

Clinico-Biological Factors and Ocular Complications during Preeclampsia

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ABSTRACT

Goal: To analyze the association between clinico-biological factors and ocular complications in pre-eclamptic patients.

Patients and Methods: This was a cross-sectional observational study with a descriptive and analytical purpose conducted from January 1, 2023 to October 1, 2023 in Libreville. It involved 93 preeclamptic patients, including 13 with ocular complications (C+) and 80 without any complication (C-). Maternal data, systolic blood pressure (SBP), diastolic blood pressure (DBP), blur vision; visual acuity (VAC) and biology were collected. These parameters were compared between C+ and C- ($p < 0.05$).

Results: The hospital prevalence of preeclampsia was 5.8% and that of ocular complications during this pathology 14.0%. Among the C+, 7 (53.8%) were workers versus 19 (23.8%) among the C- [OR = 3.7; CI = (1.1 - 12.5); $p = 0.032$]. In C+, 11 (84.6%) patients had a SBP ≥ 160 mmHg against 43 (53.8%) in C- [OR = 4.7; CI = (1.0 - 22.7); $p = 0.033$]. The C+ all had severe preeclampsia (100.0%) versus 53 (66.3%) in the C- ($p = 0.05$). In C+, 6 (23.1%) patients had an VAC $< 3/10^{\text{th}}$ against 4 (2.5%) in C- [OR = 7.3; CI = (1.9 - 27.3); $p = 0.006$].

Conclusion: These results suggest that professional activity, the severity of the pathology, the elevation of SBP and the decrease in visual acuity are predictive factors for the occurrence of ocular complications during preeclampsia.

Keywords

Pre-eclampsia, Ocular complications, Libreville.

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Introduction

Preeclampsia is the onset from 20 weeks of amenorrhea (SA), systolic arterial hypertension (SAP) greater than or equal to 140 mmHg and/or diastolic (DAP) greater than or equal to 90 mmHg associated with proteinuria greater than or equal to 300 mg/24h

[1-3]. Its pathogenesis is not clearly elucidated. It would be linked to a placental disorder in early pregnancy, followed by generalized inflammation and progressive endothelial dysfunction [4,5]. This pathology remains to this day a public health problem. Indeed, it is one of the top 3 causes of maternal mortality in the world [5-10].

It is also responsible for neonatal mortality varying between 9.4% and 21.8% depending on the studies [9,11-13]. Beyond mortality, preeclampsia can cause maternal-fetal morbidity.

In 10% of cases, it progresses to a severe form, which can lead to acute organ dysfunction, sometimes persistent in a medium and a long term [1,14-16]. At the ocular level, the complications of preeclampsia are essentially hypertensive retinopathy (HYR), serous retinal detachment (SRD), optic nerve ischemia (ONI), vitreous hemorrhage (VHE) and vascular occlusions (VOC) all of which can lead to blindness [10,17-19]. They are due to a disruption of vascular regulation and endothelial dysfunction responsible for choroidal ischemia [19,20]. These ocular lesions concern about 25% to 65.14% of women with severe preeclampsia and eclampsia [6,10,17,21-23]. In Burkina Faso they affected 31.29% of preeclamptics in 2018 and in Cameroon their prevalence was 48.8% in 2015 [10,21]. Currently in Gabon, there is no data on the prevalence of ocular complications related to this pathology. Although some studies have reported that these complications occur most often during severe preeclampsia and eclampsia, there are still questions about the different factors of their predictivity [22,23]. Authors also suggest that patients with certain complications such as HELLP syndrome have a higher risk of presenting with serous retinal detachment [24-26]. We believe that apart from high blood pressure (HTA), there are other factors that can predict the onset of ocular complications. To confirm this hypothesis, we proposed to analyze the association between clinical and biological factors and ocular complications in patients suffering from preeclampsia.

Population and Methods

Population

This was a cross-sectional observational study with a descriptive and analytical purpose conducted from January 1 to October 1, 2023. Patients were recruited in the obstetrics gynecology department of the Jeanne Ebori Foundation Mother Child University Hospital in Libreville (JEFMCUH). The target population was made of parturients who consulted at the JEFMCUH emergency service during the study period. In this population, were recruited the preeclamptic patients who constituted our sample. All patients aged 15 and over who had preeclampsia according to WHO criteria [1] and who had consented to the study were included. Patients with pre-existing ocular pathologies that could prevent fundus examination were not included, as well as those with superimposed preeclampsia or impaired consciousness. During recruitment, the patient's bedside exclusion criteria were checked and an interview allowed the collection of demographic data, medical history and functional signs (visual blurring). Information was collected from the maternal physical examination (blood pressure, complications) and paraclinical (biological). In a second step, an ophthalmological examination was carried out in the unit of ophthalmology.

