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ORIGINAL RESEARCH

Ascending infection is the leading cause of antepartum hemorrhage: A case–control study

Iván Rabinovich Orlandi[1,2] | Guido Patricio Gromadzyn[3] | Marta C. Cohen[1,4,5]

[1]Sheffield Children NSH FT, Sheffield, UK

[2]Dr. Prof. Bernardo A. Houssay Hospital, Buenos Aires, Argentina

[3]Dr. Juan P. Garrahan Hospital, Buenos Aires, Argentina

[4]Sheffield Teaching Hospital. Sheffield UK, Sheffield, UK

[5]University of Sheffield, Medicine and Population Health, Sheffield, UK

Correspondence
Marta C. Cohen, Sheffield Children Hospital FT, Western Bank, S10 2TH Sheffield, UK.
Email: marta.cohen@nhs.net

Abstract

Introduction: Placental abruption is a significant obstetric complication characterized by the premature separation of the placenta from the uterine wall, affecting 2–3 per 100 pregnancies. This condition presents a dual diagnostic challenge: obstetricians rely on clinical signs such as antepartum hemorrhage, abdominal pain, and ultrasound findings to suspect abruption, often leading to emergency cesarean delivery. Conversely, pathologists diagnose abruption through macroscopic and microscopic examination of placental tissue, identifying hematomas and signs of maternal vascular malperfusion. Notably, there is often a poor correlation between clinical diagnosis and pathological findings, with sensitivity reported as low as 30.2%. This study seeks to elucidate placental conditions associated with antepartum hemorrhage that may indicate abruption and emphasizes the importance of histopathological referral in understanding recurrence risks in subsequent pregnancies. By enhancing diagnostic accuracy, we aim to improve clinical outcomes for affected patients. Our objective is to evaluate placental conditions associated with antepartum hemorrhage and assess the correlation between clinical diagnoses and histopathological findings.

Material and Methods: A retrospective analysis of 285 placental histopathology reports from Sheffield Children NHS FT (January–December 2021) was conducted. This included 181 cases with clinical diagnoses of antepartum hemorrhage/abruption and 104 controls with well-controlled gestational diabetes mellitus. Histopathological findings were compared between groups.

Results: Significant placental findings associated with clinical antepartum hemorrhage/abruption included adherent blood clots (OR = 3.89, 95% CI: 1.88–8.04), umbilical cord hypercoiling (OR = 0.56, 95% CI: 0.33–0.96), and ascending infection/chorioamnionitis (OR = 3.08, 95% CI: 1.38–6.91). Histological abruption and chorioamnionitis were independently associated with antepartum hemorrhage (OR = 3.15, 95% CI: 1.21–9.87 and 3.13, 95% CI: 1.42–7.65 respectively), but there was no

Abbreviations: AMS, acute marginal separation; APH, antepartum hemorrhage; GDM, gestational diabetes mellitus; MVM, maternal vascular malperfusion; PA, placental abruption; TGDM, treated and well-controlled gestational diabetes mellitus.

Iván Rabinovich Orlandi and Marta C. Cohen contributed equally to this study.

significant association with maternal vascular malperfusion (OR = 1.46, 95% CI: 0.65–3.30). Gestational age was lower in the antepartum hemorrhage group (33 weeks) versus controls (39 weeks).

Conclusions: The most frequent placental conditions presenting as antepartum hemorrhage are ascending infection (leading to acute deciduitis) and histological abruption, suggesting a multifactorial spectrum. This is most relevant to the clinical implications involved, such as outcome and recurrence risk.

KEYWORDS
abruption, antepartum hemorrhage, chorioamnionitis, infection, maternal vascular malperfusion, obstetrics, placenta, placental abruption

1 | INTRODUCTION

Placental abruption (PA) is the premature separation of the placenta from the uterine wall, affecting 2–3 per 100 pregnancies.[1] There are two main diagnostic definitions of abruption, which are not necessarily coincidental:

I *For the obstetrician*, abruption is characterized by the presence of signs and symptoms (including ultrasound evidence) of placenta separation during gestation, encompassing antepartum hemorrhage (APH), abdominal pain, uterine contractions and/or uterine tenderness. When clinical abruption is suspected, an emergency cesarean section is often performed. The presence of adherent blood clots provides the obstetric team with diagnostic confirmation.[2–5]

II *For the anatomic pathologist*, abruption is characterized by the macroscopic finding of recent or remote retroplacental or marginal hematomas indenting the placenta, with or without circumvallation, excessive fibrin deposition with or without an underlying infarction (Figure 1). Microscopically, two main and distinct patterns are described: (1) marginal abruption with a peripheral clot, sometimes extending retro-membranous, (Acute Marginal Separation (AMS)); and (2): central retroplacental hematoma, often associated with maternal vascular malperfusion (MVM).

