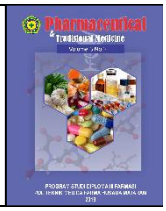
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THERAPEUTIC APPROACH TO EVANS SYNDROME IN PREGNANCY: A CASE SERIES

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ABSTRACT

Evans syndrome (ES) is a rare autoimmune disorder characterized by the combination of autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP), occasionally accompanied by autoimmune neutropenia. While it affects both children and adults, it shows a higher prevalence in adult females. The occurrence of ES during pregnancy is exceptionally rare, and standard therapeutic guidelines for its management remain lacking. To evaluate therapeutic approaches and clinical outcomes in pregnant women with Evans syndrome through a case series and literature review. A literature review and case series evaluation were conducted, focusing on pregnant women with ES treated across several hospitals. Data were retrieved from electronic databases and supplemented by manual searches up to late 2018. Six cases of pregnant women with ES were analyzed. First-line therapies comprised corticosteroids and intravenous immunoglobulin (IVIG), whereas second-line management utilized immunosuppressive agents such as rituximab and cyclosporine. Splenectomy was reserved for refractory cases. Primary complications included infections, venous thromboembolism, and fetal growth restriction. Multidisciplinary collaboration was vital in optimizing both maternal and perinatal outcomes. Evans syndrome in pregnancy presents significant diagnostic and therapeutic challenges due to its rarity. Treatment strategies must be tailored individually, balancing maternal and fetal safety within a multidisciplinary management framework. This case series serves as a valuable reference for establishing future clinical guidelines.

Keyword: *Evan Syndrome, pregnancy, therapeutic approach, case series*

BACKGROUND

Evans' syndrome (ES) was first described by Evans in 1951 and is defined as the simultaneous or sequential occurrence of immune thrombocytopenia (ITP) and autoimmune hemolytic anemia (AIHA). Anemia in ES is caused by AIHA involving warm antibodies, typically of the IgG isotype and occasionally IgA, thereby ruling out the role of cold agglutination.

Additionally, autoimmune neutropenia (AIN) may also form part of ES, with an incidence of approximately 15% in adults and 20% in children. This condition can affect both children and adults, showing a higher prevalence in adult females (female-to-male ratio of 2:1), whereas in children, it is more frequently observed in males (Audia et al., 2020; Fattizzo et al., 2021; Muley et al., 2023). Clinically, Evans syndrome (ES) is a chronic disorder marked by frequent relapses and spontaneous remissions. While AIHA has an annual incidence of 0.8–3 per 100,000 individuals and ITP affects 6.6 per 100,000 adults, the exact incidence of ES remains unknown, though it affects 1.8% to 10% of ITP patients. During pregnancy, ITP occurs in 1–5 per 10,000 cases with up to a 14% risk of neonatal thrombocytopenia, whereas AIHA is exceptionally rare yet capable of causing severe maternal anemia and fetal complications. First described by Dr. Robert Evans in 1951, with the initial pregnancy case reported in 1966, only a very limited number of ES cases during pregnancy have been documented to date (Lefkou et al., 2010; Manjula et al., 2019).

The pathogenesis of Evans syndrome involves specific autoantibodies targeting red blood cells and platelets simultaneously or separately, with IgG autoantibodies attacking platelet surface glycoproteins and leading to premature destruction by the reticuloendothelial system. Evans syndrome can occur independently or concurrently with other autoimmune diseases, such as systemic lupus erythematosus, antiphospholipid syndrome, and autoimmune lymphoproliferative syndrome, and may be associated with immunodeficiency syndromes, myelodysplastic syndrome, non-Hodgkin lymphoma, or as a side effect of certain medications. In some cases, Evans syndrome can serve as an early sign of the development of myelodysplasia or non-Hodgkin lymphoma years later (Audia et al., 2020; Muley et al., 2023).

