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Optic nerve sheath diameter measurement in healthy South Iranian adults from a cross-sectional ultrasonographic study

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The measurement of optic nerve sheath diameter (ONSD) is a rapid, safe, and non-invasive method for assessing increased intracranial pressure (ICP). This study aimed to determine the mean ONSD in a healthy Iranian adult population and its correlation with demographic and anthropometric factors. Given that normal ONSD values can vary based on sex, age, ethnicity, and ultrasound techniques, establishing a local reference can enhance clinical assessment. In this cross-sectional study, 100 healthy Iranian adults (mean age 38.7 ± 9.8 years; 60 females) underwent ultrasonographic examination of the left optic nerve sheath. ONSD was measured 3 mm behind the globe in two planes, and the average of these measurements was calculated. The mean axial length (AL) was 23.53 mm (SD ± 0.94), and the mean ONSD was noted at 6.3 mm (SD ± 0.42). Statistical analysis did not reveal significant correlations between ONSD and various demographic or anthropometric factors (P:0.236). This study contributes to the literature by providing local reference values for ONSD in a healthy Iranian adult population, establishing an upper limit of 6.3 mm, and highlighting the consistency of these values with international norms, thereby improving the assessment of ICP in diverse populations.

Keywords Optic nerve sheath diameter, Optic nerve ultrasound, ONSD, Ocular ultrasonography, Raised intracranial pressure

Intracranial hypertension (ICP) is a common complaint in emergency and ophthalmology departments worldwide[1]. If undiagnosed or untreated, it can lead to significant cerebral hypoxia, permanent disability, and even death[1,2]. In South Africa, the incidence of head injuries is estimated at about 316 per 100,000 per year, which is higher than the estimated incidence of 90.5 per 100,000 population in the United States of America[1] and 200 per 100,000 population per year in Europe[2]. ICP can be detected through radiographic methods, using computed tomography (CT) or magnetic resonance imaging (MRI), and by ultrasound measuring the distension of the optic nerve sheath that surrounds the optic nerve.

The optic nerve originates from the retinal nerve fiber layer of the retina. Upon exiting the globe posteriorly, it is enveloped by the meninges—specifically, the dura mater, arachnoid mater, and pia mater—thereby forming the optic nerve sheath[2]. The optic nerve then traverses the orbit and optic canal to the optic chiasm. Consequently, there exists free communication between the intracranial subarachnoid space and the perineural subarachnoid space surrounding the optic nerve[2,3]. Fluctuations in ICP can be monitored by evaluating the distension of the optic nerve sheath, which exhibits maximum distensibility approximately 3 mm behind the globe, with maximum distension reaching up to 7.5 mm. Beyond this point, distension plateaus at 7.5 mm, despite continued increases in intracranial pressure[3].

Ultrasonographic measurement of the optic nerve sheath diameter (ONSD) has been established in numerous studies as a specific and sensitive predictor of elevated intracranial pressure[4–7]. As a result, many emergency departments worldwide have incorporated this non-invasive bedside technique as a screening tool for identifying this condition. Recent investigations have expanded the application of optic nerve ultrasound to a wider array of ophthalmic disorders[4–7]. This includes its use in the initial screening of idiopathic intracranial hypertension (IIH) and the subsequent monitoring of treatment response by performing serial measurements

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of ONSD[8]. Additionally, this modality is employed in the detection of various optic nerve pathologies, such as inflammatory and ischemic optic neuritis[9,10], as well as normal-tension glaucoma[11,12].

However, various studies conducted worldwide have demonstrated significant disparities in the mean and range of ONSD across different population groups[13–17]. Specifically, the mean ONSD has been reported to vary from 3.68 mm in a Canadian cohort[14] to 5.1 mm in a Chinese cohort[16]. Understanding the variations in the size, shape, and unique characteristics of the optic canal can assist clinicians when approaching this structure during invasive procedures, such as optic nerve decompression. Recent studies have shown that the depth of the optic canal is notably larger on the left side in females, which correlates with several surrounding structures[18]. This highlights the clinical significance of these anatomical variations. Moreover, the optic chiasm can exhibit variations in its morphology (e.g., complete, partial, or absent crossing of fibers), which can impact visual field deficits and surgical planning[18]. This relationship between anatomical variations and clinical implications is further elaborated by Ay[19], who discusses the associations of these variations with nearby structures and their clinical impacts.