A recent abruption (either PA or AMS) is characterized by the presence of a retro placental or marginal fresh blood clot, with villous stromal hemorrhage, congestion and oedema (Figure 2). In chronic cases, hemosiderin laden macrophages in the decidua and adjacent infarcted villi indicate remote hemorrhage (Figure 3). In some cases, features of MVM are also present, including small placenta (<10th centile), decidual atherosis and infarcts distant from the abruption site, suggesting that an underlying vascular pathology is related to the PA[4,6–8] (Figure 4). While these findings support a diagnosis of abruption, they are not pathognomonic and may be absent even in clinically confirmed cases.[8]

Key message

Chorioamnionitis is more common in patients with antepartum hemorrhage than in those with histological abruption with or without maternal vascular malperfusion. The ascending infection causes acute inflammation, necrosis, and bleeding of the decidua.

In most cases of clinical abruption, there is poor correlation with pathology, with a reported sensitivity ranging from 30.2%, especially after considering the timing of the abruption[4,6,9] to 10% in more recent series.[7,10] Most studies suggest that acute abruption usually shows few or no findings on gross and/or histological examination, while these are almost always identified in chronic (remote) abruption. These findings highlight the existence of distinct clinical, macroscopic, and histologic differences between early and late abruption.[7] The clinical and pathological diagnosis of abruption bears an important prognostic value,[2,11,12] including a risk for recurrence of miscarriage and/or stillbirths if associated with maternal vascular malperfusion.[13,14]

One of the most common and objective clinical findings in abruption (acute or chronic) is the occurrence of APH or vaginal bleeding (VB), defined as any hemorrhage found in or from the genital tract during the second half of pregnancy.[15] Antepartum hemorrhage has an incidence of 3.5% and is principally caused by placental pathologies (>90%), with PA being the leading condition, alongside placenta previa and placenta accreta spectrum.[15] The proportion of APH related to PA varies according to multiple epidemiological studies showing a prevalence that ranges between 19% and 68.3%.[10,16–18]

This study aims to evaluate placental lesions in cases of APH, with a focus on the histological spectrum of abruption—including retroplacental hematoma and acute marginal separation—and its differential diagnosis, particularly in relation to chorioamnionitis and MVM. In addition, we intend to demonstrate the relevance of placental referral to histopathology, as identifying the precise condition leading to abruption may be of clinical relevance in further pregnancies (i.e., recurrence risk).

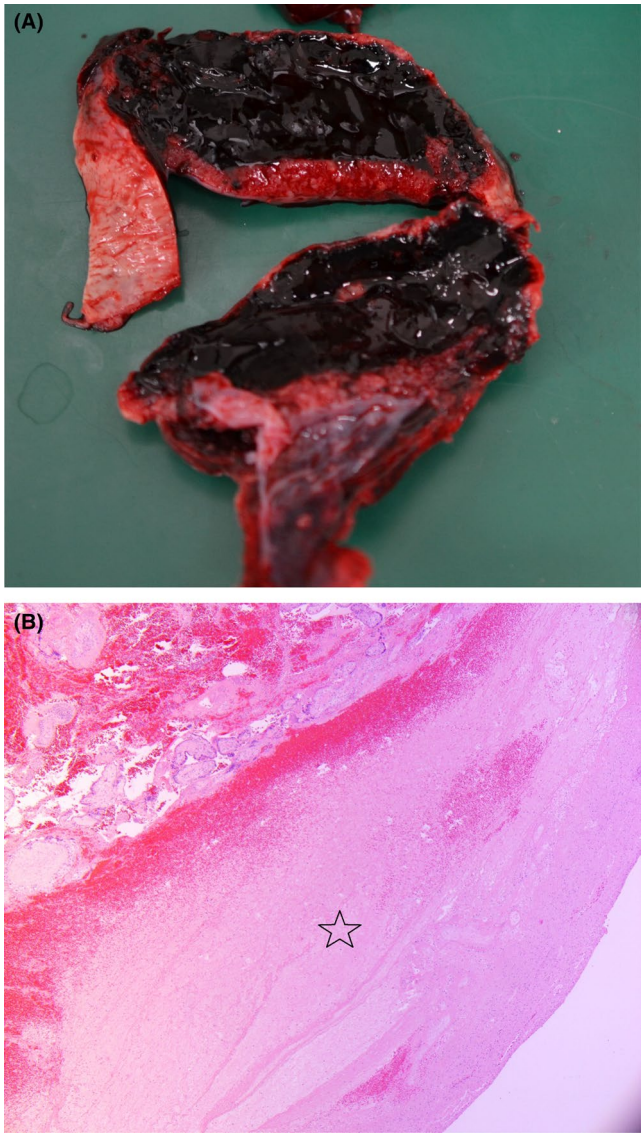

FIGURE 1 (A) Gross appearance of a fresh retroplacental hematoma. (B) Histological appearance of a fresh retroplacental hematoma, with fibrinous clot (star) (H&E ×10).

