

Management and Maternal-Fetal Prognosis of Placental Abruption: A Retrospective Study of 130 Cases

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Abstract

Objective: To describe the epidemiological, clinical and prognostic factors and assess treatment of placental abruption in the obstetrics gynecology department of the Dakar Principal Hospital. Patients and Method: We carried out a retrospective observational study of 130 successive cases of placental abruption, which occurred from January 2015 to December 2017 at the Level 3 Maternity Unit of the Dakar Principal Hospital. Data were collected from noncomputerized obstetric records and analyzed using Excel and Epi info software. Results: There were 130 cases of placental abruption, that is a prevalence of 1.5%. The average age of onset of placental abruption was 30 years. The history of hypertension concerned 32.3% of patients, the average gestational age of 32.5 weeks at the time of diagnosis, grade 3 of Sher was found in 48.5% of cases. The outcome of the pregnancy was a caesarean section in 79.2% of cases, the average weight of newborns was 2058 g. The management of the complications required a blood transfusion and intensive care. A haemostasis hysterectomy was performed in 6.2% of cases. Stillbirth rate was 53.7% and maternal mortality was zero. Discussion and Conclusion: Placental abruption, a severe complication of pregnancy, is associated with high perinatal morbidity and mortality linked to the severity of the clinical picture, despite an improved maternal prognosis.

Keywords

Placental Abruption, Perinatal Mortality, Maternal Morbidity

1. Introduction

The main etiology of maternal morbidity and perinatal morbidity and mortality, placental abruption constitutes a medico-obstetric emergency of sudden onset, unpredictable, with clinical polymorphism. Its variable incidence worldwide, between 0.5% and 5% of pregnancies [1], is difficult to estimate due to the clinical, ultrasound and/or pathological diagnostic criteria used.

It is responsible for fetal complications dominated by induced prematurity, intrauterine growth retardation and fetal death in utero; and maternal such as hemorrhagic shock, coagulation disorders and in extreme cases death.

The objectives of our study were to:

- Determine the frequency of this condition;
- Identify etiological factors;
- Describe its clinical and paraclinical characteristics;
- Describe its therapeutic modalities;
- Assess maternal and neonatal prognosis.

2. Patients and Method

We carried out a retrospective, descriptive and analytical study, at the Level 3 Maternity Unit of the Principal Hospital of Dakar, over a period of 3 years between January 2015 and December 2017. Included in this study were patients with signs of placental abruption received and supported in the service.

The diagnosis of placental abruption was retained after direct visualization of a placental abruption on the delivery and/or in front of a very evocative clinical context (association of several clinical signs among the following: metrorrhagia, abdominopelvic pain, uterine hypertonia, non-reassuring fetal condition, hypertension pregnancy, fetal death in utero), or sometimes during antenatal ultrasound. Only pregnancies after 24 weeks were taken into account.

The data listed on the survey sheet were collected from non-computerized obstetric records, fully exploited despite some missing data, using Excel software.

The variables studied for each patient concerned the socio-demographic characteristics, the antecedents, the clinical, paraclinical and therapeutic aspects, the maternal-fetal prognosis.

The statistical test used for the comparisons was that of Chi2 for the qualitative variables or the Student test for the quantitative variables. Significance was set at a value of $p \le 0.05$.

3. Results

We collected 130 cases of placental abruption among the 8657 deliveries, that is a frequency of 1.5%.

 Table 1 summarizes the sociodemographic characteristics and patient history.

The prevalence of placental abruption was 1.5%. The average age of onset was 30 years with extremes of 17 and 47 years. The 25 - 35 age group was the most represented. The pauciparous were more represented (39.2%). The history of

| Socio-demographic characteristics | Ν | % |
|--------------------------------------|-----|------|
| Age (years) | | |
| <25 | 21 | 16.2 |
| 25 - 35 | 65 | 50.0 |
| >35 | 44 | 33.8 |
| Socioeconomic status | | |
| Down | 8 | 6.2 |
| Medium | 117 | 90.0 |
| Raised | 5 | 3.8 |
| Marital status | | |
| Married | 126 | 96.9 |
| Single | 4 | 3.1 |
| Obstetric history | | |
| Parity | | |
| Primiparous | 45 | 34.6 |
| Pauciparous | 51 | 39.2 |
| Multiparous and big multiparous | | |
| Peculiarities of obstetric history | 34 | 26.2 |
| Pregnancy hypertension, preeclampsia | 74 | 56.9 |
| Spontaneous miscarriage | 36 | 27.7 |
| Fetal death in utero | 11 | 8.5 |
| Placental abruption | 02 | 1.5 |
| None | 07 | 5.4 |

