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Pregnancy Favism and Severe Hemolytic Anemia in a Patient with Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency: A Case Report

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ABSTRACT

Introduction: Favism is a genetic disease-causing hemolytic anemia in Mexico, primarily due to glucose-6-phosphate dehydrogenase (G6PD) deficiency. Factors triggering favism include infections, pregnancy, certain drugs, and eating beans. The disease is inherited recessively and is more common in men. Diagnosing and managing favism during pregnancy is crucial, as it can lead to severe hemolytic anemia and neonatal jaundice.

Case presentation: A female patient, aged 18, presented with severe anemia and thrombocytopenia during her 20-week pregnancy. During pregnancy, the patient experienced jaundice and anemia at 21.5 weeks of gestation. Despite not presenting evidence of bleeding, transfusions were performed due to critical hemoglobin levels. G6PD deficiency was confirmed at 9 days of hospital admission, indicating severe hemolytic anemia.

Clinical discussion: The hemolytic crisis in a pregnant woman with favism was triggered by pregnancy and repeated infections of candidiasis. Clinical symptoms of hemolysis were confirmed through G6PD and Coombs tests, and blood transfusion was recommended to prevent complications. The patient's hemoglobin was monitored for signs of active intravascular hemolysis, and a folic acid tablet was recommended during the crisis. Post-crisis management involved periodic controls of hemoglobin, hematocrit, lactate dehydrogenase, and bilirubin.

Conclusion: Favism, a prevalent condition in Mexico, should be considered in patients with a family history of hemolytic anemia or compatible symptoms. Early diagnosis and proper management are crucial to prevent complications in the mother and fetus. A multidisciplinary approach, genetic counseling, and medical education are essential for effective management.

ARTICLE DETAILS

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INTRODUCTION

Favism is a genetic disease that presents as a form of hemolytic anemia, triggered mainly by consuming beans (*vicia faba*) in people with glucose-6-phosphate dehydrogenase (G6PD) deficiency. This enzyme is essential for protecting red blood cells from oxidative damage. In individuals with G6PD deficiency, exposure to triggers such

as beans, certain drugs or infections can induce massive hemolysis, leading to severe anemia. (1)

It is inherited recessively linked to the X chromosome. Women develop the disease if they inherit the gene from both parents. The deficiency may not be evident in heterozygous women, but in some cases, they may manifest milder clinical forms of the disease. This hereditary pattern makes favism more common in men. (2)

On the other hand, favism is more prevalent in malaria-endemic regions, such as the Mediterranean, sub-Saharan Africa, and some areas of Asia. G6PD deficiency provides partial protection against malaria, which explains the higher prevalence in these regions. Although favism is uncommon in Mexico, isolated cases are reported, mainly in people with ancestry from areas where the disease is more frequent. (3)

The WHO classifies the deficiency of G6PD variants into five classes considering the percentage of residual enzyme activity, manifestations (Table 1), and biochemical characteristics, more than 200 mutations that produce dG6PD have been described. In Mexico, the most common variant is G6PD-A and G6PD Santamaría representing 82% of the population. (4)

Table 1. WHO classification of G6PD deficiency variants.

Classification	Enzymatic activity	Characteristics
Type I	< 1%	Patients may have spontaneous hemolysis without oxidative stress. It may be associated with severe non-spherocytic chronic hemolytic anemia.
Type II	< 10%	May or may not have severe episodes of acute hemolytic anemia, favism, drug induced.
Type III	10 – 60%	May or may not have moderate to mild episodes of hemolytic anemia, usually asymptomatic
Type IV	60 – 100%	Usually, asymptomatic
Type V	> 100%	One case reported

Factors that trigger favism include infections, pregnancy, certain drugs (such as sulfonamides), and eating beans. These triggers cause oxidative stress in the red blood cells of people with G6PD deficiency, which can lead to accelerated destruction of the red blood cells and a hemolytic crisis. People with this deficiency must avoid these risk factors to prevent serious complications (Table 2). (5)

Table 2. Hemolysis triggers in patients with dG6PD.

