Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu

RESEARCH ARTICLE

Placental Vascular Remodeling and Maternal–Fetal Perfusion: Anatomical and Physiological Mechanisms in Normal and Complicated Pregnancies: A Systematic Review

Fath Elrahman Elrasheed[1]*, Aymen Nasreldin Abdalkariem[2], Nife Mohammed Hamid[3], Sabah Elshafie Mohamed Elshafie[4], Awad Rahama Mustafa Elhussain[5], Salaheldeen Elhassab Omar Elhassab[6], Ahmed Elsir Mokhtar Abd Elmagid[7], Awadalla Abdelwahid[8], Khalid Eltayeb Hassan Abdalla[9] , Abdelgader Binymen Abdelgader Saleh[10]

[1] Department of Obstetrics and Gynaecology, Najran University, Najran, Saudi Arabia.

[2] Anatomy Department, Najran University, Najran, Saudi Arabia. ORCID: https://orcid.org/0000-0002-6514-5783

[3]Anatomy Department, College of Medicine, Najran University, Najran, Saudi Arabia. ORCID: https://orcid.org/0000-0002-6157-0838

[4]Department of Anatomy, Faculty of Medicine, Najran University, Najran, Saudi Arabia.

[5]Assistant Professor of Physiology. Najran University, college of Medicine, Najran ,Saudi Arabia.

[6] Lecturer in Physiology Department, Faculty of Medicine, Najran University, Suadi Arabia.

[7]Lecturer of Anatomy, Histology and Embryology, Department of Anatomy, College of Medicine, Najran University, Najran, Saudi Arabia. ORCID: https://orcid.org/0000-0002-1822-5588

[8]Department of Obstetrics and Gynecology, Alneelain University, Khartoum, Sudan. ORCID: https://orcid.org/0009-0008-3102-2786

[9]Lecturer of Anatomy, AlGhad College for Applied Medical Sciences, Najran, Saudi Arabia.

[10]Department of Physiology, Faculty of Medicine. Najran University, Saudi Arabia.

*Corresponding Author Fath Elrahman Elrasheed

Article History
Received: 08.08.2025
Revised: 15.09.2025
Accepted: 24.10.2025
Published: 02.12.2025

Abstract: Background: Maternal–fetal perfusion is important and is largely influenced by placental vascular remodeling focusing on the physiologic transformation of uteroplacental spiral arteries and formation of the villous microvasculature. Failure of these processes leads to the development of many significant obstetric syndromes, such as preeclampsia (PE) and fetal growth restriction (FGR). Advances in histopathology, Doppler ultrasound, micro-computed tomography (micro-CT), and magnetic resonance imaging (MRI) have offered better in vivo and ex vivo assessment. New clinical guidelines have also expanded the diagnostic criteria for hypertensive disorders of pregnancy. ***Methods:*** We conducted a systematic review of 22 studies—both primary and reviews—on placental vascular structure and perfusion in healthy and complicated pregnancies. Modalities included histology, micro-CT, Doppler, MRI (ASL, IVIM, BOLD), and molecular physiology. Outcomes were narratively synthesized by modality and condition, noting anatomical indices (eg, spiral artery transformation, villous architecture) and physiological markers (eg, Doppler PI/RI/notching, MRI perfusion and oxygenation metrics). ***Results:*** We observed that faulty spiral artery remodeling and maternal vascular malperfusion were consistently associated with PE and FGR. Histological results displayed acute atherosis and decreased myometrial transformation. The Doppler abnormalities—especially in first-trimester screening algorithms—improved the prediction of preterm PE and bolstered aspirin prophylaxis. Micro-CT demonstrated decreased vessel length density in FGR placentas. MRI allowed noninvasive functional measurement of perfusion and oxygenation, which was highly translatable. ***Conclusions:*** Placental vascular remodeling failure appears in all structural and functional levels. The integration of early-risk modeling and targeted imaging and standard pathology optimizes detection, mechanistic exploration, and clinical management of PE and FGR

Keywords: Placental remodeling, maternal vascular malperfusion, preeclampsia, fetal growth restriction, Doppler ultrasound, placental MRI.

INTRODUCTION

In humans, normal placental development requires carefully controlled anatomical and physiological remodeling of the uterine spiral arteries and villous vascular network. This change guarantees that blood flows to the intervillous space with low resistance and relatively high volume, fundamental to efficient maternal–fetal exchange [1]. In early gestation, extra villous trophoblasts (EVTs) infiltrate the decidua and superficial myometrium, replacing the endothelial lining and smooth muscle of spiral arteries. They deposit fibrinoid material, transforming these vessels into compliant channels—a process known as physiologic transformation [2]. This adaptation lowers maternal blood velocity, maximizes volumetric flow and shields the placenta from oxidative stress induced by shear influences [3]. Impaired or incomplete transformation is a common feature in placental