Methods

Diagnosis of Preeclampsia

The diagnosis of preeclampsia was based on arterial hypertension

discovered after 20 weeks and proteinuria. In order to measure blood pressure, a mercury sphygmomanometer (Spengler®) was used with a cuff of the appropriate size for the patient [27]. Proteinuria was measured using a urine dipstick (Gima®). It was significant from a cross (300 mg) [28]. The classification of preeclampsia was based on the value of systolic and/or diastolic blood pressure, as well as that of proteinuria [29].

Diagnosis of Ocular Complications

The ophthalmological examination consisted of measuring distance visual acuity in monocular with optical correction (Monoyer) and measuring intraocular pressure (Tomey™). Then, the anterior segment of the eye was examined using a slit lamp (Tomey™). Pharmacological pupillary dilation (Tropicamide, Phenylephrine) to perform a fundus examination made it possible to look for ocular complications. At the end of our examination, patients with ocular complications benefited from optical coherence tomography (OCT) and ocular fluorescein angiography. A follow-up appointment was offered to these patients. In addition, patients who could not be mobilized benefited from an examination in bed. Distance visual acuity was measured using a monocular using a paper reading scale. The anterior and posterior segments were examined using an ophthalmoscope (Riester®), after pupillary dilation using mydriatic. In these patients, intraocular pressure was not measured.

Definition of Variables

Epidemiological variables

Maternal age was expressed in years. The women were divided according to whether they had a professional activity or not.

Clinical variables

Systolic hypertension was defined as a value greater than or equal to 140 mmHg. Diastolic hypertension was defined as a value greater than or equal to 90 mmHg. The history of preeclampsia and ophthalmological pathologies were sought. The presence or absence of visual blurring was noted during the interview. Visual acuity from afar was expressed in decimal scale, it was said to be normal for a value of 10/10th. Ocular complications were listed. Serous retinal detachment (SRD) was defined as a separation of the neurosensory retina from the underlying retinal pigment epithelium resulting from impaired barriers and reabsorption functions in the retinal pigment epithelium [17]. Hypertensive retinopathy (HYR) was defined according to the Kirkendall classification [30]. Vascular occlusions were obliterations of the central retinal artery or central retinal vein or one of their branches [31]. Optic nerve ischemia was defined as ischemia of the anterior part of the optic nerve [32].

Biological Variables

Proteinuria was expressed as a cross. One cross corresponded to 300 mg/L, two crosses was equal to 1000 mg/L, three crosses was equivalent to 3000 mg/L and four crosses corresponded to a value greater than 20,000 mg/L. Aspartate aminotransferase (ASAT) was expressed in IU/L, its normal value was between 5 and 37

IU/L. Alanine aminotransferase (ALAT) was expressed in IU/L, its normal value was between 4 and 41 IU/L [33]. Hepatic cytolysis was defined on the basis of ALAT and ASAT levels raised to more than three times normal. Uremia was expressed in mmol/L, its normal value was between 2.5 and 8 mmol/L. Serum creatinine was expressed in $\mu\text{mol/L}$, its normal value was between 45 and 105 $\mu\text{mol/L}$. Uric acid was expressed in $\mu\text{mol/L}$, its normal value was between 150 and 360 $\mu\text{mol/L}$ [34]. The platelet count was expressed in IU/mm^3 , its normal value was between 150,000 to 450,000 IU/mm^3 [35].

Statistical Methods

The data was collected on a survey form and then entered into a Microsoft Office[®] Excel file. Statistical analysis was performed using Stata[®] 12.0 software. It allowed calculations of proportions, means and standard deviations. The Cochran-Mantel-Haenszel chi-square test was used to compare the proportions and thus to determine a correlation between them. The Student test allowed the comparison of the average ages. The difference was statistically significant when the p (p-value) was less than 0.05.

Ethical Aspects

This work was carried out according to the recommendations of the Helsinki declaration of ethics [36] on the use of living beings. Permission from hospital officials has been obtained. Likewise, informed consent was obtained from the participants. It was guaranteed to all, respect for the confidentiality of the data collected during the investigation.

