

Genetic factors contributing to development of neonatal jaundice

Jaundice

Icterus, neonatal jaundice has long been recognized. In early 19th century, the term Kernicterus was introduced, referring to the yellow colour development of basal ganglia in neonates, who died of jaundice. Due to high incidence of Kernicterus and Rh haemolytic diseases scientists focus on treatment of jaundice.¹

Neonatal jaundice

In neonates pale colour of stools and urine are appearance of liver disease that should be investigated urgently.² Neonatal jaundice is a common heterogeneous condition that usually resolves after 2 weeks of birth known as jaundice or icterus.³ If it is icterus of conjugated type, than it will last beyond two weeks time. When total serum bilirubin is less than 5mg/dL and conjugated serum bilirubin is higher than 1mg/dL than it is considered abnormal. Mutations in the regulatory region and exon of the gene encoding UDP-glucuronosyltransferase 1A1 (*UGT1A1*) enzyme leads to 30-70% decrease in the activity of enzyme. Enzyme is responsible for conjugation of bilirubin, and mutations in its gene are responsible for structural and functional defects.³ Previous studies showed that in patients showing iatrogenic factors such as glucose-6-phosphate dehydrogenase deficiency, hereditary spherocytosis, thalassemia or ABO incompatibility have homozygous polymorphism in the promoter region and homozygous or heterozygous mutations in exon1 of the *UGT1A1* gene in Asians.⁵⁻⁷

Hereditary predominantly unconjugated hyperbilirubinemia

Inside endoplasmic reticulum bilirubin conjugation is catalysed by *UGT1A1* enzyme. When mutations in the gene occur, it leads to disruption in the expression of the gene, which in turn lead to complete or partial inactivation of enzyme. Phenobarbital (PB) administration increases the expression of *UGT1A1* gene. PB response activity is delineated to a 290-bp distal enhancer module sequence (-3483/-3194) glucuronosyltransferase phenobarbital response enhancing motif (gtPBREM) of the human *UGT1A1*. Human constitutive active receptor (hCAR), a nuclear orphan receptor is involved in activation of (gtPBREM). PB treatment results into translocation of cytoplasmic receptors like CAR into the nucleus; it binds to retinoid X receptor and forms a heterodimer, which leads to activation of PB response enhancer element.⁸ *UGT1A1* activity at different levels is found in three different types of inherited predominantly unconjugated bilirubinemia namely Criglar-Najjar syndrome type I (CN I), type II and Gilbert syndrome.

Hereditary predominantly conjugated hyperbilirubinemia

Bilirubin chemically bound to a glucuronide in the liver, which is excreted in bile by the liver and stored in the gallbladder or transferred to the duodenum. Dubin Johnson and Rotor syndrome are the two known types of hereditary conjugated jaundice. Patients suffering from both diseases are characterized by the presence of >50% bilirubin in conjugated form.⁹

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Conflict of Interest

The author declares no conflict of interest.

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