

Original Article

Asian Pacific Journal of Reproduction

Journal homepage: <https://journals.lww.com/apjr/>

doi: 10.4103/apjr.apjr_140_25

An anatomopathological examination of placentas associated with adverse pregnancy outcomes in Moroccan women – A case series

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ABSTRACT

Objective: To characterize placental morphologic features in Moroccan women with adverse outcomes, across different clinical contexts, based on the Amsterdam consensus classification.

Methods: A prospective analysis was conducted on placentas with umbilical cords collected fresh between March 1, 2024 and July 15, 2024 from women with adverse pregnancy outcomes. Clinical data (age, parity, gravidity, complications) were retrieved. Macroscopic parameters (weight, dimensions, cord insertion, membranes, lesions) were assessed, followed by systematic sampling. Tissue was processed by standard histology (formalin fixation, paraffin embedding, hematoxylin and eosin staining), and lesions were classified per Amsterdam criteria.

Results: 16 placentas from patients with adverse pregnancy outcomes were included. The median maternal age was 30 years. Adverse conditions included placental abruption (50%), intrauterine growth restriction (IUGR, 38%), intrauterine fetal death (IUFD, 31%), pre-eclampsia/eclampsia (19%), premature rupture of membranes (13%), and oligohydramnios (13%). Several placentas were associated with more than one adverse condition. Histopathology revealed maternal vascular malperfusion lesions in 94%, particularly in pre-eclampsia, IUGR, and IUFD. Fetal vascular malperfusion was found in 88%, mainly in IUGR and IUFD. Inflammatory lesions, dominated by acute maternal and fetal responses stage 3 (necrotizing chorioamnionitis and funisitis), were primarily linked to IUFD.

Conclusions: Placental examination enhances understanding of the pathophysiology underlying adverse pregnancy outcomes, supports diagnostic confirmation, and guides preventive strategies for recurrence. This study highlights the prevalence of maternal vascular malperfusion in Moroccan women and emphasizes the importance of systematic placental histopathology in obstetric care.

KEYWORDS: Placenta; Anatomopathological examination; Adverse pregnancy outcomes; Pathological lesions; Amsterdam consensus; Maternal vascular malperfusion; Fetal vascular malperfusion

Key Points

Question: What are the predominant placental lesions in Moroccan women with adverse pregnancy outcomes?

Findings: In this prospective study of 16 placentas, maternal vascular malperfusion predominated, observed in 94% of the cases, most often associated with pre-eclampsia, intrauterine growth restriction (IUGR), and intrauterine fetal death (IUFD). Fetal vascular malperfusion occurred in 88%, mostly in IUGR and IUFD. Inflammatory lesions were found in 44%, particularly in IUFD.

Meaning: These findings highlight the predominance of maternal vascular malperfusion, which underscores the importance of systematic placental histopathology for understanding adverse pregnancy outcomes, informing preventive measures, and guiding clinical management in high-risk pregnancies.

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How to cite this article: Hilali C, Alaoui AM, Lamalmi N, Malki MY. An anatomopathological examination of placentas associated with adverse pregnancy outcomes in Moroccan women - A case series. *Asian Pac J Reprod* 2026; 15(1): 23–33.

Article history: Received: 7 June 2025; Revision: 10 October 2025; Accepted: 12 November 2025; Available online: 31 December 2025

1. Introduction

The placenta is a complex, highly specialized organ essential for fetal growth and development. It ensures the exchange of gases, nutrients, and waste between the maternal and fetal circulations, thereby conditioning the proper course of pregnancy. At term, it contains a capillary network estimated to be nearly 550 km in length, covering approximately 15 m², forming the villous tree indispensable for efficient materno-fetal exchange. Alterations in these finely regulated processes of angiogenesis and vasculogenesis may result in placental malperfusion, now recognized as a major factor contributing to adverse pregnancy outcomes[1].

According to the World Health Organization (WHO), around 810 women worldwide die every day due to preventable complications during pregnancy, delivery, or the postpartum period[2]. While global maternal mortality declined by approximately 34% between 2000 and 2020, 95% of these deaths still occur in low- and middle-income countries. In Morocco, the 2018 National Survey on Population and Family Health estimated perinatal mortality at 24.9%, and maternal mortality at 44.6 per 100 000 live births, with 44.6% of women experiencing at least one complication during pregnancy. Such figures highlight the urgent need for improved understanding and management of pregnancy-related complications[3].

Placental anatomopathological examination constitutes a fundamental diagnostic tool for exploring and elucidating adverse pregnancy outcomes. However, accurate interpretation necessitates comprehensive integration with maternal and fetal data to mitigate the risk of contextual misinterpretations[4]. It is therefore essential to acknowledge the pathologist's expertise in interpreting data on the mother's medical history, particularly in the anatomopathological examination of the placenta. In addition, the anatomopathological diagnosis should be made by the team of doctors from both specialties, obstetrics and anatomopathology.

The placenta has been understudied and underappreciated for many years. In 2016, the consensus statement of the placental workshop group recommended a diagnostic framework for placental lesions[5]. The Amsterdam classification of pathological lesions of the placenta encompasses all the major processes of placental pathology, including maternal vascular malperfusion (MVM), fetal vascular malperfusion (FVM), and inflammatory processes[5].

