Clinical retinal findings during the immediate postpartum period in patients with preeclampsia in a Mexican hospital

Manifestaciones clínicas retinianas durante el puerperio inmediato en pacientes con preeclampsia en un hospital de México

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Abstract

Introduction and objective: Hypertensive disorders during pregnancy are one of the main obstetric complications in many countries. In preeclampsia, patients may perceive optical phenomena that can predict the evolution from preeclampsia to eclampsia, because ophthalmic changes manifest as a hypertensive retinopathy. The aim of this study is to describe the clinical retinal findings in patients diagnosed with preeclampsia in the immediate postpartum by indirect ophthalmoscopy.

Material of methods: Descriptive, observational, prospective and cross-sectional study performed from August to December 2014, in patients diagnosed with preeclampsia admitted to a mother and child hospital, in the immediate postpartum, who underwent ophthalmic examination by indirect ophthalmoscopy. Fundus eye examination was performed describing clinical findings, and hypertensive retinopathy grading was done if present. Also, we evaluated a possible correlation between different factors that may influence the degree of hypertensive retinopathy. **Results:** Twenty-six patients with severe preeclampsia, 5 patients with mild preeclampsia and 1 patient with incomplete HELLP syndrome were examined, with a total of 32 patients enrolled. The prevalent clinical signs observed were vasospasm and arteriovenous crossings. We observed grade II hypertensive retinopathy in 34.61% of patients diagnosed with severe preeclampsia. Age was the main factor correlated with the degree of hypertensive retinopathy, with statistical significance ($p = 0.044$). **Conclusions:** Different grades of hypertensive retinopathy (grade I, II and III) were observed in patients with severe preeclampsia. No patients showed hypertensive neuropathy or choroidal ischemia associated with serous retinal detachment. Age is the main factor associated with the severity of hypertensive retinopathy.

Key words: Preeclampsia. Hypertensive retinopathy. Vasospasm. Retinal ischemia.

Resumen

Introducción y objetivo: Los trastornos hipertensivos durante la gestación son algunas de las principales complicaciones obstétricas en muchos países del mundo. En la preeclampsia, las pacientes pueden percibir fenómenos ópticos que pueden predecir la evolución de preeclampsia a eclampsia, ya que los cambios oftalmológicos se manifiestan como una retinopatía hipertensiva. El objetivo de este estudio es describir los hallazgos clínicos retinianos, mediante oftalmoscopia indirecta, en pacientes con preeclampsia durante el puerperio inmediato. **Material y métodos:** Estudio descriptivo, observacional,

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prospectivo y transversal, realizado de agosto a diciembre de 2014, en pacientes con preeclampsia hospitalizadas en un hospital materno-infantil de la Ciudad de México durante el puerperio inmediato, a quienes se les realizó una exploración oftalmológica mediante oftalmoscopia indirecta. Se revisó el fondo de ojo y se describieron los hallazgos clínicos y la clasificación de retinopatía hipertensiva en caso de existir. Así mismo, se identificó la relación de factores que puedan influir en el grado de retinopatía hipertensiva. **Resultados:** Se valoraron 26 pacientes con preeclampsia severa, 5 pacientes con preeclampsia leve y 1 paciente con síndrome de HELLP incompleto, de un total de 32 pacientes incluidas en el estudio. Los signos clínicos identificados con mayor frecuencia fueron vasoespasmo y la presencia de cruces arteriovenosos. El 34.61% de pacientes diagnosticadas con preeclampsia severa presentaron retinopatía hipertensiva grado II. La relación del grado de retinopatía hipertensiva con la edad tuvo una significancia estadística de $p = 0.044$. **Conclusiones:** Diferentes grados de retinopatía hipertensiva (grado I, II y III) fueron observados en pacientes con preeclampsia severa. No se encontraron pacientes con neuropatía hipertensiva o con datos de isquemia coroidea asociados a desprendimiento de retina seroso. La edad fue el factor con mayor asociación al grado de retinopatía hipertensiva.

Palabras clave: Preeclampsia. Retinopatía hipertensiva. Vasoespasmo. Isquemia retiniana.

Introduction

Hypertensive disorders during pregnancy are one of the main obstetric complications in many countries of the world, and constitute one of the leading causes of maternal, fetal and neonatal morbidity and mortality. The reported frequency shows great variability, ranging from 12 to 22%. Mexico shows similar figures. Preeclampsia/eclampsia causes 70% of hypertensive disorders during pregnancy, the other 30% is due to pre-existing chronic hypertension.

In 2000, the National Health System of Mexico reported 466 deaths from hypertensive disorders during pregnancy, that represent 35.17% of the causes of maternal mortality¹.

