

Spectrum of Pregnancy Outcomes in Systemic Lupus Erythematosus: A Three-Case Series Highlighting Diagnostic and Therapeutic Challenges

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ABSTRACT

Pregnancy in women with systemic lupus erythematosus (SLE) carries substantial maternal and fetal risks, including disease flares, lupus nephritis, preterm birth, and haemorrhagic complications. We present a three-case series from a tertiary care teaching hospital illustrating the breadth of obstetric challenges encountered in SLE pregnancies. Case 1 describes a 35-year-old multigravida with known SLE and chronic hypertension who developed acute cervical shortening at 26 weeks (effective cervical length 6 mm), managed with an Arabin pessary, and subsequently required emergency lower segment caesarean section (LSCS) at 30 weeks for meconium-stained liquor, with the delivery complicated by refractory atonic postpartum haemorrhage (PPH) necessitating stepwise surgical escalation culminating in right internal iliac artery ligation. Case 2 describes a 25-year-old primigravida with a precious dichorionic diamniotic (DCDA) twin pregnancy conceived via intrauterine insemination (IUI), who was newly diagnosed with SLE (mucocutaneous involvement, strong anti-RNP/Sm positivity) and clinically labelled as having lupus nephritis on the basis of persistent nephrotic-range proteinuria, elevated blood pressure, and strongly positive serology — renal biopsy having been contraindicated by twin gestation. She was commenced on immunosuppressive therapy and delivered alive twin babies following emergency LSCS at 31+6 weeks for preterm premature rupture of membranes (PPROM) in the setting of an SLE flare. Case 3 describes a 21-year-old primigravida with biopsy-proven International Society of Nephrology/Renal Pathology Society (ISN/RPS) Class IV lupus nephritis who had failed sequential therapy with mycophenolate mofetil and rituximab without achieving remission, and who conceived at 4 weeks of gestation despite counselling against pregnancy. In the context of active uncontrolled nephritis, worsening renal failure, persistently elevated blood pressure, and concurrent teratogenic drug exposure, medical termination of pregnancy was performed for maternal safety. Together, these cases underscore the heterogeneity of SLE-related obstetric outcomes and the critical importance of pre-conception counselling, multidisciplinary surveillance, and tailored pharmacological management in this high-risk population.

Key Words: Systemic lupus erythematosus; lupus nephritis; postpartum haemorrhage; preterm premature rupture of membranes; mycophenolate mofetil teratogenicity; case report.

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INTRODUCTION

Systemic lupus erythematosus is a chronic multisystem autoimmune disease that predominantly affects women of reproductive age, with peak incidence between the ages of 15 and 45 years. Pregnancy in sle is associated with a significantly elevated risk of adverse maternal and fetal outcomes, including lupus flares, lupus nephritis, preeclampsia, fetal growth restriction, preterm birth, and maternal mortality [1,2]. Although advances in disease monitoring and immunosuppressive therapy have improved outcomes, sle pregnancies continue to be classified as high-risk and mandate close multidisciplinary oversight involving obstetrics, rheumatology, and nephrology [3,4].

The clinical course of sle in pregnancy is highly variable and influenced by disease activity at the time of conception, the presence of lupus nephritis,

concurrent antiphospholipid antibodies, chronic hypertension, and the class of immunosuppressive therapy in use [5]. Lupus nephritis, present in approximately 50% of sle patients during their lifetime, confers a particularly adverse obstetric prognosis, significantly increasing the risks of preeclampsia, renal flare, preterm delivery, and caesarean section [6,7,8]. A recent systematic review and meta-analysis confirmed that prior lupus nephritis is independently associated with reduced livebirth probability (or 0.62), increased preterm birth (or 2.00), and markedly elevated risk of preeclampsia (or 3.11), while chronic hypertension further compounds these risks [9].

Despite this broad understanding of aggregate risk, individual cases of sle in pregnancy continue to present unique diagnostic and therapeutic challenges — ranging from the management of refractory postpartum haemorrhage and acute cervical insufficiency, to the complexities of initiating or

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continuing immunosuppression in the setting of active renal disease and a concurrent pregnancy. The challenge is further amplified in situations involving multi-fetal gestation, where standard diagnostic procedures such as renal biopsy may be contraindicated, or where a patient conceives while on established teratogenic agents.