2 | MATERIAL AND METHODS

We conducted a retrospective analysis of all placental histopathology reports referred to Sheffield Children NHS FT during a 12-month period (January–December 2021) with the clinical diagnosis of "*antepartum hemorrhage* (APH)," "*vaginal bleeding*" (VB), and/or "*abruption*," occurring at or after 20 weeks of gestation. In England, placentas in 2021 were sent to histopathology following the Tissue Pathway for Histopathological Examination of the Placenta.[19] As the placentas are referred when there is a clinical indication, a control group was constituted with placentas referred with the clinical indication of treated and well-controlled gestational diabetes mellitus (TGDM). The reasoning behind choosing the control group was based on the numbers, usually normal findings, not presenting with APH, and gestational age diagnostic criteria of TGDM of more than 20 weeks. Controls with well-controlled gestational diabetes mellitus (GDM) were selected due to their systematic referral, minimizing selection bias. We excluded any case of preeclampsia, fetal growth restriction, or macrosomia. Statistical analysis confirmed no significant increase in MVM in controls compared to cases. No case in the APH group was diagnosed with GDM, and no patient in the control group presented with vaginal bleeding.

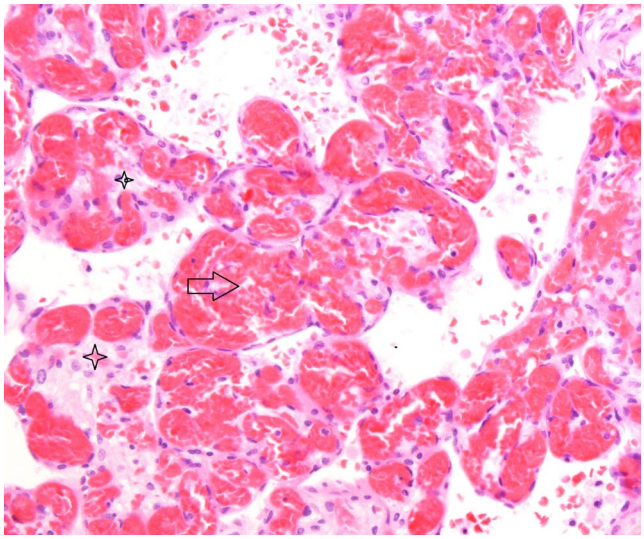

FIGURE 2 Villous vascular congestion (stars) and stomal hemorrhage (arrow) in placental abruption (H&E ×40).

With the objective of reducing the amount of confounding variables, we excluded placentas corresponding to stillbirths, COVID positive and/or twin gestations. In each placenta report (cases and controls), the following clinical and pathological information was retrieved: month of birth, gestational age (classified following the preterm birth definitions and classifications of the WHO 2023),[20] clinical diagnosis of abruption/APH/VB, macroscopic features, microscopic features, and final diagnosis. Placentas were mostly reported by four trained pediatric and perinatal consultant pathologists with proven and vast expertise in the topic. Table 1 shows the relevant macroscopic and histological features standardly described in placental reports (these latter were assessed following the Amsterdam Placental Workshop Group Consensus Statement (APWGCS)).[21] Reference ranges used at SCH are based on percentiles published in the Armed Forces Institute of Pathology (AFIP) placental pathology guidelines.[22] Abruption was defined histologically according to Amsterdam criteria as fresh retroplacental or marginal hematomas with adjacent stromal hemorrhage and edema with or without infarction or features of chronicity (e.g., siderophages). Timing was not available in most cases due to retrospective design. Finally, we filtered the cases with clinical diagnosis of abruption/APH/VB and compared the frequencies of the histopathologic diagnoses between the case and control groups.