The objective of our study was to determine the mean ONSD in a healthy adult population from southern Iran and to evaluate whether this measurement significantly differs from those reported in various populations studied across different regions of the world. Additionally, we aimed to correlate these measurements with the demographic and anthropometric characteristics of the study participants.

Materials and methods

A cross-sectional descriptive study was conducted at Imam Khomeini Hospital in Ahvaz, Iran, from January to July 2024. In light of the COVID-19 pandemic and the subsequent post-pandemic circumstances, all procedures adhered to the biosafety protocols mandated by the hospital and local and national authoritie.

This study received approval from the institutional research ethics committee (Approval number: IRIN-5224–2024), and all participants provided written informed consent prior to inclusion.

Participants

Healthy adult volunteers aged 18 and older, with no history of neurological or neuro-ophthalmological diseases and normal neurological examinations, were included in the study. Individuals with any disease, condition, or treatment that could potentially affect the ultrasound measurements or intracranial pressure, as determined by the investigators, were excluded. The study primarily involved healthy adult volunteers from the Ophthalmology Department, including hospital staff and relatives of patients, who were invited to participate. For all participants, data collected included sex, age, height, weight, and body mass index (BMI). Each participant underwent a thorough bilateral fundoscopy, and a slit lamp biomicroscopic examination was performed to evaluate the fundoscopic appearance of the optic nerve head. Intraocular pressure (IOP) measurements were taken using a Perkins applanation tonometer (PAT) on the left eye of each participant. Subjects were included in the study if both the optic nerve examination and IOP readings fell within normal limits, as defined later. Height was measured in meters using a standard wall-mounted meter scale, while weight was recorded in kilograms using a calibrated electronic scale.

Optic nerve health ultrasound

Ultrasound measurements of ONSD were performed by a single ophthalmologist with prior experience and training in optic nerve sheath ultrasound, using a portable Edge Sonosite Fujifilm ultrasound system. A standard orbital two-dimensional (2D) imaging mode was employed with a 10–13 MHz linear ultrasound probe set to maximum gain, at a depth of 6 cm and a greyscale level of 0). The system's error in B mode within the range of 0–26 cm was less than ±2% for axial, lateral, and diagonal distances. All measurements were taken with participants in a supine position, with their heads elevated at a 30-degree angle. The probe was applied to the upper eyelids using coupling gel, positioned at the superolateral margin of the orbit while the eyes were in primary gaze (Fig. 1). This alignment was crucial for proper visualization of the optic nerve and to minimize pressure on the eye. The probe's position was adjusted to clearly visualize the optic nerve's entry into the globe. For the study, measurements were taken from the left eye, starting with the maximal exophthalmic distance (ETD) followed by the ONSD in the transverse plane, measured 3 mm behind the posterior globe margin. The ONSD was measured from the inner edge to the inner edge of the optic nerve sheath (Fig. 2A, B). Each optic nerve sheath was measured twice with the probe oriented in two different planes at angles of at least 30 degrees, and the average of the two measurements was used to enhance accuracy.

Statistical analysis

A required sample size of ninety-seven participants was determined based on a standard deviation of 0.5, a margin of error of 0.1 mm, and a significance level of 5% (Type I error), utilizing the Canadian study by Goeres et al.[13,17] as a reference for the calculation. The Kolmogorov–Smirnov test for normality revealed that intraocular pressure, as well as both first and second optic nerve sheath diameter measurements along with the mean optic nerve sheath diameter, were all normally distributed. Descriptive statistics for the ONSD were computed, including the mean, standard deviation (SD), minimum, maximum, and the 95th percentile for quantitative data. Qualitative data were presented as percentage and frequency. To evaluate the reliability of the repeated ONSD measurements within individuals, a two-way mixed model Intraclass Correlation Coefficient (ICC) for absolute agreement was employed. An independent t-test was conducted to examine differences based on gender and co-morbidities, while linear regression was utilized to assess the influence of age on ONSD, adjusting for gender, as well as the impact of gender on ONSD, adjusting for age. A p-value of 0.05 was considered significant. Statistical analyses were performed using SPSS version 27. The costs associated with the study were funded by the corresponding author, ensuring there were no costs for the participants and no external funding was received.

