Acute Hypoxemic Respiratory Failure and ARDS in 26 Pediatric ICU in 2006 in China

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Background

- Pediatric acute hypoxemic respiratory failure (AHRF) is characterized as persistent and severe hypoxemia and one of the hallmarks of ALI and ARDS
- A common reason of mortality in pediatric ICU
- High incidence, mortality and cost
- Incidence of AHRF in PICU in west 2%-4.4%; mortality 72%? 25-30%

Background

2005, Trachsel D, Toronto

- **Incidence** 2.3% (135/5677), mortality 27% (55/131)
- **Primary disease** pneumonia (50%); sepsis (46%); trauma (11%)

2005, multi-center pediatric ARDS study in China

- **Incidence**: 1.44%; mortality 61%
- **Limitation**: only ARDS, observational study
- **No protocol for lung protective ventilation and PICU level approximate that of west in later 80’s**

Yu WL. Unpublished data
Objective

- To obtain epidemiological data of pediatric AHRF, ALI and ARDS in China
- To evaluate the influence of collaborative clinical study on incidence, mortality and cost of AHRF, ALI and ARDS in comparison to the data from 2004-2005 ARDS study
- To assess clinical cost-effectiveness of severe respiratory failure in PICU
Importance

- To constitute a network-based collaborative group in PICU in China
- To have a good understanding of epidemiology of AHRF, ALI and ARDS
- To set up relevant and identical therapeutic procedure, and improve outcome and mortality
- Fundamental for interventional epidemiologic study and international collaboration
Method

- **Design:** multi-center prospective, observational clinical epidemiologic study
- **Study period:** 2005.12.1-2007.6.30 (enrollment for 12 consecutive months)
- **Patient:** 29 days = age = 15 years
- **Data collection:** demographic data, diagnosis, ventilator settings, major complication, cost, etc
- **Endpoint:** discharge, death, 28 d of entry, 48 h after weaning from ventilation, whichever occurred first.
Entry criteria of AHRF, ALI, ARDS

- **Spontaneous breathing, hypoxemia** defined by
  \[ \text{PaO}_2 = 50 \text{ mmHg} \text{ (or } \text{PaO}_2/\text{FiO}_2 = 250 \text{ mmHg}), \text{ for at least 6 consecutive hours} \]

- **Mechanically ventilated, requiring** \( \text{FiO}_2 = 30\% \), \( \text{PEEP} = 2 \text{ cmH}_2\text{O} \) to achieve \( \text{SpO}_2 = 90\% \text{ or } \text{PaO}_2 = 60 \text{ mmHg} \) for at least 6 hours

- **1994 AECC definition for ALI and ARDS**
  
  Acute onset (7 days), \( \text{P/F}<300/200 \text{ mmHg} \)

  Bilateral infiltration on CXR and no cardiogenic edema
Collaborative centers

- The study was conducted at 26 PICU
- 12 of them are university affiliated; 11 from relatively developed area such as Shanghai, Beijing, Zhejiang, Guangdong, Fujian, etc.
- Other 14 are provincial children’s hospital
- Each center serves population 5-10 million
- All were numbered 1-26 according to the alphabet order of the name
## Collaborative centers: 26 PICU

<table>
<thead>
<tr>
<th>Children’s Hospital of Fudan University</th>
<th>Children’s Hospital of Suzhou University</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beijing Children’s Hospital of Capital Medical University</td>
<td>Dalian Children’s Hospital</td>
</tr>
<tr>
<td>Children’s Hospital of Chongqing Medical University</td>
<td>Chengdu Children’s Hospital</td>
</tr>
<tr>
<td>Shanghai Children’s Medical Center of Shanghai Jiaotong University</td>
<td>Jinan Children’s Hospital</td>
</tr>
<tr>
<td>Children’s Hospital of Capital Institute of Pediatrics</td>
<td>Shanxi Children’s Hospital</td>
</tr>
<tr>
<td>Peking University First Hospital</td>
<td>Second Hospital &amp; Yuying Children’s Hospital of Wenzhou Medical College</td>
</tr>
<tr>
<td>Tianjing Children’s Hospital</td>
<td>Shenzhen Children’s Hospital</td>
</tr>
<tr>
<td>Guangzhou Children’s Hospital</td>
<td>Quanzhou Children’s Hospital</td>
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<tr>
<td>Hebei Children’s Hospital</td>
<td>Second Hospital of Chinese Medical University</td>
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<tr>
<td>Harbin Children’s Hospital</td>
<td>Kunming Children’s Hospital</td>
</tr>
<tr>
<td>Hubei Children’s Hospital</td>
<td>Guiyang Children’s Hospital</td>
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<tr>
<td>Changchun Children’s Hospital</td>
<td>Wuhan Children’s Hospital</td>
</tr>
<tr>
<td>Second Hospital of Hebei Medical University</td>
<td>Jiangxi Children’s Hospital</td>
</tr>
</tbody>
</table>
Protocol execute
Supervision