Diagnosing ES in pregnancy involves complete blood counts, peripheral smears, and Coombs tests. Although ES often follows a milder clinical course during gestation and improves postpartum, transplacental antibody transfer can cause severe fetal complications, morbidity, or mortality. Given its extreme rarity, incidence data during pregnancy remain highly limited. Management primarily relies on corticosteroids as first-line therapy, alongside intravenous immunoglobulin (IVIG) when thrombocytopenia is prominent or steroid response is inadequate. Second-line immunosuppressants like rituximab, mycophenolate mofetil, and azathioprine require caution due to teratogenicity and limited safety data, while splenectomy is reserved for refractory cases in the second trimester. Delivery mode is guided by obstetric indications rather than ES, avoiding instrumental delivery to minimize bleeding risks. Careful monitoring is essential for maternal complications such as preeclampsia, HELLP syndrome, postpartum hemorrhage, placental abruption, and elevated venous thromboembolism (VTE) risks as well as neonatal screening for antibody-mediated cytopenias. Ultimately, achieving optimal maternal and neonatal outcomes relies heavily on multidisciplinary collaboration among obstetrics, hematology, anesthesia, and neonatology (Fontana et al., 2025; Santosa et al., 2021; Vadlamudi & Keerthy, 2020).

Cases of Evans syndrome during pregnancy are extremely rare, and their treatment is constrained by concerns regarding the teratogenic effects of the medications used. Because Evans syndrome is an exceptionally rare condition, standardized specific therapeutic guidelines for its management during pregnancy do not yet exist. Consequently, case management is typically tailored to individual patient conditions and involves a multidisciplinary team to provide optimal care. Moreover, in pregnancy complicated by autoimmune hemolytic anemia (AIHA) which forms part of Evans syndrome immune thrombocytopenic purpura (ITP) may develop postpartum, necessitating

long-term patient monitoring. The primary complication of ITP in pregnancy is the risk of fetal thrombocytopenia, which can lead to intracranial hemorrhage, albeit with low frequency. Due to limited data and existing guidelines, case series concerning Evans syndrome in pregnancy are compiled to aggregate clinical experience and therapeutic outcomes, which are expected to assist in the development of future treatment guidelines.

METHODS

Evans syndrome is an autoimmune disorder characterized by the combination of autoimmune hemolytic anemia and immune thrombocytopenia, which can lead to serious complications, particularly during pregnancy. Although cases of Evans syndrome in pregnancy are rare, a thorough understanding of its clinical manifestations, diagnosis, and management is crucial for optimizing maternal and perinatal outcomes. Therefore, we conducted a systematic review of the available literature by searching electronic databases such as PubMed, EMBASE, the Cochrane Library, and Google Scholar up to the end of 2018. The search was performed using keywords related to Evans syndrome in pregnancy and other hematological autoimmune conditions (ITP, AIHA, or AIN), supplemented by manual searches of recent review articles and reference lists.

1. Case 1

A 23-year-old pregnant woman was diagnosed with Evans syndrome (ES) at 38 weeks of gestation. In this case, the patient presented in active labor with spontaneous rupture of membranes and blood-tinged vaginal discharge. She had a history of easy bruising and one episode of epistaxis two weeks prior, with no known prior medical history. Initial laboratory evaluations were pending when an epidural was placed for pain control. After delivering a healthy baby boy via spontaneous vaginal delivery, laboratory results revealed severe anemia (hemoglobin 5.6 g/dL) and thrombocytopenia (platelets <10,000/μL). Peripheral blood smears and a positive direct antiglobulin test (DAT) confirmed warm autoantibodies consistent with Evans syndrome. The clinical course involved management with immunosuppressive therapy, including steroids and rituximab. The patient experienced postpartum complications, including COVID-19 infection and acute pulmonary embolism, highlighting the elevated risks of infection and venous thromboembolism (VTE) associated with Evans syndrome and its treatment. The use of epidural anesthesia in this 23-year-old G2P1001 patient at 38 weeks of gestation was appropriate for controlling labor pain, particularly given her advanced cervical dilation (8 cm) and anticipated rapid delivery. The epidural catheter was removed postpartum when repeat laboratory testing demonstrated severe thrombocytopenia (<10K/μL), as low platelet counts increase the risk of epidural hematoma and neurological complications (Vadlamudi & Keerthy, 2020).

