The Hidden Side of the Story between the Placenta and Preeclampsia: Preliminary Results of a Prospective Cohort of Pregnant Women in Cameroon

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Abstract

Introduction: Pre-eclampsia is a complication of pregnancy that generally occurs in the third trimester. It is associated with a maternal and foetal mortality rate of around 27%. In view of the grim picture painted by this condition for both mother and newborn, studies have been carried out into the early detection of patients at risk of developing pre-eclampsia. These make it possible to introduce pregnancy-specific monitoring and preventive strategies to reduce the incidence of the condition. **Objective:** To establish the link between placental ultrasound characteristics and the onset of pre-eclampsia. **Methodology:** A multicentre prospective cohort study was conducted in two hospitals in Yaoundé, namely the Yaoundé Gynaecological-Obstetrics and Paediatrics Hospital and the Nkolndongo Health and Social Animation Centre, in the gynaecology and radiology departments over a period of 11 months, from October 2022 to August 2023. It included pregnant women who had undergone obstetric ultrasound between 12 and 18 weeks' gestation. In addition to routine obstetric ultrasound, we performed obstetric Doppler measurements in these patients. The resistance index of the left and right uterine arteries, the umbilical artery and the placental volume were the characteristics sought. At the end of this examination, two groups were formed: cases (pathological Doppler group) and controls (normal Doppler group). Blood pressure and urine dipstick were taken at each antenatal visit until delivery, then during the immediate postpartum period and finally at 7 days, 21 days and 42 days after delivery. **Results:** Sixty-seven (67)

patients were included. Of these, 35 (47.8%) had pathological Dopplers. Sixteen patients had arterial hypertension associated with proteinuria and were therefore labelled as pre-eclampsia (PE). This gives a prevalence of 23.9%. Fifteen (42.8%) of these patients belonged to the exposed group and one to the unexposed group. The mean IR of the pre-eclampsia patients was significantly higher than that of the patients without pre-eclampsia; respectively 0.74 ± 0.096 and 0.49 ± 0.097 for the right uterine arteries and 0.71 ± 0.13 and 0.52 ± 0.089 for the left uterine arteries. We found that an increase in the uterine artery resistance index was significantly associated with the onset of pre-eclampsia, with a relative risk of 13.7 and a p value < 0.001. The overall sensitivity, specificity and positive and negative predictive values of Doppler ultrasound for predicting pre-eclampsia were 93.7%, 60.7%, 42.9% and 96.9% respectively. Arterial spectrum disorders accounted for 7.4% and were unrelated to the occurrence of pre-eclampsia, as were placental volume and umbilical artery resistance index. **Conclusion:** Abnormal Doppler ultrasound between 12 and 18 weeks of amenorrhoea had good overall sensitivity for predicting pre-eclampsia. Among the Doppler indices, the uterine artery resistance index was the only one significantly associated with pre-eclampsia.

Keywords

Pre-Eclampsia, Doppler, Ultrasound, Placenta

1. Introduction

Pre-eclampsia is the leading cause of maternal mortality worldwide. It is a placental vascular pathology whose frequency and complications are highest in Africa and developing countries [1], yet prevention of this pathology is possible. To prevent it, we need to know how to predict it. In recent years, several studies have been carried out to determine the factors that predict the disease. Doppler studies of the uterine and umbilical arteries, as well as placental volume, have been shown to be factors whose elevated resistance indexes are associated with the onset of pre-eclampsia [2] [3] [4]. Given the limited number of studies in our context, this study was conducted with a view to obtaining data specific to our population for the prediction of the occurrence of the pathology.

2. Methodology

2.1. Type of Study

We conducted a prospective multicentre cohort study from November 2022 to August 2023 at the Yaoundé Gynaecological Obstetrics and Paediatrics Hospital and the Nkolndongo Health and Social Animation Centre. Our target population consisted of all pregnant women receiving consultations in these hospitals.