The literature describes the importance of an adequate fundus examination and the valuable information that it can provide. During pregnancy there are physiological eye changes, such as ocular hypotension mediated by an increase in aqueous humor outflow², a decrease in corneal sensitivity with probable edema³, pathological changes that may result in the development of central serous chorioretinopathy⁴, growth of uveal tumors⁵ or progression of diabetic retinopathy⁶. In preeclampsia, patients may perceive optical phenomena that can predict the evolution from preeclampsia to eclampsia, since ocular changes manifest as hypertensive retinopathy. The most frequent clinical sign is arteriolar spasm, reported in 40 to 100% of patients with pre-eclampsia and accompanied by areas of retinal ischemia⁷. Bleeding, exudates, diffuse retinal edema, and papilledema may occur. Serous retinal detachments are reported in 10% of patients with eclampsia and in 1 to 2% of patients with severe preeclampsia⁸.

Ophthalmoscopy helps to estimate the vascular status of the placenta and to predict the increase in the severity of toxemia.

The pathophysiology of preeclampsia involves a loss of balance of angiogenic factors, such as vascular endothelial growth factor and platelet-derived growth factor. These factors are overexpressed during pregnancy and their inhibition produces hypertension and dose-dependent proteinuria⁹.

Some studies have evaluated the severity of hypertensive retinopathy and the degree of systemic alterations due to preeclampsia, and a direct correlation has been observed¹⁰.

The objective of this study is to describe the findings observed by fundus examination during the immediate puerperium in patients previously diagnosed with pre-eclampsia. This, in order to evaluate and compare the findings of this study with those described in the literature in populations other than the Mexican, and thus to establish the importance of ocular examination in patients with preeclampsia.

Material and methods

This was a descriptive, observational, prospective and cross-sectional study that was conducted from August 2014 to December 2014. We examined female patients hospitalized due to pre-eclampsia in a maternal and child hospital in Mexico City during the immediate postpartum period. In case of severe pre-eclampsia, they were examined in the intensive care unit, and in the case of mild preeclampsia, they were examined in the complicated puerperium department.

An informed consent was obtained from each patient to review and collect data for the study. All procedures were carried out in accordance with the ethical standards of the institutional research committee of the Fundación Hospital Nuestra Señora de la Luz and in compliance with the ethical principles of the Declaration of Helsinki.

Patients underwent an eye fundus exam using an indirect ophthalmoscope (Vantage Plus LED, Keeler Ophthalmic Instruments, United Kingdom) under pharmacological mydriasis with tropicamide/phenylephrine (TP Ofteno, Laboratorios Sophia, Mexico) and a 20 D lens (Volk Optical, Inc., USA), using minimal illumination and punctal occlusion to minimize systemic absorption of eye drops. There were no adverse events related to eye drops application or ocular examination.

The degree of hypertensive retinopathy was staged using the Keith-Wagener-Barker (KWB) classification¹¹. Laboratory results and vital signs data, as well as the instituted antihypertensive treatment, were taken from the patients' clinical records.

Preeclampsia was classified according to the guidelines proposed by the American College of Obstetricians and Gynecologists¹².

For the statistical analysis, a linear regression model was performed to correlate the degree of hypertensive retinopathy with liver enzyme levels, platelet count, mean blood pressure, proteinuria, the presence of lower extremity edema, age, and antihypertensive treatment. We used the SPSS program, New York, USA, and a value of $p \leq 0.05$ was considered statistically significant.

Results

Thirty-two female patients with a mean age of 23.84 years (SD $\pm$ 5.7) were examined in the immediate puerperium at a maternal and child hospital in Mexico City (Table 1).

According to the degree of preeclampsia, the patients were divided in three groups: 1) severe pre-eclampsia, 6 (23.07%) patients had grade III hypertensive retinopathy, 9 (34.61%) had grade II, 5 (19.23%) had grade I and 6 (23.07%) had grade 0; 2. mild preeclampsia, 2 (40%) patients showed grade II hypertensive retinopathy, 1 (20%) grade I and 2 (40%) grade 0; and 3) incomplete HELLP syndrome, 1 (100%) patient had grade I hypertensive retinopathy.

In patients with severe preeclampsia, vasospasm (80.76%) and arteriovenous crossovers (57.69%) predominated as clinical signs. Patients with mild preeclampsia had similar results, 40% had arteriovenous crossovers and 60% had vasospasm. The patient with incomplete HELLP syndrome showed vasospasm (100%) (Table 2).

On examination, 16 patients had lower extremity edema, and the main clinical manifestations were arteriovenous crossovers (56.2%) and vasospasm (68.7%); 14 patients showed proteinuria, and the majority had

Table 1. Demographic data

Number of patients	32
Average age (SD)	23.8 ($\pm$ 5.7)
Mild preeclampsia, n (%)	5 (15.6%)
Severe preeclampsia, n (%)	26 (81.2%)
Incomplete HELLP syndrome, n (%)	1 (3.1%)
Visual symptoms (phosphenes), n (%)	2 (6.2%)
Mean arterial pressure	104.04

vasospasm (85.7%) as predominant clinical sign, followed by arteriovenous crossovers (71.42%). Altered liver enzymes were identified in 10 patients, who showed vasospasm (80%) as the most frequent ocular finding (Table 3).

Patients with preeclampsia and lower extremity edema showed clinical data compatible with KWB-grade II and III hypertensive retinopathy with more frequency. In patients with proteinuria, grades II and III were identified in up to 70% of patients, whereas in patients with altered liver enzymes, grade I hypertensive retinopathy was predominant (40%) (Table 4).

