Rapid Communication

Effectiveness of cord blood as a strategy to rule out conjugated hyperbilirubinemia

Miray Kurtca[1], Sanjiv Harpavat[2], Sridevi Devaraj[3*]

[1]*Department of Pathology and Immunology, Baylor College of Medicine Texas Children's Hospital, Houston, TX, USA*
[2]*Department of Pediatrics, Division of Gastroenterology, Hepatology, and Nutrition, Baylor College of Medicine and Texas Children's Hospital, Houston, TX. USA*
[3]*Department of Pathology and Immunology, Baylor College of Medicine Texas Children's Hospital, Houston, TX, USA*

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Author of correspondence:
Sridevi Devaraj;
E-mail: sxdevara@texaschildrens.org;
Address:
Department of Pathology and Immunology, Baylor College of Medicine Texas Children's Hospital, Houston, TX, USA

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Abstract

Early detection of biliary atresia is crucial for timely intervention and improved outcomes in infants with elevated conjugated bilirubin levels. This study aims to investigate the viability of cord blood gas analysis as a novel method for assessing conjugated bilirubin levels. Infants with high heel stick levels also showed elevated cord blood bilirubin levels, indicating that cord blood testing could replace the need for repeat heel stick tests, especially benefiting low birth weight infants. Ongoing research, including larger cohorts and alternative bilirubin measurement methods, will further validate this innovative screening approach. Infants with biliary atresia have high conjugated bilirubin levels at birth. As a result, infants can be screened with newborn conjugated bilirubin measurements, to allow for early detection, timely treatment, and the best chances of delaying or even avoiding the need for a liver transplant [1]. An important limitation of screening, however, is that infants must undergo a separate blood test. To overcome this limitation, we investigated whether conjugated bilirubin measurements from cord blood could be useful.

We compared conjugated bilirubin from 2 sample types, from infants born at Texas Children's Hospital between October 2022-March 2023. The first sample type was from umbilical venous cord blood, collected in a heparin syringe for cord gas measurements. Leftover samples were stored in the dark at 4°C until time of analysis, ranging from 4-48 hours after collection. The second sample type was heel-stick blood, obtained in the first 60 hours of life as part of routine newborn clinical care. Conjugated bilirubin in cord blood (plasma) and heel stick (serum) was measured with the neonatal bilirubin spectrophotometric method (BuBC) using the Vitros 7600 system, and levels >0.2 mg/dL were considered high. There were 3361 births during the study period, including 3295 infants (98.0%) who had conjugated bilirubin measured by heel stick. These included 3278 infants (99.5%) with normal heel stick levels of <0.1 mg/dL, 12 infants (0.4%) with normal heel stick levels of 0.1-0.2 mg/dL, and 5 infants (0.2%) with high heel stick levels of >0.2 mg/dL (Figure1). Of the infants with heel stick levels of <0.1 mg/dL, 184 infants had cord blood available for measurement; all these infants had cord blood levels of 0.0 mg/dL. Of the infants with heel stick

levels of 0.1-0.2 mg/dL, 9 infants had cord blood available for measurement including one with transient alterations in liver function and a high cord blood level of 0.3 mg/dL (Table 1). Finally, of the infants with heel stick levels of >0.2 mg/dL, 3 infants had cord blood available for measurement. All had high conjugated bilirubin levels in cord blood, including one premature infant with an omphalocele and 2 infants with maternal antibodies directed against red blood cells. These preliminary results show that in most cases conjugated bilirubin levels of cord blood (collected at birth) and heel stick (collected in the first 60 hours of life) samples correlate perfectly and are 0.0 mg/dL. Thus, the negative predictive value of a cord blood bilirubin of 0.0 mg/dL in our study was 99.8%. Only 7 out of the high heel stick Bc level infants would need to be re-screened using this strategy. In addition, cord blood conjugated bilirubin levels that are elevated in infants with high heel stick levels perhaps reflect disease processes that have already started before birth. Future larger studies are needed to include patients with biliary atresia, compare levels from umbilical veins and arteries, and in addition, test the commonly-used diazo method which measures "direct bilirubin." Such studies will indicate that another blood draw or heel stick is unnecessary for most infants with a cord blood Bc of 0.0 mg/dL and will be important, especially in low birth weight infants.

AUTHOR'S DISCLOSURE

SH is a member of a Data Safety Monitoring Board coordinated by Syneos Health..

ETHICAL APPROVAL AND COMPLIANCE

This single-center study was conducted in strict adherence to the ethical guidelines for medical research involving human subjects. The study protocol received approval from the Institutional Review Board (IRB) at Baylor College of Medicine.