Despite its central role, placental histopathological examination remains underutilized in clinical practice. Adverse pregnancy outcomes are frequent, multifactorial, and often poorly understood. In this context, standardized placental analysis according to the international Amsterdam consensus is a crucial tool, as it enables classification of the main placental lesions and ensures consistent, comparable interpretation of findings across different populations and studies. It also contributes to a better understanding of placental

lesions, which, in other contexts, may help identify diagnostic, etiological, or prognostic markers and improve the prevention and management of at-risk pregnancies.

This study aims to investigate the anatomopathological characteristics of placentas from Moroccan women with adverse pregnancy outcomes by analyzing their morphological profiles (macroscopic and microscopic) across various clinical contexts and classifying placental abnormalities according to the Amsterdam consensus. This approach seeks to identify the most frequent anatomopathological entities in our setting and contribute to the broader understanding of placental findings across different populations.

2. Methods

2.1. Study design

Our study was a prospective descriptive case series focused on Moroccan women who experienced adverse pregnancy outcomes, including placental abruption, pre-eclampsia/eclampsia, intrauterine growth restriction (IUGR), or intrauterine fetal death (IUFD).

Data were collected prospectively in real-time between March 1, 2024, and July 15, 2024. Placentas were included consecutively as they became available and met predefined inclusion criteria.

2.2. Study population study

The included placentas were obtained consecutively from patients who delivered at the Department of Obstetrics and Gynecology of Ibn Sina University Hospital Center in Rabat, Morocco, and whose placentas were sent to the Department of Pathology for anatomopathological examination. All cases meeting the predefined inclusion criteria were collected consecutively between March 1, 2024, and July 15, 2024.

From an initial population of 30 Moroccan women who experienced complications during pregnancy, we selected a final sample of 16 placentas based on predefined criteria. The selection was performed consecutively, based on the availability of complete clinical and histopathological data, and the relevance of adverse pregnancy outcomes as defined by the inclusion criteria. No randomization or sampling method was used.

These cases involved patients who delivered with adverse pregnancy outcomes at the Department of Obstetrics and Gynecology, which recorded approximately 4 500 deliveries during the study period (from March 1st to July 15th, 2024). The included patients had a gestational age at term or near term (mean gestational age = 33 weeks), and their placentas were submitted to the Department of Pathology for anatomopathological examination.

Placentas resulting from spontaneous abortions, molar pregnancies, multiple pregnancies, or cases with incomplete clinical or obstetric records were excluded to avoid heterogeneity in placental pathology and ensure comparability of cases.

2.3. Data collection

The clinical and obstetrical data of the cases were collected from the patients' medical records, in accordance with the Declaration of Helsinki[6]. This included maternal age, parity, gravidity, medical and surgical and obstetrical history, and pregnancy-related complications. IUFD was defined as fetal death ≥ 20 weeks of gestation; IUGR as estimated fetal weight < 10 th percentile; and pre-eclampsia as hypertension ≥ 20 weeks of gestation accompanied by proteinuria or maternal organ dysfunction.

All patient data were fully anonymized prior to analysis; each case was assigned a unique study ID number, and all identifiable information was removed to ensure confidentiality. Informed consent was obtained from all participants. Data were anonymized and entered into SPSS (version 13.0) for analysis.

2.4. Anatomopathological examination of the placenta

The placenta was promptly delivered to the Department of Pathology for an anatomopathological examination. Upon arrival, a macroscopic examination was immediately conducted, following the technical processes described by L'Herminé-Coulomb *et al*[7]. The macroscopic examination allowed a precise description of the weight, dimensions, placental configuration, cord insertion, membranes, and visible lesions. Placentas were then fixed in 10% buffered formalin for 48 to 72 h. Following fixation, a detailed description was completed using a standardized macroscopy form in accordance with the Amsterdam consensus[5], which includes placental biometry, configuration, umbilical cord, amniotic membranes, chorionic plate, and basal plate[7]. The placenta was then cut into 1-2 cm strips according to standard histological techniques, and lesions observed on section were described. Sampling was performed in accordance with the Amsterdam consensus, including the umbilical cord (both fetal and maternal ends), free membranes and amniotic fluid, any macroscopic lesion, and placental parenchyma encompassing both the basal and chorionic plates. Additional blocks were taken based on clinical indications or macroscopic findings, such as areas of infarction, calcifications, hematomas, or thrombosis. The tissue cassettes were then processed following the standard laboratory protocol: dehydration in graded ethanol (70%–100%), clearing in xylene, and paraffin infiltration at 58 °C–60 °C. After embedding, sections 4–6 μm thick were cut using a microtome and stained with hematoxylin and eosin (H & E). Histological classification was evaluated based on a standard pathology protocol, as outlined in the

consensus statement of the Amsterdam Placental Workshop Group[5]. All placentas were examined by the same pathology team using a standardized Amsterdam consensus protocol to minimize observer bias.

2.5. Statistical analysis

Data were entered and analyzed using SPSS software (version 13.0, IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages [$n(\%)$], and continuous variables were expressed as medians with ranges to provide a clear summary of the data distribution. All variables were complete, and results are presented descriptively to highlight the main patterns and associations observed in the study population.

