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Ultrasonography For Fluid Assessment in Parturients with Preeclampsia Undergoing Elective Cesarean Section Under Spinal Anesthesia

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ABSTRACT

Background: Preeclampsia is a syndrome characterized by hypertension and organ system involvement. Fluid assessment is essential to avoid complications. Point of care ultrasonography (POCUS) is noninvasive tool used in assessment of parturients with preeclampsia. **Objective:** This study evaluated perioperative ultrasonography for assessment of lung congestion, optic nerve sheath diameter (ONSD), and IVC diameters in parturients with preeclampsia. We hypothesized a difference in pulmonary congestion over time during cesarean delivery.

Patients and methods: This was a prospective observational study of one hundred ASA II-III parturients with preeclampsia, singleton pregnancy undergoing elective cesarean delivery under spinal anesthesia. Lung ultrasonography, IVC diameters and ONSD ultrasound performed at baseline, at 1 h and 2 h after spinal anesthesia, Lung ultrasound for quantification of the Echo Comet Score (ECS). The maximum and minimum IVC diameters assessed using the subcostal long-axis view. ONSD measured 3 mm behind the globe.

Results: No significant difference in the ECS and ONSD at 1 hour and 2 hours compared with baseline (P=0.46), (P=0.16) respectively. The maximum and minimum IVC diameters were larger at 1 h and 2 h compared with baseline (P<0.0001).There was a positive correlation between the ECS and ONSD at 2 h. (r^2 = 0.689, P<0.001).

Conclusion: No significant difference in the ECS and ONSD at 1 hour and 2 hours after spinal anesthesia compared with baseline. Non-invasive POCUS used for fluid assessment in parturients with preeclampsia.

Keywords: Preeclampsia, Lung ultrasonography, Inferior vena cava diameters, Optic nerve sheath diameter.

INTRODUCTION

Preeclampsia is a multifocal syndrome characterized by hypertension and organ system involvement. It is associated with serious complications such as hemorrhage pulmonary edema, cerebrovascular accidents and coagulopathy. The risk for these complications is 10 to 30 folds higher among parturients with severe preeclampsia [(1)].

Judicious fluid resuscitation is essential in women with preeclampsia management. Hypovolemia exacerbates acute kidney injury, and volume overload results in pulmonary edema [(2)]. Therefore, using noninvasive monitoring for hemodynamic is associated with decreased morbidity and mortality [(3)].

Point-of-care ultrasonography (POCUS) is a highly sensitive method for detecting pulmonary edema, which can occur even in the absence of cardiomyopathy or heart failure, especially when a large amount of fluid has been given. Lung ultrasonography can be used to detect pulmonary congestion in women with preeclampsia before they become critically ill [(4)].

The inferior vena cava (IVC) is a highly compliant vessel that changes its diameter in response to variations in blood volume and central venous pressure. Using ultrasound to measure IVC diameters and the collapsibility index (CI) to determine volume status in many settings such as trauma, intensive care, and dialysis units has been examined. The IVC-CI can be used to measure volume status in both healthy and high-risk parturients, such as those with preeclampsia [(5)].

Cerebral edema is predominantly vasogenic and may be related to failure of cerebral autoregulation, blood brain barrier (BBB) disruption, and endothelial cell dysfunction [(6,7)]. Ultrasonographic measurements of the optic nerve sheath diameter (ONSD) correlates with signs of raised intracranial pressure (ICP). A dural sheath and a subarachnoid area containing cerebrospinal fluid surround the optic nerve (CSF). In the case of increased pressure in the cerebrospinal fluid, the optic nerve becomes distensible three millimeters behind the globe, within its fatty environment [(8)].

This study evaluated the use of perioperative ultrasonography for assessment of lung congestion, ONSD, and IVC diameters in parturients with preeclampsia undergoing cesarean delivery under spinal anesthesia. We hypothesized that there would be a difference in pulmonary congestion over time during cesarean delivery.

PATIENTS AND METHODS

This was a prospective observational study of 100 ASA II-III parturients with preeclampsia, singleton pregnancy undergoing elective cesarean delivery under spinal anesthesia. The study was done at Mansoura University Hospitals' Obstetric Department from June 2020 to December 2021.

Patients:

Inclusion criteria were American Society of Anesthesiologists physical status II-III parturients, singleton pregnancy, under spinal anesthesia elective cesarean delivery, parturients with preeclampsia without severe features defined per the American College of Obstetricians and Gynecologists (ACOG) guidelines as: blood pressure ≥140/90 mmHg after 20 weeks of gestation and proteinuria ≥300 mg/24h urinary

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protein or ≥1+ dipstick in urine [9]. Parturients with severe preeclampsia defined per ACOG guidelines by one or more of the following: systolic arterial pressure ≥160 mmHg and/or diastolic arterial pressure ≥110 mmHg while the patient is on bed rest, on more than one occasion at least 4 h apart unless before this time antihypertensive therapy had been initiated, elevated liver enzymes, severe persistent right upper quadrant or epigastric pain, new-onset cerebral and visual disturbances [9].

Exclusion criteria include age <19 or >40 years, gestational age <32 weeks, body mass index (BMI) ≥40 kg/m^2, women presenting in labor, significant cardiovascular disease, cerebrovascular disease, diabetes mellitus, or renal disease, other obstetrical or uteroplacental pathologies, abruptio placentae, known fetal abnormalities, acute lung pathology prior to enrollment, contraindications to spinal anesthesia, platelet count <100,000 /mm^3, serum creatinine level >1.1 mg/dL, previous thoracic surgery, ocular surgery or trauma, or glaucoma and evident pulmonary edema.

