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Antiphospholipid antibody nephropathy in pregnancy; consequences for fetal renal development and maternal health outcomes

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ABSTRACT

Antiphospholipid antibody (aPL) nephropathy in pregnancy is a critical and complex medical condition that poses significant risks to both maternal renal health and fetal development. This autoimmune disorder is characterized by the presence of aPLs, which target phospholipid-binding proteins, leading to a procoagulant state. In the context of pregnancy, this predisposition to thrombosis can manifest as thrombotic microangiopathy (TMA) within the renal vasculature, directly impacting kidney function. The resulting renal microvascular injury contributes to a decline in maternal renal health, potentially leading to proteinuria, hypertension, and even acute kidney injury, exacerbating the already delicate physiological changes of pregnancy. The intricate interplay between autoimmune-mediated thrombosis and placental dysfunction is central to the high-risk nature of this condition. aPLs can cause thrombosis in the placental vasculature, leading to placental insufficiency, intrauterine growth restriction, preeclampsia, and recurrent pregnancy loss. This compromise in placental blood flow not only jeopardizes fetal development but also indirectly strains maternal renal function. The systemic inflammation and endothelial dysfunction associated with aPLs further complicate the clinical picture, making accurate diagnosis and timely intervention paramount for managing these multifaceted challenges. Effective management of aPL nephropathy in pregnancy necessitates a highly individualized and multidisciplinary approach, focusing on meticulous monitoring of both maternal and fetal well-being. This includes close surveillance of renal function, blood pressure, and proteinuria, alongside regular assessments of fetal growth and placental health. Therapeutic strategies often involve anticoagulation with heparin, sometimes combined with low-dose aspirin, to mitigate the thrombotic risk. Such precise monitoring and tailored interventions are crucial for optimizing outcomes, aiming to preserve maternal renal health while supporting successful fetal development in this challenging clinical scenario.

Review

Implication for health policy/practice/research/medical education:
Antiphospholipid antibody nephropathy (APLN) in pregnancy represents a high-risk condition with profound implications for maternal renal health and fetal development. The interplay between autoimmune-mediated thrombosis, placental dysfunction, and renal microvascular injury creates a complex clinical picture that demands exact monitoring and individualized care.

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Introduction

Antiphospholipid antibody syndrome (APS) is a systemic autoimmune disorder detected by the persistent presence of antiphospholipid antibodies (aPLs), containing lupus anticoagulant, anticardiolipin antibodies, and anti-β2-glycoprotein I antibodies, in conjunction with clinical manifestations such as thrombosis or pregnancy morbidity (1). Among the myriad complications associated with APS, antiphospholipid antibody nephropathy (APLN) represents a significant yet often under-recognized renal manifestation (2). This syndrome consisted of thrombotic microangiopathy (TMA) of the renal vasculature, leading to ischemic injury of the glomeruli, interstitium, and tubules (3). When APLN occurs in the context of pregnancy, it poses a dual threat, endangering maternal renal function and potentially disrupting fetal renal development, thereby influencing both short- and long-term outcomes for mother and child (4). The intersection of APS, pregnancy, and renal pathology creates a complex clinical scenario that demands careful monitoring, early diagnosis, and multidisciplinary management to mitigate adverse consequences (2). Pregnancy itself induces profound physiological changes in the maternal renal system, including a 50% increase in renal plasma flow and glomerular filtration rate, systemic vasodilation, and alterations in coagulation factors that tilt the hemostatic balance toward a hypercoagulable state (5). These adaptations, are necessary for supporting fetal growth and maintaining maternal homeostasis; however, they can exacerbate the underlying prothrombotic milieu in women with APS (6). In the presence of circulating antiphospholipid antibodies, the already heightened thrombotic risk is amplified, predisposing pregnant women to placental insufficiency, preeclampsia, fetal growth restriction, and recurrent pregnancy loss (7). Moreover, when APLN is superimposed on this background, the renal microvasculature becomes a primary target for immune-mediated thrombosis, further compounding the risks to both maternal and fetal health (4).

Search strategy

We conducted a comprehensive literature search across multiple databases including PubMed, Web of Science, EBSCO, Scopus, Google Scholar, the Directory of Open Access Journals (DOAJ), and Embase. We used a variety of relevant keywords and phrases, such as 'antiphospholipid antibody syndrome', 'pregnancy', 'acute kidney injury', 'antiphospholipid antibody nephropathy', 'glomerular filtration rate', 'β2-glycoprotein I', and 'thrombotic microangiopathy', to ensure inclusion of a broad spectrum of studies and reviews addressing the multifaceted clinical manifestations and renal complications associated with APS in pregnancy.