2.6. Ethics statement

This study was an observational study; there were no costs or interventions for patients, and data were collected from medical records. Data were kept confidential. Per established regulations and guidelines in our country, ethical approval was not deemed necessary for this particular study due to the anonymous nature of the data and the classification of the placenta as hospital waste. Informed consent was obtained from the patients.

3. Results

3.1. Patient characteristics

This study included 16 placentas collected from patients with adverse pregnancy outcomes at the Department of Pathology. The median age of our patients was 30 years (range 20–40 years). 69% of the patients were multiparous. Regarding the history of the patients, we found a history of early miscarriages (one to multiple miscarriages) in 50% of the cases, the causes of which are unknown due to the absence of complete clinical data on these patients, hypothyroidism in 6%, gestational hypertension, and pre-eclampsia in 25% of the patients. IUFD was noted in 25% of the patients, whereas 13% reported no particular history. The mean gestational age of our patients at delivery was preterm (33 weeks).

3.2. Clinical diagnoses during pregnancy

In our case series, the pathologies resulting from clinical diagnoses encountered by patients during pregnancy, either occurring independently or in combination with each other, were placental abruption found in 50% of the cases, IUGR in 38%, IUFD in 31%, pre-eclampsia and eclampsia in 19%, premature rupture of membranes and oligohydramnios in 13% of the cases each.

3.3. Macroscopic placental findings

3.3.1. Placental configuration abnormalities

In terms of placental configuration, we found 38% of the placentas of normal configuration, while 6% of the placentas were fragmented, and 13% of the placentas were placenta praevia associated with placenta accreta. Regarding placenta size pre-fixation, 31% of the placentas were below the 10th percentile weight, and 13% of the placentas had placentomegaly (Table 1).

3.3.2. Amniotic membrane abnormalities

In our case series, the amniotic membranes showed abnormalities of tinted appearance (the membranes showed hemorrhagic remodelling) in 31% of the placentas, and yellow-green discoloration in 13% of the placentas. Concerning translucency, the amniotic membranes are cloudy in 19% of the placentas and semi-translucent in 6% of the placentas (Table 1).

3.3.3. Umbilical cord abnormalities

All the umbilical cords of the placentas in our study contained 3 vessels, one vein, and two umbilical arteries. Regarding cord

insertion, marginal cord insertion (<2 cm from disc edge) was found in 19% of the placentas. The cords were excessively long in 6% of cases. A hypercoiled aspect of the cord without knots was observed in 13%, a hypocoiled aspect in 6%. The discoloration of the cords was diffuse red in 31%, yellow in 6% of the placentas. For cord morphology, a thin morphology was noted in 25%, and an edematous cord (>4 cm in diameter) in 13% of the placentas (Table 1).

3.3.4. Chorionic plate findings

On macroscopic examination of the chorionic plate, 31% of the placentas appeared normal, including 6% of the placentas that showed subchorionic fibrin deposition, within the spectrum of normal. The discoloration was yellow-green in 13% of the placentas. The chorionic vessels were dilated in 44% of the placentas; note the caliber of the vessel, which was dilated at least four times that of adjacent nondistended counterparts. The chorionic vessels were the site of thrombosis varying between 0.5 cm × 0.5 cm and 1.5 cm × 1.0 cm in 13% of the other placentas (Table 1).

3.3.5. Lesions at section slice

At section slice, the majority of placentas had an infarct (Figure 1A), infarction hematoma in 44% of cases, hypertensive in 19% of cases, and marginal in 13% of cases.

3.3.6. Basal plate findings

On macroscopic examination of the basal plate, retroplacental hematoma was observed in 50% of the placentas (Figure 1B); 13% of the placentas had a shredded aspect (the missing cotyledons) (Table 1); 31% of the other placentas had calcifications in the basal plate. In contrast, 6% of the placentas had a basal plate with normal morphology.

Table 1. Distribution of placental macroscopic abnormalities in the case series (16 cases).

Macroscopic abnormalities	n(%)
Placental configuration	
Fragmented	1(6)
Placental size	
Weight below the 10th percentile	5(31)
Placentomegaly	2(13)
Amniotic membrane	
Aspect	
Tinted (hemorrhagic remodelling)	5(31)
Yellow-green discoloration	2(13)
Translucency	
Cloudy	3(19)
Semi-translucent	1(6)
Characteristics of the umbilical cord	
Insertion	
Marginal	3(19)
Aspect	
Hypercoiled	2(13)
Hypocoiled	1(6)
Discoloration	
Diffuse red	5(31)
Yellow	1(6)
Length	
Excessively long (>70 cm)	1(6)
Morphology	
Thin	4(25)
Edematous	2(13)
Chorionic plate	
Yellow-green discoloration	2(13)
Dilated chorionic vessels	7(44)
Thrombosed chorionic vessels	2(13)
Basal plate	
Shredded (the missing cotyledons)	2(13)
Retroplacental hematoma	8(50)
Calcifications	5(31)



Figure 1. Macroscopic appearance of placental lesions. (A) Sectional slice of a placenta with an old whitish infarct, highlighted by the white arrow, indicative of prolonged interruption of uteroplacental blood flow and chronic villous ischemia, typically associated with sustained maternal vascular underperfusion; (B) Macroscopic appearance of a retroplacental hematoma at the basal plate, corresponding to acute bleeding between the uterus and the basal plate. This figure corresponds to the placenta of a 39-year-old patient, Gravida 3, Para 2 (G3P2), admitted at 28 weeks of gestation for placental abruption, which progressed to intrauterine fetal death (IUFD).

