The role of pleural fluid PCR in the diagnosis of pediatric community acquired parapneumonic Empyema

Goor Zamir[1,2], Itzhak Levy[3], Dganit Adam[1], Yuval Geffen[4], Hannah Sprecher[4], Elhanan Nahum[1], Tommy Schonfeld[1]

[1] Pediatric Intensive Care Unit, Schneider Children's Medical Center of Israel, Petach Tikva, Israel. [2] Pediatric Intensive Care Unit , Emek medical center, Afula.[3] Infectious Disease Unit, Schneider Children's Medical Center of Israel (affiliated with Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv), Petach Tikva, Israel. [4] Microbiology Laboratory, Rambam Medical Center, Haifa, Israel

Introduction

- Parapneumonic empyema is a serious complication of pediatric community acquired Pneumonia.
- The causative pathogen is often difficult to diagnose as pleural fluid is frequently sterile at the time of culture, as are blood cultures
- polymerase chain reaction (PCR) assay of the pleural fluid may provide a better diagnostic tool then blood and pleural cultures, but it is not yet considered standard of care.

Study Objective

- **Objective:**
  - The aim of this study was to investigate the impact of PCR assays on the management of children with parapneumonic empyema.
  - To define the etiological pathogens and their incidence in our patients.
- **Hypothesis:** PCR Analysis of pleural fluid increases organism identification ratio compared to pleural fluid and blood cultures and decreases the number of days the child is exposed to unnecessary antibiotic treatment.

Methods

- **Methodology:** A retrospective review of case notes.

- **Study population:** The study group consisted of all infants and children with pleural effusion in which pleural fluid was collected for assessment by PCR between January 1st 2008 and December 31st 2011.

Methods (Cont.)

- **Inclusion criteria:**
  - Age between 0-18 years
  - a clinical and radiological diagnosis of parapneumonic effusion
  - A pleural fluid sample collected during the acute phase of the disease and analyzed by 16s rDNA PCR.
- **Exclusion criteria:**
  - an Immuno-compromised status (such as recent administration of chemotherapy or bone marrow transplantation) or a primary immune deficiency
  - a long standing chronic disease associated with a degraded immune status

Methods (Cont.)

- **Data collected:**
  - demographic data, comorbidity, number of days of ABX prior to admission, and duration of in-hospital treatment were obtained from the patients medical records. Laboratory markers of pleural fluid, blood and pleural fluid cultures and PCR result were also collected.
- **Outcome measures:**
  - number of positive PCR samples.
  - Type of bacteria detected in pleural fluid PCR
  - number of patients in whom antibiotic treatment was changed following the result of pleural fluid PCR analysis.

Results

- 128 children meet the inclusion criteria
- 32 children were excluded according to the exclusion criteria
- 96 children were included in the study

Results (Cont.)

- 55 boys and 41 girls.
- Average age 59 ± 48 months, median 46.
- Background medical problems were reported in 12 (12.5%), seven of which were recurrent pneumonia.
- Sixteen patients (16.6%) were transferred from other hospitals

Results (Cont.)

- Previous antibiotic treatment in 50 patients (52%).
- Duration of Previous antibiotic treatment was 5.5 ± 5 days, median 4, range 0-28 days, interquartile range (IQR) 2-8 days.
- Length of hospitalization was 13 ± 15 days, median 11.5, range 2-85, IQR 9-15.