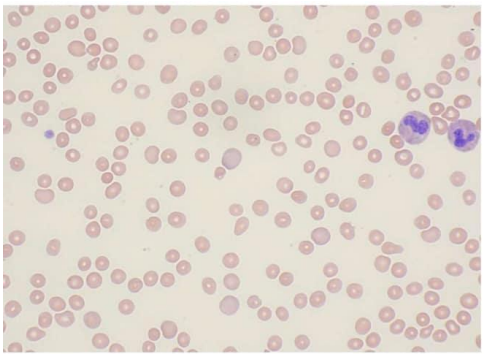


Figure 1. Peripheral blood smear showing microcytic hypochromic anemia, anisocytosis, and polychromasia, accompanied by thrombocytopenia and mild leukocytosis. Teardrop cells, reticulocytes, and small spherocytes are present, with no schistocytes, cell fragmenta

2. Case 2

In early February 2023, a 32-year-old woman was hospitalized at a local facility due to severe anemia (hemoglobin 7.9 g/dL) and moderate thrombocytopenia (platelet count 56,000/mm^3) at 6 weeks and 5 days of gestation. Her medical history revealed a diagnosis of juvenile-onset systemic lupus erythematosus (SLE) since the age of 14, with evidence of autoimmune hemolytic anemia (AIHA) and immune

thrombocytopenia (ITP) subsequently diagnosed as Evans syndrome (ES). During hospitalization, she received combination therapy comprising corticosteroids, cyclosporine A (CyA), intravenous immunoglobulin (IVIG), and rituximab (RTX) due to a partial response to initial treatment. Pregnancy was closely monitored through fetal evaluations, which demonstrated normal development until the third trimester, despite a thrombocytopenia flare and intrauterine growth restriction (IUGR) at 34 weeks of gestation. The patient underwent an elective cesarean section at 34 weeks and 6 days, delivering a premature female infant with low birth weight who remained stable following neonatal intensive care. Postpartum, the mother's condition improved with the normalization of platelet and hemoglobin levels, and treatment was maintained with hydroxychloroquine and CyA. The infant also developed well and received routine immunizations on schedule (Fontana et al., 2025).

3. Case 3

A 29-year-old Indonesian woman was admitted to Dr. Kariadi General Hospital with a confirmed 5-day history of COVID-19. She was a gravida 2, para 1, abortus 0 (G2P1A0) at 39 weeks of gestation, presenting with complaints of gross hematuria, dry cough, fever, shortness of breath, nausea, anosmia, and fatigue. She was a housewife with no prior medical history or complications during her first pregnancy and had consistently attended antenatal care. There was no family history of hematological disorders, and no signs of labor were present. Upon admission, she was fully conscious with stable vital signs, an oxygen saturation of 100% on a 2 L/min nasal cannula, and an estimated fetal weight of 4,000 g with a fetal heart rate of 142 bpm and no signs of fetal distress. Supportive investigations revealed bilateral bronchopneumonia on chest radiography, mild anemia (hemoglobin 10 g/dL), severe thrombocytopenia 2 x 10^9/L), a neutrophil-to-lymphocyte ratio (NLR) of 11, lymphopenia, as well as 2+ proteinuria, gross hematuria, and pyuria on urinalysis. Spherocyte features on the peripheral blood smear pointed toward an autoimmune hemolytic process.

