

Role of Orbital Ultrasound in the Assessment of Clinically Detected Papilledema

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Abstract

Background: Increased intracranial pressure (ICP) is frequently seen, and it is considered a serious problem that needs a careful assessment and management, especially by easy and least invasive modalities. **Objective:** The objective of the study is to assess the optic nerve sheath diameter (ONSD) using transorbital ultrasound (US) as a marker and indicator for diagnosing raised intracranial pressure. **Patients and Methods:** It is a prospective study that was carried out in Neurology and/or Ophthalmology Clinics, Baghdad Teaching Hospital in the Medical City Complex during the period from June 2016 to May 2017; in this study, 40 patients seeking medical help for other causes were considered to be a control group and the other 40 patients who were complaining of raised ICP symptoms and suggested of having optic disc swelling by ophthalmoscopy examination. All the patients and the control group were examined by transorbital US to measure the ONSD, and then, only the patients with symptoms of raised intracranial underwent a lumbar puncture (LP). **Results:** Pearson's correlation test was used, demonstrating a very significant correlation between the ultrasonographic ONSD and the measurements of LP ($R > 0.9$) and ($P < 0.001$). Transorbital US yielded high sensitivity (91.6%) with modest specificity (75%) and high accuracy (90.0%) of ONSD was considered the normal the cutoff value of (5 mm) obtained from the control group. The US also showed the crescent sign and the optic disc bulging with lower sensitivity than the ONSD (61.1% and 41.6%, respectively) but with very high specificity (100%) for both. **Conclusion:** ONSD by transorbital ultrasonography is highly accurate, easily performed, and noninvasive procedure for the detection of raised ICP. Routine daily monitoring of ONSD could be of help in intensive care units when invasive ICP monitoring is not available or contraindicated; it also has a good role in early recognition of intracranial hypertension.

Keywords: Intracranial hypertension, optic nerve sheath diameter, papilledema, transorbital ultrasound

INTRODUCTION

Papilledema is defined as bilateral optic disc swelling usually resulting from raised intracranial pressure.^[1,2] Transient blurred vision is the usual presenting symptom of papilledema; a headache is also a common but not a constant association, visual acuity is not affected by papilledema unless it is severe, chronic, or accompanied by macular edema and bleeding.^[1]

Differentiating papilledema from other forms of optic disc swellings is often difficult (especially when dealing with optic neuritis or ischemic optic neuropathy) by fundus examination alone.^[1] Fundoscopic examination reveals (in order of onset) blurring of the nerve fibers layer, loss of venous pulsations (usually when the intracranial pressure [ICP] was above 200 mmHg), hemorrhage in the layers of nerve

fibers, blurring of disc margin and elevation of the disc surface, and finally, disc hyperemia.^[2]

Ultrasound (US) is a nonionizing energy, and for that, it is safe for pregnant women and children.^[3,4] In general, the differences in the interfaces of tissues from which the echoes of the US beam travel and reflect are interpreted depending on the shape and internal structure of the organ and masses.^[3]

Beside ultrasonographic measurement of the optic nerve sheath diameter (ONSD) is developing as a noninvasive method to detect the elevated ICP and increased ICP is extending to involve the subarachnoid space surrounding the

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optic nerve, resulting in optic nerve sheath dilation, and this can easily be detected using US.^[4] Some literature describes other ultrasonographic findings in differentiation between papilledema and pseudopapilledema, and for the detection of intracranial hypertension in addition to measuring the ONSD, these are the crescent sign and bulging optic disc. The crescent sign refers to an anechoic area in the anterior intraorbital nerve usually represents the separation of the nerve and its sheath by cerebrospinal fluid (CSF).^[5]

Several studies showed a close association between ONSD dilatation and raised ICP in patients with severe head injury, intracranial bleeding, or idiopathic intracranial hypertension.^[6] While decreased ONSD was seen in patients with intracranial hypotension,^[6] many studies explaining that ONSD is increased during elevations of ICP and its diameter can be used to monitor the increase in ICP indirectly.^[7] Especially, when the physical examination has significant limitations if the patient is unconscious, intubated, or paralyzed.^[8]

The transorbital US is performed by placing the linear transducer in the transverse direction; the optic nerve with its covering sheath is visible posteriorly as a hypoechoic linear shadow radiating away from the globe; and the accurate measurements of ONSD can be obtained 3 mm posterior to the globe where best contrast difference is depicted, then measuring the diameter of optic nerve sheath shadow (including the optic nerve) from side to side and width >5 mm indicating increased ICP. The normal ONSD in adults is defined as a diameter <5 mm.^[5] A normal ONSD should be <4.5 mm in children between 1 and 15 years of age while in infants, below 1 year it should be <4 mm.^[9]

PATIENTS AND METHODS

This is a prospective study that comprised 80 individuals (40 person control group and 40 patients). The 40 patients complaining of a headache and visual impairment were visited the Neurology or Ophthalmology Clinic in Baghdad Teaching Hospital at the Medical City Complex in Baghdad, Iraq, during the period from June 2016 to May 2017 and their age ranged from 22 to 53 years.