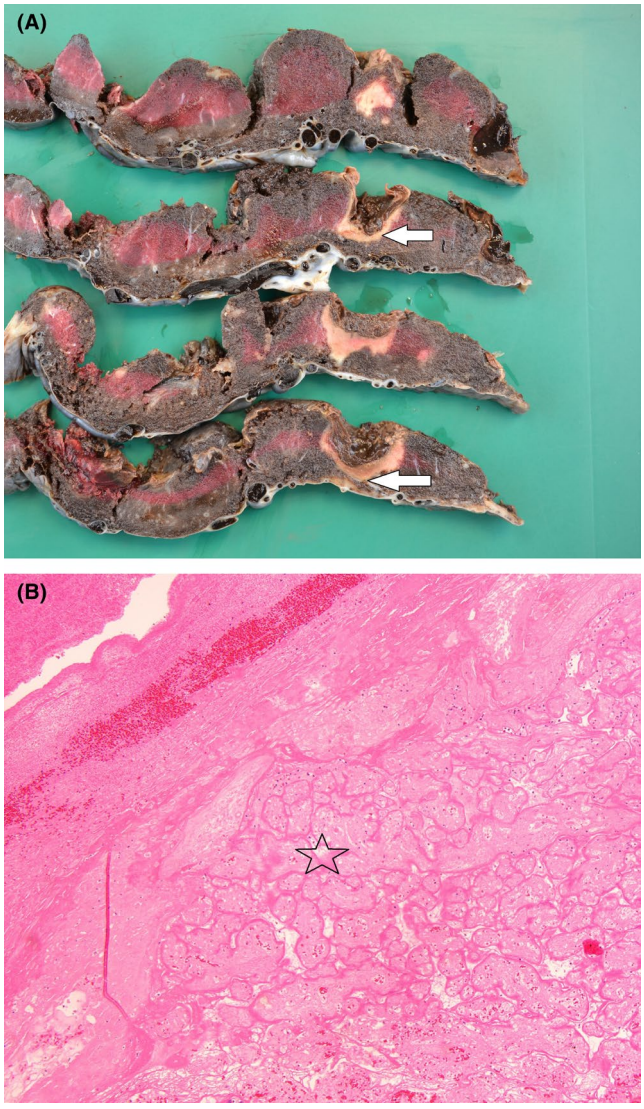

FIGURE 3 (A) Gross appearance of a less recent/chronic retroplacental hematoma, with a pale rim underneath it (white arrow). (B) Rim of infarcted villi underneath the chronic abruption (star) (H&E ×40).

2.1 | Statistical analyses

Histopathological diagnosis with categories was described using the distribution of absolute frequencies (number of cases within each category of the variable) and relative frequencies (percentage distribution of observations within each category). The normality of continuous variables' distribution was assessed using the Shapiro–Wilk test and quantile-quantile plots and described according to their normality or lack thereof. The explanatory variables were evaluated based on their association with the APH/A group when dichotomized against the TGDM group. The association between categorical variables was analyzed using the Chi-square test or Fisher's exact test as appropriate, and for continuous variables, the Wilcoxon or T-test was employed according to previously assessed normality. The association of gestational age (GA) and other variables was also analyzed. ANOVA test was used to assess differences in the median GA for categorical variables

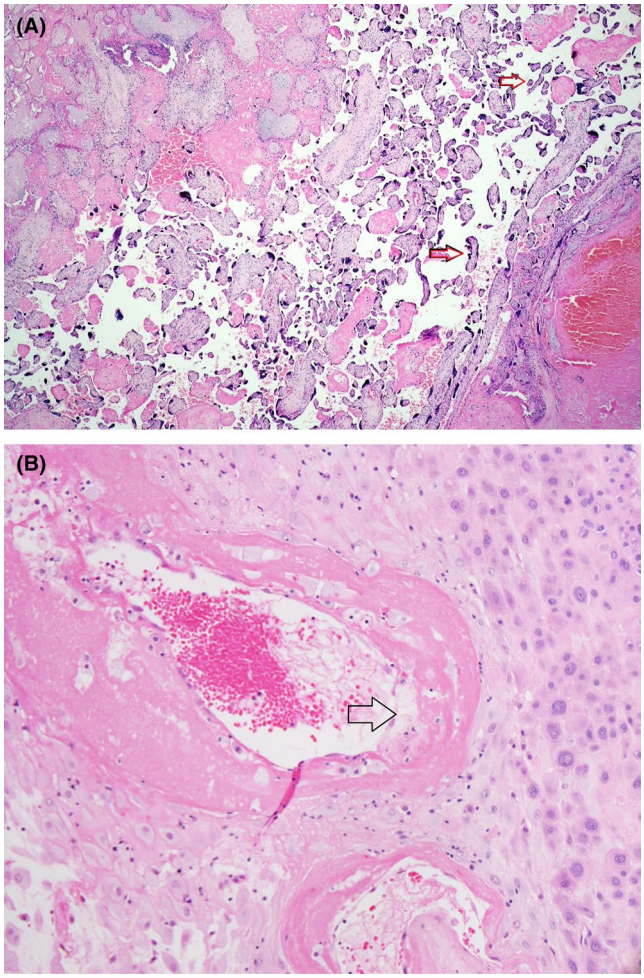

FIGURE 4 (A) Villous infarction and hypoplastic villi in a placenta with features of maternal vascular malperfusion (arrows) (H&E ×40). (B) Atherosis with foamy histiocytes and fibrinoid material in the wall of the decidual artery (arrow) (H&E ×100).

TABLE 1 Macroscopic and histological findings retrieved in each case and control placenta.