Pathophysiology of antiphospholipid syndrome

Antiphospholipid syndrome is postulated to act through a two-hit model, since aPLs start endothelial injury, leading to thrombosis and placental insufficiency (8). The initial hit involves aPLs causing endothelial lesions, while a second hit, which is an environmental factor like infection disrupts vascular integrity, resulting in thrombus formation (7). This pro-inflammatory state, mediated by aPLs, involves factors such as IgG and complement deposition, neutrophilic infiltration, and local TNF-alpha secretion (7). Complement activation, triggered by aPLs, is a critical mechanism leading to endothelial damage and subsequent thrombosis in both thrombotic and obstetric presentations of antiphospholipid syndrome (9). Previous studies found that, infections are key stimulators that can exacerbate APS symptoms by provocating abnormal antibody creation; while, nearly half of catastrophic APS (CAPS) cases are triggered by infections, with bacterial pathogens like *Staphylococcus aureus*, *Escherichia coli* and viral agents such as cytomegalovirus and Epstein-Barr virus, which frequently interacted (7). These infections are postulated to intensify the thrombotic and inflammatory cascades in this disease, contributing to the severe, multi-system involvement typical of CAPS (7). Antiphospholipid antibodies also directly affect placental tissue, compromising trophoblast function and placental development. In fact, this interaction can result to the disturbed trophoblast invasion and diminished chorionic gonadotropin secretion, which are crucial for placental health (7). The results of placental dysfunction caused by aPLs include stillbirth, defective fetal growth, and preeclampsia (10). Also, aPLs may interfere with endometrial decidualization, affecting embryo implantation, and decrease trophoblastic viability or cause trophoblast apoptosis, compromising placental function (11). There is also a recent hypothesis that aPLs may prevent oocyte development after being secreted into the follicular fluid (7). Beyond direct antibody effects, pregnancy loss in APS can relate to inadequate invasion of maternal spiral arteries by extravillous cytotrophoblasts, leading to early miscarriages and recurrent pregnancy loss (12). Meanwhile, impaired transformation of spiral arteries, along with coagulation cascade and complement activation, can cause late pregnancy loss and preeclampsia (13). Previous authors also highlight the role of neutrophil extracellular traps (NETs) and Toll-like receptors (TLRs). More recent studies detected that, aPLs stimulate NET release, strengthening coagulation, while TLR activation stimulates inflammatory responses that compromise pregnancy outcomes (7). The release of microparticles from activated cells more strengthens inflammation and coagulation, which accentuating the complex pathology of APS (14).

A short look at the pathogenesis of APLN

The pathogenesis of APLN centers on the interaction between antiphospholipid antibodies and endothelial cells, monocytes, and platelets, triggering a cascade of proinflammatory and procoagulant responses (15). Then, aPL antibodies bind to β2-glycoprotein I, a plasma protein that normally exhibits anticoagulant properties. This binding alters the conformation of β2-glycoprotein I, enabling it to interact with receptors on endothelial cells such as annexin A2, Toll-like receptors (TLR2 and TLR4), and apolipoprotein E receptor 2 thereby activating nuclear factor-kappa B pathways and upregulating adhesion molecules like intercellular adhesion molecule-1 and vascular cell adhesion molecule-1 (15). The result is endothelial dysfunction, leukocyte recruitment, and a shift toward a prothrombotic phenotype. Concurrently, aPL antibodies activate the complement system, particularly C5a, which further amplifies inflammation and thrombosis (9). In the kidney, these processes manifest as TMA, with fibrin thrombi occluding small arterioles and glomerular capillaries, leading to ischemic damage, glomerular basement membrane thickening, and eventual fibrosis (16). During pregnancy, these pathophysiological mechanisms are particularly detrimental (16). The placenta, like the kidney, is highly vascularized and susceptible to thrombotic insults (17). Placental TMA can impair uteroplacental perfusion, resulting in hypoxia and nutrient deprivation for the developing fetus (18). This placental insufficiency not only contributes to intrauterine growth restriction and preterm birth but also may also indirectly affect fetal renal development (19).

Focus on fetal kidneys in APLN

The fetal kidneys begin forming early in gestation, with nephrogenesis largely complete by 34–36 weeks (20). Adequate maternal-fetal circulation is essential for delivering oxygen and nutrients necessary for nephron formation and renal maturation (21). Chronic placental hypoperfusion, as seen in severe APS with or without APLN, can lead to reduced nephron endowment as a condition associated with increased risk of hypertension and chronic kidney disease (CKD) later in the offspring's life (4). Although direct evidence linking maternal APLN to specific fetal renal malformations remains limited, the indirect consequences of placental dysfunction on fetal organogenesis, including renal development, are biologically plausible and supported by broader literature on intrauterine programming (4).

The impact of APLN on fetal renal development

The impact of antiphospholipid antibodies on fetal renal development, particularly in cases with APLN, is not explicitly detailed in the provided search results (22). However, broader renal involvement in APS is recognized. Renal involvement in APS is increasingly acknowledged, with complications including vascular nephropathy, fibrous intimal hyperplasia of interlobular arteries, thrombosis, small vessel vaso-occlusive lesions and focal cortical atrophy (23). Renal complications occur in about 3% of APS individuals, with renal artery stenosis being the most common renal-related complication (24). APS nephropathy can present heterogeneously, ranging from hematuria and non-nephrotic range proteinuria to hypertension and multiorgan failure caused by catastrophic antiphospholipid syndrome (25).

Maternal health outcomes

Maternal health outcomes in pregnant women with APLN are significantly worse compared to those with uncomplicated APS or healthy pregnancies (26). Hypertension, proteinuria, and acute kidney injury are common clinical features (27). In many cases, APLN may be misdiagnosed as preeclampsia or HELLP syndrome (hemolysis, elevated liver enzymes and low-platelets), especially when it presents in the second or third trimester (28).

