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Maternal and Perinatal Complications of Vascular Pathologies Associated with Pregnancy: Frequency and Associated Factors in a Third Level Maternity in Benin

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Abstract: Background and aims: Vascular pathologies (hypertensive disorders and diabetes) associated with pregnancy are important public health problem in Benin because of their frequencies and their complications. This study aims to analyze maternal and perinatal complications of vascular pathologies associated with pregnancy. Methods: This analytical cross-sectional study used retrospective data collected over a three-year period. All mothers who presented a vascular pathology and their newborns during the study period at the Clinique Universitaire de Gynécologie obstétrique (CUGO) of Centre National Hospitalier Universitaire Hubert Koutoukou Maga (CNHU-HKM) of Cotonou were included. Maternal complications associated neurological, hematological, cardio-pulmonary and renal complications whereas perinatal complications included intrauterine growth restriction, fetal asphyxia, prematurity, neonatal resuscitation, low birthweight and perinatal death. Factors associated to the complications were identified by using chi-square test and a multivariate binary logistic regression model. Analyzes were performed with SAS software version 9.4. Results: The frequency of vascular pathologies associated with pregnancy was 14.95%. Diabetes was associated in 4.57%. Their evolutions were marked by the occurrence of numerous maternal complications dominated by retroplacental hematoma (12.08%), eclampsia (08.37%) which passed through signs of eclampsism (21.07%); and hellp syndrome. Perinatal complications were dominated by prematurity (43.07%), low birthweight (29.12%), fetal asphyxia (12.32%) and perinatal death (18.59%). These complications were associated with the precocity of the diagnosis, admission mode and the importance of proteinuria. Conclusion: Maternal and perinatal complications of vascular pathologies associated with pregnancy are frequent in current obstetric practice. It is therefore urgent to implement health promotion interventions targeting the factors associated with them in order to reverse the trends.

Keywords: Complications, Maternal, Perinatal, Vascular Pathologies, Pregnancy

1. Background

Hypertensive disorders and diabetes associated with pregnancy are major public health problem not only because of their high prevalence but also because of their maternal and fetal consequences. According to the World Health Organization (WHO), hypertensive disorders of pregnancy (HDP) are the second leading cause of maternal death and the first cause of perinatal morbidity and mortality in the world [1]. Their incidence varies from 10 to 15% [2]. This incidence differs according to the level of development of

the countries with a rate between 10.6% in the United States, 7% in Canada, 9% in China [3-5]. In developing countries, the frequencies are higher, 17% in Guinea, 12.3% in Lomé, 12.5% in Benin [5-7]. These vascular pathologies are a major cause of maternal and perinatal morbidity and mortality. They are the cause of 18% of all maternal deaths [1] after immediate post-partum hemorrhage. However, there are disparities between countries. United Nations statistics report a rate of 16% of maternal deaths attributable to hypertensive disorders in high level income countries [7]. In Asia and Africa, nearly 10% of maternal deaths are associated with HDP. The complications which lead to this death are: eclampsia, HELLP syndrome, retroplacental hematoma (RPH), acute pulmonary edema (APO), and strokes.

The complications of vascular pathologies can hold back on the fetus and the newborn. These complications are dominated by prematurity, perinatal asphyxia, intrauterine growth restriction (IUGR) and fetal death in utero. In France, the neonatal mortality rate due to vascular pathologies is 12.5% [8]. In Africa, a case-control study carried out in Niamey (Niger) showed a fetal mortality rate four times higher in the group of hypertensive pregnant women compared to the group of normotensive pregnant women [8].

In addition to complications, several factors are associated with poor perinatal prognosis of vascular pathologies in low-income countries. These are young maternal age, existence of a pathological obstetrical history, absence of antenatal care visits (ANC), a number of ANC less than 4, poor surveillance, low gestational age at the time of the diagnosis of the disease, delay in the decision to terminate the pregnancy, delay in referral to level II or III maternity hospitals [9].

