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Research article

Investigating the relationship between ultrasound measured optic nerve sheath diameter and preeclampsia

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Abstract: *Background:* Increased intracranial pressure (ICP) is one of the main consequences of preeclampsia, which could be manifested by a change in the optic nerve sheath diameter as a radiologic and clinical sign. However, the effect of preeclampsia on the ultrasound measured optic nerve sheath diameter (ONSD) and its possible applications are rarely investigated. The aim of this study was to determine the relationship between ultrasound measured optic nerve sheath diameter and the risk of preeclampsia. *Methods:* This case-control study was performed on 38 pregnant women with normal blood pressure and 38 pregnant women with preeclampsia in Alzahra hospital in Rasht during 2018. A checklist was used to record demographic and clinical data. Measurements were made using a high resolution transducer, by placing the focal point and a cursor line at 3 mm behind the globe, perpendicular to the optic nerve axis (measuring the mean of two eyes). Data were analyzed by SPSS software version 21. *Results:* The mean age of patients with preeclampsia and normal pregnant women were 31.42 ± 6.2 years and 29.76 ± 3.46 years, respectively. Differences in gravidity ($P = 0.854$) and the history of hypertension ($P = 0.946$) in both groups were not statistically significant ($P < 0.05$). The mean optic nerve sheath diameter in women with preeclampsia was significantly higher than pregnant women with normal blood pressure ($P = 0.001$). The area under the ROC curve for the ONSD was 0.82 and the cut-off point for this index was calculated as 4.55 mm, which at this point, sensitivity and specificity were 78.9% and 73.7%, respectively. *Conclusion:* There was a relationship between the risk of preeclampsia and ONSD, in the way that the ONSD in preeclampsia patients was higher than that of normal subjects. However, the mean ONSD in two groups of mild and severe preeclampsia were not significantly different.

Keywords: preeclampsia; ultrasound; optics nerve sheath; pregnant women

1. Introduction

Preeclampsia is an exclusive complication of pregnancy that is defined as high blood pressure with proteinuria after 20 weeks of gestational age [1]. However, in the absence of proteinuria, preeclampsia is diagnosed as hypertension in association with thrombocytopenia, impaired liver function, renal insufficiency, pulmonary edema, or new-onset cerebral or visual disturbances [2]. It affects 5 to 10 percent of pregnant women and accounts for about 12 percent of maternal mortality [3]. In fact, preeclampsia is the third most common cause of maternal mortality worldwide [4]. Major complications that threaten a patient with preeclampsia includes severe hypertension and hypertension emergencies (Intracranial hemorrhage, hypertensive encephalopathy), acute renal failure, congestive heart failure, placental abruption, disseminated intravascular coagulation (DIC), increased intracranial pressure (ICP), retinal detachment and pulmonary edema [5,6]. Preeclampsia can also limit fetal growth and cause early delivery, and in some cases can leads to fetal death through increasing the incidence of placental complications [7].

Various studies conducted in Iran showed the preeclampsia prevalence of 1 to 8% [8]. Despite widespread research, the onset or exacerbation of preeclampsia due to pregnancy is unclear, and still there is no definite prevention for it, and its management is based on reducing risk factors, early onset screening and management of complications [9]. Several pathophysiologic procedures are involved in the development of preeclampsia, which ultimately lead to endothelial dysfunction, hypertension and proteinuria [10]. One of the accepted theories about preeclampsia is the reduction of trophoblastic invasion into spiral arteries of the placental bed, which is mediated by immunologic factors and leads to a reduction of blood flow in the placenta-embryonic axis [11]. In some studies obesity, employment of mother, having a sister with a history of preeclampsia, chronic hypertension, diabetes mellitus, urinary tract infection, seasons and blood type, low education of mother, and smoking have an effect on hypertension during pregnancy [12,13].