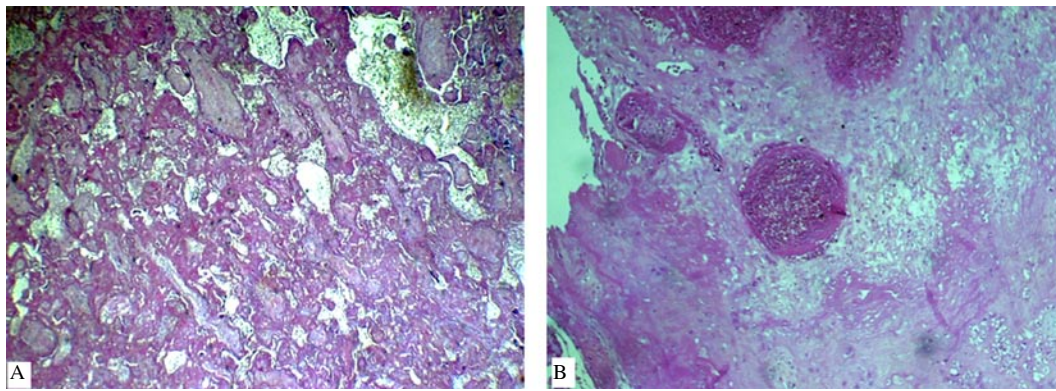


Figure 2. Histological section of maternal placental vascular malperfusion (MVM). (A) Chronic placental infarction (H & E, ×10), showing villous coagulative necrosis and collapse of the intervillous space, compatible with prolonged ischemic injury; (B) Decidual arteriopathy from the basal plate (H & E, ×10), demonstrating luminal arterial thrombosis with fibrinoid necrosis and persistence of muscular arterial walls, consistent with defective spiral artery remodeling. This placenta belongs to a 40-year-old patient, Gravida 2, Para 1 (G2P1), with a history of early miscarriage, admitted at 36 weeks for severe pregnancy complications, including placental abruption, severe intrauterine growth restriction (IUGR), and threatened preterm labor. The newborn was liveborn with a congenital malformation (Trisomy 21).

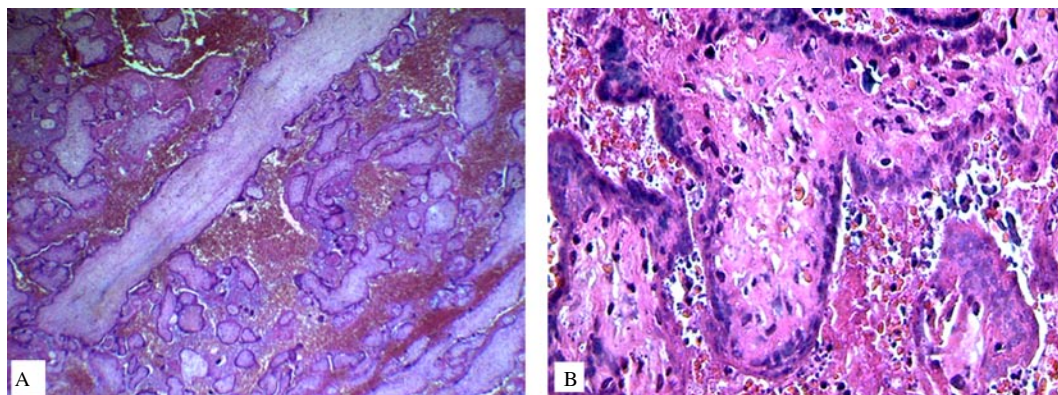


Figure 3. Histological section of fetal placental vascular malperfusion (FVM). (A) Avascular villi (H & E, ×20), showing terminal villi lacking capillaries with stromal fibrosis and preserved syncytiotrophoblasts, consistent with prolonged fetal vascular obstruction; (B) Villous stromal-vascular karyorrhexis (H & E, 40), characterized by nuclear fragmentation of fetal endothelial and stromal cells, with associated stromal apoptosis, hemorrhagic extravasation, and congestion. This placenta corresponds to a 33-year-old patient, Gravida 1, Para 0 (G1P0), with a history of early miscarriages and a previous intrauterine fetal death (IUFD). In the current pregnancy, she presented at 23 weeks of gestation with maternal infection, evolving into IUFD.

3.4. Microscopic placental findings

The different placental abnormalities and histological lesions found and evaluated based on the consensus statement of the Amsterdam placental workshop group were dominated by MVM lesions, which were present in 94% of the placentas, followed by FVM lesions, which were present in 88% of the cases, and then inflammatory lesions, which represented 44% of the placentas, and other placental abnormalities such as mesenchymal dysplasia and placenta accreta represented a percentage of 19%. In 88% of the cases, there was an association between MVM and FVM lesions.