Besides HDP, diabetes, whether pre-existing or not, can complicate pregnancies. The prevalence of gestational diabetes is increasing worldwide with rates ranging from 1.8% to 23% depending on the study population and diagnostic criteria [10]. A 2017 WHO study showed that the incidence of gestational diabetes was estimated at 16.2% in pregnant women aged 20-40 years [11]. In the same study, it was shown that 21.4 million children born to diabetic mothers with more than 90% from low-income countries had neonatal complications. The most common fetal complications were macrosomia, IUGR, prematurity, congenital malformations, especially cardiovascular and renal, and chromosomal anomalies. Macrosomia is the most frequent complication [12]. Its risk is doubled in cases of gestational diabetes compared to a normal pregnancy. Its incidence in newborns of diabetic mothers varies between 17 and 30%, compared to only 10% in the general population. Newborns from diabetic mothers are more able to have fetal trauma (skull and clavicle fractures) and metabolic disorders such as hypoglycemia in the first hours of life and hypocalcemia [13, 14].

In a precarious health environment, such as that of BENIN, where the medical devices are insufficient, it is essential to screen the population of pregnant women at risk of hypertension or diabetes in order to improve the prognosis of the pregnancy with a multidisciplinary approach. Several studies have been done on hypertensive disorders and diabetes associated with pregnancy; however, very few have linked patient characteristics to maternal and perinatal outcome. The objective of this study is to analyze maternal and perinatal complications of vascular pathologies associated with pregnancy in a third level maternity hospital in Cotonou (Benin) by determining 1) their frequency and 2) their associated factors.

2. Methodology

2.1. Data

This analytic cross-sectional study with retrospective data collection over a 3-year period, from January 1, 2016, to December 31, 2018 included the records of all mothers with vascular pathology and their newborns during the study period at the Clinique Universitaire de Gynécologie obstétrique (CUGO) of Centre National Hospitalier Universitaire Hubert Koutoukou Maga (CNHU-HKM) of Cotonou which is a third level maternity. The records of patients who had given birth but had not developed vascular pathologies during pregnancy, delivery, or postpartum were ruled out. The same applies to newborns of mothers who had a vascular pathology associated with pregnancy but did not deliver at CUGO (outborn). Permission from the heads of the CUGO and pediatric departments of the CNHU-HKM were obtained. Data were collected with respect to confidentiality and anonymity, both for the babies and their parents.

2.2. Variables

Dependent variable was the maternal and perinatal complications of vascular pathologies. Independent variables were related to sociodemographic characteristics (age, occupation, education level, residence); clinical characteristics (obstetric, medical, surgical, and family history, mode and reason for admission, type of delivery); physical examination data (blood pressure, weight, height, body mass index, level of consciousness using GLASGOW scale, neurosensory signs, lower limb edema, uterine height, fetal heart sounds, albuminuria); paraclinical data. For children, variables were related to clinical characteristics (birth term, weight, sex, notion of resuscitation, fetal asphyxia, prematurity, low birthweight, respiratory distress, hypothermia). Maternal complications included: neurological (eclampsia, stroke), hematological (retroplacental hematoma, HELLP syndrome), cardiopulmonary and renal complications. Perinatal complications included IUGR, fetal asphyxia, prematurity, neonatal resuscitation, hypotrophy and perinatal death. The different maternal and perinatal complications were used as binary variables.

2.3. Statistical Analyses

Study sample was described in terms of sociodemographic

characteristics (age, occupation, level of education, residence), mode and reason for admission, obstetrical and medical-surgical history. Obstetrical examination, paraclinical check-up, delivery modalities as well as the maternal and perinatal complications were also described. Quantitative variables were expressed as mean with standard deviation and qualitative variables as proportions with confidence intervals. Factors associated with maternal and perinatal complications were identified by using bivariate analyses to select candidate variables (chi-2 test for qualitative variables), and then a multivariate model was performed by binary logistic regression model. Analyses were performed with SAS software 9.4 (SAS Institute, Inc, Cary, NC). A p value less than 5% was significant.

