Use of Placental Cord Blood for Neonatal Admission Labs

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<u>Clinical Question:</u> For neonates < 35 weeks, what is the quality, quantity, and consistency of the evidence for use of placental cord blood compared to heel sticks, resulting in accurate admission laboratory work and decreased iatrogenic blood loss?

Conclusions: There is consistent, moderate quality evidence that it is feasible and reliable to draw baseline admission labs from the placental cord for premature neonates. 1,4,5,6,8,9 A very low birth weight (VLBW) neonate can lose between 2-10% of circulating blood volume 1,3,4,5,6,7 when admission blood is drawn directly after birth. Through use of placental blood, clinicians can spare neonates the pain of an admission blood draw. Although this review is only on use of placental blood for admission labs, authors relayed that delayed cord clamping and/or cord milking along with use of placental blood for admission labs may decrease neonatal blood loss. 1,2,4,5,9 Positive neonatal outcomes are emerging in studies when this procedure was tested in practice. Where placental blood was used for admission labs, neonates < 35 weeks or cited as VLBW had higher hemoglobin levels, 1,4 less vasopressor use, 1 decreased number of transfusions, 1,2,4 and delayed time to first transfusion. More RCTs and comparative studies are needed to assess whether placental cord blood draws instead of neonatal draws improve neonatal outcomes 5

Correlations and differences in paired samples (placental cord blood vs neonatal blood draw)

Commonly cited admission laboratory tests obtained from placental blood were CBC, ^{2,4,5,8,9} WBC, ^{5,7,9} and platelets^{4,5,7,9}; type & cross, ^{2,3,4} and blood cultures. ^{1,2,4,7} There was consistent evidence for moderate to strong statistically significant Pearson's correlations ^{5,7,9} on paired laboratory samples. See Table 1, page 2, for the full list of cited admission laboratory tests completed on placental blood draws and Pearson's correlations.

There are conflicting results when differences in paired group laboratory results were examined statistically. One author cited no significant differences in Hgb, platelets, or WBC count when placental blood was paired with neonatal arterial or venous blood.⁸ Other authors reported statistical differences on select lab results.^{7,9} The amount of difference in paired group comparisons also varied between placental blood draws and whether compared to either neonatal venous, arterial, or capillary draws.^{7,9} However, authors in the review were consistent in reporting that paired samples of placental cord blood versus blood drawn from the neonate were *clinically equivalent* ^{2,3,6,9} or otherwise stated, that differences in sources (placental cord blood versus neonatal venous or capillary draw) were not *clinically significant* ^{5,7,8} to change medical decisions.⁶

Education/training and procedural competency for drawing placental blood for admission labs

- <u>Education is essential</u> to operationalize this procedure in practice and should include sterile and standardized technique, ^{1,2,6,7,9} competency validation, ^{1,6} and clarity of team roles and responsibilities that lead to quality samples. ^{1,6,9}
- An interdisciplinary team approach^{2,4,5,6,7} was promoted. NICU RNs^{1,2,5,7} in addition to Neonatal Nurse Practitioners,^{4,7} MDs,⁴ and Neonatal Fellows^{2,5} were the clinicians trained to draw placental blood.
- Several articles reported the actual placental blood draw process with common elements of prepping the placental umbilical vein with providone iodine, 1,2,4,5 drawing between 3 to 10 ccs of blood, 1,4,5 with a 18 gauge needle 1,4,5,7 and 10 cc syringe. 1,4,7 Sterile gloves with sterile technique were emphasized, 1,5,6,7 especially sterile transfer to inoculate blood culture bottles. 1,7
- Key reported processes were good specimen labeling,^{4,6} timely draws, and prompt transport to lab.⁵

Recommendations/Future Research:

- Placental umbilical blood remains underutilized.⁶ Misconceptions about placental cord blood may be a barrier to embedding this procedure into practice,⁶ such as the procedure being new/different, not enough blood, and contamination concerns.⁶
- More RCTs and comparative studies are needed to assess whether placental cord blood draws instead of neonatal draws improve neonatal outcomes.^{5,9}
- Further utilization of placental cord blood for blood cultures may be optimal for there is more blood available to demonstrate true pathogens.^{5,7}
- Clinically important rates of false positive thrombocytopenia using placental blood can be mitigated with repeat labs from direct neonatal sampling.⁹

Table 1.