Sample size calculation:

We conducted a pilot study before beginning the research on 10 women with preeclampsia and measured the baseline ECS. The mean (SD) was 12 (10) B-lines. Assuming α=0.05 and β=0.2 (power=80%), using paired *t* test, A total number of 90 women were required to identify a difference of 3 B-lines between baseline and at 2 hours after spinal anesthesia. This difference was considered the minimal clinically important difference. One hundred subjects were enrolled in the study to compensate for drop outs.

Preoperative Management:

All subjects were assessed preoperatively in the pre-anesthesia room by medical history, clinical examination, chest and cardiac examination. Preoperative routine laboratory investigations were evaluated including full blood count, serum creatinine level, serum albumin level, liver function tests, and INR.

The study subjects fasted 8 h for solid food and were allowed to drink clear fluids until 2 h before surgery. Baseline and all subsequent ultrasound scans were performed for all enrolled subjects, saved for offline analysis, and recorded by the principal investigator at the end of each case.

Intraoperative management:

The study subjects entered the operating room without receiving any premedication, and laid supine with slight left lateral table-tilt. Pulse oximetry, noninvasive blood pressure (BP), and electrocardiography were used as standard monitors. The baseline systolic blood pressure, oxygen saturation, and heart rate were measured after adequate rest; the baseline records were the average of three measures done two minutes apart with a difference of not more than 10%.

All baseline ultrasound examinations were performed by the principal investigator with the study subjects lying supine with slight left lateral table-tilt and subsequent ultrasound examinations at 1 hour and 2 hours were performed with the study subjects lying supine. In a large forearm vein, an 18-gauge IV cannula was inserted. An anesthesiology resident not participating in our study used a 25-gauge spinal needle to provide spinal anesthesia at the L3-L4 or L4-L5 interspace while the patient was sitting; 12.5 mg of hyperbaric bupivacaine (2.5 mL 0.5%) and 15 μg of fentanyl were injected intrathecally. Urinary catheter was inserted for urine output monitoring.

After intrathecal injection, Ringer`s acetate 250 mL was administered over 5 minutes (using a pressurizer adjusted to 200 mm Hg), followed by 500 mL over 55 minutes, then 250 mL over 60 minutes (total 1000 mL Ringer's acetate over 2 hours). This is the fluid regimen routinely used in our institution for women with preeclampsia. No other fluids had been given to the patients till the end of the study period (2 hours after spinal anesthesia).

After achieving a T6 or greater upper sensory level, assessed with loss of cold sensation, surgery began. After 20 minutes, if the upper sensory level was below T6, the patient was regarded to have failed spinal anesthesia and was excluded from the study. The Pfannenstiel incision was used to perform a lower segment caesarean delivery.

Systolic blood pressure (BP), diastolic BP, heart rate, and SpO_2 were recorded every 1 minuntes before delivery and every 3 min after delivery till the end of surgery. Intravenous ephedrine 3, 5, and 10 mg boluses were given when the systolic BP decreased below 120, 110, and 90 mmHg, respectively. Bradycardia (heart rate less than 50 beats per minute) was treated with IV atropine 0.2 mg, which was repeated as needed.

The presence of nausea and/or vomiting (as stated by the patient) was noted; nausea or vomiting that occurred without hypotension or persisted after correction of hypotension was treated with IV metoclopramide 10 mg. Syntocinon 10 IU were introduced to the Ringer's acetate solution immediately after delivery. If SpO_2 decreased below 95%, patients received oxygen therapy by a simple O_2 mask.

The spinal-to-delivery time (time between intrathecal injection and umbilical cord clamping) and the time for spinal-to-skin closure (duration from intrathecal injection to skin closure) were recorded. At 1 minute and 5 minutes following delivery, the Apgar score of the newborn was recorded, obtained by a neonatologist not involved in the study. During intraoperative ultrasound examination, a sterile drape separated the investigator from the surgery field, and the ultrasonography probe was covered with a sterile cover [5].

Postoperative management:

After surgery, all patients were transferred to the post anesthesia care unit (PACU). Standard monitoring included heart rate, SpO_2, non-invasive BP. Urine output was recorded at 1 and 2 hours after spinal

anesthesia. IV Furosemide 10 mg was administered when total urine output after 2 hours of spinal anesthesia was <60 mL.

Measurements:

Lung Ultrasound (LUS) Examination:

Lung ultrasound was performed using 2-5 MHz transducer, curved array (SonoAce R3; Samsung Medison, Seoul, South Korea). The 28-rib interspaces technique was used to calculate the Echo Comet Score (ECS), which divides the chest wall into 12 areas on the left (from the second to the fourth intercostal space) and 16 areas on the right (from the second to the fifth intercostal space) in each hemithorax, divided by the parasternal, midclavicular, anterior, and mid axillary lines. Multiple B-lines or "comet tails" can indicate an increased amount of extravascular lung water (EVLW). B-lines are vertical hyperechoic reverberation artifacts that start from the pleural line and reach to the bottom of the screen without fading, and move synchronously with lung sliding. The ECS, which represents the amount of EVLW, is calculated by adding the overall number of B-lines observed on each of the 28 chest-wall locations and corresponding to the degree of pulmonary congestion. Scans were longitudinal with the probe orientation towards patient's head where the pleural line was seen between two ribs [(10)] **(Figure 1)**.

