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ORIGINAL ARTICLE

STUDY OF ASSOCIATION OF FUNDAL CHANGES AND FETAL OUTCOMES IN PREECLAMPSIA

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ABSTRACT: BACKGROUND: Pre eclampsia is characterized by endothelial dysfunction and vasospasm of vessels which can be observed by an ocular fundal examination. The fundus usually develops changes like hypertensive retinopathy, papilledema, exudative retinal detachment, vitreous and pre retinal hemorrhages. Retinopathy is associated with placental insufficiency and intra uterine growth retardation. **AIM**: To assess the prevalence of fundal changes in preeclampsia and to study the association between degrees of hypertensive retinopathy changes in fundus and fetal outcome. **METHODS:** 100 patients presenting at department of obstetrics and gynecology diagnosed as pre eclampsia at R. L. Jalappa hospital from December 2011-June 2013 were recruited in the study. Patient recruited underwent ocular examination using snellens chart, pupillary examination, slit lamp examination and dilated fundal examination. The retinopathy was graded according to Keith and Wagner classification. The fetal parameters considered were birth weight, APGAR score, still birth and neonatal death. **RESULTS**: Patients age ranged from 17-28 years of age with average of 23.28±3.37. Average systolic and diastolic blood pressures were 156.9±17.961 and 104.88±13.58. All patients had normal anterior segment. 98% of patients had vision of 6/6.2%of them had 6/9. Based on retinopathy classification, we found 34 patients with grade 1 and 13 patients with grade 2 hypertensive retinopathy. Only 3 patients presented with grade3 hypertensive retinopathy. There was significant association of retinopathy with proteinuria, serum uric acid levels and the fetal birth weight with p value <0.05. **CONCLUSION**: Fundoscopy of retina is a simple, non- invasive, safe and reliable procedure to interpret the vascular changes. Therefore, it may be concluded that the degree of hypertensive retinopathy in women with preeclampsia is a valid and reliable prognostic factor that gives valid prognostic information on assessment of the severity of pre eclampsia and neonatal outcome.

KEYWORDS: Pre eclampsia, fetal outcome, hypertensive retinopathy, proteinuria, serum uric acid.

INTRODUCTION: Pregnancy causes changes in the metabolism, blood circulation and the hormonal profile of the mother which in turn affects the ocular functions and can also have adverse effect on developing foetus. This study focuses to identify fundal changes occurring in pre eclampsia and any association with fetal outcome.

Pre eclampsia is one of the hypertensive disorders of pregnancy defined as hypertension and proteinuria occurring after 20 weeks of pregnancy. It affects multiple organ system that include cardiovascular changes, haematological abnormalities, neurological or cerebral manifestation, hepatic and renal impairment. Pre eclampsia and its potential impact on ocular fundus has been documented.[1,2]

Pre eclampsia is characterised by endothelial dysfunction and vasospasm of vessels in fundus.[3] The vasospasm activity can be observed by an ocular fundal examination. The fundus

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develops characteristic changes like hypertensive retinopathy, papilledema, exudative retinal detachment, vitreous and pre retinal haemorrhages and central serous chorioretinopathy. Retinopathy in pre eclampsia might be associated with placental insufficiency and intra uterine growth retardation. These changes are indicative of the progression of hypertension in the mother and foetal outcome.

As the retinal, cerebral and renal vessels are closely related to each other, the eye serves as a window to study the state of vessels in the brain and parenchyma of the kidneys. The documentation of fundal changes occurring in preeclampsia provides us with good opportunity to study the ocular changes and if any association exists in relation to foetal outcome.

It's a simple, non-invasive and cost effective procedure which could be the initial finding in an asymptomatic patient who may require immediate management which may help in saving lives of both the mother and the baby. The ocular fundus has proved to be valuable and a valid prognostic procedure on assessment of severity of pre eclampsia and neonatal outcome.[4]

MATERIALS AND METHODS: This study was conducted on patients diagnosed with pre eclampsia in the department of obstetrics and gynaecology at R. L JALAPPA HOSPITAL and RESEARCH CENTER attached to SRI DEVARAJ URS MEDICAL COLLEGE, Tamaka, olar. The duration of study was from December 2011- June 2013.Cases with pre-existing vascular/renal disease, diabetes, any underlying ocular co-morbidity like glaucoma or cataract, Cases with placental abnormalities, Cases with congenital defects in foetus and eclampsia were excluded.

Ethical clearance was obtained from institutional ethics committee. Patients who were willing to give informed written consent were included in the study. A proforma containing detailed information of each patient was designed according to study protocol. Patients underwent ocular examination including detailed clinical history on the presenting day and during antenatal follow upto 6 weeks post-partum period.

