Global burden of pediatric influenza

Dr. Harish Nair
MB BS, DCH, DNB (Paeds.), MSc.

Centre for Population Health Sciences,
The University of Edinburgh
&
Public Health Foundation of India

6 June, 2012   Bali, Indonesia
Global burden of respiratory infections due to seasonal influenza in young children: a systematic review and meta-analysis

Outline

• Background

• Methods

• Incidence rates and number of new cases in young children (0-59 months)

• Mortality estimates
Background

• Globally, ~156 million new episodes\(^1\) and 1.56 million deaths due to ALRI in young children\(^2\) (<5 years)

• Viral aetiologies associated with majority of episodes of ALRI in young children

• RSV associated with:
  ▶ ~34 million ALRI episodes
  ▶ ~3.4 million severe ALRI episodes
  ▶ 3-9% ALRI deaths in children 0-4 years\(^3\)

• Global burden of respiratory infections associated with seasonal influenza- unknown

1. (Rudan et al., Bull WHO, 2008); 2. (Black et al., Lancet, 2010); 3. (Nair et al., Lancet 2010)

ALRI = acute lower respiratory infection, RSV = respiratory syncytial virus
Natural history of influenza infection in children

ALRI = acute lower respiratory infection, AURI = acute upper respiratory infection
4058 records identified through database searching

1625 records after duplicates removed

1625 records screened

120 full-text articles assessed for eligibility

27 full-text articles reported incidence

12 full-text articles reported CFR

13 records identified through other sources

1505 records excluded as not relevant to topic

88 full-text articles excluded
Reason:
49 did not satisfy inclusion criteria;
4 reported prevalence;
35 relate to 2009(H1N1A) pandemic
4058 records identified through database searching

1625 records after duplicates removed

1625 records screened

120 full-text articles assessed for eligibility

1505 records excluded as not relevant to topic

88 full-text articles excluded
Reason: 49 did not satisfy inclusion criteria; 4 reported prevalence; 35 relate to 2009(H1N1A) pandemic

27 full-text articles reported incidence

12 full-text articles reported CFR

43 studies reported incidence (included in meta-analysis)

16 population based unpublished studies identified for supplementary data
Location of published and unpublished studies (n=43)
Methods

• Systematic review of studies published from 1995 to October 2010 – 27 studies

• Influenza Study Group – contributed unpublished data from 16 sites

• Common case definitions

• Adjustment for missing data

• Meta-analysis using random effects model

• Incidence applied to 0-4 year population in 2008 to estimate number of new episodes in 2008
Case definitions

- Influenza-associated acute lower respiratory infection (ALRI):
  - Influenza positive child with cough or difficulty breathing
  - AND tachypnea
Influenza-associated severe acute lower respiratory infection (ALRI):

- Influenza positive child with:
  - a) cough or difficulty breathing AND lower chest wall indrawing
  - OR
  - b) hospitalization for ALRI
Case definitions

- **Influenza episodes** — reflects overall burden of respiratory infections associated with influenza
  
i.e. Influenza positive:
  - ILI
  - + Influenza-associated ALRI
  - + Influenza-associated severe ALRI
Influenza in children 0-59 months per 1000 children / yr

<table>
<thead>
<tr>
<th></th>
<th>Developing countries</th>
<th></th>
<th>Industrialised countries</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Influenza episodes</strong></td>
<td><strong>Influenza-associated ALRI</strong></td>
<td><strong>Influenza-associated severe ALRI</strong></td>
<td></td>
</tr>
<tr>
<td>No. of studies</td>
<td>3</td>
<td>3</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Incidence (95% CI)</td>
<td>154 (84.2, 275)</td>
<td>35 (22.2, 55)</td>
<td>1.7 (1.1, 2.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No. of studies: 3

Incidence (95% CI):

- Developing countries:
  - Influenza episodes: 154 (84.2, 275)
  - Influenza-associated ALRI: 35 (22.2, 55)
  - Influenza-associated severe ALRI: 1.7 (1.1, 2.5)

- Industrialised countries:
  - Influenza episodes: 54.5 (28.1, 105.7)
  - Influenza-associated ALRI: 11.6 (7.5, 18)
  - Influenza-associated severe ALRI: 1.2 (0.9, 1.7)
Number of new cases of Influenza associated respiratory infections in children in 2008

<table>
<thead>
<tr>
<th></th>
<th>Influenza episodes (95% CI) million</th>
<th>Influenza-associated ALRI (95% CI) million</th>
<th>Influenza-associated severe ALRI (95% CI) million</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Developing countries</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-11 months</td>
<td>15.2 (9.7, 24)</td>
<td>2.8 (1, 7)</td>
<td>0.3 (0.2, 0.5)</td>
</tr>
<tr>
<td>0-59 months</td>
<td>87.2 (48, 156)</td>
<td>19.8 (12.6, 31)</td>
<td>0.9 (0.6, 1.4)</td>
</tr>
<tr>
<td><strong>Industrialised countries</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-11 months</td>
<td>0.6 (0.3, 1.1)</td>
<td>0.2 (0.2, 0.2)</td>
<td>.03 (.02, .03)</td>
</tr>
<tr>
<td>0-59 months</td>
<td>3.1 (1.6, 5.9)</td>
<td>0.7 (0.4, 1.0)</td>
<td>.07 (.05, .09)</td>
</tr>
<tr>
<td><strong>Global</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-11 months</td>
<td>15 (10, 24)</td>
<td>2.9 (1.2, 7.2)</td>
<td>0.4 (0.3, 0.5)</td>
</tr>
<tr>
<td>0-59 months</td>
<td>90.3 (49, 162)</td>
<td>20.5 (13, 32)</td>
<td>1.0 (0.7, 1.5)</td>
</tr>
</tbody>
</table>
Influenza associated severe ALRI in children <5 y: estimates by WHO regions