Table 1. Socio-demographic characteristics and patient history.

pregnancy-induced hypertension and preeclampsia was 56.9%, that of placental abruption 1.5%.

The main etiological factor found was hypertension (66.15%).

 Table 2 summarizes the clinical characteristics of the patients.

The most common reasons for admission were metrorrhagia (66.2%), abdominal pain/uterine contractures (63.1%) and absence of active fetal movements (36.9%), sometimes with a combination of these different signs.

The average gestational term of onset of placental abruption was 33 weeks 6 days with extremes of 24 and 42 weeks. Two out of five patients had a prenatal follow-up \ge 4 prenatal consultations.

The main clinical signs were dominated by metrorrhagia (88.5%), uterine hypertonia (60%) and high blood pressure (58.1%) which was pregnant in more than half of the cases.

Grade 3 of Sher was the most frequently found (48.5%).

Biological data had revealed an average hemoglobin level of 8.2 g/dl with

| Characteristics | Ν | % |
|--|-----|------|
| Reason for admission | | |
| Metrorrhagia | 86 | 66.2 |
| Abdominal pain/uterine contractions | 82 | 63.1 |
| Absence of active fetal movements | 48 | 36.9 |
| Preeclampsia | 29 | 22.3 |
| Hypovolemic shock | 02 | 1.5 |
| Gestational age at onset of placental abruption | | |
| <28 amenorrhea weeks | 7 | 6.4 |
| 28 amenorrhea weeks-36 amenorrhea weeks 6 days | 67 | 61.5 |
| 37 - 42 amenorrhea weeks | 35 | 32.1 |
| Prenatal follow-up | | |
| <4 prenatal consultations | 75 | 57.7 |
| ≥4 prenatal consultations | 55 | 42.3 |
| Clinical signs on admission | | |
| Metrorrhagia | 115 | 88.5 |
| Uterine hypertonia | 78 | 60 |
| Absence of fetal heart sounds | 62 | 47.7 |
| High blood pressure | 50 | 58.1 |
| Hypovolemic shock | 2 | 1.5 |
| Stage of placental abruption according to Sher's | | |
| classification | | |
| Grade 1 | 25 | 19.2 |
| Grade 2 | 42 | 32.3 |
| Grade 3a | 51 | 39.2 |
| Grade 3b | 12 | 9.3 |

Table 2. Clinical characteristics of patients.

extremes of 3.7 and 14 g/dl, a low prothrombin level of <70% in 38% of cases.

Ultrasound in the delivery room performed in 66.2% of cases made it possible to objectify the placental abruption.

The vast majority of patients (87.7%) benefited from oxytocin treatment for the induction of labor and/or for uterine retraction after childbirth; while intrarectal misoprostol was used in 67.7% of cases for the preventive or curative treatment of uterine atony. A proportion of 57.7% of cases required a blood transfusion with red blood cells and/or fresh frozen plasma.

 Table 3 specifies the distribution of patients according to obstetrical and surgical treatment.

The obstetrical-surgical management consisted of a caesarean section in about 4 out of 5 cases, and hemostasis procedures varied from triple arterial ligation to

| Obstetric-surgical treatment | Absolute frequency (n) | Relative frequency (%) |
|--------------------------------------|------------------------|------------------------|
| Induction of labour | 14 | 10.8 |
| Cesarean section | 103 | 79.2 |
| Vaginal delivery | 27 | 20.8 |
| Arterial ligation for haemostasis | 6 | 4.6 |
| Subtotal hysterectomy | 8 | 6.2 |

Table 3. Distribution of patients according to obstetrical and surgical treatment.

subtotal hysterectomy.

