

LETTER TO EDITOR (VIEWERS CHOICE)

PYRUVATE KINASE DEFICIENCY IN TWIN BABIES

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Pyruvate kinase deficiency (PKD) is the most common enzyme deficiency in the glycolytic pathway causing hemolytic anemia. The prevalence of PKD in non-spherocytic hemolytic anemia and neonatal jaundice is reported to be 6.4% in an Indian study.¹ We present a pair of twins with PKD who presented on day 1 of life with jaundice.

Dichorionic diamniotic male twin babies were born to gravid 3, para 2, abortion 1 mother. They were born by emergency cesarean section at 35 weeks gestation. Parents had consanguineous marriage. The birth weight of first and second twins were 1.9 kg and 1.84 kg respectively. Examination revealed pallor and icterus till thigh in both babies. Systemic examination was normal. Investigations are given in table 1. Peak serum bilirubin was 14.7 mg/dl and 16 mg/dl at 14 hours of life for twin 1 and twin 2 respectively (Table 1). Peripheral smear study showed numerous nucleated red blood cells (RBCs) and spiculated RBCs. Blood group was B positive in both mother and babies. Hemoglobin dropped to 6.2 g/dl in twin 1 and 7.2 g/dl in twin 2 on day 2 of life. Packed red blood cell (PRBC) transfusion was given for both twins. They received phototherapy for 4 days. Targeted gene sequencing revealed a homozygous missense variant in exon 4 of the PKLR gene (chr1:g.155265338T>C) that results in the amino acid substitution of aspartic acid for asparagine at codon 133. On follow up, both infants are receiving blood transfusions regularly and growth parameters are within normal limits.

Pyruvate kinase is the glycolytic enzyme necessary for ATP production.¹ There are 4 isoenzymes namely L, R, M1, and M2 in different tissues encoded by PKLR and PKM genes.² Pyruvate kinase deficiency is inherited in an autosomal recessive manner with clinical manifestation occurring in homozygous and compound heterozygous patients.² Although PK-LR gene abnormalities alters both RBC and liver enzymes, clinical symptoms are confined to erythrocytes as hepatic enzyme deficiency is compensated by persistent enzyme synthesis in liver.³ The ATP depleted erythrocytes have more potassium loss than sodium gain, causing obligate

Table 1. Laboratory parameters of twins at admission

	Twin 1	Twin 2
Hemoglobin (g/dl)	10.2	9.6
Packed Cell Volume	30	28
White blood cell count (cells/cumm)	19,443	15,500
MCV	92	89
MCHC	33	34
Platelet (×10 ⁵ /cu mm)	3.3	3.1
CRP (mg/L)	5	4
Total Serum Bilirubin (mg/dl)	14.7	16

osmotic water loss and cell reduction leading to rigid, spiculated RBCs.⁴ The clinical symptoms of pyruvate kinase deficiency in neonates are unconjugated hyperbilirubinemia and anemia requiring phototherapy and/or exchange transfusion.⁵ Investigation may show reticulocytosis, spiculated erythrocytes (ecchinocytes), negative Coombs test, non-spherocytic anemia, high lactate dehydrogenase (LDH), and unconjugated hyperbilirubinemia.⁴ The diagnosis of PKD is suggested by increased 2,3 diphosphoglycerate levels and confirmed by decreased PK enzyme activity and mutation in PKLR by next generation sequencing (NGS).^{6,7} The homozygous missense variant in exon 4 of the PKLR gene (chr1:g.155265338T>C) results in the amino acid substitution of aspartic acid for asparagine at codon 133 has previously been reported in a homozygous state, in a patient affected with PKD with mild clinical phenotype and this mutation was seen resulted in significantly reduced enzyme activity and had an effect on protein stability. However, in our patients, the above mutation in PKLR resulted in severe neonatal hemolytic anemia. Treatment of PKD is mainly supportive, consists of blood transfusion, splenectomy, and iron chelation therapy.⁸ Splenectomy decreases the transfusion requirement in patients with severe anemia.⁹ Bone marrow transplantation improves the survival rate if done at an age of less than 10 years.¹⁰

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Compliance with Ethical Standards

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