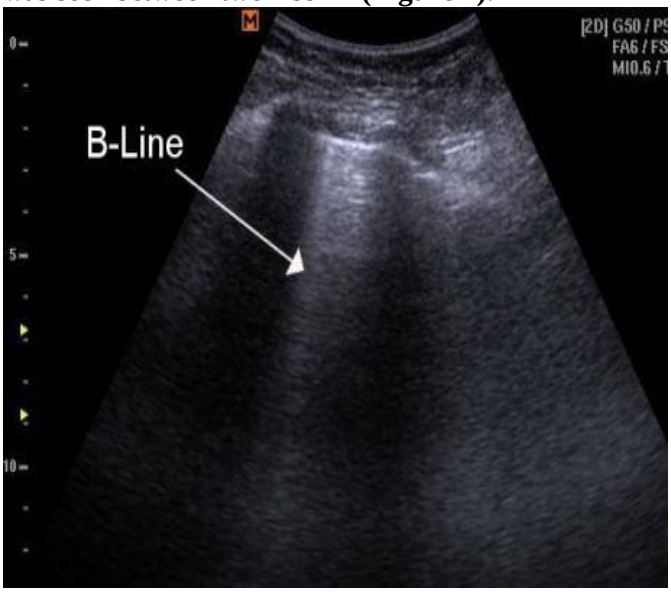

Figure (1): Lung Ultrasound showing B-line.

Each region was assessed using a two-dimensional view for the number of B-lines that was summed for analysis. The sum of B-lines found on each scanning site (from 0 to 10) provides an ECS score that is quantifiable from (0- 280), denoting the amount of extravascular lung water (from absent, ≤ 5, 6-15 mild, 16-30 moderate, >30 B-lines severe pulmonary congestion [(11)].

IVC diameters ultrasound examination:

The IVC was scanned using s2-4 MHz phased array transducer (ClearVue 350; Philips, Bothell, WA) that was implanted longitudinally in the subcostal region. During normal spontaneous breathing, the maximum and minimum IVC diameters were measured using the M-mode about 2 cm proximal (caudal) to the ostium of the right atrium and immediately proximal to the junction with the hepatic veins **(Figure 2)**.

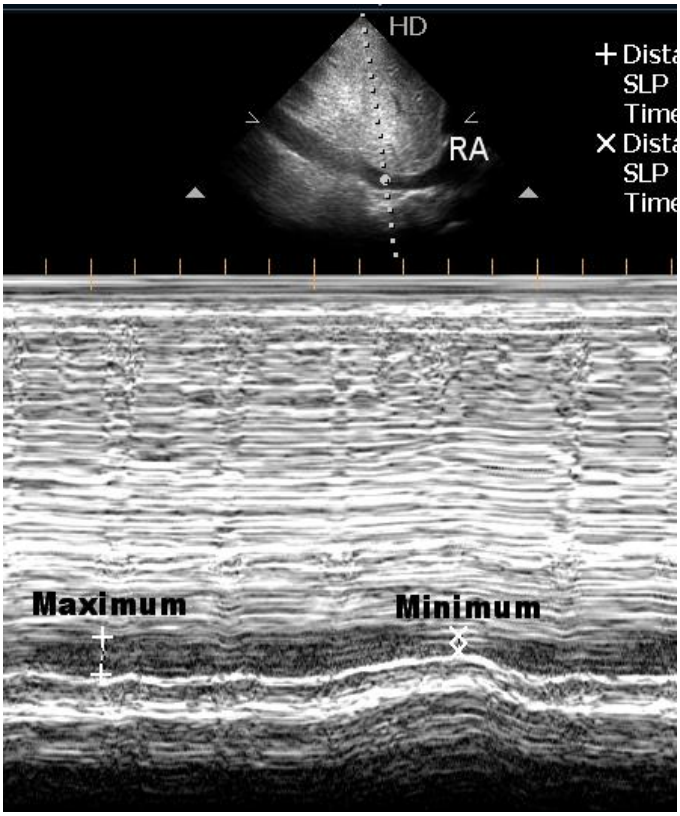

Figure (2): A 2-dimentional image showing subcostal inferior vena cava (IVC) in long axis view with the right atrium (RA) to the right of the screen.

The IVC collapsibility index (CI) was calculated by using the formula: IVC-CI = (maximum IVC diameter–minimum IVC diameter)/maximum IVC diameter, expressed as percentage. The patient was not included in our study if the IVC image quality was poor [(12)].

Optic nerve sheath diameter ultrasound examination:

Optic nerve sheath diameter measurement was conducted in two axes of transverse and oblique sagittal. Over the closed upper eyelid, a thick layer of gel was placed. The transducer used was a 12–4MHz linear array transducer (ClearVue 350; Philips, Bothell, WA, USA). To prevent excessive pressure on the eye, the hand holding the probe was put on the patient's forehead. Using two dimensional mode the position of the probe was adjusted to clearly display the entry of the optic nerve into the globe. With the use of a machine calliper, the depth of the optic nerve was located and marked at 3 mm behind the globe. The transverse diameter of the optic nerve sheath was measured at this moment. Scanning began in coronal section on the lateral side of the eye, then in the oblique sagittal plane, measuring OSND in both axes. The reported ONSD was the average of the four values obtained in the transverse and sagittal planes for both eyes for each patient [(13)] **(Figure 3).**

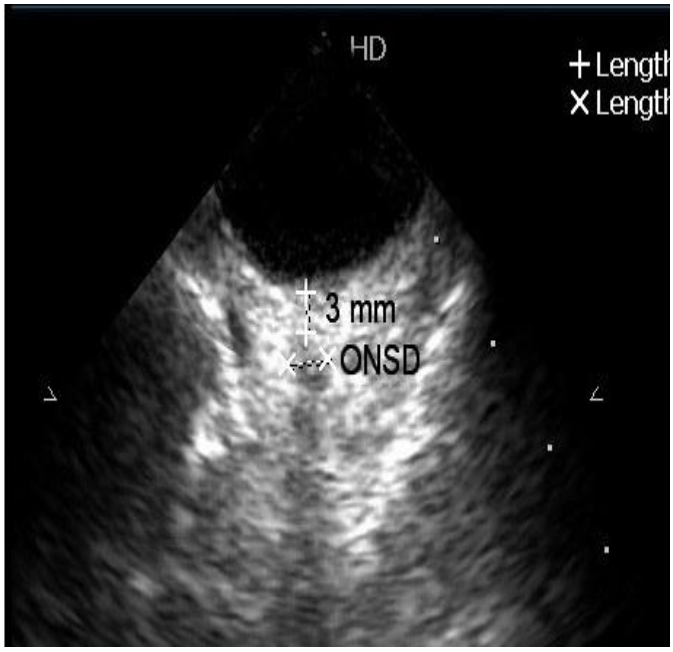

Figure (3): Ultrasonographic assessment of optic nerve sheath diameter (ONSD) 3 mm behind the ocular globe.