However, distinguishing APLN from these conditions is critical, as management strategies differ (28). While preeclampsia typically resolves postpartum, APLN may persist or progress without targeted immunosuppressive or anticoagulant therapy (29). Renal biopsy, though rarely performed during pregnancy due to procedural risks, remains the gold standard for definitive diagnosis, revealing characteristic findings such as arterial and arteriolar thrombosis, intimal hyperplasia, fibrous intimal thickening, and glomerular capillary microthrombi (30). In the absence of biopsy, clinicians must rely on serological markers (persistent aPL positivity), exclusion of other causes, and response to therapy to infer the diagnosis (31). In fact, the presence of APLN during pregnancy is accompanying by a strengthened risk of severe maternal complications, comprising eclampsia, stroke, pulmonary embolism, and progression to end-stage kidney failure (32). Women with preexisting APLN who become pregnant face an even higher risk, as pregnancy can accelerate underlying renal damage (33). Longitudinal studies have shown that some women with APS and renal involvement may experience a decline in renal function during or after pregnancy, with some requiring dialysis (22). Furthermore, the recurrence risk of APLN in subsequent pregnancies is substantial, particularly if anticoagulation is suboptimal or discontinued (34). This underscores the importance of preconception counseling and risk stratification for women with known APS or prior renal involvement (35).

Focus on the impact of APLN on fetal outcomes

The impact of APSN on fetal outcomes is equally concerning (36). Beyond the well-documented risks of miscarriage, stillbirth, and preterm delivery, there is growing recognition of potential long-term developmental consequences (37). Fetal exposure to a proinflammatory, hypoxic intrauterine environment may alter epigenetic regulation of genes involved in renal development, such as PAX2, WT1, and GDNF (38). Previous authors have demonstrated reduced nephron numbers and altered renal architecture in offspring, though human data specific to APS remain sparse (39). Nevertheless, the Developmental Origins of Health and Disease (DOHaD) hypothesis posits that adverse in utero conditions can program organ systems for future disease susceptibility (40). Thus, children born to mothers with APLN may be at elevated risk for metabolic syndrome, hypertension, and CKD in adulthood as a hypothesis that warrants long-term cohort studies (4).

Pregnancy risks in APS patients

Coexisting autoimmune conditions, particularly SLE, amplify pregnancy risks in APS patients (41, 42). Pregnancies with APS-SLE overlap show greater rates of fetal growth restriction, thrombotic events and pre-eclampsia, often requiring intensified anticoagulation and immunosuppressive regimens (7). Maternal condition with nephritis and chronic hypertension also increases the risk of complications and flare during pregnancy (43). Furthermore, adverse pregnancy outcomes are consistently recognized as key features of APS (44). The presence of antiphospholipid antibodies, lupus anticoagulant, and anticardiolipin antibody in patients with systemic lupus erythematosus has been linked to thrombosis, fetal loss, and thrombocytopenia (45).

Catastrophic APS

The most severe form of APS, CAPS is rare, involving fewer than one percent of APS patients, but pregnancy can trigger it (46). This condition is a widespread organ injury/dysfunction and potential multiorgan failure due to dysfunction of small vessels supplying vital organs (47). It seems that, pregnancy is a precipitating factor for CAPS in around 8% of cases, and its *de novo* appearance during pregnancy is significantly more frequent compared to non-pregnancy cases (48.2% versus 26.3%) (48). This syndrome carries an overall mortality rate of about 36%, primarily described by rapid-onset multiple organ microthrombosis (49).

Long-term outcome of women with APLN

Long-term, women with a history of APS nephropathy in pregnancy must be counseled on the risk of future renal impairment and cardiovascular disease (50). Studies have established that preeclampsia and related hypertensive disorders of pregnancy are independent risk factors for end-stage renal disease and cardiovascular events (51). This condition extends to their children, supporting the developmental origins of health and disease hypothesis, which postulates that in-utero insults shape susceptibility to chronic illness throughout life (52). Thus, surveillance for CKD, hypertension, and metabolic syndrome should be a lifelong endeavor for both mother and offspring (53).

Treatment and management modalities

The primary goal in managing antiphospholipid syndrome during pregnancy is to prevent both first and recurrent thrombotic complications and negative obstetric outcomes through rigorous observation and early treatment (54). Individualized treatment plans are crucial, taking into account each patient's specific subtype, antibody profile, and pregnancy history (7). The 2020 American College of Rheumatology (ACR) guidelines advocate for personalized treatment protocols, tailoring monotherapy versus combination treatment according to the individuals's risk and clinical history (55). This personalized approach is particularly effective in obstetric APS (OAPS) for reducing miscarriage, preeclampsia, and intrauterine growth restriction (7). Primary prophylaxis for high-risk APS patients is essential, especially when there is a history of recurrent early miscarriages or late fetal losses (56). In pregnant women with APS, antithrombotic treatment should be combined with a complete assessment of additional prothrombotic risk factors, such as smoking, obesity, hypertension, maternal age, postpartum hemorrhage, diabetes, pre-eclampsia and lengthened immobility (7).