An increase in ICP is one of the consequences of preeclampsia [14]. Changes in the Optic Nerve Sheath Diameter (ONSD) is an important clinical and radiographic demonstration of increased ICP [15,16]. Many studies have reported a significant relationship between increase in ICP (independent of underlying cause) and an increase in the optic nerve sheath diameter. From a physiologic standpoint, it can be stated that the increase in ICP exerts a pressure on the sub-arachnoid space around the optic nerve and causes the nerve sheath to expand [17,18]. In studies conducted so far, the relationship between the high ICP in the other pathologies with the diameter of the optic nerve sheath in ultrasound has been proven [19]. Thus it is expected that a positive relationship between preeclampsia (as one of the causes of an increased ICP) and the optic nerve sheath diameter exists and if confirmed, a routine ultrasonography as a non-invasive method, can be used to investigate the early changes attributable to an increased intracranial pressure. The goal of early screening for preeclampsia is to identify high-risk pregnancies and start preventive treatments [18]. This method can also be considered as a potential tool for monitoring the effects of preeclampsia and anticipating potential risks and complications.

2. Methods

2.1. Studied population

This case-control study was conducted on pregnant women referred to the Department of Obstetrics and Gynecology at Al-Zahra Hospital in Rasht during 2018. In this study, sequential random sampling method was used. To determine the sample size, Cochran formula was used which according to the results of Ortega et al. [20] with 95% confidence interval and 90% test reliability, the sample size of 76 individuals (38 pregnant women with normal blood pressure and 38 pregnant women with preeclampsia) was calculated.

2.2. Ethical considerations

In order to fulfill ethical considerations, ultrasonography was limited to hospitalized patients who had another clinical indications for pregnancy ultrasound exam and informed consent was obtained from the patients. The purpose of the study was explained to the studied women and they were assured that the information in this study would be used anonymously. This research has been approved by the Ethic Committee of Guilan University of Medical Sciences (with registration code IR.GUMS.REC.1397.206).

2.3. Inclusion criteria

- ✓ Pregnant woman with normal blood pressure
- ✓ Pregnant woman with preeclampsia diagnosed by a doctor
- ✓ Patients willing to participate in the study

2.4. Exclusion criteria

- ✓ The history of optic neuritis
- ✓ Severe myopia
- ✓ History of ocular surgeries
- ✓ Presence of ocular ulcers
- ✓ Any clinical or morphological conditions that prevent the ultrasound examination of the orbital area

2.5. Data gathering tool

The instruments used in this study were ultrasound device and a checklist to record patients' medical history. Information such as age, Gravidity, Gestational age by weeks, history of preeclampsia in previous pregnancies and history of chronic hypertension were used for suitable matching.

Standard diagnostic criteria for preeclampsia was used; According to American College of Obstetricians and Gynecologists definition, mild preeclampsia is defined as systolic blood pressure ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg after 20 weeks of pregnancy, and ≥ 300 mg or ≥ 1+ proteinuria in the 24-hour urine protein test. Severe preeclampsia was defined as diastolic blood

pressure ≥ 110 mmHg or ≥ 2+ proteinuria, or existing of symptoms like headache, oliguria, increased serum creatinine, thrombocytopenia, increased liver enzymes and pulmonary edema [21].

Patients with preeclampsia who did not have the above symptoms were categorized into mild preeclampsia. Pregnant women with normal blood pressure (below 140/90 mmHg) with none of the criteria for preeclampsia were considered as pregnant women with normal blood pressure.

In the third trimester hospitalized patients (for any reason) with a clinical indication for ultrasound exams (Including pregnancy surveillance, evaluation of fetal weight, biophysical profile…) an additional transorbital ultrasound was performed by an experienced radiologist which was unaware of patient's group. A GE Voluson E6 device with 11L-D Broad-spectrum linear transducer was used for measurements. Using small parts preset, a focal point and a cursor line placed at 3mm behind the globe and perpendicular to the optic nerve axis, the mean measurement of two eyes was documented. The duration of this sonography was 10 to 15 minutes (Figure 1).