The study outcomes:

The primary outcome was difference in the (ECS) detected by lung ultrasound at baseline and at 2 hours after spinal anesthesia. The secondary outcomes were difference between the (ECS) at baseline and at 1 hour after spinal anesthesia, incidence of pulmonary congestion (ECS>5) at baseline, 1h, and 2 hours, difference between the maximum and minimum IVC diameters and the IVC-CI at baseline, 1 hour, and at 2 hours after spinal anesthesia, difference between ONSD at baseline, 1 hour, and 2 hours after spinal anesthesia and correlation between the (ECS) and ONSD at 2 hours after spinal anesthesia.

Ethical consent:

Written informed consent was obtained from all participating subjects. Adhered to the Declaration of Helsinki 2013 statement of ethical principles and is presented in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement. Before subject enrollment, the study protocol was approved by the institutional review board (Code number: MD. 19.10.235) and was registered at ClinicalTrials.gov (NCT04370847; date of registration: June 1, 2020).

Statistical analysis:

Data were analyzed using the R software, version 4.0.5 (R Core Team, 2021; R Foundation for Statistical Computing, Vienna, Austria). The histogram and the Shapiro- Wilk test were used to check for normality in continuous data. Continuous normally distributed data are presented as mean ± standard deviation. Continuous non-normally data distributed are presented as median (range). Categorical data are presented as number (percentage). The ECS was compared at the 3 time points using the Friedman test. The incidence of pulmonary congestion was compared at the 3 time points using the chi-square test. The IVC diameters, the IVC-CI, and the ONSD were compared at the 3 time points using the one-way repeated measures analysis of variance (ANOVA), and pairwise comparisons were done using the paired t tests with Bonferroni adjustment. The Spearman's rank-order correlation is used to determine the strength and direction of a linear relationship between two non-normally distributed continuous variables and / or ordinal variables. A subgroup analysis for the ECS, IVC diameters, and ONSD was done for women with mild and severe preeclampsia. The ECS data were compared using the Mann Whitney U test. The IVC diameters and the ONSD were compared using the Student *t* test. Bonferroni correction was used for multiple comparisons. An overall P value ≤ 0.05 was considered statistically significant.

RESULTS

One hundred twenty subjects were assessed for eligibility, 100 subjects were included and completed the study, and their data were analyzed.

The patient characteristics and baseline data are shown in Table (1). The mean (SD) age was 29.5 (6) years, the median (range) gestational age was 34 (32-39) weeks, and the median (range) BMI was 32.6 (23-39.7) kg/m^2. Thirty-three subjects (33%) were nulliparous. Eighty subjects (80%) had one or more of severe features of preeclampsia and 20 subjects (20%) had mild preeclampsia. The baseline median (range) systolic BP and diastolic BP were 150 (129-180) mmHg and 99.5 (70-116) mmHg, respectively. The baseline median (range) heart rate and SpO_2 were 95.5 (74-138) beat/min and 100 (97-100) %, respectively. The median (range) preoperative hemoglobin level, platelets, S. albumin, S. creatinine level and proteinuria were 10.7 (9-14) g/dl, 208,500 (100,000-490,000)/mm^3, 3 (2.2-4) g/dl, 0.8 (0.5-1) mg/dl and +1 (+1 to +4), respectively.

Table (1): Patient characteristics and baseline data.

Variable	Subjects (n = 100)
Patient Characteristics	
Age (years)	29.5 ± 6
Height (cm)	165 (150-175)
Weight (kg)	89 (56-108)
Body mass index (kg/m^2)	32.6 (23-39.7)
Gestational age (weeks)	34 (32-39)
Nulliparous	33 (33%)
Baseline Measurements	
Baseline systolic BP (mmHg)	150 (129-180)
Baseline diastolic BP (mmHg)	99.5 (70-116)
Baseline heart rate (beats/min)	95.5 (74-138)
Baseline SpO_2(%)	100 (97-100)
Baseline Laboratory Values	
Hemoglobin level (g/dL)	10.7 ± 2.21
Platelets (/ mm^3)	208,500 ± 47.21
S. Albumin (g/dL)	3 ± 0.01
S. Creatinine (mg/ dL)	0.8 ±0.1
Proteinuria ***Severity***[a]	+1 (+1 to +4)
Mild preeclampsia Severe preeclampsia	20 (20%) 80 (80%)

Data are mean ± SD, median (range), or number (%).
[a] Severe preeclampsia was diagnosed when systolic arterial pressure 160 mmHg and/or diastolic arterial pressure 110 mmHg on more than one occasion at least 4 hours apart when the patient is on bed rest, epigastric pain not responding to medicinal treatment, increased liver enzymes, low platelet count syndrome (HELLP), new onset cerebral and visual manifestation.

The intraoperative, postoperative, and neonatal data are shown in Table (2).

Table (2): Intraoperative, postoperative, and neonatal data.