Data analysis
Report periodically
Figure out problems
Ask for solution

Collaborative center
investigator

Data collection
and deliver

Coordinating center

AHRF Network Website
Approval from ethical committee

Study agreement

Protocol

Data forms

Finished data forms

Newsletter

Note book for patient screen
Means of communication

- Website (http://www.shlung.com)
- E-mail
- Telephone
- Fax
- Newsletter per 2 weeks
- Periodic conference
Results—General information

16921 PICU patients in 12 m

Non-critical 5316

Scores

Critical patient 11605

Pediatric 9413 (81%)

Surgery 1526 (13%)

Others 666 (6%)
Results—General information

- Critical patient 11605

- Ventilation 2242 (19%)
  - Respiratory failure 2929 (25%)
  - Sepsis 814 (7.0%)
  - Pneumonia 5390 (60.1%)
  - Trauma 286 (2.5%)

- Death 1241
  - Mortality 10.7%
Results—General information

Report case 481

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHRF</td>
<td>104</td>
<td>29</td>
</tr>
<tr>
<td>ALI</td>
<td>62</td>
<td>18</td>
</tr>
<tr>
<td>ARDS</td>
<td>291</td>
<td>53</td>
</tr>
</tbody>
</table>

457 enrolled (3.9%)

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>353 ALI</td>
<td>3.1%</td>
<td></td>
</tr>
<tr>
<td>291 ARDS</td>
<td>2.5%</td>
<td></td>
</tr>
</tbody>
</table>
AHRF incidence in different centers

% of PICU critical patients of individual hospital
No. 27 was the mean level of all hospitals
Results—General information

- Out of 457 AHRF, male 323 (71%)
- Median age 11 m (range 29 days-15 years), and weight 9 kg (2-77 kg)
- Median onset of AHRF 72 h (0-480 h), 95% enrolled in 384 h (6 d)
- 354 (75%) patients were mechanically ventilated at enrollment, 47 (10%) CPAP and 71 (15%) without respiratory support
Results—Mortality

- AHRF hospital mortality was 40.3% (184/457, 95% CI 35.7-44.8%)
- Pulmonary origin AHRF 352, 134 died (38%)
  Extra-pulmonary AHRF 105, 50 died (48%, p=0.08)
- ARDS 43.3% (126/291, 37.6-49%), (vs. PICU 10.7%, p<0.01); vs. non-ARDS (34.9%, 58/166, P>0.05)
- Mortality was higher in patients with sepsis than those without sepsis (52% vs. 38%, x²=5.3, p<0.05; OR 1.8, 95% CI 1.1-3.1)
Summary of Mortality

- **PICU**: N=124111605
- **AHRF**: N=184/457
- **ALI**: N=143/353
- **ARDS**: N=126/291
- **2005 ARDS**: N=64/108

Mortality (%)
Mortality of AHRF caused by different diseases

- Pulmonary AHRF: N=134
- Extra-pulmonary AHRF: N=50
- Sepsis AHRF: N=36
- Non-sepsis AHRF: N=148
Mortality in different Centers

![Graph showing mortality rates in different centers for ARDS, AHRF, and PICU.](image)
Results—Mean PICU stay

- PICU: 6.5 days
- AHRF: 12 days
- ARDS: 13 days

- Total: 15 days
- Survivor: 16 days
% of patients discharged home or survived to discharge or death after enrollment

- AHRF (17)
- AHRF Survivor (22)
- Death (10)
Results—Primary disease

- Pulmonary 77%, extra-pulmonary 23%

- Pneumonia, 75%
- Sepsis, 15%
- Near-drowning, 3%
- Lung contusion, 1%
- Cardiopulmonary bypass, 2%
# Primary disease and mortality

