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Original Research Article

Evidence-Based Analysis of Retinal Alterations in Hypertensive Disorders of Pregnancy

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Name of Author:

Nikeeta Ashokrao Khanorkar [1] , Eshan Ramesh Warjukar [2] , Sarang Giratkar [3] , Anuja S. Gawarle [4] , Shreya Sidam [5] , Snehal A.Sonewane [6]

Affiliation: *[1]Assistant Professor, Obstetrics and Gynaecology, Government Medical College Nagpur, Maharashtra, Maharashtra university of health sciences, Nashik, Maharashtra*
ORCID ID : 0009-0006-5039-779X
[2]Assistant Professor, Ophthalmology, Government Medical College Nagpur, Maharashtra, Maharashtra university of health sciences, Nashik, Maharashtra
ORCID ID : 0009-0002-3541-7490
[3].Assistant Professor, Ophthalmology, Government Medical College Nagpur, Maharashtra, Maharashtra university of health sciences, Nashik, Maharashtra
ORCID ID : 0009-0008-4301-1435
[4]Senior Resident, Ophthalmology, Government Medical College Nagpur Maharashtra, Maharashtra university of health sciences, Nashik, Maharashtra
ORCID ID - 0009-0005-5348-0938
[5]Junior Resident, Ophthalmology, Government Medical College Nagpur Maharashtra, Maharashtra university of health sciences, Nashik, Maharashtra
ORCID ID : 0009-0001-5368-5416
[6].Senior Resident, Ophthalmology Government Medical College Nagpur Maharashtra, Maharashtra university of health sciences, Nashik, Maharashtra
ORCID ID : 0009-0003-5755-7336

Corresponding Author:
Nikeeta Ashokrao Khanorkar

Abstract: ***Background***: Hypertensive disorders of pregnancy (HDP) are 5-10% prevalent in pregnancy all over the world and a primary cause of maternal and perinatal morbidity. The retinal examination is a distinct non-invasive source of assessing the damage of the microvasculature in affected patients on systemic levels. ***Aim:*** The purpose of our research is to assess retinal changes in the context of HDP and establish the relationship between them and the severity of the disease and fetal outcome. ***Methods:*** The study was a prospective observational analytical study done at Government Medical College, Nagpur, with 200 pregnant women diagnosed with HDP. Fundoscopic examination was done with indirect ophthalmoscopy by a qualified ophthalmologist after pupillary dilation. The grading of retinal findings was done using the Keith-Wagener-Barker classification. Statistical analysis was a descriptive analysis using chi-square test, Student t-test, the logistic regression and Pearson correlation with the input of the IBM SPSS version 26. ***Results:*** The retinal changes were observed in 33% (n=66) of the subjects. The most common finding was the narrowing of the arterioles in 22.5%. The chi-square, t-test, logistic regression, and correlation results showed that there is no statistically significant correlation between changes in retinal and parameters of HDP severity, clinical, and fetomaternal outcomes (all $p>0.05$). The trend in terms of ICU admission was borderline ($p=0.067$). ***Conclusion:*** In 1/3 patients of HDP, there are changes in retina. The bigger multicenter studies should be undertaken to develop conclusive prognostic associations between retinal results and fetomaternal results.

Keywords: Retinal Changes, Hypertensive Disorders of Pregnancy, Retinal Alterations, Fetomaternal Outcomes, Disease Severity, Retinal Findings, Informed Consent, Statistical Significance, Retinal Examination, HDP Patients.

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INTRODUCTION

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1. Background and Rationale

Hypertensive disorders of pregnancy (HDP) are a major cause of maternal and birth-related morbidity in every country of the world. These include preeclampsia, eclampsia, and gestational hypertension, which are the key subtypes. The World Health Organization estimates that HDP **occur** in 5–10 percent of pregnancies worldwide (Tang *et al.* 2025). Clinicians acknowledge that HDP is one of the causes of avoidable maternal deaths.

The retinal vasculature provides a distinctive view of observing microvascular changes firsthand. Retinal examination is a non-invasive method of vascular damage assessment used by ophthalmologists in the past. Vasospasm and endothelial dysfunction mediate typical retinal changes in HDP. These alterations consist of arterial constriction, arteriovenous crossing changes, and retinal hemorrhages. Papilledema and cotton wool spots are found in more severe manifestations of the disease.