Common Types of Laboratory Tests Completed on Placental Cord Blood	Pearson's Correlations Between Paired Samples (Placental and Neonatal Draws for Admission Laboratory Tests)				
 CBC^{2,4,5,8,9} WBC^{5,7,9} Platelets^{4,5,7,9} Rh factor³ Type And cross^{2,3,4} Blood culture^{1,2,4,7} Coagulation profile^{2,4} C-Reactive protein² Glucose⁴ Blood gas⁴ G6PD quantitative screen² Metabolic screen^{3,4} 	 Hemoglobin (0.50)⁵, (0.55)⁷, (0.72)⁹ Platelets (0.49)⁵, (0.563)⁷, (0.76)⁹ WBC (0.84)⁵, (0.76)⁷, (0.82)⁹ 				

Key considerations: The quality of the evidence should be viewed within the context of several factors. There appears to be a core group of dedicated researchers/clinicians^{1,3,4,9} who investigate and publish on this important clinical issue. For this literature review, these researchers appeared as co-authors on each other's studies or literature. This could be viewed as a limitation, or as an emerging group of clinical experts for consultation on implementation of the technique in practice. For example, Carroll and colleagues (2012)⁹ was added to the review list as a seminal article due to frequent citation. To note, there are studies^{2,5,7} in this review with investigators outside this core group reflecting new/different settings and samples. Another consideration is small sample sizes^{1,2,4} within studies; yet frequently statistical significance was demonstrated within analyses.

REVIEW REFERENCES

- 1. Baer, V.L., Lambert, D.K., Carroll, P.D., Gerday, E. & Christensen, R.D. (2013). Using umbilical cord blood for the initial blood tests of VLBW neonates results in higher hemoglobin and fewer RBC transfusions. *Journal of Perinatology*, *33*, 363-365.
- 2. Balasubramanian, H., Malpani, P., Sindhur, M., Kabra, N., Ahmed, J., & Srinivasan, I. (2019). Effect of umbilical cord sampling versus admission blood sampling on requirement of blood transfusion in extremely preterm infants: A randomized controlled trial. *The Journal of Pediatrics*, 1-7.
- 3. Carroll, P.D. & Christensen, R.D. (2015). New and underutilized uses of umbilical cord blood in neonatal care. *Maternal Health, Neonatology, and Perinatology, 1,* 16.
- 4. Christensen, R.D., Lambert, D.K., Baer, V.L, Montgomery, D.P., Barney, C.K., Coulter, D.M., Ilstrup, S., & Bennett, S. T. (2011). Postponing or eliminating red blood cell transfusions of very low birth weight neonates by obtaining all baseline laboratory blood tests from otherwise discarded fetal blood in the placenta. *Transfusion*, *51*, 253-8.
- 5. Greer, R., Safarulla, A., Koeppel, R., Aslam, M. & Bany-Mohammed, F.M. (2019). Can Fetal umbilical venous blood be a reliable source for admissions complete blood count and culture in NICU patients. *Neonatology*, *115*, 49-58.
- 6. Moore, S.P., Newberry, D.M., & Jnah, A.J. (2017). Use of placental/umbilical blood sampling for neonatal admission blood cultures; Benefits, challenges, and strategies for implementation. *Neonatal Network*. *36*,152-158.
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- 8. Prakash, N., Decristofaro, J., & Maduekwe, E.T. (2017). One less painful procedure: Using umbilical cord blood as alternative source to admission complete blood count. *American Journal of Perinatology*, *34*, 1178-1184.
- 9. Carroll, P.D., Nankervis, C.A., Imas, J., & Kellcher, K. (2012). Umbilical cord blood as a replacement source for admission complete blood count in premature infants. *Journal of Perinatology*, *32*, 97-102.