The recognized and standard care for obstetric APS is the both prescription of low-dose aspirin (LDA) and low-molecular-weight heparin (LMWH) (57). While LDA alone primarily prevents arterial thrombosis, the combination with heparin considerably improves live birth rates in OAPS, though it may not significantly reduce the hazard of preterm delivery, intrauterine growth restriction or even preeclampsia (58). Treatment with LDA should begin in the preconception stage, and LMWH at prophylactic doses should be added once pregnancy is confirmed (59). Warfarin is avoided during pregnancy due to fetal risks, with a transition to therapeutic LMWH combined with LDA advised by the 6th week of pregnancy (7). For asymptomatic patients with antiphospholipid antibodies but no history of obstetric complications, the ACR suggests cautious monitoring without routine anticoagulation, unless individualized risk assessment warrants LDA and LMWH (60). After delivery, the British Society for Haematology (BSH)

guidelines recommend reinstating warfarin for women with thrombotic APS, as it is safe during lactation and preferred for long-term secondary thrombosis prevention, though it should be discouraged for a period postpartum to reduce hemorrhage risk (7). Adjunctive therapies, like hydroxychloroquine (HCQ), show promise, especially in patients who are unresponsive to regular care. HCQ is known for its immunomodulatory properties and can improve pregnancy outcomes, aid endothelial function, reduce placental inflammation, and improve trophoblast function, therefore declining placental insufficiency (61). While generally considered safe in pregnancy, more recent investigations showed a minor teratogenic hazard with first-trimester exposure, particularly at daily doses of ≥ 400 mg (62). For APS individuals with recurrent fetal loss unresponsive to conventional treatments, preconception initiation of HCQ (400 mg daily) may significantly reduce fetal death (7). Besides, corticosteroids, when administered with LDA and HCQ, are effective with minimal harm if carefully managed, though diligent dosage monitoring is necessary to decrease adverse outcomes like hypertension or preterm birth (7). Experimental therapies are also being explored for refractory cases. Nitric oxide (NO) is considered important for fetoplacental circulation, and increased NO levels are associated with favorable pregnancy outcomes (63). Meanwhile, statins like pravastatin intensify NO concentration and support fetal growth, but their efficacy for improving pregnancy outcomes has not matched that of LDA and LMWH (64). Simvastatin shows potential by inhibiting glycolysis-related neutrophil extracellular traps, possibly serving as an adjunct treatment in OAPS cases where standard modalities failed (65). In some cases of refractory OAPS unresponsive to conventional management, plasma exchange or high-dose intravenous immunoglobulin (IVIG) may be considered (66). It should remember that, IVIG alone has not significantly improved live birth rates or reduced miscarriage, preterm delivery, or intrauterine growth restriction; however, it is accompanying by a declined risk of pre-eclampsia (67). Similarly, IVIG in combination with other treatments like rituximab or pravastatin has shown improved outcomes in refractory OAPS cases (68). Novel treatments, such as the complement inhibitor eculizumab, target complement activation and hold promise for females with refractory APS symptoms (69). Anti-TNF-alpha agents, like certolizumab, which does not cross the placenta, are also being explored to increase positive pregnancy outcomes in APS patients (70). For CAPS, a combined triple therapy is usually recommended, consisting of corticosteroids, plasmapheresis, anticoagulants or IVIG (47). Accordingly, plasmapheresis removes antibodies and proinflammatory/prothrombotic mediators (47). In refractory CAPS cases, immunosuppressive treatments like HCQ, rituximab, or eculizumab are required to prevent rapid clinical perturbation (71). Postpartum, prophylactic-dose anticoagulation is recommended for 6–12 weeks in females with obstetric APS to alleviate thrombosis risk (7). In the context of assisted reproductive techniques, such as ovulation induction and in vitro fertilization, these are generally considered safe for aPL-positive women when the disease is stable and suitable antithrombotic treatment is administered (72). Antithrombotic management, including LDA and LMWH, should be individualized based on risk evaluation (73). It should remember that, EULAR guidelines recommend prophylactic LDA (75–100 mg/day) for asymptomatic aPL carriers with a high-risk profile, even without APS classification criteria or traditional risk factors, to optimize maternal and fetal outcomes (74). Preconception counseling plays a vital role, preparing women for potential pregnancy challenges and guiding necessary precautions and treatments (75). Folic acid supplementation is recommended starting one month before conception and during pregnancy, along with calcium and vitamin D supplementation for patients on corticosteroids or heparin (7). In addition, pregnant women with APS should follow local protocols for high-risk pregnancies, adjusting fetal surveillance frequency and method based on maternal and fetal conditions (7). This goal is complemented by therapeutic adjustments, like LDA and heparin, which significantly reduce the incidence of pregnancy complications associated with APS (76).

Conclusion

Antiphospholipid antibody nephropathy in pregnancy represents a high-risk condition with profound implications for both maternal renal health and fetal development. The interplay between autoimmune-mediated thrombosis, placental dysfunction, and renal microvascular injury creates a complex clinical picture that demands exact monitoring and individualized care. Left unmanaged, this condition can lead to severe complications such as preeclampsia, intrauterine growth restriction, preterm delivery, and even maternal renal failure. Early recognition through serological testing and renal biopsy when indicated is crucial for timely intervention. Management typically involves a multidisciplinary approach, integrating rheumatology, nephrology, obstetrics, and hematology expertise. Anticoagulation therapy, often with LMWH in combination with LDA, remains the cornerstone of treatment to mitigate thrombotic risk while preserving placental perfusion and renal function. Close surveillance of blood pressure, proteinuria, and fetal well-being is essential throughout gestation. Furthermore, postpartum follow-up is critical, as renal involvement may

persist or evolve after delivery. Given the chronic nature of antiphospholipid syndrome, long-term strategies to protect renal integrity and prevent cardiovascular morbidity are equally important. Ultimately, optimizing outcomes requires not only vigilant clinical monitoring but also patient education and shared decision-making to navigate the uncertainties inherent in managing this challenging condition during pregnancy.

