

# Pregnancy Outcome in Bernard-Soulier Syndrome Complicated by Preeclampsia

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## Abstract

This is a case report of Bernard-Soulier syndrome with pregnancy. This syndrome was first described in 1948 and is a rare autosomal recessive disorder characterized by platelet dysfunction. There is mild thrombocytopenia and a failure of platelet adhesion to the vessel wall. Our case report is the 12<sup>th</sup> case in the literature, and the first to be complicated by preeclampsia. Bernard-Soulier syndrome results in considerable morbidity due to haemorrhage and isoimmunization. Preeclampsia complicating the pregnancy, as in our patient, may be a diagnostic dilemma in uninvestigated cases, where low platelets may simulate HELLP syndrome (Hemolysis, Elevated Liver enzymes, Low Platelet count), moreover the two conditions if present together can complicate the situation further. Since there are no clear cut guidelines available for its management we suggest some basic principles for the prevention of complications and management of this syndrome

**Keywords:** Bernard-Soulier syndrome, pregnancy induced hypertension, pregnancy

## Özet

### Bernard-Soulier Sendromu ve Preeklampsi Komplikasyonları Olan Gebelikte Sonuç

Bu çalışma, gebelikte Bernard-Soulier sendromu tanılı olayların tıp literatüründe yayımlanmış raporlarının onikincisidir ve ilk defa preeklampsi komplikasyonu ile birlikte görülmüştür. Bu sendrom, ilk kez 1948'de tanımlanmış seyrek görülen, resesif otozom kalıtmı trombotik yapıda bozukluktan kaynaklanan bir durumdur. Kanda trombotik düzeyinde hafif azalma olup trombotik damar duvarlarına yapışmadığından pıhtılaşma oluşmaz ve bu durum oldukça fazla kanama ve izoimmunizasyona bağlı hastalıkla sonuçlanır. Gebelikte preeklampsi, hastamızda görüldüğü gibi üzerinde araştırma yapılmayan hastada tanısal çelişki oluşturabilir; düşük trombotik sayısı HELLP sendromunu (hemolysis, elevated liver enzymes, low platelet count: hemoliz, yüksek karaciğer enzimleri, düşük trombotik sayısı) anımsatır ve bu iki durum beraberce hastalık olayını daha da komplike hale getirir. Bu durumu kontrol altına alarak çözümlenmek için kesin yöntemler belirlenmemiş olduğundan, komplikasyonların önlenmesi ve sendromun kontrolü için bazı temel yaklaşımlar önerilmiştir.

**Anahtar sözcükler:** Bernard-Soulier sendromu, gebelikte hipertansiyon, gebelik

## Introduction

Bernard-Soulier syndrome, was first described in 1948 and is a rare (1:100 000), autosomal recessive disorder characterized by platelet dysfunction. However an autosomal dominant

form has been reported as well (1). The syndrome is characterized by mild thrombocytopenia and a failure of platelets to undergo selective Von Willebrand factor-dependent platelet interactions where this factor acts as a bridge between the sub-endothelial matrix and platelets (2). This is a result of the abnormalities in the platelet glycoprotein (GP) Ib, IX (CD 42) and V which are necessary for platelet adhesion to the vessel wall (3). Consanguinity is common in families with affected children (4). Laboratory findings include a prolonged bleeding time, unusually large platelets, the clotting factor levels are normal, but platelets fail to aggregate with ristocetin or normal serum. Clinically, patients often present in childhood

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with epistaxis, menorrhagia, spontaneous bruising, or bleeding after minor trauma (5). The differential diagnosis includes May-Hegglin anomaly, variants of Alport's syndrome and Gray platelet syndrome.

Bernard-Soulier syndrome in pregnancy is very rare and only eleven cases have been reported so far (6). Most cases of maternal thrombocytopenia at term are due to gestational thrombocytopenia, which has no impact on either the mother or the fetus unless associated with some other medical or obstetric disorder. Other causes of thrombocytopenia are pre-eclampsia and idiopathic thrombocytopenic purpura (ITP) (7). The aim of presenting this case is to sensitize obstetricians about this rare syndrome which can affect the pregnancy outcome.

### Case Report

A 26-years-old woman, known case of Bernard-Soulier syndrome was seen in the antenatal clinic after spontaneous conception at 5 weeks of gestation. She was diagnosed with Bernard-Soulier syndrome in childhood after repeated episodes of epistaxis and the laboratory investigations confirmed the disease. Since puberty she had experienced severe menorrhagia and was admitted to the ER with shock, twice. She had received multiple blood and platelet transfusions over the years. Two of her siblings also suffered from the same syndrome.

The couple had primary subfertility of three and a half years duration, for which ovulation induction was attempted with clomiphene citrate and human chorionic gonadotrophin. This led to acute abdomen and intraperitoneal bleeding. Her platelet count dropped to 20 000/mm<sup>3</sup> and haemoglobin to 6.2 g/dl. She was managed conservatively by blood and platelet transfusions. She had a history of a similar episode of intraperitoneal bleed two years ago, at the time of ovulation, without any ovulation induction which again had been managed conservatively.

