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Sonographic findings of COVID-19-related acute dacryoadenitis

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Abstract

Objectives: To evaluate the ability of grayscale sonography and color Doppler sonography in determining the involvement of the lacrimal glands in coronavirus disease (COVID-19).

Methods: A retrospective analysis was performed on a total of 25 COVID-19 patients with symptoms of acute dacryoadenitis and 25 healthy participants. The study's inclusion criteria encompassed pain, swelling, and discomfort in the superior temporal aspect of the upper eyelid and orbit, consistent with acute dacryoadenitis occurring within 30 days of a positive test for SARS-CoV-2. PCR testing yielded positive results for all patients. Inclusion criteria for healthy participants included asymptomatic orbit and upper lid, no prior trauma or surgery involving the orbit, no evidence of upper respiratory tract infection consistent with SARS-CoV-2 in the past 6 months, and no history of systemic inflammatory disorders. The evaluation of the lacrimal gland and periorbital adipose tissue involved gray-scale and color Doppler ultrasonography to assess echogenicity, homogeneity, vascularity and enlargement of the lacrimal gland. The patients involved in the study underwent orbital examination and US evaluations repeated at 3 weeks and 3 months.

Results: The mean age of the patients were 41.5±12.2 years (range, 18 to 63 years), while for the healthy participants, it was 34.4±5.2 years (range, 18 to 47 years). Significant differences were observed in the echogenicity (p=0.025), homogeneity (p=0.018), and vascularity (p<0.001), size (p<0.001) of the lacrimal gland between healthy participants and COVID-19 patients exhibiting symptoms of acute dacryoadenitis. However, no difference was noted in the perilacrimal fat tissue changes between COVID-19 patients with symptoms of acute dacryoadenitis and the control group (p=0.054).

Conclusion: Gray-scale and color Doppler ultrasonography demonstrates as a valuable radiologic technique for assessing the acute onset involvement of the lacrimal glands in COVID-19.

Keywords: acute dacryoadenitis; COVID-19; ultrasonography

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Introduction

The lacrimal gland, an exocrine gland responsible for the aqueous component of lacrimal fluid production, is located in the orbit on the lateral side of the orbital rim of the frontal bone. It is divided into two parts, palpebral and orbital, by the levator palpebrae superioris muscle. The lacrimal fluid produced by this gland drains into the nasal cavity through the lacrimal puncta, lacrimal canaliculi, lacrimal sac and nasolacrimal ducts.[1]

Dacryoadenitis is an inflammatory condition affecting the lacrimal gland. Acute dacryoadenitis (AD) is characterised by a rapid inflammatory process affecting the lacrimal gland, often seen in children and women.[2] The main causes of acute dacryoadenitis include viral, bacterial, traumatic and autoimmune factors. Among these, Epstein-Barr virus stands out as the most common pathogen, while others include adenovirus, mumps virus, herpes simplex virus and herpes zoster virus.[3,4] Typical symptoms of AD include orbital pain, painful eye movements, swelling and discomfort in the upper eyelid, and red eye appearance. Common signs of AD include tenderness, swelling, redness and droopy eyelid (ptosis) in the temporal region of the orbit (**Figure 1**).

The coronavirus disease (COVID-19) is an infectious illness caused by SARS-CoV-2. Since its emergence in 2019, COVID-19 has become a significant global health