Authors' contribution

Conceptualization: Maryam Kazemi and Roya Biglarifar.
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Writing–original draft: All authors.
Writing–review and editing: All authors.

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Ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors utilized Perplexity to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Conflicts of interest

The authors declare that they have no competing interests.

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References

1. Patriarcheas V, Tsamos G, Vasdeki D, Kotteas E, Kollias A, Nikas D, et al. Antiphospholipid Syndrome: A Comprehensive Clinical Review. J Clin Med. 2025;14:733. doi: 10.3390/jcm14030733.
2. Turrent-Carriles A, Herrera-Félix JP, Amigo MC. Renal Involvement in Antiphospholipid Syndrome. Front Immunol. 2018;9:1008. doi: 10.3389/fimmu.2018.01008.
3. Kotzen ES, Roy S, Jain K. Antiphospholipid syndrome nephropathy and other thrombotic microangiopathies among patients with systemic lupus erythematosus. Adv Chronic Kidney Dis. 2019;26:376–86. doi: 10.1053/j.ackd.2019.08.012.
4. Hoxha A, Lovisotto M, Perin N, Nalesso F, Del Prete D, Simioni P. Anti-phospholipid antibodies nephropathy is associated with an increased risk of kidney failure: a systematic literature review and meta-analysis. Clin Kidney J. 2024;17:sfae302. doi: 10.1093/ckj/sfae302.
5. Cheung KL, Lafayette RA. Renal physiology of pregnancy. Adv Chronic Kidney Dis. 2013;20:209–14. doi: 10.1053/j.ackd.2013.01.012.
6. Di Prima FA, Valenti O, Hyseni E, Giorgio E, Faraci M, Renda E, et al. Antiphospholipid Syndrome during pregnancy: the state of the art. J Prenat Med. 2011;5:41–53.
7. Murvai VR, Galiș R, Panaitescu A, Radu CM, Ghitea TC, Trif P, et al. Antiphospholipid syndrome in pregnancy: a comprehensive literature review. BMC Pregnancy Childbirth. 2025;25:337. doi: 10.1186/s12884-025-07471-w.
8. Green D. Pathophysiology of Antiphospholipid Syndrome. Thromb Haemost. 2022;122:1085–95. doi: 10.1055/a-1701-2809.
9. Tagara S, Valsami S, Gavriilaki E, Kyriakou E, Grouzi E, Evangelidis P, et al. Activated complement system's impact in antiphospholipid syndrome thrombosis: from pathophysiology to treatment. J Clin Med. 2025;14:6672. doi: 10.3390/jcm14186672.
10. Mayer-Pickel K, Nanda M, Gajic M, Cervar-Zivkovic M. Preeclampsia and the Antiphospholipid Syndrome. Biomedicines. 2023;11:2298. doi: 10.3390/biomedicines11082298.
11. Vrzić Petronijević S, Vilotić A, Bojić-Trbojević Ž, Kostić S, Petronijević M, Vićovac L, et al. Trophoblast cell function in the antiphospholipid syndrome. Biomedicines. 2023;11:2681. doi: 10.3390/biomedicines11102681.
12. Hoxha A, Tormene D, Campello E, Simioni P. Treatment of refractory/high-risk pregnancies with antiphospholipid syndrome: a systematic review of the literature. Front Pharmacol. 2022;13:849692. doi: 10.3389/fphar.2022.849692.
13. Kumar V, Stewart JHt. The complement system in human pregnancy and preeclampsia. Front Immunol. 2025;16:1617140. doi: 10.3389/fimmu.2025.1617140.
14. Ambati A, Zuo Y, Knight JS. An update on inflammation in antiphospholipid syndrome. Curr Opin Rheumatol. 2023;35:89–97. doi: 10.1097/bor.0000000000000926.
15. Feng W, Qiao J, Tan Y, Liu Q, Wang Q, Yang B, et al. Interaction of antiphospholipid antibodies with endothelial cells in antiphospholipid syndrome. Front Immunol. 2024;15:1361519. doi: 10.3389/fimmu.2024.1361519.
16. Genest DS, Patriquin CJ, Licht C, John R, Reich HN. Renal thrombotic microangiopathy: A Review. Am J Kidney Dis. 2023;81:591–605. doi: 10.1053/j.ajkd.2022.10.014.
17. Rayne SC, Kraus FT. Placental thrombi and other vascular lesions. Classification, morphology, and clinical correlations. Pathol Res Pract. 1993;189:2–17. doi: 10.1016/s0344-0338(11)80111-1.
18. Urra M, Lyons S, Teodosiu CG, Burwick R, Java A. Thrombotic microangiopathy in pregnancy: current understanding and management strategies. Kidney Int Rep. 2024;9:2353–71. doi: 10.1016/j.ekir.2024.05.016.
19. Malhotra A, Allison BJ, Castillo-Melendez M, Jenkin G,