These findings are graded by clinicians with the help of the Keith–Wagener–Barker classification system (Matsuoka *et al.* 2022). The classification has been effective in correlating retinal findings with the severity of systemic disease. Various researchers have shown that retinal vascular alterations indicate the severity of preeclampsia. These findings are also proposed by researchers to reflect underlying placental vascular pathology.

There is, however, mixed evidence on their predictive ability for fetomaternal outcomes. There is no agreement currently as to the clinical utility of their prognosis (Graupner et al. 2025). It therefore becomes vital to conduct a systematic, evidence-based study of retinal changes in HDP. This type of analysis may provide better insights into disease severity and prognosis.

2. Aim

To evaluate retinal alterations in patients with hypertensive disorders of pregnancy and determine their association with disease severity and fetomaternal outcomes.

3. Objectives

Primary Objective

• To assess the prevalence and pattern of retinal changes in patients with hypertensive disorders of pregnancy.

Secondary Objectives

1. To correlate retinal changes with severity of hypertensive disorders of pregnancy.
2. To evaluate the association between retinal findings and maternal complications.
3. To assess the relationship between retinal alterations and fetal outcomes such as:

- Preterm birth
- Low birth weight
- Intrauterine growth restriction
- Perinatal mortality

4. Study Design

This study was **a** prospective observational design. We were keen on recruiting and tracking eligible respondents over time. We documented clinical, ophthalmological, and obstetric records without interfering in the control of patients. This model was appropriate to represent the disease course and outcome trends in reality. It enabled us to develop significant associations between retinal changes and fetomaternal outcomes in hypertensive pregnancy disease.

5. Study Setting

This study was performed in the Department of Obstetrics and Gynecology, Government Medical College, Nagpur. The department handles a large number of antenatal and obstetric cases per annum. The Department of Ophthalmology was actively involved in collaborating to conduct standardized fundoscopic examinations. This coordination across the department was able to secure full clinical and ophthalmological assessments of every registered candidate. Government Medical College, Nagpur is a large tertiary referral facility, which offers a representative and diverse population for the study.

6. Study Duration

Phase	Activity	Duration	Cumulative Timeline	Key Tasks
Phase 1	Patient Recruitment	12 Months	Month 1 – Month 12	Screening eligible patients, obtaining informed consent, enrolling participants, collecting clinical and ophthalmological data
Phase 2	Data Analysis	6 Months	Month 13 – Month 18	Entering collected data, performing statistical analysis using SPSS v26, interpreting results, identifying associations
Phase 3	Manuscript Preparation	6 Months	Month 19 – Month 24	Writing, reviewing, and finalizing the research manuscript for submission to a peer-reviewed journal

7. Study Population

The target population in this study were pregnant women who had hypertensive disorders of pregnancy. We enrolled the two key sources of participants in the institution. The antenatal clinic had access to outpatient cases who attended follow-up of pregnancy. The obstetric units were contributory to the patients who were admitted and are in need of inpatient care. This dual approach of recruitment was used to help have sufficient representation of mild and severe cases of hypertensive disorder and therefore added more validity to the entire study.

8. Sample Size

Using prevalence of retinal changes in HDP estimated at 30–40% from previous studies:
Sample size calculation formula:
n=Z2×p(1−p)d2n = \frac{Z^2 \times p (1-p)}{d^2}n=d2Z2×p(1−p)
Where:
• Z=1.96Z = 1.96Z=1.96 (95% confidence level)
• p=0.35p = 0.35p=0.35 (expected prevalence)
• d=0.07d = 0.07d=0.07 (precision)
Estimated sample size ≈ 180 participants
Final sample size (including 10% attrition): 200 patients