When she first applied to the antenatal clinic, her hemoglobin was 11.1 g/dl, platelet count was 40 000/mm<sup>3</sup> using manual cell count and 23 000/mm<sup>3</sup> by histogram using hematology analyzer. She was found to have no antiplatelet antibodies in her circulation. She was managed conservatively and her first trimester remained uneventful. At 13 weeks she experienced mild bleeding from the gums, which was self-limiting. She was started on oral haematinics and calcium supplementation. Her platelet count was monitored fortnightly which remained unchanged. At 25 weeks of pregnancy she developed moderate pregnancy induced hypertension, her blood pressure ranging from 150/95 mmHg to 160/100 mmHg. She had no proteinuria and she had normal liver function tests. She was started on methyl dopa 250 mg, four times a day and serial ultrasonography was performed to monitor fetal growth. Intrauterine growth restriction was suspected at 35 weeks gestation and at 37 weeks Doppler study showed abnormal uterine and umbilical artery flow parameters. Additionally, while her platelet count were decreasing to a

level of 15 000/mm<sup>3</sup>, 24 h proteinuria had increased to 500 mg. A decision was made to perform an elective caesarean section in view of abnormal Doppler studies, preeclampsia, precious pregnancy and patient's choice.

A male baby weighing 2.5 kg with Apgar score of 8 and 10 at 1 and 5 minutes was delivered. Immediately after the delivery of the fetus, oxytocin infusion was started. The uterus was well contracted, and no untoward bleeding was encountered. The intraoperative blood loss was 500 ml. During and after the surgery one unit of fresh blood and 250 ml of screened single donor platelets (SDP) donated by the husband were transfused. Postoperatively the platelet count rose to 50 000/mm<sup>3</sup>. The oxytocin drip (20 units/L) was continued for 12 h. The patient's vaginal bleeding was within normal limits. Her sutures were removed on the eighth postoperative day and she was discharged on antihypertensive therapy and iron supplementation. At follow up in the postpartum clinic after 6 weeks her blood pressure had returned to normal.

The baby was investigated and the platelet count, morphology and function were found to be normal (platelet count 262 000/mm<sup>3</sup>). Baby was diagnosed with a ventricular septal defect (which closed spontaneously at 9 months) and patent ductus arteriosus, for which he is being followed up. Baby is now two years old and has normal milestones.

### Discussion

This is the first case report of Bernard-Soulier syndrome complicated by preeclampsia and intrauterine growth restriction as per the literature search carried out by the authors. Of the eleven previously reported pregnant patients with Bernard-Soulier syndrome, none was complicated by preeclampsia. There were no guidelines available for managing such pregnancies. The main complications encountered in reported cases were antepartum haemorrhage (8), excessive intraoperative bleeding (9), immediate and delayed postpartum haemorrhage (8,10-13), development of maternal antiplatelet antibodies leading to fetal intracranial haemorrhage (14), and neonatal alloimmune thrombocytopenia (13).

Mode of delivery was vaginal in most of the women (10,11-13), cesarean section being reserved only for obstetric indications (5,8-10), two patients were delivered using both the vaginal and cesarean routes in different pregnancies, with similar outcomes (10). Cesarean hysterectomy was carried out as a prophylactic measure against postpartum hemorrhage, in a woman who had developed antiplatelet antibodies subsequent to multiple platelet transfusions (14). One woman with uncontrollable hemorrhage had postpartum hysterectomy (11).

Intravenous gamaglobulin has been used successfully in preventing neonatal thrombocytopenia (12), while in one isoimmunized woman steroids, intravenous gamaglobulin and plasmapheresis were successfully used (5). If fetal thrombocytopenia is suspected, it is diagnosed and managed using cordocentesis and fetal platelet transfusion (9). Various mo-

dalities of therapy have been used for the control of bleeding. Prophylactic and therapeutic platelet transfusions have been used but the benefit is uncertain, intravenous desmopressin has been shown to decrease the bleeding time, without any clinical benefit (8). Intravenous oxytocin, intramuscular methylergometrine and prostaglandin F2 alpha, have been found useful (9,10,12). Postoperatively, antifibrinolytic tranexamic acid can be helpful (8). Observation up to 6 weeks postpartum is essential as delayed postpartum haemorrhage has been reported.

Preeclampsia complicating the pregnancy, as in our patient, may be a diagnostic dilemma in uninvestigated cases, where low platelets may mimic HELLP syndrome, moreover the two conditions together can complicate the situation further. We suggest that management of this syndrome should involve preventive measures as well as treatment of bleeding episodes. Since these patients need blood transfusions throughout life, Hepatitis B vaccination should be administered early in life. At menarche, hormonal treatment is often necessary to control menorrhagia. Dental hygiene is important in reducing gingival trauma. Iron and folate supplementation may be needed to prevent anemia in pregnancy. Though, most of these women would have been diagnosed during childhood, a bleeding time should always be carried out in addition to other coagulation studies in a woman with history of menorrhagia or any unexplained obstetric bleeding.

The mother may develop antiplatelet antibodies due to either platelet transfusions or fetal platelets traversing the placenta, which can pass into the fetal circulation and cause fetal thrombocytopenia and intracranial haemorrhage. Hence, it is important to detect antiplatelet antibodies during pregnancy in women with Bernard-Soulier syndrome. Meticulous hemostasis must be secured in caesarian sections. Pregnancy should be closely supervised and a diligent watch should be kept for

complications. The judicious and timely use of platelet transfusions and antifibrinolytics can result in a successful pregnancy outcome in a patient with Bernard-Soulier syndrome.

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