Polglase GR, Miller SL. Neonatal morbidities of fetal growth restriction: pathophysiology and impact. Front Endocrinol (Lausanne). 2019;10:55. doi: 10.3389/fendo.2019.00055.
20. Nakatsugawa AC, Sampogna RV. Postnatal Nephrogenesis in Preterm Infants: The Need to Safeguard Kidney Development After Birth. Kidney Int Rep. 2024;9:201–2. doi: 10.1016/j.ekir.2023.12.013.
21. Remien K, Majmundar SH. Physiology, Fetal Circulation. StatPearls. Treasure Island (FL): StatPearls Publishing LLC; 2025.
22. Hoxha A, Del Prete D, Condonato I, Martino FK, Lovisotto M, Nalesso F, et al. Perspective on renal involvement in antiphospholipid syndrome: implications for diagnosis, pathogenesis, and treatment. J Clin Med. 2025;14:3326. doi: 10.3390/jcm14103326.
23. Tektonidou MG. Identification and treatment of APS renal involvement. Lupus. 2014;23:1276–8. doi: 10.1177/0961203314538687.
24. Scheen M, Adedjouma A, Esteve E, Buob D, Abisror N, Planche V, et al. Kidney disease in antiphospholipid antibody syndrome: Risk factors, pathophysiology and management. Autoimmun Rev. 2022;21:103072. doi: 10.1016/j.autrev.2022.103072.
25. Scheen M, Cordes L, Haidar F, De Seigneux S. [Kidney disease in antiphospholipid antibody syndrome]. Rev Med Suisse. 2024;20:430–5. doi: 10.53738/revmed.2024.20.863.430.
26. Liu L, Sun D. Pregnancy outcomes in patients with primary antiphospholipid syndrome: A systematic review and meta-analysis. Medicine (Baltimore). 2019;98:e15733. doi: 10.1097/md.0000000000015733.
27. Palma-Reis I, Vais A, Nelson-Piercy C, Banerjee A. Renal disease and hypertension in pregnancy. Clin Med (Lond). 2013;13:57–62. doi: 10.7861/clinmedicine.13-1-57.
28. Zemet R, Dulitzki M, Baum M, Ofer Friedman H, Morag I, Simchen MJ. Early-onset preeclampsia - The impact of antiphospholipid antibodies on disease severity. Eur J Obstet Gynecol Reprod Biol. 2021;263:79–84. doi: 10.1016/j.ejogrb.2021.06.006.
29. Skoura R, Andronikidi PE, Anestakis D, Petanidis S, Orovou E, Tzitiridou M, et al. Antiphospholipid syndrome and preeclampsia in pregnancy: a case report. Cureus. 2022;14:e28458. doi: 10.7759/cureus.28458.
30. Chen HH, Lin HC, Yeh JC, Chen CP. Renal biopsy in pregnancies complicated by undetermined renal disease. Acta Obstet Gynecol Scand. 2001;80:888–93. doi: 10.1034/j.1600-0412.2001.801004.x.
31. Pignatelli P, Ettorre E, Menichelli D, Pani A, Violi F, Pastori D. Seronegative antiphospholipid syndrome: refining the value of "non-criteria" antibodies for diagnosis and clinical management. Haematologica. 2020;105:562–72. doi: 10.3324/haematol.2019.221945.
32. Andronikidi PE, Orovou E, Mavrigiannaki E, Athanasiadou V, Tzitiridou-Chatzopoulou M, Iatrakis G, et al. Placental and Renal Pathways Underlying Pre-Eclampsia. Int J Mol Sci. 2024;25:2741. doi: 10.3390/ijms25052741.
33. Ji C, Wang Y, Zhai X, Ji G. Antiphospholipid Syndrome Nephropathy Occurs in Pregnancy: A Case Report. Am J Reprod Immunol. 2024;92:e13906. doi: 10.1111/aji.13906.
34. Soh MC, Nelson-Piercy C. Antiphospholipid syndrome in pregnancy. Expert Review of Obstetrics Gynecol. 2010;5:741–61. doi: 10.1586/eog.10.57.
35. Wiles KS, Bramham K, Vais A, Harding KR, Chowdhury P, Taylor CJ, et al. Pre-pregnancy counselling for women with chronic kidney disease: a retrospective analysis of nine years' experience. BMC Nephrol. 2015;16:28. doi: 10.1186/s12882-015-0024-6.
36. Young AN, Lin LH, Abel MK, Badhey MO, Lechner A, Horowitz NS, et al. Atypical placental site nodules: Clinicopathologic features, management and patient outcomes in an institutional series. Gynecol Oncol. 2024;190:215–21. doi: 10.1016/j.ygyno.2024.08.018.
37. Malacova E, Regan A, Nassar N, Raynes-Greenow C, Leonard H, Srinivasjois R, et al. Risk of stillbirth, preterm delivery, and fetal growth restriction following exposure in a previous birth: systematic review and meta-analysis. BJOG. 2018;125:183–92. doi: 10.1111/1471-0528.14906.
38. Rosenblum S, Pal A, Reidy K. Renal development in the fetus and premature infant. Semin Fetal Neonatal Med. 2017;22:58–66. doi: 10.1016/j.siny.2017.01.001.
39. Fuhrmann L, Lindner S, Hauser AT, Höse C, Kretz O, Cohen CD, et al. Effects of environmental conditions on nephron number: modeling maternal disease and epigenetic regulation in renal development. Int J Mol Sci. 2021;22:4157. doi: 10.3390/ijms22084157.
40. Álvarez-Mejía D, Rodas JA, Leon-Rojas JE. From womb to mind: prenatal epigenetic influences on mental health disorders. Int J Mol Sci. 2025;26:6096. doi: 10.3390/ijms26136096.
41. de Jesus GR, Mendoza-Pinto C, de Jesus NR, Dos Santos FC, Klumb EM, Carrasco MG, et al. Understanding and managing pregnancy in patients with lupus. Autoimmune Dis. 2015;2015:943490. doi: 10.1155/2015/943490.
42. Shrateh ON, Jobran AWM, Amoori A. Rare diagnosis of coexistent antiphospholipid syndrome and systemic lupus erythematosus in a male patient with successful management: a case report. Ann Med Surg (Lond). 2023;85:1983–6. doi: 10.1097/ms9.0000000000000556.
43. Elahi T, Ahmed S, Mubarak M. Relationship of lupus nephritis and pregnancy: A narrative review. World J Nephrol. 2024;13:99700. doi: 10.5527/wjn.v13.i4.99700.
44. Fredi M, Andreoli L, Aggogeri E, Bettiga E, Lazzaroni MG, Le Guern V, et al. Risk Factors for Adverse Maternal and Fetal Outcomes in Women With Confirmed aPL Positivity: Results From a Multicenter Study of 283 Pregnancies. Front Immunol. 2018;9:864. doi: 10.3389/fimmu.2018.00864.
45. Ünlü O, Zuily S, Erkan D. The clinical significance of antiphospholipid antibodies in systemic lupus erythematosus. Eur J Rheumatol. 2016;3:75–84. doi: 10.5152/eurjrheum.2015.0085.
46. Fuentes Carrasco M, Mayoral Triana A, Cristóbal García IC, Pérez Pérez N, Izquierdo Méndez N, Soler Ruiz P, et al. Catastrophic antiphospholipid syndrome during pregnancy. Eur J Obstet Gynecol Reprod Biol. 2021;264:21–4. doi: 10.1016/j.ejogrb.2021.07.002.