This case series presents three patients managed at our institution who exemplify this spectrum — from a case of refractory atonic postpartum haemorrhage in a multigravida with known sle and cervical incompetence, to a complex twin pregnancy with newly diagnosed lupus nephritis managed without biopsy confirmation, to a patient with biopsy-proven refractory class iv lupus nephritis who conceived while on rituximab and mycophenolate mofetil. The series aims to highlight the diagnostic and therapeutic challenges inherent to each presentation and to reinforce the principles of pre-conception risk stratification and multidisciplinary care.

Table 1. Summary of all three cases

Parameter	Case 1	Case 2	Case 3
Age	35 years	25 years	21 years
Obstetric history	G4A3	Primigravida	Primigravida
Conception	Spontaneous	IUI (precious pregnancy)	Spontaneous
Type of pregnancy	Singleton	DCDA Twin	Singleton
Primary diagnosis	SLE with chronic hypertension	SLE with clinical lupus nephritis	SLE with biopsy-proven Class IV lupus nephritis
Key antenatal complication	Acute cervical shortening at 26 weeks	PPROM + SLE flare at 31+6 weeks	Active renal disease; conceived on teratogenic immunosuppressants
Mode of delivery	Emergency LSCS at 30 weeks	Emergency LSCS at 31+6 weeks	Medical termination of pregnancy (4 weeks GA)
Key intrapartum/postpartum event	Refractory atonic PPH - escalated to right	Delivery of alive twin babies; maternal disease stabilised	MTP for maternal safety and teratogen exposure

	internal iliac artery ligation		
Fetal outcome	Live preterm neonate	Two live preterm neonates	Pregnancy terminated
Maternal outcome	Recovered; haemorrhage controlled surgically	Stabilised post-delivery; immunosuppression continued	MTP performed; renal disease under ongoing management

CASE PRESENTATIONS

Case 1: SLE-Positive Pregnancy with Acute Cervical Shortening and Refractory Postpartum Haemorrhage

Patient Information

A 35-year-old woman, gravida 4, abortus 3 (G4A3), with a background of confirmed SLE and chronic hypertension, presented at 26 weeks of gestation with cervical incompetence. She had no live children from prior pregnancies. There was no family history of autoimmune disease. Her psychosocial history was unremarkable. She was on antihypertensive therapy and had been followed up in the rheumatology clinic prior to conception.

Clinical Findings and Timeline

At 26 weeks, the patient was admitted with acute cervical shortening. Transvaginal ultrasound demonstrated an effective cervical length of 6 mm, a funnel width of 2.5 cm, and a funnel length of 5.2 cm — findings consistent with significant cervical incompetence. An Arabin pessary was inserted, and the patient was maintained on strict bed rest in the antenatal ward. At 30 weeks, she developed leaking per vaginam with meconium-stained liquor (MSL), and emergency LSCS was performed.

Diagnostic Assessment

Serological investigations at admission confirmed active SLE. See Table 2 for the full investigative profile.

Table 2. Case 1: Serological and biochemical investigations

Investigation	Finding
ANA	Positive
Anti-dsDNA	Positive
Complement C3/C4	Mildly reduced
Platelets	Borderline low
Coagulation profile	Normal
Urine protein	3+
ESR / CRP	Elevated

Therapeutic Intervention and Outcome

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A live preterm male neonate was delivered by emergency LSCS. Immediately following delivery of the placenta, the patient developed severe atonic postpartum haemorrhage. A stepwise escalation of haemostatic interventions was undertaken in accordance with institutional protocol (Table 3):

Table 3. Case 1: Stepwise surgical management of postpartum haemorrhage

Step	Intervention	Response
1	Medical management (uterotonics + tranexamic acid)	Not controlled
2	Bakri balloon insertion	Not controlled
3	B-Lynch compression suture	Not controlled
4	Uterine artery ligation	Not controlled
5	Right internal iliac artery ligation	Bleeding controlled

Haemorrhage was successfully controlled following right internal iliac artery ligation. Blood transfusion and intensive care monitoring were provided postoperatively. Both the mother and neonate were stabilised and discharged in satisfactory condition.