Pleural fluid parameters

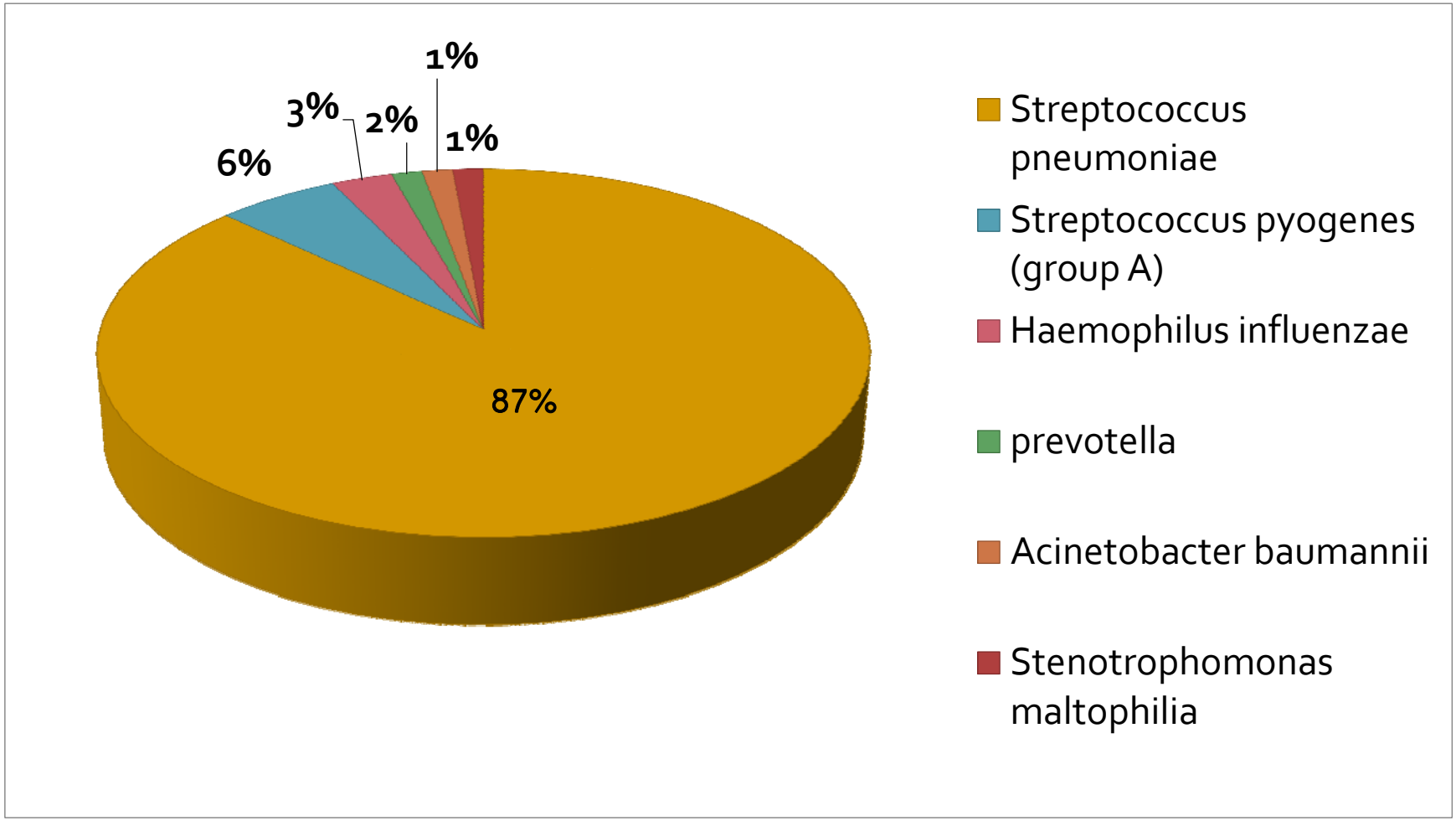
Pleural Fluid color				
unknown	clear	serotic	turbid	pus
31 (32.2%)	6 (6.25%)	17 (17.7%)	13 (13.5%)	29 (30%)

	Number of cases	Mean ± SD	Median	IQR
Protein	81/96	4.4 ± 1.1	4.5	0.5-6.8
Glucose	83/96	37 ± 37	5	1-67
LDH	81/96	16,300 ± 13,500	8,000	2,000 – 18,000
WBC	84/96	40K ± 96K	13K	2.5K – 31K
PH	77/96	7.1 ± 0.4	7.1	6.4 – 7.4

Pleural fluid PCR analysis

- 68 (70%) pleural fluid samples were positive for bacteria by PCR analysis
- 28 (30%) were negative
- In most samples only one type of bacteria was found, in one sample two types of bacteria (Streptococcus pneumoniae and Haemophilus influenzae) were reported.

Causative organisms detected by PCR



Pleural fluid parameters

	PCR (-)	PCR (+)	P value
PH	7.3 ± 0.3	7.0 ± 0.4	>0.05
WBC	15,189 ± 25,686	51,925 ± 114,850	>0.05
LDH	3,394 ± 5,535	18,494 ± 17,517	>0.05
Glucose	62 ± 36	18 ± 30	>0.05
Protein	4.6 ± 1.3	4.3 ± 0.9	0.13

Pleural fluid culture

- Positive in only 8 (8.3%) patients, PCR was positive in 7/8 patients. One patient had positive pleural fluid culture and negative PCR analysis (Streptococcus pneumoniae in culture)
- 4/8 (50%) had background medical problems

Streptococcus pneumoniae	Haemophilus influenzae	Streptococcus pyogenes (group A)	Prevotella
5	1	1	1

Pleural fluid culture

- Duration of Previous antibiotic treatment was 6.6 ± 7.7 days, median 2.5 days.
- 4/8 had less then a day of previous ABX
- 3/8 had over 11 days of ABX
- Average time for pleural fluid culture growth was 2 ± 1.6 days, median 1.5 days (considerably shorter then PCR result)

Blood culture

- Positive in only 8 (8.3%) patients, PCR was positive in all patients.
- Only one patient had both blood and pleural cultures positive.
- Duration of Previous antibiotic treatment was 2.6 ± 1.6 days, median 2.5 days.