Group	**Type**
Food	Beans
Drugs	**Antimalarials with definite risk:** Primaquine Combinations containing Dapsone Pamaquina **Antimalarials with possible risk:** Chloroquine Quinidine Quinine **Other drugs with definite risk:** Methylene blue (methylthionine chloride) Ciprofloxacin Moxifloxacin Nalidihexic acid Niridazole Nitrofurantoin Norfloxacin

	Ofloxacin Sulfamethoxazole/cotrimoxazole Rasburicasa **Other drugs with possible risk:** Acetylsalicylic acid (aspirin) Sulfadiazine Sulfasalazine Sulfonylureas Chloramphenicol Dimercaptosuccinic acid Glibenclamide Mepacrin Vitamin K analogues
Quimical products	Naphthalene
Infections	**Viral:** Hepatitis A and B Cytomegalovirus **Bacteria:** Pneumonia Typhoid fever Rickettsiosis (Tifus).

The diagnosis and management of favism during pregnancy is especially important, as the disease can have consequences for both mother and fetus. During pregnancy, women with G6PD deficiency may develop severe hemolytic anemia, which can affect newborn health, causing neonatal jaundice and other problems. (6)

This article presents a clinical case of favism in a pregnant patient with G6PD deficiency, exploring its management and the clinical implications of the disease during pregnancy.

CLINICAL CASE

A-18 years old, female patient, Mexican, 160 cm tall and 75 kg, no allergies; previous C-section because of fetal macrosomia; anemia and thrombocytopenia without clinical follow-up since the age of 12. History of son with favism diagnosis. Presented to the obstetrics department with a 20-week pregnancy (calculated by last menstrual date), asthenia, dizziness, dyspnea with minimal effort, cough, and rhinorrhea since the seventh week of gestation (Image 1).

Image 1. A patient presented jaundice, accompanied by asthenia, dizziness, dyspnea with minimal effort, cough, and rhinorrhea.

Upon admission, it was decided to carry out laboratory studies, which showed severe anemia with hemoglobin of 5.3 g/dL and hematocrit of 16.8%.An obstetric ultrasound was performed that reported a single live fetus with a heart rate of

136 ppm, fetal biometrics compatible with 21.6 weeks of gestation, estimated weight of 425 grams, normal inserted placenta, and homogeneous amniotic fluid. An abdominal ultrasound was also performed, which reported the liver with regular edges and homogeneous but increased echogenicity, compatible with hepatic steatosis and 11- and 19-mm gallstones.

During pregnancy, the patient presented episodes of jaundice and anemia at 21.5 weeks of gestation, laboratory studies showed hemoglobin of 5.3 g/dL, hematocrit of 16.8%, VGM of 115 fL, HCM of 36.0 pg., and total bilirubin of 1.78 mg/dL, with a predominance of the indirect fraction of 1.35 mg/dL.

Despite not presenting evidence of bleeding, it was decided to transfuse an erythrocyte component, which raised hemoglobin to 7.8 g/dL and hematocrit to 24.6%. However, the suspicion of hemolytic anemia persisted, so a diagnostic panel was performed, including tests for G6PD deficiency and a direct Coombs test, which turned out to be positive, suggesting an active hemolytic process.

During hospitalization, the patient was transfused three times (three erythrocyte components in total during her hospitalization) due to critical hemoglobin levels. Close monitoring was done with hemoglobin and bilirubin controls. At 9 days of hospital admission, G6PD deficiency was confirmed, which explained severe hemolytic anemia, probably precipitated by candidiasis and pregnancy-related oxidative stress.

The patient decided to be discharged voluntarily on the ninth day of hospitalization, so it was suggested that she receive close medical follow-up at prenatal check-ups and report to the obstetric emergency department in case of any alarm; However, the patient returned to the hospital until the end of the third trimester of pregnancy with premature rupture of membranes and repeated candidiasis, new laboratory control studies were conducted which reported: hemoglobin 8.6 g/dL, hematocrit of 26.6%, platelets of 187 mil/uL, leukocytes of 5.5, TP 10.1 sec and INR 0.87.

It was decided to perform a cesarean section due to the lack of cervical conditions for vaginal delivery (Image 2). The newborn, a male at 39 weeks of gestation by Capurro scale, presented a good Apgar (9/9) and a weight appropriate for the gestational age.

