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LETTER TO THE EDITOR

G71R mutation of the UGT1A1 gene is not associated with neonatal hyperbilirubinemia in India

To the Editor,

We read with interest the report entitled "Neonatal hyperbilirubinemia and G71R mutation of the UGT1A1 gene in Turkish patients" by Narter et al. [1]. We have also been studying the genetic risk factors of neonatal hyperbilirubinemia in western India. One of our interest was to look for the G71R mutation and its association with neonatal hyperbilirubinemia. As against the 39 infants with hyperbilirubinemia studied by Narter et al. [1], we enrolled 126 neonates (≥35 weeks of gestation) who developed peak serum total bilirubin (STB) levels of >15 mg/dl in the first 5 days of life as hyperbilirubinemia cases. Along with this, 180 babies who did not develop clinical jaundice or had peak STB of <15 mg/dl and had not received phototherapy or exchange transfusion were enrolled as controls. Of the 126 babies in the hyperbilirubinemic group, 50 (39.7%) were treated with phototherapy and 2 (1.5%) underwent exchange transfusion. All the mothers were healthy during pregnancy and did not receive any oxytocic drugs during delivery. These infants had no risk factors for hyperbilirubinemia such as neonatal asphyxia, ABO blood group incompatibility, haemolytic anaemia, dehydration, vomiting, polycythemia, hypoglycemia, infection, liver dysfunction and G6PD deficiency. Serum bilirubin levels were measured on an automated biochemistry analyzer (Cobas 111, Roche). DNA samples of these neonates were analysed for the G71R mutation by the PCR–RFLP method [2]. A summary of our findings is presented in Table I.

Our findings also showed that the G71R mutation is not uncommon and it's presence in the heterozygous condition was observed in 20.6% and 21.7% of neonates with and without hyperbilirubinemia, respectively. This mutation neither influenced the severity of hyperbilirubinemia nor the requirement of phototherapy. The mutant allele frequency did not differ significantly between the two groups and was significantly lower than in the Turkish patients [1] (10.4% vs. 24.3%). Unlike in their cohort, none of our patients were homozygous for the mutant allele and this could be due to the lower frequency of this allele (7.7%) in healthy Indian populations (unpublished data).

Table I. Genotypic and allelic distribution of G71R mutation in the neonatal hyperbilirubinemia and nonhyperbilirubinemia groups.

	Cases ($n = 126$)	Controls ($n = 180$)
Genotypes		
G/G	100 (79.4%)	141 (78.3%)
G/A	26 (20.6%)	39 (21.7%)
A/A	0 (0.0%)	0 (0.0%)
Alleles		
G	226 (89.6%)	321 (89.2%)
A	26 (10.4%)	39 (10.8%)

It has been reported that the high frequency of the Gly71Arg mutation of the UGT1A1 gene is associated with a high incidence of neonatal hyperbilirubinemia in Japanese, Korean and Chinese populations [3]. Contrary to these findings, our data as well as the study of Narter et al. [1] did not find any significant effect of the G71R mutation on unconjugated bilirubin levels among the newborns. Narter et al. [1] have not looked into the influence of the TA insertion in the TATA box of the promoter region in the UGT1A1 gene on the development and severity of hyperbilirubinemia, whereas we found that the G71R mutation along with the TA insertion (either in TA6/7 or TA7/7) had a significant effect on unconjugated bilirubin levels and the severity of neonatal hyperbilirubinemia in our patients (data not shown). This finding is in agreement with those reported among the Japanese neonates [4] but discordant with the results on Gilbert's syndrome patients from the eastern part of India [5]. On the other hand, a complete absence of this mutation was observed among the neonates with or without hyperbilirubinemia from north India [6]. Thus, our study indicates that the development of hyperbilirubinemia among our neonates was influenced by the TA insertion rather than the G71R mutation of the UGT1A1 gene.

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