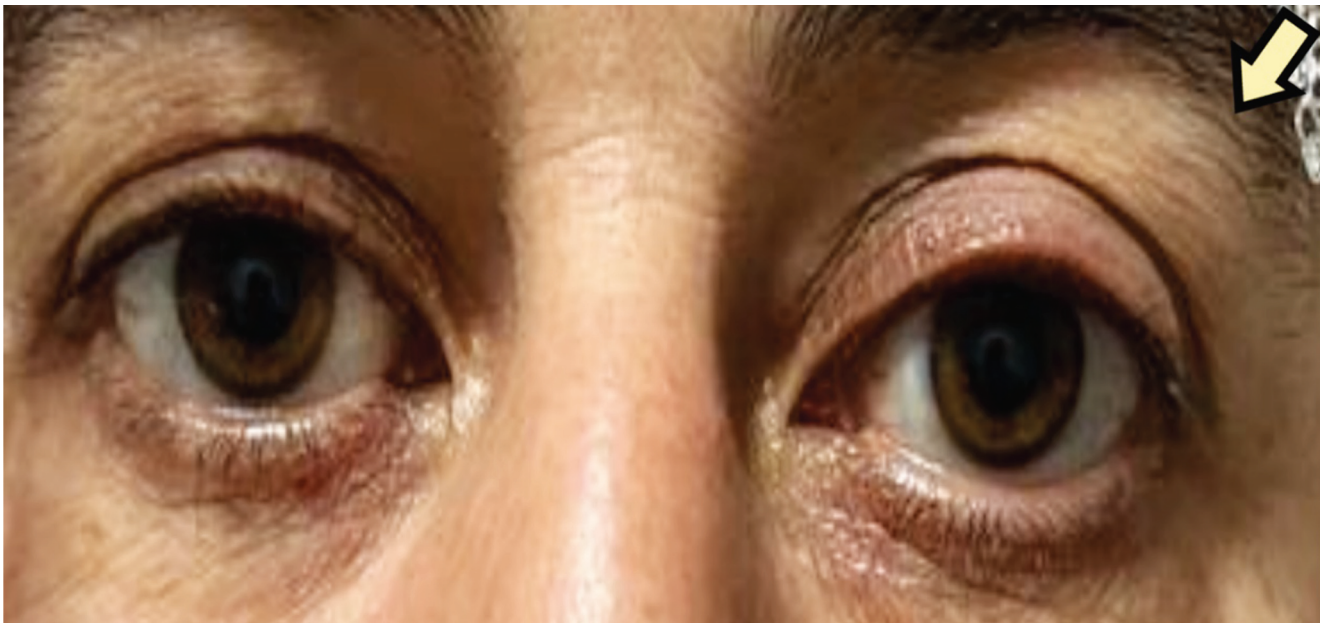

Figure 1. 42 years of female COVID-19 patient with left upper temporal eye lid swelling localized to lacrimal gland (yellow arrow).

concern, leading to widespread impacts on human health and society.[5] Recently, ocular complications associated with the coronavirus (SARS-CoV-2) have been reported. These complications include follicular conjunctivitis, inflammatory changes in both the anterior and posterior segments of the eye, orbital cellulitis, and retinal disorders such as retinal vasculitis and retinal degeneration.[6] Involvement of the lacrimal gland by SARS-CoV-2 is exceptionally rare, and only a limited number of studies and case reports have documented such occurrences, primarily presenting as acute dacryoadenitis.[2,7–10]

The diagnosis of AD is primarily established through the identification of typical clinical manifestations and physical examination findings. Additionally, a range of radiologic modalities are utilized for diagnosing AD, including conventional sonography and color Doppler ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI).[11]

Inflammatory changes, autoimmune disorders, and masses affecting the lacrimal gland can be effectively visualized using sonography and elastography techniques.[12,13] The lacrimal gland is situated in the superior lateral aspect of the globe.

The ocular globe and lacrimal artery serve as key landmarks for locating the lacrimal gland during examination. Once the lacrimal gland is identified, sonographic evaluation can be easily performed. Although the lacrimal gland presents as a homogeneous hypoechoic exocrine gland similar to other salivary glands, sonography is infrequently employed in clinical practice for diagnosing AD, despite the superficial location of the glands.

This study aimed to investigate the potential utility of sonographic imaging in diagnosing lacrimal gland involvement in COVID-19 by assessing imaging features such as echogenicity, homogeneity, vascularity and dimensions of the lacrimal gland.

Materials and Methods

Approval was obtained from the institutional review board and informed consent was obtained from all participants before starting the study. The study included 25 patients with a clinically confirmed diagnosis of COVID-19 who presented to the hospital with acute dacryoadenitis symptoms between January 2020 and January 2022 and 25 healthy participants. The inclusion criteria for this study involved the presence of pain, swelling, and discomfort in the superolateral aspect of the upper eyelid and orbit, consistent with AD within 30 days of a positive test for SARS-CoV-2. PCR testing yielded positive results for all patients. Healthy participants were included based on criteria including asymptomatic orbit and upper lid, absence of prior trauma or orbital surgery, no symptoms of upper respiratory tract infection compatible with SARS-CoV-2 within the preceding 6 months, and no history of systemic inflammatory disorders. PCR testing was negative for the control group over the preceding 6 months. Exclusion cri-

teria involved a clinical history of surgery, fracture, or other diseases affecting the lacrimal gland, such as sarcoidosis, Sjögren's syndrome, Graves' disease and wegener granulomatosis, as well as chronic progression of acute dacryoadenitis due to conditions such as syphilis, leprosy, tuberculosis, and trachoma.