2.2. Study Population

All pregnant women attending antenatal clinics who had undergone an ultra-

sound scan between 12 and 18 months' gestation.

We formed two study groups:

❖ **First group, the exposed:** These were all pregnant women with an abnormal Doppler ultrasound result between 12 and 18 BSA.

❖ **Second group, the controls:** These were all pregnant women with a normal Doppler ultrasound result between 12 and 18 BSA.

2.3. Inclusion Criteria

Pregnant women attending antenatal clinics who had undergone obstetric ultrasound between 12 and 18 weeks' gestation and who had given informed consent were included.

2.4. Non-Inclusion Criteria

We did not include patients with known diabetes, patients with chronic hypertension, patients on Aspirin, patients with chronic kidney disease, patients with multiple pregnancies.

2.5. Exclusion Criteria

Women with spontaneous or induced abortion before 20 weeks' gestation, and gestational diabetes.

2.6. Data Collection

From the outpatient department, we approached pregnant women between 12 and 18SA. After obtaining the patient's consent, sociodemographic and clinical data were collected, and they were then taken to the medical imaging department where ultrasound scans were performed using a Mindray ultrasound scanner. All data were collected and recorded on a data sheet. After 20SA, the patients' BACs were taken at each cpn and BU was performed for high BACs. At the end of the study, this enabled us to create 2 groups: EP and pregnancies without EP.

2.7. Statistical Study

The data collected were analysed using SPSS software version 23.0 (Statistical Package for Social Sciences). Quantitative variables, expressed as means ± standard deviation. Qualitative variables were expressed in terms of numbers and percentages. Chi 2 test used to assess homogeneity between groups, Student's t test used to assess homogeneity of quantitative variables. A significance threshold of less than 5% was set. The Relative Risk with its 95% confidence interval used to assess the association between variables.

3. Results

75 Patients was approached, we had 03 missed abortions, 05 patients excluded, 67 pregnant women were registered for the study. Of these, 35 had pathological

Dopplers and formed the exposed group and 32 had normal Dopplers and formed the unexposed group. The mean age in the two groups was 28.4 ± 4.9 and 25.3 ± 4.9 years respectively, and the mean parity (**Figure 1**).

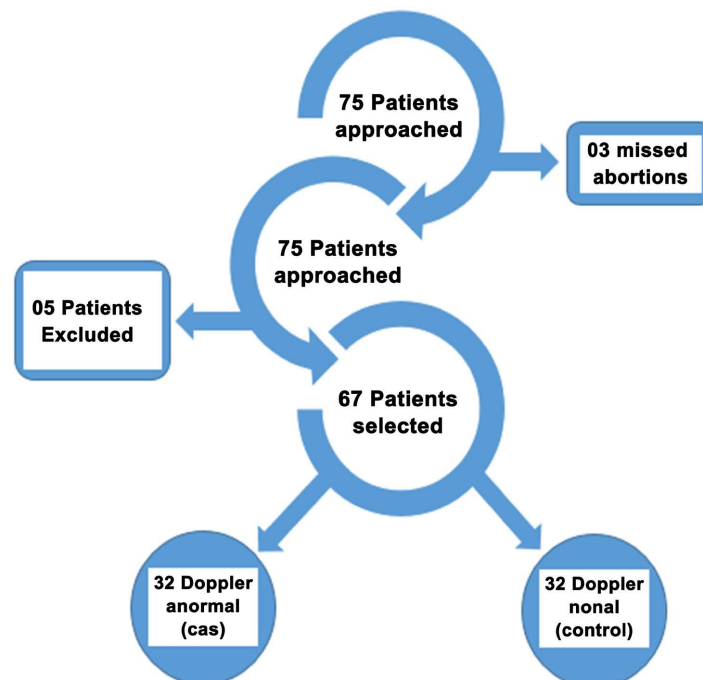### 3.1. Ultrasound Characteristics of Patients

The mean IRAUD in the exposed group was higher, 0.73, than in the unexposed group, 0.49. Similarly, the mean IRAUG in the exposed group was higher than in the unexposed group, at 0.71 and 0.52 respectively. The mean IRAO in the case group was 0.83 and in the control group 0.78. Placental volume was evenly distributed with an overall mean of 115.54 mm^3 (**Table 1**).

