Prevalence and Utility of C-Reactive Protein (CRP) in Neonatal Early Onset Sepsis

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NICHD Neonatal Research Network

Background

- CRP is proposed as a biomarker to improve diagnosis of early onset sepsis (EOS; within 72 hours of birth)
- Associations of **CRP levels and clinical presentation and outcome of neonates with EOS are unknown**

Objective

- Characterize CRP use and levels in neonates with EOS

Design / Methods

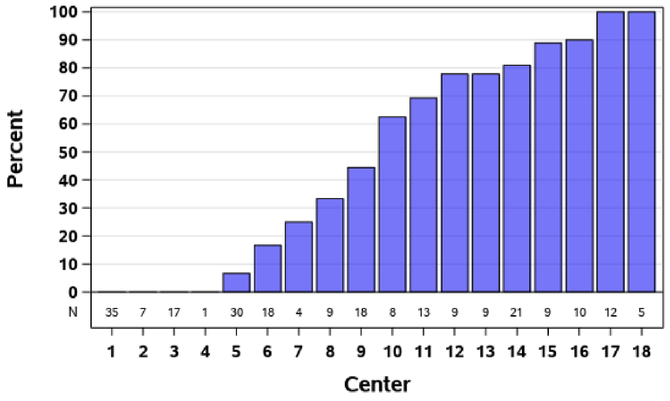
- Analysis of neonates born at 18 Neonatal Research Network clinical centers 2015-2017
- **Infants with gestational age (GA) ≥22 weeks and birth weight >400g who were diagnosed with EOS**
- Evaluated the proportion of neonates with EOS for whom CRP was obtained by **center**
- Compared median CRP concentrations among categories of neonatal **demographics**, **clinical characteristics**, **pathogen type**, and **outcome**

Results

- **235** neonates among 217,480 live births had EOS [131 (56%) born <37 weeks GA]
- At least one CRP was obtained for **96/235 (41%)** neonates with EOS, of which **71/95 (74.7%) had a CRP concentration >10 mg/L** (one value missing)
- Proportion of neonates with any CRP **varied by center** (*Figure 1*)
- No relationship between the time CRP was obtained and the concentration (*Figure 2*)
- No differences were found in the distribution of CRP concentrations by demographic or clinical characteristics
- CRP concentrations were **significantly higher with ≥5 clinical signs / symptoms of sepsis** (*Table 1*)
- **CRP concentrations were not significantly different in gram-positive compared to gram-negative EOS** (*Table 2*) or preterm neonates who died (n=13) compared to those who survived (n=46) [median (p25, p75): 38 (20, 95) vs 28 (8, 70)]

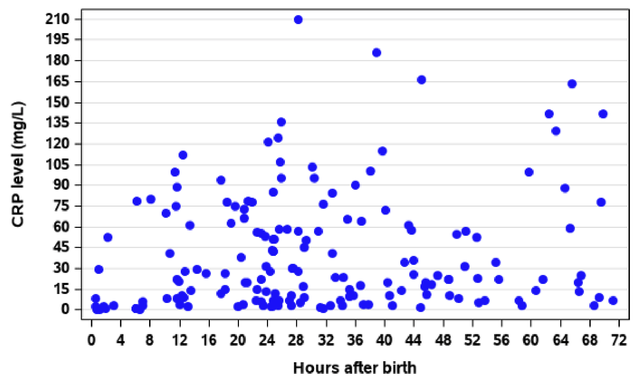
In neonates with early onset sepsis (EOS), use of CRP varied by center. CRP concentration did not differ by time of testing, demographic and clinical characteristics examined, pathogen type, or death.

Figure 1. Percent of neonates with EOS who had any CRP obtained in the first 72 hours of life by study center. The number of neonates with EOS at each center is shown below the bars in the row labeled N. No neonates at centers 1-4 and all neonates at centers 17-18 had CRP obtained.



* The proportion of neonates with any CRP varied by study center, p<0.001

Figure 2. CRP level by number of hours taken after birth. All values available are shown including multiple values per neonate where applicable. A total of 170 CRP levels were obtained for 96 neonates; CRP level was missing for 3 observations.



