parotid and submandibular glands.[15–19] As reported by these studies, impaired glandular function and acinar cells expand in the salivary glands of patients with DM, resulting in an increase in the size of acinar cells, and a dense appearance of the glands on CT. Pathological mechanisms of how DM contributes to these structural changes have not been investigated, and the vast majority of these studies have been cytologically conducted with no salivary gland imaging method used. To the best of our knowledge, only one study examined the parotid glands of patients with type 2 DM by USG, which was from a dimensional perspective.[16] In this study, the submandibular and parotid glands of both type 1 DM and type 2 DM patients were evaluated by USG in terms of size, volume, SWE values, echogenicity, margin characteristics, parenchymal homogeneity, and vascularization. As far as we know, the present study is the first to investigate submandibular and parotid glands in detail using USG in patients with DM.

TABLE 2 Comparison of right–left parotid gland echogenicity, margin properties, parenchymal homogeneity, vascularization and colour Doppler variables according to patient and control groups.

Values	Right parotid gland – Group – Patient *N* (%)	Right parotid gland – Group – Control *N* (%)	Right parotid gland *p*-value	Left parotid gland – Group – Patient *N* (%)	Left parotid gland – Group – Control *N* (%)	Left parotid gland *p*-value
Echogenicity						
Hyperechoic	1 (2.5)	0 (0.0)	.024*	1 (2.5)	0 (0.0)	.042*
Hypoechoic	6 (15.0)	0 (0.0)		5 (12.5)	0 (0.0)	
Isoechoic	33 (82.5)	40 (100)		34 (85.0)	40 (100)	
Margin properties						
Regular	12 (30.0)	11 (27.5)	.221	14 (35.0)	7 (17.5)	.032*
Focal irregular	23 (57.5)	28 (70.0)		21 (52.5)	32 (80.0)	
Significantly irregular	5 (12.5)	1 (2.5)		5 (12.5)	1 (2.5)	
Parenchyma homogeneity						
Homogeneous	0 (0.0)	0 (0.0)	.309	0 (0.0)	0 (0.0)	.009*
Minimally heterogeneous	18 (45.0)	24 (60.0)		16 (40.0)	29 (72.5)	
Significantly heterogeneous	22 (55.0)	16 (40.0)		24 (60.0)	11 (27.5)	
Vascularization						
Peripheral	19 (47.5)	32 (80.0)	.007*	19 (47.5)	27 (67.5)	.064
Central	0 (0.0)	0 (0.0)		0 (0.0)	1 (2.5)	
Central + peripheral	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	
None	21 (52.5)	8 (20.0)		21 (52.5)	12 (30.0)	
Colour Doppler						
Hypovascularization	29 (72.5)	27 (67.5)	.560	31 (77.5)	26 (65.0)	.033*
Mild hypervascularization	1 (2.5)	3 (7.5)		2 (5.0)	1 (2.5)	
Hypervascularization	1 (2.5)	0 (0.0)		3 (7.5)	0 (0.0)	
Normal	9 (22.5)	10 (25.0)		4 (10.0)	13 (32.5)	

Note: Pearson Chi-square test, Yates correction, *$P < .05$.

In the DM patient group, submandibular glands on both sides were observed to have a higher rate of isoechoic echogenicity and peripheral vascularization than the control group. In the DM patient group, parotid glands on both sides were observed to have a higher rate of hypoechoic echogenicity, significant heterogeneity, absence of blood supply and hypovascularization than the control group. Most of these parameters caused a statistically significant difference in both parotid and submandibular glands ($p < .05$). These values were determined to be higher in the type 1 DM group compared to the type 2 DM group. It was concluded that these changes in echogenicity and parenchymal homogeneity and vascularization are due to the aggressive course of type 1 DM starting at an earlier age. According to our results, significant differences were found in the submandibular and parotid salivary glands of DM patients and healthy control group and the null hypothesis was rejected.

The study by Orloff et al.[20] investigating the role of USG in the diagnosis and treatment of salivary gland diseases, concluded that salivary gland USG performed by a specialist with adequate training and experience can eliminate the need for MRI and CT. The study by Lee et al.[21] in which they examined the efficiency of different imaging methods in salivary gland neoplasms suggested the use of USG for the initial assessment of superficial lesions and nodal involvement in the submandibular and parotid glands since it provides solubility and tissue characterisation without radiation. In a meta-analysis study conducted by Delli et al.[22] on diagnostic properties of ultrasound of major salivary glands in Sjögren's syndrome, it was found that USG had a sensitivity, specificity and diagnostic rates of 69%, 92%, and 34%, respectively, for the diagnosis of Sjögren's syndrome in major salivary glands in a total of 30 studies evaluated. In a study conducted by Gandage et al.[23] with 87 patients to investigate the sensitivity and specificity of USG in examining salivary glands, USG was reported to have high sensitivity (93.33%) and high specificity (98.07%). Since USG is easier to use than other imaging methods, does not contain ionising radiation, and is a non-invasive, costly, accessible, safe imaging method, they recommended USG for the initial assessment of salivary glands, which was consistent with the literature.