Figure 1: Patient flow

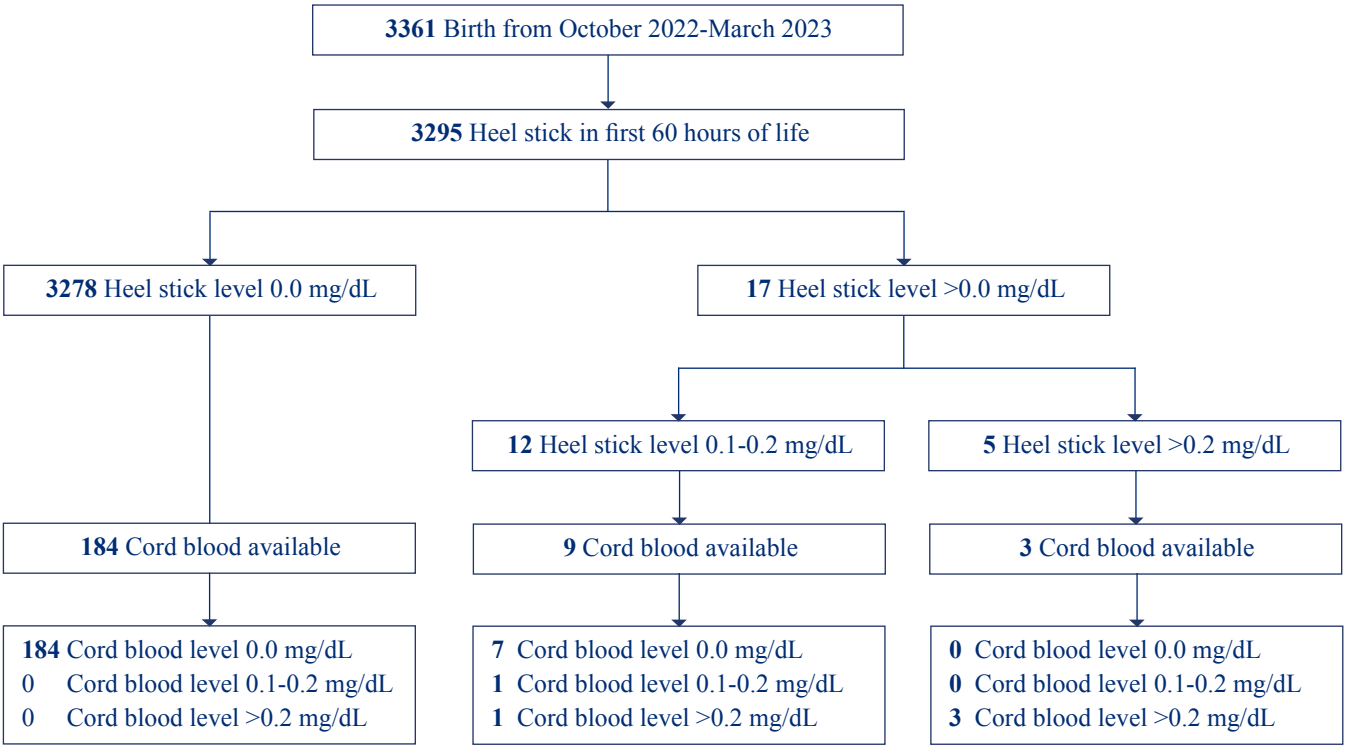

Table 1: Conjugated bilirubin levels in cord blood from infants with heel stick levels of >0.0 mg/dL

Gestational age	Additional birth factors	Cord blood level (mg/dL)	Heel stick level (mg/dL)†	Hospital length of stay
Patient heel stick Bc 0.1-0.2 mg/dL (n=12)				
33 weeks	None	*	0.1	>3 months
Term	None	*	0.1	<2 days
30 weeks	Anti-A isoimmunization	0.0	0.1	>1 month
30 weeks	Congenital anomalies	0.0	0.1	Deceased <14 days
31 weeks	Twin B	0.0	0.1	>2 months
34 weeks	Congenital anomalies	0.0	0.1	Deceased <14 days
Term	Anti-A isoimmunization	0.0	0.1	<2 days
30 weeks	Alteration in liver function	0.3	0.1	>3 months
Term	None	*	0.2	<2 days
31 weeks	Twin A	0.0	0.2	>2 months
Term	Concern for sepsis	0.0	0.2	Deceased <14 days
Term	None	0.1	0.2	<2 days
Patient heel stick Bc ≥0.2 mg/dL (n=5)				
29 weeks	Twin to twin transfusion syndrome	*	0.3	Deceased <14 days
Term	Anti-A isoimmunization	0.4	0.3	<2 days
26 weeks	Myelomeningocele	*	0.4	>4 months
35 weeks	Prematurity, omphalocele	0.3	1.3	>7 months
34 weeks	Anti-Rh isoimmunization	0.9	9.0	<1 month

* Cord blood not available

† Drawn in first 60 hours of life

REFERENCE

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