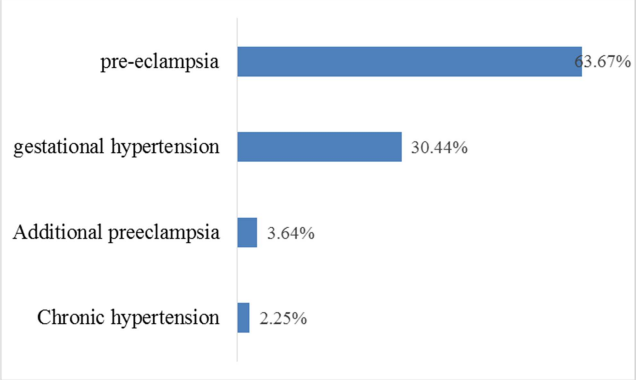

Figure 1. *Distribution of hypertensive disorders of pregnancy at CUGO of CNHU-HKM from 2016 to 2018 (n=1291).*

3. Results

Sociodemographic and clinical characteristics of patients

This study included 1291 cases of vascular pathologies associated with pregnancy out of a total of 8634 deliveries, i.e. a hospital frequency of 14.95%. Pre-eclampsia and gestational hypertension were the most frequent clinical types (Figure 1) with overall frequencies of 63.5% and 30.36% respectively. Diabetes was associated in 4.57% of cases.

The average age of the patients was 28.32 years, with the 18 to 35 age group being the most represented. As shown in Table 1, the majority of patients were not educated (43.99%) and lived in urban areas in more than half of the cases. The main reasons for referral were pre-eclampsia, lumbopelvic pain and hypertension. The majority of patients were pauciparous with a short spacing interval between births. Pregnancy was well attended in 45% of cases with 59.41% of patients who delivered by caesarean section.

Table 1. *Socio-demographic and clinical characteristics of patients.*

	Numbers	Percentages (%)
Age groups		
Youngs	34	02.62
Middle	1040	80.56
Olds	192	14.87
Missing	25	01.94
Education		
No education	568	43.99
Primary level	285	22.08
Secondary level	266	20.60
University level	172	13.33
Residence		
Urban	746	57.78
Rural	545	42.22
Admission mode		
Herself	318	24.60
Refered	973	75.40
Admission reason		
Lumbopelvic pain	325	25.17
Hypertension	221	17.12
Pre-eclampsia	356	27.57
Eclampsia	118	09.14
Loss of fluid	61	04.72
Convulsions	54	04.18
Delivery labor	161	12.47
Metrorrhagia	108	08.36
Fetal asphyxia	115	08.90
Gestation		
First gestation	401	31.00
Second gestation	422	32.70
Multigestation	468	36.30
Parity		
No delivery	127	14.32
One	224	25.22
Two	361	40.65
≥ 3	176	19.81

	Numbers	Percentages (%)
Spacing interval between births		
Short	38	07.27
Normal	485	92.73
Antenatal care visits (ANC)		
< 4 ANC	374	54.28
≥ 4 ANC	315	45.72
Gestational week (GW) at diagnosis		
Before 34 GW	537	41.60
Between 34 et 37 GW	225	17.43
More than 37 GW	559	40.98
Number of fetuses		
Singleton	1176	91.10
Twin or multiple	115	08.90
Type of delivery		
Vaginal	524	40.59
Cesarian section	767	59.41

Maternal and perinatal complications of vascular pathologies associated with pregnancy and associated factors

Table 2 shows that the main maternal complications were retroplacental hematoma (12.08%) and eclampsia (08.37%) between those who had signs of eclampsism (21.07%). Perinatal complications in this study were mostly prematurity (43.07%), low birthweight (29.12%), fetal asphyxia (12.32%) and perinatal death (18.59%).

Table 2. *Maternal and perinatal complications of vascular pathologies associated with pregnancy at the CUGO of CNHU-HKM from 2016 to 2018.*

	Numbers	Percentages (%)
Maternal complications		
Eclampsism		
Yes	272	21.07
No	1019	78.93
Eclampsia		
Yes	108	08.37
No	1183	91.63
Stroke		
Yes	08	00.62
No	1283	99.38
Retroplacental hematoma		
Yes	156	12.08
No	1135	87.92
HELLP syndrome		
Yes	25	01.94
No	1266	98.06
Acute pulmonary edema		
Yes	11	00.85
No	1280	99.15
Acute kidney failure		
Yes	38	02.94
No	206	15.95
Missing	1047	81.11
Perinatal complications		
Prematurity		
Yes	556	43.07
No	553	42.83
Missing	182	14.10
Neonatal resuscitation		
Yes	101	07.82
No	881	68.24
Missing	309	23.94
Low birthweight		
Yes	376	29.12
No	612	47.41
Missing	303	23.47
Intra-uterine growth restriction		
Yes	55	04.26
No	1236	95.74