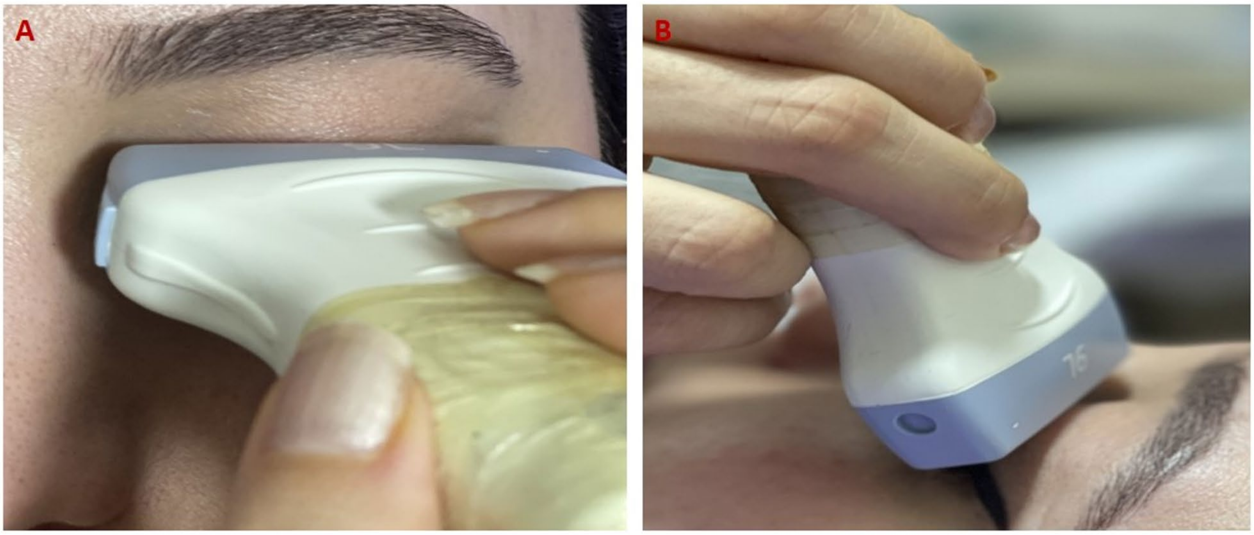

Fig. 1. Position of the ultrasonographic probe, showing the patient in the prone position, with the eye depicted in two different views: A: front view and B: lateral view.

