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Establishing an association between pregnancy-induced hypertension changes in the fundus and fetal outcomes

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Abstract---Background: Involvement of the ocular system in pregnancy is a common finding in females having PIH (pregnancy-induced hypertension). Aim: To judge the association between pregnancy-induced hypertension changes in the fundus and fetal outcomes. Methods: In 306 pregnant females with a confirmed diagnosis of pregnancy-induced hypertension, fundus changes were assessed along with fetal outcomes. The fetal outcomes included neonatal death, stillbirth, 1-minute Apgar scores, birth weight, and gestational age. Collected data were subjected to an ANOVA test and SPSS software to assess any association. Results: Among 306 subjects, 42 subjects had fundus changes and 264 subjects had no fundus changes. Mean systolic blood pressure (BP) was 182.88±33.62 in subjects with fundus changes and 150.74±12.84 mmHg in subjects without any fundus changes which was significantly higher in fundus changes. Diastolic pressure was also significantly higher, 125.26±21.34 mmHg in subjects with fundus changes compared to 100.09±9.49 mmHg in subjects without fundus changes. Fetal outcomes were comparable in subjects with or without fundus changes. A significant association was seen between optic nerve head and retinal changes with low birth weight ($p < 0.05$). Conclusion: Low birth weight has an association with changes in the optic nerve head and retina. Low Apgar scores are associated with changes in optic nerve head and choroidal changes. Evaluation of the fundus in

females with pregnancy-induced hypertension is vital for the prediction of adverse pregnancy outcomes.

Keywords---choroidopathy, fetal outcomes, optic neuropathy, PIH, retinopathy

Introduction

Pregnancy-induced hypertension (PIH) is one of the major causes of perinatal and maternal mortality along with being one of the most challenging conditions in the field of Obstetrics. Pregnancy leads to various changes in the pathological and physiological state of females.¹ PIH is seen as one of the pathologic changes of pregnancy which is a hypertensive disorder usually seen after 20 weeks of gestation without any associated cause of raised blood pressure of >140/90 mmHg evaluated twice at a minimum of 6-hour difference. PIH signifies hypertension which develops directly due to a gravid state. Hypertension leads to complications in nearly 5% to 10% of all pregnancies.²

The most vital pathologies seen with the pregnancy are PIH including eclampsia, preeclampsia, and gestational hypertension. A blood pressure level of >140/90 recorded for the first time after mid-pregnancy signifies gestational hypertension. Significant proteinuria associated with gestational hypertension (>300mg/24 hours) is termed pre-eclampsia. Eclampsia is a condition where tonic-clonic convulsions complicate the preeclampsia caused primarily by hypertension.³ Initially, edema is seen in the lower leg which later progresses to anasarca or massive edema. PIH affects multiple systems including ocular manifestations, neurological abnormalities, renal, hepatic, hematological, and cardiovascular systems. The main reason for the involvement of the visual system in PIH is retinal vascular alterations. The vessel constriction can develop after days and may persist for weeks/months.⁴

Retinal changes are seen with a rise of systolic pressure to >160mm Hg and diastolic blood pressure to >110mmHg. These changes are more noticeable when blood pressure reaches 200/130 mmHg. This disease also affects the Choroid commonly leading to choroidal infarction and ischemia along with optic nerve and occipital lobe ischemia. The recovery is usually seen except for cases with significant infarction. Visual disturbances are the common presenting symptoms with less common symptoms being hemianopia, achromatopsia, diplopia, scotomata, photopsia, and/or amaurosis.⁵ Abnormalities of retinal vasculature and retina are most commonly seen. However, the visual cortex, optic nerve, choroid, and conjunctiva can also be affected. Visual loss can also be commonly seen owing to vascular involvement. Threat to vision can be due to choroidal hemorrhage, choroidal ischemia, central retinal vein occlusion, retinal detachment, central serous retinopathy, macular tear, secondary optic atrophy, and central retinal artery occlusion.⁶

Reversible extraocular muscle palsy and cortical blindness are rare entities, however, they have been reported in the literature in subjects with eclampsia. The changes are usually correlated with the severity of hypertension. These findings

are being used as indications for pregnancy termination. Previous literature data showed a significant association between preeclampsia and gestational hypertension with hypertensive disorders. With the progression of the retinal changes associated with pregnancy-induced hypertension progression, maternal outcomes, and with the mortality of the fetus owing to similar vascular ischemic alterations in the placenta.⁷ Considering this background, the present study aimed to assess any existing association between pregnancy-induced hypertension changes in the fundus and fetal outcomes.

