Nutritional status and childhood wheezing in rural Bangladesh

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Introduction:

- Increasing international interest in the causal role of nutrition and other dietary factors in the development of asthma and allergic diseases (Nurmatov U 2012).

- Asthma and allergic manifestations are increasing, especially early in life, in both developed and developing countries (Elizabeth CM et al 2009).

- Currently asthma affects 300 million people worldwide (Braman SS 2006).
Introduction (Cont…)

➢ Obesity has been widely recognized to be more common among children with asthma and the association between higher BMI and overweight were found in many countries like UK, Japan and Taiwan (Figueroa-Munoz J 2001, Okabe Y 2012, Yao TC 2001)

➢ However, very little evidence exists on the potential association between undernutrition and current wheezing/asthma and allergic diseases.
Objectives

➢ To investigate the association between current childhood nutritional status and current wheezing among pre-school children in rural Bangladesh.
Conceptual Framework

Asthma and allergies

Genetic factors

Allergen, pollutant and endotoxin exposure

Exposure to parasites and viruses

Diet, nutrition
Methods

- This cross-sectional study was nested into a large-scale randomized clinical trial of nutrition interventions in pregnancy; the Maternal and Infant Nutrition Intervention in Matlab (MINIMat), rural Bangladesh.

- The icddr,b has been running a health and demographic surveillance system (HDSS) in the area since 1966 that covers a population of about 225,000.
The MINIMat trial was conducted in the Matlab HDSS area from November 2001 to October 2003.

The 4,436 mothers in MINIMat were followed during pregnancy when data on socio-economic status (SES) and morbidity of mothers were collected.

Information about their children’s gestational age, birth weight, birth length were also collected at delivery.
Identification of Individuals

RID (Registered Identification #): It is a 10 digit code given to all population of study area and it never changes – “1V32003202”

- First 1 digit (1) digit for census phase
- Next 3 digits (V32) for Village code
- Next to village code (0032), 4 digits is family code
- Last 2 digits (02) for Individual Number
Explanation on Phase of RID

Phase of RID: The phase of RID changes regarding the census period. Our first census was held in 1974. For this census we have used 1 as phase of the RID, like “1V32003202”.

- 1V32003202, 1 used in 1974, until the next census
- 2VB4046710, 2 used in 1982, until the next census
- 3D34013708, 3 used in 1993, until the next census
- 4C00052008, 4 used in 2000, until the next census
Identification of Individuals

- CID (Current Identification #): It is a 9 digit code given to all population of study area. This code changes when an individual moves within study area – “V32003202”

- First 3 digits (V32) for Village code
- Next to village code (0032), 4 digits is family code
- Last 2 digits (02) for Individual Number
Demographic & Health Data Collection

Household Visit of a CHRW for data collection
Responsibilities of CHRWs

- Health and demographic data collection by visiting households
- Provide diarrhoeal treatment to the patients
- Conduct pregnancy test
- Refer diarrhoeal patients either to icddr,b Sub-center or Matlab Hospital, referral of other patients to Govt. service center
- Assist in special research works
Refresher Training Among Field Staffs
Block / Sub center (contd.)

- This is the second tier of HDSS infrastructure
- Activities are planned based on Blocks
- Block is the place of meeting and refresher training for CHRWs
- CHRWs meets twice in Block in a month
MINIMat Trial

Effects of Prenatal Micronutrient and Early Food Supplementation on Maternal Hemoglobin, Birth Weight, and Infant Mortality Among Children in Bangladesh
The MINIMat Randomized Trial

JAMA, May 16, 2012; Vol 307, No 19
Methods (Cont...)

Fig 1: Flow chart of the study children

No live birth (n=845)
- Abortion (n=111)
- Miscarage (n=236)
- Still birth (n=89)
- Woman died (n=1)
- Migration out (n=188)
- Refuse (n=123)
- Woman too sick (n=1)
- Absent (n=73)
- Due to Ramadan (n=6)
- Not pregnant (n=3)
- Others (n=12)
- Pregnancy >13 weeks (n=2)

Randomized women (n=4436)

Live Birth (n=3591)
- Twin (n=34)

Excluded (n=890)
- Migrated out (n=448)
- Death (n=168)
- Refused (n=225)
- Other reason (n=49)

Follow-up at 4.5 yrs (Group A & B)
- n=2735

Group B (n=1303)
Measurements

- Total IgE was measured by human IgE quantitative ELISA kit

- Specific IgE level against house dust mites (Dermatophagoides pteronyssinus) was measured by the CAP-FEIA system.

