Role of clinical characteristics, radiographic features, and biomarkers in distinguishing bacterial vs viral etiology in childhood community-acquired pneumonia.

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Background:

- ❖ Childhood Community acquired pneumonia (CAP) is an important public health problem.
- ❖ Determination of microbial etiology at presentation is difficult.
- ❖ Distinguishing bacterial from viral etiology can help to tailor therapy, but this is not currently feasible.
- ❖ This was undertaken to identify demographic, clinical, & radiographic characteristics as well as biomarkers (CRP, Procalcitonin, Cytokines) capable of distinguishing bacterial vs viral etiology.

Methods:

- ❖ Study design: Prospective cohort
- ❖ Study duration: Jan to Jun 2015
- ❖ Inclusion: Children (1 mo to 12 y) with severe CAP (WHO IMCI criteria).
- ❖ Exclusion: Illness > 7 d, antibiotics > 24 h, immune-deficiency.
- ❖ Sample size: 222 consecutive children.
- ❖ Etiology assigned in individual children using a hierarchy of biological specimens and analytic models based on weighting potential pathogenicity of individual organisms in biological specimens.
- ❖ Various clinical and laboratory parameters compared between bacterial vs viral etiology in multiple analytic models.

Results:

- ❖ No differences for:
 - Demographics (age, sex, residence)
 - Clinical features (wheezing, crackles on auscultation, auscultatory wheeze),
 - Radiographic features (consolidation, streaky hilar opacities, normal xray)
 - Total and Differential counts
 - CRP & Procalcitonin higher in bacterial but no clinically useful cut-off value.
 - IL-6 >5000, >1000, >100 and IL-8 >1000 pg/ml could distinguish bacterial vs viral.

	Model 1		Model 2		Model 3	
	Bacterial (n=48)	Viral (n=65)	Bacterial (n=25)	Viral (n=85)	Bacterial (n=10)	Viral (n=68)
Median age (mo)	7.3 (3.4, 14.2)	7.4 (3.1, 21.6)	7.9 (4.7, 15.4)	6.4 (2.9, 18.4)	13.9 (5.9, 24.2)	6.2 (2.7, 12.2)
Crackles on auscultation (%)	89.5	83.1	92.0	84.7	80.0	88.2
Wheeze on auscultation (%)	35.4	43.1	32.0	41.2	40.0	38.2
Consolidation on xray (%)	43.8	58.5	44.0	56.5	60.0	61.8
Streaky infiltrates on xray (%)	35.4	23.1	28.0	25.9	0.0	25.0
Median TLC (/mm ³)	9850 (7525, 14750)	10200 (6900, 14900)	9800 (8200, 12000)	10300 (7200, 14200)	9800 (8550, 10350)	10500 (7475, 14425)
TLC <4000/mm ³ (%)	4.2	12.3	4.0	10.6	0.0	11.8
TLC >11000/mm ³ (%)	37.5	43.1	28.0	44.7	20.0	48.5
Median CRP (mg/l)	41.8 (8.1, 98.7)	27.2 (6.5, 100.8)	52.2 (14.1, 119.9)	24.1 (7.9, 96.9)	95.6 (57.7, 242.8)	24.1 (5.4, 85.1)
Median Procalcitonin (ng/ml)	2.35 (0.40, 15.6)	1.69 (0.25, 5.80)	5.15 (0.38, 50.46)	1.31 (0.26, 7.48)	10.50 (3.36, 46.47)	1.89 (0.25, 13.8)
Log ₁₀ IFN γ (pg/ml)	0.5076 (0.5076, 0.8439)	0.5076 (0.5076, 0.5076)	0.5076 (0.5076, 0.9991)	0.5076 (0.5076, 0.5076)	0.6819 (0.5076, 1.3329)	0.5076 (0.5076, 0.7448)
Log ₁₀ IL1-B (pg/ml)	0.0406 (0.0406, 0.0406)	0.0406 (0.0406, 0.0406)	0.0406 (0.0406, 0.4800)	0.0406 (0.0406, 0.0406)	0.0406 (0.0406, 1.0665)	0.0406 (0.0406, 0.0406)
Log ₁₀ IL-4 (pg/ml)	0.8443 (0.8443, 0.8443)	0.8443 (0.8443, 0.8443)	0.8443 (0.8443, 0.8443)	0.8443 (0.8443, 0.8443)	0.8443 (0.8443, 0.8443)	0.8443 (0.8443, 0.8443)
Log ₁₀ IL-6 (pg/ml)	1.6873 (1.0761, 2.1946)	1.4955 (1.0298, 2.1214)	1.9987 (1.6063, 2.3911)	1.5709 (1.1126, 2.0485)	2.2859 (1.9845, 3.1066)	1.4955 (1.4955, 1.4955)
Log ₁₀ IL-8 (pg/ml)	1.9969 (1.7977, 2.3625)	1.9423 (1.6736, 2.3896)	2.1114 (1.9519, 2.7476)	1.9572 (1.6881, 2.4219)	2.0882 (1.9947, 3.1066)	2.0446 (1.7046, 2.4823)
Log ₁₀ CCL22 (pg/ml)	3.2331 (3.0063, 3.3761)	3.2310 (3.0556, 3.3299)	3.1987 (3.0096, 3.3342)	3.2534 (3.0681, 3.3610)	3.1541 (2.9979, 3.2922)	3.2534 (3.0527, 3.3697)

Log10 (Absolute value)	Parameters [CI]	IL-6	IL-8
>4.0 (>10,000 pg/ml)	LR+ LR-	Infinity [NaN to Infinity] 0.8 [0.587 to 1.091]	Infinity [NaN to Infinity] 0.8 [0.587 to 1.091]
>3.69897 (>5,000 pg/ml)	LR+ LR-	13.333 [1.354 to 136.581] 0.812 [0.595 to 1.108]	3.39 [0.713 to 16.216] 0.85 [0.62 to 1.165]
>3.0 (>1,000 pg/ml)	LR+ LR-	4 [1.131 to 14.283] 0.757 [0.501 to 1.141]	4.054 [1.148 to 14.501] 0.756 [0.501 to 1.14]
>2.69897 (>500 pg/ml)	LR+ LR-	2.913 [0.897 to 9.469] 0.78 [0.516 to 1.18]	2.273 [0.736 to 6.985] 0.806 [0.532 to 1.223]
>2.0 (>100 pg/ml)	LR+ LR-	1.852 [1.006 to 3.419] 0.592 [0.272 to 1.286]	1.323 [0.832 to 2.102] 0.637 [0.239 to 1.698]
>1.69897 (>50 pg/ml)	LR+ LR-	1.754 [1.171 to 2.629] 0.368 [0.104 to 1.294]	1.333 [1.162 to 1.529] 0 [0 to NaN]
>1.0 (>10 pg/ml)	LR+ LR-	1.172 [1.062 to 1.294] 0 [0 to NaN]	1.015 [0.986 to 1.045] 0 [0 to NaN]

Conclusion:

- ❖ None of the clinical, radiographic and laboratory features can distinguish bacterial from viral pneumonia.
- ❖ IL-6 >5000 pg/ml, IL-8 >1000 pg/ml and the combination IL-6 >1000 pg/ml + IL-8 >1000pg/ml, could differentiate bacterial from viral pneumonia.
- ❖ Combination of IL-6 >1000 pg/ml & IL-8 >1000pg/ml showed LR+ of 10.345 [CI 1.937 to 53.725], and LR- of 0.721 [CI 0.48 to 1.084].
- ❖ Although these findings are highly encouraging, application in routine clinical use requires further validation in other cohorts.

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