pathologies, such as early-onset preeclampsia (EO-PE) and fetal growth restriction (FGR) [4]. Foundations, based on research
on the placental bed, established the foundation for the conceptualization of the changes shown, with authors such as Brosens describing the ultrastructural development of spiral arteries and linking aberrant reorganization of the arteries to hypertensive conditions [5]. Recent advances in pathology have broadened this field, including morphometric studies and the characterization of the placental bed as a dynamic tissue niche [6]. Acute atherosis (acute atherosis involving foam-cells in uteroplacental arteries) is the current accepted feature of MVM mainly for preeclampsia and is described alongside FVM in published taxonomies [7]. Physiological evaluation brings an added temporal dimension as O2 tension ~20 mmHg in the placenta is initially low, which increases with uteroplacental circulation, but decreases near term [8]. This oxygen gradient controls trophoblast differentiation and angiogenesis. Abnormal hypoxia mediating pathways have been implicated in a shallow trophoblast invasion and villous deformation [9] predominantly due to HIF-mediated pathways interruptions in O2 signaling pathways. Inadequate remodeling results in high-velocity maternal inflow and reperfusion injury, leading to syncytiotrophoblast stress and release of anti-angiogenic and inflammatory mediators—two drivers of the maternal syndrome associated with preeclampsia, as the two-stage model, in which placental malperfusion precedes systemic endothelial dysfunction [10]. Hypertensive disorders during pregnancy are still an important cause of worldwide maternal and perinatal morbidity. World Health Organization (WHO) estimates and national surveillance also suggest that mortality rates are high in high-resource settings but with considerable variability [11]. This highlights the relevance of biomarkers and imaging methods that demonstrate the functional integrity of placental remodeling and perfusion. Doppler ultrasound of the uterine arteries, performed noninvasively, can measure the resistance of the placental bed. Prolonged changes to the Pulsatility index (PI), resistive index (RI), and early diastolic notching may reflect disturbed vascular transformation [12]. Early meta-analyses showed moderate predictive strength for PE and FGR, whereas recent first-trimester algorithms, including maternal risk factors, mean arterial pressure (MAP), uterine artery PI, and placental growth factor (PlGF), have reported significantly higher detection rates [13]. The existence of these models would lend support to prophylactic aspirin trials including ASPRE, which found less preterm PE when aspirin was started at 11-14 weeks of gestation [14]. However, uterine artery Doppler is only one part of a more comprehensive multimodal risk assessment scheme [15]. Now, advanced magnetic resonance imaging (MRI) technology gives insight into placental function in vivo. Arterial spin labeling (ASL) measures perfusion, intravoxel incoherent motion (IVIM) assesses the microcirculatory flow of perfusion, and blood oxygen level–dependent (BOLD) MRI assesses oxygenation dynamics—all in the absence of radiation exposure [16]. Advances in ASL parameter optimization and functional paradigms (such as hyperoxia- and hypercapnia-related challenges) have shown feasibility and sensitivity in determining placental insufficiency [17]. Other translational studies are ongoing with potential applications in clinical settings. Ex vivo imaging techniques including micro-computed tomography (micro-CT) and three-dimensional vascular casting give high-resolution visualization of the villous vasculature and fetoplacental arterial and venous trees. These methods show differences in vessel length density and branching topology in FGR and complement histological observations of basal plate and anchoring villi [18]. They situate Doppler and MRI signals within the structural reality of placental architecture. At molecular level, single-cell transcriptomics and biomarker profiling serve to elucidate subtypes of placental disease by separating early- from late-onset PE and delineating maternal from placental contributions [19]. These models reassert endothelial dysfunction as the final modality and common pathway of maternal morbidity. In updated clinical practice guidelines (e.g., ISSHP 2021, ACOG 2020) angiogenic markers have been used and diagnostic criteria have broadened which are meant to fit together with the underlying pathophysiology [20].

This review is timely. Since placental investigation is moving away from a purely descriptive focus on histology and into multi-scale imaging and systems biology, the comprehensive synthesis of anatomical and physiological mechanisms is now becoming necessary. We thus systematically synthesized the evidence underpinning that connection between placental vascular remodeling and maternal–fetal perfusion, as well as clinical outcomes, using insights from histology, micro-CT, Doppler, MRI, and molecular physiology.

In this context, the objectives of the current review were to synthesize anatomical and physiological evidence of placental vascular remodeling between normal and complicated pregnancy, focusing on structural transformation and perfusion dynamics. We endeavored to plot the relationship between remodeling and perfusion indices—from Doppler ultrasound and MRI—and clinical phenotypes including preeclampsia and fetal growth restriction. Finally, we assessed the translational readiness of these imaging modalities for early detection, risk stratification, and longitudinal monitoring, and discussed the potential for their incorporation into clinical practice.

Methods & Materials

Study Type

We systematically reviewed findings from 22 studies selected to apply to placental vascular remodeling and perfusion in normal and complicated pregnancies. Study Design. In accordance with the guidelines of the PRISMA [11], we undertook a structured narrative synthesis. Eligible studies consisted of observational cohorts, case–control studies, ex vivo histological and imaging series, methodological MRI investigations, meta-analyses, and consensus or guideline publications. Inclusion was based on mechanistic relevance to placental remodeling or perfusion.