Both the control group and patients underwent examination using gray-scale and color Doppler sonography (LOGIQ S7 Expert, GE Medical Systems, Chicago, IL, USA utilizing a 5–11 MHz linear-array transducer, performed by a radiologist with 5 years of experience. In our study, all participants were positioned supine on a stretcher with their heads turned to the opposite side and their eyelids closed. Following the application of a conductive gel, the 5–11 MHz linear array transducer was placed directly over the skin corresponding to the lacrimal fossa region. The examination of the lacrimal gland began obliquely, with the scanning plane parallel to the superotemporal aspect of the supraorbital margin. Landmarks such as the ocular globe and lacrimal artery were used to locate the lacrimal gland. Once identified, the longitudinal and transverse diameters of the lacrimal gland were measured by orienting the probe in transverse and craniocaudal directions. Gray scale and color Doppler sonography were performed using the 5–11 MHz linear array transducer. Doppler parameters were adjusted to detect low velocity or low volume flow, or both.

Anterior segment examination and dilated fundoscopy revealed normal findings, with no signs of intraocular inflammation. The patients involved in the study underwent orbital examination and ultrasonography (US) evaluations repeated at 3 weeks and 3 months.

All statistical analyses were conducted using SPSS software (version 26.0, IBM Corp., Armonk, NY, USA). Continuous variables were described using the median and range, while categorical variables were described using counts and percentages. The normality of distribution for variables was assessed using the Kolmogorov-Smirnov test. To compare continuous variables between healthy participants and patients, the Mann-Whitney U test and Kruskal-Wallis test were employed. Categorical variables were analyzed using the chi-square test and Fisher exact test. A p-value <0.05 was considered statistically significant.

Results

The study included a total of 50 participants, divided into two groups: 25 patients and 25 healthy participants. Among the 50 participants in the study, 21 were males and 29 were females. Of the 25 patients, 9 were male and 16 were female. Of the 25 participants in the control group, 12 were male and 13 were female. The mean age of the patients was 41.5±12.2 years and ranged between 18 and 63 years. The mean age of healthy participants was 34.4±5.2 years and ranged between 18 and 47 years. There was no significant difference between patients and healthy participants for age and gender (p=0.345 and 0.312 respectively). In 25 patients with clinically confirmed COVID-19 and symptoms of acute dacryocystitis, 11 patients had unilateral right lacrimal gland involvement, 12 patients had unilateral left lacrimal gland involvement, and 2 patients had bilateral lacrimal gland involvement. The participants included in this study had a total of 27 lacrimal glands with symptoms compatible with AD and 50 normal lacrimal glands. The mean time to the onset of symptoms of AD after COVID-19 infection was 17.7 days±6.8, with a range of 7 to 30 days. These baseline characteristics of the participants were summarized in **Table 1**.

The echogenicity of the lacrimal gland was increased in 23 out of 25 patients (92%). The homogeneity of the lacrimal gland was inhomogeneous in 18 out of 25 patients (72%). The vascularity of the lacrimal gland was increased in 20 out of 25 patients (80%). The resistive index in patients was low resistance flow (0.65±0.05).

Table 1
Demographic data of COVID-19 patients with symptoms of acute dacryoadenitis and control group.

	COVID-19 patients with acute vertebral level dacryoadenitis findings (n=25)	Control group (n:25)	p-value
Age	33.5±12.2 (min: 18; max: 43)	29.95±5.8 (min: 18; max: 34)	0.345
Male/female	9/16	12/13	0.312
Mean time to AD symptoms after COVID-19	17.7±6.8 (min: 7; max: 30) days	-	
Lacrimal gland involvement	right: 11 left: 12 bilateral: 2	-	

Perilacrimal fat tissue was normal in 18 out of 25 patients (72%). The mean transverse diameter of the lacrimal gland in patients group was 14.19±2.38 mm, ranged between 9 mm to 18.2 mm. The mean anteroposterior (AP) diameter of the lacrimal gland in patients with AD was 8.08±1.9 mm, ranging from 5.5 mm to 12 mm.