	Numbers	Percentages (%)
Fetal asphyxia		
Yes	159	12.32
No	1132	87.68
Perinatal death		
Yes	240	18.59
No	1051	81.41

As shown in Table 3 below, in bivariate analysis, the frequency of maternal complications was significantly higher in middle-aged patients, in cases of significant proteinuria, in patients referred, in patients with poor antenatal care and in those who had caesarean section. On the other hand, the occurrence of perinatal complications decreased significantly with the term at diagnosis. In multivariate analysis, only the effects of significant proteinuria (OR=5.83; 95% CI [2.85-11.9]) and term at diagnosis persisted with a linear trend of significant reduction of the risk of maternal and perinatal complications in the latter (OR=0.49; 95% CI [0.34-0.70]).

Table 3. *Factors associated with maternal complications of vascular pathologies associated with pregnancy at the CUGO of the CNHU-HKM.*

	Maternal complications		**p-value**	**OR***	**95%CI***
	Yes	**No**			
Age groups			0.04		
Youngs	16 (03.14%)	18 (02.38%)		1.26	[0.66-2.30]
Middle	431 (84.68%)	609 (80.45%)		1	
Olds	62 (12.18%)	130 (17.17%)		0.77	[0.38-1.55]
Type of hypertensive disorders			<0.0001		
Without significant prateineria	62 (12.04%)	360 (46.39%)		1	
With significant prateineria	453 (87.96%)	416 (53.61%)		5.83	[2.85-11.92]
Admission mode			<0.0001		
Herself	71 (13.79%)	247 (31.83%)		1	
Refered	444 (86.21%)	529 (68.17%)		1.12	[0.55-2.27]
First delivery			0.12		
No	387 (75.15%)	553 (71.26%)		1	
Yes	128 (24.85%)	223 (28.74%)		0.96	[0.51-1.80]
Gestational week (GW) at diagnosis			<0.0001		
Before 34 GW	128 (24.85%)	401 (51.68%)		1	
Between 34 et 37 GW	92 (17.86%)	133 (17.14%)		1.70	[1.20-3.81]
More than 37 GW	295 (57.28%)	242 (31.19%)		4.14	[2.02-8.50]
Test for linear trend				*0.49*	*[0.34-0.70]*
Type of delivery			0.002		
Vaginal	183 (35.53%)	435 (56.06%)		1	
Cesarian section	332 (64.47%)	341 (43.94%)		1.67	[0.88-3.18]
Spacing interval between births			0.55		
Short	181 (91.98%)	304 (93.25%)		1	
Normal	16 (8.12%)	22 (6.75%)		0.95	[0.35-2.58]
Antenatal care visits (ANC)			0.001		
< 4 ANC	93 (37.65)	222 (50.23%)		1	
≥4 ANC	154 (62.35%)	220 (49.77%)		1.04	[0.58-1.87]

Abbreviations:
OR: Odd ratio
CI: Confidence intervals
*Multivariable logistic regression model
Bold indicates statistical significance

As shown in Table 4 below, the frequency of perinatal complications was significantly higher in patients with significant proteinuria, in referred patients, in patients with less antenatal care visits or short spacing interval between births, and in those who delivered by cesarean section. On the other hand, their frequencies decreased significantly with the term at diagnosis. In multivariate analysis, the effects of mode of admission, significant proteinuria, and earliness of diagnosis persisted with a significant linear trend test for the latter (OR=0.06 IC95% [0.02-0.14].

Table 4. *Factors associated with perinatal complications of vascular pathologies associated with pregnancy at the CUGO of the CNHU-HKM.*

	Perinatal complications		**p-value**	**OR***	**CI***
	Yes	**No**			
Age groups			0.14		
Youngs	24 (02.85%)	10 (02.36%)		1.33	[0.75-2.15]
Middle	702 (83.37%)	338 (79.72%)		1	