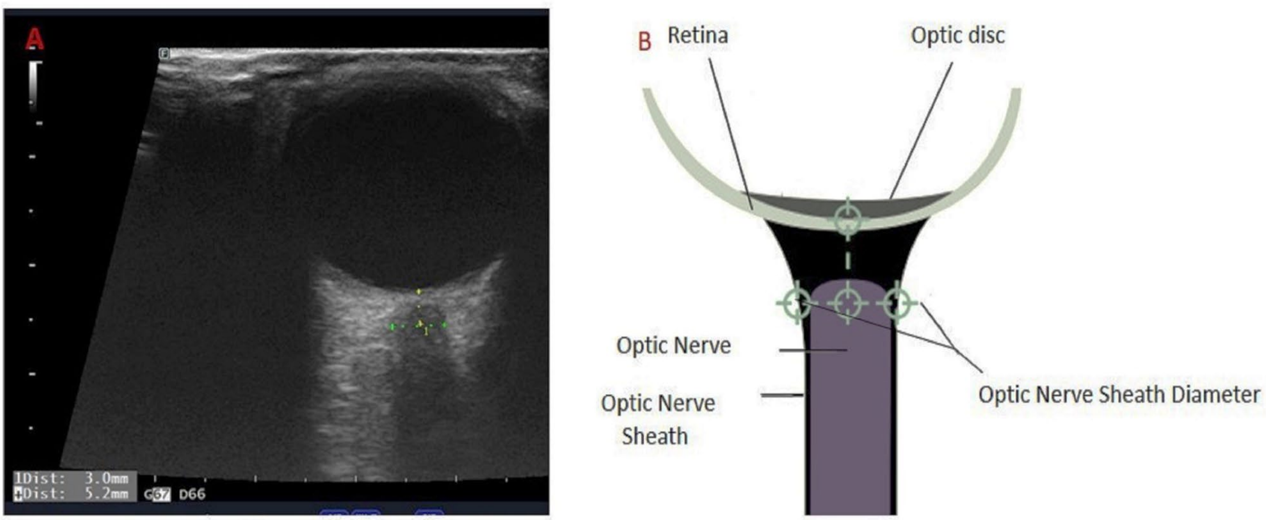

Fig. 2. A: Ultrasonography images of the optic nerve sheath, demonstrating the sheath located 3 mm behind the retina. The hyperechoic sheath elegantly surrounds the center of the optic nerve. B: A corresponding illustration labels the structures of the eye, providing a direct comparison with the clinical image and the ONSD measurement.

Result

A final sample of 100 healthy volunteers was obtained, with a mean age of 32.7 ± 6.3 years (SD), 59 of whom were male. The mean weight, height, and BMI were 67.71 ± 8.46 kg (SD), 170.2 ± 9.45 cm (SD), and 23.34 ± 1.15 kg/m^2 (SD), respectively (Table 1).

The range of ONSD measurements in our adult population was found to be 4.6 mm to 8.2 mm (Fig. 2). The mean ONSD for all participants is summarized in Table 2. The overall mean ONSD was 6.3 mm (SD ± 0.42), with a 95th percentile of 6.6 mm. The reliability of ONSD measurements was assessed using Intraclass Correlation Coefficient (ICC) analysis, yielding a value of 0.94 (95% confidence interval: 0.900–0.956), indicating a high level of reliability (Fig. 3).

Upon evaluating the influence of gender on ONSD, no significant difference was observed between the mean ONSD of males (6.44 mm) and females (6.28 mm), with a p-value of 0.652. Linear regression analysis indicated that age and gender explained only 4% of the variance in ONSD (R^2 = 0.028; F(2, 16) = 1.315; p = 0.236). When considered together as independent variables, neither age (β = 0.076; p = 0.102) nor gender (β = 0.080; p = 0.593) emerged as significant predictors of ONSD.

	(*n*,%)/ (mean ± SD)	Minimum	Maximum
Sex-Male	41 (41%)		
Age (years)	32.7 ± 6.3	20	73
Weight (kg)	67.71 ± 8.46	45	87
Height (cm)	170.2 ± 9.45	152	188
BMI (kg/m^2)	23.34 ± 1.15	19.5	25
IOP (mmHg)	12.6 ± 1.82	20	10
Axial length (mm)	23.53 ± 0.94	21	28

Table 1. Summary of enrolled participants' demographic data ($n = 100$).

Variable (mm)	Mean	SD	95% CI	Minimum	Maximum
ONSD 1	6.42	0.34	6.0–6.4	4.3	6.8
ONSD 2	6.10	0.44	6.0–6.1	4.5	8.2
Mean ONSD	6.30	0.42	6.0–6.6	4.3	8.2

Table 2. Summary of the descriptive statistical analysis for the ONSD measurements taken in two different planes (at least Thirty degrees apart) and the mean of the two readings for all participants. All measurements were found to be normally distributed, as confirmed by the Kolmogorov–Smirnov test.