Discussion / Future Directions

- There is a **lack of consensus** regarding use of CRP in management of EOS among United States NICUs
- CRP concentration **did not differ by timing, demographic and clinical characteristics, pathogen type, or death** in this cohort
- Among infants with EOS, CRP was higher in infants with multiple **(≥5) clinical signs of sepsis**, as well as when **cyanosis**, **acidosis**, **neutropenia**, and **bleeding / thrombocytopenia** are present
- Results should be viewed in the context of the small number of neonates for whom CRP was obtained
- Prospective studies that include neonates without EOS are warranted to evaluate the diagnostic and predictive utility of CRP

Table 1. Clinical signs/symptoms of sepsis at ≤72 hours and highest CRP level in the first 72 hours after birth in neonates with EOS[a]

Clinical sign/symptom	Sign present median (p25, p75) CRP level [n]	Sign absent median (p25, p75) CRP level [n]	P-value[b]
Temperature ≥38.0° C	58 (18, 95) [16]	31 (10, 72) [79]	0.15
Temperature ≤36.0° C	26 (12, 100) [17]	43 (10, 72) [78]	0.95
Cyanosis with use of oxygen (>60 min)	57 (18, 94) [40]	26 (10, 58) [55]	0.04
Tachypnea (respiratory rate>60 breaths/min) for ≥30 min documented twice	34 (9, 75) [61]	40 (20, 72) [34]	0.75
Grunting, flaring, retractions	45 (10, 84) [59]	29 (13, 58) [36]	0.38
Hypotension[c]	52 (14, 88) [37]	30 (9, 70) [58]	0.14
Acidosis[d]	55 (20, 95) [50]	23 (7, 58) [45]	0.008
Tachycardia (heart rate>160 bpm)	36 (12, 78) [70]	42 (10, 61) [25]	0.46
Apnea and/or intermittent bradycardia	40 (8, 57) [34]	34 (13, 75) [61]	0.37
Lethargy	51 (14, 103) [19]	35 (10, 71) [76]	0.40
Irritability	43 (17, 88) [19]	36 (10, 72) [76]	0.45
Hypoglycemia (lowest blood glucose level <40 mg/dL)	57 (10, 100) [30]	30 (11, 61) [65]	0.11
Neutropenia (ANC <1000/μL)	58 (43, 87) [20]	28 (9, 72) [75]	0.02
Bleeding, petechiae, thrombocytopenia (platelets <100,000/μL)	64 (26, 103) [23]	29 (9, 61) [72]	0.01
Abdominal distention or >1 episode of bilious emesis	65 (27, 115) [6]	38 (10, 72) [89]	0.29
Clinical seizures (proven or suspect)	35 (12, 59) [4]	38 (10, 78) [91]	0.81
Any signs of sepsis in the first 72 h	40 (10, 77) [92]	23 (20, 50) [3]	0.62
≥3 clinical signs of sepsis	42 (10, 78) [79]	28 (14, 58) [16]	0.53
≥5 clinical signs of sepsis	56 (18, 95) [56]	23 (7, 54) [39]	0.002

[a] A total of 96 neonates with EOS had at least 1 CRP obtained in the first 72 hours of life. CRP level was missing for 1 neonate. If more than one CRP level was obtained for an neonate in the first 72 hours the highest CRP level was used.
[b] P-value by Kruskal-Wallis test.
[c] Hypotension was defined as mean arterial pressure less than estimated GA or treated with fluid boluses or pressors (such as dopamine, epinephrine, norepinephrine, or vasopressin).
[d] Acidosis was defined as peripheral or cord blood gas analysis with pH of less than 7.25

Table 2. CRP levels in neonates with EOS by pathogen type

Median (p25, p75)[a] [n]	Gram positive	Gram negative	P-value[b]	GBS	E coli	P-value[b]
CRP ≤24 h	22 (7, 61)	31 (13, 78)	0.19	22 (7, 66)	29 (10, 78)	0.39
	[25]	[25]		[15]	[22]	
CRP >24-72 h	30 (14, 61)	42 (10, 96)	0.66	44 (24, 86)	54 (18, 100)	0.85
	[39]	[35]		[20]	[25]	
CRP ≤72 h	43 (15, 72)	51 (12, 89)	0.63	51 (27, 78)	53 (12, 96)	0.96
	[47]	[43]		[25]	[34]	

[a] If more than one CRP level was obtained for a neonate during the specified time interval the highest CRP level was used.
[b] P-value by Kruskal-Wallis test.

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Disclosures: The authors have no financial relationships to disclose or conflicts of interest to resolve. Any real or apparent conflicts of interest related to the content of this poster have been resolved. This poster does not involve discussion of unapproved or off-label, experimental or investigational use of a drug.

Acknowledgements: The National Institutes of Health and the Eunice Kennedy Shriver National Institute of Child Health and Human Development provided grant support for the Neonatal Research Network. We are indebted to the infants and their parents who agreed to take part in this study and to our medical and nursing colleagues at: Brown University; Case Western Reserve University; Cincinnati Children's Hospital Medical Center; Duke University; Emory University; Nationwide Children's Hospital/Ohio State University, RTI International; Stanford University; University of Alabama at Birmingham; University of Iowa; University of New Mexico; University of Pennsylvania, University of Rochester; University of Texas Southwestern Medical Center; University of Texas Health Science Center at Houston; University of Utah.

NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development