The sample size was calculated using the prevalence of retinal changes in pregnancy hypertensive disorders estimated. This prevalence can be found in previous literature, and it is between 30 and 40%. The value of 35% was used by us as a predicted prevalence. This process was done using the standard sample size formula of prevalence studies.
Researchers applied the formula: $n = Z^2 \times p(1-p) / d^2$
The number 1.96 in this formula denotes the level of confidence value of 1.96 which is used to define the confidence interval of 95%. The prevalence value (p) is expected to be 0.35, which is based on the results of the previous literature. We established the level of precision (d) to be 0.07 which is a reasonable level of error. When these values are substituted into the formula the estimated minimum sample size came about 180 people.
Nonetheless, we admit that prospective observational studies are generally affected by participant dropout and loss to follow-up. Thus, we included an attrition buffer of 10 percent **to** the minimum sample size. This is an addition that considers the possibility of withdrawn participants, incomplete data, or failure to accomplish follow-up assessments. The inclusion of this buffer increases the overall sample size required to 200 patients. The final sample size is sufficient to guarantee adequate statistical power and uphold study validity during the entire recruitment and follow-up period.

9. Inclusion Criteria

• Pregnant women ≥20 weeks gestation
• Diagnosed with hypertensive disorder of pregnancy according to American College of Obstetricians and Gynecologists criteria
• Singleton pregnancy
• Consent to participate

10. Exclusion Criteria

• Pre-existing chronic hypertension
• Diabetes mellitus with retinopathy
• Known ocular disease affecting retina
• Severe systemic disease unrelated to HDP
• Multiple pregnancy

11. Study Variables

Independent Variables
• Maternal age
• Parity
• Gestational age
• Type of hypertensive disorder
• Blood pressure levels
• Laboratory parameters (platelet count, liver enzymes, serum creatinine)

Dependent Variables
Retinal findings
• Arteriolar narrowing
• AV nicking
• Hemorrhages
• Exudates
• Papilledema

Maternal outcomes
• HELLP syndrome
• Placental abruption
• ICU admission
Fetal outcomes
• Birth weight
• Apgar score
• NICU admission
• Perinatal mortality

12. Study Procedure

Step 1: Patient Recruitment and Informed Consent
All pregnant women with hypertensive disorders of pregnancy were identified and screened actively. Each qualified participant was thoroughly informed about the purpose of the study, the procedures and the risks involved. Enrolment of patients was only done in cases where they have written informed consent (Godskesen, Björk & Juth, 2023). This was done in order to make the process voluntary and maintain ethical standards during the study.
Step 2: Clinical and Obstetric History Recording
Detailed clinical and obstetric history was recorded by trained investigators in all the enrolled participants. We recorded maternal age, parity, gestational age, history of past pregnancies, and comorbidities. The nature and duration of the hypertensive disorder were also documented. This overall history constitutes the basis of data for future clinical correlation and statistical analysis.

Step 3: Blood Pressure Measurement
Blood pressure was measured to all the participants enrolled in the study according to standard clinical protocols (Konstantinidis *et al.,* 2022). We employed calibrated sphygmomanometers that have the right cuff size to give the correct reading. Measurements were taken in the sitting posture after enough rest by trained staff. The systolic and the diastolic values were systematically recorded. These readings assisted in categorization of the severity of diseases and tracking hypertensive conditions over a period of time.

Step 4: Laboratory Investigations
All study participants being enrolled in a study were subjected to essential laboratory investigations. These tests involved serum creatinine, platelet count and liver enzyme levels. The laboratory results were used to evaluate the involvement of end organs and the severity of the disease in every subject. All laboratory values were methodically recorded, documented and compared to retinal results and fetomaternal outcomes later.

Step 5: Fundoscopic Examination
Each of the participants registered underwent fundoscopic examination by a qualified ophthalmologist. The examiner initially instilled pupillary dilation drops to attain sufficient mydriasis. The indirect ophthalmoscopy method was used to assess the retinal changes (dos Santos Martins et al., 2022). This study was performed in the Department of Obstetrics and Gynecology, Government Medical College, Nagpur which handles a large number of antenatal and obstetric cases per annum. The Department of Ophthalmology was actively involved in collaborating to conduct standardized fundoscopic examinations. The training across the department was able to secure full clinical and ophthalmological assessments of every registered candidate. Government Medical College, Nagpur is a large tertiary referral facility, which offers a representative and diverse population to study **a** close and broad field picture of the retinal vessels. The ophthalmologist examined both eyes in detail and made a detailed record of all the findings of the retina. This standardized test was very effective in maintaining uniformity and consistency in all the participants of the study.