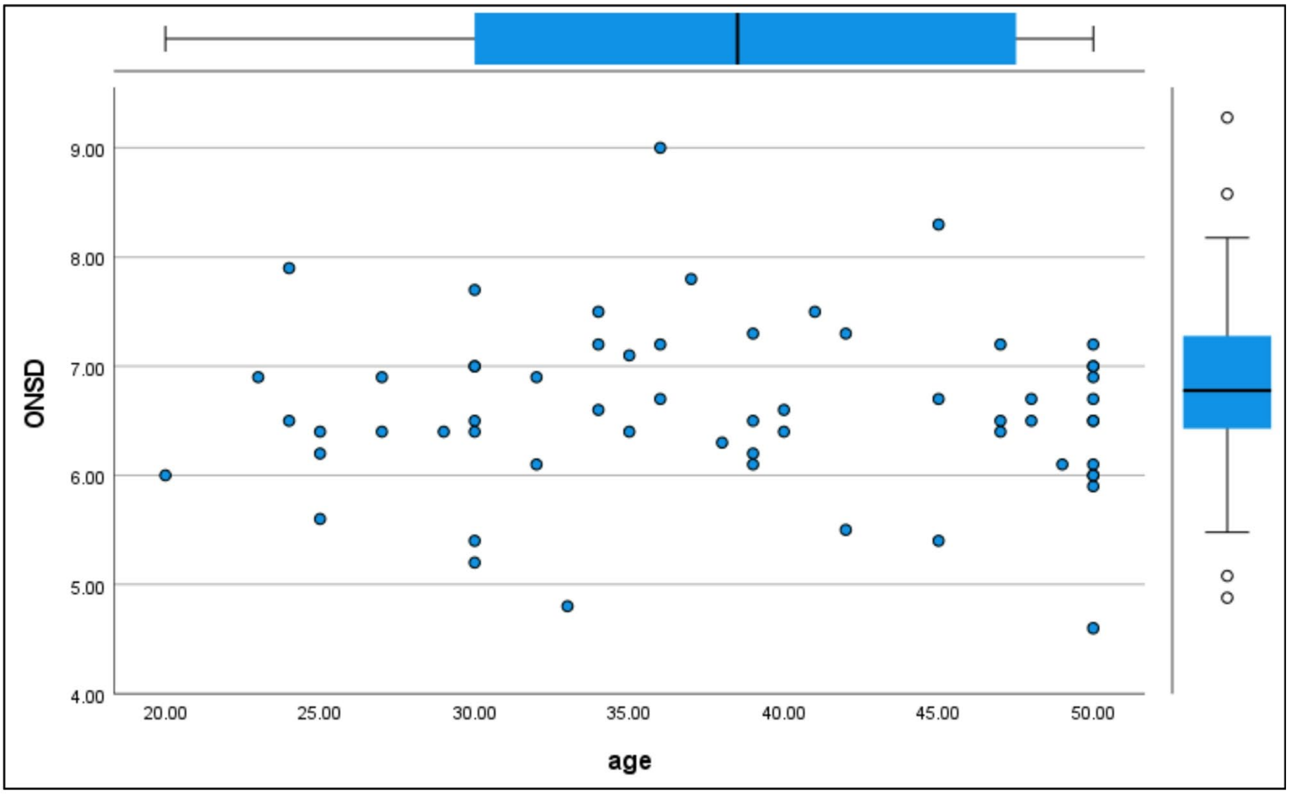

Fig. 3. Distribution of ONSD among different age groups.

Discussion

This study provides the first comprehensive assessment of ONSD in a healthy Iranian adult population, revealing an average measurement of 6.3 mm (SD ± 0.42) with a 95th percentile of 6.6 mm. These findings significantly contribute to the existing literature by establishing a normative database that can facilitate more accurate clinical evaluations and interventions for intracranial hypertension. Our results indicate that the mean ONSD in this population is notably higher than the mean reported in a Canadian cohort (3.68 mm, 95% CI 2.85–4.40 mm)[13] and a Chinese population (5.1 mm)[15]. This emphasizes the critical necessity for localized studies to determine accurate diagnostic criteria.

