Case Report

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# Aplastic anemia in pregnancy

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**Abstract:**

Aplastic anemia (AA) is a rare hematological disorder which is life-threatening in pregnancy. It is mainly caused by the destruction of pluripotent stem cells of bone marrow. There is high risk in pregnancy due to risk of hemorrhage and infection due to pancytopenia. Fetus is also at high risk of intrauterine growth restriction, risk of intrauterine death, and preterm labor. Hence, managing aplastic anemia in pregnancy is a great challenge for obstetricians. It requires a multidisciplinary approach involving hematologist, obstetrician, and critical care specialist for the management of AA in pregnancy. We report a case of AA with pregnancy diagnosed during first trimester.

**Keywords:**

Anemia, aplastic anemia, pancytopenia, pregnancy, thrombocytopenia

## Introduction

Aplastic anemia (AA) is a rare hematological disorder, which is caused by the destruction of pluripotent stem cells of bone marrow, with an incidence of 1–2 cases per million per year.[1] This entity was recognized during pregnancy by Ehrlich in 1888, and since then its pathogenesis has remained illusive.[2] There have been some observations made that due to increase in synthesis of placental lactogen, erythropoietin, and estrogen during pregnancy, an imbalance occurs between these three hormones, which leads to hypoplasia of bone marrow.[3] Effect of pregnancy on AA is still not clear, but pregnancy with AA is a serious condition, due to risk of hemorrhage and infection. There is no direct effect of AA on fetus, but fetal complications such as intrauterine growth restriction, risk of intrauterine death, and preterm labor are due to maternal anemia.[1] There are anecdotal reports in the literature regarding fetal thrombocytopenia, placental anomaly, and severe oligohydramnios.[1] We report a case of AA with pregnancy diagnosed during first trimester.

## Case Report

A 24-year gravida 2 para 1 live 0 women, 8 weeks 6-day period of gestation came for routine antenatal checkup. She had got complete blood count showing hemoglobin (Hb) 8.5 gm%, total leukocyte count (TLC) 4500/cumm, and platelet count 20,000/cumm. There was a history of easy fatiguability, weakness off, and on palpitations on exertion (NYHA I). She gave a history of previous preterm vaginal delivery, 2 years back, of male stillborn fetus weighing 1.6 kg. She had received repeated blood transfusions during her last pregnancy. Total of 30 packed cell (PC) and 26 platelet-rich plasma (PRP) were transfused. Postdelivery, there was doubtful history of loss of consciousness, for 3–4 days for which she remained hospitalized for 1 month. Bone marrow aspiration was done in postnatal period which was suggestive of decreased blood cell lines (amegakaryocytic thrombocytopenia). Chromosomal analysis showed karyotype 46 XX with no significant structural aberrations. Tablet cyclosporine 100 mg twice a day was started postdelivery which she took and stopped on her own after 6–7 months. There has been no episode of bleeding or blood transfusions since then.

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During her current pregnancy, an opinion from hematology was obtained, and she was investigated. The reports were as follows; Hb 8.9 gm%, TLC 4840/cu mm, ANC 2370/cu mm, platelet count 28,000/cu mm, reticulocyte count 2.37%, MCV 107.4 fl, peripheral smear normocytic normochromic, macrocytic, Vitamin B12 257 pg/ml, and ferritin 233 ng/ml. Liver function tests, renal function tests, LDH, viral markers, test for paroxysmal nocturnal hemoglobinuria, and stress cytogenetics were normal. Bone marrow biopsy showed 15% to 20% cellularity, erythroid myeloid ratio 1:1, with erythroid predominance, and no megakaryocyte. All her other routine antenatal investigations were normal. Tablet folic acid 400 micrograms once a day, Vitamin B12, and tablet cyclosporine 100 mg twice daily were started. Regular ANC checkup was done monthly. In first trimester, dual marker test and ultrasound for nasal bone and nuchal translucency were done, which were normal. She was told not to take iron tablets in view of normal ferritin levels. An anomaly scan at 18 weeks ruled out any gross congenital anomalies. She continued to follow up in the hematology outpatient department and came for regular antenatal checkups.

At 20-week period of gestation, she had an episode of gum bleeding. On investigation, her Hb was 8.2 gm% and platelet count – 15,000/cumm. Four units of PRP was transfused.

At 30 weeks, 2 days of gestation, she gave a history of bleeding gums 15 days back which lasted for 1 week, but she did not report to the hospital. On investigation, her platelet count was 15,000/cumm, and Hb was 6 g/dl. This time she was transfused 1 unit PC and 2 unit PRP. At 32-week period of gestation, she had a nasal bleed and her platelet count again fell to 15,000/cumm for which she was transfused 4 units PRP. In view of repeated bleeding episodes and need for repeated platelet transfusion, cyclosporine trough levels were done which was below 100. The dose of cyclosporine was changed to 150 mg in the morning and 100 mg at night. The hematologist also advised to start eltrombopag, but it could not be started due to nonavailability of drug at that time in the hospital. PC and single donor platelet were arranged for further consumption if required. Till 37 weeks of gestation, she required total 11 PRP and 4 PC.