Materials and Methods

The present prospective clinical study aimed to assess any existing association between pregnancy-induced hypertension changes in the fundus and fetal outcomes. The study population was comprised of pregnant females with the diagnosis of pregnancy-induced hypertension of Ayodhya city.

The study included 306 females admitted to the Obstetrics ward of the institute with a confirmed diagnosis of pregnancy-induced hypertension. After explaining the detailed study design, informed consent was taken from all the study participants in both written and verbal format. After the final inclusion of the study subjects, detailed history was recorded for all the subjects followed by general examination and systemic examination along with demographics were noted at the baseline.

Following this, an ocular examination of all the subjects was done including detailed slit-lamp examination, pupillary examination, ocular alignment and motility, BCVA (best corrected visual acuity) in possible subjects following refraction, and visual acuity with Snellen's chart was done. Evaluation of the fundus was done under mydriasis using tropicamide was done. The changes in the fundus were recorded as choroidal changes, optic nerve head changes, extravascular retinal changes including hard exudates, cotton wool spots, hemorrhages, vascular changes, and no changes in the retina. Fetal outcomes were assessed as neonatal death, stillbirth, 1-minute Apgar scores recording, birth weight, and gestational age.

The data collected were assessed statistically using logistic regression and multivariate statistical techniques. The data were presented in tabulated and descriptive formats. SPSS version 22.0, 2013, Armonk, NY: IBM Corp and ANOVAs test were utilized. The data were expressed as mean and standard deviations and as percentages and numbers with a 0.05% significance level.

Results

The study included 306 females admitted to the Obstetrics ward of the institute with a confirmed diagnosis of pregnancy-induced hypertension. Among 306 subjects, 42 subjects had fundus changes and 264 subjects had no fundus changes. The mean age of the study subjects with and without fundus changes was 23.84 ± 5.53 years and 24.34 ± 5.67 years respectively. The mean gravida state was 1.73 ± 1.25 and 1.72 ± 1.17 respectively for subjects with and without fundus changes and pregnancy-induced hypertension incidence was higher in

primigravida state compared to multi-gravida. The mean parity was 0.64 ± 1.05 and 0.56 ± 1.13 respectively in subjects with and without fundus changes. Mean systolic blood pressure (BP) was 182.88 ± 33.62 in subjects with fundus changes and 150.74 ± 12.84 mmHg in subjects without any fundus changes which was significantly higher in fundus changes. Diastolic pressure was also significantly higher, 125.26 ± 21.34 mmHg in subjects with fundus changes compared to 100.09 ± 9.49 mmHg in subjects without fundus changes. Other demographic data for age, gravida, and parity were comparable at baseline in subjects with or without fundus changes.

Concerning the fundus changes in study subjects, it was seen that the most common fundus change was optic nerve changes seen in 35.71% (n=15) study subjects followed by retinal changes observed in 30.95% (n=13) study subjects. Other changes seen were choroidal change seen in 23.80% (n=10) study subjects and vascular changes seen in 9.52% (n=4) study subjects respectively as shown in Table 1.

On assessing the fetal outcomes in study subjects with or without fundus changes, it was seen that no neonatal death was reported in subjects with PIH and fundus changes, whereas, 1.51% (n=4) neonatal deaths were reported in subjects with no fundus changes which was the non-significant difference with $p=0.55$. Stillbirths in subjects with and without fundus changes were 4.76% (n=2) and 4.54% (n=12) which was also statistically non-significant with $p=0.94$. 1 min Apgar scores of <5 was seen in 23.80% (n=10) neonates with fundus change mother compared to 14.39% (n=38) neonates from females with no fundus changes. This was also statistically non-significant with $p=0.25$. Low-birth weight neonates were significantly higher in females with PIH and fundus changes with 23.80% (n=10) neonates compared to 26.51% (n=70) neonates from females without fundus changes with $p=0.01$. The gestational age of <37 weeks was seen in 23.80% (n=10) subjects from fundus changes and 31.06% (n=82) subjects with no fundus changes. This was statistically non-significant with $p=0.3$. Pregnancy induced hypertension with fundus changes was more common in primigravida females with 73.80% (n=31) females compared to multigravida females with 26.19% (n=11) females as shown in Table 2.

