

SUPPLEMENTARY MATERIALS AND METHODS

State-wide multi-center retrospective linkage study of all children <16-years requiring PICU admission in Queensland, Australia, from January 1st 2008 until December 31st 2013(1). During this 6-year period, two units (19-bed PICU; Mater Children`s Hospital, and 8-bed PICU; Royal Children`s Hospital) provided pediatric intensive care services for the state of Queensland and northern New South Wales, capturing a pediatric population of 987,481 (2015 census). The institutional review board approved the protocol including waiver of informed consent. The prospective PICU and microbiology databases of both institutions including the statewide public laboratory system (Queensland Pathology) were linked using unique patient identifier numbers, date of birth, date of pathology result and PICU admission and discharge dates.

Case definition

Patients with severe *Mycoplasma pneumoniae* infection were defined as children admitted to the PICU with *both* positive laboratory results and a clinical presentation consistent with *M. pneumoniae* infection. Clinical phenotypes included in the study were: Atypical pneumonia, tracheobronchitis, acute respiratory distress syndrome, myocarditis, encephalitis, acute disseminating acute encephalitis, Steven-Johnson syndrome, erythema multiforme, Guillain-Barre Syndrome, myasthenia gravis, and other autoinflammatory conditions possibly linked to *Mycoplasma pneumoniae*. During the study period it was routine practice at both tertiary institutions to request testing for *Mycoplasma* if the patients had symptoms suggestive of *Mycoplasma* infection. In addition, prolonged treatment with macrolide antibiotics for >48 hours required infectious disease specialist approval which was not usually provided in the absence of *Mycoplasma* testing.

Cases were reviewed by two clinicians (KM, LS). We searched the institutional microbiology databases for test results in all patients admitted to PICU, within a time window ranging from 72 hours before PICU admission to day of PICU discharge. Detection of *M. pneumoniae* in respiratory samples (from nasopharyngeal or endotracheal aspirates, or bronchoalveolar lavage) was performed using Polymerase-Chain Reaction (PCR).

In addition, the prospective institutional PICU databases were searched for *M. pneumoniae* infections using the Australia and New Zealand Pediatric Intensive Care Registry specific diagnostic coding(1), which had been entered by trained PICU nurses supervised by a pediatric intensivist. In patients coded as positive for *M. pneumoniae* infection who had no laboratory evidence of infection in the initial result search, we expanded the search for microbiological results outside the defined time-window to confirm evidence of *M. pneumoniae* infection by either PCR or serological testing (requiring titers >1:160).

The serology test used at both institutions was the gelatin particle agglutination assay measures that measures total immunoglobulin (both IgG and IgM anti—Mycoplasma pneumonia antibodies; but the manufacturer claims predominately IgM is detected) from SERODIA®-MYCO II from Fujirebio incorporated (see <https://www.fujirebio-europe.com/products-services/product-browser/serodiar-myco-ii-25t>).

Statistics

Length of PICU stay was defined as the primary outcome. *M. pneumoniae* cases were compared with PICU patients admitted non-electively with an infection. Subgroups were compared using the Mann Whitney U test and proportions were compared using Fisher exact

or Chi square test. Logistic and linear regression were used to explore associations between binary and log-transformed continuous outcomes. For multivariate analyses, we adjusted for factors that showed a trend for difference between groups ($p < 0.10$). All analyses were conducted using SPSS, Version 22, IBM statistics.

REFERENCES

1. Moynihan K, Barlow A, Alphonso N, Anderson B, Johnson J, Nourse C, et al. Impact of Viral Respiratory Pathogens on Outcomes After Pediatric Cardiac Surgery. *Pediatr Crit Care Med*. 2017;18(3):219-27.