<table>
<thead>
<tr>
<th>WHO Region (number of studies)</th>
<th>Incidence per 1000 children / year (95% CI)</th>
<th>Number of new episodes (95% CI) thousands</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americas (15)</td>
<td>1.2 (0.8, 1.8)</td>
<td>94 (63, 140)</td>
</tr>
<tr>
<td>Western Pacific (7)</td>
<td>2.1 (0.9, 5.1)</td>
<td>255 (105, 620)</td>
</tr>
<tr>
<td>Europe (6)</td>
<td>1.1 (0.7, 1.6)</td>
<td>55 (37, 82)</td>
</tr>
<tr>
<td>SE Asia (4)</td>
<td>1.4 (0.4, 5.6)</td>
<td>257 (65, 1020)</td>
</tr>
<tr>
<td>Africa (7)</td>
<td>1.4 (0.7, 2.5)</td>
<td>180 (97, 332)</td>
</tr>
<tr>
<td>Global estimate</td>
<td></td>
<td>1001 (665, 1503)</td>
</tr>
</tbody>
</table>
Influenza in children: mortality estimation

- 12 full text articles reported CFR data on influenza positive children hospitalised for severe ALRI

- Additionally 8 unpublished studies provided CFR data on influenza positive children with severe ALRI

- Meta-estimates of CFR (9 studies) in developing countries in children 0-59 months – 2.96% (0.79, 5.13)

- Meta-estimates of CFR (8 studies) in industrialised countries in children 0-59 months – 0.17% (0.08, 0.26)
Influenza in children: mortality estimation (lower bounds)

• Using number of new episodes of influenza severe ALRI and CFR meta-estimates, lower bounds of mortality attributable to influenza in children in year 2008

  ► ~28,000 (95% CI- 7400 to 48,000) deaths in <5 year children

  ► True mortality higher - 54% to 90% of ALRI deaths in children occur outside a health facility*

Influenza in children:
upper bound mortality estimate

• Similar to methods used for RSV (Nair et al., Lancet, 2010)

• Using data from VA confirmed ALRI deaths in community by month in a site with clear seasonal influenza peak
  > excess ALRI mortality during influenza season attributed to influenza

• Such data available from Ballabgarh, India (2006-08)

• Based on these data upper bound of estimated global mortality due to influenza-associated ALRI in <5y children
  > ~ 111,500 (range 21,000 to 245,000)

• Over-estimate
  > attributing all excess deaths during influenza season to influenza
  > shared seasonality with other respiratory pathogens (RSV)
Etiology of childhood pneumonia cases: incidence & mortality

**Influenza pneumonia - year 2008**
- 20.45 million episodes (13%) of pneumonia
- ~1 million episodes (7%) of severe pneumonia
- 28-111,500 (2-7%) deaths from pneumonia in children (0-4 years)

**RSV pneumonia - year 2005**
- 33.8 million episodes (22%) of pneumonia
- 3.4 million episodes (23%) of severe pneumonia
- 53-199,000 (3-9%) deaths from pneumonia in children (0-4 years)

**PC pneumonia - year 2000**
- 13.8 million episodes (9%) of pneumonia
- 741,000 deaths (~37%) from pneumonia in 0-<5y children

**Hib pneumonia - year 2000**
- 7.9 million episodes (5%) of pneumonia
- 292,000 deaths (~15%) from pneumonia in 0-<5y children

Limitations

• Preliminary estimates with large uncertainty ranges

• Of all estimates, those for severe episodes most robust as based on relatively large number of data points with narrow 95% Confidence Interval

• Mortality estimates are very crude

• Better data are required for more precise estimates
Acknowledgements

Influenza Study Group

- Harry Campbell, Igor Rudan, V Evans, Evi Theodoratou- CPHS, Edinburgh
- Thailand- Mark Simmerman, Sonja Olsen
- Bangladesh- Abdullah Brooks
- Japan- Peter Wright, Masatoki Sato
- Philippines-Eric Simoes, Marilla Lucero
- India- Anand Krishnan, Shobha Broor
- Cambodia- Sirenda Vong, Philippe Buchy
- Kenya- Mark Katz, Maurice Ope, James Berkley, R Breiman, Walter Ochieng
- Gambia- Steve Howie, T Briese, R Tokarz
- S Africa- Shabir Madhi, Cheryl Cohen, M Venter
- Mozambique- Anna Roca, C O’Callaghan-Gordo
- Egypt - Erica Dueger
- Nicaragua- Aubree Gordon, Eva Harris
- Guatemala- Kim Lindblade
- USA- Eric Simoes, Laurie Kamimoto
- American Indians - Niranjan Bhat
- Marc-Alain Widdowson- CDC
- Brad Gessner- AMP
- Anthony Wayne Mounts- World Health Organization, Geneva