- Anti-DP IgE >0.70 UA/ml was considered positive.

- Fresh stools from the participants were collected in the morning for parasite-egg examination.
Measurements (Cont....)

- Immediate hypersensitivity reaction was tested by a skin prick test using mite allergen (Dermatophagoides pteronyssinus).

- Children’s weight was measured to the nearest 100g with a TANITA digital scale.

- Height was measured to the nearest 0.1cm with a Holtain Stadiometer.

- Stunting, wasting and underweight were calculated using the WHO Anthro.
Measurements (Cont....)
Measurements (Cont....)

- Stunting was defined as height-for-age z-score < -2, wasting as weight-for-height z-score < -2, and underweight as weight-for-age z-score < -2

- Current wheezing, ever wheezing and ever asthma were identified using the International Study on Asthma and Allergies in Childhood (ISAAC) questionnaire
## Results

### Table 1: Characteristics of the study participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>480</td>
<td>52.6</td>
</tr>
<tr>
<td>Low birth weight (&lt;2500gms)</td>
<td>241</td>
<td>26.4</td>
</tr>
<tr>
<td>Prematurity (GA&lt;37 weeks)</td>
<td>125</td>
<td>13.9</td>
</tr>
<tr>
<td>Stunting (Height for Age Z-Score &lt; -2)</td>
<td>289</td>
<td>31.7</td>
</tr>
<tr>
<td>Wasting (Weight for Height Z-Score &lt; -2)</td>
<td>158</td>
<td>17.3</td>
</tr>
<tr>
<td>Underweight (Weight for Age Z-Score &lt; -2)</td>
<td>371</td>
<td>40.7</td>
</tr>
<tr>
<td>Ever wheezing</td>
<td>412</td>
<td>45.2</td>
</tr>
<tr>
<td>Current wheezing</td>
<td>180</td>
<td>19.7</td>
</tr>
<tr>
<td>Ever asthma</td>
<td>164</td>
<td>18.0</td>
</tr>
</tbody>
</table>
Table 2: Geometric mean of serum total IgE and positivity of anti-DP IgE, mite antigen skin prick test and helminthes eggs

<table>
<thead>
<tr>
<th></th>
<th>Geo mean (95% CI)</th>
<th>Positive %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total IgE (IU/ml)</td>
<td>526.44 (172.93 - 3039.15)*</td>
<td></td>
</tr>
<tr>
<td>Anti-DP IgE (UA/ml)</td>
<td></td>
<td>44.3</td>
</tr>
<tr>
<td>Mite antigen skin prick test (&gt;5mm)</td>
<td></td>
<td>15.2</td>
</tr>
<tr>
<td>Ascaris lumbricoids eggs (159/912)</td>
<td></td>
<td>17.4</td>
</tr>
<tr>
<td>Trichuris trichura eggs (160/912)</td>
<td></td>
<td>17.5</td>
</tr>
</tbody>
</table>

*Mean (range), IgE-Immunoglobulin E, DP-Dermatophyte Pteronyssinus
Table 3: Association between current wheezing and different parameters