DATABASE SEARCH STRATEGIES AND FINDINGS

Evidence Search Strategies: A literature review on the selected clinical question was conducted during June 2019. This review examined the quantity, quality, and consistency of the evidence for use of placental cord blood compared to heel sticks, resulting in accurate admission laboratory work and decreased iatrogenic blood loss for neonates < 35 weeks.

Search terms were broad and included "premature," "umbilical cord blood", "blood count", "preterm", "umbilical cord", and "admission" either alone or in combination. Limitors included English language and human. Electronic databases included PubMed, CINAHL, Google Scholar, and Cochrane Library. Searches were individualized for each database for years 2010 to 2019 (See Database Search Methodology, Page 6).

This review yielded 7 relevant hits after initial de-duplication from 275 total hits between databases (excluding Google Scholar). Two contextual references were included, as they addressed the clinical question. A total of 9 citations were included in the review. The citations were ranked using the Academy of Evidence-Based Practice Evidence Leveling System and ranked/graded using the Johns Hopkins Evidence Appraisal tools (See Page 5). The strength and the final grade of the evidence was appraised to be of moderate quality.

<u>Evidence Review Results</u>: There were 6 comparison/paired sample or case matched cohort studies, 1 RCT, and 2 literature reviews within this review. Limitations are stated in the key considerations section of the report.

Title

©Academy of Evidence Based Practice Academy of EBP® Evidence Leveling System (ELS)						
LEVEL	DESCRIPTION	RELEVANT ARTICLES	ARTICLE NUMBER			
A	Meta-analysis of multiple large sample or small sample* randomized controlled studies, or meta-synthesis of qualitative studies with results that consistently support a specific action, intervention, or treatment					
В	Well-designed controlled studies, both randomized and nonrandomized, prospective or retrospective studies, and integrative reviews with results that consistently support a specific action, intervention, or treatment	6	1; 2; 5; 7; 8; 9			
С	Qualitative studies, descriptive or correlational studies, concept analyses, integrative reviews, systematic reviews, or randomized controlled trials with inconsistent results	1	4			
D	Peer-reviewed professional organizational standards, with clinical studies to support recommendations					
E	Theory-based evidence from expert opinion or multiple case reports, case studies, consensus of experts, and literature reviews	2	3; 6			
MA	Manufacturer's recommendation; Anecdotes					
LR	Laws and Regulations (local, state, federal; licensing boards; accreditation bodies, etc.)					
	Total	9				

A large sample has adequate power to detect the observed effect with confidence (as seen in significant Confidence Intervals). A small sample may lack confidence in the power of the desired effect (Polit & Beck, 2008). Designed by Emma M. Cuenca and Cecelia L. Crawford, Academy of EBP; ©Kaiser Permanente SCAL Regional Nursing Research Program, May 2011. Adapted from AACN Evidence Leveling System (2009) and Canadian Medical Association & Centre for Evidence-Based Medicine

High Quality: #2, #5, #9

(Consistent, generalizable results; sufficient sample size for the study design; adequate control; definitive conclusions; consistent recommendations based on comprehensive literature review that includes thorough reference to scientific evidence OR expertise is clearly evident; draws definitive conclusions; provides scientific rationale; thought leader in the field)

Moderate Quality: #1, #6; #7, #8

(Reasonably consistent results; sufficient sample size for the study design; some control, and fairly definitive conclusions; reasonably consistent recommendations based on fairly comprehensive literature review that includes some reference to scientific evidence OR expertise appears to be credible; draws fairly definitive conclusions; provides logical argument for opinions).

Low Quality: #3, #4,

(Little evidence with inconsistent results; insufficient sample size for the study design; conclusions cannot be drawn OR expertise is not discernable or is dubious; conclusions cannot be drawn.