Patients advised for hospitalization were evaluated at the bedside. Patients were examined for pallor, pedal oedema, pulse, blood pressure and urine protein at the time of ocular examination. Patient's blood pressure was recorded before ocular examination and was carried out during each phase of evaluation. The selected patients retinopathy status, age, and blood pressure will be included for analysis purpose.Anterior segment was examined with torch light on the bed itself. 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.

The fundoscopic examinations of both eyes were documented. The hypertensive retinopathy was graded and staged according to KEITH WAGNER classification:[13]

Grade 1: Mild-moderate narrowing or sclerosis of the arterioles.
Grade 2: Moderate to marked narrowing of the arterioles, Local and/or generalised narrowing of the arterioles, exaggeration of the light reflex, arteriovenous crossing changes.
Grade 3: Retinal arteriolar narrowing and focal constriction, retinal edema, cotton wool spots, hemorrhages.
Grade 4: As Grade 3, plus papilledema.

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The fetal outcome was assessed under birth weight, APGAR score at 1 minute and 5th min, still birth and neonatal death. Proteinuria was tested using dipsticks method and was graded as + = 0.3gm/L, ++ =1gm/L, and +++ = 3gm/L.

STATISTICAL ANALYSIS: The demographic data was analyzed using descriptive statistics and expressed as mean ± standard deviation. Categorical data was analyzed by chi square test. P value of 0.05 or less was considered statistically significant.

RESULTS: One hundred patients with pre eclampsia, who were referred to Department of Ophthalmology, were included in this study. Detailed ocular examination including fundoscopy was done in all patients and results were interpreted.

In our study, the mean age of the patients was 23.28± 3.37 years. 88% of patients belonged between age groups of 20-29 years.48.86 % of the patients in that age group had retinopathy findings. 6% of patients belonged to patients aged above 30 years and.83.3% of them presented with retinopathy findings. 74% of patients were primigravida and 26% were multigravida.

28% of our patients complained of pedal edema. 35% patients complained of headache along with pedal edema. 13% complained of blurring of vision. All our patients had good vision on 3 month follow up. 54% had mild preeclampsia while 46% had severe preeclampsia. A mean systolic blood pressure was 156.9±17.96 and mean diastolic blood pressure was 104.88±13.58.

All our cases had normal anterior segment. Out of 100 cases, 50% of cases had no retinopathy findings. Thirty four (34%) patients had grade I hypertensive changes. Grade II and Grade III changes were seen in 13% and 3% respectively. The percentage of patients developing retinopathy due to preeclampsia increased as we moved from mild preeclampsia group to severe preeclampsia. Our study had retinal hemorrhages, a: v nipping of blood vessels, silver wiring, and cotton wool spots. We did not encounter any cases of retinal detachment, vitreous hemorrhage or cortical blindness.

All patients had proteinuria of varying severity ranging from 1+ to 4+ with patients with severe proteinuria of 4+ having greater chance of developing retinopathy. It was significantly associated with retinopathy with p value <0.05. In this study, it was found that the value blood urea ranged from 10-34 mg% with mean value of 18.7 and 19.7 mg% in mild and severe preeclampsia. Serum uric acid levels ranged from 2.5- 11.0 in mild preeclampsia and 2.7-9 mg% in severe preeclampsia is also increased. The mean value was 5.76mg% and 5.60 mg%.

The fetal outcomes to pre eclamptic mother were also assessed. The mean birth weight was 2300.20±616.75. Fetal birth weight was less than 2500g of 63 of mothers, out of which 69 mothers, 39 of them had retinopathy changes. Birth weight and retinopathy were significantly associated with p value of 0.002.

Variables	Mean±SD
Age	23.28± 3.37
Systolic blood pressure	156.9±17.961
Diastolic blood pressure	104.88±13.58
Blood urea levels	19.29±5.87
Serum uric acid levels	5.69±1.77

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Variables	Mean±SD
Birth weight	2300.20±616.75
Apgar score at 1 min	6.63±2.34
Apgar score at 5th min	8.5±2.95

There was statistical association between retinal changes and blood pressure, proteinuria and fetal outcome. The association between retinal changes and different parameters is shown in tables:

Proteinuria	No. of patients	Percentage	Retinopathy (%)	P value
+	65	65%	30(46.8%)	
++	25	25%	10(40%)	
+++	7	7%	7(100%)	**0.03**
++++	3	3%	3(100%)	