Maternal morbidity was dominated by anemia (62%), coagulation disorders such as Disseminated Intravascular Coagulation DIC (15.5%), hemorrhage due to uterine atony (9.9%), acute renal failure (5.6%). No maternal deaths were noted. This morbidity was greater in the case of placental abruption grade 3 of Sherwith 42.8%(p = 0.001).

A total of 136 births were counted (6 cases of twin pregnancy), with 63 live births (46.3%) including 6 who died secondarily in neonatology. An Apgar score at the 5th minute \leq 7 was noted in 49.3% of cases. The average weight of newborns at birth was 2058 g with extremes of 600 and 4200 g, patients having given birth before term in most cases. Neonatal mortality was statistically higher (58.9%) in patients who delivered by caesarean section (p = 0.019; OR = 2.7).

4. Discussion

Placental abruption has a variable incidence according to epidemiological studies, depending on the populations and the diagnostic criteria used (clinical, ultrasound, anatomo-pathological).

African series have found rates similar to that of our study (1.5%): 1.55% in Cocody [1], others higher (6%) such as Thiam [2]. This high incidence, contrasting with that of developed countries: 0.78% in Strasbourg [3], 0.49% in the United States [4], could have as explanatory factors the preponderance of hypertension, largely linked to lifestyle, climatic and seasonal factors [5], socio-demographic and economic characteristics specific to each population.

The risk factors for placental abruption are well identified in the literature [6]: maternal age <20 years or \geq 35 years, parity \geq 3, tobacco, chronic hypertension, history of preeclampsia, multiple pregnancies.

The hypertension in our series presents a rate (66.15%) higher than those of Kovovski 37.6% [7]. A personal history of pre-eclampsia increases the risk of recurrence of uteroplacental ischemia, whereas the risk of placental abruption is multiplied by more than 10 in the event of a history of severe pre-eclampsia in the second trimester [8]. The history of pregnancy loss as a risk factor was found in our series: 27.7% spontaneous miscarriage and 8.46% fetal death in utero, proportions different from those of Oyelese [4] respectively of 3%, 9% and 23%.

A history of abortions and fetal death in utero are responsible for endometrial and myometrial alterations that promote placental abruption [4].

Different series, including ours, confirm the consideration of placental abruption as an accident of the third decade [1] [4] [9].

The clinical picture of our series found metrorrhagia (88.5%), abdominal pain (66.2%), uterine hypertonia (60%), fetal death in utero (47.7%).

Our rates for metrorrhagia are identical to those of Nayama 89.9% [10] and Saulieres 78% [11], and higher than those of Gueneuc 60% [3] and Tikkannen 70% [12].

Abdominal pain and/or contractures were noted in 51% and 43% of cases according to Tikkannen [12] and Guennec [3], whereas the classic clinical form was observed by Bohec in 1 out of 3 cases [13].

The seriousness of the clinical pictures, as well as the delay in consulting patients explain the high proportions of these signs in sub-Saharan Africa, which is confirmed by the rate of 48.5% of grade 3 Sher in our serie.

The average hemoglobin level according to Gueneuc [3] was 9.3 g/dl (8.2 g/dl for our series) with extremes ranging from 1.2 g/dl to 14.4 g/dl. The prevalence of anemia, often multifactorial, is significant in our population, and it increases the risk of placental abruption from 1.9 to 2.45 [14] [15]. The same is true for vitamin deficiencies and folate deficiencies, whose influence on the course of pregnancy is evidenced by the reduction in the risk of placental abruption in the event of folate supplementation alone (OR = 0.81) or multivitamin. (OR = 0.72) [16].

The prevention or correction of systematic anemia, in our country, in wellmonitored pregnant women, cannot be affirmed in our series because of the insufficient quality of the follow-up (57.7% of patients had less than 4 consultations prenatal). In our context, anemia is also due to haemorrhage.