Regarding antihypertensive treatment, 46.87% of the patients received nifedipine, 15.62% had a combined treatment with propranolol and nifedipine and 37.5% did not require hypotensive treatment, with a mean arterial pressure of 104.04 in the three groups.

The comparison between the degree of hypertensive retinopathy and age was statistically significant ($p = 0.044$); this was not the case when comparing liver enzymes, proteinuria, lower extremity edema, mean blood pressure, and platelet count (Table 5).

Discussion

The most frequent fundoscopic findings were arteriovenous crossovers and arteriolar vasospasm in the three groups.

In all groups, the most frequent finding was generalized vasospasm; however, this are different findings compared to those published by Rasdi, et al, who reported that up to 70% of patients had a normal fundus and no hypertensive retinopathy in up to 82%, but they did not distinguish between groups according to the severity of pre-eclampsia. In their study they report one patient with bilateral serous retinal detachment, while in our study no patient showed serous retinal detachment¹².

Table 2. Clinical signs according to the severity of preeclampsia

	Intraretinal hemorrhages	Soft exudates	Arteriovenous crossovers	Vasospasm	Vascular tortuosity
	N (%)	N (%)	N (%)	N (%)	N (%)
Mild preeclampsia	0 (0)	0 (0)	2 (40)	3 (60)	0 (0)
Severe preeclampsia	3 (11.5)	5 (19.2)	15 (57.6)	21 (80.7)	3 (11.5)
Incomplete HELLP syndrome	0 (10)	0 (0)	0 (0)	1 (100)	0 (0)

Table 3. Clinical signs in patients with lower extremity edema, proteinuria and liver enzymes alteration

	Intraretinal hemorrhages	Soft exudates	Arteriovenous crossovers	Vasospasm	Vascular tortuosity
	N (%)	N (%)	N (%)	N (%)	N (%)
Lower extremity edema	1 (6.2)	3 (18.7)	9 (56.2)	11 (68.7)	1 (6.2)
Proteinuria	1 (7.14)	3 (21.42)	10 (71.42)	12 (85.7)	2 (14.28)
Liver enzymes alteration	1 (10)	2 (20)	4 (40)	8 (80)	1 (10)

Table 4. Degree of hypertensive retinopathy in patients with lower extremity edema, proteinuria and liver enzymes alteration

KWB classification	Lower extremity edema	Proteinuria	Liver enzymes alteration
	N (%)	N (%)	N (%)
IV	0 (0)	0 (0)	0 (0)
III	4 (25)	4 (28.5)	2 (20)
II	5 (31.2)	6 (42.8)	2 (20)
I	2 (12.5)	2 (14.2)	4 (40)
0	5 (31.2)	2 (14.2)	2 (20)

KWB: Keith-Wagener-Barker.

Table 5. Linear regression model comparing the degree of hypertensive retinopathy with age, liver enzymes, mean blood pressure, proteinuria, thrombocytopenia, and lower extremity edema

Degree of hypertensive retinopathy vs.	F value	Significance
Age	4.424	0.044
AST	0.118	0.734
ALT	0.001	0.972
Mean blood pressure	0.499	0.485
Proteinuria	1.657	0.208
Thrombocytopenia	0.219	0.643
Lower extremity edema	0.375	0.545

ALT: alanine aminotransferase; AST: aspartate aminotransferase.

Tadin, et al, reported an important correlation between the degree of hypertension and the severity of hypertensive retinopathy, in contrast to our study, where this finding was not consistent; however, the group of patients studied by Tadin were still pregnant¹⁰.

There is a higher degree and proportion of hypertensive retinopathy in patients with severe pre-eclampsia than in patients with mild pre-eclampsia.

The group with the highest degree of severity of hypertensive retinopathy was the group associated with proteinuria, followed by the group associated with lower extremity edema.

The results of fundus findings are homogeneous between groups.

Only visual symptoms, such as phosphenes, occurred in 2 patients (6.2%), without reports of metamorphopsia, micropsy, or changes in color perception.

No patients had grade IV hypertensive retinopathy or serous retinal detachment. Age was the factor with the highest correlation to the degree of hypertensive retinopathy, perhaps explained by the progressive development of atherosclerosis with age, which would justify

the clinical findings described despite finding blood pressure figures with a tendency to normality.

Among the limitations of the study are the need of a larger sample to validate the findings and a control group to conduct a comparative study with a healthy population. Another limitation is the lack of blood pressure records prior to the introduction of antihypertensive treatment; this would have allowed the identification of higher blood pressure figures and their correlation with the degree of hypertensive retinopathy.

Conclusions

This study describes fundus findings in patients with pre-eclampsia in a Mexican hospital. Hypertensive retinopathy grades I, II and III was observed in patients with severe preeclampsia, while hypertensive retinopathy grades I and II was observed in patients with mild preeclampsia. Age is an important factor that correlates with the degree of microvascular damage secondary to high blood pressure and, therefore, the ocular manifestations that can be identified.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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