The ultrasonographic assessment of ONSD has emerged as a quick, non-invasive, and portable method for monitoring ICP fluctuations. The relationship between ONSD and ICP is well documented in the literature. For instance, the scoping review by Martínez-Palacios et al. reports that ultrasonographic ONSD measurement demonstrates a strong correlation with invasive ICP methods, making it a suitable non-invasive alternative for assessing ICP in traumatic brain injury (TBI) patients[20]. Additionally, Lioi et al. further support the utility of ONSD as a first-line screening tool for identifying patients needing invasive monitoring in emergency situations[21]. Ferreira et al. corr oborate these findings, demonstrating a positive correlation between ONSD and intracranial pressures measured via intraparenchymal monitoring[22].

The accessibility of the ultrasonographic technique is further enhanced by its ability to be executed by trained non-radiologists, as highlighted by Potgieter et al., where novice operators could achieve high accuracy after brief training[23,24]. This feature is particularly valuable in resource-limited settings, such as rural hospitals in southern Iran, where ultrasound can mitigate barriers associated with advanced radiological investigations.

Our study found a range of ONSD measurements spanning from 4.3 mm to 8.2 mm, with no significant correlations noted between ONSD and demographic factors such as age or gender. This finding is consistent with international research where such correlations were found lacking[15,16,25–27]. Furthermore, our unilateral focus on ONSD measurement aligns with previous evidence indicating that significant discrepancies between right and left side measurements are rare[12,15].

The results of our study contribute to the growing body of evidence regarding the variability of mean ONSD observed across diverse population groups globally. Numerous factors have been proposed to account for these discrepancies in ONSD as reported in various studies. One principal factor is the variability in measurement techniques utilized[25,26]. ONSD is defined as the distance between the external margins of the hyper-echoic optic nerve sheath and the arachnoid mater[23,28]. If measurements are taken from the internal boundaries of the hyper-echoic sheath, they reflect the diameter of the optic nerve itself, resulting in an underestimation of the mean ONSD[23,28,29]. Conversely, including the hypoechoic region outside the optic nerve sheath leads to measurements that encompass the dura mater, retrobulbar fat, and surrounding artifacts, which can result in an overestimation of ONSD[29,30]. Typically, ONSD measurements are performed three millimeters posterior to the globe, a site believed to be the most distensible and therefore the most sensitive to variations in intracranial pressure[23,30]. To enhance the accuracy of ONSD assessments, several methodologies have been proposed. These include the application of color Doppler imaging to visualize central retinal vessels, thus confirming the course of the optic nerve and minimizing artifact[30,31]. Additionally, employing A-scan ultrasonography can mitigate the "blooming effect" often associated with the B-scan mode if a standardized gain setting is not utilized[30]. Emerging imaging modalities, such as high-frequency ultrasound elastography, have shown promise in detecting subtle changes in ocular structures prior to their visibility on traditional B-scan ultrasonography[31]. However, further investigation is warranted to ascertain the practicality of this technique in optic nerve sheath imaging.

Ethnic and genetic heterogeneity may contribute to the observed variations in ONSD. A comprehensive review of existing literature indicates a notable absence of studies focused on racial and ethnic differences in ocular anatomy among Iranian adult populations, particularly in southern Iran, but we proposed that adults from this region, specifically Khuzestan, exhibit higher intraocular pressures and reduced central corneal thickness (CCT) compared to other ethnic groups in Iran. For instance, previous research has demonstrated that Black African populations tend to have a higher ONSD in contrast to both European and Canadian populations[32]. Additionally, studies utilizing OCT reveal that Black African adults possess significantly thicker retinal nerve fiber layers when compared to the normative values derived from European cohorts established by the manufacturers of OCT machines[28]. Though not directly applicable to the Iranian adult population, international studies have reported ethnic disparities in various ocular parameters, including anterior chamber depth and angle morphology[27–29]. Moreover, research examining optic disc characteristics has indicated that individuals of African descent have an optic disc area approximately 26% larger than that of Caucasian individuals[19]. Similar investigations have revealed that Black individuals demonstrate significantly larger vertical disc diameters on optic disc imaging compared to their Caucasian counterparts[33,34]. The findings by Ferreira et al.[21] also showed significant variability and emphasized the need for standardization in measurement techniques due to differences in equipment and methodologies across studies[2,19,28]. This variability presents both a challenge and an opportunity for further investigation.

