INTRODUCTION

Elevated C-reactive protein (CRP) is known to be associated with pneumococcal pneumonia and, more generally, with bacterial pneumonia [1]. We describe the distribution of CRP levels among severe and very severe pneumonia cases with suspected bacterial and viral etiology factors with the aim of determining if CRP may be a useful tool to inform or validate the PERCH etiology results.

METHODS

- **PERCH** is a 7-country case-control study; **cases:** aged 1-59 months hospitalized with WHO-defined severe and very severe pneumonia; **controls:** age-frequency-matched to cases, randomly selected from the community without pneumonia.
- Enrollment blood CRP levels were measured for all PERCH cases.
- Case groups representing likely bacterial or viral pneumonia were defined as:
  - Confirmed bacterial pneumonia: bacteria detected by blood culture or by lung aspirate or pleural fluid culture or PCR, including confirmed pneumococcal (Spn) and confirmed *H. influenzae* (Hinf) pneumonia
  - Viral pathogen positivity: detected by PCR from na/o/oropharyngeal (NP/OP) swab or induced sputum specimen (assessed 17 viruses)
  - Cases with respiratory syncytial virus (RSV) were considered likely viral pneumonia cases since PCR density ratio compared to controls was 10.6 (8.8-12.7)
  - High-density Spn: Spn PCR density in NP/OP > 6.6 log_{10} copies/mL, > 4.4 log_{10} copies/mL for children with prior antibiotics or whole blood (WB) > 2.2 log_{10} copies/mL (thresholds derived comparing confirmed Spn cases to controls)
  - High-density Hinf: Hinf PCR density in NP/OP > 5.9 log_{10} copies/mL
  - Evidence of bacterial infection: high-density Spn or high-density Hinf or confirmed bacterial pneumonia
- Odds ratios and 95% confidence intervals (95%CIs) for elevated CRP adjusted for site and age (aORs) were calculated for the defined bacterial/viral case groups, overall and by site.
- An optimal CRP cut-off was obtained using ROC analysis comparing RSV+ without evidence of bacterial infection to confirmed bacterial cases.

RESULTS

- **CRP > 40 mg/L was consistently associated with bacterial case groups (all p<0.05)**
  - Strongly assoc. with Confirmed Spn and Non-Spn bacterial pneumonia (**FIGURE 1**)
  - High density Spn, in NP/OP and/or whole blood, and any Spn positivity
  - High density Hinf in NP/OP and any Hinf positivity
- **CRP > 40 mg/L was inconsistently associated with viral case groups** (**FIGURE 1**)
  - No association found for cases positive for any virus vs. negative for all viruses (aOR=0.92; 95%CI: 0.73,1.15) (not shown)
  - Elevated CRP was less common in RSV+ compared to RSV− cases (p=0.08)
  - Elevated CRP was more common in human metapneumovirus (hMPV)+ cases (p=0.05) and also for influenza+ but did not reach statistical significance

CONCLUSIONS

- Elevated CRP was positively associated with confirmed pneumococcal and non-pneumococcal bacterial pneumonia in PERCH and negatively associated with RSV positivity; its usefulness to inform or validate etiology in PERCH cases is being further evaluated.
- Variation by site suggests that bacterial etiologies may be more common in the African than Asian sites; this may in part be due to early treatment with antibiotics in the Asian sites with high access to care (e.g., the Bangladeshi site was nested in active respiratory disease case-finding surveillance).
- While elevated CRP was uncommon in RSV+ cases, especially CRP > 40 mg/L (only 2.1%), elevated CRP was positively associated with influenza and hMPV. Although this may indicate synergistic bacterial co-infection in these cases, the association remained after excluding cases with evidence of bacterial infection.
- The increased frequency of elevated CRP in RSV+ cases with high density Spn and Hinf compared to RSV− cases without evidence of bacterial infection may provide a clue as to the proportion of RSV+ cases with a concurrent bacterial infection.

References:

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