	Perinatal complications		p-value	OR*	CI*
	Yes	No			
Olds	116 (13.78%)	76 (17.92%)		0.71	[0.28-1.80]
Type of hypertensive disorders			<0.0001		
Without significant prateineria	182 (21.26%)	240 (55.17%)		1	
With significant prateineria	674 (78.74%)	195 (44.83%)		3.22	[1.43-7.26]
Admission mode			<0.0001		
Herself	149 (17.41%)	169 (38.85%)		1	
Refered	707 (82.59%)	266 (61.15%)		2.49	[1.12-5.53]
First delivery			0.06		
No	637 (74.42%)	303 (69.66%)		1	
Yes	219 (25.58%)	132 (30.34%)		0.70	[0.31-1.61]
Gestational week (GW) at diagnosis			<0.0001		
Before 34 GW	175 (20.44%)	354 (81.38%)		1	
Between 34 et 37 GW	215 (25.12%)	10 (02.30%)		20.70	[10.2-30.81]
More than 37 GW	466 (54.44%)	71 (16.32%)		44.18	[12.6-154.8]
Test for linear trend				*0.06*	*[0.02-0.14]*
Type of delivery			0.25		
Vaginal	338 (39.49%)	186 (42.76%)		1	
Cesarian section	518 (60.51%)	249 (57.24%)		0.94	[0.43-2.06]
Spacing interval between births			0.03		
Short	298 (90.85%)	187 (95.90%)		1	
Normal	30 (09.15%)	08 (04.10%)		1.24	[0.28-5.32]
Antenatal care visits (ANC)			0.02		
< 4 ANC	189 (42.57%)	126 (51.43%)		1	
≥4 ANC	225 (57.43%)	119 (48.57%)		1.24	[0.59-2.63]

Abbreviations:
OR: Odd ratio
CI: Confidence intervals
*Multivariable logistic regression model
Bold indicates statistical significance.

4. Discussion

Hypertensive disorders of pregnancy and diabetes are frequent in the world, regardless of the level of development of the countries, but with an increasing trend in low-income countries. The frequency of HDP in Africa varies from 12.3% [15] in Togo to 17.5% in Guinea [16]. Our frequency of 14.95% falls within this range. In general, the rates reported in high-income countries are low, ranging from 7 to 10% in Canada and the United States [4, 17, 18]. However, there is little data on all HPD with pregnancy, which makes comparisons difficult. The available data are mostly related to pre-eclampsia, which is the main clinical form of hypertension associated with pregnancy (63.5% of all forms of hypertension in our study). Like the association between hypertension and pregnancy, pre-eclampsia is more frequent in low-income countries than in high-income ones, with rates varying from 3 to 7%, particularly in the United States, the United Kingdom and France [18-20]. However, there are limitations to this comparison, as the rates calculated in high-income countries are related to the total number of pregnancies, whereas in low-income countries they are expressed in relation to the number of deliveries, which is the case in our study.

Besides HDP, the association of diabetes and pregnancy represents a potential risk for both mother and child. The frequency of diabetes associated with pregnancy is very diversely assessed in the literature; it varies from 1% to 17% according to Western and Asian studies and from 5% to 38% according to African studies [20]. Our frequency of 4.57% takes into account gestational diabetes and type 2 diabetes. The tendency of Africans to adopt a westernized diet combined with a sedentary lifestyle explains the increase in diabetes rates.

The average age of the patients was 28 ± 6.36 years. According to the authors, these ages correspond to the period of maximum fertility [21]. In Africa, the age of childbearing is lower because of early marriage and unschooling of young girls. However, this age tends to increase, as is the case in northern countries where the age of childbirth is decreasing. The patients did not attend school in 43.99% of cases, corresponding to an unfavorable socioeconomic profile. Multigestation and pauciparous women were the most numerous in our study with respective rates of 36.3% and 40.6%. The same result was found in other African samples [22, 23].

HDP discovering in this study was late in almost half of the cases. In fact, it was the term at which the diagnosis was made, explained by the poor monitoring of the pregnancy and late referral of the patients. In fact, three quarters of the patients in this study were referred from local hospitals, health centers or private clinics when they presented a hypertensive attack before or during labor. There were no ANV or this one was irregular in 54.3% of cases. The situation is similar for most low-income countries. Lower rates of ANC were found in two studies from Senegal (65.4%) and Morocco (60.4%) [22, 23]. Studies have already identified the factors that explain the low use of prenatal services. These are economic and socio-cultural factors and poor health coverage in low-income countries [24, 25].