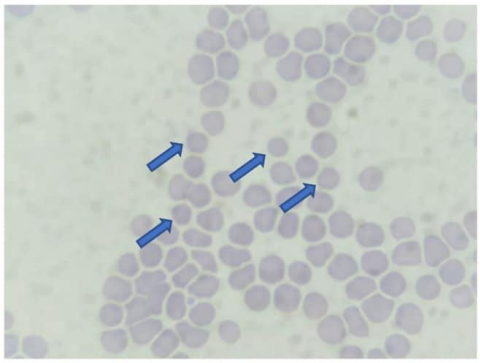


Figure 2. Spherocytes in blood smear

Viral serology markers for HIV, cytomegalovirus (CMV), and hepatitis B and C were negative. Initial therapy included remdesivir, moxifloxacin, dexamethasone, tranexamic acid, N-acetylcysteine (NAC), vitamins C and D3, zinc, and transfusions of platelets and blood concentrates. However, platelet counts continued to decline, and anemia worsened due to ongoing hematuria. On the third hospital day, the patient's condition deteriorated with increasing dyspnea and hematuria, prompting an emergency cesarean section due to gestational maturity and a high risk of bleeding. Postoperatively, the patient developed disseminated intravascular coagulation (DIC) with hematemesis, melena, and hematuria, alongside a significant decrease in hemoglobin and elevated D-dimer levels, requiring admission to the intensive care unit (ICU) for mechanical ventilation. Follow-up examinations revealed a positive direct Coombs test, elevated bilirubin, and serial chest X-rays demonstrating worsening pulmonary edema and bronchopneumonia. Additional therapy comprised convalescent plasma, dexamethasone, eltrombopag, and diuretics. The patient's condition began to improve by the seventh day, but platelet counts and hemoglobin levels remained unchanged, leading to a regimen switch to

methylprednisolone and cyclosporine. By day 13, platelet counts increased dramatically, and the patient stabilized until discharge on day 19 with a platelet count of 45 $x10^9$/L Throughout hospitalization, she received multiple blood and plasma transfusions without any adverse drug reactions. Two months after recovering from COVID-19, her condition was healthy, hemoglobin and platelet levels had returned to normal, and all medications were discontinued. The final diagnosis established was secondary Evans syndrome (Santosa et al., 2021).

4. Case 4

A 23-year-old woman, gravida 2, para 1, with no known medical history, presented at 38 weeks of gestation complaining of spontaneous rupture of membranes, contractions, and blood-tinged vaginal discharge. Upon hospital admission, her vital signs were within normal limits, and cervical examination revealed an 8 cm dilation. Because the patient desired pain relief and a rapid delivery was anticipated, anesthesia was consulted for neuraxial analgesia. Her previous obstetric history showed a normal, uncomplicated delivery at 38 weeks of gestation. Initial laboratory evaluations at that time showed a hemoglobin level of 12.5 g/dL and a platelet count of 223 K/μL. The patient had no prior history of thrombocytopenia; therefore, an epidural was administered before the complete blood count results became available, in accordance with hospital policy. Subsequent laboratory results revealed a hemoglobin level of 7.1 g/dL, a hematocrit of 22.1%, a mean corpuscular volume of 74.7 fL, and a platelet count of <10 K/μL. Upon further clinical inquiry, the patient reported experiencing easy bruising and epistaxis two weeks prior, with no history of heavy menstruation, hemarthrosis, or bleeding gums.

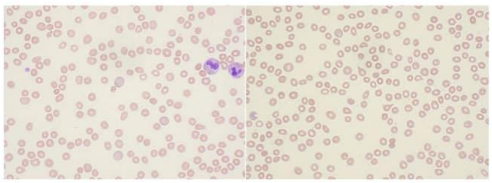


Figure 3. Peripheral blood smear showing microcytic hypochromic anemia with anisocytosis and polychromasia, accompanied by thrombocytopenia and mild leukocytosis, featuring teardrop cells, reticulocytes, and small spherocytes without schistocytes, erythrocyte fragmentation, overt dysplasia, or blast.

Physical examination revealed no pallor, bruising, or organomegaly. Due to concerns regarding hemodilution or laboratory error, blood was redrawn. While awaiting repeat results, the patient delivered a baby boy spontaneously with an estimated blood loss of approximately 400 mL. The epidural catheter was removed immediately after delivery. Repeat laboratory results confirmed severe anemia (hemoglobin 5.6 g/dL, hematocrit 17.7%) and severe thrombocytopenia (<10 K/μL), with no coagulopathy or liver dysfunction, though iron and vitamin B12 deficiencies were noted. The peripheral blood smear showed microcytic anemia with anisocytosis, polychromasia, and thrombocytopenia, without schistocytes or erythrocyte fragmentation. Antibody testing was positive for warm autoantibodies, and the direct antiglobulin test (DAT) was also positive, leading to a diagnosis of Evans syndrome (ES). The patient received red blood cell and platelet transfusions, iron supplementation, and oral dexamethasone. Her platelet count increased to 55 K/μL, and she was discharged with a plan for weekly laboratory monitoring alongside prednisone, folic acid, and vitamin B12 therapy. On day 9 postpartum, her platelet count dropped back to <10 K/μL, prompting a repeat course of dexamethasone with a favorable response. However, on day 18 postpartum, her platelet count decreased again to 16 K/μL, and she received dexamethasone and intravenous immunoglobulin (IVIG). Due to a suboptimal response to steroids, rituximab therapy was initiated. On day 34