Table 13: Proteinuria and association with retinopathy

Grades	No. of Patients	Percentage
No retinopathy changes	50	50%
Grade 1 retinopathy	34	34%
Grade 2 retinopathy	13	13%
Grade 3 retinopathy	3	3%
Grade 4 retinopathy	0	0

Table 9: Fundus changes according to grades of retinopathy

DISCUSSION: Mean age of the patients in our study was 23.28± 3.37 years and 88% of the patients were between the age groups of 20-29 and 6% were aged between 30-35 years who had retinopathy findings of 48.8% and 83.3% respectively. In Tadin et al study, out of 40 women with pre-eclampsia 45% showed abnormalities of the fundus. The average age was 29.1 years.[4] Studies have shown those in younger and older age groups are associated with higher risk factors for developing pre eclampsia.[5]

In our study, 35% of patients had headache as one of the complaints while 14% of patients complained of visual symptoms like blurred vision and diplopia. In our study no patients presented with symptoms of flashes of light or black spot in visual field. Visual disturbances such as scotoma, diplopia and dimness of vision are seen in 30-50% of patients with eclampsia and 20-25% of patients with pre eclampsia.[6]OberRR have reported that headache has long been known to be harbinger of eclamptic convulsions.[7] Belfort MA concluded that headache is most common symptom among patients with preeclampsia.[8]

In our study there was association between blood pressure and retinopathy changes, especially in severe preeclampsia patients. This was also observed in studies by Tandin et al and Vanden Born et al.[4]

Our data contradicted Gupta et al, Kaliaperumal et al and Rasdi et al, studies who reported that severity of retinopathy might be independent of systemic blood pressure.[9, 10]

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Visual system are affected in 30-100% of patients with preeclampsia.[11] Visual symptoms are few in patients with preeclampsia and often absent unless macula is involved.[11] In our study, 98% of patients had visual acuity of 6/6 and 2% had vision of 6/9. All the patients gained vision of 6/6 during postnatal follow up. There was no patient with visual acuity of 6/12 or worse during all assessment period.

In Karki e al study, 153 cases did not show any signs of visual disturbances. Most of them had visual acuity between 6/6 to 6/9.[12] In A.R Rasdi study, 96.7% of patients had visual acuity of 6/6 in both eyes and 3.3% had visual acuity of 6/9.[13]

Literature studies have considered the progression of retinal vascular changes a sign of increasing severity of preeclampsia and have correlated with fetal mortality. Our findings support the preexisting data on fundoscopic signs of hypertensive disorders in pregnancy.

Study	Prevalence rate
Tadin et al	45%
Rasdi et al	21.5%
Karki et al	13.7%
Reddy et al	53.4%
Saglireddy study	59%
Our study	50%

Comparison of prevalence of retinal changes in pre eclampsia in other studies

In our study, 50% of patients with pre eclampsia had retinal changes, which correlates with studies reported by Sunness JS and Beck RW et al in which retinal changes were observed in 40-100% patients with preeclampsia.[14] In our study 34% of patients belonged to grade 1 hypertensive retinopathy, followed by 13% patients of grade 2 hypertensive retinopathy and 3 patients with grade 3 retinopathy.

In our study, majority of the patients had arteriolar narrowing which were supported by studies conducted by Hallum where the most common ocular finding was constriction of arterioles occurring in approximately 60% of patients with pre-eclampsia.[15] Beck R W reported hallmark of abnormal ocular findings is terminal arteriolar vasospasm.[16] Wagener reported spastic lesions of retinal arterioles in 70% cases of pre eclampsia.[17] Arteriolar narrowing of generalized nature is seen later and may resolve following pregnancy.[18] Our study co-relates with previous study which states arteriolar narrowing is the most common fundus finding in patients with pre eclampsia.[19]

Our study revealed retinal hemorrhages, a: v nipping, silver wiring of vessels and cotton wool spots. The absence of hard exudates in this present study is supported by Jaffe and Schatz.[12] Presence of multiple hard exudates in retina may indicate albuminuric retinopathy and possibility of damage of the kidney. Jaffe and Schatz from USA reported significant co relation between the reduction in a: v ratio, number of focal arteriolar constrictions and severity of preeclampsia.[12] Rasdi et al study reported retinal changes like arteriolar narrowing, cotton wool spots, retinal hemorrhages and serous retinal detachment.