For the evaluation of the association between fundus changes and different fetal outcomes, choroidal changes did not show any significant association with any adverse fetal outcomes including stillbirth, 1 min Apgar scores <5 , gestational age <37 weeks, and low birth weight <2.5 kgs with respective p-values of 0.63, 0.84, 0.63, and 0.63. Similar results were seen for vascular changes where no significant association was seen for any adverse fetal outcomes including stillbirth, 1min Apgar scores <5 , gestational age <37 weeks, and low birth weight <2.5 kgs with p-values of 0.73, 0.54, 0.51, and 0.54 respectively. Retinal changes in study subjects showed a significant association with low birth weight <2.5 kgs with $p=0.04$, and a non-significant association with stillbirth, 1 min Apgar scores <5 , and gestational age <37 weeks with $p=0.12$, 0.24, and 0.83 respectively. Optic nerve changes in study subjects were significantly associated with low birth weight <2.5 kgs in neonates with 0.03. However non-significant association was seen in optic nerve changes and stillbirth, 1min Apgar scores <5 , and gestational age <37 weeks with $p=0.54$, 0.46, and 0.24 respectively (Table 3).

For mean fetal outcome values in study participants with fundal changes, choroidal change was seen in subjects with a mean gestational age of 38.22 ± 1.62 weeks, 1 min Apgar score <5 with 5.42 ± 2.49 , and mean birth weight of 2.882 ± 0.587 kgs. Optic nerve changes were seen in subjects of mean gestational age of 37.36 ± 1.53 weeks, mean birth weight of 2.427 ± 0.360 kgs, and mean 1 min Apgar score of 5.27 ± 1.37 . Retinal changes were following similar patterns, with mean values of 5.85 ± 2.84 , 2.469 ± 0.530 , and 36.69 ± 2.86 for mean gestational age, mean birth weight and mean 1 min Apgar scores respectively. Vascular changes were also seen for gestational age, mean birth weight, and mean 1 min Apgar score with respective mean values of 37.02 ± 2.81 weeks, 2.952 ± 0.786 kgs, and 6.52 ± 0.73 respectively as shown in Table 4.

Discussion

The study results showed that concerning the fundus changes in study subjects, it was seen that the most common fundus change was optic nerve changes seen in 35.71% (n=15) study subjects followed by retinal changes observed in 30.95% (n=13) study subjects. Other changes seen were choroidal change seen in 23.80% (n=10) study subjects and vascular changes seen in 9.52% (n=4) study subjects respectively. These findings were consistent with studies of Karki P et al⁸ in 2010 and Reddy SC⁹ in 2012 where authors reported the most common fundus changes as optic nerve change and retinal changes as in the present study.

For adverse fetal outcomes, no neonatal death was reported in subjects with PIH and fundus changes, whereas, 1.51% (n=4) neonatal deaths were reported in subjects with no fundus changes which was the non-significant difference with $p=0.55$. Stillbirths in subjects with and without fundus changes were 4.76% (n=2) and 4.54% (n=12) which was also statistically non-significant with $p=0.94$. 1 min Apgar scores of <5 was seen in 23.80% (n=10) neonates with fundus change mother compared to 14.39% (n=38) neonates from females with no fundus changes. This was also statistically non-significant with $p=0.25$. Low-birth weight neonates were significantly higher in females with PIH and fundus changes with 23.80% (n=10) neonates compared to 26.51% (n=70) neonates from females without fundus changes with $p=0.01$. The gestational age of <37 weeks was seen in 23.80% (n=10) subjects from fundus changes and 31.06% (n=82) subjects with no fundus changes. This was statistically non-significant with $p=0.3$. These results were in agreement with the previous studies of Rasdi AR et al¹⁰ in 2012 and Javedkar SD et al¹¹ in 2013 where authors reported a higher incidence of low-birth-weight infants in subjects with PIH with fundus changes in their respective studies.