Macroscopy	Histology
• Placental and fetal-placental weight centile. • Adherent (attached to the maternal surface) or significant (>500 g) amount of loose (found on the specimen bag) blood clots. • Umbilical cord coiling index (number of coils by the length of the umbilical cord, taking 0.08 to 0.30 as normal reference values). • White or hemorrhagic lesions on cut surface. • Circumvallation. • Accessory lobes.	• Maternal vascular malperfusion (MVM) • Fetal vascular malperfusion (FVM) • Villitis of unknown etiology (VUE) • Delayed villous maturation (DVM) • Ascending intrauterine infection (AII), including maternal (chorioamnionitis and subchorionitis) and foetal inflammatory responses staging and grading. • Abruption: retroplacental central or marginal hematoma indenting and/or causing infarction on the immediate placental tissue. • No significant findings or NOS (non-otherwise specified).

of more than 2 categories. Post hoc analysis was performed in these cases using Tukey multiple comparison test.

The crude odds ratio (OR) and its corresponding 95% confidence interval (CI) were calculated for each explanatory variable using a simple logistic regression model, considering the association with the APH/A group as the response variable. Multiple logistic regression models were constructed, including variables that were statistically significant in the previous analysis. The potential association between some explanatory variables was also evaluated, and the variance inflation factor (VIF) was used to check for problematic multicollinearity. The Hosmer–Lemeshow test was used to assess the goodness of fit of the model. Adjusted ORs and 95% CIs were obtained for the variables in the selected multiple logistic models. Statistical significance was considered for probabilities less than 5% ($p < 0.05$). All of the statistical analysis was conducted using R software version 4.3.0 (2023-04-21, R Foundation) through the RStudio development environment version 2023.03.0 + 386.

3 | RESULTS

3.1 | General information

A total of 3969 placentas were received in the pathology department of Sheffield Children NHS Foundation Trust between January and December 2021. After applying exclusion criteria, a total of 285 patients were recruited, consisting of 181 cases with a clinical diagnosis of Antepartum Hemorrhage and/or Abruption (APH/A) and 104 controls with only treated/well-controlled Gestational Diabetes Mellitus (TGDM). Also excluded from the analysis were 80 patients that had a diagnosis of clinical Abruption without mention of APH and 8 patients that had APH with placenta previa diagnosis. Distribution of cases and controls by gestational age groups is shown in Table 2. The median gestational age for the APH/A placentas was 33 ± 4 weeks, while that of the TGDM was 39 ± 1 weeks (OR = 0.72 (CI95% 0.64–0.78); p-value < 0.001).

Cases and controls were distributed in the gestational age groups as per WHO recommendations (25), demonstrating that APH/A placentas were predominantly preterm (72%) and TGDM placentas were primarily term (87%). See Table 2.

3.2 | Macroscopy

Table 3 shows the macroscopic characteristics of the placentas in both groups. As shown, the placental weight and the fetal-placental weight ratio showed no significant difference between APH/A and GDM. The most common findings in the APH/A group were the presence of adherent blood clots (29%), hypercoiling of the umbilical cord (22%), and loose blood clots (16%). However, only the presence of adherent blood clots, umbilical cord hypercoiling, and/or significant amounts of loose blood clots were statistically significant and positively correlated with APH/A. TGDM placentas lacked significant association with the presence of pathological findings (OR = 0.31 (CI95%: 0.18–0.54)). Among the adherent blood clots, marginal hematomas—defined as clots located at the placental border—were significantly associated with APH. In multivariate analysis, marginal hematomas showed an odds ratio of 5.51 (95% CI: 2.09–19, $p = 0.002$).

3.3 | Microscopy

Each case and control was categorized according to the Amsterdam consensus of placental pathology diagnosis.[21] In addition, we categorized each case as histological abruption and non-significant findings. As shown in Table 4, the most common histological diagnosis on the APH/A group corresponded to: chorioamnionitis (20.4%), histological evidence of abruption (17.1%), and maternal vascular malperfusion (12.2%). Superposition of histological abruption with chorioamnionitis was seen in 11 cases (6.1%) and 0 controls (Figure 5), and with maternal vascular malperfusion in only one case (0.6%) and one control (1.0%). Of these, significant and positively associated diagnoses with APH/A were: chorioamnionitis, including Maternal Inflammatory Response (MIR)-2 and 3 with low-grade inflammation and histological abruption. On the contrary, the ones negatively associated with APH/A characterized the cases with TGDM (control group) were delayed villous maturation and the absence of significant findings (OR = 0.48 (CI95%: 0.3–0.79)). No significant association was seen with maternal vascular malperfusion (OR = 1.46 (CI95%: 0.65–3.30)). In total, 81/104 (78%) control placentas and 95/181 (52%) APH placentas were reported with no specific abnormal findings.

TABLE 2 Gestational age at birth.

By gestational age groups	APH/A ($n = 181$)	TGDM ($n = 104$)	OR (95% CI)	p-value
Term (>37 w)*	51 (28%)	90 (87%)	0.06 (0.03–0.11)	<0.05
Late preterm (32–37 w)*	59 (33%)	9 (9%)	5.10 (2.40–10.81)	<0.05
Very preterm (28–32 w)*	34 (19%)	3 (3%)	7.79 (2.33–26.04)	<0.05
Extremely preterm (<28 w)*	37 (20%)	2 (2%)	13.10 (3.09–55.60)	<0.05

*Statistically significant difference between cases and control placentas.

