



Co-Relation of Ocular Fundus Changes and Pregnancy Induced Hypertension and Its Foetal Outcomes

Mohmed Kandeel^{1*}, Hoda El-Sobky², Ahmed Shalah³ and Essam A. Amin¹

¹Department of Obstetrics and Gynecology, Faculty of Medicine, Menoufia University, Egypt.

²Department of Ophthalmology, Faculty of Medicine, Menoufia University, Egypt.

³Department Obstetrics and Gynecology, Ministry of Health, Egypt.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Pregnancy-Induced Hypertension (PIH) is a stigmatizing condition in obstetrics and a significant cause of maternal and neonatal death. It is a kind of pregnancy-related hypertension that develops after 20th week of pregnancy with no presence of other reasons of high blood pressure.

Objectives: To study the relation between grades of ocular fundus changes & degree of features severity of pregnancy induced hypertension and its maternal and foetal outcomes.

Subjects and Methods: This is a prospective observational follow up study, the research lasted about 16 months and included 121 pregnant women diagnosed with PIH. Ocular examinations were performed using a direct ophthalmoscope, a slit lamp and grades of retinopathy were recorded and linked to the severity of PIH and its consequences. The data were analyzed statistically.

Results: Results of the study revealed that most of the patients 62% had no abnormal fundus changes while 29.8% of the patients were grade I retinopathy and 7.4% of the patients were grade

II retinopathy & There was significant difference between grades of retinopathy and degree of features of severity of PIH & some of its important maternal & foetal outcomes.

Conclusion: Grades of ocular fundus alterations are associated with the severity of PIH's characteristics and are predictive of maternal and fetal comorbidity.

Keywords: Pregnancy induced hypertension; foetal outcomes; ocular fundus changes.

1. INTRODUCTION

Pregnancy-Induced Hypertension (PIH) is a stigmatizing condition in obstetrics and a significant cause of maternal and neonatal death. It is a kind of pregnancy-related hypertension that develops after 20th week of pregnancy with no presence of other reasons of high blood pressure (B.P.) that is >140/90 mm Hg measured twice with a minimum of 6-hour interval. 5-10% of all pregnancies are complicated by hypertensive disorders [1].

PIH is a serious pregnancy condition that has been linked to preterm birth, HELLP (Hemolysis, Low platelet count, Elevated liver enzymes), abruptio placentae and intrauterine fetal as well as maternal mortality. [2].

Complications for the fetus and the mother may be avoided by early identification of PIH. The pathological alterations associated with this disease seem to be linked to vascular endothelial dysfunction and the repercussions of this dysfunction (generalized vasospasm and capillary leak). [3].

Fundus changes associated with PIH (Clinical Manifestations) may be classified into four categories: Grade I: Spastic narrowing of arteriolar of the retina, Grade II: Irregular constriction of the lumen, Grade III: Narrowing and constriction are more fixed with cotton wool patches and hemorrhages, Grade IV: Diffuse retinitis with papilledema. [4].

2. METHODOLOGY

Prospective observational follow up study aims to study relation between grades of ocular fundus changes, degree features severity of pregnancy induced hypertension and its maternal and foetal outcomes. Duration of the study is about 16 months.

Inclusion criteria: Age group between 18 and 35 years, ≥ 34 weeks of pregnancy and patients with PIH (high blood pressures, SBP ≥ 140 mmHg & DBP ≥ 90 mmHg) and appeared for the first time in pregnancy.

Exclusion criteria: Pre-existing diabetic patients, chronic pre-gestational hypertension, renal pathology, patients with cardio-vascular diseases, patients with anaemia and connective tissue disorders ocular pathologies [such as glaucoma, cataract, corneal, opacities, history of ocular trauma, surgery or previous laser treatment and having hazy media which hinders the fundus examination were excluded from the study].

Methods: All the patients were subjected to: (A) Obstetrics evaluation, (B) Ocular evaluation and (C) evaluated of foetal outcomes.