3.2. Evolutionary Characteristics of Patients

The occurrence of pre-eclampsia was the only variable with a heterogeneous distribution. In fact, 15 patients in the pathological Doppler group developed PE and only one in the control group, for a prevalence of 23.9% (16 patients). Most deliveries were vaginal (95.5%) and at term (91.5%) in both groups. Male newborns were more numerous in both groups and represented 61.1% of the general population. Most were eutrophic and 98.5% had an Apgar score greater than 7 at 5^e minutes. All these variables were homogeneously distributed (**Table 2**).

3.3. Evolution of Pregnancies According to the Occurrence of Pre-Eclampsia

The vaginal delivery route was the most frequent in both groups at 95.5%. 04.5% of all babies were premature and 94% of them had a birth weight greater than

Figure 1. Flow chart.

Table 1. Ultrasound characteristics of women.

Variables	Abnormal Doppler n = 35	Normal Doppler n = 32	Total n = 67	P-value
IRAUD				
Averages	0.73	0.49	0.62	**0.000***
Min; **Max**	0.68; 0.90	0.29; 0.52	0.29; 0.90	
IRAUG				
Averages	0.71	0.52	0.62	**0.000***
Min; **Max**	0.54; 0.96	0.29; 0.64	0.29 - 0.96	
IRAO				
Averages	0.83	0.78	0.81	0.492
Min; **Max**	0.62; 0.98	0.62; 0.90	0.62 - 0.98	
VOLUPLA				
Averages	111.21	120.27	115.54	0.629
Min; **Max**	23.88; 151.33	37.63; 191.34	39.74 - 191.34	

Table 2. Pregnancy outcome according to Doppler.

Variables	Abnormal Doppler n = 35	Normal Doppler n = 32	Total n = 67	P-value
Average GA	38.1	39.0	38.5	0.137
AG (min; max)	24; 4	36; 41	24; 41	
AG Class				
<33 SA +6 days	02 (05.7)	00 (00.0)	02 (03.0)	
34 - 36 SA + 6 days	01 (02.8)	02 (06.2)	03 (04.5)	
37 - 42 SA	32 (91.4)	30 (93.7)	62 (91.5)	
Delivery route				
Low track	32 (91.4)	32 (100)	64 (95.5)	0.090
Caesarean section	03 (08.5)	00 (00.0)	03 (04.4)	
Evolution				
PE	15 (42.8)	01 (03.1)	16 (23.9)	**0.002***
Without PE	20 (57.1)	31 (96.8)	51 (76.1)	

2500 g. The mean GA was 38SA + 5 days with a mean birth weight of 3123.1 g and height of 50.2 cm. 97% had an Apgar greater than 7 at 5^e min. The complications of EP recorded were 02 premature deliveries at 24 and 31 AU associated with severe EP and the death of one of the newborns (Table 3).

3.4. Doppler Profile of Uterine and Umbilical Arteries in the Study Population

This study enabled us to verify the existence of a link between uterine Doppler measurements and the occurrence of EP, as summarised in Table 4.

IRAUD: index of resistance of the right uterine artery IRAUG: index of resistance of the left uterine artery IRAO: index of resistance of the umbilical artery PE: pre-eclampsia GSP: pregnancies without pre-eclampsia

Table 3. Pregnancy outcomes by stage.