The control group represents the patients who do not complain from any neural or ophthalmic problems and visited the outpatient clinic for abdominal US examination for any urological/gynecological or hepatobiliary complaints, they were asked for the permission to do the orbital US. The age and gender distribution were similar to age and gender of a study group.

We explained the examination technique of our research for all included patients before starting data collection. All patients who were included in our research gave their oral agreement; furthermore, they had the choice to stop cooperating with our project whenever they wanted. Furthermore, we explained that our study was noninvasive which would not harm anybody.

All patients included in our study met the following inclusion criteria; 20 years of age, bilateral suspected papilledema by ophthalmoscopic examination which was done by ophthalmologist or neurologist, the presence of clinical symptoms and signs of raised ICP, including a headache, nausea and vomiting, in the absence of any contraindication for a lumbar puncture (LP).

Patients who have a history of glaucoma, known orbital injury or prior ocular surgery, patients whom magnetic resonance imaging nor computed tomography scans revealed any lesions or causes which could be the reason for raised ICP that turned them contraindicated for LP, history of bleeding diatheses such as coagulopathy and thrombocytopenia, skin infection at puncture site, sepsis, abnormal respiratory pattern, and patients who refuse to undergo LP were excluded from the study.

The suspected papilledema cases by ophthalmology examination were referred to the radiology department for a transorbital US which was performed by a radiologist using Philips HD11XE US machine. The examination was done using a linear probe (7.5–12 MHz) which was placed gently on the superior and lateral aspect of upper eyelid with the eyes closed. Copious amount of gel was sited over the eyelids which allowed the floating of the probe and to avoid placing direct pressure on the ocular structures. The probe then angled slightly caudally and medially in transverse view until the optic nerve was clearly visualized as a linear hypoechoic structure with clearly defined margins posterior to the globe. ONSD was measured 3 mm behind the globe from side to side of the optic nerve shadow, and the results were documented for both eyes and the presence or absence of crescent sign and bulging or flat papillae was recorded as well, patients then were referred for LP.

LP was performed for all patients in a special, fully equipped room by neurologists with their medical assistance. They prepared the patient to perform the procedure in a correct position under a full sterile condition. The needle was inserted in L3–L4 interspace which was attached to a manometer to collect the CSF and to measure the pressure, and then the results were recorded. Following LP, the patients were positioned in a comfortable recumbent position for 30–60 min before safely discharged home. We compared the US with the LP results which are considered a gold standard method for measuring ICP in each patient.

The study sample is illustrated in figures as mentioned below; Figure 1 shows normal ONSD of both the eyes “Control Group” measuring 4.6 mm was obtained 3 mm behind the globe; Figure 2 illustrates the transorbital US of a 32-year-old patient who was diagnosed with benign intracranial hypertension, it demonstrates dilated ONSD of both sides (right 6.5 mm) and (left 7 mm), they were measured 3 mm behind the globe; and Figure 3a demonstrates transorbital US of a patient with sagittal sinus thrombosis showing dilated left ONSD 7.5 mm at 3 mm behind the globe and Figure 3b shows US image of the same patient demonstrating crescent sign “arrowhead” and optic disc bulging “straight arrow” in the same eye.

RESULTS

A total of 80 individuals (40 person control group and 40 patients) were registered in our study, and the mean age of them is 35.1 ± 8.72015 standard deviation (SD) for the patient age ranging between (22 and 53 years). About 42.5% were male while females represent 57.5% as shown in Tables 1 and 2. The

Table 1: Demographic age characteristic of the studied patient group

Age	n (%)
20-29	12 (30)
30-39	14 (35)
40-49	10 (25)
>50	4 (10)
Total	40 (100)
Mean±SD	35.100±8.72015

SD: Standard deviation



Figure 1: Normal optic nerve sheath diameter of both eyes measuring 4.6 mm of control person

mean ONSD of the patients' group for both right and left sides was measured by the US represent 5.65 ± 0.18771 as shown in Table 3. It is considered high in comparison to the mean ONSD of the control group which was represented in Table 4. As shown earlier, the mean ONSD of the control group of both right and left sides was 4.2749 ± 0.11308 mm as measured by the US; however, a cutoff ONSD value of 5 mm was chosen as an upper normal diameter for more accuracy. Furthermore, the correlation of ONSD with ICP was assessed by measuring lumbar pressure, and the 20 mmHg was considered to be a maximum cutoff upper normal pressure value. A Pearson's correlation test and a scatterplot of ICP as a function of ONSD demonstrate this relationship, a highly statistically significant correlation was found ($R > 0.9$) and ($P < 0.001$) in Figure 4. The sensitivity of US examination of both the right and left sides was high (91.6%) with modest specificity (75.0%) and very good accuracy (90.0%) as shown in Table 5.