Image 2. The multidisciplinary team was present during the C-section, which was performed at 39.3 weeks gestation. The patient had a hemoglobin of 8.6 g/dL before the cesarean section, and the procedure showed minimal bleeding (<50 ml).

During her postoperative period, she was treated with analgesics and intravenous antibiotics. The post-surgical control laboratories revealed a hemoglobin of 8.8 g/dL, hematocrit of 26.8%, and platelets of 186 mil/uL, without evidence of low cardiac output, so no new blood transfusion was performed. The patient showed improvement in her hematological parameters in the postoperative period and was discharged after a favorable evolution with medical follow-up by the gynecology and obstetrics service.

DISCUSSION

Favism, or hemolytic anemia triggered by bean intake, is caused by a deficiency in glucose-6-phosphate dehydrogenase (G6PD), an enzyme vital to protecting red blood cells from oxidative stress. (7)

In individuals with this deficiency, exposure to certain oxidant factors such as infections, some drugs (sulfonamides), or consumption of beans may induce massive hemolysis, which is the most common form of onset, resulting in severe anemia. (8)

In our case, pregnancy and repeated infections of candidiasis were probably the factors that increased oxidative stress and precipitated hemolytic crisis. The inheritance of this disease is linked to the X chromosome, affecting mainly men, although heterozygote women may also have clinical forms of the disease. (9)

Our patient, despite being a woman, had clinical symptoms of hemolysis and a family history compatible with favism. Confirmation of diagnosis was by measuring the enzymatic activity of G6PD and a positive direct Coombs test; this was crucial to establishing appropriate treatment. In addition,

monitoring with biomarkers such as reduced hemoglobin and hematocrit, high reticulocyte levels, elevated lactate dehydrogenase (LDH), and increased unconjugated bilirubin are associated with increased hemolysis. Therefore, to prevent complications in pregnant women during acute hemolytic crises, blood transfusion should be the immediate pre-determined treatment. (10)

Frequent transfusions are evaluated as a function of hemodynamic stability after transfusion of hematin concentrate (15-20 ml/kg). If hemoglobin is <7 g/dl, as in our patient (Hb 5.3 g/dl), blood transfusion is indicated. If hemoglobin is between 7-9 g/dl, blood transfusion should be considered if there are signs of active intravascular hemolysis (such as hemoglobinuria), and if no active hemolysis, clinical control observation should be chosen. (12)

On the other hand, foods, and drugs that could trigger hemolysis in patients with favism were also avoided.

It is recommended to implement a 5 mg/day folic acid tablet during the hemolytic crisis, once passed the hemolytic crisis stage, subsequent management will be with periodic controls of hemoglobin, hematocrit, lactate dehydrogenase (LDH), and bilirubin's, until the resolution of pregnancy; knowing that the most effective strategy is the prevention of hemolysis, as well as constant monitoring with a multidisciplinary team of hematology, obstetrics and neonatology, which in this case allowed a favorable development for both mother and newborn. (13)

An important point to mention is that mothers with favism can breastfeed their babies by avoiding the triggers of hemolysis. In the presence of hemolytic crisis in the mother, unconjugated bilirubin circulating in the plasma is bound to albumin so that passage into breast milk is minimal. The amount of conjugated bilirubin that passes through the newborn is metabolized in the intestine, having little effect on it. (14)

CONCLUSION

Favism during pregnancy, although not a prevalent condition in Mexico, should be considered in patients with a family history of hemolytic anemia or with compatible symptoms such as fatigue, jaundice, and coluria. G6PD deficiency can be triggered by a variety of factors, including infections and certain drugs, making it essential to know and prevent the triggers of hemolysis. Early diagnosis and proper management of this condition are critical to preventing serious complications in the mother and fetus.

This case highlights the importance of a multidisciplinary approach, including genetic counseling and careful obstetric management, especially in populations at risk. Medical education about G6PD deficiency is crucial to improving outcomes in these patients. There is currently no very recent information on the management of Favism in pregnant patients, so our case report could serve as a tool to strengthen the current literature.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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