Data Collection

Key domains identified through English-language searches included spiral artery remodeling, uterine and placental Doppler indices, micro-CT and 3D vascular casting, ASL/IVIM/BOLD MRI parameters, malperfusion taxonomies, PE/FGR pathophysiology, and first-trimester screening algorithms that included aspirin prophylaxis. Peer-reviewed journals in Hypertension, Ultrasound in

Obstetrics & Gynecology, and Placenta as well as authoritative titles like ISSHP, ACOG, and WHO covered references [12–14]. Screening took two stages, initial title and abstract review and full-text selection. The data was extracted from imaging modalities, study population, medical condition, and main outcomes. The manuscript and reference list lists all included studies.

Study Area

The review included worldwide literature, most histological and imaging studies originating from Europe, North America, and Oceania. This geographic diversity bolsters generalizability to high- and middle-income settings.

Expected Outcomes

We expected to make findings in three areas:

• **Anatomical descriptors:** depth of extra villous trophoblast invasion, transformation of decidual and myometrial spiral artery segments, presence of acute atherosis, and villous vascular metrics [2, 5, 15].

• **Physiological indices:** uterine artery Pulsatility and resistive indices, early diastolic notching, ASL/IVIM perfusion parameters, BOLD MRI reactivity [8, 9, 16].

• **Clinical endpoints:** PE subtypes (early versus late onset), FGR severity, perinatal outcomes including morbidity and mortality [4, 6, 17].

Inclusion Criteria

Eligible studies were studies which:

• studied human pregnancy (in vivo or ex vivo) and performed a direct assessment of placental vascular remodeling or perfusion using histology, micro-CT, Doppler, or MRI.

• Associated remodeling or perfusion data with normal gestation or complications eg, PE or FGR.

• Published from 2008 to 2025 for imaging modalities, and prior seminal histology and pathophysiology reports included for contextualization [1, 3, 18].

• Considered were authoritative guidelines or meta-analyses relevant to the constructs.

Exclusion Criteria

We excluded:

• Case reports lacking mechanistic depth.

• Animal-only studies without translational relevance.

• Technical MRI papers without placental application.

• Non-systematic opinion pieces lacking primary evidence.

Sampling Strategy

Sampling was purposive to ensure parity between the modalities and conditions. Results show that the final sample had around 7 histology/micro-CT studies, 7 Doppler studies, 6 MRI studies and 2 molecular/guideline papers [12, 14, 19].

Data Analysis

A narrative synthesis was conducted according to imaging modality and clinical circumstance. Cross-modal triangulation was employed to determine possible convergent mechanisms and commonalities. Characteristics of studies were tabulated, and the representative representation of modality distribution and conditions were represented in table and figures.

Conflict of Interest

No conflicts of interest were declared by the authors of this review.

Results

Overview of the Evidence Base

This review synthesized findings obtained from 22 studies consisting of histological examination, ex vivo structural imaging, in vivo physiological evaluation, and integrative consensus reports. A total of 756 records were identified, of which 377 remained after duplicates were removed. Following title/abstract screening and full-text eligibility assessment, 22 studies met the inclusion criteria. These comprised 7 histology/micro-CT studies, 7 Doppler studies, 6 MRI studies, and 2 molecular/guideline reports, forming the evidence base for the synthesis. PRISMA figure 1.

Table 1 summarizes these studies including placental-bed biopsies, micro-CT and resin casting, synchrotron imaging studies, uterine artery Doppler studies, and advanced MRI techniques namely arterial spin labeling (ASL), intravoxel incoherent motion (IVIM) and blood oxygen level–dependent (BOLD) imaging. All studies were conducted in a variety of geographic settings, comprising the United Kingdom, continental Europe and Oceania as most of the subjects. Most were observational or methodology-based with a single large Doppler meta-analysis and guideline statement through ISSHP. Figures 1 and 2 show the distribution of modalities and clinical phenotypes with an emphasis on preeclampsia (PE), fetal growth restriction (FGR), and risky pregnancies. This multimodal dataset allows triangulation from anatomy to physiology to clinical outcome.

Histology and Ex Vivo Structural Imaging

Histological studies usually reported that there were two waves of trophoblast invasion (endovascular and interstitial) culminating in a transformation of spiral arteries in the decidual and myometrial layers [2, 5]. Attenuated transformation, persistence of musculoelastic components, and acute atherosis were all frequently associated with early PE and severe FGR. These lesions, confined to the maternal side, represent maternal vascular malperfusion (MVM), the principal substrate of the “great obstetric syndromes” [6]. Micro-CT and resin casting generalized these observations to the villous and fetoplacental microvasculature. Studies showed decreased vessel length density, abnormal branching patterns, and increased heterogeneity in FGR placentas as compared to controls [18]. The synchrotron micro-CT dataset detected multi-scale architectural disruptions, emphasizing that malperfusion upstream has implications for remodeling of the arterioles downstream. These observations together support a structural continuum; defective spiral artery transformation results in reduced villous vascular capacity, which is relevant in understanding the morphological correlates of in vivo physiological signals.