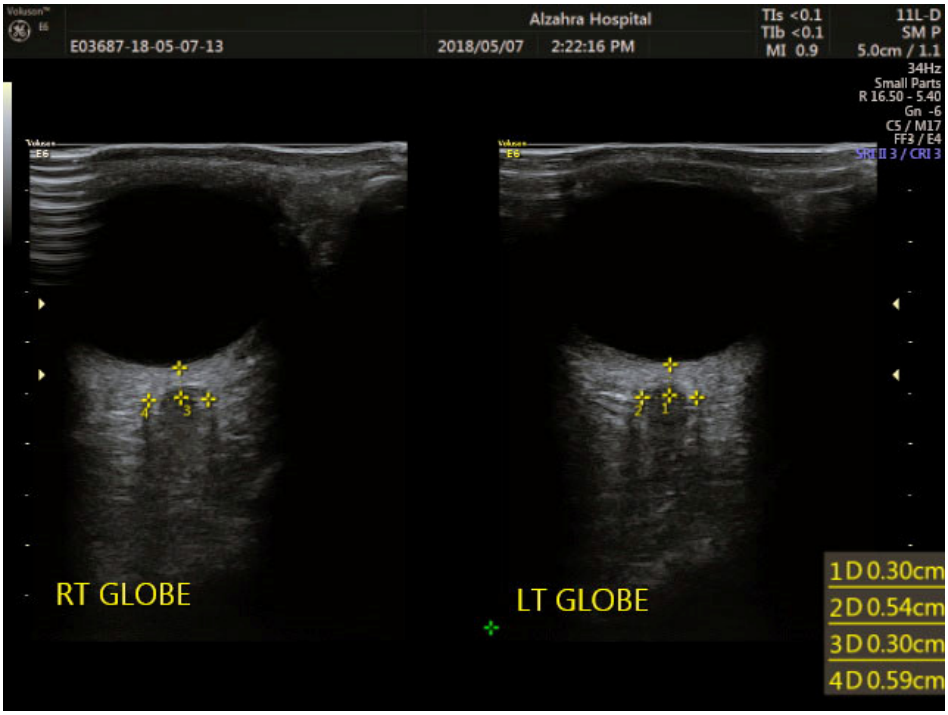

Figure 1. Measurement of diameter of the optic nerve sheath using transorbital ultrasound.

2.6. Statistical analysis

After collecting, the data were entered into SPSS version 21 software. The qualitative variables were characterized by frequency, and quantitative variables were characterized by mean, standard deviation, maximum, minimum and median. Mann-Whitney U test was used to compare the continuous data between groups. Chi-Square test was also used. ROC analysis was used to determine the appropriate cut-off point. The significance level of the tests was considered as $P < 0.05$.

3. Results

One of the limitations of the current research was the unwillingness of some patients to participate in the study, which in most cases after sufficient explanation and proper answers to their questions, cooperation was sought. The demographic data of women showed that the mean age of pregnant women with preeclampsia was 31.42 ± 6.02 years, and in pregnant women with normal blood pressure was 29.76 ± 3.46 years. In terms of gestational age, patients were in the range of 28–39 weeks. The prevalence of positive history of preeclampsia in pregnant women with current preeclampsia and women with normal blood pressure were 21.05% and 7.89%, respectively.

Chi-square test showed that there was no significant difference in the gravidities (P = 0.375) and the history of hypertension between two groups (P = 0.779). Independent t-test showed that there was no significant difference between the mean age and gestational age in pregnant women with preeclampsia and pregnant women with normal blood pressure (P > 0.05). Statistical tests showed that the ONSD was significantly higher in women with preeclampsia compared with women with normal blood pressure (P < 0.001) (Table 1). However, the ONSD in severe and mild preeclampsia patients were not significantly different (P = 0.727) (Table 2).

Table 1. Relationship between preeclampsia and the studied variables.

Variables	Group	Mean ± SD	P-Value
Age (years)	Preeclampsia	31.42 ± 6.02	0.146
	Normal	29.76 ± 3.46	
Gestational age (weeks)	Preeclampsia	34.08 ± 2.03	0.307
	Normal	33.50 ± 2.81	
ONSD (millimeters)	Preeclampsia	5.37 ± 0.96	0.001
	Normal	4.26 ± 0.55	

Table 2. Comparison of ONSD in mild and severe preeclampsia.

Variable	Group	Mean (millimeters)	Standard deviation	T	P-value
Preeclampsia	Mild	5.33	0.89	−0.366	0.727
	Severe	5.55	1.36		

The results obtained from the ROC curve analysis showed that the best cut-off point for the ONSD was 4.55 mm for diagnosing the risk of preeclampsia, with sensitivity and specificity of 78.9% and 73.7%, respectively. Also, the area under the curve (AUC) was 0.82 (Figure 2).