Variables	PE n = 16 (%)	GSP n = 51 (%)	p-value
Delivery route			
Low track	14 (87.5)	50 (98.04)	0.075
Caesarean section	02 (12.5)	01 (01.96)	
Prematurity			
Yes	02 (12.5)	01 (01.96)	0.075
No	14 (87.5)	50 (98.04)	
Gender			
Female	02 (12.5)	01 (01.96)	0.9
Male	14 (87.5)	50 (98.04)	
Birth weight			
Averages	2936.2	3181.7	
Min; Max	540; 3900	1530; 3970	0.283
<2500 g	02 (12.5)	02 (03.92)	
>2500 g	14 (87.5)	49 (96.08)	
Birth size			
Averages	49.53	50.39	
Min; Max	38; 53	44; 53	0.387
<2500 g	02 (12.5)	02 (03.92)	
>2500 g	14 (87.5)	49 (96.08)	
APGAR			
Averages	9.31	9.7	
<7 at 5^e min	01 (06.25)	01 (01.96)	0.277
>7 at 5^e min	15 (93.75)	50 (98.04)	
Children's short-term development			
Favourable	15 (93.75)	51 (100)	0.072
Deaths	01 (06.25)	00 (00.0)	

Table 4. Comparison of resistance index averages.

Average resistance indexes	PE	GSP	p-value
IRAUD	0.74	0.58	<0.01*
IRAUG	0.70	0.58	0.018*
IRAO	0.83	0.80	0.37

IRAUD: index of resistance of the right uterine artery IRAUG: index of resistance of the left uterine artery IRAO: index of resistance of the umbilical artery PE: pre-eclampsia GSP: pregnancies without pre-eclampsia.

In our study population, the mean uterine artery resistance indexes in pre-eclampsia patients (0.74 ± 0.07 and 0.68 ± 0.13) were significantly higher than those in patients with pregnancy outcomes without EP (0.58 ± 0.14 and 0.60 ± 0.14), p value < 0.001.

Increased uterine artery resistance was significantly associated with the occurrence of EP, with an RR of 8.6 (p < 0.001) for AUD and 2.8 (p = 0.01) for AUG. Patients with abnormal Doppler were therefore 13.7 (p < 0.001) times

more likely to develop EP during their pregnancies than those with normal Doppler (Table 5).

3.5. Uterine and Umbilical Artery Resistance Index Values Predictive of Pre-Eclampsia

The ROC curve here presents the occurrence of pre-eclampsia as the reference category and considers pathological Dopplers as the test. We note that the area on the curve is 0.773, so our area is significant (Figure 2).

The ROC curve here presents the occurrence of pre-eclampsia as the reference category and takes placental volume as the test. We note that the area on the curve is 0.496, so our area is not significant (Table 6 and Figure 3).

Table 5. Relationship between resistance indexes and the onset of pre-eclampsia.

| Variables	RR (confidence interval)	p-value
IRAUD increase	8.6 (1.25 - 2.50)	<0.01*
IRAUG increase	2.8 (0.38 - 1.90)	0.018*
IRAO increase	2.1 (0.38 - 6.19)	0.37
Doppler pathology results	13.7 (1.26 - 2.27)	<0.01*

RR: relative risk IRAUD: index of resistance of the right uterine artery IRAUG: index of resistance of the left uterine artery IRAO: index of resistance of the umbilical artery.

Table 6. Predictive values of increased uterine artery resistance indexes.

