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Incidence Of Increased Optic Nerve Sheath Diameter (ONSD) Measured By Ocular Ultrasonography In Normal Antenatal Women And In Patients With Severe PIH And Eclampsia

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ABSTRACT

Background: It is a well-known fact that pregnancy-induced hypertension is a most common type of hypertension encountered during pregnancy, and has the most serious consequences for the mother and the baby. Therefore, it is always desirable to know the extent of its severity by a real-time and easily accessible modality such as ultrasound.

Aims: The aim of the study was to estimate the incidence of increased optic nerve sheath diameter (ONSD) using ocular ultrasonography in normal antenatal women and in patients with severe pre-eclampsia and eclampsia.

Setting and design: This study design wasprospective observational. Methods: This study was carried out during the year 2021 - 2022 after obtaining approval from the Institutional Ethics Committee of the Department of Anaesthesiology and the Department of Radiodiagnosis, GMC, Srinagar. The study was designed in three cohort groups: Group I (Normal antenatal women), Group II(severe preeclampsia), and Group III(eclampsia).Demographic profiles, hemodynamic parameters, laboratory markers for the severity of PIH and ultrasonographic OSND were measured.

Statistical analysis used: Data were statistically analysed using Chi-Square tests or Fisher's Exact test for qualitative variables. The quantitative variables were analysed using one way analysis of variance technique. Value of $P < 0.05$ was considered statistically significant.

Results: The maternal age of the patients in our three study groups did not differ significantly from each other. However, there was a significant difference in gravida and parity between the three groups ($p < 0.0001$). Gravida and parity appeared to be the lowest in the eclampsia group. Gestational age was also the lowest in the eclampsia group. Other than liver enzymes, the analysis of laboratory data did not show a significant difference in our study. Aspartate transaminase (AST) and alanine transaminase (ALT) values were the highest in severe preeclampsia. Within each group, the ONSD in the transverse and sagittal planes did not differ much from each other, nor did the

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diameters of the right eye differ significantly from those of the left eye. However, there was a significant difference in the ONSD measurements between three study groups($p < 0.0001$). **Conclusions:** We conclude that the USG measurement of ONSD can be used as a surrogate for the measurement ofICP in severe preeclampsia and eclampsia. We are also of the opinion that if all pregnant women are subjected to this relatively harmless noninvasive investigation routinely on antenatal check-ups, that may help a great deal in early detection of suspected cases as well as in grading the severity of raised ICP in PIH patients noninvasively.

Keywords: Eclampsia, PIH, optic nerve sheath diameter, severe preeclampsia, ocular ultrasonography.

INTRODUCTION:

Hypertension during pregnancy is one of the leading causes of maternal and foetal morbidity and mortality around the world [1]. It also accounts for the increased hospitalisation and utilisation of resources by mothers and their babies [2]. Preeclampsia, also called pregnancy-induced hypertension (PIH), is the most common type of hypertension encountered during pregnancy and has the most serious consequences for the mother and the baby. It causes more than 500 000 foetal and neonatal deaths and more than 70000 maternal deaths each year, worldwide [3]. Approximately 14% of maternal deaths are attributed to PIH and its complications [4].

PIH complicates around 3 – 4 % of gestations globally,[5] and therefore comprises almost half of the 5 – 10 % of pregnancies affected by hypertensive disorders worldwide.[6] Women with PIH are at increased risk of developing maternal complications such as pulmonary oedema, abruptio placentae, cerebrovascular events, cardiac or renal complications, haemolysis and disseminated intravascular coagulation.[7,8] However, it is the neurological complications of PIH, including intracranial haemorrhage and cerebral oedema that are responsible for most maternal deaths from this diagnosis.[9] Although there is a direct relationship between the degree of hypertension and the risk of occurrence of these complications,[10] this is not a universal antecedent. Some patients suffer neurological sequelae without previously having severe hypertension.[11] Therefore, it remains challenging to predict who will suffer neurological complications from preeclampsia.