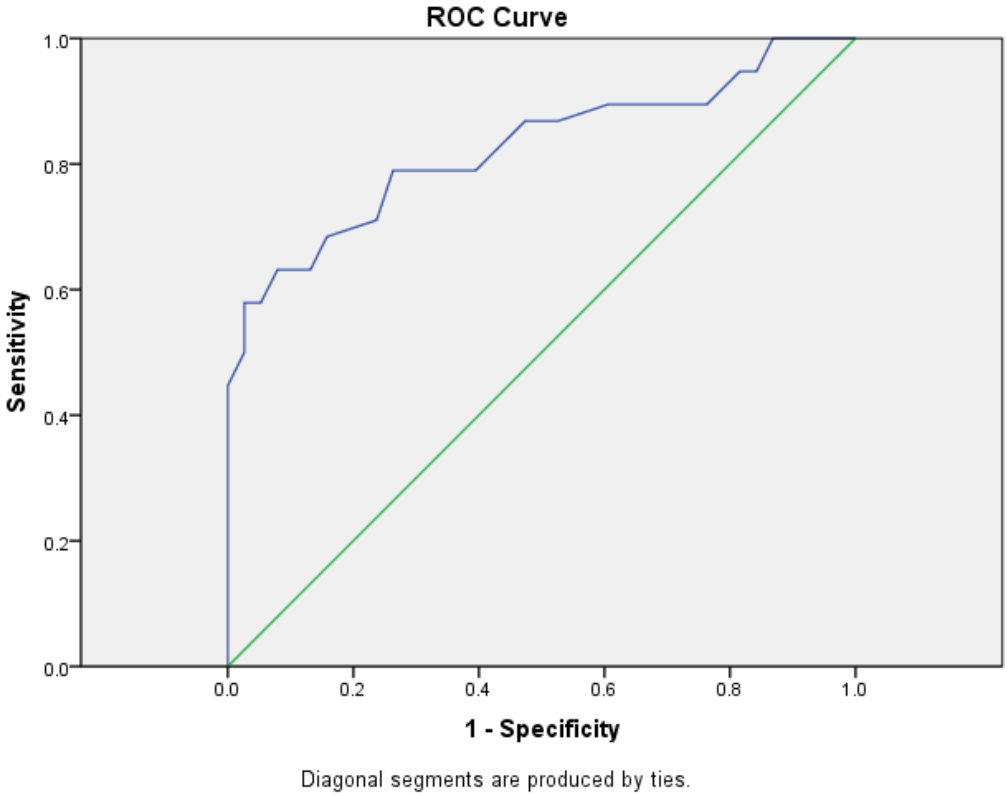

Figure 2. ROC Curve to determine the suitable cut-off point of the ONSD for preeclampsia.

The results of linear regression model showed that none of the possible intervening variables had a significant correlation with the ONSD (Table 3).

Table 3. Relationship between the ONSD and age, gestational age, gravidity, history of preeclampsia and history of hypertension using linear regression model.

Variables	Standardized Coefficients Beta	t	P-Value
Age	0.245	1.983	0.051
Gestational age	−0.068	−0.583	0.562
Gravidity	−0.025	−0.185	0.854
History of preeclampsia	0.006	0.045	0.964
History of hypertension	−0.037	−0.299	0.766

4. Discussion

In the present study, there was no significant difference between age and gestational age in two groups of pregnant women with preeclampsia and normal blood pressure pregnant women, which was consistent with the study by Davaryari et al. [22] and Dargahi et al. [23]. However, there are contradictory results in this regard, such as the study by Samierad et al. [24] which age had a significant difference between two groups of patient and control women. Also, in the present study, the results showed that the gravidity and the history of hypertension in the two groups of pregnant women with preeclampsia and pregnant women with normal pressure had no significant differences, which was consistent with the study by Nikpour et al. [25]. Even though, this finding is not consistent with Tessema et al. [26]. It seems that this differences can be attributed to the different categorization of patients, sample size and the sampling method in current study which was conducted only on hospitalized patients and did not include patients who were not hospitalized during pregnancy.

In agreement with other recent studies, the mean ONSD in two groups of women with preeclampsia and women with normal blood pressure were significantly different. The mean diameter of the optic nerve sheath in the normal blood pressure group, mild preeclampsia and severe preeclampsia were 4.26 ± 0.55, 5.33 ± 0.89 and 5.55 ± 1.39 millimeters respectively, which was similar to the results of Singh et al. (4.7, 5.6 and 5.8 millimeters, respectively) [27].