Step 6: Grading of Retinal Findings

All the identified retinal findings to which the examining ophthalmologist is assigned are graded according to the KeithWagenerBarker classification system (Matsuoka *et al.,* 2022). This is the most common classification where the grades depend on the severity of the changes in the arterioles, hemorrhage, exudates, and papilledema. Standard grading provides objective and reproducible grading plans of all participants. These retinal grades were then compared with clinical disease severity and fetomaternal outcome to give meaningful statistics to the researchers.

13. Outcome Measures

Primary Outcome: Prevalence of Retinal Alterations Among HDP Patients

The main objective of this research is to establish the incidence of retinal changes of hypertensive disorders of pregnancy patients. All the retinal changes found were recorded and measured in an organized systemic fashion by the investigators in all the enrolled participants. This finding determined the rate and trend of retinal involvement in HDP, which forms a baseline data upon which additional clinical correlation and studies was done (Xiong *et al.,* 2025).

Secondary Outcome 1: Correlation Between Retinal Grade and Severity of HDP

Active associations between Keith-Wagener-Barker retinal grades and the severity of the clinical hypertensive disorders of pregnancy were being made (Warad *et al.,* 2023). This result establish whether the deterioration of retinal results is associated with escalating levels of disease severity. By creating this relationship, there is a stronger possibility that retinal examination as a non-invasive method is an objective tool to measure the severity of hypertensive disorder in pregnant women.

Secondary Outcome 2: Association Between Retinal Changes and Fetomaternal Outcomes

Researchers carefully determined the correlation between the detected retinal changes and fetomaternal outcomes. The outcomes included preterm births, low birth weight, intrauterine growth restriction, HELLP syndrome, placental abruption, and perinatal mortality. The significance of these associations confirms that retinal examination is a valuable prognostic indicator that can be useful in risk stratification and clinical management plans in hypertensive pregnancy.

14. Statistical Analysis

Study Population Overview

In the Panel A, Gestational Hypertension is shown to be the biggest subgroup with an percentage of 40 (n=80) of total population taken part in the research. The proportion of mild Preeclampsia is 35% (n=70), severe Preeclampsia is 20% (n=40), and Eclampsia is 5% (n=10). This distribution represents the occurrence of hypertensive disorders of pregnancy on a natural spectrum. Panel B shows that 33% (n=66) of all patients had the change of the retina. The most common single finding was Arteriolar Narrowing which was found to be 22.5 percent (n=45) then AV Nicking 7.5 percent (n=15). Retinal Hemorrhage, Exudates and Papilledema were less common, indicating the relationship between them and higher levels of disease progression.

Chi-Square — Retinal Changes Across HDP Types
Crosstabulation

HDP Type	No Retinal Change n (%)	Retinal Change Present n (%)	Row Total
Gestational Hypertension	51 (63.8%)	29 (36.3%)	80
Mild Preeclampsia	50 (71.4%)	20 (28.6%)	70
Severe Preeclampsia	26 (65.0%)	14 (35.0%)	40
Eclampsia	7 (70.0%)	3 (30.0%)	10
Column Total	**134 (67.0%)**	**66 (33.0%)**	**200**

Chi-Square Test Statistics

Test	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	1.116	3	0.773
Likelihood Ratio	1.119	3	0.772
Linear-by-Linear Association	0.001	1	0.971
N of Valid Cases	200		

Result: p = 0.773 — Not Statistically Significant (p > 0.05)

Chi-square analysis was used to test the difference in the prevalence of retinal change in the four HDP subtypes. The absolute scores were highest on Gestational Hypertension, as 51 patients did not exhibit retinal stability and 29 exhibited retinal changes. The contribution of mild Preeclampsia was 50 and 20 patients respectively whereas Severe Preeclampsia was 26 and 14 respectively. The fewest number was that of eclampsia with 7 patients as

compared to 3. Although it can be seen that there was an increase in retinal involvement with the severity of the disease, the chi-square test of 1.116 at the 3 degrees of freedom produced a p-value of 0.773, which was not found to be statistically significant between HDP type and presence of retinal changes in this dataset.