TABLE 3 Macroscopic findings.

	APH/A ($n=181$)	TGDM ($n=104$)	OR (95% CI)	p-value
Placental weight[22]				
Adequate	138 (73%)	84 (81%)	0.76 (0.42–1.38)	0.376
Small	16 (8%)	6 (6%)	1.58 (0.60–4.18)	0.353
Large	27 (19%)	14 (13%)	1.13 (0.56–2.26)	0.736
Foetal-placental weight ratio[22]				
Adequate	146 (73%)	83 (80%)	1.05 (0.58–1.93)	0.861
Small	23 (21%)	14 (13%)	0.94 (0.46–1.90)	0.855
Large	12 (6%)	7 (7%)	0.98 (0.37–2.58)	0.973
Macroscopical findings				
Normal features*	95 (52%)	81 (78%)	0.31 (0.18–0.54)	<0.05
Pathological findings*	86 (48%)	23 (22%)	3.19 (1.84–5.51)	<0.05
Specific findings**				
Adherent blood clot*	53 (29%)	10 (10%)	3.89 (1.88–8.04)	<0.05
Loose blood clot*	28 (16%)	4 (4%)	4.57 (1.56–13.44)	<0.05
Umbilical cord hypercoiling*	40 (22%)	35 (34%)	0.56 (0.33–0.96)	<0.05
Placental lesions	7 (4%)	3 (3%)	1.35 (0.34–5.35)	0.665
Circumvallation	12 (7%)	3 (3%)	2.39 (0.66–8.68)	0.185

*Statistically significant difference between cases and control placentas. **The total is not equal to the sum of the parts because some categories overlap.

TABLE 4 Microscopic findings.

	APH/A ($n=181$)	TGDM ($n=104$)	OR (95% CI)	p-value
Non-otherwise specified	72 (40%)	60 (57%)	0.48 (0.30–0.79)	<0.05
Pathological diagnosis	109 (60%)	44 (42%)	2.06 (1.26–3.37)	<0.05
Specific findings**				
Maternal vascular malperfusion	22 (12%)	9 (9%)	1.46 (0.65–3.30)	0.363
Fetal vascular malperfusion	9 (5%)	4 (4%)	1.31 (0.39–4.36)	0.661
Chorioamnionitis*	37 (20%)	8 (8%)	3.08 (1.38–6.91)	<0.05
Subchorionitis	23 (13%)	9 (9%)	1.54 (0.68–3.46)	0.299
Villitis of unknown etiology	6 (3%)	8 (8%)	0.41 (0.14–1.22)	0.109
Abruption*	31 (17%)	5 (5%)	4.09 (1.54–10.88)	<0.05
Delayed villous maturation*	2 (1%)	11 (11%)	0.095 (0.021–0.44)	<0.05

*Statistically significant difference between cases and control placentas. **The total is not equal to the sum of the parts because some categories overlap.

3.4 | Multivariate regression

We calculated the adjusted OR for each variable following a multivariate regression model which showed that the only independent risk factors that stayed significantly associated with APH/A were the presence of *adherent blood clots* (OR = 4.26 (CI95%: 1.57–15)), chorioamnionitis (OR = 3.13 (CI95%: 1.42–7.65)), and *histological evidence of abruption* (OR = 3.15 (CI95%: 1.21–9.87)). We included gestational age as a covariate in multivariable models to adjust for this difference. Subgroup analysis of cases >34 weeks ($n=98$) also failed to show a significant association between MVM and APH (OR = 1.32, $p=0.41$).

3.5 | Gestational age differences in chorioamnionitis, subchorionitis, and abruption

The mean gestational ages differed significantly among the chorioamnionitis, subchorionitis, and the group without either condition ($F=19.75$, $p<0.001$), with the lowest mean gestational age observed