TABLE 3 Comparison of right–left submandibular and parotid glands size, volume and SWE variables according to patient group and control groups.

Values	Group: Patient Mean ± SD	Patient Median (Min.–Max.)	Control Mean ± SD	Control Median (Min.–Max.)	*p*-value
Right submandibular gland					
Antero-posterior (mm)	3.39 ± 0.42	3.42 (2.37–4.11)	3.17 ± 0.41	3.18 (2.02–4.02)	.021*
Supero-inferior (mm)	1.71 ± 0.23	1.73 (1.12–2.12)	1.62 ± 0.27	1.67 (1.11–2.36)	.148
Medio-lateral (mm)	2.05 ± 0.32	1.98 (1.53–2.86)	1.98 ± 0.33	1.94 (1.51–2.96)	.329
Volume (mL)	6.3 ± 1.74	6.21 (3.44–10.2)	5.45 ± 1.92	5.28 (2.62–11.4)	.043*
SWE (kPa)	12.04 ± 3.44	11.51 (6.28–20.24)	11.51 ± 3.04	11.09 (7.02–20.65)	.381
Left submandibular gland					
Antero-posterior (mm)	3.34 ± 0.47	3.32 (2.48–4.44)	3.18 ± 0.37	3.11 (2.38–4.18)	.094
Supero-inferior (mm)	1.63 ± 0.28	1.65 (1.05–2.31)	1.57 ± 0.31	1.57 (0.99–2.24)	.410
Medio-lateral (mm)	1.98 ± 0.28	1.98 (1.53–2.69)	1.93 ± 0.31	1.87 (1.48–2.89)	.222
Volume (mL)	5.69 ± 1.63	5.58 (2.73–10.07)	5.17 ± 1.91	4.93 (2.39–11.85)	.197
SWE (kPa)	13.12 ± 4.03	12.36 (7.4–25.54)	11.8 ± 3.26	11.03 (7.37–21.17)	.112
Right parotid gland					
Antero-posterior (mm)	4.05 ± 0.51	4.02 (2.61–4.91)	4.02 ± 0.55	4.14 (2.85–4.85)	.787
Supero-inferior (mm)	2.21 ± 0.27	2.24 (1.63–2.83)	2.14 ± 0.31	2.12 (1.28–2.81)	.312
Medio-lateral (mm)	1.53 ± 0.21	1.51 (1.05–2.04)	1.36 ± 0.22	1.35 (0.86–2.01)	.001*
Volume (mL)	7.21 ± 1.86	6.8 (4.1–12.83)	6.1 ± 1.54	5.96 (3.33–9.08)	.005*
SWE (kPa)	17.24 ± 7.59	14.47 (9.38–39.25)	15.17 ± 4.81	14.53 (8.51–26.33)	.424
Left parotid galnd					
Antero-posterior (mm)	4.05 ± 0.47	4.16 (2.96–4.92)	4.03 ± 0.45	4.08 (2.89–4.83)	.886
Supero-inferior (mm)	2.22 ± 0.25	2.22 (1.59–2.81)	2.15 ± 0.31	2.17 (1.45–2.76)	.245
Medio-lateral (mm)	1.45 ± 0.22	1.45 (1.05–1.84)	1.42 ± 0.26	1.38 (0.79–2.24)	.450
Volume (mL)	7.02 ± 2.03	6.63 (3.68–13.6)	6.56 ± 2.16	6.4 (2.98–12.34)	.334
SWE (kPa)	21.36 ± 9.71	20.25 (7.92–50.32)	15.06 ± 5.3	13.98 (7.55–27.01)	.001*

Note: Independent sample *t*-test; Mann Whitney *U*-test; $^{*}p < .05$.

Abbreviations: SWE, Shear Wave Elastography; SD, standard deviation; Min., minimum; Max., maximum.