Whatever the mechanism, cerebral oedema can cause increased intracranial pressure (ICP).[12] It is not easy to interpret the clinical signs of elevated ICP during pregnancy because these signs are not specific and can manifest late. Furthermore, the gold standard method for ICP measurement is based on the use of invasive procedures, such as the placement of an intraventricular cannula. Such invasive manoeuvres can cause complications such as infection and haemorrhage and can even be contraindicated in some cases due to the presence of coagulopathies. There has always been an interest in finding non-invasive methods under such circumstances. One such method that has recently emerged and has become quite popular is ocular ultrasonography.

In recent years, emphasis has been on measuring the optic nerve sheath diameter (ONSD) noninvasively using ocular ultrasound. The optic nerve sheath (ONS) is a continuation of the intracranial meninges. About 3 mm behind the confluence of the optic nerve with the globe, the optic nerve is covered only by fat, and its sheath is readily distensible at this point in case there is an increase in ICP. This provides an opportunity to measure ONSD by ultrasound and correlate its findings with the incidence of PIH. It has been observed that the diameter of the optic nerve sheath can give insight into the severity of elevated ICP.

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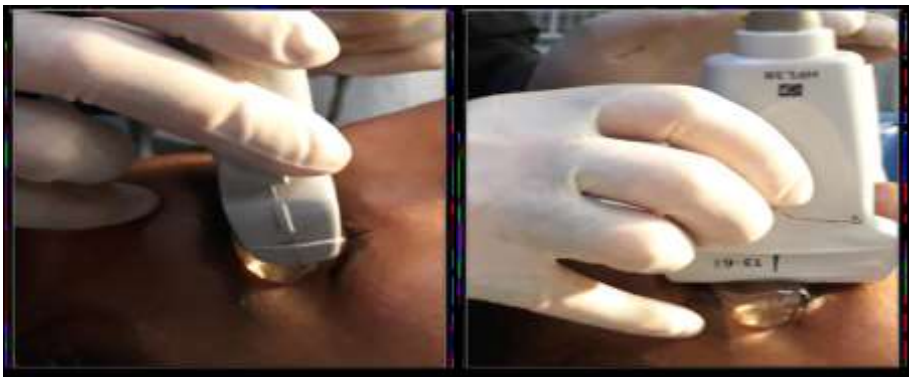
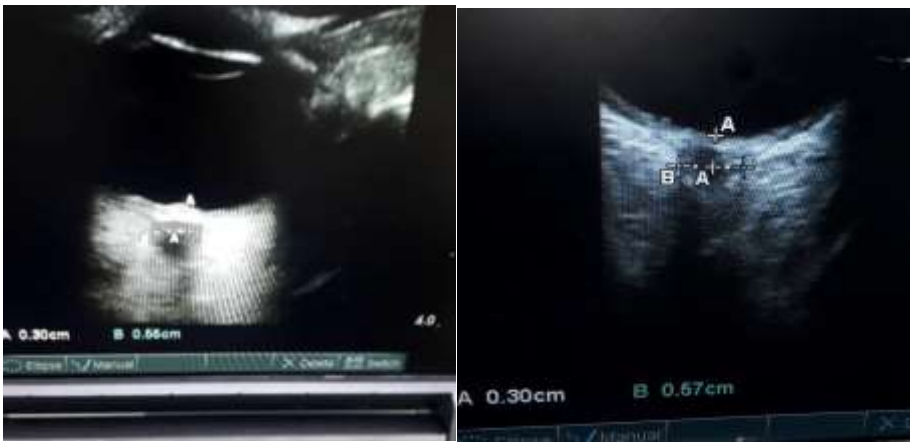
METHODS:

This prospective observational study was conducted on patients after obtaining their written informed consent and in accordance with the STROBE statement for the performance of the observational studies [13]. All studies were carried out at the Government Lalla Ded Hospital (LDH), Srinagar.

Patients who presented to the LDH operation theatre for an emergency Caesarean section and met our inclusion criteria were enrolled for the study. Proper counselling was done with the patients and they were educated about the procedure. Written informed consent was taken. Demographic profiles, hemodynamic parameters, laboratory markers for the severity of PIH were noted. The monitors (pulse oximeter, ECG, NIBP) were applied and the baseline values were recorded. Standard ASA monitoring was done throughout the procedure.