In this present study we did not find any case of serous retinal detachment or other conditions like cortical blindness, purtschers like retinopathy. Retinal detachment was seen in 1-2% of all patients with pre eclampsia.[20]

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Studies by Prado and Reddy et al did not report cases with vitreous hemorrhage, serous retinal detachment, purtscher like retinopathy or cortical blindness.[21] Reddy et al study also reported presence of macular edema or papilledema or retinal detachment which are warning signs for termination of pregnancy to save vision of the mother.[21]

Proteinuria is an important sign of pre eclampsia. The minimum criteria for diagnosis of preeclampsia are hypertension and proteinuria which may be minimal or severe.[22]in our study, all 100 patients had proteinuria and it ranged from 1+ to 4+. Patients with severe proteinuria (4+) have greater chance of developing retinopathy than less severe proteinuria. There is significant association was found between retinopathy grade and proteinuria with P value of 0.03.

In present study, blood urea levels in mild pre-eclampsia group ranged from 10 to 34 mg% with an average of 18.7 mg % whereas in severe pre eclampsia it ranged 10 to 34 mg% with an average value of 19.7 mg%. The result of our study correlates with the studies by Tandon and Kishore, the increasing level of mean blood urea level is seen with increasing severity of preeclampsia.[23] In their study the blood urea level in mild preeclampsia ranged from 19.5 to 30.0 mg% with an average of 24.6 mg% while in severe preeclampsia group it ranged from 24.0 to 103.0 mg%.[23]

Knowledge of blood urea level offers information which is useful in complicated cases of toxemia. The rising level is almost always associated with increasing severity of toxemia and falling levels with improvement. In complicated cases this additional means of assessment can be of considerable assistance in management.[23]

In the present study, the mean value of blood uric acid in mild and severe preeclampsia is 5.76 mg% and 5.60 mg% respectively. There was an increase in the mean value of blood uric acid with increase in severity of preeclampsia. In study by Tandon and Kishore, serum uric acid level in mild preeclampsia ranged from 4.6 to 6.4 mg% with an average of 5.2 mg% whereas in severe preeclampsia it ranged from 4.2 to 8.0 mg% with a mean value of 5.63 mg%. Our study is also supported Gupta et al study which reported that retinopathy was found to be significantly associated only with serum uric acid levels among all lab parameters. They showed retinal changes showed a positive association with uric acid.[24]

Thus, it may be inferred that there is a clinico-biochemical correlation with respect to blood uric acid levels and severity of pre eclampsia and that blood uric acid level are of considerable value in predicting severity of pre eclampsia.

Our study showed that presence of fundus changes in a patient of pre eclampsia was not significantly associated with fetal outcomes in terms of APGAR score at 1 minute, still birth and intra uterine death. There was significant association between birth weight and fundal changes. Four intrauterine deaths and eight still born were reported, but they were not associated to retinopathy changes.

Karki et al showed presence of fundal changes in pregnancy was not associated significantly with fetal outcomes in terms of gestational age, APGAR score 1, still birth and neonatal death but it was associated with low birth weight and they assessed the fetal outcome in these patients and concluded that retinal and optic nerve head changes were associated with low birth weight.[21] They also reported that choroidal and optic nerve head changes were associated with low APGAR score.

They concluded that choroidal and optic nerve head changes were associated with low APGAR score.[22]Our study contradicted Gupta et al study which reported that the outcome of

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pregnancy in terms of fetal birth weight was inversely associated with the severity of retinopathy. They also stated that low birth weight was due to intrauterine growth retardation.[23]

The severity of maternal retinopathy may reflect the state of the placental vasculature and hence might correlate with the severity of preeclampsia and fetal morbidity. Study done by Oliver M observed that changes that can be observed in the retinal vasculature like vasospasm may indirectly indicate the level of placental vascular status and hence placental insufficiency and fetal birth weight.[24]

CONCLUSION: Our study was conducted on 100 diagnosed cases of preeclampsia. Fundoscopy of retina is a simple, non- invasive, safe and reliable procedure to interpret the vascular changes.

Our study revealed that a retinopathy change was more common in primigravida and older age group. Headache was the most common symptom encountered. Systolic and diastolic blood pressures were both significantly associated with retinopathy.

Our study reported that common retinal findings was grade 1 hypertensive retinopathy and generalized arteriolar narrowing. Serum uric acid was significantly associated with retinopathy findings. The retinal changes were more often seen in patients with severe hypertension, severe proteinuria and severity of pre eclampsia in our study. Retinal changes was not associated with APGAR score at 1 min but was significantly associated with fetal birth weight.

Our findings suggest the degree of hypertensive retinopathy in women with preeclampsia is a valid and reliable prognostic factor that gives valid prognostic information on assessment of the severity of pre eclampsia and neonatal outcome.

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