(A) Obstetrics evaluation

- 1- History: Age, obstetrics history: Gravidity, parity, mode of delivery, menstrual history: 1st day of last menstrual period (LMP), past history of medical or surgical disorders, family history of same condition.
- 2- Complain: Asymptomatic, or symptoms such as: Headache, blurring of vision, epigastric pain and vomiting.
- 3- Body mass index (BMI).
- 4- Blood pressure measurement by sphygmomanometer.
- 5- Urinary dipstick tested for proteinuria.

Classification of severity of the patients with PIH:

- In this study we classified pregnant women into gestational hypertension, hypertension with mild and severe features.
- According to clinical classifications of the PIH and based on following finding:
 - Gestational hypertension: BP $\geq 140/90$ mmHg, without or Trace Proteinuria.
 - Pre-eclampsia with mild features: BP $\geq 140/90 - 159/109$ mmHg, Proteinuria +1* and ++*.
 - Pre-eclampsia with sever features: Blood pressure $\geq 160/110$ mmHg, Proteinuria +++ **, Presence of symptoms.
- Proteinuria was graded as *+ = 0.3 gm/l, **++ = 1gm/l, ***+++ = 3gm/l.

(B) Ocular evaluation

Pregnant women with PIH attended to ophthalmology department and subjected to the following:

1. History for any eye symptoms was taken.
2. Technique:
 - Pupils in both eyes were dilated with 1% tropicamide eye drops, and then the fundus was examined directly with an ophthalmoscope (ri-scope) (Welch Allyn 3.5V, United states) and Slit lamp Volk 90D (HS, Shin-Nippon model BP900 CE 00952).
3. The alterations to the retina (hypertensive retinopathy) will be graded using Keith Wagener’s categorization system: Grade 1 –mild generalized arterial attenuation, particularly of small branches; grade II – more serve grade I + focal arteriolar attenuation; grade III - grade II + hemorrhage, cotton wool spots, hard exudates; grade IV – grade III = swelling of optic disc (papilloema).

(C) Fetal outcomes evaluation:

- 1- Fetal gestational age per (weeks): if it was 37 0/7 weeks gestational (term) or less than 37 weeks (preterm).
- 2- Apgar score recording of the test was done at the 1st and 5th minutes after delivery and was repeated later if the score remained low, however scores of 7 and above were generally normal; 4 to 6, fairly low and might admitted to NICU.

- 3- Fetal birth weight: if it was normal weight (term delivery): 2,500–4,200g, Low birth weight: less than 2,500 g.
- 4- Perinatal mortality.

3. RESULTS

Patients’ age ranged 18 – 35 years with mean BMI 27.92 kg/m². Mean GA 37.21 weeks. Table (1).

Most of the patients were pre- eclampsia with mild features by 49.5% and the least was pre-eclampsia with sever features by 24.8%.Table (2).

Most of the patients (62%) had no ophthalmoscopic changes while 29.8% of the patients were grade I retinopathy and 7.4% of the patients were grade II retinopathy. Table (3).

Foetal outcomes included mean GA was 37.21 ± 2.78 weeks, mean birth weight was 2.69 ±1.06 kg, and mean Apgar at 1 min was 6.53 ±1.27 and at 5 min was 8.5 ± 1.09. there were 2 cases of perinatal mortality and 13 cases of NICU admission. Table (4).

There is a significant difference between the grades of ocular fundus changes regarding age, BMI, SBP and DBP. Table (5).

There is a significant difference between the grades of ocular fundus changes regarding proteinuria and severity. Table (6).

There is no significant difference between grades of ocular fundus changes regarding mode of delivery. Table (7).

Table 1. Demographic characteristics among studied patients

Demographic characteristics	Patients [n=121]
Maternal age [years]	27.46 ± 4.57
Mean ± SD	18 – 35
Range	
Gestational age [weeks]	37.21 ± 2.78
Mean ± SD	≥34 (34 – 40)
Range	
BMI [kg/m ²]	27.92 ± 3.65
Mean ± SD	22 – 35
Range	

This table shows that patients’ age ranged 18 – 35 years with mean BMI 27.92 kg/m². Mean GA 37.21 weeks

