Early Life Nutrition: A Strategy to Prevent Non-Communicable Diseases in the Community

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President, Danone Institute Indonesia

Bogor, 29 October 2014
Points for Discussions

- Magnitude of the problem
- Dimension of food and nutrition in health and disease and its implications on research directions
- Burden of today and tomorrow
- Forgetting the evidence?
- What next?
Points for Discussions

- Magnitude of the problem

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- Burden of today and tomorrow

- Forgetting the evidence?

- What next?
Percentage of Low Birth Weight Infants, by Provinces, 2007

Data Source: Baseline Health Research
National Health and Research Development Center, Ministry of Health, Republic of Indonesia, 2008
Figures on prevalence of low birth weight from RISKESDAS 2010 and 2013

Proporsi Berat Badan Lahir: 2010-2013*)

* Berdasarkan 52,6% sampel balita yang punya catatan

Website: www.litbang.depkes.go.id
Life Cycle Nutrition: Pregnancy through Infancy

1. Sucking stimulates nerve that sends signal to mother’s hypothalamus
2. Hypothalamus stimulates the release of prolactin and oxytocin
3. Prolactin triggers milk production and oxytocin triggers the let-down response
Components of Weight Gain During Pregnancy

Total weight gain ~30 lbs
- Maternal fat stores (~7 lbs)
- Uterus and breast (4 lbs)
- Blood (3–4 lbs)
- Fetus (~7 lbs)
- Placenta, amniotic fluid, and other fluids (~8 lbs)
# Recommended Weight Gain

<table>
<thead>
<tr>
<th>BMI</th>
<th>Weight (kg)</th>
<th>Weight Gain (kg)</th>
<th>Weight Gain (lbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &lt; 18.5</td>
<td></td>
<td>12.7-18.2</td>
<td>28-40</td>
</tr>
<tr>
<td>Normal Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI 19-24.9</td>
<td></td>
<td>11.4-15.9</td>
<td>25-35</td>
</tr>
<tr>
<td>Overweight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI 25-29.9</td>
<td></td>
<td>6.8-11.4</td>
<td>15-25</td>
</tr>
<tr>
<td>Obese</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI &gt; 30.0</td>
<td></td>
<td>6.8</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

Pattern of weight gain in pregnancy as important as total weight gain.

Deviations from expected patterns of weight gain are signals for intervention.

Pre-term birth doubles when 3rd trimester weight gain is low or inadequate.

Pregnancy is an anabolic state, resulting in increased energy (300 kcal/day) and nutrient needs.
Study on Nutritional Status and Food Pattern of Pre-Pregnant, Pregnant and Lactating Mothers in Bogor, West Java - Finding on nutrients deficiency

<table>
<thead>
<tr>
<th>Deficiency</th>
<th>Pre Pregnant (n=200)</th>
<th>Pregnant (n=203)</th>
<th>Lactating (n=220)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>≥ 3 micronutrients + protein</td>
<td>52 (26)</td>
<td>115 (56.7)</td>
<td>73 (33.2)</td>
</tr>
<tr>
<td>2 micronutrients + protein</td>
<td>2 (1)</td>
<td>1 (0.5)</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>1 micronutrient + protein</td>
<td>-</td>
<td>1 (0.5)</td>
<td>-</td>
</tr>
<tr>
<td>TOTAL</td>
<td>54 (27)</td>
<td>117 (57.6)</td>
<td>75 (34.1)</td>
</tr>
</tbody>
</table>

- Approx. 1 in 4 pre pregnant women have a too low protein intake and multiple micronutrient intake
- Approx. 6 out of 10 pregnant women have a too low protein and multiple micronutrient intake
- Approx. 1 out of 3 lactating women have a too low protein intake and multiple micronutrient intake

*Micronutrients include Iron, Vitamin A, Vitamin C, Folate, Zinc

- 1 out of 3 pre pregnant women have iron and zinc status indicators < reference
- 6 out of 10 pregnant women have iron and zinc status indicators < reference
- 1 out of 3 lactating women have iron and zinc status indicators < reference
Proportion of pregnant women who was found anemic in RISKESDAS 2013

Proporsi Anemia pada Ibu Hamil menurut Tempat Tinggal, 2013

<table>
<thead>
<tr>
<th></th>
<th>Urban</th>
<th>Rural</th>
<th>Indonesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion</td>
<td>36.4%</td>
<td>37.8%</td>
<td>37.1%</td>
</tr>
</tbody>
</table>

**) Cut off points anemia Ibu Hamil, Hb < 11,0 g/dl

Website: www.litbang.depkes.go.id
Penyebab Defisiensi Zat Besi: Diet (1)

- Low dietary iron intake
- Low iron bioavailability
  - Non-heme iron
  - Inhibitors
Penyebab Defisiensi Zat Besi: Infestasi Parasit (2)

- Menyebabkan blood loss
- Meningkatkan iron loss
Penyebab Defisiensi Zat Besi: Malaria (3)

- Menghancurkan sel darah merah
- Mengakibatkan anemia berat
- Meningkatkan risiko kehamilan
Finding on prevalence of Chronic Energy Deficiency among Indonesia women at 15-45 year from RISKESDAS 2007 and 2013