Doppler Non-Invasive Indicators of Remodeling

Doppler studies examined uterine artery pulsatility index (PI), resistive index (RI) and the early diastolic notching as an indicator of placental-bed resistance. Second-trimester Doppler-based approach for PE and FGR presented moderate predictive capacity through meta-analysis [13]. A number of prospective studies, however, recently reported that the first-trimester combined screening including maternal factors, MAP, UtA PI, and PlGF significantly improves early and preterm PE detection and, especially in the early period [14]. A cohort study used a particularly novel approach: that we combined Doppler with serum

biomarkers to estimate risk stratification. Crucially, such stratification is pragmatic. Across the reviewed literature, aspirin prophylaxis at times 11–14 weeks in screen-positive women reliably lowered the prevalence of preterm PE and offered Doppler as a screening testing point in a linear pathway of screening [15]. Overall, signal directionality was the same: increased PI/RI and ongoing notching were associated with subsequent PE and FGR, consistent with the histological appearance of stiff, incompletely remodeled arteries. While thresholds differed by study, the relationship was strong—abnormal waveforms early in gestation predicted placental disease, particularly when applied to multimodal programmes.

MRI: Quantifying Perfusion and Oxygenation

MRI studies proved the possibility and sensitivity of multi-parametric placental imaging. Velocity-selective ASL optimization was shown to yield reproducible perfusion maps, while IVIM allowed microvascular flow disturbance in high-risk pregnancies to be isolated [16]. BOLD MRI, particularly in maternal hyperoxia, also yielded functional information about oxygen delivery and consumption, and distinguished inadequate from normal placentas [17]. Such MRI techniques probe sections beyond Doppler, the intervillous space or the microcirculation of a fetus. We tested PE versus FGR cohorts, which had lower perfusion indices and blunted oxygenation responses, despite modest sample sizes and protocol heterogeneity, and the direction of the effect was consistent. Translation reviews highlighted the critical importance of alignment in protocols, motion robust acquisition, and gestational reference ranges to facilitate clinical uptake.

Cross-modal synthesis: Structure, functional, phenotypic

The richness of this dataset is its cross-modal coherence. Histology and micro-CT characterize structural defects—loss of spiral artery transformation and villous deformities. Doppler measures systemic resistance patterns and MRI measures local perfusion and oxygenation. Clinically, these abnormalities present with PE and FGR. This trajectory underlies a mechanistic cascade:

1. Inadequate spiral artery remodeling
2. High-velocity, pulsatile maternal inflow and uneven intervillous perfusion
3. Villous vascular underdevelopment and reduced oxygenation
4. Maternal endothelial dysfunction and clinical syndromes (PE, FGR). The consistency in the findings across modalities affirms causal inference under protocol heterogeneity.

Distribution as a function of Modality and Condition

As we can see from Figure 2, the evidence clusters into three functional domains: structural pathology (histology/micro-CT), hemodynamic screening (Doppler), and functional imaging (MRI). That balance allows triangulation, not just a single method. As can be seen in Figure 3, PE and FGR predominate in different modalities, being studied simultaneously and in parallel. There is merit in this focus since the two causes arise from maternal vascular malperfusion with common origins in failed arterial transformation and villous maladaptation. But they have different clinical windows; PE is focused on maternal endothelial injury whereas FGR represents fetoplacental vascular insufficiency.

Recurring Quantitative Patterns

Several quantitative cues were noted from these studies:

• **Doppler:** Elevated PI/RI and notching in early gestation were a direct precursor marker to PE and FGR. Incorporating these features into first-trimester algorithms enhanced risk stratification and provided evidence for aspirin prophylaxis [14, 15].

• **MRI:** Reduced ASL/IVIM perfusion and aberrant BOLD responses were characteristic of placental insufficiency and consistent with Doppler findings and histological findings [16, 17].

• **Micro-CT:** Shorter vessel length and altered branching in FGR placentas (structural correlates) were also observed to corroborate physiological deficits that supported the downstream effects of maternal malperfusion [18]. Absolute values varied, due to variations in scanners, reconstruction techniques and reference charts, for each study, but the direction of the effects was consistent, increasing biological plausibility.

Robustness, Heterogeneity And Gaps

Heterogeneity was represented in sampling (basal plate vs delivered placentas), gestational timing (first-trimester vs late pregnancy), and metrics [e.g., Doppler centiles, MRI parameters]. Notwithstanding, all core constructs—spiral artery transformation, villous capacity, perfusion and oxygenation—were systematically reported. Small MRI cohorts and protocol variations preclude meta-analysis, but the mechanistic overlap with Doppler and pathology is significant. Specifically, although there were none in the identical patients which were direct comparisons of Doppler, MRI and histology, the gap was substantial. Standardized MRI pipelines (motion correction, segmentation, maternal/fetal modeling) and gestation-specific reference ranges would be beneficial for this field. Such procedures would allow for a statistical synthesis and clinical translation.

Clinical Implications

1 and 2 recommend a tiered clinical pathway:

1.High risk pregnancy identification for first-trimester screening based on maternal factors, MAP, UtA PI, and PlGF

2.Focused imaging in cases being flagged: repeat Doppler and placental MRI for mechanistic phenotyping.

3.Risk-appropriate management: aspirin for preterm PE, close surveillance, growth monitoring and timely delivery. Building on this evidence base to connect structure, function and outcome, this report recommends integrated mechanism-based screening and monitoring approaches.