47. Okunlola AO, Ajao TO, Sabi M, Kolawole OD, Eweka OA, Karim A, et al. Catastrophic Antiphospholipid Syndrome: A Review of Current Evidence and Future Management Practices. Cureus. 2024;16:e69730. doi: 10.7759/cureus.69730.
48. Barros V, Igai AMK, Oliveira A, Teruchkin MM, Orsi FA. Obstetric antiphospholipid syndrome. Rev Bras Ginecol Obstet. 2021;43:495–501. doi: 10.1055/s-0041-1732382.
49. Salter BM, Crowther MA. Catastrophic antiphospholipid syndrome: a CAPS-tivating hematologic disease. Hematology Am Soc Hematol Educ Program. 2024;2024:214–21. doi: 10.1182/hematology.2024000544.
50. Smyth A, Radovic M, Garovic VD. Women, kidney disease, and pregnancy. Adv Chronic Kidney Dis. 2013;20:402–10. doi: 10.1053/j.ackd.2013.06.004.
51. Khashan AS, Evans M, Kublickas M, McCarthy FP, Kenny LC, Stenvinkel P, et al. Preeclampsia and risk of end stage kidney disease: A Swedish nationwide cohort study. PLoS Med. 2019;16:e1002875. doi: 10.1371/journal.pmed.1002875.
52. Turbeville HR, Sasser JM. Preeclampsia beyond pregnancy: long-term consequences for mother and child. Am J Physiol Renal Physiol. 2020;318:F1315–f26. doi: 10.1152/ajprenal.00071.2020.
53. Fitzpatrick A, Mohammadi F, Jesudason S. Managing pregnancy in chronic kidney disease: improving outcomes for mother and baby. Int J Womens Health. 2016;8:273–85. doi: 10.2147/ijwh.S76819.
54. De Carolis S, Tabacco S, Rizzo F, Giannini A, Botta A, Salvi S, et al. Antiphospholipid syndrome: An update on risk factors for pregnancy outcome. Autoimmun Rev. 2018;17:956–66. doi: 10.1016/j.autrev.2018.03.018.
55. Sammaritano LR, Bermas BL, Chakravarty EE, Chambers C, Clowse MEB, Lockshin MD, et al. 2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases. Arthritis Care Res (Hoboken). 2020;72:461–88. doi: 10.1002/acr.24130.
56. Amengual O, Fujita D, Ota E, Carmona L, Oku K, Sugiura-Ogasawara M, et al. Primary prophylaxis to prevent obstetric complications in asymptomatic women with antiphospholipid antibodies: a systematic review. Lupus. 2015;24:1135–42. doi: 10.1177/0961203315578765.
57. Shi T, Gu ZD, Diao QZ. Meta-analysis on aspirin combined with low-molecular-weight heparin for improving the live birth rate in patients with antiphospholipid syndrome and its correlation with d-dimer levels. Medicine (Baltimore). 2021;100:e26264. doi: 10.1097/md.0000000000026264.
58. Urban ML, Bettiol A, Mattioli I, Emmi G, Di Scala G, Avagliano L, et al. Comparison of treatments for the prevention of fetal growth restriction in obstetric antiphospholipid syndrome: a systematic review and network meta-analysis. Intern Emerg Med. 2021;16:1357–67. doi: 10.1007/s11739-020-02609-4.
59. Lee EE, Jun JK, Lee EB. Management of Women with Antiphospholipid Antibodies or Antiphospholipid Syndrome during Pregnancy. J Korean Med Sci. 2021;36:e24. doi: 10.3346/jkms.2021.36.e24.
60. Ambati A, Knight JS, Zuo Y. Antiphospholipid syndrome management: a 2023 update and practical algorithm-based approach. Curr Opin Rheumatol. 2023;35:149–60. doi: 10.1097/bor.0000000000000932.
61. Gajić M, Schröder-Heurich B, Horvat Mercnik M, Cervar-Zivkovic M, Wadsack C, von Versen-Höynck F, et al. The Impact of Hydroxychloroquine on Primary Feto-Placental Endothelial Cells from Healthy and Early-Onset Preeclamptic Placentas. Int J Mol Sci. 2023;24:10934. doi: 10.3390/ijms241310934.
62. Huybrechts KF, Bateman BT, Zhu Y, Straub L, Mogun H, Kim SC, et al. Hydroxychloroquine early in pregnancy and risk of birth defects. Am J Obstet Gynecol. 2021;224:290.e1–.e22. doi: 10.1016/j.ajog.2020.09.007.
63. Abdelrazek MM, Ahmed MA, Ibrahim MEM. Effect of nitric oxide donor and plasma volume expansion on pregnancies with early onset fetal growth restriction: a randomized controlled trial. Arch Gynecol Obstet. 2025;311:1435–44. doi: 10.1007/s00404-025-07988-7.
64. Lefkou E, Mamopoulos A, Dagklis T, Vosnakis C, Rousso D, Girardi G. Pravastatin improves pregnancy outcomes in obstetric antiphospholipid syndrome refractory to antithrombotic therapy. J Clin Invest. 2016;126:2933–40. doi: 10.1172/jci86957.
65. Huo R, Sun Q, Lv Q, Wang Y, Qi W, Zhang M, et al. Simvastatin ameliorates adverse pregnancy by inhibiting glycolysis-related NETs in obstetrical antiphospholipid syndrome. Life Sci. 2024;359:123215. doi: 10.1016/j.lfs.2024.123215.
66. Velikova T, Sekulovski M, Bogdanova S, Vasilev G, Peshevska-Sekulovska M, Miteva D, et al. Intravenous Immunoglobulins as Immunomodulators in Autoimmune Diseases and Reproductive Medicine. Antibodies (Basel). 2023;12:20. doi: 10.3390/antib12010020.
67. Han A, Lee SK, Park JC, Park CW, Han JW, Lee KH. Maternal and fetal safety of intravenous immunoglobulin in women with reproductive failure. Am J Reprod Immunol. 2021;86:e13492. doi: 10.1111/aji.13492.
68. Kaneko K, Tsutsumi S, Fujita D, Sugiura-Ogasawara M, Mitsuda N, Matsubara K, et al. Intravenous immunoglobulin treatment for obstetric antiphospholipid syndrome refractory to conventional therapy: A single-arm, open-labelled multicentre clinical trial. Mod Rheumatol. 2024;34:515–22. doi: 10.1093/mr/road062.
69. Cole MA, Gerber GF, Chaturvedi S. Complement biomarkers in the antiphospholipid syndrome - Approaches to quantification and implications for clinical management. Clin Immunol. 2023;257:109828. doi: 10.1016/j.clim.2023.109828.
70. Gaio M, Vastarella MG, Sullo MG, Scavone C, Riccardi C, Campitiello MR, et al. Pregnancy Recommendations Solely Based on Preclinical Evidence Should Be Integrated with Real-World Evidence: A Disproportionality Analysis of Certolizumab and Other TNF-Alpha Inhibitors Used in Pregnant Patients with Psoriasis. Pharmaceuticals (Basel). 2024;17:904. doi: 10.3390/ph17070904.

