Low Birth Weight, Stunting and the Intestinal Microbiota in Children in an Urban Slum in South India
D. Dinh, M. Chatterjee, C. Wanke, A. Kane, H. Ward
Tufts Medical Center,
Tufts School of Medicine

E. Naumova, P. Braunstein, S. Hassoun
Tufts School of Engineering

B. Ramadoss, D. Kattula, S. Ajjampur, R. Sarkar, G. Kang
Christian Medical College, Vellore, India
Malnutrition, Infection and the Intestinal Microbiota

Host Genetics

Food insecurity

Impaired Absorption, Barrier Function

Microbiome

Decreased Immune Function

Infection

MALNUTRITION

• Malnutrition is associated with nearly half (45%) of all deaths (~3.1 million) in children <5 years
• 165 million children <5 years were stunted in 2011
• Most of these children live in South Asia
• Largest number of stunted children live in India (61 million, 48% of children <5 years are stunted

DIARRHEAL DISEASE

• Globally 1.3 billion cases per year
• 2nd leading cause of death in children < 5 years
• Causes 11% of ~8 million childhood deaths per year
• Proportion of deaths attributable to diarrhea in children <5 years of age is highest in South Asia
• 31% of deaths due to diarrhea in children < 5 years of age in South Asia

Global causes of childhood deaths

The Burden of Diarrheal Diseases in India

Table 3. **Countries accounting for three-quarters of deaths due to diarrhoea in the developing regions of the world, 2004**

<table>
<thead>
<tr>
<th>Country</th>
<th>WHO subregion</th>
<th>Deaths due to diarrhoea (thousands)</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>SEAR D</td>
<td>535</td>
</tr>
<tr>
<td>Nigeria</td>
<td>AFR D</td>
<td>175</td>
</tr>
<tr>
<td>Democratic Republic of the Congo</td>
<td>AFR E</td>
<td>95</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>AFR E</td>
<td>86</td>
</tr>
<tr>
<td>Pakistan</td>
<td>EMR D</td>
<td>77</td>
</tr>
<tr>
<td>China</td>
<td>WPR B</td>
<td>74</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>SEAR D</td>
<td>69</td>
</tr>
<tr>
<td>Afghanistan</td>
<td>EMR D</td>
<td>65</td>
</tr>
<tr>
<td>Indonesia</td>
<td>SEAR B</td>
<td>39</td>
</tr>
<tr>
<td>Angola</td>
<td>AFR D</td>
<td>34</td>
</tr>
<tr>
<td>Niger</td>
<td>AFR D</td>
<td>33</td>
</tr>
<tr>
<td>Uganda</td>
<td>AFR E</td>
<td>28</td>
</tr>
<tr>
<td>Myanmar</td>
<td>SEAR D</td>
<td>26</td>
</tr>
<tr>
<td>United Republic of Tanzania</td>
<td>AFR E</td>
<td>25</td>
</tr>
<tr>
<td>Mali</td>
<td>AFR D</td>
<td>24</td>
</tr>
<tr>
<td><strong>Total of 15 countries</strong></td>
<td></td>
<td><strong>1384</strong></td>
</tr>
</tbody>
</table>
Immune Responses to Cryptosporidiosis in a Birth Cohort of Children in South India

Honorine Ward, Geographic Medicine and Infectious Diseases, Tufts Medical Center, Boston, USA
Gagandeep Kang, Gastrointestinal Sciences, Christian Medical College, Vellore, India
STUDY SITE

- semi-urban slum area
- population ~ 41,000
- 2.2 Sq Km area
- birth rate is 20 per 1000 population - ~ 800 births per year
- infant mortality rate is 37.9/1000 live births
- diarrhea causes 23.3% of the deaths
- diarrhea causes 43% of deaths in the 1st month of life

Immune responses to Cryptosporidiosis in a Birth Cohort of Children in South India

• Parent Study
  • birth cohort study on humoral and cell-mediated immune responses to specific antigens in cryptosporidiosis in children in South India
  • 400 children followed from birth to 3 years of age
    • clinical and epidemiological data (twice a week),
    • anthropometric data (once a month)
    • stool (once in 2 weeks and whenever child has diarrhea)
    • blood (every 6 months)
• Pilot Study using data and samples from parent study
  • 10 children with low birth weight (<2.5Kg) and stunting
  • 10 children with normal birth weight and no stunting
  • Studied from birth to 2 years of age
  • Clinical data twice a week
  • All enteric pathogens whenever child had diarrhea
  • Stool samples collected at 3, 6, 9, 12, 15, 18, 21 and 24 months of age (total of 160 samples) stored at -80°C used for microbiota analysis
Objectives

• Effect of age on diversity and relative abundance of intestinal microbiota
• Differences in intestinal microbiota in children with low and normal birth weight
• **Microbial Community profiling:** V4 region of 16S rRNA genes from stool DNA PCR amplified and amplicons sequenced using Illumina MiSeq platform (200 x 100 PE) average of 37,050 sequences per sample

• **Computational and bioinformatics analysis with QIIME**
  - Alpha and Beta Diversity Metrics
  - Relative Abundance of Taxa

• **Statistical Analysis**
  - LEfSe [http://huttenhower.sph.harvard.edu/lefse/](http://huttenhower.sph.harvard.edu/lefse/)
  - Mathematical models
    - Generalized Additive Model (GAM)
    - Generalized Linear Model (GLM)
    - Linear Mixed Effects Model (LMEM)
Growth and Nutritional Status

Height (cm)

Weight (Kg)

HAZ

WAZ

Age in Months

Tufts CGPH Tufts Center for Global Public Health
Nutritional status, Diarrhea and Antibiotic use in LBW children
Age-related effect on alpha and beta diversity
Differential abundance of taxa and function

- Low_Birthweight
- Normal_Birthweight

- a: g_vadinCA11
- b: f_Methanomassiliicocccae
- c: o_E2
- d: g_Odoribacter
- e: f_Odoribacteraceae
- f: f_S24_7
- g: g_Capnocytaphaga
- h: o_YS2
- i: f_Clostridiaceae
- j: g_Phascolarctobacterium
- k: g_Catenibacterium
- l: g_Eubacterium
- m: g_Desulfovibrio
- n: f_Desulfovibrionaceae
- o: o_Desulfovibrionales
- p: o_Campylobacterales
- q: f_Rs_045
- r: o_Y025
- s: g_Thermus
- t: f_Thermaceae
- u: o_Thermales

Peptidases (ko01002)
Fructose and Mannose Metabolism (ko00051)
Future Studies

• Metagenomics (predictive and whole genome sequencing)
• Metabolomics
• Larger numbers
• Associations with environmental enteropathy, inflammation, immune activation, barrier function, absorption
• Clinical trials of interventions to modulate the gut microbiome
Potential Interventions to Modulate Gut Microbiota

• Diet, Nutrients
• Prebiotics, Probiotics, Synbiotics
• Fermented Foods
• Functional foods
• Antibiotics
• Microbiome transplantation
• ? Novel targeted designer “Biotics”
Thank you!
Happy Thanksgiving!