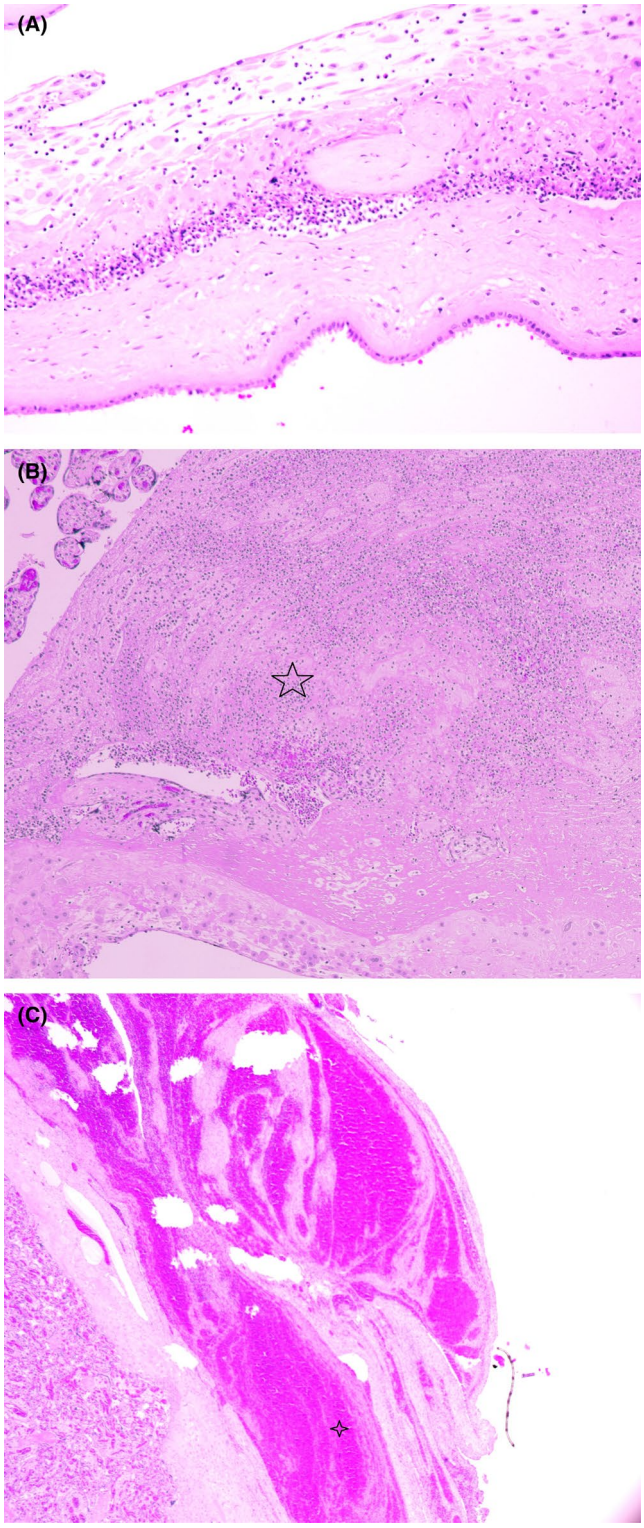

FIGURE 5 (A) Placental membranes demonstrating ascending infection with acute inflammation in the membranous decidua and acute chorioamnionitis (H&E ×40); (B) Basal decidua with acute inflammation and decidua (star) (H&E ×40). (B) Basal decidua with acute inflammation and decidua (star) (H&E ×40). (C) Retroplacental hematoma associated with ascending infection and acute chorioamnionitis (star) (H&E ×20).

in the chorioamnionitis group at 31.2 weeks. In the post hoc analysis, a significant difference was found between the group without and the chorioamnionitis group (Tukey, $p < 0.001$).

Similarly, the median gestational age in the abruption group was significantly lower at 33 weeks (IQR 10.86) compared to the "no abruption" group at 37.84 weeks (IQR 5.65), as indicated by the Wilcoxon test ($p < 0.001$).

4 | DISCUSSION

Antepartum hemorrhage (APH) is an important cause of maternal and perinatal morbidity and mortality, corresponding to one of the most frequent emergencies in obstetrics.[17] Over 90% of cases of APH are due to placental causes such as abruptio placentae (abruption) and placenta previa, but in some cases, the exact cause of bleeding cannot be determined.[17,23] Up to 35% of APH bleedings can be associated with abruption, but it is not a homogeneous diagnosis, as these can include acute inflammation, chronic inflammation, and vascular dysfunction as part of its pathogenesis[23] Histologic abruption is not addressed by the Amsterdam consensus classification, leading to under-recognition of key entities such as AII and MVM, despite their distinct prognostic implications.[2,14] This is most relevant as each of these conditions has different clinical and prognostic implications. AII has an infectious origin related to ascending invasion of microorganisms from the genital tract. While in most cases, AII is a consequence of a premature rupture of the chorioamnionic membrane,[24] it may also occur with intact membranes due to ascending subclinical infection.[25] AII has limited recurrence risk, particularly associated with preterm birth, and is generally managed with antibiotics to reduce neonatal sepsis risk; MVM has a high recurrence rate (~25%) due to genetic and epigenetic determinants, and histologic abruption may recur in up to 15%,[26]

Our results show that Chorioamnionitis is not just a coincidental finding in patients with APH, as it was more frequent than histological abruption, even taking into consideration that the most common macroscopic finding was the presence of adherent blood clots, often corresponding microscopically to acute deciduitis. After applying statistical multivariate regression, acute chorioamnionitis, alongside histological abruption, was the only two significant histological findings in patients with APH. This opens a new window for placental pathology research through the eyes of clinical presentation. Whether AII precedes or results from rupture remains uncertain. Some authors consider that abruption, as is AII, is not homogeneous and that acute abruption differs from chronic abruption in pathogenesis and prognosis.[23] Further research needs to contemplate the conundrum, as APH has multiple clinical contexts consisting of Chorioamnionitis (leading to acute deciduitis), marginal hematomas, MVM, Acute Abruption, and/or Chronic Abruption, and therefore introducing the concept of the APH spectrum of etiologies and prognosis. Chronic Abruption, marked by extensive fibrin deposition, remote infarcts,

and siderophages, may serve as a substrate for a superimposed acute-on-chronic abruption, carrying its own prognostic implications. Future studies should address the clinical outcomes associated with these subtypes to better refine recurrence risk estimates.