Table 2. Severity distribution studied patients

Features of Severity	Patients[n=121]	
	N	%
Gestational Hypertension	31	25.6
Pre- eclampsia with mild features	60	49.5
Pre- eclampsia with sever features	30	24.8

Most of the patients were pre- eclampsia with mild features by 49.5% and the least was pre- eclampsia with sever features by 24.8%

Table 3. Grades of retinopathy by Keith Wagener classification among studied patients

Grades of retinal fundus changes	Patients[n=121]	
	N	%
No changes	75	62
Grade I	36	29.8
Grade II	9	7.4
Grade III	1	0.8
Grade IV	0	

Most of the patients 62% had no ophthalmoscopic changes while 29.8% of the patients were grade I retinopathy and 7.4% of the patients were grade II retinopathy

Table 4. Neonatal outcomes distribution among studied patients

Neonatal outcomes	Patients [n=121]
GA [weeks]	37.21 ± 2.78
Mean ± SD	
Birth weight [kg]	2.69 ± 1.06
Mean ± SD	
Apgar at 1 min	6.53 ± 1.27
Mean ± SD	
Apgar at 5 min	8.5 ± 1.09
Mean ± SD	
Perinatal mortality, n (%)	2 (2.2%)
NICU admission, n (%)	13 (10.7%)

This table shows that mean GA was 37.21 ± 2.78 weeks, mean birth weight was 2.69 ± 1.06 kg, and mean Apgar at 1 min was 6.53 ± 1.27 and at 5 min was 8.5 ± 1.09. there were 2 cases of perinatal mortality and 13 cases of NICU admission

Table 5. Association of grades of retinopathy with different variables among studied patients

	No changes [n=75]	Grade I [n=36]	Grade II [n=9]	Grade III [n=1]	F	p
Age [years]	28.56 ± 4.31	33.7 ± 4.91	34.1 ± 2.12	31	6.64	.000*
Mean ± SD						
BMI [kg/m²]	28.29 ± 3.69	30.12 ± 3.39	31.60 ± 1.84	30	7.09	.001*
Mean ± SD						
SBP	<150 mmHg	9 [25%]	2 [22.2%]	0	28.3	.000*
	≥150 mmHg	27 [75%]	7 [77.8%]	1 [100%]		
DBP	<100 mmHg	14 [38.9%]	3 [33.3%]	0	9.91	.019*
	≥100 mmHg	22 [61.1%]	6 [66.7%]	1 [100%]		
Gravidity	Primigravida	23 [63.3%]	5 [55.6%]	0	1.81	.613
	Multigravida	13 [36.1%]	4 [44.4%]	1 [100%]		

This table shows there is a significant difference between the grades of ocular fundus changes regarding age, BMI, SBP and DBP

Table 6. Association of grades of retinopathy with proteinuria grades and severity among studied patients

		No changes [n=75]	Grade I [n=36]	Grade II [n=9]	Grade III [n=1]	F	p
Proteinuria	Trace	27 [36%]	4 [11.1%]	0	0	30.3	.000*
	1+	29 [38.6%]	11 [30.5%]	2 [22.2%]	0		
	2+	9 [12%]	6 [16.6%]	3 [33.3%]	0		
	3+	10 [13.3%]	15 [41.6%]	4 [44.4%]	1 [100%]		
Severity	Gestational Hypertension	27 [36%]	4 [11.1%]	0	0	21.4	.006*
	Pre E with mild features	38 [50.6%]	17 [47.2%]	5 [55%]	0		
	Pre E with sever features	10 [13.3%]	15 [41.6%]	4 [44.4%]	1 [100%]		

This table shows there is a significant difference between the grades of ocular fundus changes regarding proteinuria and severity

Table 7. Association of grades of retinopathy and mode of delivery among studied patients

	CS [n=50]		VD [n=71]		P
	N	%	N	%	
No changes	31	62%	44	62%	.672
Grade I	14	28%	22	31%	
Grade II	4	8%	5	7%	
Grade III	1	2%	0	--	

There is no significant association between mode of delivery and retinopathy grades

Table 8. Association of grades of retinopathy and maternal morbidity & mortality among studied patients