Furthermore, other ultrasonographic findings were detected, including crescent sign and bulging papillae. Concerning

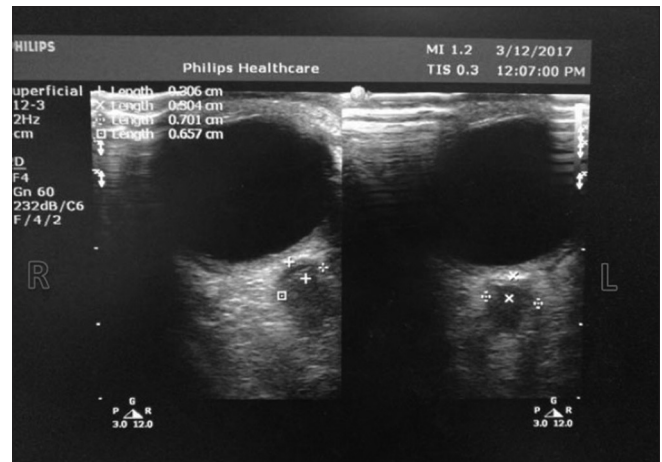


Figure 2: The transorbital ultrasound of the patient diagnosed with benign intracranial hypertension aged 32 years old demonstrate dilated optic nerve sheath diameter of both sides; right 6.5 mm and left 7 mm

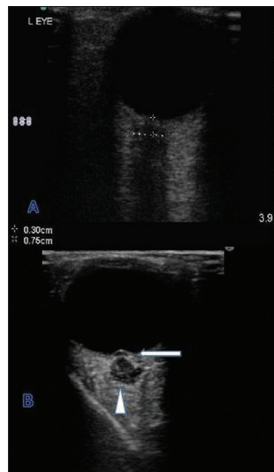


Figure 3: (A) Transorbital US of a patient with sagittal sinus thrombosis demonstrate dilated LT ONSD (7.5 mm) of 3mm behind the globe. (B) US image of the same patient demonstrate crescent sign (arrowhead) and optic disc bulging (straight arrow) in the same eye

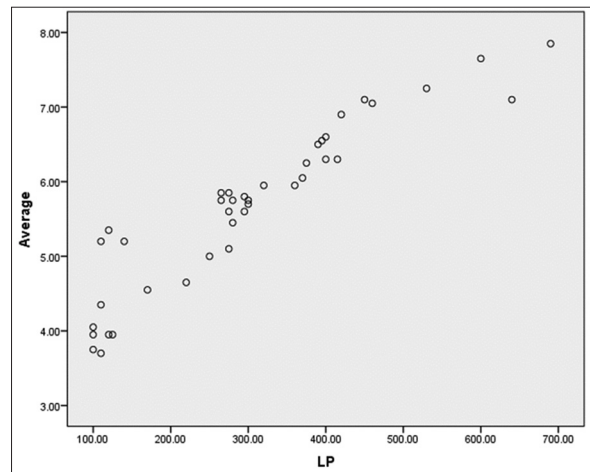


Figure 4: Scattergram of increased intracranial pressure versus average of the right and left optic nerve sheath diameter

Table 2: Demographic gender characteristic of the patient group

Sex	Frequency (%)
Female	23 (57.5)
Male	17 (42.5)
Total	40 (100.0)

Table 3: Nerve sheath diameter mean values measured by ultrasound for the right and left sides distributed by gender of patient's group

ONSD (mm)	n	Minimum	Maximum	Mean±SD
Left female	23	3.70	7.90	5.8391±1.16492
Right female	23	3.80	7.80	5.7957±1.14355
Left male	17	3.70	7.00	5.4824±0.97419
Right male	17	3.70	7.20	5.5059±1.07615
Total	40	-	-	5.6558±0.18771

ONSD: Nerve sheath diameter, SD: Standard deviation, US: Ultrasound

Table 4: Mean nerve sheath diameter of the right and left sides distributed by gender of the control group