Among the 50 lacrimal glands examined in the 25 control healthy group, the echogenicity of the lacrimal gland was normal in 44 out of 50 glands (88%). The homogeneity of the lacrimal gland was normal in 49 out of 50 glands (98%). Vascularity of the lacrimal gland and echogenity of perilacrimal fat tissue showed normal sonography parameters in healthy participants. The resistive index in healthy participants was low resistance flow (0.62±0.04). The mean transverse diameter of the lacrimal gland in healthy participants was 7.89±1.5 mm, ranged between 9 mm to 18.2 mm. The mean AP diameter of the lacrimal gland in healthy participants was 5.14±1.05 mm, ranged between 3.2 mm to 7.7 mm.

The echogenicity of the lacrimal gland exhibited significant differences between healthy participants and COVID-19 patients (p=0.025). The homogeneity of the lacrimal gland exhibited significant differences between healthy participants and COVID-19 patients (p=0.018). Vascularity of the lacrimal gland exhibited significant differences between healthy participants and COVID-19 patients (p<0.001). The transverse diameter of the lacrimal gland in patients (14.19±2.38 mm, range: 9–18.2 mm) was significantly increased compared to healthy participants (7.89±1.5 mm, range: 9–18.2 mm) (p<0.001). Additionally, the AP diameter of the lacrimal gland in patients (8.08±1.9 mm, range: 5.5–12 mm) was significantly increased compared to healthy participants (5.14±1.05 mm, range: 3.2–7.7 mm) (p<0.001). However, there was no significant difference observed in the perilacrimal fat tissue changes between COVID-19 patients and the control group (p=0.054). And, no significant differences in the RI were measurable between AD (RI: 0.65±0.5) and control group (RI: 050.62±0.04) (p=0.078).

The sonographic characteristics of participants were summarized in **Table 2**.

Discussion

The ocular complications associated with SARS-CoV-2 infection include follicular conjunctivitis, inflammatory changes in the anterior and posterior segments, orbital cellulitis, and retinal disorders such as retinal vasculitis and retinal degeneration. However, lacrimal gland involvement due to SARS-CoV-2 infection is remarkably rare. Only a few studies and case reports have documented lacrimal gland involvement in the form of acute dacryoadenitis.[2,6–9]

There are limited previous studies regarding the evaluation of the effectiveness and reliability of lacrimal gland US in gland pathology. Giovagnorio et al.[14] evaluated that sonography was able to visualize 12 out of 30 lacrimal glands in 6 out of 15 patients affected by Sjögren's syndrome as significantly larger than normal (major axis: 7.6±0.9 mm; minor axis: 3.5±0.4 mm). Our study also revealed that the gland diameter was significantly enlarged in COVID-19-related AD patients compared to the control group. Ali et al.[15] demonstrated that the vascular flow around the lacrimal sac was increased with higher flow velocities in primary acquired nasolacrimal ducts obstruction compared to normal conditions. Moreover, Martinoli et al.[16] reported that color and power Doppler sonography could be utilized in the diagnosis and differentiation of chronic inflammatory processes and malignant tumors of

Table 2
Sonographic evaluation of COVID-19 patients with acute dacryoadenitis findings and control group.

Sonographic findings		Acute dacryoadenitis (n=25)	Control group (n:25)	p-value
The echogenicity of lacrimal gland	Normal	4	44	0.025
	Increased	23	6	
Homogeneity of lacrimal gland	Homogeneous	9	49	0.018
	Inhomogeneous	18	1	
Vascularity of lacrimal gland	Normal	7	50	<0.001
	Increased	20	-	
Perilacrimal fat tissue changes	Normal	18	50	**0.054**
	Increased	9	-	
Lacrimal gland transverse diameter		14.19±2.38 (min: 9; max: 18.2) mm	7.89±1.5 (min: 9; max: 18.2) mm	**<0.001**
Lacrimal gland AP diameter		8.08±1.9 (min: 5.5; max: 12) mm	5.14±1.05 (min: 3.2; max: 7.7) mm	**<0.001**