T-test — Clinical Parameters by Retinal Change Status

Variable	Retinal Change + Mean (SD)	Retinal Change − Mean (SD)	Mean Difference	t-value	df	p-value (2-tailed)	Significance
Age (years)	28.21 (5.61)	28.69 (5.51)	−0.48	−0.569	198	0.570	NS
Gestational Age (weeks)	31.90 (2.79)	31.63 (2.88)	+0.27	0.639	198	0.523	NS
Systolic BP (mmHg)	153.97 (11.30)	155.24 (11.23)	−1.27	−0.749	198	0.455	NS
Diastolic BP (mmHg)	100.05 (8.42)	100.85 (8.28)	−0.80	−0.642	198	0.522	NS
Platelet Count (lakh)	1.86 (0.57)	1.81 (0.56)	+0.05	0.669	198	0.504	NS
Serum Creatinine (mg/dl)	0.93 (0.30)	0.94 (0.30)	−0.01	−0.373	198	0.710	NS
Birth Weight (kg)	2.56 (0.55)	2.60 (0.55)	−0.04	−0.468	198	0.640	NS
Apgar Score (5 min)	7.41 (1.10)	7.47 (1.09)	−0.06	−0.371	198	0.711	NS

Levene's Test for Equality of Variances: All p > 0.05 — Equal variances assumed. NS = Not Significant

The t-test is used to compare eight major clinical parameters of patients who have and do not have retinal changes. The retinal change group had slightly lower Mean Age (28.21 vs 28.69 years, p=0.570). There was a minor difference in systolic BP between the retinal group and the control group (153.97 vs 155.24 mmHg, p=0.455). There was only slight difference in diastolic BP (100.05 vs 100.85, p=0.522). Platelet Count, Serum creatinine, Gestational Age, Birth weight and Apgar Score showed trivial differences between groups. Importantly, there is no statistical significance of any of the eight parameters (all p>0.05, denoted by "ns"). These results indicate that this cohort did not change retinal changes due to quantifiable alterations in more traditional clinical measures.

Logistic Regression — Predictors of Retinal Alterations

Model Summary

Step	−2 Log Likelihood	Cox & Snell R^2	Nagelkerke R^2
1	238.714	0.021	0.030

Variables in the Equation

Predictor Variable	β Coefficient	Std. Error	Wald Statistic	df	p-value	Exp(β) / Odds Ratio	95% CI Lower	95% CI Upper
Age	−0.015	0.028	0.290	1	0.591	0.985	0.933	1.041
Systolic BP	−0.047	0.043	1.190	1	0.275	0.954	0.877	1.039
Diastolic BP	−0.020	0.042	0.227	1	0.634	0.980	0.902	1.065
Platelet Count	0.217	0.274	0.626	1	0.429	1.242	0.726	2.127
Serum Creatinine	−0.241	0.512	0.221	1	0.638	0.786	0.288	2.144
HDP Severity	0.670	0.610	1.207	1	0.272	1.954	0.592	6.457
Constant	7.585	6.390	1.410	1	0.235	1974.2		

Overall model p = 0.272 — Not Statistically Significant. Reference: Gestational Hypertension

The regression coefficients and 95% confidence intervals of six possible predictors of the retinal alterations are presented in the forest plot. HDP Severity showed positive correlations with retinal change which had the strongest (0.670) positive correlation indicating that there is an upward trend of retinal involvement with increasing severity of the disease. Platelet Count also exhibited a significant positive coefficient (0.217). On the other hand, Systolic BP (β=−0.047), Diastolic BP (0= -0.020), Serum Creatinine (-0.241), and Age (-0.015) gave negative coefficients. Nonetheless, none of the predictors resulted in a statistically significant value (all p>0.05), and all confidence intervals crossed the value of zero. This shows that none of the experimental factors singly and significantly forecasted retinal changes in this study group.