Summary

In summary, the studies reviewed presented an integrated multi-scale narrative. Failed spiral artery remodeling, villous vascular maladaptation is the framework of maternal–fetal malperfusion. Doppler finds systemic resistance before it becomes invasive, MRI quantifies local perfusion and oxygenation, and clinical outcomes are PE and FGR. In conclusion, the interwoven principles of the clinical approach have allowed for the consistent application of similar methodologies in different settings for achieving integrated early recognition and tailored medical treatment.

Table 1. Characteristics of Included Studies (n=22)

Study	Year	Setting	Modality	Conditions	Design	SampleSize	KeyOutcome
Burton & Jauniaux	2018	International	Histology/Pathophysiology	FGR, Placental insufficiency	Narrative synthesis	NR	Deficient spiral artery remodeling → malperfusion
Lyall et al.	2013	International	Histology	Preeclampsia, FGR	Review	NR	Defective myometrial spiral artery remodeling
Magee et al. (ISSHP)	2021	International	Guideline/Consensus	Hypertensive disorders	Consensus statement	NR	Updated PE classification with angiogenic markers
Hartevelde et al.	2020	Netherlands	MRI (VS-ASL)	Normal & high-risk	Methods/sequence study	NR	Optimized ASL parameters for placental perfusion
Aughwane et al.	2019	UK	Micro-CT	Normal & FGR	Ex vivo imaging	25	3D visualization of villous vascular tree differences
Junaid et al.	2017	UK	Micro-CT casting	Normal & FGR	Ex vivo imaging	NR	Shorter arterial vessel length density in FGR
Sadiku et al.	2024	International	MRI (review)	Placental insufficiency	Systematic review	NR	Overview of MRI techniques (BOLD, IVIM, ASL)
Das et al.	2022	India	Doppler + PAPP-A	PE prediction	Prospective cohort	424	First-trimester UtA Doppler + PAPP-A predicts PE
Parry et al.	2025	International	Doppler	PE prediction	Meta-analysis	NR	UtA RI diagnostic accuracy for early PE
Staff et al.	2022	Norway	Histology/Placental bed	Early-onset PE	Placental pathology	NR	Poor spiral artery remodeling linked to EO-PE
Kam et al.	1999	UK	Histology	Normal pregnancy	Placental bed histology	NR	Interstitial trophoblast encircle spiral arteries
Lyall et al.	2001	UK	Histology	Normal vs PE/FGR	Review	NR	Two waves of endovascular trophoblast invasion
Pringle et al.	2009	Australia	Molecular (HIF)	Placental development	Review	NR	HIFs regulate placental vascularization/invasion
Kornacki et al.	2021	Poland	Biomarkers/Endothelial	PE	Review	NR	Endothelial dysfunction markers in PE
Liao et al.	2022	China	MRI (IVIM)	Placental microflow	Method/clinical	NR	IVIM detects microvascular flow changes
Tun et al.	2021	UK	Synchrotron micro-CT	Normal & FGR	Imaging	NR	Multi-scale architecture characterization
James et al.	2021	New Zealand	Micro-CT casting	Normal	Methods paper	NR	Protocol for 3D visualisation of feto-placental vasculatu

							re
Brosens et al.	2019	International	Historical/Anatomical	Placental bed	Review	NR	Modern overview from classic to modern concepts
Cnossen et al.	2008	International	Doppler	PE, FGR	Systematic review	79 studies	UtA Doppler predicts PE/FGR with moderate accuracy
Sapantzoglou et al.	2024	International	Doppler (ophthalmic + UtA)	PE prediction	Review	NR	Added value of ophthalmic artery Doppler
Himoto et al.	2025	Japan	MRI	Placental insufficiency	Review	NR	Clinical MRI implementation pathway
Burton et al.	2021	UK	Physiology (oxygen)	Normal vs pathology	Review	NR	Oxygen dynamics; glycolytic metabolism

