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## **Preeclampsia/Eclampsia and Retinal Micro Vascular Characteristics Affecting Maternal and Foetal Outcome: A Prospective Study amongst South Indian Pregnant Women**

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### **Abstract:**

*The association of hypertension with pregnancy is still an unsolved puzzle. This problem confronted by the obstetrician is quite challenging, considering the high incidence of maternal and foetal complications associated with preeclampsia/ Eclampsia syndrome. It is extremely difficult to identify the clinical features or any parameter which would alarm the high risk to the mother or the foetus. Vasospasm is basic to the patho-physiology of preeclampsia. Clinical evidence of vasospasm may be obtained by ophthalmologic examination. The various pathological changes in different organs of body can be studied by directly studying the ocular fundus and may give a true index of changes in vascular system of brain and kidneys.*

*The aim of the study: To analyse the presence of retinal changes in preeclampsia and its relevance to maternal and foetal outcome.*

*Study design –Prospective study, conducted at the Government Lady Goschen Hospital, Mangalore, Karnataka India, during the years from June 1997 to June 1999, as a Postgraduate Dissertation work with recent updates.*

*Method: 100 consecutive patients with preeclampsia were included in the study. Necessary laboratory investigations from samples of blood and urine were performed. Special investigations like Ultrasonography and fundoscopy were conducted. Maternal and perinatal complications were studied in patients with preeclampsia with retinal changes.*

*Results: 60% of patients with preeclampsia showed fundal changes. Those who had retinal changes suffered complications like abruptio-placentae, Eclampsia, preterm delivery, low birth weight and perinatal deaths.*

*Conclusions: Significant proportion of women with preeclampsia had retinal changes. These women are found to be at a greater risk for adverse pregnancy outcome. Prompt termination of pregnancy would prevent maternal complications; improve foetal outcome thereby reducing perinatal mortality.*

**Key words:** Preeclampsia, Retinopathy, Fundoscopy, Syndrome

### **1. Introduction**

The Preeclampsia/Eclampsia syndrome is a multisystem disorder that can include cardio-vascular changes, hematologic abnormalities, hepatic and renal impairment, neurologic and cerebral manifestations<sup>1</sup>. It can also affect eye and visual pathways. Vasospasm is the basic to the patho-physiology of preeclampsia/Eclampsia. This concept first advanced by Volhard (1918)<sup>2</sup> is based upon direct observations of small blood vessels in the nail beds, ocular fundus, bulbar conjunctivae and it has been surmised from histo-pathology changes seen in various affected organs. Vascular constriction causes resistance to blood flow and accounts for the development of arterial hypertension. The various pathological changes in different organs of the body in preeclampsia can be studied directly visualizing the ocular fundus and may give a true index of changes in vascular system of brain and retina.

Even though two retrospective studies on Eclampsia have been published from Malaysia<sup>2,3</sup>, there is no mention of retinal changes in these studies. There is paucity of data available in the published literature on the prevalence of retinal changes in preeclampsia from other parts of the world especially from India.<sup>4,5,6</sup>. Therefore, this study was undertaken to determine the prevalence of retinal changes in Preeclampsia / Eclampsia and association between the retinal changes and blood pressure, and severity of the disease.

## 2. Materials and Methods

### 2.1. Study Population

This observational study was conducted over a period of twenty four months (June 1997-June 1999). All the patients who fulfilled the diagnostic criteria of PIH (>20 weeks of pregnancy, high arterial blood pressure and proteinuria) admitted in the Obstetric ward, at the Government Lady Goschen Hospital, Mangalore, Karnataka State in South India, intending to eventually deliver in the above named hospital were included in this study. Patients who had preexisting diabetes or hypertension or renal disease or hazy media which did not permit fundus visualization were excluded from the study.

We analyzed data from the inclusion criteria, which were citizens of age  $\geq 18$  year, age range 18 to 38 years, attending the antenatal clinic. 100 consecutive patients with preeclampsia were included in this study, detailed history, clinical evaluation, blood and urine investigations, Ultrasonography and fundoscopy were performed.