Variables	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
IRAU increase	93.7	60.7	42.9	96.9
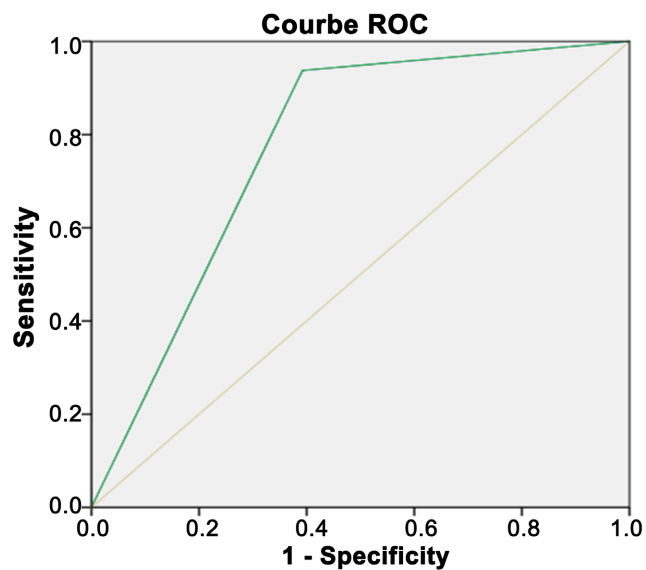
Figure 2. ROC curve of uterine arteries. Diagonal segments are generated by ties. Zone: 0.773.
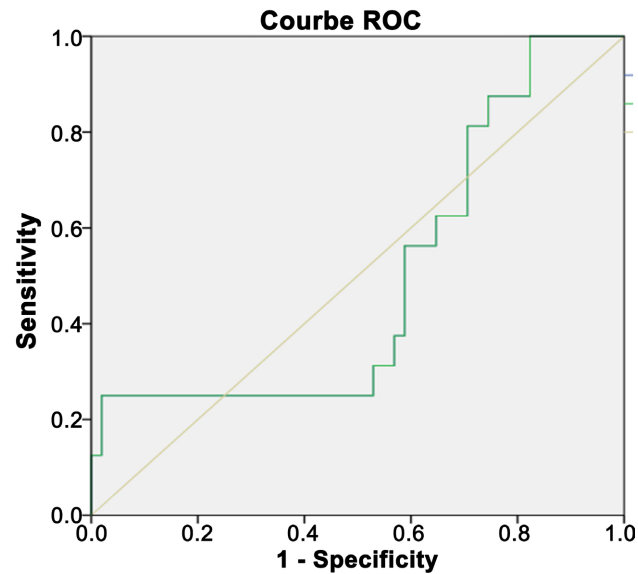
Figure 3. ROC curve for placental volumes. Diagonal segments are generated by ties. Zone: 0.496.

4. Discussion.

4.1. Sample Size

The mean age of patients with normal Doppler was 25.34 ± 4.95 years; that of patients with pathological Doppler was 28.45 ± 4.95 years. The age range most represented in the case group was 26 - 30 years, while that most represented in the control group was 21 - 25 years. These results are superimposed on those of Naguet *et al.* who found an average age of patients with abnormal Doppler of 28.1 ±5.4 years [5]. In the general population, 64.2% of these women were between 21 and 30 years of age. These results are similar to those of D. Boiro *et al.* in 2018 and Mariem Sidi Mohamed *et al.* in 2017, who respectively found an average age of 27.5 years and 29.16 years, with extremes ranging from 16 to 47 years and 15 to 47 years [6] [7]. This could be explained by the fact that this is a period of intense reproductive activity for women.

4.2. Ultrasound Characteristics of Patients

In the abnormal Doppler group, the mean values for IRAUD and IRAUG were significantly higher than those for the normal Doppler group, at 0.73 (±0.078) and 0.71 (±0.13) respectively (p < 0.01). Similarly, the means of the RAOIs were significantly higher in the case group than in the control group. The difference in placental volumes, on the other hand, was not significant in the two groups, p = 0.62. M. Para-Cordero *et al.* in Chile in 2016 found similar results to ours. The difference in means in the two groups was significant, higher in the case group than in the control group [8].

4.3. Pregnancy Outcome

Regarding the uterine and umbilical artery Doppler results, 52.20% were patho-

logical and 48.80% were normal. 15 women in the case group developed EP and 1 in the control group developed EP. This gives a prevalence of EP of 23.9%. This result is higher than that of H Essome *et al.* at Hôpital Laquintinie and Benjelloun *et al.* in Greater Cassablanca, who found a prevalence of 6.12% and 07% respectively. This could be explained by the small size of our sample compared to theirs [9].