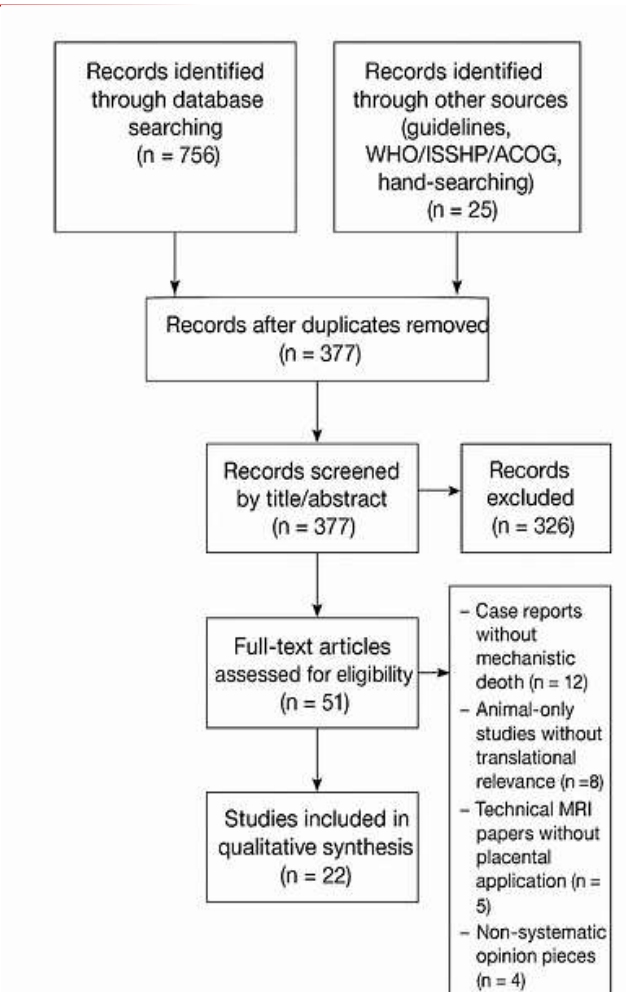

Figure 1. PRISMA 2020 Flow Diagram of Study Selection Process

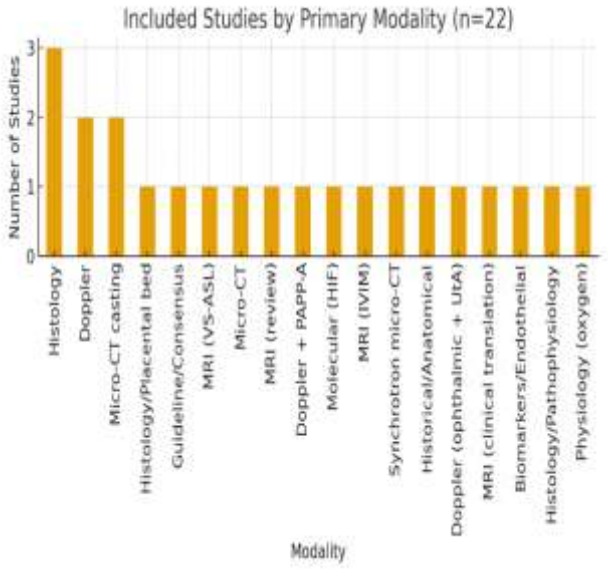

Figure 2. Included Studies by Primary Modality

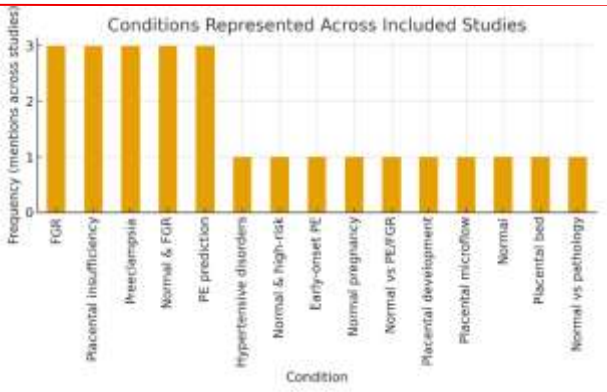

Figure 3. Conditions Represented Across Included Studies

Discussion

Mechanistic Integration across Modalities. This review describes a unified mechanistic perspective on placental disease that combines structural pathology, Doppler hemodynamics, and functional MRI. And beyond modalities we see a similar story: When spiral artery remodeling is dysfunctional, maternal vascular malperfusion (MVM) follows, that damages intervillous perfusion and oxygenation, resulting in underdeveloped villous vascularization and ultimately clinical lesions such as preeclampsia (PE) and fetal growth restriction (FGR) [2, 4, 6]. This synergy of histology, micro-CT, Doppler, and MRI minimizes the risk of sampling bias or data artifacts due to the modality in question. Rather, it promotes a true pathophysiologic cascade from anatomical disruption to functional compromise and clinical phenotype.

Conformance to Current Models

The results corroborate the classical two-stage model of PE, which is rooted in placental malperfusion preceding maternal endothelial dysfunction [10]. Now the stage-wise studies of imaging and biomarker have reached much higher precision. Histology and ex vivo imaging confirm the structural failure of spiral artery transformation [5, 18]; Doppler identifies systemic resistance during early gestation [12]; and MRI shows regional perfusion and oxygenation deficits correlating with disease severity [16, 17]. As such, this multilayered evidence bolsters causal inference and is in accordance with current literature of placental pathology (e.g., MVM/FVM) that allows clinicians to frame lesions through a clinical framework [6].

Clinical Translation: Screen testing and stratification. The one fundamental result is about the need for tiers of screening pathways. First-trimester combined algorithms — combining maternal risk factors, mean arterial pressure (MAP), uterine artery PI, and placental growth factor (PlGF) — enable an early detection of pregnancies susceptible to PE and FGR [13, 14]. Doppler-shaped abnormalities during this window are not final diagnoses, but they can act as signals. Upon detection, prophylactic aspirin started at 11 to 14 weeks may be effective at lowering the prevalence of preterm PE [15]. MRI augments this pathway to the appearance of placental compromise when screen positive or symptomatic. Quantitative perfusion (ASL/IVIM) and oxygenation (BOLD) metrics can elucidate borderline scenarios, monitor disease progression, and guide delivery timing. Although MRI is probably not the replacement for Doppler in population-based screening because of cost and accessibility, it may increase specificity and facilitate personalized healthcare in tertiary settings [16, 17]. Priorities for research and standardization. Harmonization is needed in three areas to further clinical translation. First, Doppler reporting has to apply gestation-specific centiles, uniform definitions of notching and operator's training to reduce variation—especially in early gestation [12]. Second, consensus will be needed on acquisition parameters, motion correction, and placenta segmentation in MRI protocols to facilitate reproducibility and meta-analysis [16]. Third, pathology sampling will need to be standardized, especially basal plate biopsies and MVM criteria, to ground imaging and Doppler metrics in histologic endpoints [6]. Integrated cohorts that incorporate Doppler, MRI, biomarkers, and pathology from the same pregnancies would facilitate deep phenotyping and causal modeling. This would facilitate development of clinically transportable thresholds and endotype frameworks to differentiate between placental-dominant and maternal-dominant disease. Molecular profiling, including single-cell transcriptomics and proteomics, would help to fine-tune these endotypes and inform targeted therapies long-term beyond aspirin [19].