	No changes [n=75]	Grade I [n=36]	Grade II [n=9]	Grade III [n=1]	F	p
No morbidity n (%)	59(78.6%)	22 (61.1%)	1 (11.1%)	0	20.14	0.0005
Placental abruption n (%)	2 (2.6%)	2 (5.5%)	1 (11.1%)	0	22.3	0.007*
Eclampsia n (%)	0	0	1 (11.1%)	0	12.55	0.005*
Impaired coagulation n (%)	4 (5.3%)	2 (5.5%)	0	1(100%)	16.8	0.006*
Intraoperative complication: Uterine atony with B lynch sutures n (%)	1 (1.3%)	1 (2.7%)	1 (11.1%)	0	3.22	0.359
Postpartum hemorrhage n (%)	5 (6.6%)	4 (11.1%)	2 (22.2%)	0	2.69	0.442
ICU admission n (%)	4 (5.3%)	4 (11.1%)	2 (22.2%)	0	3.64	0.303
HELLP n (%)	0	1 (2.7%)	1 (11.1%)	0	6.51	0.189
Maternal mortality n (%)	0	0	0	0	---	---

This table shows there is significant difference between the grades of ocular fundus changes with maternal morbidity regarding placental abruption, eclampsia and impaired coagulation and no case of mortality

Table 9. Association of retinopathy with Neonatal outcomes

	No changes [n=75]	Grade I [n=36]	Grade II [n=9]	Grade III [n=1]	F	p
GA [weeks] Mean ± SD	37.44 ± 0.927	36.89 ± 0.808	35.2 ± 0.629	40	3.26	.021*
Birth weight [kg] Mean ± SD	2.71 ± 0.435	2.62 ± 0.338	2.57 ± 0.134	2	.873	.421
Apgar at 1 min Mean ± SD	7.11 ± 1.65	6.49 ± 2.26	6.1 ± 1.54	6	3.88	.023*
Apgar at 5 min Mean ± SD	8.86 ± 1.21	8.81 ± 2.92	8.71 ± 0.499	9	1.38	.256
Still birth, n (%)	0	0	2 (22.2%)	0	--	--
NICU, n (%)	5 (6.7%)	3 (8.3%)	5 (55.6%)	0	20	.000

This table shows there is a significant difference between the groups regarding Gestational age, Apgar score at 1 min and NICU

There is significant difference between the grades of ocular fundus changes with maternal morbidity regarding placental abruption, eclampsia and impaired coagulation and no case of mortality. Table (8).

There is a significant difference between the grades of ocular fundus changes regarding Gestational age, Apgar score at 1 min and NICU admission. Table (9).

4. DISCUSSION

Pregnancy-Induced Hypertension is a stigmatizing condition in obstetrics and a significant cause of maternal and neonatal death. Pregnancy brings a slew of physiological and pathological changes with it.

When the systolic pressure exceeds 160 and the diastolic pressure exceeds 100 mm of Hg, retinal abnormalities are likely to develop and are noticeable when these limits approach 200/130 mm of Hg. The choroid is also often involved in the disease; ischemia and infarction of the choroid may develop.

- Our Patient's age ranged 18 – 35 years with mean 27.46 years and mean BMI 27.92 kg/m². Mean GA 37.21 weeks. Our results were supported by study of Bhavya et al., [5] as they reported that the study was conducted on a total of 120 patients with ages ranging from 19 years to 36 years. 24% of the participants were below 20 years old, 75 percent were in the range of 21-30 years old, while only 1% was above 30 years old. In 84 cases [70%], they were primigravidae while 36 [30%] cases were multigravida, Furthermore, Kapil et al., [6] showed that 117 individuals

were evaluated, the majority of them were between the ages of 31 and 40 years. [46.15%]. Only 5 patients were over 40 years old [4.27%] while 7 were adolescents [5.98%].