Results

Frequency of Ocular Complications

We identified 143 preeclamptic patients out of 2487 parturients treated at the JEFMCUH, i.e. a hospital prevalence of 5.8%. In total, 93/143 (65%) preeclamptic patients were retained, including 13 with ocular complications (14.0%) (C+) and 80 without (C-) (Figure 1). Hypertensive retinopathy and serous retinal detachment accounted for 76.9% and 15.4% of ocular complications of preeclampsia in this study, respectively (Table 1).

Table 1: Distribution of ocular complications.

Parameters	Quantities	Percentages (%)
Serous retinal detachment (SRD)	2	15.4
Hypertensive retinopathy	10	76.9
Optic nerve ischemia	1	7.7
Total	13	100

Epidemiological variables

The average age of C+ was 32 ± 5.4 years, and that of C- was 28.4 ± 6.9 ($p = 0.079$). Female workers accounted for 53.8% (7) of the C+ workforce and 23.8% (19) of the C- workforce [OR = 3.7; CI = (1.1 - 12.5); $p = 0.032$].

Clinical variables

Ocular complications are listed in Table 2. Comparisons of clinical variables between C+ and C- have been grouped in Table 2. In C+,

11 (84.6%) patients had a SBP ≥ 160 mmHg against 43 (53.8%) in C- [OR = 4.7; CI = (1.0 - 22.7); $p = 0.033$]. All C+ had severe preeclampsia against 53 (66.3%) in C- ($p = 0.05$). In C+, 6 (23.1%) patients had distance visual acuity $< 3/10^{\text{th}}$ against 4 (2.5%) in C- [OR = 7.3; CI = (1.9-27.3); $p = 0.006$].

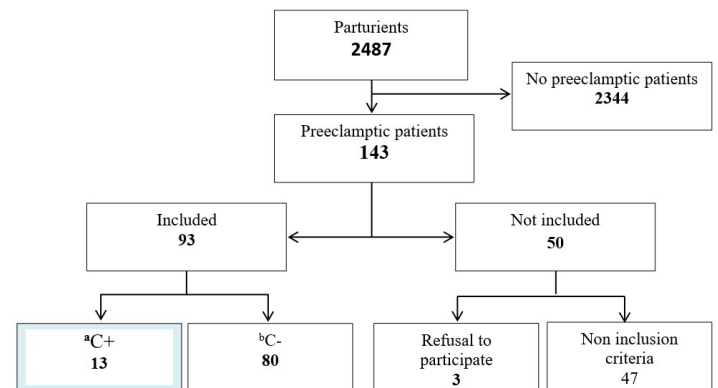


Figure 1: Flow diagram describing the selection of the study population. ^aC+ preeclamptic patients with ocular complications, ^bC- preeclamptic patients without ocular complications.

Table 2: Population epidemiological and clinical variables.

Parameters	^a C+ (N=13) n (%)	^b C- (N=80) n (%)	OR	p
Profession (n = 93)			3.7 [1.1 – 12.5]	0.032
Student/Jobless	6 (46.2)	61 (76.2)		
Workers	7 (53.8)	19 (23.8)		
History of preeclampsia (n = 93)			0.5 [0.1 – 2.5]	0.323
Yes	2 (15.4)	21 (26.2)		
No	11 (84.6)	59 (73.8)		
Ophthalmological history (n = 93)			0.4 [0.1 – 3.6]	0.378
Yes	1 (7.7)	13 (16.2)		
No	12 (92.3)	67 (83.8)		
Visual blur (n = 93)			2.9 [0.9 – 9.5]	0.073
Yes	7 (53.8)	23 (28.7)		
No	6 (46.2)	57 (71.3)		
Systolic Blood Pressure (n = 93)			4.7 [1.0 – 22.7]	0.033
< 160 mmHg	2 (15.4)	37 (46.2)		
≥ 160 mmHg	11 (84.6)	43 (53.8)		
Diastolic Blood Pressure (n = 93)			2.3 [0.7 – 7.5]	0.151
< 110 mmHg	7 (53.8)	58 (72.5)		
≥ 110 mmHg	6 (46.3)	22 (27.5)		
Preeclampsia Classification (n = 93)			0.0	0.05
Light	0 (0.0)	9 (11.2)		
Moderate	0 (0.0)	18 (22.5)		
Severe	13 (100.0)	53 (66.3)		
Eclampsia (n = 93)			2.1 [0.5 – 9.0]	0.383
Yes	3 (23.1)	10 (12.5)		
No	10 (76.9)	70 (87.5)		

HRP (n = 93)			0.00	0.335
Yes	0 (0.0)	7 (8.7)		
No	13 (100.0)	73 (91.3)		
HELLP syndrome (n = 93)			2.1 [0.2 – 22.3]	0.458
Yes	1 (7.7)	3 (3.7)		
No	12 (92.3)	77 (96.3)		
Distance visual Acuity (n = 186 yeux)			7.3 [1.9 – 27.3]	0.006
< 3/10 th	6 (23.1)	4 (2.5)		
≥ 3/10 th	20 (76.9)	156 (97.5)		

^agroups of patients with ocular complications; ^bgroups of patients without ocular complications; ^cRetroplacental hematoma.