Defibrination first has a biological translation and is highlighted by the haemostasis assessment [17]: fibrinogen level < 2 g/l, platelets < 150,000/mm³, PDF > 20 µg/ml, prothrombin time < 50% of witness. Placental abruption is the main cause of hemostasis disorders in obstetrics, and the frequency of DIC complicating placental abruption varies from 3.33% to 31% [14].

Ultrasound can be performed (66.2% in our series) for diagnostic confirmation but should not delay management. A placental abruption can be visualized on ultrasound as a peripheral abruption of the placenta or an increase in its thickness, with a threshold of 5 to 6 cm, associated with a hyper to iso-echoic zone, of mixed echogenicity, hypo-echoic, or even anechoic, depending on the age of the hematoma [6].

Caesarean section as the preferred delivery route seems to be a consensual attitude in the case of placental abruption in a live child [18], whereas the vaginal route is favored in the case of fetal death in utero, by associating induction of labor and close maternal clinical and biological monitoring [6].

Our indications for caesarean section (79.2%) were dominated by maternal

salvage, living child placental abruption and association with placenta previa. Our rate, close to that of Gueneuc (79%) [3], is lower than that of Nayama 94.1% [10]. Vaginal delivery was performed mainly in the crude forms (20.76%). Immediate obstetric care depends on the term of the pregnancy, fetal vitality and the degree of maternal complications, according to Oyelese who proposes a management algorithm [4]. Caesarean section interrupts the vicious circle of coagulation in the event of placental abruption; the opening of the hematoma in the intervillous chamber favoring the passage into the maternal circulation of decidual thromboplastins and activated coagulation factors, leading to DIC aggravating the bleeding (phenomenon that persists as long as childbirth has not taken place).

The maternal prognosis is mainly linked to anemia (62%), due to hemorrhage which is the direct consequence of coagulation disorders associated with uterine inertia, and occurring on a sometimes precarious ground. Disorders of hemostasis (15.5% in our series) occurring in identical proportions: 4.5% in Burkina Faso [19], are observed in most cases during deliveries of stillbirths, and could be of variable intensity ranging from simple asymptomatic defibrination to severe DIC [20] [21]. The recommended diagnosis-expulsion time for uterine evacuation should not exceed 4 to 12 hours [4] to prevent the onset of coagulation disorders: 2.61 hours in our series. Cesarean delivery was correlated with a high rate of maternal complications, most often with fetal death in utero.

Maternal mortality is nil in our series, comparable to those of Boisramé [6], and Downes [22]. Nayama [10] and Akpadza [23] reported respectively 14.3% and 3.6% of maternal deaths for vaginal delivery, against 4.5% and 1.9% for caesarean section. Our result can be explained by the quality of obstetric care and resuscitation, the correct technical platform, and the almost constant availability of blood products.

The fetal prognosis depends on the severity of the clinical picture, the degree and type of abruption, the uterine evacuation time and the gestational age [24] [25] [26]. According to Downes' meta-analysis [22], the perinatal mortality rate varies from 4% to 56.3%. Neonatal mortality (53.7%) in a context of neonatal suffering was lower than that of Nayama [10] in Niger (75.5%), Thiam [2] in Senegal (60%) and high compared to Boisramé series (19%) [6].

There is a high rate of perinatal deaths (55%) associated with placental abruption and attributed to preterm birth, but the risk remains high despite adequate management of morbidities related to prematurity and growth retardation, the other cause of death is intrauterine asphyxia attributable to placental abruption [22]. The direct correlation between the fetal prognosis and the time elapsed before uterine evacuation allows a significant reduction in neonatal morbidity by reducing the extraction time from 30 to 20 minutes [24]. The stillbirth could be explained by a significant rate of crude forms (19.2%). Fetal morbidity in our series was dominated by low birth weight due to prematurity, growth retardation and acute fetal distress.

5. Conclusion

Placental abruption, a severe and unpredictable complication of pregnancy, is responsible for significant perinatal morbidity and mortality, despite an improvement in maternal prognosis, favored by rapid diagnosis and appropriate management. It is imperative to insist on a preventive attitude through better monitoring of pregnancy, detection and correct management of identified risk factors.

Declaration of Interests

The authors declare that they have no conflicts of interest in relation to this article.