Final Summary of the Body of Evidence = Moderate

Electronic Database Search Methodology

Date(s): February to June-2019; October to December 2019

Literature search topic/clinical question: For neonates less than 35 weeks, what is the quality, quantity, and consistency of the evidence for use of placental cord blood compared to heel sticks, resulting in accurate admission laboratory work and decreased iatrogenic blood loss

Inclusion Criteria: infants < 35 weeks; acute care

Exclusion Criteria: Infants >35 weeks, delayed cord clamping, cord milking, setting other than acute care

Limiters: English, 2019, 2010, human

Database	Key Word(s) and/or Controlled Vocabulary Terms#	Total References Identified (hits)	No. Relevant References	No. Total Duplicate Articles	No. Articles Selected for Review	No. Articles Excluded	Final Total Relevant References
PubMed* Years: 2010-2019	Umbilical cord AND premature AND admission	86	3	*	3	0	3
PubMed* Years: 2010-2019	Placental AND Neonatal AND blood count	89	1	0	1	0	1
PubMed* Years: 2010-2019	Neonatal and cord blood and blood culture and umbilical	37	2	1	1	0	1
CINAHL Years: open	Umbilical cord AND premature AND admission	24	2	2	0	0	0
CINAHL Years: Open	Cord blood AND admission	31	2	1	1	0	1
Cochrane database for systematic reviews	Premature and admission and umbilical cord	0 systematic reviews; 6 trials	0	0	0	0	0
Cochrane database for systematic reviews	Premature and umbilical cord and blood count	0 systematic reviews; 9 trials	0	0	0	0	0
Google Scholar 5 pages in	Premature and admission and umbilical cord	32 by date 25,400 by relevance	4	3	1		1
	TOTALS						7

^{*}Use the first database as the main comparison for subsequent database searches and identifying duplicate articles

*Reference/Contextual Links

Christensen, R.D., Lambert, D.K., Baer, V. L., Montgomery, D.P., Barney, C.K., Coulter, D.M., Ilstrup, S., and Bennett, S.T. (2011). Postponing or eliminating red blood cell transfusions of very low birth weight neonates by obtaining all baseline laboratory blood tests from otherwise discarded fetal blood in the placenta. *Transfusion, 51*, 253-58. Doi: 10.1111/j.1537-2995.2010.02827.x

Carroll, P.D., Nankervis, C.A., Imas, J. & Kellcher, K. (2012). Umbilical cord blood as a replacement source for admission complete blood count in premature infants. *Journal of Perinatology*, 32, 97-102.

Total Articles Included in Literature Review: Database (7) + Contextual Links (2) = 9

Clinical Question						
Population and/or Patient(s)	Intervention/Interest Area	Comparison Intervention (current practice)	Outcome	Time Period (If Applicable; Optional)		
P: neonates<35 weeks and less than 1500 grams	I: use of placental blood for admission labs	C: Heel stick/venous labs drawn in NICU	O: Accuracy of placental blood and decreased iatrogenic blood loss	T: placental blood draw within 30 minutes of birth		

Final Clinical Question: For neonates < 35 weeks, what is the quality, quantity, and consistency of the evidence for use of placental cord blood compared to heel sticks, resulting in accurate admission laboratory work and decreased iatrogenic blood loss.

Searchable Question

Key Search Terms: premature, umbilical cord blood, admission, complete blood count, preterm, umbilical cord, heel stick*

MESH Terms: Infant, premature, before 37 weeks; infant, extremely premature <28 weeks; fetal blood, umbilical cord blood; blood specimen collection; blood specimen collection, heel.

Inclusion Criteria: infants < 35 weeks (see above); acute care

Exclusion Criteria: Infants > 35 weeks, delayed cord clamping, cord milking; setting other than acute care

Limiters (Open year or year ranges, age ranges, and language, etc.): English, 2018-2010, humans

Databases: PubMed, CINAHL, Cochrane Library, OneSearch, Google Scholar

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