The patients were made to lie in the supine position with the head in neutral position, and were asked to close their eyes tight. An ample amount of sterile coupling gel was applied to the eyelids as a medium between the eyelids and the transducer. High-frequency linear probe (7 – 12 MHz) of the USG machine (Sonosite M Turbo) was placed over the upper eyelids in an axial or sagittal plane as required while applying minimal pressure to the eyeball. The operator's hand was stabilised by resting the little finger on the orbital ridge, allowing the least possible pressure on the globe. B-mode imaging alone was used to obtain a still image of the optic nerve. The nerve was assessed in two planes: transverse and sagittal, the latter requiring rotation of the probe 90 degrees. The probe was adjusted with subtle movements caudally and medially to obtain a fairly clear image of the globe along with the lens, vitreous, optic nerve, and optic nerve sheath. The optic nerve sheath was visualised as a thin hypoechoic line on either side of the hyperechoic area (optic nerve). The images were stored in the machine. Using the machine callipers, the cursors were placed parallel to and in the middle of the optic nerve 3.0 mm posterior to the junction of the optic nerve and the retina. The second measurement was made perpendicular to this line at the 3.0 mm mark, measuring the diameter of the ONS. Two measurements were made for each optic nerve (right and left), one in the transverse plane and the other in the sagittal plane, measuring ONSD in both axes. The mean of these four values (2 per eye) was recorded as ONSD for each patient.





All the patients underwent Caesarean section after the procedure. Postoperative patients were transferred to the recovery ward. Those patients who had an increase in mean ONSD (> 5.0 mm) were observed for two days after delivery for any sort of complications such as convulsions, TIA, stroke, reduction in GCS.

STATISTICAL METHODS

The recorded data was compiled and entered into a spreadsheet (Microsoft Excel) and then exported to data editor of the SPSS - Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD and categorical variables were summarised as percentages.
Qualitative variables were analysed using Chi-Square tests or Fisher's Exact test, whichever appropriate. Quantitative variables were analysed using one-way analysis of variance technique.
A p- value of <0.05 was considered statistically significant.

Conflict of interest: Nil
Funding: Nil

RESULTS:

A total of 150 patients were enrolled in this observational study for statistical purpose. Patients were divided into three groups: Group I (N=55): Normotensive Antenatal Women, Group II (N=49): Women with severe preeclampsia and Group III (N=46): Women with eclampsia. The demographic profile of the study groups in depicted in table 1.

Table 1: Demographic profile of the study population

Variables	Group I	Group II	Group III	P Value
Age (years)	27.72±3.43	29.12±3.01	28.32±3.70	0.114
Gestational age(weeks)	36.89±1.78	34.36±3.56	31.23±3.04	<0.0001*
Gravida	3.14±2.38	2.72±1.86	2.34±1.89	<0.0001*
Parity	2.52±2.38	1.35±1.61	0.98±1.44	<0.0001*

*** Statistically significant difference (p valve < 0.05)**

The mean ONSD in group I subjects was 4.30 ± 0.24 mm (95% CI: 4.23 - 4.37); in group II patients, the mean ONSD was 5.06 ± 0.54 mm (95% CI: 4.91 – 5.22), and in group III patients, the mean ONSD was 5.41 ± 0.39 mm (95% CI: 5.29 – 5.52). The difference in the mean ONSD of patients was statistically extremely significant between the three groups (p < 0.0001).

Table 2: Optic nerve sheath diameter measurement among the study groups.

ONSD	Group I	Group II	Group III	P Value
Right eye transverse diameter	4.03±0.26	5.08±0.53	5.43±0.40	<0.0001*
Right eye sagittal diameter	4.29±0.28	5.06±0.56	5.40±0.38	<0.0001*
Left eye transverse diameter	4.32±0.23	5.06±0.55	5.40±0.40	<0.0001*

Left eye sagittal diameter	**4.29±0.25**	**5.05±0.58**	**5.40±0.40**	**<0.0001***

*** Statistically significant difference (p valve < 0.05)**

Of 55 patients in group I, none had ONSD > 5.0 mm while in group II, 24 of 49 patients had ONSD > 5.0 mm, and in group III 37 of 46 patients had ONSD > 5.0 mm [Table 3].