References

- Mian, D.B., Angoi, V., N'guessan, K.L.P., Abauleth, Y.R., Kouakou, F. and Boni, S. (2014) Hématome retro placentaire et mort foetale in utéro: À propos de 70 cas et revue de la littérature. *Saraf*, **19**, Numéro 1.
- Thiam, O., Mbaye, M., Diouf, A.A., Touré, F.B., Gueye, M., Niang, M., Moreau, J.C., *et al.* (2014) Aspects épidémiologiques, pronostiques et thérapeutiques de l'HRP dans une maternité de référence en zone rurale. *The Pan African Medical Journal*, 17, Article No. 11. <u>https://doi.org/10.11604/pamj.2014.17.11.3554</u>
- [3] Gueneuc, A., Carles, G., Lemonnier, M., Dallah, F., Jolivet, A. and Dreyfus, M. (2015) Hématome rétroplacentaire: Terrain et facteurs pronostiques revisités à propos d'une série de 171 cas en Guyane francaise. *Journal de Gynécologie Obstétrique et Biologie de la Reproduction (Paris)*, **45**, 300-306. https://doi.org/10.1016/j.jgyn.2015.04.003
- [4] Oyelese, Y. and Ananth, C.V. (2006) Placental Abruption. *Obstetrics and Gynecology*, 108, 1005-1016. <u>https://doi.org/10.1097/01.AOG.0000239439.04364.9a</u>
- [5] Yackerson, N.S., Piura, B. and Friger, M. (2007) The Influence of Weather State on the Incidence of Preeclampsia and Placental Abuption in Semi-Arid Areas. *Clinical* and Experimental Obstetrics & Gynecology, 34, 27-30.
- [6] Boisrame, T., Sanane, N., Fritz, G., Boudier, E., Viville, B., Aissi, G., Favre, R. and Langer, B. (2014) Hematome retroplacentaire. Diagnostic, prise en charge et pronostic maternofœtal: Étude rétrospective de 100 cas. *Gynecologie Obstetrique & Fertilite*, 42, 78-83. https://doi.org/10.1016/j.gyobfe.2013.06.012
- [7] Kozovski, I., Bozova, S., Patanov, N., Protopopov, F. and Shopova, P. (1989) Abruptio Placentae in the Data from the Obstetrical Clinics in Varma, Tolbukhin and Shumen during 1984-1987. *Akush Ginekol (Sofiia)*, 28, 26-30.
- [8] Tica, V., Serbanescu, L. and Tica, I. (2006) Etiologic, Clinical and Prognostic Correlations in Abruptio Placentae. *Revista Medico-Chirurgicala a Societatii de Medici si Naturalisti din Iasi*, 110, 633-638.
- [9] Thieba, B., Lankoande, J., Akotionga, M., Kyelem, C., Ouedraogo, A., Ouedraogo, C.M. and Koné, B. (2003) Hématome retroplacentaire. Aspects épidémiocliniques et pronostiques à propos d'une série de 177 cas. *Gynécologie Obstétrique & Fertilité*, 31, 429-433. <u>https://doi.org/10.1016/S1297-9589(03)00117-6</u>
- [10] Nayama, M., Tamakloe Azamesu, D., Garba, M., Idi, N., Djibril, B., et al. (2007) Abruption Placentae Management in a Reference Nigerien Maternity: Prospective Study about 118 Cases during One Year. Gynécologie Obstétrique & Fertilité, 35, 975-981. https://doi.org/10.1016/j.gyobfe.2007.05.023