Follow-up and Outcomes

The mother made a full recovery without further surgical intervention. Postoperative review confirmed haemodynamic stability, and she was referred for continued rheumatological and obstetric follow-up. The neonate required neonatal intensive care support commensurate with extreme prematurity.

Case 2: SLE with DCDA Twin Pregnancy (IUI Conception), Clinical Lupus Nephritis, and PPROM

Patient Information

A 25-year-old primigravida conceived a dichorionic diamniotic (DCDA) twin pregnancy following intrauterine insemination (IUI). This constituted a precious pregnancy. She had no prior diagnosis of autoimmune disease. Antenatal booking investigations prompted autoimmune serological workup in view of a facial rash noted during the early second trimester, leading to a new diagnosis of SLE. She was also known to have hypothyroidism and chronic hypertension, for which she was on levothyroxine and antihypertensive therapy.

Clinical Findings and Timeline

At 14 weeks of gestation, the patient developed erythematous facial lesions consistent with a malar rash, which did not respond to topical therapy or antihistamines. ANA testing was performed and returned strongly positive. Further antibody profiling revealed RNP/Sm (RNP): +++ and Sm: +++. Urine PCR was 3.3, with urine protein 2+. Blood pressure was elevated. A diagnosis of SLE with mucocutaneous involvement was made.

Renal biopsy was planned at 16 weeks in view of persistent nephrotic-range proteinuria (24-hour urine protein >3.5 g). However, prone positioning — a prerequisite for the percutaneous renal biopsy procedure — was not feasible due to the twin gestation. In the absence of histological confirmation, a clinical diagnosis of lupus nephritis was established on the basis of: persistent nephrotic-range proteinuria, elevated blood pressure, strong positive ANA and anti-Sm/RNP serology, and the presence of active SLE with mucocutaneous manifestations. The patient was commenced on immunosuppressive therapy — prednisolone (Wysolone), azathioprine, and hydroxychloroquine — and disease remained controlled through the second trimester.

At 31 weeks and 6 days, the patient presented with complaints of abdominal pain, leaking per vaginam, and exaggerated facial rashes indicating an SLE flare. Preterm premature rupture of membranes (PPROM) was confirmed. She was administered magnesium sulphate for neuroprotection and antenatal corticosteroids for fetal lung maturation. Emergency LSCS was performed.

Diagnostic Assessment

Table 4 details the full serological and biochemical profile of this patient.

Table 4. Case 2: Serological and biochemical investigations

Investigation	Finding
ANA	Positive
RNP/Sm (RNP)	+++ (strong positive)
Sm antibody	+++ (strong positive)
Anti-dsDNA	Mild elevation
Complement C3/C4	Low-normal
Urine PCR	3.3
Urine protein	++ (persistent)
24-hour urine protein	>3.5 g/day (nephrotic range)
Serum creatinine	Stable / mildly elevated
ESR / CRP	Elevated (flare)
TSH / Thyroid profile	Hypothyroid — on levothyroxine
CBC	Mild anaemia
Urine microscopy	Occasional RBCs; proteinuria pattern

Therapeutic Intervention and Outcome

Emergency LSCS was performed at 31+6 weeks. Both twin babies were delivered alive with acceptable Apgar scores. Maternal haemodynamic status remained stable throughout the procedure. Postoperatively, the patient was continued on her immunosuppressive regimen. The SLE flare was managed with dose optimisation of prednisolone. The maternal condition stabilised and she was discharged with close rheumatological and neonatal follow-up arranged.

Follow-up and Outcomes

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Both neonates required neonatal intensive care admission commensurate with their degree of prematurity. The mother was followed up in rheumatology clinic, where immunosuppressive therapy was continued and the lupus nephritis was monitored. A postnatal renal biopsy was planned to enable histological classification of the nephritis.

Case 3: Biopsy-Proven Class IV Lupus Nephritis — Rituximab and Mycophenolate Mofetil Exposure in Early Pregnancy Necessitating Medical Termination

Patient Information

A 21-year-old primigravida presented with a confirmed intrauterine pregnancy at 4 weeks of gestation. She had a pre-existing diagnosis of SLE with biopsy-proven lupus nephritis and had been managed by a combined rheumatology and nephrology team for over 12 months prior to conception. Despite being explicitly counselled against conception in view of active disease and ongoing teratogenic therapy, she conceived.