<table>
<thead>
<tr>
<th>Primary</th>
<th>N (%)</th>
<th>Death (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pulmonary</strong></td>
<td>352 (77)</td>
<td>134 (73)</td>
<td>38</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>343 (75)</td>
<td>131 (72)</td>
<td>38</td>
</tr>
<tr>
<td>Lung hemorrhage</td>
<td>3 (0.6 )</td>
<td>3 (2)</td>
<td>100</td>
</tr>
<tr>
<td>Lung contusion</td>
<td>6 (1.3 )</td>
<td>0 (0)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Extra-pulmonary</strong></td>
<td>105 (23)</td>
<td>50 (27)</td>
<td>48</td>
</tr>
<tr>
<td>Sepsis</td>
<td>68 (15)</td>
<td>36 (20)</td>
<td>53</td>
</tr>
<tr>
<td>Near drowning</td>
<td>12 (3)</td>
<td>3 (2)</td>
<td>25</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Bypass</td>
<td>7 (1.5)</td>
<td>1</td>
<td>33.3</td>
</tr>
<tr>
<td>Aspiration</td>
<td>3 (0.6)</td>
<td>1</td>
<td>44.4</td>
</tr>
<tr>
<td>Others</td>
<td>13 (3)</td>
<td>8 (4)</td>
<td>62</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>457 (100)</td>
<td>184 (100)</td>
<td>40</td>
</tr>
<tr>
<td>Preexisting medical conditions</td>
<td>Case(%)</td>
<td>Death(%)</td>
<td>Mortality(%)</td>
</tr>
<tr>
<td>------------------------------------------------</td>
<td>---------</td>
<td>----------</td>
<td>--------------</td>
</tr>
<tr>
<td>Bronchopulmonary dysplasia</td>
<td>4 (0.9)</td>
<td>3 (1.6)</td>
<td>75.0</td>
</tr>
<tr>
<td>Pulmonary Hemosiderosis</td>
<td>5 (1.1)</td>
<td>2</td>
<td>40.0</td>
</tr>
<tr>
<td>Post-operation</td>
<td>22 (4.8)</td>
<td>10 (5.4)</td>
<td>45.5</td>
</tr>
<tr>
<td>Malignant disease</td>
<td>17 (3.7)</td>
<td>9 (4.9)</td>
<td>52.9</td>
</tr>
<tr>
<td>Aspiration of gastric contents</td>
<td>8 (1.8)</td>
<td>6 (3.3)</td>
<td>75</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>3 (0.7)</td>
<td>1</td>
<td>33.3</td>
</tr>
<tr>
<td>Others</td>
<td>195 (42.7)</td>
<td>87 (47.3)</td>
<td>44.6</td>
</tr>
<tr>
<td>None</td>
<td>203 (44.4)</td>
<td>66 (35.9)</td>
<td>32.5</td>
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</tbody>
</table>
Results—— Cost in PICU

- PICU critical patients: mean cost $6113 (924/d)
- AHRF: mean cost $20,417 (1,722/d), survivor $23,170 (1,563/d)
- ARDS: mean cost $23,100 (1,833/d), survivor $27,444 (1,638/d)
- Unit in Yuan (CNY), 1 USD=8 CNY
PICU cost (x1, 000 Yuan, CNY)
PICU cost in different Centers

1. ARDS
2. AHRF
3. PICU
PICU cost/d in different Centers

- AHRF
- AHRF survivor
- PICU

- ARDS
- ARDS survivor
- PICU

1000 CHY/d

Code of Centers
## Data from different area or level

<table>
<thead>
<tr>
<th>Area</th>
<th>Incidence</th>
<th>Mortality</th>
<th>Mean cost</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AHRF</td>
<td>ARDS</td>
<td>AHRF</td>
</tr>
<tr>
<td>Developed (14)</td>
<td>3.6%</td>
<td>2.4%</td>
<td>40%</td>
</tr>
<tr>
<td>Undeveloped (12)</td>
<td>4.4%</td>
<td>2.2%</td>
<td>41%</td>
</tr>
<tr>
<td>University (12)</td>
<td>3.7%</td>
<td>2.5%</td>
<td>44%</td>
</tr>
<tr>
<td>Non-university (14)</td>
<td>4.2%</td>
<td>2.4%</td>
<td>36%</td>
</tr>
</tbody>
</table>
Discussion

● This study is the first prospective, multicenter, observational, epidemiologic study of AHRF, ALI and ARDS in China

● Participants came from 18 provinces and 4 municipalities, covered most part of the nation except the western regions

● 11 centers from relative developed area and 12 were university affiliated

● The results of this study represent real situation of respiratory care in leading PICU in China
Discussion

- Incidence of AHRF was 3.9%, similar to those in Peters’s and Trachsel’s studies
- Incidences of AHRF widely varied between the 26 centers (range 0.6-31%), a control of inclusion criteria is not efficient
- The mortality of AHRF (40.3%) was higher than that in the developed countries (20-25%)
- Fundation for conducting interventional (controled) investigation in AHRF