However, in the present study, the results showed that the difference between the mean ONSD was not significant in two groups of mild and severe preeclampsia. This might be due to the low number of patients with severe preeclampsia in this study (7 patients), nonlinear changes in optic nerve sheath diameters in ICP elevation, as well as the lack of more severe intracranial changes in some patients with severe preeclampsia (only one patient with severe preeclampsia had neurological symptoms).

In this study, the ROC curve analysis showed that the best cut-off point of ONSD for diagnosing existing preeclampsia was 4.55 mm, with the sensitivity, specificity, and area under the curves of 78.9%, 73.7% and 0.82, respectively. There is no agreement on the cut-off point for numerical optic nerve sheath diameter, and it seems that various factors such as the underlying cause of ICP elevation, the duration of this phenomenon, and individual characteristics are involved. In the study by Goeres et al. [28], the mean diameter of the optic nerve sheath in non-pregnant healthy women was 3.60mm (95% CI: 2.83–4.11), which is close to that of the non-pregnant women in the study by Ortega et al. [20].

In some pioneer studies, diameter above 5.8 mm was considered equivalent to ICP above 20mmHg. In our study, 13 patients with preeclampsia (34.2%) had diameter equal to or greater than 5.8mm. In the control group, diameters of all patients were below this value. Similarly, in the study by Brzan Simenc et al. which was conducted on patients with severe preeclampsia, none of the patients in the control group had diameter more than 5.8mm, while in 43% of patients with severe preeclampsia, the diameter of the optic nerve sheath was measured above this level [29].

5. Conclusion

The results of this study shows that there is a relationship between preeclampsia and ONSD, in a way that the ONSD in preeclampsia patients is higher than that of normal subjects. However, the ONSD in two groups of mild and severe preeclampsia were not significantly different. Researchers of this study believe that considering the confirmation of this finding in ours and other recent studies, additional and comprehensive prospective studies should be conducted, with focus on the usefulness

of transorbital ultrasound as an accessible and noninvasive tool for monitoring of preeclampsia (specially response to treatment) and the prediction of complications (occurrence of eclampsia, preterm delivery, pregnancy bleedings, etc.).

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Conflict of interest

There is no conflict of interest.

References

1. Duhig K, Vandermolen B, Shennan A (2018) Recent advances in the diagnosis and management of pre-eclampsia. *F1000Res* 7: 242.
2. ACOG (2013) Hypertension in pregnancy. Report of the American college of obstetricians and gynecologists' task force on hypertension in pregnancy. *Obstet Gynecol* 122: 1122–1131.
3. Fayyaz S, Agrawal N, Yadav P, et al. (2018) Can high first trimester NLR and PLR is early predictor for preeclampsia ?: An experience of single tertiary care center. *Arch Reprod Med Sex Health* 1: 3–7.
4. Peres GM, Mariana M, Cairrão E (2018) Pre-Eclampsia and eclampsia: An update on the pharmacological treatment applied in Portugal. *J Cardiovasc Dev Dis* 5: pii: E3.
5. Bokslag A, van Weissenbruch M, Mol BW, et al. (2016) Preeclampsia; short and long-term consequences for mother and neonate. *Early Hum Dev* 102: 47–50.
6. Ghulmiyyah L, Sibai B (2012) Maternal mortality from preeclampsia/eclampsia. *Semin Perinatol* 36: 56–59.
7. Grotegut CA (2016) Prevention of preeclampsia. *J Clin Invest* 126: 4396–4398.
8. Safari M, Yazdanpanah B (2003) Preeclampsia and maternal and fetal side effects prevalence in women visiting maternity of Yasuj Imam sajjad hospital. *J Shahrekord Univ Med Sci* 5: 47–53.
9. Anderson UD, Gram M, Åkerström B, et al. (2015) First trimester prediction of preeclampsia. *Curr Hypertens Rep* 17: 1–8.
10. Jadli A, Sharma N, Damania K, et al. (2015) Promising prognostic markers of preeclampsia: New avenues in waiting. *Thromb Res* 136: 189–195.
11. Brunelli VB, Prefumo F (2015) Quality of first trimester risk prediction models for pre-eclampsia: A systematic review. *BJOG* 122: 904–914.
12. Vahidroodsari F, Ayati S, Ebrahimimonfared M (2009) Before pregnancy BMI effect on incident of pregnancy blood pressure and preeclampsia. *J Babol Med Sc Univ* 11: 49–53.