Regarding the histological lesions of MVM (Figure 2), the most common in the case series were acute infarct in 81% of the placentas, retroplacental hematoma (50%), and lesions of decidual arteriopathy (44%), represented by arterial thrombosis (25%), absence of spiral artery remodelling (13%). In our study, the most common histological lesions in FVM were vascular thrombosis (50%) and

avascular villi (25%) (Figure 3). However, the inflammatory lesions found in our study were dominated by acute inflammatory lesions (Figure 4) and represented mainly by acute maternal inflammatory response stage 3 (necrotizing chorioamnionitis) in 19% of the placentas and acute fetal inflammatory response stage 3 (necrotizing funisitis) in 25% of the placentas, followed by chronic inflammatory response, represented by chronic villitis, which was determined by infectious staining as a chronic villitis of unknown aetiology, chronic intervillitis, chronic chorioamnionitis, chronic histiocytic intervillitis in 6% of the cases each (Table 2).

4. Discussion

It is commonly recognized that the placenta plays a crucial role in fetal development and survival, and the mother's state of health

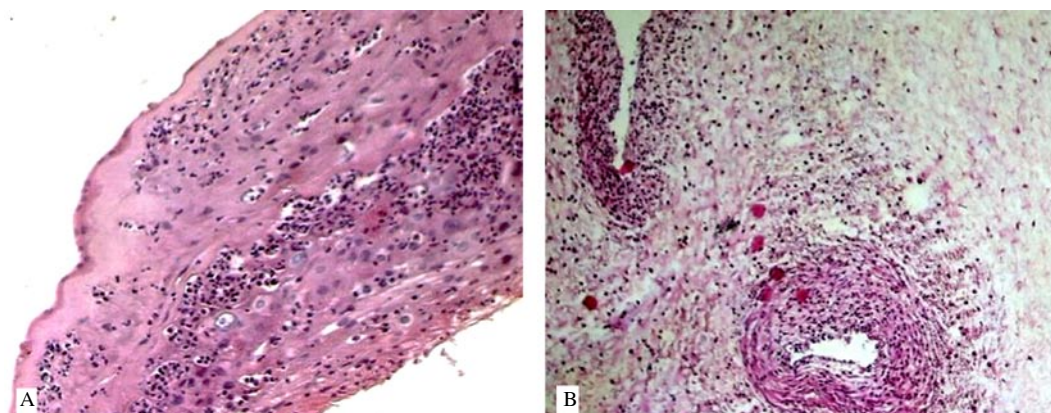


Figure 4. Histological section of inflammatory lesions. (A) Acute maternal inflammatory response stage 2 (acute chorioamnionitis) (H & E, $\times 40$). This lesion reflects an advanced maternal inflammatory reaction, marked by the progression of neutrophilic infiltration into the deeper chorioamniotic tissues; (B) Acute fetal inflammatory response stage 2 (umbilical arteritis) (H & E, $\times 20$). The involvement of the umbilical arteries indicates systemic activation of the fetal immune response, a characteristic of severe fetal inflammation. Panel (A) corresponds to a placenta from a 35-year-old patient, Gravida 4, Para 0 (G4P0), with maternal infection, diabetes, placental abruption, and intrauterine fetal death (IUFD) associated with congenital malformation. Panel (B) corresponds to a placenta from a 33-year-old patient, G1P0, with a history of early miscarriages and a previous IUFD; during the current pregnancy, she was admitted at 23 weeks for maternal infection that progressed to IUFD.

Table 2. Distribution of placental histological lesions according to the Amsterdam consensus (16 cases).

Placental abnormalities	n(%)
Maternal placental vascular malperfusion (MVM)	
Placental hypoplasia	4(25)
Infarct	
Acute infarct	13(81)
Chronic infarct	7(44)
Retroplacental hematoma	8(50)
Marginal hematoma	2(13)
Decidual arteriopathy	
Acute atherosclerosis	1(6)
Arterial thrombosis	4(25)
Absence of spiral artery remodelling	2(13)
Intervillous thrombi	
Subchorionic	2(13)
Central	1(6)
Fetal placental vascular malperfusion (FVM)	
Vascular thrombosis	8(50)
Avascular villi	4(25)
Villous stromal-vascular karyorrhexis	1(6)
Chorangioma	4(25)
Inflammatory processes	
Acute maternal inflammatory response	
Acute subchorionitis or chorionitis (stage 1)	1(6)
Acute chorioamnionitis (stage 2)	1(6)
Necrotizing chorioamnionitis (stage 3)	3(19)
Acute fetal inflammatory response	
Umbilical phlebitis (stage 1)	1(6)
Umbilical arteritis (stage 2)	2(13)
Necrotizing funisitis (stage 3)	4(25)
Chronic inflammatory response	
Chronic villitis of unknown aetiology	1(6)
Chronic intervillitis	1(6)
Chronic chorioamnionitis	1(6)
Chronic histiocytic intervillitis	1(6)
Other placental processes	
Placenta accreta	2(13)
Mesenchymal dysplasia	1(6)

during pregnancy[8]. Although anatomopathological examination of the placenta is not routinely recommended, its value is systematically proven. It has an indisputable interest in the management of patients and their children, particularly in explaining certain perinatal complications and detecting recurrent pregnancy disorders[7]. The criteria of Moroccan triage methods for examining placentas in the Department of Pathology include indications in which placental pathology has clinical relevance, such as IUFD, suspected placental abruption, pre/eclampsia, IUGR, suspected chorioamnionitis, premature rupture of membranes, oligohydramnios, non-reassuring fetal heart testing requiring urgent delivery, preterm birth, placental insertion anomalies (placenta accreta), fetal malformation, and maternal infection. It should be noted that the study only involves pathological placentas, making it challenging to include normal placentas in the analysis.