- Our present study showed that most of the patients were pre-eclampsia with mild features by 49.5% and the least was pre-eclampsia with sever features by 24.8%. However, Reddy., [162] revealed that thirty [38.5%] had preeclampsia with mild features, 46 [59%] had pre-eclampsia with sever features and 2[2.5%] had eclampsia, in the study of Jayashree et al., [1] most of the patients had pre-eclampsia with sever features 71[47.3%], 34[22.6%] had preeclampsia with mild features, 32[21.3%] had eclampsia and 13 [8.t7] had gestational hypertension. Furthermore, Varija et al., [7] revealed that out of 423 patients, 81 [19.1%] had preeclampsia with mild features, 99 [23.4%] had pre-eclampsia with sever features and 153 [36.2%] had imminent eclampsia with associated symptoms of blurring of vision, severe headache and in the remaining 90 [21.3%] had eclampsia.
- Our research demonstrated that several phases of fundus alterations during PIH [hypertensive retinopathy] were detected and evaluated using the Keith Wagener classification into:- grade I: mild generalized arterial attenuation, particularly of small branches; grade II: more serve grade I+ focal arteriolar attenuation; grade III: grade II + haemorrhage, hard exudates, cotton wool spots; grade IV: grade III + optic disc swelling [papilloedema].

- In our study most of the patients [62%] had no ophthalmoscopic changes while 29.8% of the patients were grade I retinopathy and 7.4% of the patients were grade II retinopathy, our results were supported by study of Nellore et al., [8] as they reported that grade I retinal alterations were observed in 33[47.14%] and grade II in 4 [6.15%] patients. According to Reddy et al., [9] research, grade I retinal changes were seen in 41[52.46%] and grade II in 5[6.4%]. Another study by Shah et al., [3] showed Grade I retinal changes in 12 [8%] and Grade II in 6 [4%]. In Reddy et al, Shah et al. studies, no hemorrhages, cotton wool spots and/or retinal detachments were found. This observation attribute in providing appropriate prenatal care and also early detection of pregnancy caused hypertension patients, thus avoiding further them to advance. Ranjan et al., [10] research established that fundus alterations occur in 70% of patients with grade I hypertensive retinopathy, 20% of patients with grade II hypertensive retinopathy, and 10% of patients with grade III hypertensive retinopathy. Meanwhile, Tadin et al., [11] reported 10 cases [25%] with grade I hypertensive retinopathy, 6 [15%] cases with grade II hypertensive retinopathy and 2 cases [5%] with grade III hypertensive retinopathy in their study while Rasdi et al., [12] reported 50 patients with hypertensive retinopathy among which, 24 patients [48%] had Grade I hypertensive retinopathy, 21 patients [42%] had Grade II, 4 patients [8%] had Grade III and 1 patient [2%] had Grade IV hypertensive retinopathy changes. In Bhandari et al., [13] study, 56% did not have any ocular fundus alterations in 100 PIH patients. In their study, grade III retinal vascular changes were observed in 3% and grade IV were observed in 2%.
- In our study, mean GA at time of delivery was 37.2 ± 2.78 weeks, mean birth weight was 2.69 ± 1.06 kg, and mean Apgar at 1 min was 6.5 ± 1.27 and at 5 min was 8.5 ± 1.09 and 13 neonates were admitted to NICU. Furthermore, Pragitara et al., [14] discovered that approximately 47.14% of neonates born to pre-eclamptic women were born between 32 and 37 weeks gestation, 50.00 percent were born with low birth weight, 52.86% had an Apgar score of 7 in the first minute, and 72.86% had an Apgar score of 7 in the fifth minute.
- We found a significant difference between the grades of ocular fundus changes regarding age, SBP and DBP. In the study of Bakhda et al., [15] Young individuals are more vulnerable to PIH, and patients aged 18 to 25 years frequently have positive fundus findings. 36 patients, out of 66, under the age of 20 had positive fundus findings [54.55%], while 61 patients in the age range 21-25 years had positive fundus findings [51.26%]. They have correlated systolic blood pressure with fundus changes. In the study of Varija et al., [16] women aged 20-25 years had a greater prevalence of retinal alterations [48.3%] and a larger percentage of Grade III and Grade IV changes [8%] than women of other ages, and this difference is statistically significant. Our results were supported by study of Shah et al., [3] as they reported that of 72 patients who had >160 mmHg systolic and >100 mmHg diastolic blood pressure, 4 [5.56%] patients had developed hypertensive retinopathy changes while out of 78 patients who had ≥ 160 mmHg systolic and/or ≥ 100 mmHg diastolic blood pressure, 14 [17.95%] patients developed hypertensive retinopathy changes. There was significant [P = 0.037] association between retinopathy changes and blood pressure readings in the present study which is similar to reported by Tadin et al., [11], Karki et al., [17]. Furthermore, Bhandari et al., [13], demonstrated that the degrees of retinopathy was correlating with the severity of the disease and levels of hypertension.
- In our study there is a significant difference between the grades of ocular fundus changes regarding severity and proteinuria. Our results were supported by study of Tadin et al., [11] as they demonstrated that there is a directly proportional relationship between the degree of retinopathy and severity of preeclampsia. Therefore, hypersensitive retinopathy can be relied on in the prognosis of preeclampsia severity]. In the study of Bhavya et al., [5] there was less prevalence rate of fundus changes but the