At 37 weeks, she went into spontaneous labor and delivered a male baby weighing 2.68 kg with Apgar score of 7, 8. Active management of third stage of labor was done. During the intrapartum period, 1 unit PC and 4 units PRP were transfused. Cord blood was sent for Hb, TLC, and platelet. Postpartum day 2, her Hb was 8.2, TLC-2800/cumm, and platelets were 20,000/cumm.

She was discharged on postpartum day 3 with an advise to continue cyclosporine, folic acid, and Vitamin B12. At follow-up visit at 4 weeks later, her Hb was 6.8, TLC – 3950/cumm, and platelet count was 60,000/cumm. She was counseled regarding contraception and the definitive management of AA.

## Discussion

AA is a diagnosis of exclusion, where in 70%–80% are idiopathic in nature. It is characterized by pancytopenia with hypocellularity in bone marrow in the absence of fibrosis or abnormal cells in the bone marrow.[4] Severity of AA is based on modified Camitta criteria with severe AA is defined as marrow cellularity of <25% plus at least 2 of the following-neutrophils $<0{\cdot}5 \times 10^9$/l, platelets, or reticulocyte count $<20 \times 10^9$/l. Very severe AA has neutrophils $<0{\cdot}2 \times 10^9$/l.[5]

Acquired AA is found to be more common than the hereditary form. It is more prevalent among young adults who have peripheral pancytopenia in the absence of any other hematological diseases.[6] In around 20% of cases of AA, the etiological factor such as drugs, infections specially hepatitis has been enumerated. Pathophysiology of AA is explained by two mechanisms, first is immune-mediated suppression of hematopoietic stem cells and second is abnormality of marrow cell progenitors which prevents them in maturing to normal hematopoietic cells.[6]

Treatment of AA is dependent on number of factors such as age of patient during diagnosis, comorbid conditions, and severity of pancytopenia. The management is either symptomatic or curative. Symptomatic treatment involves transfusion of blood and platelets and controlling and treatment of infections which occur due to pancytopenia. Curative treatment involves bone marrow transplantation or use of immunosuppressive agents. In nonpregnant women, treatment such as antithymocyte globulin (ATG), methylprednisolone, specific colony-stimulating factors, and cyclosporine is preferred.[1,7]

Management of AA in pregnancy is generally symptom-based. In the first reported case of AA with pregnancy, the patient died after delivery due to postpartum hemorrhage.[2] Spontaneous resolution of AA is seen after delivery.[3] Our case was also asymptomatic after first delivery and was also showing recovery after second delivery.

The need for repeated blood transfusion and high risk of infection makes the management of AA quite challenging. Curative treatment for AA is bone marrow transplantation which is contraindicated in pregnancy.[1] In pregnancy, the aim is to keep platelets above $20 \times 10^9$/l with platelet transfusions.[4] Our patient was also

managed with blood transfusions and cyclosporine. Cyclosporine is the first line of management and is considered safe in pregnancy specially in those who need blood transfusions.[8] Cyclosporine can cause preterm delivery and low-birth-weight babies, the patient needs to be counseled regarding this. Such side effects are not found to be associated with ATG but use of ATG during pregnancy is not recommended.[4] If immunosuppressants are used prednisolone, prednisone and hydrocortisone are preferred as it does not cross placenta.[1]

Role of termination of pregnancy in first trimester in patients with AA for maternal benefit is still unclear, with no specific recommendation. Our patient presented to us in first trimester with a doubtful history of AA and was not advised termination. Termination can be considered if a triggering factor such as infection or drug reaction leading to bone marrow suppression is identified and the drug cannot be discontinued due to maternal benefit or pregnancy is causing hindrance to treatment of infection.[1]

Our patient had a vaginal delivery in first pregnancy and again had a spontaneous vaginal delivery in the current pregnancy. According to various studies, vaginal delivery is preferred and cesarean is recommended for obstetric indications only.[4] Our patient was also counseled for contraception such as barrier contraception, long-acting reversible contraception, or permanent contraception which is preferred in patients with AA.[1]

## Conclusion

AA in pregnancy is a life-threatening condition for both mother and baby. It is a challenge to manage such patients in pregnancy as drugs used are toxic to fetus, and curative treatment such as bone marrow transplantation is contraindicated in pregnancy. Supportive treatment such as blood transfusion with a multidisciplinary approach is needed throughout pregnancy.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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