Streptococcus pneumoniae	Haemophilus influenzae	Multiple bacterial growth
7	1	1

Treatment

- In 28 patients ABX treatment was changed following PCR result (41% of positive PCR), ABX being downgraded in all.
- In 13 patients (19% of positive PCR) no ABX treatment change was necessary (treated with Ceftriaxone).
- No statistically significant difference in length of hospitalization (P=0.16).

Discussion

- This is the largest series of pleural fluid PCR analysis reported in pediatric literature to date.
- The first large pleural fluid PCR series reported in our region.
- PCR analysis yielded a bacterial causative agent in 70% of patients compared to 16% using only blood and pleural fluid cultures.

Discussion (Cont.)

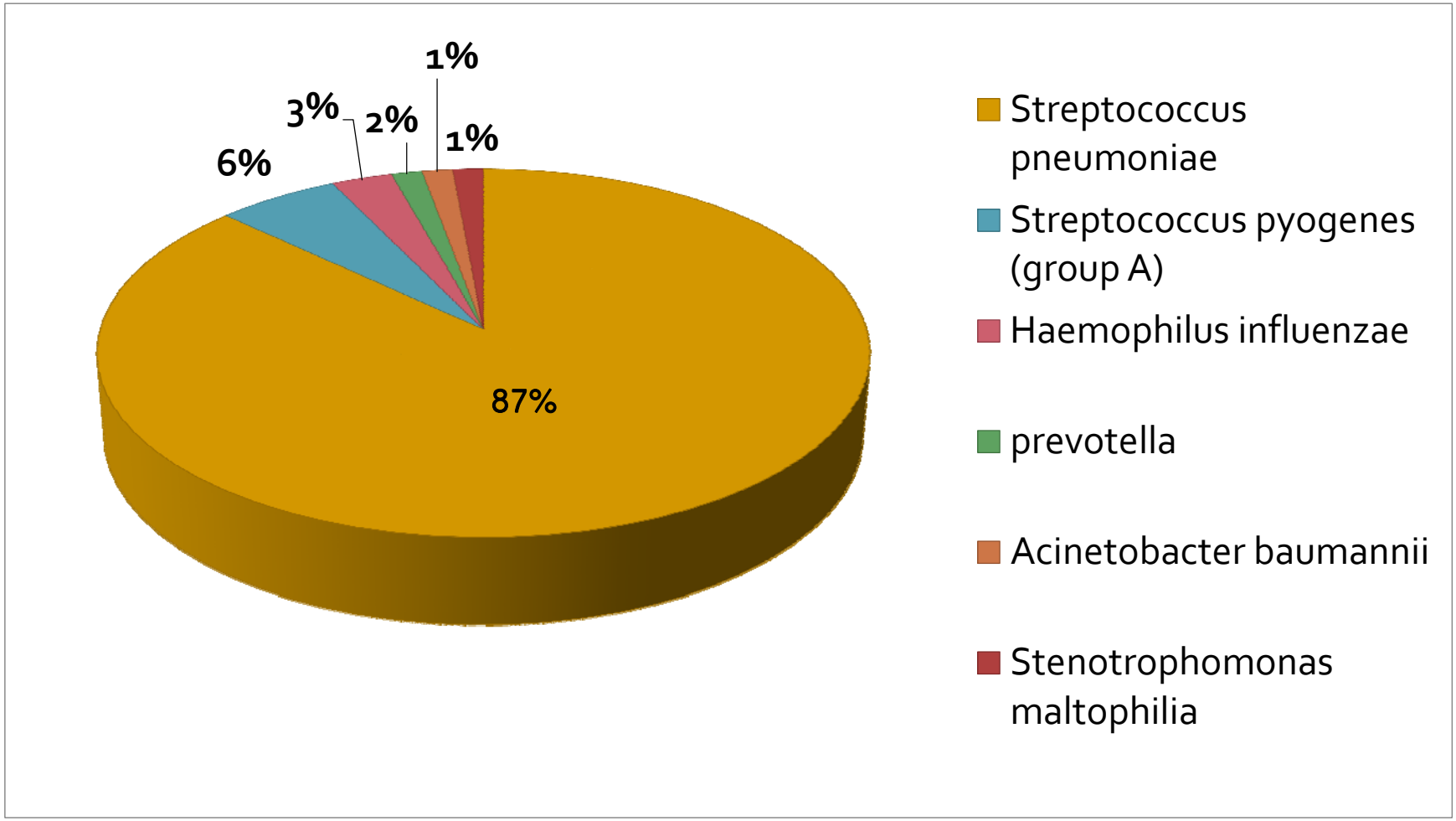
Author	finding	country
Obando et al. 2008	67/99 (67%)	Spain
Hernandez-Bou et al. 2009	72 /111 (64%)	Spain
Strachan et al. 2012	43/79 (54%)	Australia
Eastham et al. 2004	32/43 (75%)	England