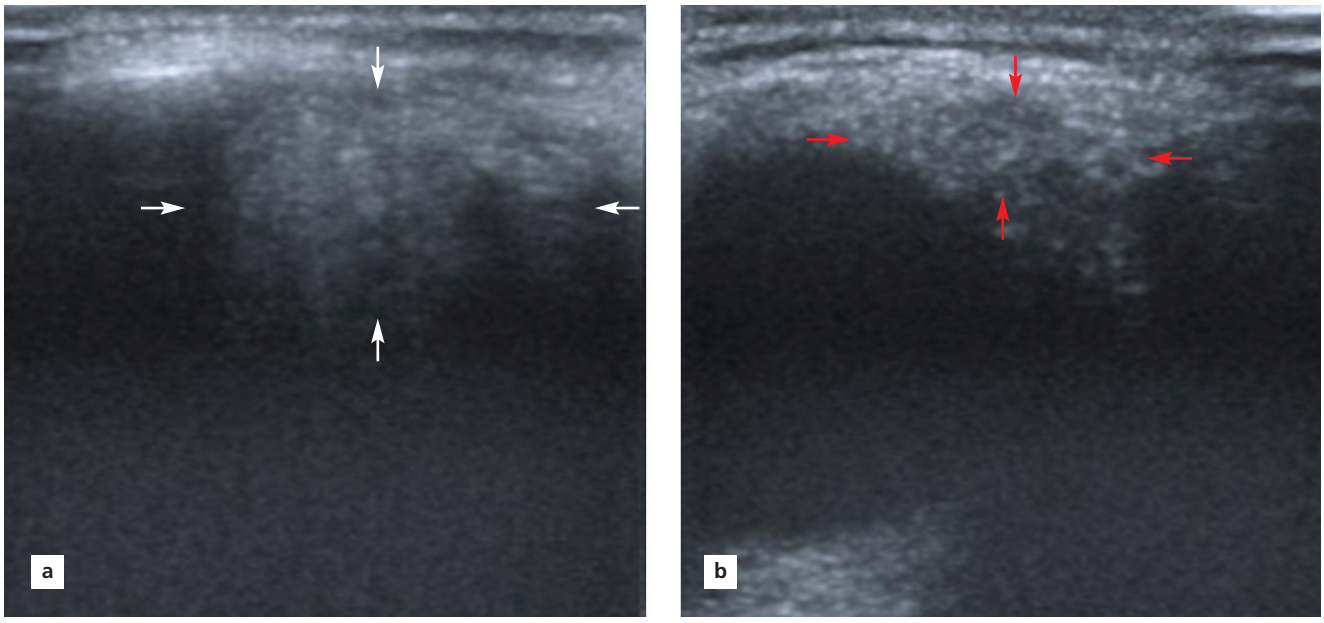

Figure 2. (**a**) B mode sonography findings of increased echogenicity, inhomogeneity, and enlargement of lacrimal gland (right side) (**white arrows**), compared to (**b**) healthy participant (**red arrows**).

the salivary glands. Additionally, Lecler et al.[17] demonstrated that non-epithelial lesions and acute dacryoadenitis were significantly more likely to present with high vascular intensity, both central and peripheral vascularization, tree-shaped vascularization, and a low resistance index (RI). Our study is consistent with previous studies that increased vascular flow in lacrimal dacryoadenitis. De Lucia et al.[18] revealed that lacrimal gland ultrasonography (US) is reliable imaging for the evaluation of US features in healthy subjects with a good-excellent intra and inter-rater reliability and the inter-rater agreement for the glandular parenchyma visibility, homogeneity, and size was good, and moderate for fibrous gland appearance.

All patients exhibited symptoms of pain, swelling, and discomfort in the superolateral aspect of the upper eyelid and orbit, consistent with AD, within 30 days of testing positive for SARS-CoV-2 (**Figures 2** and **3**). Anterior segment examination and dilated fundoscopy revealed normal