Variable	Subjects (n = 100)
Intraoperative Data	
Upper sensory level[a]	T4 (T2-T6)
Spinal to delivery time (min)[b]	13 (9-20)
Spinal to skin closure time (min)[c]	51 (40-62)
Total ephedrine dose (mg)	10.5 ± 2.31
Hypotension[d]	84 (84%)
Severe hypotension[e]	8 (8%)
Bradycardia[f]	2 (2%)
Need of O_2[g]	14 (14%)
Nausea and/or vomiting	30 (30%)
Postoperative Data	
Urine output at 2 h (mL)	130 (26-350)
Need of diuretic[h]	27 (27%)
Neonatal Data	
Apgar score at 1 minute	8 (5-10)
Apgar score at 5 minutes	10 (7-10)

Data are median (range) or number (%).
[a] Assessed using loss of cold sensation at 20 minutes after spinal anesthesia.
[b]. Time between intrathecal injection and umbilical cord clamping.
[c] . Time from intrathecal injection till the completion of skin closure.
[d] Defined by decrease of systolic blood pressure <120 mmHg.
[e] Defined by decrease of systolic blood pressure <90 mmHg.
[f] Defined by heart rate <50 beats / min.
[g] application of O_2 mask if SpO_2 decreased <95%.
[h] IV Furosemide 10 mg administered when the total urine output at 2 h <60 mL.

The main outcomes of the study are shown in table (3).

There was no statistically significant difference in the ECS score at the 3 time points (p=0.46) (Figure 4). The median (range) ECS at baseline and at 2 h after spinal anesthesia was 9 (0-35) and 10 (0-35), respectively; median difference (95% CI) was -0.000001 (-1 to 0.00005); P=0.36. There was no statistically significant difference between the baseline ECS and the ECS at 1 hour (P=0.5). Moreover, there was no statistically significant difference between the ECS at 1 h and 2 h after spinal anesthesia (p =0.64).

Table (3): Outcome data of participated patients.

Variable	Baseline	At 1 hour	At 2 hours	*P* value
Echo Comet Score	9 (0-35)	9.5 (0-35)	10 (0-35)	0.46
Incidence of pulmonary congestion[a]	66 (66%)	68 (68%)	69 (69%)	0.9
IVC diameters				
IVC-max (cm)	1.14 ± 0.2	1.42 ± 0.24	1.36 ± 0.24	<0.0001[b]
IVC-min (cm)	0.64 ± 0.17	0.77 ± 0.19	0.74 ± 0.18	<0.0001[c]
IVC-CI (%)	43.6 ± 10.9	46 ± 10.4	45.4 ± 9.5	0.06
Optic nerve sheath diameter (mm)	5.12 ± 0.61	5.11 ± 0.61	5.11 ± 0.59	0.16

Data are median (range), number (%). or mean ± SD.
[a] Defined by Echo comet score >5.
[b] Significant difference using the repeated measures ANOVA. Pairwise comparisons at the 3 time points were done using the paired t tests with Bonferroni adjustment. Significant differences exist between the IVC-max at 1 h and at 2 h compared with the baseline IVC-max (P <0.0001). No significant difference exists between the IVC-max at 1 h compared with the IVC-max at 2 h (P = 0.23).
[c] Significant difference using the repeated measures ANOVA. Pairwise comparisons at the 3 time points were done using the paired t tests with Bonferroni adjustment. Significant differences exist between the IVC-min at 1 h compared with the baseline IVC-min (P <0.0001) and between the IVC-min at 2 h compared with the baseline IVC-min (P = 0.00016). No significant difference exists between the IVC-min at 1 h compared with the IVC-min at 2 h (P >0.99).

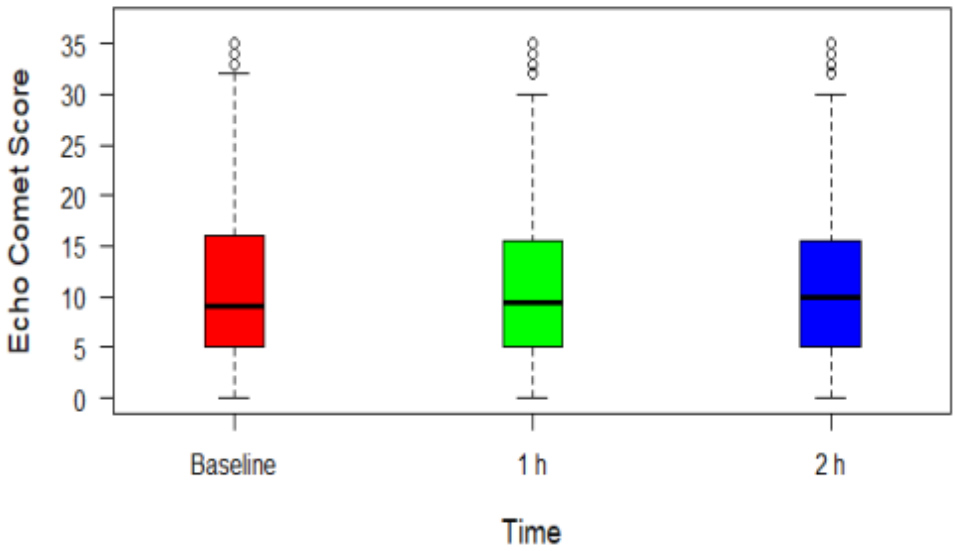

Figure (4): Box plots of the Echo comet score at baseline, 1 hour, and 2 hours after spinal anesthesia. No significant differences exist between the 3 time points.

The number of cases who had pulmonary congestion (ECS >5) detected at baseline, 1 hour, and 2 hours after spinal anesthesia were 66 cases (66%), 68 cases (68%), and 69 cases (69%) respectively. There was no significant difference in the incidence of pulmonary congestion (ECS>5) detected at the 3 time points (P =0.9).

Figure (5) shows the serial changes in the IVC diameters. There was a significant difference in the maximum IVC diameter between the 3 time points. The maximum IVC diameter was larger at 1 h and 2 h after intrathecal injection compared with baseline. There was no significant difference in the maximum IVC diameter at 1 hour and 2 hours after spinal anesthesia.