postpartum, the patient presented to the emergency department complaining of chest pain and shortness of breath; evaluations revealed an elevated D-dimer level, and a CT scan demonstrated acute pulmonary embolism alongside ground-glass opacities. The patient also tested positive for COVID-19 via PCR, resulting in the temporary postponement of rituximab and the initiation of anticoagulant therapy. During readmission, her platelet count remained stable above 200 K/µL (Vadlamudi et al., 2020).

5. Case 5

In June 2015, a 20-year-old primigravida married for 11 months presented to the Obstetrics & Gynecology outpatient clinic at Nishtar Medical College and Hospital, Multan, with 6 months of gestational amenorrhea. She complained of generalized body weakness for the preceding 3 months, a rash for 2 months, and hematochezia (blood in stool) for four days. Following evaluation, she was diagnosed with Evans syndrome based on low hemoglobin (3.3 g/dL), severe thrombocytopenia (20,000/mm^3), and a positive direct Coombs test. Other laboratory investigations—including antinuclear antibodies, smooth muscle antibodies, antimitochondrial antibodies, serum haptoglobin levels, and rheumatoid factor—were within normal limits. She received vaccinations against Haemophilus influenzae and Streptococcus pneumoniae, alongside transfusions of 4 units of platelets and 3 units of packed red blood cells, which raised her hemoglobin to 8.8 g/dL and platelet count to 69,000/mm^3. The fetus was viable and healthy with a normal anomaly scan. The patient was prescribed high-dose oral prednisolone at 40 mg daily and discharged. One month later, she presented with generalized tonic-clonic seizures, gingival bleeding, and elevated blood pressure, leading to a diagnosis of eclampsia associated with Evans syndrome. Due to deteriorating maternal condition and the risk of poor fetal outcomes, labor was induced with plans for vaginal delivery. She delivered stillborn diamniotic male twins approximately 6–7 hours post-induction, without significant primary postpartum hemorrhage. Postpartum, despite maintaining prednisolone therapy, her platelet count dropped back to 20,000/mm^3 on the fifth postpartum day. A splenectomy was planned, and she was referred to the surgical department. Following a successful splenectomy, the patient was lost to follow-up (Parveen et al., 2019).

6. Case 6

A 35-year-old woman who conceived via intracytoplasmic sperm injection (ICSI) presented to the hospital at 9 weeks of gestation. Her previous obstetric history was unremarkable, with one uncomplicated delivery. She had a history of asthma and had only taken cephem antibiotics during the ICSI procedure for infection prophylaxis. Initial blood tests confirmed she was RhD-positive, with no irregular antibodies and a hemoglobin level of 14.4 g/dL. At 28 weeks of gestation, acute macrocytic anemia was detected, with a hemoglobin level of 7.9 g/dL, mean corpuscular volume (MCV) of 108.1 fL, and mean corpuscular hemoglobin (MCH) of 35.3 pg. Further evaluations ruled out HELLP syndrome, hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), and systemic lupus erythematosus (SLE). Signs of hemolysis—including elevated reticulocytes, elevated lactate dehydrogenase (LDH), and decreased haptoglobin—were evident, and the direct antiglobulin test (DAT) was positive for IgG, establishing a diagnosis of warm autoimmune hemolytic anemia (warm AIHA). She received iron supplementation, and her hemoglobin level improved to 10.1 g/dL at 31 weeks of gestation. Fetal ultrasound monitoring demonstrated normal development until spontaneous delivery at 40 + 1 weeks, resulting in a healthy female infant. Postpartum, the DAT remained positive, and on day 203, severe thrombocytopenia

(8,000/µL) was detected, leading to hospital admission and a diagnosis of primary immune thrombocytopenia (ITP) which, alongside AIHA, indicated Evans syndrome. Corticosteroid therapy successfully elevated her platelet count, and following treatment, her condition stabilized with normal hemoglobin and platelet levels up to one year post-treatment completion (Suzuki et al., 2019).