Regarding placental weight abnormalities, we found that 31% of the placentas in our study had a pre-fixation weight below the 10th percentile; this finding is often observed in the following circumstances: IUGR and placental abruption. Furthermore, placental hypoplasia has been reported to be associated with IUGR[8], and it has also been suggested to be linked with certain aneuploidies[9]. In addition, 13% of the placentas in our case series had placentomegaly; these placentas are often observed in placental abruption, including one case associated with placental mesenchymal dysplasia. In fact, a study of French pregnant women infected with the Zika virus showed that placentomegaly was observed more frequently in women from pregnancies with Zika virus[10]. In addition, previous studies have shown that placentomegaly can be caused by hydrops, unbalanced maternal diabetes, congenital nephrotic syndrome, Beckwith-Wiedemann syndrome, and placental mesenchymal dysplasia[7].

Regarding placental configuration, we observed 13% of cases with placenta accreta, one of which was associated with IUGR. However, other studies of pregnant women diagnosed with placenta accreta spectrum have shown that placenta accreta is not associated with IUGR. Additionally, it causes significant maternal and perinatal morbidity and mortality[11,12].

The normal umbilical cord averages about 0.2 coils/cm. For umbilical cord coiling abnormalities, hypercoiled cords are generally considered to be those in which the coiling index is >0.3 coils/cm, and hypocoiled cords are those in which the coiling index is <0.1 coils/cm[7]. In our case series, 13% of umbilical cords were hypercoiled and associated with IUGR, and 6% were hypocoiled and associated with IUFD. Indeed, a previous study showed that umbilical cord hypercoiling is associated with IUGR and IUFD, as well as preterm delivery and congenital abnormalities[13]. For umbilical cord hypocoiling, another study has shown that it is associated with fetal abnormalities, fetal distress, chromosomal errors, and increased fetal and neonatal morbidity and mortality[14]. While for umbilical cord insertion abnormalities, Pinette *et al*[14] found that marginal cord insertion has been shown to be strongly associated with IUGR. These findings are consistent with our study, which found that 18.8% of cases with marginal umbilical cord insertion were associated with IUGR.

In our case series, histopathological results show a predominance of MVM lesions, accounting for 94%. The most common histological lesions of MVM are acute infarcts in 81% of the placentas, retroplacental hematoma (50%), and decidual arteriopathy lesions (44%) represented by arterial thrombosis (25%) and absence of spiral artery remodelling (13%). MVM was observed in our study, mainly in the following conditions: pre-eclampsia, IUGR, and IUFD. Indeed, the incidence of MVM may be difficult to determine from the existing literature. The classic maternal clinical association with MVM is pre-eclampsia[15], characterized by high blood pressure during pregnancy (>20 weeks of gestation) and at least one other associated complication, including proteinuria, maternal organ dysfunction or uteroplacental dysfunction[15], which is compatible with some cases found in our series that had a pregnancy complicated by pre-eclampsia superimposed on gestational hypertension, in which histopathological examination of the placentas showed MVM lesions, consisting of infarcts and decidual arteriopathy. In addition, a retrospective American study of 16 345 placentas on the frequency of acute atherosclerosis lesions (decidual arteriopathy), indicative of MVM, showed that this lesion was more frequent in patients with pre-eclampsia (10.2%) than in uncomplicated pregnancies (0.4%)[16]. In our case series, histopathological examination of all placentas associated with IUGR showed MVM lesions consisting of infarcts and decidual arteriopathy. In fact, MVM lesions are classically associated with IUGR. Dutch, Australian, and American studies have shown that MVM lesions are significantly

more frequent in placentas with IUGR[7,17–19]. Multiple and central infarcts in the placentas at term are strongly associated with pre-eclampsia and IUGR[20], which is consistent with the placenta of a patient in our case series, who had a complicated pregnancy with IUGR and pre-eclampsia; on histopathological examination, her placenta showed a central infarct. However, placental MVM lesions may also be associated with other important clinical pathologies, such as IUFD. Since extensive placental infarction can be considered a cause of IUFD. A recent study found that infarcts and distal villous hypoplasia were the most common histologic components of MVM, a lesion significantly associated with IUFD. It is also associated with IUFD in cases of maternal hypertension, placental haemorrhage, and IUGR[21]. Man *et al*[22] found that MVM was the largest category of placental abnormalities in placentas associated with IUFD in the United Kingdom. Similarly, an American study found that acute atherosclerosis, indicative of MVM, was present at higher frequencies in patients with IUFD[16]. In addition, MVM lesions are associated with oligohydramnios, preterm delivery, eclampsia, hemolysis, elevated liver enzyme, low platelets (HELLP) syndrome, and abnormal uterine artery Doppler flow[17]. Moreover, the presence of MVM lesions is associated with a 10%-25% risk of recurrence in subsequent pregnancies[5].