### 2.2. Blood Pressure Measurements

Upper arm blood pressure was measured using the Mercury Sphygmomanometer (ELKO B.P APPARATUS) after 5 minutes of rest, according to standard protocols. All of the participants were seated in an upright position with back support. A cuff was placed around the non-dominant upper arm, which was supported at the level of the heart; with the bladder midline over the brachial artery pulsation, the average of 3 separate measurements was taken.

### 2.3. Definitions

Preeclampsia is a clinical syndrome that afflicts 3–5% of pregnancies and is a leading cause of maternal mortality, especially in developing countries.<sup>3, 4</sup> It is a multisystem hypertensive disorder, with the clinical spectrum including severe preeclampsia; Eclampsia; hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome; and HELLP syndrome with Eclampsia. Preeclampsia is defined as the new onset of hypertension and proteinuria during the second half of pregnancy.<sup>1</sup> The diagnosis of preeclampsia requires a blood pressure  $>140/90$  mm Hg on two occasions combined with urinary protein excretion  $>300$  mg/day<sup>1, 4, 5</sup>. Edema is a classic feature of the disease; however, it is no longer considered a diagnostic feature given its lack of sensitivity or specificity.<sup>1, 2, 4, 5</sup> Eclampsia is an acute and life-threatening complication of pregnancy characterized by the appearance of tonic-clonic seizures, usually in a patient who had developed preeclampsia.<sup>2</sup>

### 2.4. Fundoscopy

Fundus examination was done with Direct Ophthalmoscopy, on admission after dilating the pupils with 1% Tropicamide drops (one drop in each eye at 15 minutes interval for 3 times) and this examination was repeated weekly till delivery and in case who showed abnormal fundal changes, fundus examination was continued until 10 days after delivery in the post-partum period.

### 2.5. Direct Ophthalmoscopy

Both pupils were dilated with 1% Tropicamide eye drops and fundus examination was done by ophthalmologist with direct ophthalmoscope in a semi dark room in the ward. Hypertensive retinopathy changes seen in right or left or both eyes, was taken as positive findings in that patient. Age, para, gravida, blood pressure, proteinuria were noted. The PIH was graded as preeclampsia (mild and severe) and Eclampsia. All the findings were noted on a data sheet. The retinal changes (hypertensive retinopathy) were graded according to Keith Wagener classification:

<b>Grade I</b>	<b>Mild to moderate narrowing or sclerosis of arterioles</b>
<b>Grade II</b>	Moderate to marked sclerosis of retinal arterioles
	Exaggeration of light reflex
	Arterio venous compression changes
<b>Grade III</b>	Generalized /localized narrowing of arterioles
	Retinal arteriolar narrowing and focal constriction; retinal oedema; cotton wool spots; hemorrhage
<b>Grade IV</b>	Papilloedema with associated Grade III changes.

*Keith Wagener Classification of Hypertensive Retinopathy*

## 3. Results

A total of 100 patients were examined; 65 % of cases were un-booked (had no prior antenatal checkup). The mean age of patients was  $25.7 \pm 6.2$  years (range 18-38 years). The gestation period ranged between 24 and 41 weeks. 65 (65%) were primi gravida (first time pregnant), 25 (25%) were multi gravida (2-4 pregnancies), and 10 (10%) were Grand Multi (5 or more deliveries) 38 (38%) had mild preeclampsia, 50 (50%) had moderate to severe preeclampsia and 12 (12%) had Eclampsia.

Retinal changes (hypertensive retinopathy) were noted in 60 (60%) patients (Table 1) and gravida were not associated with occurrence of retinopathy in our study. In mild preeclampsia 29% suffered Grade I retinal changes, whereas 79% moderate to severe preeclampsia patients suffered Grade II and Grade III retinal lesions indicating progressive severity of disease process.