ONSD (mm)	n	Minimum	Maximum	Mean±SD
Right male	11	3.80	4.60	4.1818±0.29939
Left male	11	3.80	4.60	4.1727±0.31013
Right female	29	3.80	4.80	4.3828±0.30714
Left female	29	3.80	4.80	4.3621±0.32006
Total	40	-	-	4.2749±0.11308

ONSD: Nerve sheath diameter, SD: Standard deviation, US: Ultrasound

crescent sign, the US had lower sensitivity and accuracy but with higher specificity than ONSD, as shown in Table 6; US validity of crescent sign around optic nerve in detecting raised ICP among 40 cases was as follows: sensitivity 61.1%, specificity 100%, and accuracy 65.0%.

Bulging papillae of the optic nerve head are another ultrasonographic feature in the detection of raised ICP with lower sensitivity and accuracy than ONSD and crescent sign but with higher specificity, as shown in Table 7; US validity of bulged optic disc in the detection of raised ICP among 40 cases was as follows: sensitivity 41.6%, specificity 100%, and accuracy 47.5%.

Among 36 patients who were confirmed to have raised ICP, 22 of them had ICP measurement >300 mmHg; those patients demonstrate crescent sign in US examination as shown in Table 8.

DISCUSSION

ICP monitoring techniques are numerous, however, before selecting the best to use, especially in a critical situation, several issues need to be taken in consideration; the accuracy of measurements, the charge of the device, the possible problems, and mechanical difficulties associated with each individual technique as well.^[10]

Table 5: Validity of nerve sheath diameter in detection of raised elevated intracranial pressure of both the right and left eyes

ONSD	LP		Total
	Raised	Normal	
Right × LP crosstabulation			
RT eye			
Dilated	33	1	34
Not dilated	3	3	6
Total	36	4	40
Left × LP crosstabulation			
LT eye			
Dilated	33	1	34
Not dilated	3	3	6
Total	36	4	40

ONSD: Nerve sheath diameter, LP: Lumbar puncture, RT: Right, LT: Left

Table 6: Validity of crescent sign in detection of raised intracranial pressure

Variables	Crescent sign versus LP crosstabulation		Total
	Raised	Normal	
Crescent sign versus LP crosstabulation			
LP			
Crescent sign			
Present	22	0	22
Percentage within LP	61.1	0.0	55.0
Absent	14	4	18
Percentage within LP	38.8	100.0	45.0
Total (%)	36	4	40
Percentage within LP	100.0	100.0	100.0

LP: Lumbar puncture

Table 7: Validity of bulging papillae in detection of intracranial pressure

Variables	Bulging papilla versus LP crosstabulation		Total
	Raised	Normal	
Bulging papilla versus LP crosstabulation			
LP			
Bulging papilla			
Bulged	15	0	15
Percentage within LP	41.6	0.0	37.5
Flat	21	4	25
Percentage within LP	58.3	100.0	62.5
Total (%)	36	4	40
Percentage within LP	100.0	100.0	100.0

LP: Lumbar puncture

Optical coherence tomography is one of the proved methods to diagnose mild papilledema and differentiating it from pseudopapilledema or a normal optic disc,^[11] this was done by assessing the retinal fibers' thickness, when its normal, that indicates the pseudopapilledema, and if its thickened,

Table 8: Percentage of patients with positive crescent sign among patients have cerebrospinal fluid pressure >300

LP (range)	n (%)	Positive crescent sign	Negative crescent sign
160-≤300	14 (38.8)	0.0	14
>300	22 (61.1)	22	0.0
Total (%)	36 (100)	22 (61.1)	14 (38.8)

LP: Lumbar puncture

then papilledema is the diagnosis, in our center and in Iraq, in general, it is still under development and does not fully enter the practical use up till the time of our study.^[12]

In the current study, we aimed to find the correlation between ONSD and the raised ICP, we also attempted to evaluate the accuracy of transorbital US in detecting raised ICP by measuring ONSD in a group of Iraqi patients who were examined by neurologists and were suspected to have raised ICP.