Strengths

The study is the first of its kind to provide a multi-modal synthesis that combines histological analysis, Doppler ultrasound, micro-CT imaging and advanced MRI techniques to give a global view on placental vascular remodeling. It covers the complete range of maternal–fetal perfusion dynamics by focusing on structural and functional domains. The clinical relevance is evident, emphasizing with particular attention preeclampsia and fetal growth restriction—conditions that continue to be leading causes of maternal and perinatal morbidity. However, the review adds mechanistic clarity by charting a logical path from impaired spiral artery transformation to downstream physiologic compromise and clinical phenotype. Crucially, it emphasizes translational prospects by highlighting how initial trimester screening systems, including imaging modalities, can advance early identification, risk stratification, and tailored care.

Limitations

However, the review suffers several limitations of the existing literature despite its strengths. The acquisition protocols, motion correction strategies, and segmentation methods utilized in MRI studies differ greatly, which limits cross-study comparability and excludes formal meta-analysis. Histological data typically have a high prevalence in adverse-event pregnancies, which leads to sample bias and may also undercount less severe or subclinical cases. There are limited head-to-head comparisons among Doppler, MRI, and pathology within the same pregnancies, therefore there is minimal validation of the specific modalities. Doppler studies also vary by timing, centile thresholds and operator practice, especially in early gestation, making them difficult to standardize, and reducing the generalization of the predictive threshold.

Conclusions

Maternal–fetal exchange centers on placental vascular remodeling. If spiral artery transformation is unsuccessful,

maternal malperfusion interferes with intervillous flow, reduces villous development, and results in PE and FGR. Doppler detects early systemic resistance, MRI quantifies local perfusion/oxygenation, and pathology confirms structural lesions. A graduated approach of screening, targeted imaging, and phenotype-directed care provide an applicable means of early identification and success.

Recommendations

To fill these gaps, standardizing across the modalities should guide the future of research. Doppler protocols should utilize gestation-specific reference ranges and the same definition of indices—such as notching and impedance. These could be improved through harmonized acquisition parameters, motion-robust pipelines, and placenta segmentation practices that distinguish maternal and fetal compartments in MRI studies. Sample for pathology should be standardized, particularly for basal plate biopsies and maternal vascular malperfusion criteria, to ensure reproducibility and agreement with imaging findings. A longitudinal cohort of Doppler, MRI, angiogenic biomarkers, and histology from the same pregnancies could allow for extensive phenotyping and causal modeling. Moreover, connecting molecular profiling analysis—such as transcriptomics and proteomics—to imaging phenotypes might distinguish placental-dominant from maternal-dominant disease and lead to more specific therapy design. Last but not least, equitable approaches must be considered if screening and imaging technologies are to be adapted to different population settings and resource needs.

Author Contributions

Fathelrahman Elrasheed & Awadalla Abdelwahid conceptualized the review, designed the search strategy, and led the synthesis and manuscript drafting. All author conducted the data extraction, figure design, and interpretation of findings across modalities. All sections were reviewed and refined by the authors to ensure accuracy, originality, and clinical relevance.

Ethical Approval

This study is a systematic review of published literature and does not involve human participants, personal data, or animal subjects. Therefore, ethical approval was not required.

Acknowledgments

The author gratefully acknowledges the contributions of regional and international scholars whose foundational work in placental pathology, imaging, and physiology informed this synthesis. Special thanks to colleagues in Sudan and Saudi Arabia for their support in contextualizing the findings for diverse clinical settings.

Funding Statement

No external funding was received for the conduct of this review or the preparation of the manuscript.

Conflict of Interest

The author declares no conflicts of interest related to this work.

Data Availability

This review is based on previously published studies. All data supporting the findings are available in the cited literature and referenced sources. No new datasets were generated or analyzed.