Retinal changes	Preeclampsia(n=88)				Eclampsia(n=12)		
	Mild(n=38)		Moderate-severe(n=50)		Retinal changes	n	%
	n	%	n	%			
normal	27	71	13	26	normal	nil	Nil
Grade I	11	29	21	42	Grade I	8	66.67%
Grade II	nil	nil	15	30	Grade II	4	33.33%
Grade III	nil	nil	1	2	Grade III	Nil	Nil
Grade IV	nil	nil	nil	nil	Grade IV	nil	Nil

Table 1: Distribution of retinal changes in preeclampsia/Eclampsia

In mild preeclampsia 29% suffered Grade I retinal changes, whereas 79% moderate to severe preeclampsia patients suffered Grade II and Grade III retinal lesions, indicating progressive severity of disease process. Table II: Relationship of preeclampsia and abruptio-placentae. Of the 100 cases we encountered 8 cases with abruptio of placenta, and majority of these 7/8 (87.5%) showed Grade II and Grade III retinopathy changes, which was a significant observation.

Retinal changes	Abruptio placentae	
	N	Percentage
normal	Nil	Nil
Grade I	1	12.5%
Grade II&III	7	87.5%

Table 2: Correlation of retinal changes with abruptio placentae

Table III. Showing correlation of Retinopathy with perinatal mortality. The present study shows high incidence of perinatal mortality (81.8 %) which were associated with severe Grades of Retinopathy.

Retinal changes	Perinatal Death	
	n	Percentage (%)
Normal	nil	nil
Grade I	4	18.2%
Grade II & Grade III	18	81.8%

Table 3: Correlation of Retinal Changes with Perinatal Mortality (Maternal Outcome)

Retinal changes	Preterm(<37wks)	Term(≥ 37wks)
Normal ( n=40)	8	32
Grade I ( n=36)	29	7
Grade II & III ( n=4)	3	1
Grade IV	nil	nil

Table 4: Correlation of Retinal Changes with Preterm Delivery (Foetal Outcome)

Retinal changes	Birth weight			
	<2.5kgs		>2.5kgs	
	SGA	AGA	SGA	AGA
Normal(n=40)	3	20	nil	17
Grade I (n=40)	26	10	nil	Nil
Grade II (n=4)	4	nil	nil	Nil

Table 5: Retinal Changes and Foetal Outcome.

SGA-small for gestational age

AGA-appropriate for gestational age

Preterm delivery had high incidence in patients who suffered from retinopathy, (Table IV). All the patients who had retinal changes i.e., 44, delivered babies with birth weight<2.5kgs, 75% of them being small for gestational age. (SGA).(Table V). 26 out of 40 i.e.,

65% of patients with Grade I retinopathy had SGA babies, whereas, the incidence of SGA babies was still higher in patients, (4/4 i.e., 100%) with Grade II and Grade III retinal damage.

#### 4. Discussion

In the present study, hypertensive retinopathy changes (Grade I and II) were seen in 60% of patients with preeclampsia / Eclampsia. Majority of the patients had no antenatal check-up until they first presented with complications in the third trimester, these findings were similar as in the study by Rasdi et.al<sup>5</sup>. Retinal detachment was not seen in any of the patients in this study. Jaffe and Schatz<sup>16</sup>, found a significant relationship between reduced arteriole to vein ratio and preeclampsia, suggesting retinal vasospasm and resistance to blood flow as a possible explanation for visual symptoms. Although visual disturbances are quiet common, complete blindness is rare, with an incidence of 1–3%.<sup>6–8</sup>. Severe arteriolar spasm is the most common fundoscopic finding, occurring in 70% of preeclampsia cases.<sup>9, 15, and 22</sup>.