13. Nasiriamiri F, Aghajanidelavar M, Mohammadpourtahmtan RA (2009) Survey on mean arterial pressure diagnostic value in second three month pregnancy in preeclampsia prediction. *J Mazandaran Univ Med Sci* 45: 67–73.
14. Ferro F, Rocha E, Nobrega L, et al. (2016) Transorbital ultrasonographic measurement of the optic nerve sheath diameter in preeclampsia [24J]. *Obst Gyn* 127: 87.
15. Dehnadi Moghadam A, Alizadeh A, Yousefzadeh Chabok SH, et al. (2015) Evaluation of correlation between optic nerve sheath diameter and intracranial pressure in patients with head trauma. *J Guilan Univ Med Sci* 23: 44–49.
16. Sekhon MS, Griesdale DE, Robba C, et al. (2014) Optic nerve sheath diameter on computed tomography is correlated with simultaneously measured intracranial pressure in patients with severe traumatic brain injury. *Intensive Care Med* 40: 1267–1274.
17. Whiteley JR, Taylor J, Henry M, et al. (2015) Detection of elevated intracranial pressure in robot-assisted laparoscopic radical prostatectomy using ultrasonography of optic nerve sheath diameter. *J Neurosurg Anesthesiol* 27: 155–159.
18. Dip F, Nguyen D, Sasson M, et al. (2016) The relationship between intracranial pressure and obesity: An ultrasonographic evaluation of the optic nerve. *Surg Endosc* 30: 2321–2325.
19. Gagnon A, Wilson RD (2008) Obstetrical complications associated with abnormal maternal serum markers analytes. *J Obstet Gynaecol Can* 30: 918–932.
20. Ortega J, Urias E, Arteaga C (2015) Comparative study measuring optic nerve sheath diameter by transorbital ultrasound in healthy women, pregnant women and pregnant with preeclampsia/eclampsia. *Intensive Care Med Exp* 3: A992.
21. Cuningham FG, Gant NF, Leveno KJ, et al. (2001) Williams obstetrics. 21st ed. New York: Mc Graw-Hill, 568–569.
22. Davaryari N, Razavi Panah R, Homayoon Mehr S, et al. (2011) A comparison of serum level of selenium in women with preeclampsia and normal pregnant women. *Med J Mashhad Univ Med Sci* 54: 80–85.
23. Dargahi R, Shahbazzadegan S, Naghizadeh-Baghi A, et al. (2018) Expression levels of Drosha and Dicer enzymes and DGCR8 protein in pre-eclamptic patients. *Iran J Obstet Gynecol Infertility* 20: 40–49.
24. Samiee Rad F, Jahani Hashemi H, Sofiabadi M, et al. (2017) Evaluation of severity of preeclampsia with mother's serum high sensitive C-reactive protein (Hs-CRP). *SSU_J* 25: 556–563.
25. Nikpour S, Atarodi Kashani Z, Mokhtarshahi S, et al. (2007) Study of the correlation of the consumption of Vitamin C-Rich foods with preeclampsia and eclampsia in women referred to Shahid Akbar Abadi Hospital in Tehran, 2004. *Razi J Med Sci* 14: 179–192.
26. Tessema GA, Tekeste A, Ayele TA (2015) Preeclampsia and associated factors among pregnant women attending antenatal care in Dessie referral hospital, Northeast Ethiopia: A hospital-based study. *BMC Pregnancy Childbirth* 15: 73.
27. Singh SK, Bhatia K (2018) Ultrasonographic optic nerve sheath diameter as a surrogate measure of raised intracranial pressure in severe pregnancy-induced hypertension patients. *Anesth Essays Res* 12: 42–46.

28. Goeres P, Zeiler FA, Unger B, et al. (2016) Ultrasound assessment of optic nerve sheath diameter in healthy volunteers. *J Crit Care* 31: 168–71.
29. Brzan Simenc G, Ambrozic J, Prokselj K, et al. (2018) Ocular ultrasonography for diagnosing increased intracranial pressure in patients with severe preeclampsia. *Int J Obstet Anesth* 36: 49–55.

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