RESULT AND DISCUSSION

During a healthy pregnancy, platelet counts gradually decrease as gestation advances due to physiological changes such as hemodilution, increased platelet consumption, and heightened platelet aggregation, dropping from an average of about 250,000/µL in the first trimester to around 225,000/µL near term, though this reduction is considered normal and most women remain within the reference range of 140,000–440,000/µL. However, in pregnancies complicated by Autoimmune Hemolytic Anemia (AIHA), the risk of life-threatening severe anemia reaches 40–50%, with a 35–40% probability of fetal demise or severe postpartum hemolytic anemia in infants. Common complications of autoimmune thrombocytopenia include maternal and fetal hemorrhages due to low platelet counts, alongside frequent antenatal complications such as preeclampsia and intrauterine growth restriction (IUGR) at approximately 25% each, oligohidramnion at around 50%, and intrauterine death in 25% of cases. Fetuses are also at risk of anemia and mortality from transplacental autoimmune antibodies, making fetal anemia monitoring essential, while maternal autoimmune thrombocytopenia can induce neonatal thrombocytopenia with a 1–3% risk of fatal or neurologically damaging intracranial hemorrhage. Furthermore, postpartum hemorrhage and placental abruption can emerge as serious complications for mothers suffering from AIHA and autoimmune thrombocytopenia (Eslick & McLintock, 2020; Manjula et al., 2019).

Diagnosis of autoimmune hemolytic anemia (AIHA) is based on detecting regenerative hemolytic anemia alongside a positive Direct Antiglobulin Test (DAT) for IgG and/or complement component C3d. Meanwhile, for diagnosing immune thrombocytopenia (ITP), routine detection of anti-platelet antibodies is not recommended due to the low specificity and sensitivity of currently available methods. Other rare manifestations of Evans syndrome include autoimmune neutropenia, which has not been documented in pregnancy likely due to physiological pregnancy-related neutrophilia. In ITP, treatment is typically considered if the platelet count drops below 20,000–30,000/µL, or if significant bleeding occurs or surgical intervention is planned (Fontana et al., 2025).

Hematological therapy during pregnancy is challenging due to the risk of drug teratogenicity, with primary options consisting of steroids with or without intravenous immunoglobulin (IVIG). Evans syndrome (ES) treatment in pregnancy generally begins with high-dose glucocorticoids as first-line therapy due to their efficacy and speed of onset, whereas life-threatening conditions may be managed with pulse methylprednisolone up to 15 mg/kg/day for 3 days. Although glucocorticoids are generally considered safe during pregnancy, high doses increase maternal risks of gestational diabetes, hypertension, preeclampsia, and osteoporosis, as well as fetal growth restriction and preterm birth if administered in the third trimester, alongside potential long-term intrauterine effects on brain development, endocrine dysregulation, and cognitive or behavioral functions. Prednisone is the most frequently used corticosteroid due to relatively low transplacental fetal exposure, with initial doses typically ranging from 0.25–1 mg/kg/hari (current trends favoring 0.25–0.5 mg/kg/day to minimize maternal side effects like hypertension, gestational diabetes, insomnia, mood changes, and infection risks). Response time to prednisone is