In the present study we interestingly found in the age group of 16-25 years 59% of the subjects having changes on direct ophthalmoscopic examination. This observation was in accordance with the findings of S.C.Reddy et.al. Who evidenced 53% in the same age group patients as ours, and in age group of 26-40 years fundal changes were found in 60.8% when compared with 56% reported by S.C.Reddy et.al.<sup>8</sup>. The present study observed the retinal changes were found in primigravida to an extent of 63.7 % where as S.C.Reddy.et.al<sup>23</sup>., observed a proportional statistics of only 55.3 % in the similar group. The multigravida exhibited retinal changes to an extent of 55% in our study, which was similar to the findings of S.C.Reddy et.al<sup>23</sup>.. Of 54.3 % in the corresponding group.

Our present study observed 72.7% of patients with 20-32wks of gestation, 55.9% with 33-36 weeks of gestation and 51.5% with 37-40 weeks of gestation had fundal changes comparable with the study of S.C.Reddy et.al., conducted at Andhra Pradesh, South India in a cross-sectional, randomized study on 200 patients. In their study retinal changes were found in 60.3% with 35-36 wks and 42% with 37-40 wks of gestation. The earlier the development of preeclampsia greater the chances of retinopathy<sup>15-18</sup>.. The fundal changes were observed more frequently in moderate to severe cases (74%) than in mild cases (29%) of Preeclampsia. S.C.Reddy ET .al<sup>23, 27</sup>. Found retinal changes in 90% of severe and 30% of mild cases of Preeclampsia. In our present study 54.5% with preeclampsia and 100% with Eclampsia had fundal changes. Hallum made similar observations, among the 38 cases of mild preeclampsia, 29% had retinal changes which were all Grade I changes. In cases of moderate to severe preeclampsia 26% had normal fundus, 42% had Grade I, 30% had Grade II and 2% Grade III. None of the patients had Grade IV changes and retinal detachment. There was no significant difference in the incidence of retinal changes age wise or parity wise, but they were frequently seen in patients with early onset preeclampsia and severe cases of preeclampsia. When fundus examination was repeated on 10<sup>th</sup> postpartum day in patients who showed retinal changes in the ante partum period 95% of them had normal fundus in our study. Other 5% in whom the changes persisted were lost for follow up.

##### 4.1. Maternal Outcome

Out of 100 patients 8 had abruptio placentas out of which 87.5% had Grade II and Grade III retinal changes. Majority of patients were delivered by vaginal route and only 20% had LSCS out of which 40% had normal fundus and 60% had retinal changes. The study done by Dr. Binayendra Nath et.al<sup>10</sup>. Showed that caesarean section rate was 37.5% with normal fundus and 62.5% in mothers having retinal changes.

##### 4.2. Perinatal Outcome

Out of 60 patients with retinal changes, 40 had live births and 20 still births perinatal deaths occurred in 36.7%. Out of the 40 live born babies 30 had birth weight <2.5 Kg, 75% of them small for gestational age (SGA). 2 babies died in neonatal period due to complications of prematurity comparable to study done by Hemmadi et.al<sup>11</sup>., where 63.3% of babies weighed less than 2.5 Kg and Perinatal deaths accounted for 20%. It has been suggested that retinal changes in preeclampsia may indirectly indicate the level of placental vascular status and, hence, placental insufficiency and fetal birth weight.<sup>9–12</sup>. Conflicting opinions exist on whether maternal or fetal outcome is worse in patients with fundoscopic signs<sup>10</sup>. Some studies reported poor fetal prognosis, while others reported no prognostic implications on the foetus.<sup>15, 18</sup>.

Since the antenatal check up of pregnant mothers has improved very much in India, hypertension was detected early during the antenatal visits and treatment was started immediately<sup>21</sup>. This could be the probable reason for the absence of Grade IV Retinal changes and Retinal detachment in our study.

#### 5. Conclusion

Progressive fundal changes in preeclampsia indicate worsening of patho-physiological status and helps in the management. Visual disturbances are very common among pregnant women with preeclampsia/Eclampsia. Physicians should have a firm understanding of the various ocular conditions associated with these disturbances. In addition, it is very important to be vigilant about the rare and serious conditions that may occur in pregnant women with visual complaints. Prompt evaluation may be required and the immediate transfer of care of the patient may help saving the lives of both the mother and the baby.

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