Abstract for PAS

Title
Assessment of the impact of multiplex PCR panels in sepsis evaluations of young febrile infants

Background
The management of febrile infants under the age of 3 months has long been a controversial topic, often requiring them to be subject to a battery of tests, antibiotics, and hospitalization. Multiplex polymerase chain reaction (PCR) panels can provide a rapid diagnosis, but their role in managing these patients is still unknown.

Objective
Our objective was to determine if multiplex respiratory and meningitis/encephalitis PCR panels decreased antibiotic duration of therapy (DOT) and hospital length of stay (LOS) when used in sepsis evaluations of febrile infants less than 90 days of age.

Methods
We performed a retrospective chart review of infants younger than 90 days old admitted to the pediatric ward for concerns of fever or sepsis from 1/1/2016 through9/30/2019. Subjects with bacterial infections were excluded. Our primary outcomes were differences in DOT and LOS between patients admitted before and after PCRs became available (Pre-PCR era and PCR era). Secondary outcomes were differences in DOT and LOS between infants diagnosed with a viral infection versus those without a definitive diagnosis.

Results
118 subjects were included in our analysis with 28 (39%) in the Pre-PCR group and 44 (61%) in the PCR Era group. Descriptive statistics of demographic data, DOT, and LOS, stratified by both eras, are available in Tables 1 and 2. The overall median DOT and LOS were decreased by 10 and 7 hours, respectively, (p=.07) after PCR panels became available. Using linear regression models (Tables 3 and 4), we found that the overall DOT for patients admitted during the PCR era was 13 hours less than the Pre-PCR era (p=.019, 95% CI: 2.3; 23.9). A diagnosis of viral infection in either period decreased DOT by 21 hours (p<.01, 95% CI: 6; 37).Within the PCR era, DOT decreased by 19 hours (p<.001, 95% CI: 10; 29) and LOS by 16 hours (p<.01, 95% CI: 5; 27) in patients diagnosed with a viral infection by PCR compared to those with no diagnosis.

Conclusion
We conclude that multiplex PCR panels can potentially influence the management of young febrile infants admitted for sepsis evaluations by rapidly diagnosing viral infections and thus decreasing DOT and LOS. In turn, that may improve patient outcomes and satisfaction, as well as possibly decrease costs. Multiplex PCR panels should be considered as part of routine sepsis evaluations in young febrile infants. Larger studies are needed, including in depth cost analysis.

	Both Eras (n=72)	Pre-PCR (n=28)	PCR Era (n=44)
Age (days)	33.2 [-14.8; 81.2]	31.3 [-16.1; 78.7]	34.5 [-14.1; 83.1]
Gestational age (weeks)	38.3 [34.7; 41.9]	38 [35; 41]	38.5 [34.7; 42.3]
Birth weight (grams)	3155 [2090; 4220]	3080 [2036; 4123]	3203 [2124; 4283]
LOS (hours)	47.4 [6.6; 88.2]	51.7 [11.1; 92.3]	44.7 [4.3; 85.1]
DOT (hours)	24.5 [-19.5; 68.5]	30.6 [-12.6; 73.8]	20.6 [-22.6; 63.8]

Table 1: **Descriptive statistics for continuous variables**, with mean values shown [and 95% confidence intervals in brackets]. The first column of numbers represents the pooled totals, and the second and third columns represent the "Pre-PCR era" and "PCR era", respectively. Age represents age on admission. ***Abbreviations:*** *LOS=Length of stay; DOT=Duration of therapy with antibiotics*