In our study, FVM lesions were the second most common, with a prevalence of 88% of the placentas. The most frequent histological components indicative of FVM in our case series were vascular thrombosis (50%) and avascular villi (25%). It has been noted that FVM lesions are found most frequently in placentas associated with IUGR and IUFD in our series. For many pregnancy outcomes, particularly fetal death, a thorough examination of the placenta is crucial to determine the exact cause of death. Taking into account the possibility that some FVM lesions observed in cases of IUFD may be attributed to post-mortem changes, rather than pre-existing vascular malperfusion issues, which may result in FVM-like lesions, our study found that avascular villi were the most common component of FVM in placentas associated with IUFD, whereas extensive thrombosis was seen in placentas associated with IUGR. Concerning literature, Kulkarni *et al*[21] found that placentas associated with IUFD had a lower incidence of FVM (19.0%) compared to MVM (58.4%) in India and Pakistan. Indeed, recent studies have found that FVM lesions were significantly more frequent in the placentas of pregnant women with IUGR in India[23] and in the placentas of pregnant women with recurrent IUGR in Israel[24]. In fact, the major causes that can lead to FVM are thrombosis of umbilical vessels and the umbilical cord pathology, resulting in compromised blood flow[25]. Other contributing factors to FVM may frequently include pre-eclampsia, thrombophilia, polycythemia, cardiac dysfunction or malformation, large vascular abnormalities, and sometimes maternal diabetes[26]. FVM lesions can be global or segmental, classified by grade, high or low. In our study, global

FVM lesions were identified as being more frequent than segmental FVM lesions, and were associated with IUGR, oligohydramnios, placental abruption, and IUFD. In particular, they consisted of avascular villi in placentas significantly associated with IUFD. In fact, an Indian study has shown that global FVM is strongly associated with IUGR, low Apgar, asphyxia, poor neonatal survival, and fetal distress[23]. Moreover, other studies have found that central nervous system abnormalities are strongly associated with global FVM lesions, such as avascular villi, which were significantly increased in the placentas of newborns with cerebral palsy, and in the placentas of newborns with neonatal encephalopathy. Vascular intramural fibrin deposition has been associated with IUGR, umbilical cord entanglements, and fetal distress[27]. Furthermore, global FVM with an at-risk umbilical cord (entanglement, prolapse, hypercoiling, torsion, excessive cord length) is associated with a low risk of recurrence[26]. Regarding segmental FVM lesions in our case series, the most common histological findings were extensive avascular villi, observed in placentas associated with IUFD, and extensive thrombosis, observed in placentas associated with placental abruption. Indeed, an American study has shown that specific findings of segmental FVM, such as extensive avascular villi and thrombosis, have been strongly associated with IUGR, IUFD, oligohydramnios, fetal heart defects, and neonatal coagulopathies[26]. Furthermore, segmental FVM is associated with an increased risk of cases with inherited coagulopathies and a history of maternal or neonatal thromboembolic disease[26]. Regarding chorangiosis, our study identified its presence in 25% of the cases, with a higher frequency observed in placentas associated with IUGR, IUFD, preeclampsia, placental abruption, and premature rupture of membranes. Indeed, chorangiosis most commonly affects placentas at or near term, and it is associated with an increased risk of prenatal and neonatal morbidity and mortality[28]. A recent study conducted in Saudi Arabia found that no statistically significant associations were observed between potential maternal risk factors such as age, body mass index (BMI), type of gestation, gravidity, and parity, and the presence of chorangiosis. However, chorangiosis was found to be significantly associated with IUFD, an elevated number of abortions, and low neonatal APGAR scores at 5 minutes[29]. A case-control study conducted in Iran, which included 308 cases of chorangiosis compared to an equal number of controls, revealed several notable findings. In the chorangiosis group, there was a significantly higher prevalence of preeclampsia, IUFD, maternal hematocrit, oligohydramnios, diabetes mellitus, fetal anomaly, maternal hemoglobin, and various placental features, including retroplacental hemorrhage, calcification, fundal location, acute chorioamnionitis, and perivillous fibrin deposition. Additionally, the chorangiosis group exhibited lower birth weight, lower amniotic fluid index, lower 1st- and 5th-minute Apgar scores, and lower cord pH[30].