Biological variables

In C+, 10 (76.9%) preeclamptic patients had proteinuria ≥ 3 crosses (Table 3) versus 48 (60.0%) in C- [OR = 0.22; CI = (0.6-8.6); p=0.357]. In the C+ group, 9 (18.2%) patients had a level of their enzyme ASAT ≥ 40IU/L versus 7 (10.9%) in the C- [OR = 1.8; CI = (0.3 - 10.1); p=0.612]. In the C+, 1 (12.5%) patient had an ALAT ≥ 41UI/L versus 7 (10.6%) in the C- [OR = 0.8; CI = (0.1-7.2); p=0.842].

Table 3: Biological variables of the study population.

Parameters	C+ (%)	C- (%)	OR [IC95%]	p
Proteinuria (croix) (n= 93)			2.2 [0.6 – 8.6]	0.357
≤ 2	3 (23.1)	32 (40.0)		
≥ 3	10 (76.9)	48 (60.0)		
ASAT^a (UI/L) (n=75)			1.8[0.3 – 10.1]	0.612
< 40	9 (81.8)	57 (89.1)		
≥ 40	2 (18.2)	7 (10.9)		
ALAT^b (UI/L) (n = 74)			0.8 [0.1 – 7.2]	0.842
< 41	7 (87.5)	59 (89.4)		
≥ 41	1 (12.5)	7 (10.6)		
Platelets (mm³/L) (n= 88)			2.5 [0.8 – 8.5]	0.181
< 150000	6 (46.2)	19 (25.3)		
≥ 150000	7 (53.8)	56 (74.7)		
Uric Acid (μmol/L) (n= 33)			1.4[0.1 – 24.2]	0.676
≤ 360	1 (50.0)	18 (58.1)		
> 360	1 (50.0)	13 (41.9)		
Urea (mmol/L) (n = 70)			0.00	0.47
≤ 8	10 (100.0)	57 (95.0)		
> 8	0 (0.0)	3 (5.0)		
Creatinine (μmol/l) (n= 77)			0.00	0.201
≤ 105	12 (100.0)	52 (80.0)		
> 105	0 (0.0)	13 (20.0)		

^aaspartate aminotransferase; ^balanine aminotransferase

Discussion

Limitations of the Study

This study encountered several difficulties, in particular the unavailability and the short period of recruitment of parturients. All these constraints had the impact of a small sample size and a disproportion between the number of C+ and that of C-.

However, despite these limitations, it appears that the hospital prevalence of preeclampsia was 5.8% and that of ocular complications during this pathology, 14.0%. Female workers were 4 times more likely to develop an ocular complication during preeclampsia [OR = 3.7; CI = (1.1 - 12.5); p = 0.032]. When the SBP was greater than or equal to 160 mmHg, the risk of an ocular complication was multiplied by 5 [OR = 4.7; CI = (1.0 - 22.7); p = 0.033]. This risk was multiplied by 7 when distance visual acuity was less than 3/10th [OR = 7.3; CI = (1.9 - 27.3); p = 0.006].

These results suggest that occupational activity, increased SBP and decreased visual acuity are predictive factors for the occurrence of ocular complications during preeclampsia. Furthermore, we did not find a link between maternal, obstetrical and fetal biological factors and the occurrence of ocular complications.

Epidemiological Variables

Frequency of Ocular Complications

Hypertensive retinopathy was the most common ophthalmologic complication of preeclampsia in our study population. This result is corroborated by the work of Diallo et al., Ngwanou et al. and Rajaona et al. [10,21,23]. This is because the first response of the retinal vasculature to systemic hypertension is vascular narrowing and extravasation of fluid to extravascular spaces due to increased vascular permeability. These pathophysiological mechanisms are responsible for the appearance of all the retinal lesions described during preeclampsia [18].