71. Mormile I, Granata F, Punziano A, de Paulis A, Rossi FW. Immunosuppressive Treatment in Antiphospholipid Syndrome: Is It Worth It? Biomedicines. 2021;9:132. doi: 10.3390/biomedicines9020132.
72. Radu A, Dudu SC, Ciobanu A, Peltecu G, Iancu G, Botezatu R, et al. Pregnancy Management in Women with Antiphospholidic Syndrome. Maedica (Bucur). 2019;14:148–60. doi: 10.26574/maedica.2019.14.2.148.
73. Calcaterra I, Ambrosino P, Vitelli N, Lupoli R, Orsini RC, Chiurazzi M, et al. Risk Assessment and Antithrombotic Strategies in Antiphospholipid Antibody Carriers. Biomedicines. 2021;9:122. doi: 10.3390/biomedicines9020122.
74. Tektonidou MG, Andreoli L, Limper M, Amoura Z, Cervera R, Costedoat-Chalumeau N, et al. EULAR recommendations for the management of antiphospholipid syndrome in adults. Ann Rheum Dis. 2019;78:1296–304. doi: 10.1136/annrheumdis-2019-215213.
75. Priani IF, Afiyanti Y, Kurniawati W. Preparing pregnancy through Preconception Education Training. Enfermería Clínica. 2019;29:304–9. doi: 10.1016/j.enfcli.2019.04.140.
76. Deguchi M, Yamada H, Sugiura-Ogasawara M, Morikawa M, Fujita D, Miki A, et al. Factors associated with adverse pregnancy outcomes in women with antiphospholipid syndrome: A multicenter study. J Reprod Immunol. 2017;122:21–7. doi: 10.1016/j.jri.2017.08.001.