In the present study, the inflammatory lesions were predominantly

acute (44%), represented essentially by the acute maternal inflammatory response stage 3 (necrotizing chorioamnionitis) and the acute fetal inflammatory response stage 3 (necrotizing funisitis), and were mainly found in placentas associated with IUFD. This is in line with the findings of Cox *et al*[31], who demonstrated that the maternal inflammatory response is associated with neonatal morbidity and mortality, as well as preterm delivery and premature rupture of membranes in the United Kingdom. In addition, a meta-analysis study has shown that the maternal inflammatory response can also have serious consequences for the preterm or term newborn, such as cerebral palsy, ulcerative colitis, neonatal encephalopathy, periventricular leukomalacia, and chronic lung disease[9,32]. Recent Dutch and Israeli studies have shown that the maternal inflammatory response is present in IUGR placentas[17,33]. Regarding the fetal inflammatory response, represented by the necrotising funisitis lesion, it is associated with neonatal mortality and morbidity[5], closely associated with IUGR[7], and associated with a risk of cerebral palsy[32]. Furthermore, necrotizing funisitis has been suggested to be an important risk factor for the development of chronic lung disease in preterm infants. Additionally, the fetal inflammatory response has been associated with bronchopulmonary dysplasia[34]. In our case series, chronic inflammatory response lesions were observed in 25% of the cases, including unknown aetiology, chronic chorioamnionitis, chronic histiocytic intervillitis, and chronic intervillitis, each occurring in 6% of the cases. These lesions were predominantly found in placentas associated with premature rupture of membranes and IUFD. Our results align with the existing literature. A British study revealed an association between unknown aetiology and IUFD[35]. However, Feist *et al*[36] found that unknown aetiology was linked to a birth weight below the 10th percentile and hypertensive disorders during pregnancy in Germany. Unknown aetiology has also been associated with preterm and term IUGR, pre-eclampsia, foetal death, and preterm labour. In addition, infants with a placenta affected by an unknown aetiology are at risk of adverse outcomes such as mortality and neurodevelopmental abnormalities at 2 years of age[37]. An American study found that gestational diabetes and hypertension were associated with a diagnosis of unknown aetiology[38]. With regard to chronic chorioamnionitis, a Korean study found that this lesion was the most common lesion in preterm deliveries, especially late ones, and also in IUFD[39]. For chronic histiocytic intervillitis, it has been associated with significant implications, such as IUGR, premature delivery, poor neurological outcome in live newborns, miscarriage, stillbirth, and recurrence risk in future pregnancies[40,41]. Similarly, Feist *et al*[36] found that miscarriage and IUFD were associated with chronic histiocytic intervillitis in Germany. Concerning chronic intervillitis, a meta-analysis study showed that it was strongly associated with placental insufficiency, IUGR, IUFD, recurrent first-trimester miscarriages

with normal karyotype, and a high risk of recurrence in subsequent pregnancies[42].

Our findings contribute to the existing body of knowledge by offering a detailed examination of placental abnormalities in a Moroccan population with adverse pregnancy outcomes. This research not only identifies prevalent anatomopathological entities but also provides insights into the specific contexts in which these abnormalities manifest. By sharing our findings, we aim to help enhance the understanding of placental pathology across diverse populations and contribute to the broader discourse on adverse pregnancy outcomes.

This study holds critical significance for clinicians, researchers, and healthcare policymakers due to its insights into placental pathology and its links to adverse pregnancy outcomes. Understanding these associations directly impacts clinical practice by aiding diagnosis, risk assessment, and management. The study's revelations about placental features contribute to the development of diagnostic criteria and the identification of early markers, thereby enhancing healthcare decision-making. Moreover, this knowledge is pivotal for public health strategies aimed at addressing complications such as pre-eclampsia, IUGR, and IUFD. It also lays a foundation for future research, offering a global perspective by focusing on placentas from Moroccan women and contributing to a broader understanding of placental variation across populations.

There are some limitations of the study. The practice of anatomopathological examination of the placenta remains limited by a lack of interest among practitioners, a lack of standardisation in histological reports, and a lack of multidisciplinary consultation. In addition to its late nature, the examination is conducted after the child's birth. The clinical implications of histological diagnoses are not always immediately apparent, which limits the interest of pathologists and gynecologists. In addition to the non-availability of data for monitoring patients' pregnancies before their hospitalisations, there is an unrepresentative sample and the absence of national standardised curves adapted to our population. It is therefore important to respect the pathologist's knowledge of the data related to the mother's medical history, particularly in the anatomopathological examination of the placenta.

In conclusion, our study highlights the importance of anatomopathological examination of the placenta in cases of adverse pregnancy outcomes. It suggests that such examinations can help explain perinatal complications and detect recurrent pregnancy disorders, which can be valuable for patient management. By examining a series of placentas with umbilical cords from women with adverse pregnancy outcomes, our study aims to shed light on the pathological changes associated with these complications, share knowledge about different placental findings across various populations, and inform clinical practice and future research in this area.

The most frequent anatomopathological entities in our context from a cohort of 16 Moroccan pregnant women were MVM lesions, including acute infarct, retroplacental hematoma, and decidual arteriopathy lesions characterized by arterial thrombosis and absence of spiral artery remodelling. These findings underscore the specific burden of MVM in our population and highlight the crucial role of systematic placental examination in informing obstetric management and enhancing perinatal outcomes.

Conflict of interest statement

The authors have declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

The authors received no financial support for the research, authorship and/or publication of this article.

Authors' contributions

Chaimae Hilali conceived and designed the study, performed the methodology, analysis, investigation, visualization, and drafted the manuscript; Asmaa Mdaghri Alaoui, Najat Lamalmi, and Mounia Yousfi Malki supervised the work, contributed to data interpretation, and critically revised the manuscript; all authors approved the final version.

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Edited by Lin LY