statistical correlation maintained. Reddy et al., [9] from India has reported retinal changes in 53.4% preeclampsia and in 71.2% in eclampsia patients [over all 59%, 236 out of 400]. The most often observed retinal alteration was arteriole narrowing [45.7%, 183 of 400%]. He found that retinal changes were significantly more in patients with severe hypertension. In the study of Varija et al., [16] significant correlation was observed between the severity of PIH and the development of retinopathy changes where in as the severity of the PIH increased the Odds of women developing retinopathy also increased substantially from OR: 17.6; 95% CI: 3.1 - 136.3 in severe PIH to OR: 253; 95% CI: 47.2 - 1935 in Imminent eclampsia. Furthermore, In Bhandari et al., [13] study observations, out of 100 cases, 49% of cases have 1+ proteinuria on urine dipstick method followed by 27% cases having 2+ proteinuria. Patients with 3+ and 4+ proteinuria constituted 17% and 7% respectively. Retinal vascular changes observed in 27%, 44%, 71% and 100% of cases with proteinuria 1+, 2+, 3+ and 4+ respectively. This showed that retinal vascular changes were observed in more cases with high degree of proteinuria. Jayashree et al., [1] demonstrated that patients with proteinuria more than 3+ had greater chances of developing retinopathy.

- In our study there is no significant difference between grades of ocular fundus changes regarding mode of delivery. According to Kapil et al., [17], it was found that there was a statistically significant association of parity [P=0.002] and mode of delivery, [P=0.00] with the fundus changes detectable.
- In our study there is significant difference between the grades of ocular fundus changes with maternal morbidity regarding placental abruption, eclampsia and impaired coagulation. According to S. Cansun Demir et al., [18] study that showed there was no statistically significant difference between the complicated cases of PIH with hypertensive retinopathy and uncomplicated cases regarding abruption placenta, eclampsia, impaired coagulation,

HELLP syndrome and intraoperative complication.

- In our study, there is a significant difference between the grades of ocular fundus changes regarding foetal outcomes included Gestational age at time of delivery, NICU admission and Apgar score at 1 min. Our results were in contrary with study of Karki et al., [100] as They found that individuals with pregnancy-induced hypertensive fundus alterations had a substantially higher prevalence of low birth weight [2.5 Kg]. No statistically significant relationship was found between hypertensive retinopathy and the Apgar score at 1 minute. In the study of Sirenden et al., [19] low birth weight was found more in the preeclampsia with sever features with maternal complications group [37.5%]. The APGAR score of 7–10 in the first and fifth minutes was high in both groups. 41.7% of fetal complications occurred in the group of preeclampsia with sever features complication.

5. CONCLUSION

Retinal alterations develop in accordance with the degree of PIH, and visual symptoms are minimal or nonexistent in individuals with PIH, unless the macula is affected. Routine fundus examinations should be done on individuals with PIH, with the presence of various grades of retinal fundus alterations serving as an indirect indicator of the severity of the disease and a critical technique for predicting adverse fetal and maternal outcomes.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

As per international standard or university standard, patient's consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It was approved by the local ethical committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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