Age

There was no significant difference between the mean age of C+ and C- in the study population. Age was therefore not a risk factor for the occurrence of ocular complications during preeclampsia. However, the preeclamptic patients in our study were young. Our results thus agree with those of the African literature [10,21,23,26] and suggest that age is a risk factor for the onset of preeclampsia [29].

Professional activity

The proportion of female workers among the C+ was significantly higher than among the C-. Female workers were 4 times more likely to develop ocular complications from preeclampsia. Spinillo et al. had carried out an analytical study on the effect of professional activity during pregnancy and the risk factors for severe preeclampsia [37]. They had found that parturients with moderate and intense activities during professional activity were twice as likely to develop severe preeclampsia. Similarly, Østerdal et al. found that physical activity exceeding 270 minutes per week in the first trimester of pregnancy increased the risk of severe preeclampsia [38]. Knowing that ocular complications occur

most often in cases of severe preeclampsia [22,23], there would probably be an indirect link between professional activity and the occurrence of these.

Clinical variables

Visual Blur and Visual Acuity

In the C+, more than half of the patients showed visual blurring, a higher proportion than in the C-. Although our results do not demonstrate a link between this symptom and the onset of ocular complications, it was nevertheless noted that the risk of finding ocular complications during preeclampsia was multiplied by 7 when distance visual acuity was less than 3/10th. Indeed, the C+ had presented more visual impairment than the C-. During preeclampsia, this visual loss is related to a disturbance of vascular regulation and dysfunction of the chorioretinal endothelium. These disturbances can give rise to ophthalmological lesions visible on the fundus or go unnoticed. Removal of the placenta is usually accompanied by an improvement in visual acuity within a few weeks [17,39].

Severity of Preeclampsia

Systolic blood pressure (SBP)

When the SBP was greater than or equal to 160 mmHg, the risk of an ocular complication was multiplied by 5. Tadin et al. had also found a significant link between the rise in systolic blood pressure and the occurrence of these complications [40]. Along the same lines, Karki et al. found an average SBP of 182.86 mmHg in preeclamptics with ocular complications versus 150.72 mmHg in those without [41].

The occurrence of ocular complications during preeclampsia is related to changes in the retinal arterioles caused by hypertension. Indeed, the main response of the retinal vasculature to systemic arterial hypertension is vascular narrowing. This answer has several consequences. First, it causes focal or diffuse vasoconstriction with extravasation of fluid to extravascular spaces due to increased vascular permeability responsible for superficial retinal hemorrhages, retinal edema and deep exudates. Similarly, occlusions of the choriocapillaris may appear and be responsible for ischemia and necrosis of the retinal pigment epithelium leading to serous retinal detachment. Furthermore, this arterial hypertension may be responsible for hypoperfusion of the anterior part of the optic nerve [14,18,30].

Diastolic blood pressure (DBP)

In the C+ group, there were more patients with a DBP \geq 110 mmHg than in the C- group. However, we have not established a link between the elevation of DBP and the occurrence of ocular complications. However, other studies have established this link during preeclampsia. This is the case of Tadin et al. who found a link between the severity of hypertensive retinopathy and that of diastolic blood pressure [40]. The fact that we have diverging results could be explained by the small size of our sample.

Biological variables

Proteinuria

C+ had more preeclamptic patients with proteinuria \geq 3 crosses than C-. However, we did not find a link between the occurrence of ocular complications and the existence of proteinuria \geq 3 crosses. However, this link has been established by Tadin et al. Indeed, they had found a significant link between the severity of hypertensive retinopathy and that of proteinuria in preeclamptic patients [40].

The HELLP Syndrome

The HELLP syndrome was more present in C+ than in C-. However, we did not find a link between this complication and the ocular complications of preeclampsia. On the other hand, Vigil-De Gracia et al. had also found many cases of serous retinal detachment (32.14%) associated with HELLP syndrome in preeclamptic patients in their series [26].

Classification

All of our patients with ocular complications (C+) had a severe form of preeclampsia. We found a significant link between the severity of preeclampsia and the occurrence of ocular complications in our study. These facts are corroborated by literature data [22,23]. Rajaona et al. found the most advanced hypertensive retinopathy in cases of severe preeclampsia [23].

Conclusion

This work aimed to analyze the association between clinical and biological factors and ocular complications in preeclamptic patients. It appears that the hospital prevalence of preeclampsia was 5.8% and that of ocular complications during this pathology, 14.0%. The number of workers, the value of systolic blood pressure and the severity of preeclampsia were significantly higher in preeclamptic patients with ocular complications compared to the others.

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