Table 3: Number of patients with ONSD > 5.0 mm in each group

Variable	Group I (N=55)	Group II (N=49)	Group III(N=46)
ONSD≤5.0mm	**55**	**25**	**9**
ONSD>5.0mm	**0**	**24**	**37**

None of our patients in Group I (normotensive antenatal womem) had ONSD > 5.0 mm. However, 24 out of the 49 patients in Group II (severe preeclampsia) had increased ONSD, accounting for 49 % of the group. On the other hand, 80% of the patients (37 out of 46) in Group III (eclampsia) had increased ONSD [Fig 1].

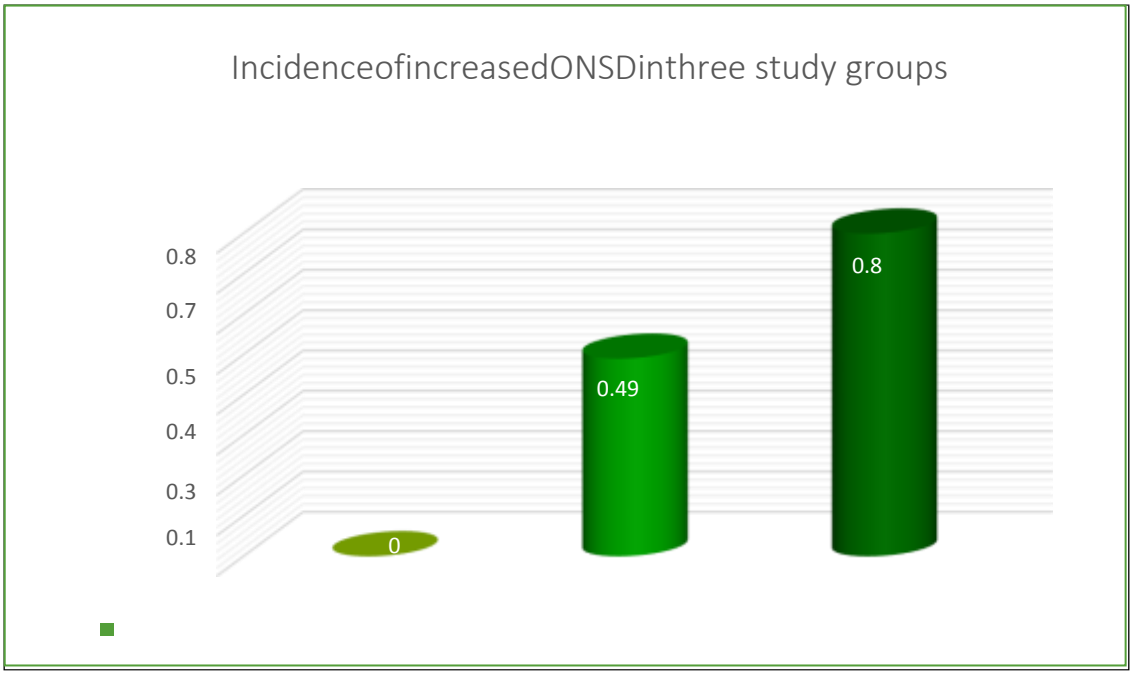


Fig 1

61 of our patients had increased ONSD, 24 in group II and 37 in group III. 15 of them suffered some type of complications – 4 from group II and 11 from group III [Fig 2].
4 patients in group II had complications while 12 patients in group III