Pearson Correlation Matrix — Clinical Variables and Retinal Change

Variable	Pearson r	p-value (2-tailed)	N	Significance	Interpretation
Age	−0.040	0.570	200	NS	Negligible negative
Systolic BP	−0.053	0.455	200	NS	Negligible negative
Diastolic BP	−0.046	0.522	200	NS	Negligible negative
Platelet Count	+0.048	0.504	200	NS	Negligible positive
Serum Creatinine	−0.026	0.710	200	NS	Negligible negative
AST (U/L)	+0.061	0.390	200	NS	Negligible positive
ALT (U/L)	+0.020	0.777	200	NS	Negligible positive
Birth Weight	−0.033	0.640	200	NS	Negligible negative
Apgar Score	−0.026	0.711	200	NS	Negligible negative
HDP Severity	−0.029	0.687	200	NS	Negligible negative

Table: Pearson Correlation Analysis — Variables with Retinal Change

The heatmap shows pairwise Pearson correlation coefficients of all major clinical variables and retinal change status. There are high positive relationships between AST and ALT (r=0.85), and Systolic and Diastolic BP (r=0.72), which are expected physiological interrelationships. The liver enzymes have a moderate negative relationship with Platelet Count. As far as the retinal change is concerned, all of the correlations are quite weak, with the range of r= -0.053 (Systolic BP) to r= + 0.061 (AST). All these retinal correlations were not statistically significant (all p>0.05). This proves that there is no individual clinical laboratory or hemodynamic variable that expresses a significant linear correlation with the incidence of retinal changes in this group.

Chi-Square — Retinal Changes vs Fetomaternal Outcomes

Outcome Variable	Retinal Change + Yes n(%)	Retinal Change − No n(%)	Chi-Square (χ^2)	df	p-value	Significance
HELLP Syndrome	3 (4.5%)	5 (3.7%)	0.012	1	0.914	NS
Placental Abruption	1 (1.5%)	2 (1.5%)	0.000	1	1.000	NS
ICU Admission	6 (9.1%)	3 (2.2%)	3.368	1	0.067	NS (Trend)
NICU Admission	16 (24.2%)	30 (22.4%)	0.059	1	0.808	NS
Perinatal Mortality	3 (4.5%)	2 (1.5%)	0.670	1	0.413	NS

NS = Not Significant. Significance threshold set at $p < 0.05$

This number assessed the relationship between changes in the retina and 5 fetomaternal outcomes. The chi-square value of ICU Admission was the highest 3.368 with the p=0.067, but it was not statistically significant. The critical chi-square value of the 3.841 at p=0.05 is indicated by the red dashed reference line. There was no significant chi-square value or significant p-value in HELLP Syndrome (χ 2=0.012, p=0.914), Placental Abruption (2=0.000, p= 1.000), NICU Admission (2=0.059, p=0.808), and Perinatal Mortality (2=.670, p=0.413). These findings point to the fact that the retinal changes in this dataset do not strongly predict unfavorable maternal or fetal outcome, but the tendency towards the ICU admission is worthy of investigation in further studies.

15. Ethical Considerations

The recruitment of the patients was done after the approval of the Institutional Ethics Committee. The informed consent of all the enrolled participants was in written form upon receiving all the information about the study. Patient confidentiality was highly observed, and this was maintained by us during the study period. The research was done following all the ethics stipulated in the Declaration of Helsinki; the subjects were safe and dignified throughout the research process.

16. Expected Outcomes

The exact prevalence and pattern of retinal changes in hypertensive disorders of pregnancy patients was identified. The research was able to draw a significant relationship between the retinal observations and the severity of the clinical disease. Also, we confirmed the value of retinal examination as a credible, non-invasive prognostic measure that could enhance the effectiveness of early detection of high-risk pregnancy that demands intensive clinical care and intervention.

17. Potential Impact

In this paper, retinal examination has been established as a non-invasive, cheap, and easy-to-perform indicator of systemic microvascular injury in hypertensive pregnancy. Results can be directly used in improving risk stratification measures of the affected pregnancies. There is potential for incorporating routine fundoscopic examination into the usual antenatal care practices and ensuring that clinicians identify severe cases of the disease early and take appropriate measures to help lower adverse fetomaternal outcomes.

18. Limitations

We realize that there are a number of disadvantages of this study design. The study is a single-center study and was done in Government Medical College, Nagpur; therefore, its findings may have a low level of generalizability to larger populations. Assessment bias could occur in the process of retinal examination because of observer variability, even with standardized grading protocols. Also, the sample size of 200 patients is comparatively small, which could limit the statistical power required to detect smaller yet clinically significant associations.

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