Concerning the association between fundus changes and different fetal outcomes, choroidal changes did not show any significant association with any adverse fetal outcomes including stillbirth, 1 min Apgar scores <5 , gestational age <37 weeks, and low birth weight <2.5 kgs with respective p-values of 0.63, 0.84, 0.63, and 0.63. Retinal changes in study subjects showed a significant association with low birth weight <2.5 kgs with $p=0.04$, and a non-significant association with stillbirth, 1 min Apgar scores <5 , and gestational age <37 weeks with $p=0.12$, 0.24, and 0.83 respectively. Optic nerve changes in study subjects were significantly associated with low birth weight <2.5 kgs in neonates with 0.03.

These results were similar to the previous studies of Ranjan R et al¹² in 2014 and Sheth BP¹³ in 2001 where retinal and optic nerve changes were shown to have a significant association between retinal changes and low-birth-weight infants.

The study results also showed that choroidal change was seen in subjects with a mean gestational age of 38.22 ± 1.62 weeks, 1 min Apgar score <5 with 5.42 ± 2.49 , and mean birth weight of 2.882 ± 0.587 kgs. Optic nerve changes were seen in subjects of mean gestational age of 37.36 ± 1.53 weeks, mean birth weight of 2.427 ± 0.360 kgs, and mean 1 min Apgar score of 5.27 ± 1.37 . Retinal changes were following similar patterns, with mean values of 5.85 ± 2.84 , 2.469 ± 0.530 , and 36.69 ± 2.86 for mean gestational age, mean birth weight and mean 1 min Apgar scores respectively. Vascular changes were also seen for gestational age, mean birth weight, and mean 1 min Apgar score with respective mean values of 37.02 ± 2.81 weeks, 2.952 ± 0.786 kgs, and 6.52 ± 0.73 respectively. These findings were closely associated with findings of Bhakda RN¹⁴ in 2015 and Tadin I¹⁵ in 2001 where authors suggested similar findings for fundus changes and adverse fetal outcomes as in the present study.

Conclusion

Considering its limitations, the present study concludes that low birth weight has an association with changes in the optic nerve head and retina. Low Apgar scores are associated with changes in optic nerve head and choroidal changes. Evaluation of the fundus in females with pregnancy-induced hypertension is vital for the prediction of adverse pregnancy outcomes. The limitations of this study were smaller considered population, short monitoring, and biased related to the geographic location warranting further long-term studies planned longitudinally.

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TABLES

Table 1: Fundus changes seen in the study subjects

Fundus changes	%	n=42
Choroidal changes	23.80	10
Optic nerve changes	35.71	15
Retinal changes	30.95	13
Vascular changes	9.52	4

Table 2: Fetal outcomes in subjects with or without fundus changes

Fetal outcomes	Fundus changes		No fundus changes		p-value
	%	n=42	%	n=264	
Neonatal death	0	0	1.51	4	0.55
Stillbirths	4.76	2	4.54	12	0.94
1 min Apgar scores <5	23.80	10	14.39	38	0.25
Low birth weight <2.5 kgs	52.38	22	26.51	70	0.01
Gestational age <37 weeks	23.80	10	31.06	82	0.3
Primigravida	73.80	31	42.80	113	<0.05
Multigravida	26.19	11	57.19	151	

Table 3: Association between fundus changes and different fetal outcomes

Fundus changes	Stillbirth		1 min Apgar scores <5		Gestational age <37 weeks		Low birth weight <2.5 kgs	
	n (%)	p-value	n (%)	p-value	n (%)	p-value	n (%)	p-value
Choroidal changes (n=10)	0	0.63	2 (20)	0.84	2 (20)	0.63	2 (20)	0.63
Optic nerve changes (n=15)	0	0.54	4 (26.6)	0.46	1 (6.66)	0.24	10 (66.6)	0.03
Retinal changes (n=13)	2 (15.38)	0.12	4 (30.76)	0.24	4 (30.76)	0.83	8 (61.53)	0.04
Vascular changes (n=4)	0	0.73	0	0.54	2 (50)	0.51	2 (50)	0.54

Table 4: Mean fetal outcome values in subjects with fundus changes

Fundus changes	Mean 1 min Apgar score	Mean birth weight	Mean gestational age
Choroidal changes	5.42±2.49	2.882±0.587	38.22±1.62
Optic nerve changes	5.27±1.37	2.427±0.360	37.36±1.53
Retinal changes	5.85±2.84	2.469±0.530	36.69±2.86
Vascular changes	6.52±0.73	2.952±0.786	37.02±2.81