4.4. Doppler Profile of Uterine and Umbilical Arteries in the Study Population

In the EP group, the mean values for IRAUD and IRAUG were significantly higher than those for the group of pregnancies without pre-eclampsia, at 0.74 (±0.078) and 0.68 (±0.13) respectively (p < 0.01). These results are similar to those of K Harrington *et al.* who found mean resistance indices of 0.80 [2]. An increase in RI was significantly associated with the occurrence of EP, with a relative risk of 13.7 and a p-value < 0.01. M. Para-Cordero *et al.* in 2016 in Chile found similar results. An increase in the vascular characteristics of the uterine arteries used was significantly associated with the occurrence of EP. [8]. Similarly, K. Harrington *et al.* and G. Okwudire *et al.* found similar results [3]. These results are in line with the literature. During a normal pregnancy, CTEV cells from the placenta invade the uterus (decidua and myometrium) and also the uterine arteries, mainly the spiral arteries. Following this invasion, the smooth muscle and endothelial cells of the arteries disappear, leaving the VTEC in their place. The arteries become atonic, insensitive to vasoactive molecules, which enlarges their diameter and improves perfusion of the intervillous chamber [10]. However, during a pre-eclampsia pregnancy, the endo- and perivascular invasion of the spiral arteries is defective. Vascular remodelling by the CTEV does not occur. Trophoblastic cells do not replace smooth muscle and endothelial cells. The diameter of the uterine spiral arteries remains unchanged and they retain their vasoconstrictor capacity. This lack of trophoblastic invasion and uterine remodelling leads to an increase in resistance in the uterine arteries, reduced vascularisation of the uteroplacental unit and placental hypoxia.

The mean IRAO was 0.83 (±0.08) and the difference with the opposite group was not significant (p = 0.155). This result is in total contradiction with the literature; it should be noted that the umbilical artery transports blood from the foetal heart to the placenta. EP is responsible for an increase in resistance in the placenta and in the network downstream of the umbilical artery, which by retrograde effect will also increase resistance in this artery.

Finally, we found that the mean placental volumes in the case group were reduced compared with the controls, but the difference was not significant p = 0.42. Patients in the case group had an average of 104 mm^3 and those in the control group 119.15 mm^3. Estelle Perdriolle Galet *et al.* in 2011 found similar results to ours, placental volumes were not different between the two groups. On the other hand, Cécile Fanget *et al.* in 2016 in France and Andréa Suranyi *et al.* in 2017 in Hungary found that placental volume was significantly smaller in pa-

tients who had developed EP [11]. These differences could be explained by the small size of our sample.

4.5. Correlation between Uterine and Umbilical Artery RI Values Predictive of Pre-Eclampsia

The increase in uterine artery resistance indexes had sensitivity values of 93.7%. Specificity was 60.7% and positive and negative predictive values 42.9% and 96.9% respectively. These results are similar to those of Nadia Shahid *et al.* in 2021, who found good sensitivity and a good negative predictive value of 71.4% and 74.1% respectively for the increase in resistance indexes [12]. Another study by Espinoza J *et al.* found a lower sensitivity and positive predictive value of 36% and 11% respectively. The negative predictive value was just as high, at 98%, and the specificity higher, at 90%. Their sample size was much larger than ours, which could explain the discrepancy between some of our results [13].

5. Conclusion

Pre-eclampsia is a preventable and predictable complication of pregnancy. This study showed that an increase in the uterine artery resistance index was the only ultrasound parameter significantly associated with the onset of PE, with good positive and negative predictive values. Uterine Doppler pathology thus increased the risk of developing pre-eclampsia during pregnancy fourteen-fold. The difference in mean placental volumes and umbilical artery resistance indexes in the two groups was not significant, so no link was found with the onset of pre-eclampsia.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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