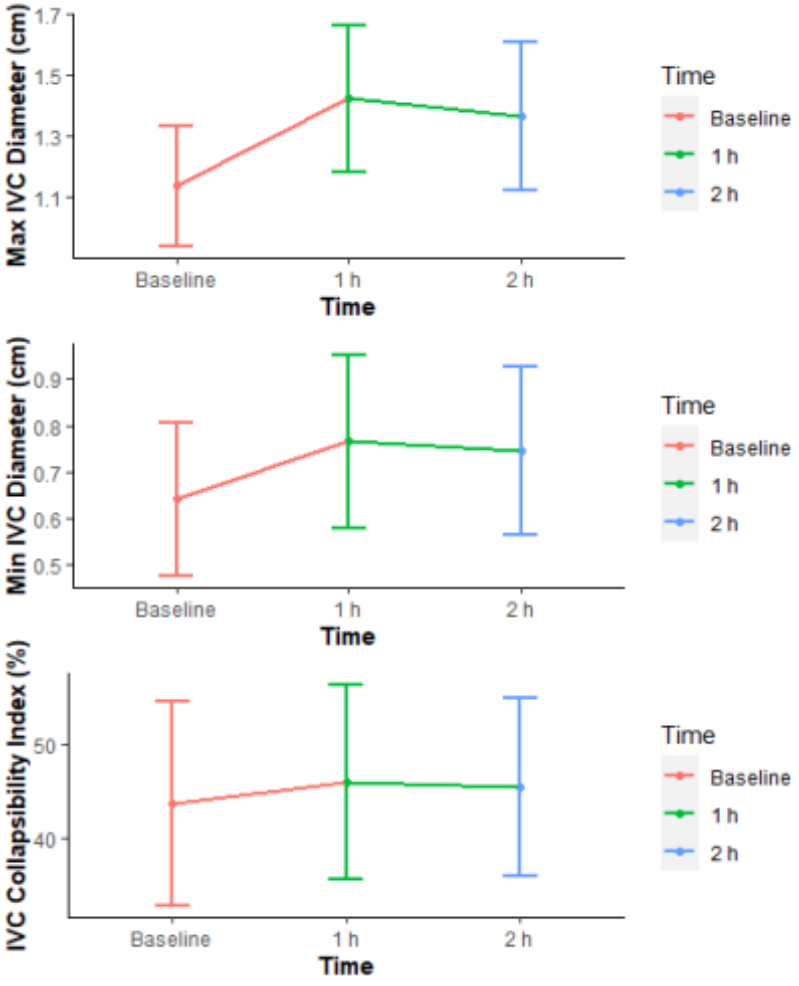

Figure (5): At baseline, 1 hour, and 2 hours following spinal anaesthesia, maximum and minimum inferior vena

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cava (IVC) diameters and collapsibility index (CI) were measured. The IVC collapsibility index was calculated as (maximum IVC diameter – minimum IVC diameter) / maximum IVC diameter. When compared to 1 hour and 2 hours, the maximum and minimum IVC diameters are larger compared with the baseline. No significant differences in the IVC-CI exist between the 3 time points. Data are represented as mean ± SD.

There was a significant difference in the minimum IVC diameter between the 3 time points. The minimum IVC diameter was larger at 1 and 2 hours after intrathecal injection compared with baseline. There was no significant difference in the minimum IVC diameter at 1 and 2 hours after spinal anesthesia. Both the maximum and minimum IVC diameters are greater at 1 hour and 2 hours compared with the baseline. There was no significant difference in the IVC-CI between the 3 time points.

There was no significant difference in the ONSD between the 3 time points (p=0.16) (**Figure 6**).

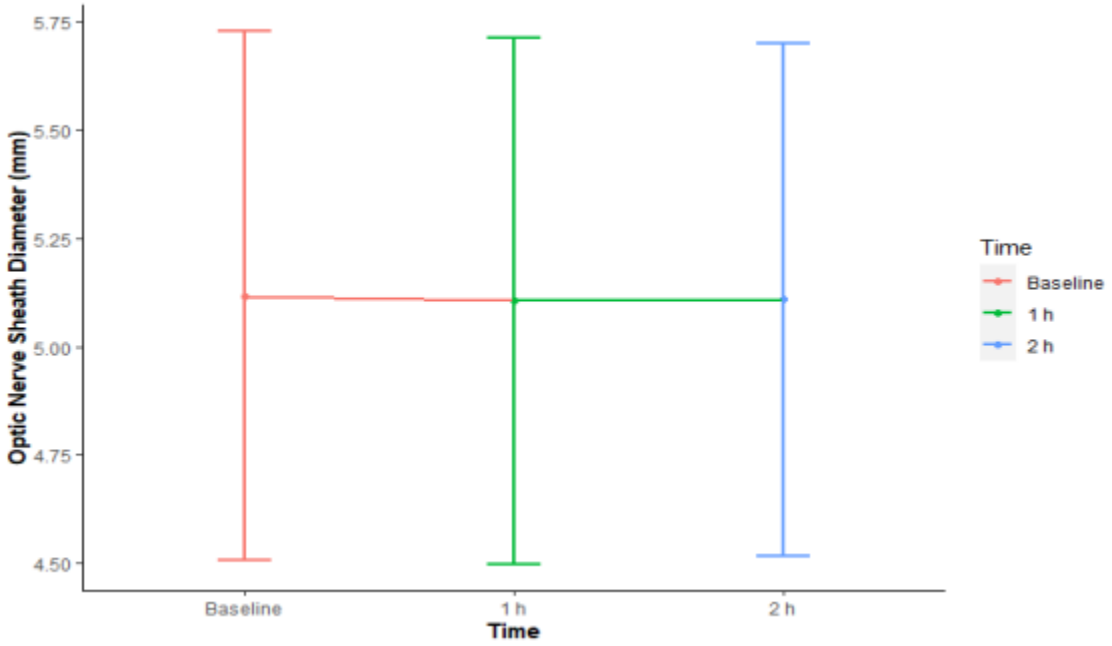

Figure (6): The optic nerve sheath diameter at baseline, 1 h, and 2 h after spinal anesthesia. No significant differences exist between the 3 time points. Data are represented as mean ± SD.

