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Letter to the Editor

211 G to A variation of *UGT1A1* and severe neonatal hyperbilirubinemia

To the Editor,

We read with great interest the article by Yang et al.[1] that reported that *UGT1A1* variation, Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency, and thalassemia may contribute to severe neonatal hyperbilirubinemia in southern China. Although this is an interesting and important finding that may have clinical implications, this study has some limitations, and we would like to make some comments on this article.

Neonatal hyperbilirubinemia is common in Asian populations. The incidence and severity of neonatal hyperbilirubinemia are much higher in full-term Asian and American Indian neonates compared to those in Caucasian and black populations. If hazardous levels of bilirubin develop, accumulation of bilirubin in certain brain regions may result in irreversible damage.

UGT1A1 variation, including promoter TATA box variation and coding region 211 G to A (Gly71Arg) variation, has been shown to be associated with an increased incidence and severity of neonatal hyperbilirubinemia.[2] In the present study,[1] Yang et al. demonstrated that coding region 211 G to A was the most frequent *UGT1A1* variant, and they also confirmed the strong association between this common variant and severe hyperbilirubinemia in their study cohort. These data fully support our previous finding. We found that both heterozygous and homozygous coding region 211 G to A variations in the *UGT1A1* gene were the independent risk factor for developing early-onset neonatal hyperbilirubinemia.[3]

Interestingly, Yang et al. found that there were more heterozygotes of the (TA)7 repeat variant in the control group. This finding is in contrast to previous reports in Caucasian population.[2] However, it is consistent with our previous finding in Taiwan and also in Japan. This indicates that the promoter TATA box variation in the *UGT1A1* gene may not contribute, and may even have a protective effect, to neonatal hyperbilirubinemia in Asian population.

However, in this study, there were no data providing how many neonates with the *UGT1A1* variation were breastfeeding or fed with infant formula. We had previously found that neonates carrying the 211 G to A variation of the *UGT1A1* gene were susceptible to breastfeeding jaundice. Furthermore, a statistically significant dose effect for 211 G to A variation of the *UGT1A1* gene was found on both the peak bilirubin level and the incidence of hyperbilirubinemia among exclusive breastfeeding babies. In addition, we also demonstrated that neonates carrying a homozygous 211 G to A variation of the *UGT1A1* gene with a maximal body weight loss of $>$7.33% had a higher relative risk of developing neonatal hyperbilirubinemia.[3] Thus, body weight loss may be another confounding factor that may affect the severity of hyperbilirubinemia in neonates with *UGT1A1* mutation.

In conclusion, screening the *UGT1A1* coding region 211 G to A variation, instead of the promoter TATA box variation, could be taken into consideration to identify the risk group who tend to be suffering from severe neonatal hyperbilirubinemia in Asian populations.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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