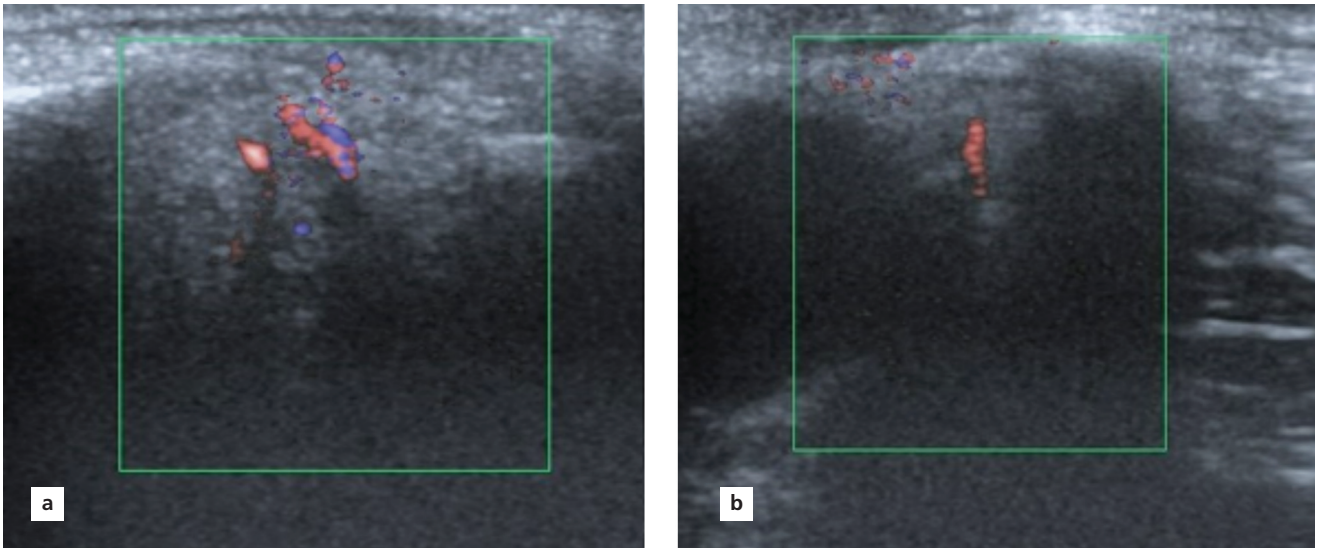

Figure 3. (**a**) Color Doppler sonography findings increased increased vascularity of the right lacrimal gland (right side), compared to (**b**) healthy participant.

findings, with no signs of intraocular inflammation. All patients' symptoms improved with one week of topical antibiotic-steroid and oral non-steroidal anti-inflammatory treatment. Normal visual and orbital functions were observed during the 3rd week and 3rd month follow-up examinations. During the 3-week follow-up examinations, increased echogenicity in the lacrimal gland persisted. And all sonographic parameters were observed to be normal during the 3-month follow-up examinations.

To our knowledge, this is the first study to evaluate acute dacryoadenitis after coronavirus (SARS-CoV-2) disease using sonographic and Doppler ultrasound. There are few case reports regarding coronavirus-related acute dacryoadenitis. Only three case reports have shown acute onset of lacrimal gland involvement in COVID-19 disease.[5–10] This study demonstrates that sonography and color doppler ultrasound is a reliable diagnostic tool for clinically confirmed COVID-19 patients with symptoms of Acute dacryoadenitis and US features such as increased echogenicity, inhomogeneity, increased vascularity, and enlargement of lacrimal gland are important US findings for AD. While the diagnosis of lacrimal gland involvement in AD in COVID-19 disease relies on clinical and laboratory criteria, evaluating structural changes in the glands and periorbital inflammation involvement necessitates diagnostic imaging modalities such as CT and MRI. Sonography is able to provide noninvasively volumetric and structural information needed by the clinician. Based on our experience, gland enlargement, increased echogenicity, and vascularity were found to correlate with lacrimal gland involvement in the disease process. Sonography accurately allowed for the assessment of gland dimensions, as it can identify the optimal plane in real time for measuring both transverse and anteroposterior diameters. Changes in echotexture of gland, periorbital echogenicity and vascularity, were reliably identified, making ultrasonography a viable tool for monitoring and follow up structural changes during disease progression.

Several limitations need to be acknowledged in this study. Firstly, ultrasonography imaging is a highly operator-dependent modality. We did not assess interobserver and intraobserver variability. To avoid sampling error, we measured the diameter of the lacrimal gland twice and calculated an average measurement. Secondly, histopathological correlation of AD was not conducted as the gold standard test, due to the invasive nature of the procedure. Thirdly, there was no radiologic correlation between ultrasound and other imaging modalities such as CT and MRI. Lastly, the study's sample size for both healthy participants and the disease group was small.

Conclusion

Lacrimal gland grey scale and colour Doppler ultrasonography are emerging as promising and valuable sonographic techniques to assess acute-onset involvement of the lacrimal glands in COVID-19, and reliable sonographic parameters such as echogenicity, homogeneity, vascularity and enlargement of the lacrimal gland contribute to the diagnostic accuracy of the disease.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author Contributions

SE: designed the research study, performed the research, analyzed the data and wrote the manuscript; MCÖ: performed the research, analyzed the data and wrote the manuscript; MB: designed the research study; all authors have read and approve the final manuscript.

Ethics Approval

Approval for this retrospective study was obtained from the institutional ethics committee (Ethics Committee of Ankara Bilkent City Hospital, Ankara, Turkey, decision number: ABCH-EK-2023/09-E2-23-4907).

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