At 2 hours after spinal anesthesia, there was a strong positive correlation found between the ECS and the ONSD measurements ($r^2 = 0.689$, $P<0.001$) (Figure 7).

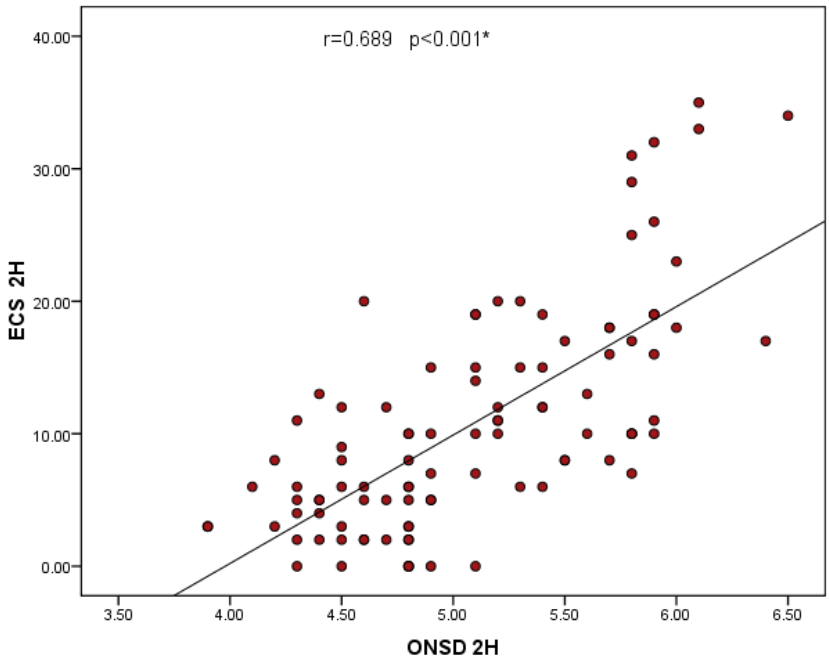

Figure (7): Scatter plot diagram showing correlation between ECS and ONSD at 2 h after spinal anesthesia among studied subjects.

The subgroup analysis for the baseline values for subjects with mild and severe preeclampsia is shown in Table (4). The baseline ECS was higher in subjects with severe preeclampsia than those with mild preeclampsia (P<0.001) and a greater number of subjects had pulmonary congestion. The ONSD was larger in subjects with severe preeclampsia than in subjects with mild preeclampsia (P<0.001).

Table (4): Subgroup analysis for the baseline data between subjects with mild and severe preeclampsia.

Variable	Mild preeclampsia (N = 20)	Severe preeclampsia (N = 80)	Estimated treatment effect	*P* value
Echo Comet Score	2 (0-13)	10 (0-35)	-8 (-5 to -11)[a]	<0.0001
Incidence of pulmonary congestion	2 (10%)	64 (80%)	-70 (-89 to -51)[b]	<0.0001
IVC diameters				
IVC-max (cm)	1.06 ± 0.22	1.16 ± 0.19	-0.1 (-0.21 to 0.01)[c]	0.076
IVC-min (cm)	0.63 ± 0.19	0.64 ± 0.16	-0.01 (-0.11 to 0.08)[c]	0.76
IVC-CI (%)	40.2 ± 11.2	43.9 ± 10.6	-3.7 (-9.4 to 2)[c]	0.19
Optic nerve sheath diameter (mm)	4.6 ± 0.29	5.24 ± 0.6	-0.65 (-0.84 to -0.47)[c]	<0.0001

[a] The difference in median between the 2 groups' (95% nonparametric confidence interval).
[b] The difference in proportions between the 2 groups (95% confidence interval).
[c] The difference in means between the 2 groups (95% nonparametric confidence interval).

DISCUSSION

This prospective observational study demonstrated no significant difference in the ECS and ONSD at 1 hour and 2 hours after spinal anesthesia compared with baseline in parturients with preeclampsia undergoing cesarean delivery. The maximum and minimum IVC diameters were larger at 1 hour and 2 hours after spinal anesthesia compared with baseline. There was no significant difference in the IVC-CI at the 3 time points. At 2 hours after spinal anesthesia, there was a strong positive correlation between the ECS and the ONSD. The baseline ECS and ONSD were higher in subjects with severe preeclampsia than those with preeclampsia.

Bajwa *et al.* [14] demonstrated the role of POCUS in their meta-analysis, including the ECS and ONSD as markers in volume status assessment and early detection of pulmonary edema in parturients with severe preeclampsia.

Three studies compared ECS before and after delivery in women with severe preeclampsia. **Mowafy and Elsayed** [15] demonstrated that the ECS in severe preeclampsia was significantly lower at 24 h after delivery compared with before delivery. **Ambrozic *et al.*** [16] demonstrated that the ECS was higher in women with preeclampsia than in controls, before delivery and at 1 day after delivery. **Zieleskiewicz *et al.*** [3] demonstrated that the ECS was higher in parturients with severe preeclampsia than in healthy controls.

