Author’s response to reviews

Title: Umbilical cord bilirubin as a predictor of neonatal jaundice: a retrospective cohort study

Authors:

Kelsey Jones (kelseyjones@gmail.com)

Sophie Grossman (sophie.grossman8@gmail.com)

Dharshini Kumaranayakam (dharshinikumar@hotmail.com)

Arati Rao (aratirao@nhs.net)

Greg Fegan (g.w.fegan@swansea.ac.uk)

Narendra Aladangady (narendra.aladangady@homerton.nhs.uk)

Version: 1 Date: 19 Jun 2017

Author’s response to reviews:

We are grateful for the reviewers’ comments, which are addressed below:

> = Reviewer comment

>> = Our response

Reviewer 1:

> I found this article to be well written, easy to read and the information to be potentially useful in helping predict which infants among those who were a setup for developing significant jaundice. Even in centers not currently doing aUCB, this study raises the likelihood that doing it in O mothers could prevent missing clinically significant jaundice. I wondered if the authors looked Rh set-ups separately from the group as a whole and if that might also be helpful information.

>> Thank-you for this comment. Dichotomising the data on the basis of Rhesus status does not influence the predictive capacity of arterial umbilical cord bilirubin for all-cause jaundice. The area under the ROC curve for Rh +ve is 0.765, and for Rh -ve is 0.753. This reflects the fact that ABO incompatibility is a far more common cause of neonatal jaundice than Rhesus incompatibility in our setting.
Limitations were addressed. I would change the word untypical on page 13 Line 14 to atypical.

Thank-you, we have reorganised the paragraph in light of Reviewer 2’s comments and now say (page 13, line 12): “The study presents data from a single centre that is atypical compared to the wider UK population, serving an economically deprived and unusually ethnically diverse catchment area.”

Reviewer 2:

Diagnostic performance of a test needs to be studied in perspective of prior probability of the diagnosis, especially with existing work up of the patients. From this point of view one needs to know positive and negative likelihood ratios of the proposed cut-offs. What is prior probability of significant jaundice in neonates born to mothers with O blood group and how this probability is altered with information about cord bilirubin.

We have included positive and negative likelihood ratios in the tables as suggested, and have explicitly stated the pre- and post-test probabilities for development of jaundice in O+ve/-ve mothers with an umbilical cord bilirubin of >35 umol/l in our discussion (page 14, line 12), and have also included it in the abstract.

Secondly, if conducting DAT is usual practice in neonates whose mothers are of blood group O, how adding cord bilirubin test changes the probability of jaundice?

Conducting cord blood (or baby blood) DAT in neonates of mothers who are of blood group O is not routine practice in our setting, and so we are not able to answer this interesting question. Conducting DAT is part of the work-up for neonatal jaundice, which is how DAT +ve jaundice has been identified.

Of the neonates born during the study period, cord bilirubin is available only for about half neonates (2128/4069). What is the reason of this? Decision of measuring the cord bilirubin may be related to its perceived utility (e.g. if mother is O+) directly related to risk of jaundice or other perinatal event like fetal distress which may be indirectly related to risk of jaundice.

Thank-you for the comment. We have strengthened our reporting of this important limitation in the discussion section where we now say (page 13, line 12): “The study has a number of limitations. Umbilical cord blood specimens were not systematically processed during the study period, with analysis undertaken in only 52% of inborn deliveries. Cord blood analysis was not generally undertaken in deliveries under midwifery-led care, introducing an important bias into
our dataset towards complicated pregnancies and deliveries requiring medical intervention. Although these features might influence the probability of developing neonatal jaundice, it was reassuring to see that the jaundice rate in our sample was in line with previous population-based studies.”