usually 3–14 days with a 35–70% response rate in pregnancy (lower than in non-pregnant populations), and once achieved, the dose should be tapered gradually to the lowest effective level. Meanwhile, intravenous immunoglobulin (IVIG) is effective for managing thrombocytopenia in ES but not recommended for ES-associated anemia, working by inhibiting platelet phagocytosis and lowering transplacental autoimmune antibody transmission to reduce maternal IgG in fetal circulation. IVIG is typically administered as a first-line agent either alone or combined with corticosteroids—when a rapid platelet increase is needed (e.g., near delivery) at a common dose of 0.4 g/kg/day for 5 days or 1 g/kg/day for 1–2 days, yielding a response within 1–3 days and a 40–80% success rate, though potential side effects include headache, fluid overload, hypertension, hemolysis, and transient platelet responses requiring repetition every 2–4 weeks. Because there is no significant difference in platelet efficacy between IVIG and corticosteroids in pregnancy, treatment choices are based on side effects, cost, urgency, and clinical preference, with combination therapy considered in refractory cases despite increased side effect risks, and first-line therapy generally initiated if platelets fall below 10,000/μL at any time, below 30,000/μL in the second or third trimester, or in the presence of bleeding, while high-dose dexamethasone is avoided during pregnancy due to fetal risks (Eslick & McLintock, 2020; Fontana et al., 2025; Jaime-Pérez et al., 2018; Manjula et al., 2019).

At 28 weeks of gestation, a case presented with laboratory findings including a positive Direct Antiglobulin Test (DAT), low haptoglobin levels, and anemia, though the patient required no corticosteroid treatment during pregnancy as her hemoglobin levels recovered spontaneously, followed by long-term postpartum monitoring that ultimately detected immune thrombocytopenia (ITP) on day 203 postpartum, prompting authors to emphasize the critical need for extended postpartum surveillance following a diagnosis of autoimmune hemolytic anemia (AIHA) during pregnancy since ITP can develop later, as successfully managed here with an initial 3-day course of 500 mg intravenous methylprednisolone upon hospitalization (which raised platelets to 88,000/μL), subsequent oral prednisolone (60 mg) when counts dropped post-steroid cessation, and gradual tapering to 0 mg, resulting in normal hemoglobin and platelet ranges one year later. Meanwhile, blood transfusions are utilized to correct cytopenias in specific cases—packed red blood cells being administered for AIHA associated with Evans syndrome (ES) when necessary, while platelet transfusions are typically reserved for life-threatening bleeding conditions given alongside immunomodulatory drugs, though they lack consistent efficacy and carry risks of serious transfusion reactions. For resistant cases or persistent hemorrhage, rituximab serves as a primary option, alongside alternative therapies such as splenectomy, thrombopoietin receptor agonists (though romiplostim and eltrombopag have very limited safety data in pregnancy and are not routinely recommended), and hematopoietic stem cell transplantation (Angelopoulos et al., 2021; Suzuki et al., 2019; Yacoub et al., 2025).

Immunosuppressive agents such as azathioprine and cyclosporine can be used in refractory ITP particularly during the first and second trimesters—despite their slow response and notable side effects, while anti-RhD immunoglobulin may also be utilized in Rhesus-positive mothers though its use remains limited by risks of hemolysis and anemia. Although frequently used in non-pregnant populations, rituximab has been reported as safe in several pregnancy cases despite its potential to cause neonatal lymphopenia, whereas splenectomy serves as a last resort for refractory patients—ideally performed laparoscopically after the second trimester to eliminate antibody production sources and sequestration,

albeit carrying risks of obstetric and perioperative complications as well as less optimal long-term remission compared to standard ITP. Additionally, adjunctive therapies such as plasmapheresis (which replaces antibody-bound platelets and red blood cells without altering IgG concentration) and chemotherapy are employed in severe cases. For instance, as illustrated in Case 5, a pregnant patient who initially responded well to high-dose corticosteroids experienced a drastic platelet drop to 20,000/mm³ postpartum despite ongoing steroid therapy, ultimately requiring a successful splenectomy (Eslick & McLintock, 2020; Jaime-Pérez et al., 2018; Navakumar, 2022; Parveen et al., 2019)