Eclampsia is the first complication of HDP. It is also the main complication in most African and Western samples, 77.8% in Côte d'Ivoire [26], 32.35% in Morocco [09] and 10.75% in Japan [27]. The differences between the series reported in the literature are related to the level of health development of the countries with a much lower frequency of eclampsia in high-income countries. In addition to eclampsia, retroplacental hematoma (RPH) appears to be the second most common complication of HDP, 12.08% in this study. This rate is close to that reported in Mali (11.6%). These two main complications associated with hellp syndrome, which is still under-diagnosed in our working conditions, explain the lethality rate of HDP, which is 1.54% in this study. Obstetrically, cesarean section was the main delivery method (59.4%). Indeed, most of the patients presented a severe clinical picture, endangering the vital prognosis of the mother and the fetus, which indicated that a vaginal delivery was not appropriate.

HDP has also fetal and neonatal consequences. Fetal consequences include IUGR, acute fetal asphyxia, in utero death, and prematurity. IUGR is the result of chronic fetal suffering and can lead to very low birthweight. In this study, the rate was 4.26%. Higher rates have been found in other African series, 18.1% in Nigeria [28], 19.4% in Congo [29]. In general, IUGR rates are lower in series from high-income countries, thus the rate of IUGR from vascular causes was 7.2% in the United States [30], and 9% in Switzerland [31]. When considering the different rates reported in the literature, the IUGR rate in our study would be comparable to those of Western series. However, this rate is underestimated in our study firstly due to selection bias and secondly to the diagnostic criteria for IUGR which lack precision in most African series. Besides IUGR, one of the frequent complications of vascular pathologies associated with pregnancy is prematurity (43.07% in this study). This is a prematurity caused by maternal and/or fetal complications such as eclampsia, eclampsia, hellp syndrome, IUGR, hyperuricemia greater than 80 mg/L, abnormalities in the fetal heartbeat and pathological umbilical and cerebral dopplers. In-utero death occurs at the end of a severe IUGR or during an acute event (eclampsia, retroplacental hematoma, hellp syndrome). In our series, perinatal mortality was 18.59%, higher than in some African studies 11.3% in Morocco [09], 13.2% in Congo [29].

Significant proteinuria was associated with maternal and perinatal complications. Indeed, it increases the risk of eclampsia, retroplacental hematoma, and hellp syndrome and leads to induced prematurity with a high morbidity and mortality. Other studies had already reached the same conclusions [32, 33]. Moreover, early diagnosis was associated with the occurrence of maternal and perinatal complications. Indeed, it has been shown that early forms of vascular pathologies associated with pregnancy are more serious [34]. This severity associated in our working conditions with the diagnostic delay linked to the late recourse to care explains the unfavorable maternal and perinatal outcome. Perinatal complications were significantly more frequent in referred patients. This is related to the status of the CNHU of Cotonou which is the center of last resort in BENIN health pyramid. It was not possible in this study to specify whether there were dysfunctions in the referral that could have an impact on maternal and perinatal prognosis. However, studies have already shown that referrals in health systems in developing countries are characterized by the first and second delays [35].

This retrospective study has inherent shortcomings in this type of data collection, particularly in most developing countries. Out of 1533 records expected from the delivery registers, only 1400 records were found, including 109 records that could not be used because of the absence of important data such as maternal and perinatal prognosis. These deficiencies are related to poor archiving of data and lack of computerization of records. This may result in an underestimation of the true frequency of vascular pathologies associated with pregnancy, and of the proportions of the different variables studied. Ideally, this selection bias should have been explored by comparing those excluded with those included. However, as the number of files retained was comparable to what is observed in similar studies, this exclusion was not likely to significantly influence the trend of our results. Despite these limitations, the strengths of this study include the large sample size and the analysis methodology (logistic regression) to control for potential confounders.

5. Conclusion

At the end of this hospital study, it was found that the frequency of vascular pathologies associated with pregnancy was 14.95%. Their evolution was marked by the occurrence of numerous maternal complications dominated by retroplacental hematoma, eclampsia which was characterized by signs of eclampsism, and hellp syndrome. Perinatal complications were mostly prematurity, low birthweight, fetal asphyxia and perinatal death. These different complications were associated with the earliness of the diagnosis, the mode of admission and the importance of proteinuria. Thus, early management of these pathologies will improve the maternal and perinatal prognosis. Prenatal consultations are therefore essential to detect the first evocative clinical signs in order to limit maternal and perinatal morbidity.

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