Relevant Past Interventions and History

Following renal biopsy confirming ISN/RPS Class IV lupus nephritis (diffuse proliferative), the patient was commenced on mycophenolate mofetil (MMF) as first-line therapy. After six months of treatment, remission was not achieved. The regimen was escalated with the addition of injection rituximab, of which two doses were administered. Remission remained elusive. Blood pressure was persistently elevated throughout her treatment course and nephrotic-range proteinuria persisted with progressive worsening of renal function.

Clinical Findings and Diagnostic Assessment

At the time of pregnancy confirmation, all investigations reflected active, unremitted disease. See Table 5.

Table 5. Case 3: Investigations at time of pregnancy confirmation

Investigation	Finding
ANA	Positive
Anti-dsDNA	Positive
Direct Coombs test	Positive
Serum creatinine	Worsening — progressive renal failure
24-hour urine protein	>3.5 g/day (nephrotic range)
Complement C3/C4	Low
Blood pressure	Persistently elevated
Renal biopsy	Diffuse lupus nephritis — ISN/RPS Class IV (A)
Gestational age at pregnancy confirmation	4 weeks

Medications at conception	Mycophenolate mofetil + Rituximab (2 doses completed) + Azathioprine
Disease status at conception	Active — remission NOT achieved

Therapeutic Intervention: Rationale for Medical Termination

A joint decision for medical termination of pregnancy (MTP) was reached by the multidisciplinary team - comprising obstetrics, rheumatology, and nephrology and discussed at length with the patient and her family. The following factors underpinned this decision:

(i) Active, uncontrolled Class IV lupus nephritis with worsening renal failure: Continued pregnancy in the setting of progressive renal deterioration carried a high risk of end-stage renal disease, a recognised risk that is substantially amplified by active nephritis at conception.

(ii) Persistently elevated blood pressure and nephrotic-range proteinuria: These independently confer a high risk of preeclampsia, fetal growth restriction, and preterm delivery.

(iii) Teratogenic risk of mycophenolate mofetil: MMF is a well-established human teratogen. It has been associated with a characteristic pattern of congenital malformations — including external ear and other facial anomalies, cleft palate, and distal limb defects — as well as increased risk of first-trimester pregnancy loss.

(iv) Teratogenic risk of rituximab: Rituximab is a chimeric anti-CD20 monoclonal antibody that crosses the placenta, particularly in the second and third trimesters. Neonatal B-cell depletion and haematological abnormalities have been reported following in-utero exposure.

Given the compound risks of active maternal renal disease and dual teratogenic drug exposure, medical termination of pregnancy was performed at 4 weeks of gestation for maternal safety.

Follow-up and Outcomes

Post-termination, the patient was continued on rheumatology and nephrology follow-up. MMF was maintained as part of her induction regimen, with plans to transition to azathioprine once remission was achieved, in preparation for any future pregnancy attempts. The patient was counselled extensively regarding the importance of achieving sustained disease remission prior to any future conception, with a minimum remission period of six months as a prerequisite, in alignment with EULAR guidelines.

DISCUSSION

This three-case series illustrates the heterogeneity of sle-related obstetric outcomes and the distinct diagnostic and therapeutic challenges that arise at different points along this spectrum. Each case contributed a clinically significant and

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independently instructive narrative — from refractory surgical haemorrhage and cervical incompetence, to a twin pregnancy with clinically diagnosed lupus nephritis, to the termination of an early pregnancy complicated by active refractory nephritis and teratogenic drug exposure.

Cervical incompetence and postpartum haemorrhage in sle (case 1)

The first case highlights two distinct but compounding complications. Cervical shortening in sle may reflect underlying systemic inflammation and endothelial dysfunction, which impair normal cervical remodelling [9]. The use of an arabin pessary is well-supported for the management of cervical insufficiency in singleton pregnancies and has demonstrated efficacy in reducing preterm delivery at gestational ages below 34 weeks [10,11]. In the context of sle-associated chronic hypertension and borderline placental reserve, the patient ultimately delivered by emergency lscs at 30 weeks following development of meconium-stained liquor. The subsequent refractory atonic pph required stepwise surgical escalation through five interventions, culminating in right internal iliac artery ligation. Postpartum haemorrhage is a recognised complication of sle pregnancies, driven by borderline platelet counts, endothelial dysfunction, and abnormal uterine vascular tone [1]. A comprehensive review of uterine-sparing surgical procedures documented the relative efficacy of available surgical options — noting that internal iliac artery ligation carries approximately 70% effectiveness but is technically demanding, and that no single procedure has demonstrated superiority over others [12]. The stepwise approach employed in this case — consistent with international management guidelines — reflects best practice for preserving uterine fertility while achieving haemostasis [12].