In late 2019, a novel viremic disease emerged in China and rapidly spread worldwide, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a coronavirus family member presenting with flu-like symptoms and a high affinity for the human respiratory tractwhose infections can impair proper immune responses and trigger severe immune-inflammatory reactions like cytokine storms and autoimmunity, notably linked to rare autoimmune disorders such as Evans syndrome (ES), which is characterized by autoimmune cytopenia in at least two blood cell lines (including autoimmune hemolytic anemia and immune thrombocytopenia) driven by immune dysregulation. In clinical practice, this intersection is exemplified by cases such as a 23-year-old pregnant woman presenting with severe anemia and thrombocytopenia during active labor who was diagnosed with ES via a positive Direct Antiglobulin Test, subsequently experiencing postpartum COVID-19 and acute pulmonary embolism that heightened management complexity. While immunosuppressive therapies like steroids and rituximab carry risks of respiratory infections and warm AIHA elevates venous thromboembolism (VTE) risks further compounded by IVIG, pregnancy, and the postpartum state combination therapy using steroids and intravenous immunoglobulin remains an effective first-line approach for managing ES in pregnancy, achieving favorable outcomes when administered alongside precise multidisciplinary monitoring (Fazeli et al., 2022; Vadlamudi et al., 2020).

In Case 2, initial oral prednisone (1 mg/kg/day) yielded only a partial response, prompting the addition of cyclosporine A, intravenous immunoglobulin (IVIG), and rituximab (RTX) chosen for its efficacy in refractory AIHA and ITP despite guidelines recommending cessation six months pre-conception which successfully controlled the disease without teratogenic effects or neonatal lymphocyte abnormalities, though complicated by a maternal sepsis episode successfully treated with antibiotics (Fontana et al., 2025; Gall et al., 2010).

In Case 3, a term pregnant woman developed secondary Evans syndrome triggered by severe COVID-19 infection, resulting in worsened maternal condition that required emergency delivery despite low platelet counts. Characterized by immune dysregulation such as reduced regulatory T cells and CD8+ T cell activation—the condition was successfully managed with a combination of glucocorticoids, thrombopoietin receptor agonists, and cyclosporine, ultimately achieving hematological recovery alongside the resolution of COVID-19 symptoms (Santosa et al., 2021).

In Case 4, a 23-year-old multigravida presenting in active labor with severe anemia and thrombocytopenia was diagnosed with Evans syndrome and initiated on immunosuppressive therapy for persistent ITP, receiving initial management consisting of oral dexamethasone (40 mg daily for four days), packed red blood cells, and platelets, while planned rituximab infusions were postponed until several weeks postpartum due to active COVID-19 infection and stable platelet counts (Vadlamudi et al., 2020).

Managing Evans syndrome in pregnant COVID-19 patients presents

unique challenges due to overlapping immune dysfunction, requiring cautious first-line therapy with corticosteroids and intravenous immunoglobulin (IVIG) alongside meticulous laboratory monitoring. While secondary ES often shows better treatment responsiveness, refractory cases may require second- and third-line agents—such as rituximab or immunosuppressants—though their use demands careful risk-benefit evaluation due to heightened infection and thrombosis risks. Ultimately, successful maternal and fetal outcomes rely on early recognition, supportive care, and a coordinated multidisciplinary approach (Santosa et al., 2021; Vadlamudi et al., 2020; Yacoub et al., 2025).

During pregnancy, no reliable parameters exist to definitively predict fetal platelet status or pregnancy outcomes, as maternal treatment response does not guarantee desired results, leaving a patient's prior neonatal history as the sole predictive parameter. In such cases, platelet antibody levels must be measured because these maternal antibodies can cross the placenta and bind to fetal platelets, potentially causing fetal thrombocytopenia (Navakumar, 2022).

SUMMARY

Evans syndrome in pregnancy is an extremely rare and complex autoimmune condition characterized by a combination of autoimmune hemolytic anemia and immune thrombocytopenia, which may be accompanied by neutropenia. This condition can potentially cause serious complications for both mother and fetus, such as hemorrhage, severe anemia, thromboembolism, and the risk of perinatal morbidity and mortality. Diagnosis requires complete blood counts and Coombs tests, while primary management involves administering corticosteroids as first-line therapy, with additional IVIG and second-line therapies for refractory cases, which must be performed cautiously given the risks to the fetus. Obstetric management must be individualized based on obstetric indications, supported by multidisciplinary monitoring to optimize maternal and infant outcomes. Due to its very low incidence and limited data, there are no standard treatment guidelines, so management is tailored to the patient's condition and clinical experience, highlighting the importance of case reports for the development of future guidelines.

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