	Both Eras	Pre-PCR	PCR Era
Sex			
Male *(ref)*	43 (59.7%)	19 (67.9%)	24 (54.5%)
Female	29 (40.3%)	9 (32.1%)	20 (45.5%)
Race			
White *(ref)*	35 (48.6%)	7 (25.0%)	28 (63.6%)
Black	14 (19.4%)	8 (28.6%)	6 (13.6%)
Asian	2 (2.8%)	1 (3.6%)	1 (2.3%)
Other	21 (29.2%)	12 (42.9%)	9 (20.5%)
Infectious Diagnosis			
Viral	49 (68.1%)	17 (60.7%)	32 (72.7%)
FUO *(ref)*	8 (11.1%)	3 (10.7%)	5 (11.4%)
Non-infectious	15 (20.8%)	8 (28.6%)	7 (15.9%)
Lumbar puncture			
LP done	37 (51.4%)	15 (53.6%)	22 (50.0%)
LP not done *(ref)*	35 (48.6%)	13 (46.4%)	22 (50.0%)
PCR Results			
Not Done *(ref)*	32 (44.4%)	28 (100.0%)	4 (9.1%)
Negative	28 (38.9%)	0 (0.0%)	12 (27.3%)
Viral	28 (38.9%)	0 (0.0%)	28 (63.6%)

Table 2: **Descriptive statistics for categorical variables**, with number of subjects in each group given (and column percentages for each category in parentheses). The first column of numbers represents the pooled totals, and the second and third columns represent the "Pre-PCR era" and "PCR era", respectively. For the PCR Results, *Viral* indicates one or more of the PCR panels returned positive for a virus (excluding HSV) while *Negative* indicates that the patient had $\geq$1 PCR panel but all results were negative. If neither the Respiratory nor CSF PCR panel was done, the patient was categorized in the *Not Done* group. ***Abbreviations:*** *`FUO`=Fever of unknown origin; `LP`=Lumbar puncture; `ref`=Reference level in linear regressions*

	DOT
Intercept	54.07 (8.79)***
Pre-PCR Era	13.07 (5.40)*
Infectious diagnosis	
Dx: Non-infectious diagnosis	−31.10 (9.21)**
Dx: Viral infection	−21.73 (7.74)**
Demographics	
Age (days)	−0.22 (0.11)·
Sex: Female	−4.89 (5.00)
Race: Asian	−19.50 (14.78)
Race: Black	−3.66 (6.99)
Race: Other	−10.23 (6.00)·
R^2	0.28
Adj. R^2	0.19

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$; ·$p < 0.1$

Table 3: **Linear regression predicting duration of antibiotic therapy (DOT) based on PCR era**, infectious diagnosis, and demographics. Coefficients are shown for each predictor (with standard errors in parentheses). A similar regression for LOS was conducted but is not included as its F-statistic was not significant. ***Reference levels:*** *Infectious diagnosis=Fever of unknown origin; Sex=Male; Race=White*

	LOS	DOT
Intercept	43.34***	38.63***
	(9.98)	(8.75)
PCR Results		
Negative	6.49	4.95
	(7.05)	(6.19)
Viral	−16.17**	−19.43***
	(5.60)	(4.91)
Demographics		
Age (days)	−0.06	−0.12
	(0.12)	(0.10)
Sex: Female	−2.98	−6.39
	(4.62)	(4.06)
Race: Asian	−9.14	−14.07
	(13.74)	(12.05)
Race: Black	−6.75	−4.38
	(6.43)	(5.64)
Race: Other	−8.26	−8.87
	(5.56)	(4.88)
Had LP done	14.82**	21.17***
	(5.01)	(4.39)
Infectious diagnosis		
Dx: Non-infectious diagnosis	8.40	−17.73*
	(8.90)	(7.81)
Dx: Viral infection	10.54	−6.09
	(8.20)	(7.20)
R^2	0.30	0.54
Adj. R^2	0.18	0.46

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$; $p < 0.1$

Table 4: **Linear regression predicting DOT and LOS based on PCR results**, demographics, if a lumbar puncture (LP) was done, and infectious diagnosis. Coefficients are shown for each predictor (with standard errors in parentheses). ***Reference levels:*** *PCR Results=Not done; Sex=Male; Race=White; Had LP done=No (meaning the coefficient represents those who did have a LP); Infectious diagnosis=Fever of unknown origin*