Epidemiological data of AHRF/ARDS

<table>
<thead>
<tr>
<th>Author</th>
<th>Pub.</th>
<th>Period</th>
<th>Case</th>
<th>Incidence (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHRF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Debruin</td>
<td>1992</td>
<td>86/7-90/3</td>
<td>100</td>
<td>4.4</td>
<td>72</td>
</tr>
<tr>
<td>Peters</td>
<td>1998</td>
<td>95/8-97/5</td>
<td>118</td>
<td>14</td>
<td>22</td>
</tr>
<tr>
<td>Randolph</td>
<td>2003</td>
<td>00/10-01/4</td>
<td>303</td>
<td>6</td>
<td>1.6</td>
</tr>
<tr>
<td>Trachsel</td>
<td>2005</td>
<td>95/6-97/4</td>
<td>134</td>
<td>2.3</td>
<td>27</td>
</tr>
<tr>
<td>ARDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timmons</td>
<td>1991</td>
<td>87/8-90/8</td>
<td>44</td>
<td>1.5</td>
<td>75</td>
</tr>
<tr>
<td>Kühl</td>
<td>1996</td>
<td>92/1-93/1</td>
<td>112</td>
<td>0.7</td>
<td>46</td>
</tr>
<tr>
<td>Lu</td>
<td>2003</td>
<td></td>
<td>21</td>
<td>1.34</td>
<td>71.4</td>
</tr>
<tr>
<td>Flori</td>
<td>2005</td>
<td>96/7-00/5</td>
<td>221</td>
<td></td>
<td>26</td>
</tr>
<tr>
<td>Yu</td>
<td>2005</td>
<td>04/1-04/12</td>
<td>104</td>
<td>1.44</td>
<td>61</td>
</tr>
</tbody>
</table>

Pub=Publication year
Discussion

- In this study, pneumonia was the predominant primary disease (75%), followed by sepsis (15%), which differed from other studies with 30-50% and 24-46% respectively.
- None of 457 AHRF had underlying diseases as bone marrow or liver transplant.
- Difference in the disease severity may exist compared to the published reports.

### Primary disease of AHRF/ARDS (%)

<table>
<thead>
<tr>
<th>Author</th>
<th>Pn.</th>
<th>Sep.</th>
<th>Tra.</th>
<th>ND.</th>
<th>As.</th>
<th>BMT.</th>
<th>IS.</th>
<th>LT.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AHRF</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Debruin</td>
<td>84</td>
<td>13</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Randolph</td>
<td>37</td>
<td>34</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>8</td>
<td>34</td>
<td>9</td>
</tr>
<tr>
<td><strong>ARDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timmons</td>
<td>14</td>
<td>16</td>
<td>7</td>
<td>18</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lu</td>
<td>29</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>47</td>
<td>0</td>
</tr>
<tr>
<td>Flori</td>
<td>35</td>
<td>13</td>
<td>0</td>
<td>9</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Yu</td>
<td>55</td>
<td>23</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

Pn=Pneumonia; Sep=Sepsis; Tra=Trauma; ND=Near drowning; As=Aspiration; BMT=Bone marrow transplant; IS=Immunosuppression; LT=Liver transplant
Discussion

- 291 patients AHRF and ARDS had a higher mortality vs non-ARDS AHRF
- PICU cost was higher in centers from developed compared with underdeveloped area, but there were no difference between these two groups in mortality of AHRF and ARDS
- Reason: more give up due to economics
Regional Economic Development

- 2004 GDP 21,239 + 15,001 (Median 15,000, range 8,867-54,510) Yuan (CNY)
- 2004 Urban resident income: 10,130 + 2,871 (Median 9,221, range 7,471-16,683) Yuan (CNY)
- 2004 average annual income: 5,645 Yuan

8 Yuan = 1 US Dollar
1 kg meat = 20-30 Yuan, 1 kg rice = 0.4 Yuan
1 L gasolin = 5 Yuan, 1 kwh electricity = 1 Yuan
**Discussion**

- Compared to non-university centers, both mortality and cost of AHRF and ARDS were higher in university centers, patient severity.
- Modalities of treatments in AHRF were with considerable variation between the 26 centers, this might be one of the reasons for the wide variation of mortalities between the centers.
Conclusion

- The mortality of AHRF in China was higher than that in developed countries.
- There are significant differences between the hospitals in cost and treatment level.
- Interventional efforts should be made to ensure facility, protocol identity, staff competence, and quality of the investigation.