The strengths of our study include its designation as the first investigation, to our knowledge, aimed at determining the mean ONSD in healthy South Iranian adults. Notably, while the majority of studies identified in the literature review did not incorporate ocular examinations in participants undergoing optic nerve sheath ultrasonography, we included an assessment of the optic nerve head using slit lamp biomicroscopy, as well as intraocular pressure measurements via applanation tonometry. These additional evaluations were implemented to further exclude potential optic nerve pathologies that could confound the data collection necessary for establishing a normative database. To enhance the accuracy of our ONSD measurements and minimize artifacts, the optic nerve sheath was assessed in two distinct cross-sectional planes that were at least thirty degrees apart, with the average of the two readings being used for each participant. We anticipate that our findings regarding the normal range of ONSD and the established upper limit cut-off value will serve as a foundational reference for future studies exploring the utility of ONSD in detecting and monitoring various pathological conditions of the optic nerve, including optic neuritis and idiopathic intracranial hypertension (IIH).

This study has several important limitations that should be acknowledged. First, all ONSD measurements were obtained by a single investigator. While the investigator had substantial experience in optic nerve ultrasound and was trained in Level One ultrasonography, there remains a potential risk of observer bias. Although a second ophthalmologist reviewed the images and measurements, the inclusion of a second independent investigator, with masked measurement comparisons, would have enhanced the robustness of the findings and allowed for an assessment of interobserver variability. Although a second ophthalmologist reviewed the images, incorporating independent measurements could further strengthen the findings. Future research should explore the use of various ultrasound devices to examine inter-device variability, as noted by Ferreira et al. The environment in which this study was conducted—an emergency department during off-hours—also introduced specific constraints[21]. Due to these circumstances, only participants with a cup-to-disc ratio greater than 0.4 on fundoscopy were required to undergo a normal OCT assessment of the retinal nerve fiber layer (RNFL) prior to data analysis. Future studies could benefit from performing OCT on all participants to further bolster the evaluation of the optic nerve and to eliminate the possibility of undetected subclinical optic neuropathy. Finally, this study was not adequately powered to investigate the impact of individual comorbidities on ONSD. Exploring this relationship in future studies could provide valuable insights into how various medical conditions may influence optic nerve sheath dynamics.

Conclusions

Optic nerve sheath ultrasound is a rapid, cost-effective, and non-invasive bedside tool that provides an accurate assessment of raised intracranial pressure and optic nerve-related pathology. This modality has demonstrated high sensitivity and specificity for detecting changes in intracranial pressure; however, further population-based studies are necessary to establish definitive cut-off values. This need arises from the significant heterogeneity observed in normal ONSD values reported in international literature. In our study, which included healthy South Iranian adult volunteers, we determined the mean ONSD to be 6.3 mm (SD ± 0.33). Notably, ONSD was found to be independent of gender, age, and the presence of comorbidities. Based on our findings, we recommend an upper limit cut-off value of 6.3 mm for ONSD assessment in South Iranian adults, which may facilitate more accurate screening for raised intracranial pressure.

Data availability

Data will be available on request from the corresponding author.

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Author contributions
A.M: received and designed the analysis, collected data, contributed data or analysis tools. M.H: received and designed the analysis, performed the analysis. M.A: received and designed the analysis, collected data, contributed data or analysis tools, performed the analysis and wrote the paper. A.S: Collected data, contributed data or analysis tools. M.K: Collected data and wrote.

Competing interests
The authors declare no competing interests.

Informed consent
Informed consent was obtained from all participants (or their legal guardians) for the use and publication of clinical information and images in this online open-access publication.

Additional information
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