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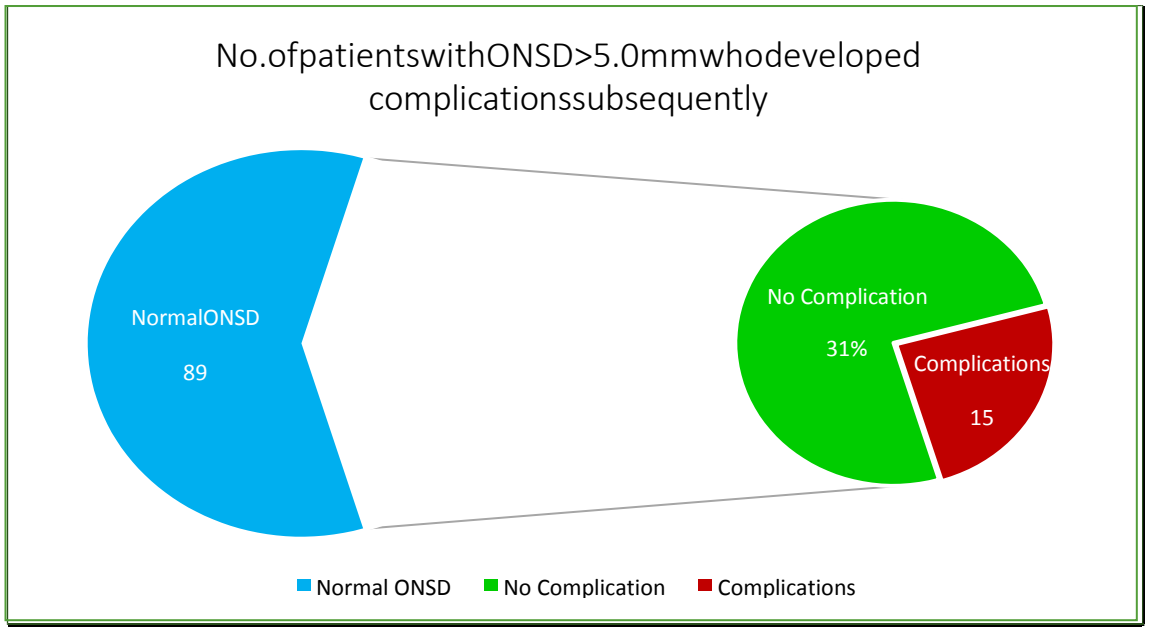

Fig 1

4 patients in group II had complications while 12 patients in group III developed complications. However, one of these patients belonging to group III had normal ONSD and developed PRES. Therefore, she was not included in our calculation, as our study of complications included only patients with increased ONSD. All other patients who developed complications had increased ONSD [Fig 3].

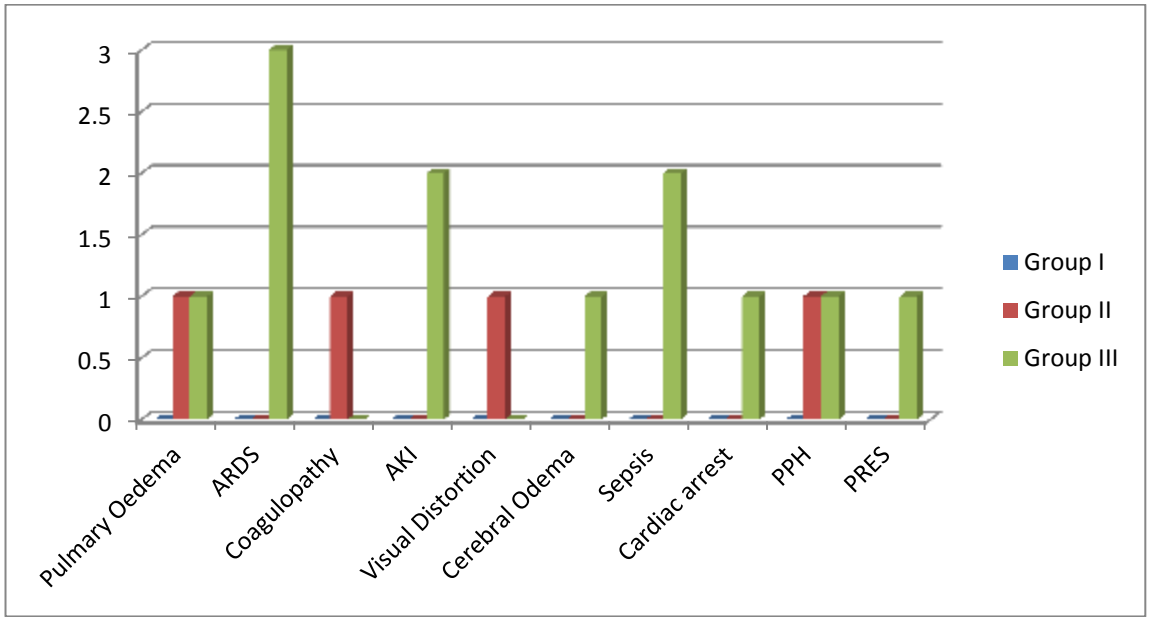

Fig 3

DISCUSSION:

Ultrasound measurement of the optic nerve sheath diameter (ONSD) isnowconsideredareasonableproxyforintracranialpressure(ICP),withtheadvantages that it is non-invasive, can be repeated frequently and does notrequireshiftingofthepatienttotheradiodiagnosisfacility.ONSDmeasuredby different techniques like magnetic resonance imaging (MRI), computedtomography(CT)andultrasoundallgivecomparablevalues.StudieswhichhavecorrelatedONS

DwithconcomitantICPmeasurementsusinginvasivemethods haveshownasensitivityof 88% andspecificityof93%.[14]

Sonographic assessment of the ONSD can be easily achieved by anexperienced operator. It is measured as the average of the diameters in twoplanes (axial and sagittal). No studies have compared the ONSD with in vasive means of assessingntracranial pressurein pregnancy.

In our study the mean ONSD in group I subjects was 4.30 ± 0.24 mm (95% CI: 4.23 - 4.37); in group II patients, the mean ONSD was 5.06 ± 0.54 mm (95% CI: 4.91 – 5.22), and in group III patients, the mean ONSD was 5.41 ± 0.39 mm (95% CI: 5.29 – 5.52). The difference in the mean ONSD of patients was statistically extremely significant between the three groups ($p < 0.0001$). **Dubost, Le Gouez etal**.[15]in 2012 found that medianONSD values were significantly greater inpreeclamptic patients compared with healthy pregnant women at delivery (5.4mm(95%CI:5.2,5.7)vs.4.5mm(95%CI:4.3,4.8),P<0.0001).Intheirstudy, about20%ofpreeclampticpatientshadONSDvaluescompatiblewithintracranialpressureof>20mmHg.T heresultsintheirstudywereinaccordancewithourstudy.

JanS,NazirO,HussainAetal. (2022) [16]measuredONSDinpre-eclampticpatients and compared it to healthy pregnant women. A total of 90 subjectswererecruited,andweredividesintothreegroupswith30patientsineachgroup.GroupI– Normalpregnantwomen,groupII–mildpreeclampsia,andgroupIII – severepreeclampsia.Theyfoundthatopticnervesheathdiameterwassignificantly higher in patients with preeclampsia compared to controls (p<0.001).The mean of ONSD in group I was 4.5±0.2 mm, versus 5.7±0.2 mm in group II,versus,5.9±0.3mmingroupIII.

There is no consensus regarding cut-off valve of normal ONSD. However,majority of studies that have been done so far have taken 5.0 mm as the upperlimitofnormalONSD. Inourstudy,thecut-offvalueofnormalONSDwastaken5.0mm.Anyvalue5.0mmONSDwasconsideredincreasedwhile5.0m morbelowwere categorized asnormalONSD.

Based on this cut-off point (5.0 mm), the incidence of increased ONSD (> 5mm)inourthree studygroupswas GroupI –0outof 55subjects –0% , GroupII–24out of49patients–49% and GroupIII– 37out of46patients–80%.**Singh and Bhatia** (2018) [17]evaluated the incidence of raised intracranialpressure(ICP)in patients withseverepreeclampsiaandeclampsiausingocularultrasonography with optic nerve sheath diameter (ONSD) measurement. Themean ONSD in the severe preeclamptic group was 5.6 ± 0.37 mm, while in theeclampsia group, it was 5.8 ± 0.36 mm. Overall, 56% of pre-eclamptic patientshadONSDs>5.7mm.

Brzan Simenc, Ambrozic et al. (2018)[18]examined thirty patients withsevere preeclampsia at a median gestation of 32 weeks and 5 days, in whom theONSDwasstatisticallysignificantlygreaterantenatallyandondaysoneandfourpost-partumthaninhealthycontrols.43%ofthepatientswithseverepreeclampsia had an ONSD > 5.8 mm, while none in the control group reachedthisdimension.

