Role of Influenza Among Pediatric Hospitalizations for Respiratory Disease: A Review of the Literature

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**Background**

- **Estimating** influenza disease burden
  - Population-based studies
  - Model-based estimation
- **Uses** of prevalence data
  - Influenza testing as part of surveillance/etiology studies
  - Proportion of respiratory illness positive for influenza: parameter for disease burden
  - Complement incidence-based estimates
Objective

Summarize published data on the proportion of respiratory illness positive for influenza virus

• Emphasis on severe illness
• By age, setting, case definition

Focus on pediatric inpatients
Literature Search

- All indexed articles published since 1996
  - Pubmed, Embase, Web of Science
  - Search terms:
    - (Respiratory infection, influenza-like illness, SARI, ILI, ALRI, pneumonia, bronchiolitis)
    + (influenza, viral etiology)
    + (surveillance, epidemiology)
- Laboratory confirmation of influenza
Inclusion Criteria

• Articles containing:
  • Original human data
  • Community-acquired infection
  • At least 12 continuous months influenza testing
  • Criteria/case definition for influenza testing
  • Influenza diagnostic test type
  • Total tested and total influenza positive
  • N \geq 50 tested
Data Abstraction

- **Key data elements included:**
  - Study location/setting
  - Time frame/year
  - Age range
  - Case definition
  - Diagnostic test used
  - Number tested for influenza
  - Number positive, by subtype if available
  - Additional data: underlying conditions, severity, co-infections
Article Review

4644 Citations identified → 3648 Citations excluded

996 Articles reviewed → 737 Articles excluded

259 Articles included → 180 Articles without pediatric inpatient data

79 Articles with pediatric inpatient data + 21 Additional articles from outside search
Description of Included Articles

\((N=100)\)

- 97 Data sets
- 34 Countries:
  - All WHO regions
  - All World Bank income categories
- 1 – 20 Years of data, covering 1980 – 2010
- Most common:
  - Study age range: Less than 5 years
  - Case definition: Acute Respiratory Infection (ARI)
  - Testing: Multiple tests, RT-PCR alone, IFA alone
Africa Articles

- **Kenya:**

- **Morocco:**

- **Mozambique:**

- **Nigeria:**

- **South Africa:**
<table>
<thead>
<tr>
<th>Country</th>
<th>First Author</th>
<th>Year</th>
<th>Test Used</th>
<th>Percent Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>Hussey</td>
<td>2000</td>
<td>culture</td>
<td>0.6%</td>
</tr>
<tr>
<td>South Africa</td>
<td>Smuts</td>
<td>2008</td>
<td>IFA</td>
<td>0.9%</td>
</tr>
<tr>
<td>South Africa</td>
<td>Venter</td>
<td>2011</td>
<td>IFA, PCR</td>
<td>1.7%*</td>
</tr>
<tr>
<td>Morocco</td>
<td>Barakat</td>
<td>2011</td>
<td>IFA, culture</td>
<td>1.7%</td>
</tr>
<tr>
<td>Mozambique</td>
<td>O'Callaghan-Gordo</td>
<td>2011</td>
<td>PCR</td>
<td>4.8%</td>
</tr>
<tr>
<td>Kenya</td>
<td>Berkley</td>
<td>2010</td>
<td>PCR</td>
<td>5.8%</td>
</tr>
<tr>
<td>South Africa</td>
<td>Madhi</td>
<td>2000</td>
<td>DFA, culture</td>
<td>8.6%</td>
</tr>
<tr>
<td>Nigeria</td>
<td>Johnson</td>
<td>2008</td>
<td>IFA, paired serology</td>
<td>15.6%</td>
</tr>
</tbody>
</table>

*Tested for influenza A only
## Overall Percent Influenza Positive

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Median</th>
<th>Interquartile Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Children 0-18*</td>
<td>93</td>
<td>5.0%</td>
<td>2.4% – 8.4%</td>
</tr>
<tr>
<td>Influenza A</td>
<td>68</td>
<td>4.0%</td>
<td>1.6 – 7.1%</td>
</tr>
<tr>
<td>Influenza B</td>
<td>64</td>
<td>0.6%</td>
<td>0.1 – 1.7%</td>
</tr>
<tr>
<td>Under 5 Years</td>
<td>52</td>
<td>4.7%</td>
<td>2.5 – 8.2%</td>
</tr>
<tr>
<td>Under 2 Years</td>
<td>25</td>
<td>3.7%</td>
<td>1.7 – 5.6%</td>
</tr>
</tbody>
</table>

*Age range of 1 study extended inpatients at pediatric hospital up to 20 years*
### Influenza Positive by Key Variables

<table>
<thead>
<tr>
<th>By Income Level:</th>
<th>N=</th>
<th>Median</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low/Middle</td>
<td>44</td>
<td>5.1%</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>49</td>
<td>4.9%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>By Case Definition:</th>
<th>N=</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory Infection (ARI/ARTI)</td>
<td>35</td>
<td>3.6%</td>
</tr>
<tr>
<td>Lower Respiratory Infection (ALRI/LRTI)</td>
<td>23</td>
<td>5.3%</td>
</tr>
<tr>
<td>Pneumonia (CAP)</td>
<td>18</td>
<td>7.3%</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>6</td>
<td>4.1%</td>
</tr>
<tr>
<td>High Risk (HIV, cancer)</td>
<td>7</td>
<td>5.1%</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>3.7%</td>
</tr>
</tbody>
</table>
# Influenza Positive by Diagnostic Test

<table>
<thead>
<tr>
<th>Test Used:</th>
<th>DFA</th>
<th>IFA</th>
<th>PCR</th>
<th>Culture</th>
<th>Multiple</th>
<th>Other</th>
<th>KW test p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=</td>
<td>8</td>
<td>18</td>
<td>24</td>
<td>7</td>
<td>33</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Median:</td>
<td>3.3%</td>
<td>2.6%</td>
<td>5.0%</td>
<td>4.5%</td>
<td>7.0%</td>
<td>1.7%</td>
<td>0.015</td>
</tr>
</tbody>
</table>

![Box plot showing percent positive for different diagnostic tests](image-url)
Influenza Positive, PCR/Culture

<table>
<thead>
<tr>
<th>Test Used:</th>
<th>PCR +/- Culture</th>
<th>All Other Tests</th>
<th>Rank Sum p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=</td>
<td>60</td>
<td>33</td>
<td>0.015</td>
</tr>
<tr>
<td>Median:</td>
<td>5.5%</td>
<td>3.1%</td>
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The table above shows the comparison between PCR +/- Culture and All Other Tests in terms of the median percent positive. The rank sum p-value indicates a statistically significant difference (p < 0.05).
Limitations

• Heterogeneity of data/limited data
  • Predominant strain
  • Vaccine coverage/immunity
  • Time from onset

• Differences in hospitalization/testing practices
  • Between studies
  • Over time
Summary and Next Steps

• Broad global representation
• Consistent percent positive
  • Across age groups, income levels, case definitions
  • Similar to incidence-based studies
• Variation by diagnostic test used
• Next steps:
  • Pooled estimates for children
  • Analysis of adult inpatient articles
  • Collaboration with SARI partners to summarize additional inpatient data for adults and children
Acknowledgements

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Priyanka Wardhan
Marc-Alain Widdowson
CDC PHLIC

Thank you!
### Influenza Positive, PCR/Culture

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**Median:**
- All Other Tests: 3.1%
- PCR +/- Culture: 5.5%