In the case reports published by Mandel et al.[15,17] on patients with diabetes and bilateral parotid gland enlargement, they detected bilateral enlarged parotid glands with equally increased density on CT by using CT and fine needle aspiration biopsy. Biopsy results revealed enlarged serous acinuses. They reported parotid gland enlargement induced by diabetes without any pathological mass evidence. Lee et al.[24] investigated the parotid and submandibular glands of patients with advanced Sjögren's syndrome by USG, reporting decreased parotid and submandibular gland volumes. In the study by Kyung-Ann et al.[25] in which they examined the changes in salivary glands with systemic sclerosis by USG, glandular fibrotic changes were observed in the salivary glands of patients with systemic sclerosis accompanied by a corresponding volume decrease. In the current study, unlike the study of Lee et al.[24] and Kyung-Ann et al.[25] the mean volume was observed to be higher in the patient group than in the control group. This volumetric growth of the glands is thought to act as a compensatory mechanism in the fight against xerostomia encountered in patients with DM. In the patient group, the mean volume value was observed to be higher in the type 2 DM group than in the type 1 DM group, which is thought to be due to a relative increase in volume associated with increased body mass index due to the onset of type 2 DM in advanced ages and insulin resistance, which plays a role in the developmental phase.

The study by Gupta et al.[16] in which 50 type 2 DM patients with known HbA1c values and 50 healthy control groups were examined for dimensional changes in the parotid glands with USG reported that the dimensional measurements were higher in the patient group than in the control group, while the size of parotid glands concurrently increased with increasing HbA1c in the patient group. In the present study, unlike the study of Gupta et al.[16] not only the parotid gland but also the submandibular gland was examined in patients with DM. In addition, evaluation of the dimensional and volume USG measurements of the patient group showed that the patient group exhibited higher dimensional measurements than the control

TABLE 4 Comparison of size, volume and SWE variables of right–left submandibular and parotid glands compared to type 1 DM-type 2 DM and control groups.

	Group						
	Tip 1 DM		Tip 2 DM		Control		
Values	Mean ± SD	Median (Min.–Max.)	Mean ± SD	Median (Min.–Max.)	Mean ± SD	Median (Min.–Max.)	*p*-value
Right submandibular gland							
Antero-posterior (mm)	3.33 ± 0.45	3.34 (2.37–4.11)	3.44 ± 0.38	3.55 (2.81–4.04)	3.17 ± 0.41	3.18 (2.02–4.02)	.051
Supero-inferior (mm)	1.68 ± 0.23	1.66 (1.12–2.09)	1.73 ± 0.23	1.8 (1.24–2.12)	1.62 ± 0.27	1.67 (1.11–2.36)	.289
Medio-lateral (mm)	2.01 ± 0.34	1.92 (1.53–2.86)	2.09 ± 0.31	2.01 (1.72–2.77)	1.98 ± 0.33	1.94 (1.51–2.96)	.436
Volume (mL)	6.04 ± 1.8	6.04 (3.44–10.2)[ab]	6.55 ± 1.69	6.4 (3.86–9.45)[a]	5.45 ± 1.92	5.28 (2.62–11.4)[b]	.040*
SWE (kPa)	11.95 ± 3.64	11.49 (6.28–20.24)	12.12 ± 3.33	11.52 (7.37–18.96)	11.51 ± 3.04	11.09 (7.02–20.65)	.671
Left submandibular gland							
Antero-posterior (mm)	3.41 ± 0.47	3.32 (2.74–4.44)	3.27 ± 0.47	3.34 (2.48–4.1)	3.18 ± 0.37	3.11 (2.38–4.18)	.174
Supero-inferior (mm)	1.62 ± 0.27	1.66 (1.05–2)	1.64 ± 0.29	1.63 (1.13–2.31)	1.57 ± 0.31	1.57 (0.99–2.24)	.692
Medio-lateral (mm)	2.01 ± 0.28	1.96 (1.53–2.69)	1.95 ± 0.28	2 (1.54–2.47)	1.93 ± 0.31	1.87 (1.48–2.89)	.404
Volume (mL)	5.76 ± 1.47	5.58 (3.66–10.07)	5.61 ± 1.81	5.72 (2.73–8.4)	5.17 ± 1.91	4.93 (2.39–11.85)	.220
SWE (kPa)	14.32 ± 4.68	13.7 (7.54–25.54)	11.92 ± 2.9	11.95 (7.4–20.56)	11.8 ± 3.26	11.03 (7.37–21.17)	.087
Right parotid gland							
Antero-posterior (mm)	3.95 ± 0.56	4.11 (2.61–4.85)	4.15 ± 0.45	3.99 (3.29–4.91)	4.02 ± 0.55	4.14 (2.85–4.85)	.472
Supero-inferior (mm)	2.11 ± 0.27[a]	2.18 (1.63–2.55)	2.31 ± 0.24[b]	2.31 (1.63–2.83)	2.14 ± 0.31[a]	2.12 (1.28–2.81)	.049*
Medio-lateral (mm)	1.46 ± 0.17[ab]	1.46 (1.05–1.77)	1.6 ± 0.22[a]	1.57 (1.28–2.04)	1.36 ± 0.22[b]	1.35 (0.86–2.01)	<.001*
Volume (mL)	6.31 ± 1.21[a]	6.43 (4.1–8.23)	8.11 ± 1.98[b]	8.07 (5.24–12.83)	6.1 ± 1.54[a]	5.96 (3.33–9.08)	<.001*
SWE (kPa)	18.53 ± 8.32	16.57 (9.38–39.25)	15.94 ± 6.74	13.47 (9.58–37.18)	15.17 ± 4.81	14.53 (8.51–26.33)	.382
Left parotid galnd							
Antero-posterior (mm)	3.93 ± 0.46	3.87 (2.96–4.76)	4.16 ± 0.47	4.29 (3.05–4.92)	4.03 ± 0.45	4.08 (2.89–4.83)	.296
Supero-inferior (mm)	2.14 ± 0.24	2.14 (1.59–2.79)	2.31 ± 0.24	2.3 (1.77–2.81)	2.15 ± 0.31	2.17 (1.45–2.76)	.051
Medio-lateral (mm)	1.46 ± 0.21	1.46 (1.1–1.84)	1.45 ± 0.24	1.43 (1.05–1.84)	1.42 ± 0.26	1.38 (0.79–2.24)	.720
Volume (mL)	6.46 ± 1.66	6.39 (4.45–10.5)	7.58 ± 2.25	7.06 (3.68–13.6)	6.56 ± 2.16	6.4 (2.98–12.34)	.187
SWE (kPa)	23.14 ± 11.25	23.01 (7.92–50.32)[a]	19.58 ± 7.77	18.6 (9.66–39.29)[ab]	15.06 ± 5.3	13.98 (7.55–27.01)[b]	.007*