Inourstudy,61patients outof150hadONSDof>5.0mmandofthem15developedcomplications:AKI(2),ARDS(3),coagulopathy(1),PPH(2),pulmonaryoedema(2),cerebraloedema(1),distortedvision(1),revived cardiac arrest (1), sepsis (2). In general, 25% of our patients whohad increased ONSDdeveloped

somesortofcomplications.

To our knowledge, no studies have been conducted on complications inPIH patients who have had an increase in ONSD to date.However, thereare many studies on the complications of PIH in general. **Bibi Shahnaz etal, [19]** conducted a study in 2004 to assess the frequency, epidemiologicalfactors,complications,andoutcomeofseverepreeclampsiaandeclampsia.

200patientswereenrolledinthisstudy.TheyobservedthatHELLPsyndrome,disseminatedintravascularcoagulation,acuterenalfailure, neurological complications, and acute respiratory distress syndrome werethemainmaternalcomplications,alloccurringmorefrequentlyineclampticpatients.Thefrequencyofpulmonaryoedema,placentalabruption,postpartum haemorrhage, and aspiration pneumonia was not significantlydifferent between the two groups. More than half of the patients underwentcaesarean delivery. The early neonatal mortality rate was 13% in the entirecohort.

A total of 150 patients were examined in our study. 55 of them werenormotensive while 95 belonged to the severe preeclamptic or eclampticgroups. Of these 95 patients, 61 had increased ONSD (> 5.0 mm) while 34had normalONSD(≤5.0 mm).

Of61patientswhohadincreasedONSD,14patientsgavebirthtobabieswithapoorAPGARscoreat5minutes (<7),whichisapproximately23%.While only 3 out of 34 patients with normal ONSD delivered babies withpoorAPGARat5minutes–about10%.

ThereisalackofliteratureontheoutcomeofpregnancyintermsofpoorAPGARscoresinthosepatientswithincreasedONSD. Therefore, we have compared our results with the studies conducted for foetal outcome in PIHpatients regardless of theONSD values.

Shen M, Smith G et al.,[20]in 2017 compared risk factors and outcomesofgestationalhypertensionandpre-eclampsia.7633patientswereincludedin thisstudy andtheriskfactors compared.They observedthatthere wasa strong association between preeclampsia and several adverse outcomesincluding placenta abruption, low weight babies, preterm birth and APGARscore<7atfive minutes.

Ajibo B, Wolke E et al. (2022) [21] conducted a study with the aim toidentify determents of low fifth minute APGAR score among new-bornsdelivered by caesarean section. They observed that pregnancy inducedhypertensionwasanindependentfactorassociatedwithlowAPGARscore.

LIMITATIONS:

Only those patients who presented to the emergency operation theatre at LDH for an emergency Caesarean section were included in the study. The results cannot be authentically extrapolated to those PIH patients who had normal vaginal deliveries. Ultrasound is subjected to artifacts, and measuring the ONSD in the off-axis may sometimes result in an erroneous value.

CONCLUSION:

None of the normotensive antenatal patients in our study had ONSD > 5.0 mm. While 49 % of severe preeclamptic patients and 80% of eclamptic patients had increased ONSD. These results are in agreement with those of most of the previously conducted studies.

25% of patients who had increased ONSD subsequently developed some sort of complications like ARDS, PRES, AKI etc.

While 23% of babies born of PIH patients with increase ONSD had poor APGAR (< 7) at 5 minutes, only 10% of babies born of PIH patients with normal ONSD had low APGAR at 5 minutes.

We conclude that USG measurement of ONSD can be used as a surrogate for ICP measurement in preeclampsia and eclampsia. We are also of the opinion that if all pregnant women are subjected to this relatively harmless non-invasive investigation routinely on antenatal check-ups, that may help a great deal in early detection of suspected cases as well as in grading the severity of raised ICP in PIH patients noninvasively.

Regarding complications in patients with increased ONSD and the neonatal outcome of those patients with increased ONSD, we suggest that more studies must be done to confirm or refute our results.

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