Another study by **Hammad *et al.*** [17] demonstrated that the lung ultrasound score measured before delivery was high in preeclampsia and showed an excellent ability to detect pulmonary edema. **Pachtman *et al.*** [18] demonstrated that women with severe preeclampsia had B-lines measured before delivery more frequently than women without severe features. Another 2 studies were able to detect B-patterns by LUS before delivery (indicating pulmonary interstitial syndrome) in women with severe preeclampsia [19, 20].

Despite the similar finding regarding the ECS results in the current study and previous studies**,** where the ECS has increased from baseline compared to the findings at 2 hours after spinal anesthesia, this hasn't been considered statistically significant. Furthermore, we found no significant difference in the ECS between the 3 time points.

In this study, the baseline ECS was higher in parturients with severe preeclampsia than those with mild preeclampsia. This could be related to changes in disease severity and higher pulmonary congestion in these patients, or it could be a precursor to clinical detection of pulmonary edema.

In the current study, we investigated the capacity of sonographic IVC diameters and the IVC-CI to detect early changes in the intravascular volume (fluid assessment) of parturients with preeclampsia. The maximum and minimum IVC diameters at 1 h and 2 h were larger than the baseline values with no change in the IVC-CI at the 3 time points. This could be due effect of spinal anesthesia, concomitant fluid and ephedrine administration in most of the study subjects resulting in maintained venous return.

A previous study demonstrated similar finding regarding the IVC-CI for fluid assessment in spontaneously breathing patients. They found no significant differences in the max and min IVC diameters, and the IVC-CI between the hypotensive and non-hypotensive patients after induction of spinal anesthesia followed by normal saline administration [21].

In contrast to our study, **Zhang *et al.*** [22] demonstrated in their meta-analysis that IVC-CI helped to predict hypotension after induction of general anesthesia particularly in patients on controlled mechanical ventilation and resuscitated with colloids.

Hernandez *et al.* [23] found that IVC diameters increased with concurrent fluid administration, increased somewhat following epidural block induction, and then reduced to near baseline values at 24 hours after delivery. **Kundra *et al.*** [24] demonstrated that parturients had increased maximum IVC diameter and lower CI in the left lateral position, and parturients with hypotension following spinal anesthesia had a higher CI in the recumbent with wedge position.

Another randomized controlled study found that following spinal anesthesia and delivery, the max and min IVC diameters increased compared to all pre-delivery values, and they were bigger in the colloid preload group. However, the crystalloid group had a greater IVC-CI following delivery [5].

Findings of the current study and other studies are clinically relevant because of some factors that contribute to different results. These factors include: the type of anesthesia (general versus spinal), the type of surgery, the type of the administered IV fluid (colloids versus crystalloids) and different populations.

The majority of ONSD research has been done on traumatic brain injury patients. These investigations showed that ONSD corresponds well with invasive intracranial pressure measures [27-28]. ONSD of 5.0 mm is considered normal, whereas ONSD of >5 mm is deemed abnormal [8, 13]. In patients with stroke, meningitis, epilepsy, hepatic encephalopathy, and mountain sickness, ONSD has already been used as a surrogate marker of elevated intracranial pressure [29, 30].

The alterations in the ONSD indicate a state of cerebral edema as a part of generalized edema, fluid overload and serves as a predictor of volume status in women with severe preeclampsia [31]. Three studies [15, 19, 20] demonstrated ONSD levels before delivery in preeclampsia, and one study evaluated ONSD before and after delivery in parturients with severe preeclampsia and found that ONSD was lower significantly at 24 hours after delivery compared to pre-delivery values.. In addition, they found a significant correlation between ECS and ONSD measurements both before and after delivery [15]. Another observational study on parturients with severe preeclampsia reported a significant correlation between ONSD and The ECS [19].

Dubost *et al.* [8] demonstrated that ONSD was larger in parturients with preeclampsia than healthy controls and ONSD decreased at the third day after delivery while there was no significant difference between both groups at day seven after delivery.

Similar to the above mentioned studies**,** the current study confirmed a strong significant positive correlation between the ECS and ONSD at 2 h after spinal anesthesia. The baseline ONSD was larger in parturients with severe preeclampsia than those without severe features. This could be due to differences in disease severity and indicative of increased cerebral edema among the study subjects.

In contrast to our study, another study reported that there was no significant difference in the mean values of ONSD between parturients with mild and severe preeclampsia. This could be due to the low number of patients with severe preeclampsia (only seven cases) and the lack of more severe intracranial changes as in parturients with severe preeclampsia [32].

LIMITATIONS

This study has a number of limitations. First, the sample size is relatively small (100 subjects) which may affect the generalizability of the results of the study. Second, the observational design of the study may prevent conclusions on the predictive usefulness of ECS and ONSD and IVC-CI measurements in patients with preeclampsia. Third, we perform our ultrasound examinations until 2 h after spinal anesthesia, we didn't perform the ultrasound examination to evaluate and follow up subjects days after delivery due to the paucity in research in the perioperative period in such critical subjects. Forth, the assessment of ECS with the detailed 28 ribs interspaces technique and ONSD is time consuming and requires several measurements. Therefore, more simplified ultrasound scans are needed for further studies to be evaluated.

CONCLUSIONS

Different POCUS parameters that are simple and easy to utilize can be used for fluid assessment in parturients with preeclampsia. In comparison to baseline, there was no statistically significant difference in the ECS and ONSD after 1 and 2 hours following spinal anesthesia. In parturients with preeclampsia, the quick, safe, and reproducible ultrasound measurement of ONSD is highly linked with ECS calculated by lung ultrasonography, which effectively predicts pulmonary congestion and can guide perioperative fluid administration. Furthermore, the ECS, as well as the maximum and minimum IVC diameters, are non-invasive and simple to learn measures for assessing overall fluid status in preeclampsia patients, where excessive fluid administration can lead to major consequences.

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