Note: Kruskal–Wallis H-test. a-b There is no difference between types of diabetes with the same letter.

Abbreviations: ANOVA, One-Way Analysis of Variance; Max., Maximum; Min., Minimum; SD, standard deviation; SWE, shear wave elastography.

*$p < .05$.

group, similar to the study of Gupta et al.[16] of these values, only the antero-posterior mean value of the right submandibular gland was statistically significantly different between the patient group and the control group ($p < .05$). In the current study, dimensional enlargement was higher in the type 2 DM group than in the type 1 DM group. Unlike the study of Gupta et al.[16] HbA1c values were not included in this study.

Yang et al.[26] investigated the echogenicity, parenchymal homogeneity, and margin characteristics of healthy parotid glands and parotid glands treated with radiotherapy by USG, reporting that the healthy parotid glands displayed soft tissue echogenicity, were homogeneous and had regular margins, while the parotid glands treated with radiotherapy frequently exhibited hypoechoic areas and hyperechoic bands with a heterogeneous structure and irregular margins. The study by Seleim et al.[27] in which the salivary glands of 68 patients with rheumatoid arthritis were examined by USG and detected parotid and submandibular glands with heterogeneous parenchyma with hyperechoic bands in hypoechoic echogenicity. The case reports by Fischer et al.[28] examining the parotid glands affected by sarcoidosis and the study by Vourexakis et al.[29] examining the submandibular glands affected by sarcoidosis with USG detected hypoechoic echogenicity and hypervascularization in the parotid and submandibular glands on coloured Doppler USG images. In this study, similar to the literature, USG echogenicity examination was evaluated as hyperechoic, isoechoic, and hypoechoic, and unlike the literature, margin characteristics were evaluated as regular, focal irregular, distinctively irregular, while parenchymal homogeneity was evaluated as homogeneous, minimally heterogeneous, and distinctively heterogeneous. According to the literature, salivary glands may have isoechoic and hypoechoic echogenicity, irregular margins, and heterogeneous intra-parenchymal structure. Similarly, in the present study, submandibular gland echogenicity was observed to be higher on both sides in the patient group than in the control group, while parotid gland echogenicity was observed to be higher on both sides in the hypoechoic group than in the control group. Also, the margin characteristics of the submandibular and parotid glands on both sides were found to be similar in the patient group and the control group. However, the rate of parotid glands with well-defined irregular margins was found to be higher in the type 1 DM group.

Similar to the literature, in the current study, parenchymal homogeneity was found to be minimally heterogeneous in both sides of the submandibular gland in the patient group and significantly higher in both sides of the parotid gland than in the control group. These rates were observed to be higher in the type 1 DM group compared to the type 2 DM group, which is attributed to the fact that DM causes changes in the salivary glands similar to inflammatory and non-inflammatory diseases, and that type 1 DM progresses aggressively from an earlier age and parotid gland acinar cells display a serious structure and are more prone to external effects.