Many authors define the cutoff value of the normal ONSD as (5 mm) which supports our cutoff point gained from the control group to compare it with the corresponding values of the patients.^[9,13] The current study found a highly significant statistical correlation between ONSD with direct measurement of ICP ($R = 0.933$ and $P < 0.001$), this result goes with the latest studies done in Rome, Italy, that was performed in 2017 by Toscano *et al.* whose found a strong correlation between ONSD and ICP ($R = 0.895$ and $P < 0.001$).^[14]

Another study conducted by Kimberly *et al.* in Boston in 2007, also depicted a significant correlation of ONSD with raised ICP ($R > 0.59$ and $P < 0.0005$)^[15] other study in France at 2008 by Geeraerts *et al.* found a strong correlation between ONSD and ICP (78 simultaneous measurements, $R = 0.71$ and $P < 0.0001$), and changes in ICP were strongly correlated with changes in ONSD (39 measurements, $R = 0.73$ and $P < 0.0001$).^[16]

In our study, the mean ONSD of the patients is 5.6558 ± 0.18771 SD, we set the cutoff value at 5 mm gained from the control group to evaluate sensitivity, specificity, and accuracy of transorbital US regarding the measurement of ONSD in both eyes for the detection of raised ICP, we found the sensitivity (91.6%), the specificity (75.0%), and the accuracy (90.0%). Our results are relatively in concordance with a study performed in Michigan in 2011 by Rajajee *et al.*, who demonstrate that the optimal cutoff value for detecting ICP > 20 mmHg is 4.8 mm for both eyes with (96%) sensitivity and (94%) specificity.^[17]

Old study in the USA carried out in 2007 by Tayal *et al.* evaluated 59 patients at the emergency department with suspected increased ICP and reported ONSD to have a sensitivity of 100% and specificity of 63%,^[18] whereas another study in the UK by Major *et al.* which showed that the optimal ONSD cutoff value for increased ICP is 5 mm with (86%)

sensitivity and (100%) specificity,^[19] accordingly, there is an obvious agreement of the previously mentioned results with our sensitivity, but, with lesser difference in the specificity, and this will bring to light that the US is a highly sensitive and accurate method for the detection of raised ICP but with moderate specificity.

These different reports could tell “as a matter of fact” that each research has different population with different epidemiologic features and also different number of participants; furthermore, choosing lower measures for ONSD cutoff value of optic nerve US can affect the statistical values in this regard.

A number of rare causes can result in dilatation of the optic nerve sheath, and by that lead to false-positive findings, these include optic neuritis, optic nerve infiltration, optic nerve trauma, and an anterior orbital or cavernous sinus masses,^[18] other causes of swollen optic disc by could be noticed by ophthalmoscope including pseudopapilledema, anterior optic neuropathy, and accelerated hypertension.^[5]

In our study, there was one patient considered to be a “false-positive” result because the US demonstrated bilateral dilatation of ONSD (right – 5.5 mm, left – 5.1 mm) but with normal ICP (14 mmHg) with the absence of crescent sign and flat optic disc, thereafter, the patient was diagnosed with viral meningitis.

Three other patients were considered “true-negative” results because US examination demonstrated a normal ONSD (<5 mm) with normal ICP in spite of swollen optic disc by ophthalmoscope, in which the US demonstrated optic disc drusen in two patients, and the third patient was a pregnant woman and the diagnosis is still unknown.

In this study, it was also approved, that crescent sign and optic disc bulging, for which the US is highly specific (100%), in the detection of intracranial hypertension but with a moderate sensitivity of (61.1%) for a crescent sign and (41.6%) for the bulged optic disc.

We noticed that all the patients with a positive crescent sign were having elevated ICP measuring (≥ 300 mmHg). In a recent study in India which was carried out by Bhosale *et al.* in 2017,^[20] and in another one in 2011 by Neudorfer *et al.*,^[21] it was found that the sensitivity was higher, (92%) and (90%), respectively, but they did not count the specificity because all the patients in their studies were proved to have raised ICP.

Optic disc bulging is another ultrasonographic finding that was thoroughly examined in our study with (41.6%) sensitivity and very high specificity of about (100%) and the accuracy was (47.5%). A study was carried in California during 2013 demonstrated (73%) sensitivity and (100%) specificity of the bulged optic disc in the detection of raised ICP.^[22] Those results agree with the results of the current study, but with higher values, this may be due to the greater sample size and because of the use of higher resolution machines. The presence of these

signs, as well as the dilated ONSD, gives a precise diagnosis of elevated ICP and a clear impression about the severity of the intracranial hypertension.

CONCLUSION

Transorbital ultrasonography is very accurate, available, noninvasive, safe, and easily performed procedure for the detection of raised ICP, and it also may be helpful for monitoring neurologically critical, sedated and/or mechanically ventilated patients, and others who are complaining of head trauma, especially those admitted to the emergency departments and intensive care units that develop signs of cerebral deterioration. Although this technique will not replace invasive ICP monitoring methods, it might be helpful and complimentary in choosing patients who may need furthermore invasive examination steps.

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Conflicts of interest

There are no conflicts of interest.

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