Discussion (Cont.)

- ***No*** cases of Staphylococcus aureus were found in this study (including the patients excluded from the study – 128 samples).

- Should routine ABX treatment for parapneumonic empyema include coverage for Staphylococcus aureus, or should it be limited to special cases?

Causative organisms detected by PCR

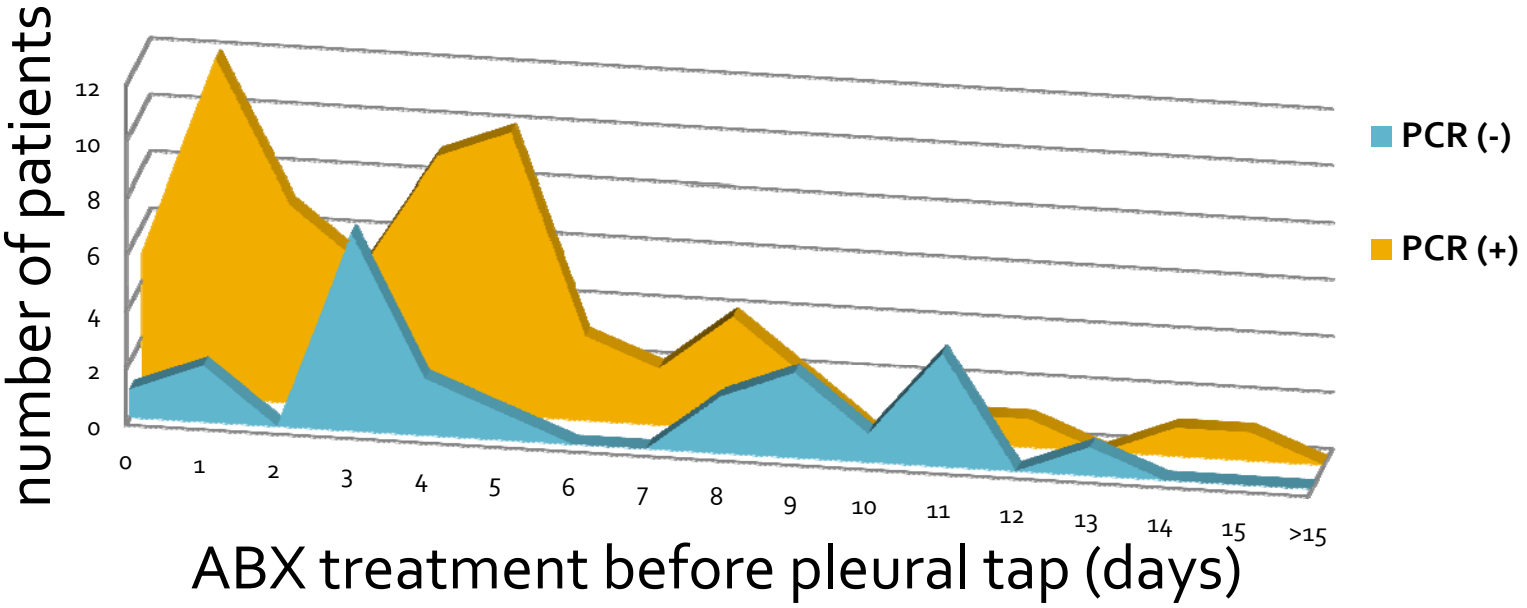


Discussion (Cont.)

- The PCR analysis, as used in this study is insensitive to *Mycoplasma* Infections, which could explain same of the negative results.

- Further research is needed in order to explore the prevalence of *Mycoplasma* Infections in these patients.

The correlation between length of ABX treatment and PCR result



Discussion (Cont.)

- PCR is affected by previous ABX treatment, but less so then pleural fluid cultures.
- Pleural fluid samples intended for PCR analysis should be obtained, delivered to the lab and performed as soon as possible in order to significantly affect treatment.

The End

- Questions?