Our data support the distinction between two major entities: acute marginal separation (AMS), predominantly inflammatory, and abruptio placentae, primarily vascular.[10] Our findings supporting a diagnosis of AMS included marginal hematomas, acute chorioamnionitis, and acute deciduitis. Conversely, findings supporting classic PA included large retroplacental hematomas, infarcts, and features of maternal vascular malperfusion such as decidual vasculopathy. However, we found that inflammatory lesions were more common than vascular lesions, favoring AMS as a dominant contributor to APH in our population. In our cohort, we identified a significant subset of adherent blood clots located at the placental margin, consistent with marginal hematomas. These lesions were significantly associated with APH, with an adjusted odds ratio of 5.51 (95% CI: 2.09–19, $p=0.002$). Although higher surface marginal clots did not reach statistical significance, this likely reflects small sample size rather than lack of biological association. The consistent overlap between marginal hematomas, acute chorioamnionitis, and histologic abruption supports the hypothesis that AMS represents a distinct, inflammation-driven subtype of PA.

We found that chorioamnionitis was more common in patients with APH than histological abruption with or without MVM, even considering the most common macroscopic finding of adherent blood clots. This relates to the presence of fresh bleeding in the decidua with acute inflammation and necrosis. The mean gestational ages differed significantly among the AII, abruption, and control groups, with the lowest mean gestational age observed in the chorioamnionitis group at 31.2 weeks, followed by the median gestational age in the abruption group, 33 weeks, and the "non abruption" (control) group at 37.84 weeks. These findings suggest that APH may have multiple clinical contexts, including chorioamnionitis, acute abruption, and chronic abruption, and that the concept of an APH spectrum of etiologies and prognosis should be considered.

It is important to acknowledge that a proportion of clinically diagnosed abruptions show no corresponding placental findings. Contrary to some earlier estimates suggesting a 30% discrepancy,[4] more recent series report that the absence of pathological findings occurs in closer to 10% of confirmed clinical abruptions.[7,10] This highlights the importance of careful gross and histological examination in suspected cases. Our results indicate that chorioamnionitis, a consequence of ascending intrauterine inflammation (AII), is not just a coincidental finding in patients with APH. Importantly, whilst AII has some risk of recurrence in specific situations, it does not usually recur in subsequent pregnancies. In contrast, MVM has been shown to present a high risk of recurrence in pregnancy.

This study is limited by its retrospective nature, reliance on information from pathology request forms, and possible interobserver variability in histopathologic diagnosis. These limitations are inherent to retrospective placental studies and emphasize the need for standardized clinical-pathologic protocols. Other important limitations of the study were that, although control cases were well-controlled cases of gestational diabetes, it would have been better if the control group corresponded to placentas of normal pregnancies. However, these placentas are not submitted for examination according to the Tissue Pathway for Histopathological Examination of the Placenta.[19]

5 | CONCLUSION

APH is a complex and multifactorial condition that requires further research to understand its underlying causes and to develop effective prevention and treatment strategies. In this cohort, acute ascending infection and histological abruption were the leading placental findings in APH. Our findings suggest that AMS with an inflammatory background is a major contributor to APH, challenging the assumption that MVM-driven abruption predominates in these cases and highlighting the importance of histologic investigation for etiologic clarification and risk stratification. The concept of an APH spectrum of etiologies and prognosis may provide new insights into this condition and lead to improved outcomes for mothers and infants.

AUTHOR CONTRIBUTIONS

Marta C. Cohen designed and led the study and contributed to writing the manuscript. Iván Rabinovich Orlandi conducted the analysis, contributed to manuscript drafting, and provided critical revisions. Guido Patricio Gromadzyn conducted the statistical analysis and contributed to writing the manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare no competing financial interests related to this work.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

ETHICS STATEMENT

This study was approved by the Sheffield Children NHS FT Clinical Governance as an Audit project (Reference Number: SE1789) on 30 May 2023. The study was conducted in accordance with the Declaration of Helsinki. The patients consented for placental examination. All cases were anonymized.

ORCID

Iván Rabinovich Orlandi https://orcid.org/0009-0009-8513-7826
Marta C. Cohen https://orcid.org/0000-0001-5534-444X

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