Zhang et al.[30] Delli et al.[22] and Ustabasioglu et al.[31] evaluated the parotid and submandibular glands of a patient group with Sjögren's syndrome and a healthy control group by colour Doppler USG, reporting hypervascularization in the parotid and submandibular glands of patients with Sjögren's syndrome. The study by Lee et al.[24] on the parotid and submandibular glands of patients with Sjögren's syndrome detected hypervascularization in the early inflammatory phase and hypovascularization in the late phase. In this study, unlike the literature, colour Doppler USG examination primarily investigated the absence of vascularization, and vascularization was evaluated as central, peripheral, or both central and peripheral, if present. In addition, vascularization was classified as hypovascularization, mild hypervascularization, hypervascularization and normal vascularization for examination. The present study yielded similar hypovascularization results to the patients with advanced inflammatory phase Sjögren's syndrome in the study of Lee et al.[24] contrary to available studies reporting hypervascularization in parotid and submandibular glands on colour Doppler images. These results are attributed to how controlled DM is and to the fact that micro and macrovascular complications are more common in people with uncontrolled diabetes, and that DM affects the salivary glands similarly to inflammatory phases (hypervascularization and hypovascularization cycle).

In the study conducted by Karaman et al.[32] where benign and malignant lesions were investigated in the major salivary glands using SWE, SWE was applied before the USG-guided fine needle aspiration biopsy for definitive diagnosis. It was observed that malignant lesions exhibited the highest stiffness (average 107 kPa) whereas benign lesions exhibited the lowest stiffness (average 20 kPa). A study conducted by Arslan et al.[33] with 53 patients with primary Sjögren's syndrome and 30 healthy controls to investigate the diagnostic value of SWE in patients with primary Sjögren's syndrome, the degree of elasticity of the submandibular and parotid glands was evaluated using SWE, and the SWE value of the parotid gland was observed to be higher than that of the healthy control group in patients with Sjögren's syndrome, while the SWE value of the parotid gland was higher than that of the submandibular gland. In the present study, the submandibular and parotid glands of the patient and control groups were evaluated via SWE, and similar to the study of Arslan et al.,[33] the SWE value was found higher in the patient group than in the control group, while the SWE value of the parotid gland was higher than that of the submandibular gland. In the patient group, the SWE value was found to be significantly higher in the type 1 DM patient group than the SWE value in the type 2 DM group, particularly for the parotid gland. These results may be attributed to the fact that DM increases the degree of stiffness in the salivary gland, causes a significant change in the gland parenchyma, and that the effects of type 1 DM on the salivary glands are more severe and prominent than type 2 DM due to the very early onset of type 1 DM.

The limitation of this study is that the duration of exposure to DM, DM medicines and insulin use, HbA1c values, and the presence of DM-related systemic complications are unknown among the type 1 DM and type 2 DM patients in the patient group. In addition, differences in mean age between the patient group and the control group is another restriction of the study. Prospective controlled studies with larger populations will enable a clearer understanding of the effect of DM on salivary glands.

5 | CONCLUSION

In this study, it was concluded that the size of the submandibular and parotid glands increased significantly in the DM patient group. In the DM patient group, a higher rate of hypoechoic echogenicity, significant heterogeneity, absence of blood supply and hypovascularization were detected in the parotid glands on both sides compared to the control group. Most of these parameters were statistically significant in both parotid glands. In addition, the SWE value was higher in the patient group than in the control group, however, the difference was statistically significant only for the left parotid gland. USG, which has many advantages in investigating the effects of DM on the submandibular and parotid salivary glands, is an effective imaging method that should be preferred primarily.

AUTHOR CONTRIBUTIONS

Concept—E.M.A.O.; Design—E.M.A.O., E.D.Y; Supervision—E.M.A.O., E.D.Y.; Resources—E.M.A.O., E.D.Y.; Materials—E.M.A.O.; Data Collection and/or Processing—E.M.A.O., E.D.Y.; Analysis and/or Interpretation—E.M.A.O., E.D.Y; Literature Search—E.M.A.O., E.D.Y.; Writing Manuscript—E.M.A.O., E.D.Y.; and Critical Review—E.M.A.O., E.D.Y.

CONFLICT OF INTEREST STATEMENT

The authors declare that no conflict interests.

PEER REVIEW

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later versions.

CONSENT

Informed consent was obtained from all patients for being included in the study.

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