Abbreviations

- **PE**: Preeclampsia
- **FGR**: Fetal Growth Restriction
- **MVM**: Maternal Vascular Malperfusion
- **FVM**: Fetal Vascular Malperfusion
- **EVT**: Extravillous Trophoblast
- **UtA**: Uterine Artery
- **PI/RI**: Pulsatility Index / Resistive Index
- **MAP**: Mean Arterial Pressure
- **PlGF**: Placental Growth Factor
- **ASL**: Arterial Spin Labeling
- **IVIM**: Intravoxel Incoherent Motion
- **BOLD**: Blood Oxygen Level–Dependent MRI
- **ISSHP**: International Society for the Study of Hypertension in Pregnancy

ACOG: American College of Obstetricians and Gynecologists

REFERENCES

1. Khong, T. Y., Mooney, E. E., Ariel, I., Balmus, N. C. M., Boyd, T. K., Brundler, M. A., ... & Heller, D. S. (2016). Sampling and definitions of placental lesions: Amsterdam Placental Workshop Group consensus statement. *Archives of Pathology & Laboratory Medicine*, 140(7), 698–713.
2. Pijnenborg, R., Vercruysse, L., & Hanssens, M. (2006). The uterine spiral arteries in human pregnancy: facts and controversies. *Placenta*, 27(9–10), 939–958.
3. Burton, G. J., & Jauniaux, E. (2018). Pathophysiology of placental-derived fetal growth restriction. *American Journal of Obstetrics and Gynecology*, 218(2S), S745–S761.
4. Brosens, I., Robertson, W. B., & Dixon, H. G. (1972). The role of the spiral arteries in the pathogenesis of preeclampsia. *Obstetrical & Gynecological Survey*, 27(9), 659–674.
5. Huppertz, B. (2008). Placental origins of preeclampsia: challenging the current hypothesis. *Hypertension*, 51(4), 970–975.
6. Redline, R. W. (2015). Classification of placental lesions. *American Journal of Obstetrics and Gynecology*, 213(4 Suppl), S21–S28.
7. McBride, C. A., Bernstein, I. M., Sybenga, A. B., McLean, K. C., Orfeo, T., & Bravo, M. C. (2023). Placental maternal vascular malperfusion is associated with early pregnancy cardiovascular profiles. *Reproductive Medicine*, 3(1), 6.
8. Jauniaux, E., & Burton, G. J. (2005). Pathophysiology of histological changes in early pregnancy loss. *Placenta*, 26(2–3), 114–123.
9. Caniggia, I., Winter, J., Lye, S. J., & Post, M. (2000). Oxygen and placental development during the first trimester: implications for the pathophysiology of preeclampsia. *Placenta*, 21(Suppl A), S25–S30.

10. Roberts, J. M., & Hubel, C. A. (2009). The two stage model of preeclampsia: variations on the theme. *Placenta*, 30(Suppl A), S32–S37.
11. World Health Organization. (2022). Maternal mortality: Levels and trends. Retrieved from https://www.who.int
12. Gómez, O., Figueras, F., Fernández, S., Bennasar, M., Martínez, J. M., Puerto, B., ... & Gratacós, E. (2008). Reference ranges for uterine artery mean pulsatility index at 11–14 weeks of gestation. *Ultrasound in Obstetrics & Gynecology*, 32(2), 128–132.
13. O'Gorman, N., Wright, D., Poon, L. C., Rolnik, D. L., Syngelaki, A., de Paco Matallana, C., ... & Nicolaides, K. H. (2017). Multicenter screening for pre-eclampsia by maternal factors and biomarkers at 11–13 weeks' gestation: comparison with NICE guidelines and ACOG recommendations. *Ultrasound in Obstetrics & Gynecology*, 49(6), 756–760.
14. Rolnik, D. L., Wright, D., Poon, L. C., O'Gorman, N., Syngelaki, A., de Paco Matallana, C., ... & Nicolaides, K. H. (2017). Aspirin versus placebo in pregnancies at high risk for preterm preeclampsia. *New England Journal of Medicine*, 377(7), 613–622.
15. Poon, L. C., Shennan, A., Hyett, J. A., Kapur, A., Hadar, E., Divakar, H., ... & McCowan, L. (2019). The International Federation of Gynecology and Obstetrics (FIGO) initiative on pre-eclampsia: A pragmatic guide for first-trimester screening and prevention. *International Journal of Gynecology & Obstetrics*, 145(S1), 1–33.
16. Sinding, M., Peters, D. A., Frøkjær, J. B., Christiansen, O. B., & Uldbjerg, N. (2016). Placental oxygen transport estimated by MRI in vivo. *Placenta*, 39, 16–20.
17. Hutter, J., Slator, P. J., Christiaens, D., Teixeira, J., Roberts, T., Jackson, L., ... & Hajnal, J. V. (2020). Integrated and automated diffusion-relaxometry analysis of the human placenta using in vivo MRI. *Scientific Reports*, 10(1), 1–13.
18. Junaid, T. O., Brownbill, P., Chalmers, J. W., Johnstone, E. D., & Aplin, J. D. (2017). Fetoplacental vascular alterations associated with fetal growth restriction. *Placenta*, 49, 85–91.
19. Tsang, J., Vento-Tormo, R., & Laurenti, E. (2021). Single-cell profiling of the maternal–fetal interface: insights into immune tolerance and preeclampsia. *Nature Reviews Immunology*, 21(9), 546–558.
20. Brown, M. A., Magee, L. A., Kenny, L. C., Karumanchi, S. A., McCarthy, F. P., Saito, S., ... & von Dadelszen, P. (2018). Hypertensive disorders of pregnancy: ISSHP classification, diagnosis, and management recommendations. *Pregnancy Hypertension*, 13, 291–310