- Saulières, H. (2002) Hématome rétroplacentaire. Journées pyrénéennes Gynécol-Obstét Tarbes; 4-5.
- [12] Tikkanen, M., Luukkaala, T., Gissler, M., Ritvanen, A., Ylikorkala, O., Paavonen, J., et al. (2012) Decreasing Perinatal Mortality in Placental Abruption. Acta Obstetricia et Gynecologica Scandinavica, 92, 298-305. <u>https://doi.org/10.1111/aogs.12030</u>
- Bohec, C. and Collet, M. (2010) Hématome rétroplacentaire. Annales Françaises d'Anesthésie et de Réanimation, 29, e115-e119. https://doi.org/10.1016/j.annfar.2010.03.011
- [14] Kramer, M.S., Usher, R.H., Pollack, R., Boyd, M. and Usher, S. (1997) Etiologic Determinants of Abruptio Placentae. *Obstetrics & Gynecology*, 89, 221-226. <u>https://doi.org/10.1016/S0029-7844(96)00478-4</u>
- [15] Levy, A., Fraser, D., Katz, M., Mazor, M. and Sheiner, E. (2005) Maternal Anemia during Pregnancy Is an Independent Risk Factor for Low Birthweight and Preterm Delivery. *The European Journal of Obstetrics & Gynecology and Reproductive Biology*, **122**, 182-186. <u>https://doi.org/10.1016/j.ejogrb.2005.02.015</u>
- [16] Nilsen, R.M., Vollset, S.E., Rasmussen, S.A., Ueland, P.M. and Daltveit, A.K. (2008) Folic Acid and Multivitamin Supplement Use and Risk of Placental Abruption: A Population-Based Registry Study. *The American Journal of Epidemiology*, 167, 867-874. <u>https://doi.org/10.1093/aje/kwm373</u>
- [17] Wang, H.X. and Wu, X.Q. (2004) Disseminated Intravascular Coagulation in Obstetrics—Clinical Analysis of Cases. *Scimago Journal & Country Rank*, **39**, 408-410.
- [18] Sholl, J.S. (1987) Abruptio Placentae: Clinical Management in Nonacute Cases. American Journal of Obstetrics and Gynecology, 156, 40-51. https://doi.org/10.1016/0002-9378(87)90200-6
- [19] Thieba, B., Lankaonde, J., Akotionga, M., Kyelem, C., Ouedraogo, A., Ouedraogo, C.M. and Koné, B. (2003) Hématome rétroplacentaire: Aspects épidémiocliniques et pronostiques à propos d'une série de 177 cas. *Gynécologie Obstétrique & Fertilité*, **31**, 429-433. https://doi.org/10.1016/S1297-9589(03)00117-6
- Hall, D.R. (2009) Abruptio Placentae and Disseminated Intravascular Coagulopathy. Seminars in Perinatology, 33, 189-195. https://doi.org/10.1053/j.semperi.2009.02.005
- [21] Kor-Anantakul, O. and Lekhakula, A. (2007) Overt Disseminated Intravascular Coagulation in Obstetric Patients. *Journal of the Medical Association of Thailand*, 90, 857-864.
- [22] Downes, K.L., Grantz, K.L. and Shenassa, E.D. (2017) Maternal Delivery and Perinatal Outcomes Associated with Placental Abruption: A Systematic Review. *Ameri*can Journal of Perinatology, 34, 935-937. https://doi.org/10.1055/s-0037-1599149
- [23] Akpadza, K., Baeta, S., Neglo, Y., Tete, V. and Hodonou, A.K.S. (1996) L'hématome rétroplacentaire à la clinique de gynécologie-obstétrique du CHU Tokoin-Lomé (TOGO) de 1988 à 1992. Médecine d'Afrique Noire, 43, 342-347.
- [24] Ananth, C.V. and Peltier, A.M. (2011) Ischemic Placental Disease: Epidemiology and Risk Factors. *The European Journal of Obstetrics & Gynecology and Reproductive Biology*, **159**, 77-78. https://doi.org/10.1016/j.ejogrb.2011.07.025
- [25] Kayani, S.I., Walkinshaw, S.A. and Preston, C. (2003) Pregnancy Outcome in Severe Placental Abruption. *BJOG*, **110**, 679-683. https://doi.org/10.1046/j.1471-0528.2003.02088.x
- [26] Ananth, C.V. and Vanderweele, T.J. (2011) Placental Abruption and Perinatal Mortality with Preterm Delivery as a Mediator: Disentangling Direct and Indirect Effects. *The American Journal of Epidemiology*, **174**, 99-108. <u>https://doi.org/10.1093/aje/kwr045</u>