<table>
<thead>
<tr>
<th></th>
<th>Current Wheezing</th>
<th></th>
<th></th>
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<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Yes</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n</td>
<td></td>
<td>n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>92</td>
<td>19.2</td>
<td>388</td>
<td>80.8</td>
<td></td>
<td></td>
<td>0.648</td>
</tr>
<tr>
<td>Female</td>
<td>88</td>
<td>20.4</td>
<td>344</td>
<td>79.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stunting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>72</td>
<td>24.9</td>
<td>217</td>
<td>75.1</td>
<td></td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>No</td>
<td>108</td>
<td>17.3</td>
<td>515</td>
<td>82.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wasting</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>30</td>
<td>19.0</td>
<td>128</td>
<td>81.0</td>
<td></td>
<td></td>
<td>0.795</td>
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<tr>
<td>No</td>
<td>150</td>
<td>19.9</td>
<td>604</td>
<td>80.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>85</td>
<td>22.9</td>
<td>286</td>
<td>77.1</td>
<td></td>
<td></td>
<td>0.046</td>
</tr>
<tr>
<td>No</td>
<td>95</td>
<td>17.6</td>
<td>446</td>
<td>82.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother’s BMI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>40</td>
<td>22.5</td>
<td>138</td>
<td>77.5</td>
<td></td>
<td></td>
<td>0.033</td>
</tr>
<tr>
<td>Normal</td>
<td>113</td>
<td>15.7</td>
<td>605</td>
<td>84.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of asthma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>75</td>
<td>37.3</td>
<td>126</td>
<td>62.7</td>
<td></td>
<td></td>
<td>0.000</td>
</tr>
<tr>
<td>Negative</td>
<td>105</td>
<td>14.8</td>
<td>606</td>
<td>85.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IgE = Immunoglobulin E, DP = Dermatophyte Pteronyssinus
Stunting = height-for-age Z-score < -2, Wasting = weight-for-height Z-score < -2, Underweight = weight-for-age Z-score < -2
Table 4 Univariate and multivariate logistic regression analyses with current wheezing as dependent variable

<table>
<thead>
<tr>
<th></th>
<th>Crude OR</th>
<th>95% CI</th>
<th>Adjusted OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stunting</td>
<td>1.58</td>
<td>1.13 – 2.22*</td>
<td>1.70</td>
<td>1.17 – 2.47*</td>
</tr>
<tr>
<td>Wasting</td>
<td>0.94</td>
<td>0.61 – 1.46</td>
<td>0.88</td>
<td>0.54 – 1.43</td>
</tr>
<tr>
<td>Underweight</td>
<td>1.39</td>
<td>1.00 – 1.94*</td>
<td>1.29</td>
<td>0.89 – 1.85</td>
</tr>
</tbody>
</table>

*P<0.05
†OR = Odds Ratio, CI = Confidence Interval
Adjustment by sex, birth weight, birth length, gestational age at birth, mother’s parity, maternal BMI, family history of asthma, socio-economic status and season of birth.
Discussion

- In this study we found that stunting, an indication of long-term chronic malnutrition was significantly associated with current wheezing in rural Bangladeshi children aged 4.5 years.

- Previous study has also shown that underweight children had lower lung function, and lower body fat was associated with higher occurrence of asthma symptoms (Berntsen S et al 2009).
Discussion (cont....)

- Earlier study suggested that there was a defective T cell response in malnourished children, and that the proportion of total B cells, and those bearing the low-affinity IgE receptor (CD23+) increased in moderately malnourished children (Hagel I et al 2003).

- And those may cause increased specific IgE, which leads to wheezing and asthma symptoms.
Discussion (Cont....)

- Strengths of this study
  - large sample size and good retention of participants.
  - 76% of eligible individuals born during the maternal trial were successfully recruited at 4.5 years of age.
Limitations

- This was a cross-sectional study, the data did not provide direct information on whether stunting is a cause of the development of current wheezing.

- We used a questionnaire based on the ISAAC to diagnose current wheezing.

- Wheezing in children may be attributed to allergic asthma, exercise-induced asthma or be a symptom of viral/other respiratory infections.
The term wheezing is also often misinterpreted by parents and this may produce overestimation or underestimation of the symptoms.

However, the ISAAC questionnaire has been extensively used worldwide and it has reportedly provided an acceptable estimation of the prevalence of asthma in children 2-6 years of age.
Conclusions

- In conclusion, our data suggest that chronic undernutrition has an influence on current wheezing in rural Bangladeshi children.

- Further analysis is required to examine the relationship between nutritional factors and asthma and allergic responses in population such as rural Bangladesh, with a high degree of undernutrition and a growing prevalence of asthma and atopic disease.
Acknowledgement

The study was supported by the International Centre for Diarrhoeal Disease Research, Bangladesh; the UK Medical Research Council; the Swedish Research Council; the UK Department for International Development; the Grant-in-Aid for Scientific Research of the Japan Society for the Promotion of Science (JSPS, Grant #18256005); the Child Health and Nutrition Research Initiative; Uppsala University; the US Agency for International Development, under the Cooperative Agreement #388-G-00-02-00125-00; the Australian International Development Agency and core donor of icddr,b. We are grateful to the study participants for their involvement in the study. We thank the field team members and data management staff for their excellent work.
Thank you all