Twin pregnancy with clinical lupus nephritis and pprom (case 2)

Case 2 illustrates a particularly challenging diagnostic scenario. In twin pregnancies, prone positioning for percutaneous renal biopsy is typically not feasible, precluding histological classification of nephritis [6]. Our patient was therefore diagnosed with lupus nephritis on clinical grounds — nephrotic-range proteinuria exceeding 3.5 g per day, elevated blood pressure, strongly positive anti-sm and anti-rnp antibodies, and active mucocutaneous sle. This approach is recognised in the literature and endorsed in the context where biopsy cannot be safely performed [13,14].

Anti-rnp positivity, as identified in this patient, has been specifically associated with an increased risk of pprom in sle pregnancies, with a reported relative risk of 3.08 (95% ci 1.39–6.78) for pprom and 3.37 for preterm pprom specifically [15]. This finding directly contextualises the membrane rupture event at 31+6 weeks. Furthermore, glucocorticoid use —

an integral component of immunosuppression in this case — has been independently associated with pprom through modulation of amnion permeability and induction of the itga8 gene in fetal membranes [16]. The preterm birth rate in sle pregnancies is well-documented to be high, with a recent systematic review reporting that approximately 31% of sle pregnancies result in preterm birth, of which 14% are spontaneous [17]. Despite the prematurity, both twin neonates were delivered alive, reflecting the favourable impact of antenatal corticosteroid administration and magnesium sulphate neuroprotection.

The immunosuppressive regimen employed — prednisolone, azathioprine, and hydroxychloroquine — is consistent with current eular recommendations for sle management in pregnancy, which designate azathioprine and hydroxychloroquine as the preferred immunosuppressive agents in this setting [18,19,20]. Hydroxychloroquine in particular has been shown to reduce the frequency and severity of sle flares during pregnancy and is recommended in all sle patients unless contraindicated [19,21].

Refractory lupus nephritis, teratogenic agents, and the decision for medical termination (case 3)

Case 3 represents the most complex scenario from an ethical, pharmacological, and clinical standpoint. The decision for medical termination was reached after systematic assessment of three converging risk factors: active, unremitted class iv lupus nephritis; worsening renal function; and dual exposure to established teratogenic agents.

Mycophenolate mofetil is contraindicated in pregnancy and is recognised as a human teratogen. Eular guidelines and multiple consensus statements explicitly mandate discontinuation of mmf at least six weeks prior to planned conception, with transition to azathioprine as the preferred alternative [18,20]. The characteristic mmf embryopathy syndrome — encompassing external ear anomalies, orofacial clefts, and limb defects — is well-documented in the literature and in case reports of lupus nephritis patients [22,23]. A directly analogous case of a lupus nephritis patient who conceived while on mmf and delivered a neonate with multiple skeletal deformities has been previously reported [22].

Rituximab, a chimeric anti-cd20 monoclonal antibody, is employed in refractory lupus nephritis as a salvage therapy [13,14]. An analysis of 153 pregnancies with known rituximab outcomes from the global drug safety database reported neonatal b-cell depletion and haematological abnormalities in exposed infants, alongside a small number of congenital malformations [24]. Current eular guidance advises discontinuation of rituximab prior to planned conception, noting insufficient safety data to support its continuation in pregnancy [18,19]. A retrospective cohort of rituximab use in multiple sclerosis pregnancies reported no increase

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in major malformations when last exposure occurred prior to conception; however, inadvertent first-trimester exposure — as in our patient — introduces substantially greater uncertainty [25].

The patient in case 3 had received two doses of rituximab and remained on mmf at the time of conception. The compound teratogenic risk, in combination with active uncontrolled nephritis — itself associated with a 37% rate of fetal complications including growth restriction, stillbirth, and preterm delivery [7] — rendered continuation of pregnancy medically untenable. Current eular recommendations on sle management state explicitly that women with active lupus nephritis should be counselled against pregnancy until sustained remission is achieved, ideally for a minimum of six months [19]. Single-dose rituximab has demonstrated approximately 79% partial or complete renal response in refractory lupus nephritis, though relapse rates at 17 months exceed 45%, underscoring the unpredictability of disease control in this subset [13]. A consensus guideline for lupus nephritis similarly reserves rituximab for cases of confirmed refractory disease and recommends robust preconception planning [14].

Overarching clinical implications

Across all three cases, several recurring themes emerge. First, multidisciplinary care — integrating obstetrics, rheumatology, and nephrology — was indispensable at every decision point, consistent with evidence demonstrating improved outcomes through specialist-coordinated surveillance [4,5,21]. Second, the primacy of pre-conception counselling cannot be overstated: the adverse outcomes in cases 1 and 3, in particular, were substantially compounded by disease-related and pharmacological factors that could have been mitigated through earlier disease optimisation [1,2,9]. Third, even in the absence of definitive histological diagnosis (case 2), clinical decision-making guided by serological and biochemical parameters — supported by multidisciplinary consensus — can be appropriately enacted [6,8]. Finally, the cases collectively affirm that sle pregnancies should be regarded as inherently high-risk irrespective of presenting severity, and that escalation protocols for haemorrhage, ppprom, and preterm delivery must be anticipated and planned in advance [3,4,17].

Strengths and Limitations

The strengths of this case series lie in the clinical authenticity of the three cases, their representation of a genuinely broad spectrum of SLE obstetric complexity, and the multidisciplinary nature of the decision-making described. The series provides a real-world counterpart to population-level data from systematic reviews, grounding abstract risk estimates in concrete clinical narratives. Limitations include the small number of cases (inherent to the case series design), the absence of long-term

maternal renal follow-up data in Cases 1 and 2, and the reliance on clinical diagnosis of lupus nephritis in Case 2 without histological confirmation.

PATIENT PERSPECTIVE

All three patients expressed gratitude for the sustained and coordinated care they received throughout their hospital admissions. The patient in Case 1 conveyed that despite the fear and uncertainty surrounding the emergency surgery and the haemorrhagic complication, she felt reassured by the clarity with which each intervention was explained to her and her family. She emphasised that being kept informed at every step was central to her sense of safety. The patient in Case 2 shared that the experience of managing a complex twin pregnancy alongside a new autoimmune diagnosis was emotionally overwhelming, but that early counselling about disease management and fetal surveillance helped her to understand the nature of the risks involved. She expressed relief at the delivery of her twins alive and appreciated the close postpartum support provided. The patient in Case 3, in her own words, described the experience of being told that continuing her pregnancy would place her life at serious risk as profoundly difficult. She expressed that she was treated with dignity and compassion throughout the counselling process and acknowledged that, with hindsight, she understood the reasoning behind the decision for termination of pregnancy, even as she continued to grieve the loss.

CONCLUSION

This three-case series demonstrates that pregnancy in SLE encompasses a wide spectrum of clinical complexity, from refractory postpartum haemorrhage and cervical incompetence, to biopsy-unconfirmed lupus nephritis in a multi-fetal gestation, to the irreversible consequences of conceiving with active renal disease on teratogenic immunosuppressive therapy. Adverse outcomes in this population are not confined to the most severely affected patients; rather, they arise at every point along the disease spectrum and are shaped by the interplay of disease activity, comorbidities, gestational complexity, and pharmacological context. Pre-conception counselling with achievement of sustained disease remission, transition to pregnancy-compatible immunosuppression, and close multidisciplinary surveillance throughout pregnancy represent the cornerstones of risk mitigation in SLE. Clinicians must maintain a high index of suspicion for complications at every gestational stage and be prepared to escalate management swiftly, particularly in the domains of haemorrhage control and preterm birth management.

INFORMED CONSENT

Written informed consent was obtained from all patients for publication of this case series and any accompanying data. Ethical review was not required for this case series as per institutional guidelines

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applicable to de-identified clinical case descriptions; however, all principles of the Declaration of Helsinki were observed throughout the care and reporting of these cases.

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