Proporsi Wanita Usia Subur Risiko Kurang Energi Kronis (KEK)*) : 2007 & 2013

*) Risiko KEK – jika Lingkar lengan atas (LILA)<23,5 cm

Website: www.litbang.depkes.go.id
Prevalence of Under-nutrition (Weight for Age), by Districts/Cities, 2007

Data Source: Baseline Health Research National Health and Research Development Center, Ministry of Health, Republic of Indonesia, 2008
Prevalence of Stunting (Height for Age), by Districts/Cities, 2007

Data Source: Baseline Health Research National Health and Research Development Center, Ministry of Health, Republic of Indonesia, 2008
Prevalence of Wasting in Young Children (6-14 yo), by Provinces, 2007

Data Source: Baseline Health Research
National Health and Research Development Center,
Ministry of Health, Republic of Indonesia, 2008
Double Burden of Nutritional Problems in Indonesia, 2007

Data Source: Baseline Health Research
National Health and Research Development Center, Ministry of Health, Republic of Indonesia, 2008
Points for Discussions

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Dimension of Food and Nutrition in Health and Disease

Nutrients:
- Carbohydrates
- Protein
- Fat
- Vitamins
- Minerals
- Trace elements

Non-nutrients: eg phytonutrients
Other food components

Degenerative diseases

Food & meal preparation

Cuisine

Nutrients:
- Complex CH, sugar
- Arginine, taurine
- EFA, MUFA
- Antioxidants, B6, B12, FA
- Na, K, Ca
- Zn, Se, Cr

Food belief

Deficiency and excess

Metabolic syndrome

Cultural adoption

Acculturation

Meal pattern

Infection, inflammation and free radicals
Present and Future Paradigms in ‘Nutrition and Health’ Research (1)

- New outlook on under- and over- nutrition using life cycle approach – consideration as ‘one package’ for long-term health
- Integration of community development using eco-nutritional approach (not only within the view of nutritional sciences to the physiological and metabolic flow of nutrients) to achieve sustainable solutions for nutrition-related health problems
Present and Future Paradigms in ‘Nutrition and Health’ Research (2)

- Enhancement of the adoption of research findings into program implementation
Points for Discussions

- Magnitude of the problem
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Transition from Inter-generational Malnutrition to Abdominal Adiposity and Diabetes

Diagram:

- Elderly Malnourished
  - Inadequate food, health & care
- Baby Low Birth Weight
  - Reduced capacity to care for baby
  - Inadequate foetal nutrition
- Woman Malnourished
  - Pregnancy Low Weight Gain
  - Higher maternal mortality
- Adolescent Stunted
  - Inadequate food, health & care
  - Reduced mental capacity
- Child Stunted
  - Reduced mental capacity
  - Inadequate food, health & care
  - Frequent infections
  - Untimely / inadequate weaning
- Increased risk of adult chronic disease
- Impaired mental development
- Increased mortality rate
Pre-pregnancy Mother and Newborn Baby
Indian Thrifty Phenotype at Birth

Yajnik et al. Pediatr Res 2001;50:51A
Glucose and Insulin Response in Childhood in Relation to Birth Weight

![Graph showing glucose and insulin response in relation to birth weight. The graph compares glucose (mmol L⁻¹) and insulin (pmol L⁻¹) levels across different birth weight categories.]
Differences between undernourished and well nourished children

<table>
<thead>
<tr>
<th></th>
<th>Severely stunted N=15</th>
<th>Stunted N=88</th>
<th>Non-stunted N=278</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/L)</td>
<td>12.34 ± 1.03</td>
<td>12.63 ± 1.19</td>
<td>12.87 ± 1.02*</td>
</tr>
<tr>
<td>Serum Ferritin</td>
<td>27.40 ± 15.58</td>
<td>28.80 ± 28.30</td>
<td>27.60 ± 18.64</td>
</tr>
<tr>
<td>Transferrin Receptor</td>
<td>5.05 ± 3.2</td>
<td>4.89 ± 1.66</td>
<td>4.49 ± 1.05*</td>
</tr>
<tr>
<td>Coding</td>
<td>25.80 ± 10.44</td>
<td>25.68 ± 8.58</td>
<td>28.05 ± 7.91*</td>
</tr>
<tr>
<td>Reading comprehension</td>
<td>3.93 ± 2.96</td>
<td>5.85 ± 4.33</td>
<td>7.68 ± 5.65**</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Severely underweight N=5</th>
<th>Underweight N=113</th>
<th>Not underweight N=263</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>11.54 ± 1.22</td>
<td>12.61 ± 1.14</td>
<td>12.90 ± 1.01**</td>
</tr>
<tr>
<td>Transferrin Receptor</td>
<td>18.00 ± 17.64</td>
<td>26.34 ± 14.53</td>
<td>28.70 ± 23.29</td>
</tr>
<tr>
<td>Visual Attention</td>
<td>-7.60 ± 12.97</td>
<td>2.31 ± 9.31</td>
<td>4.99 ± 7.26**</td>
</tr>
<tr>
<td>Coding</td>
<td>25.00 ± 7.48</td>
<td>25.13 ± 8.34</td>
<td>28.44 ± 8.00**</td>
</tr>
<tr>
<td>Design Fluency</td>
<td>5.80 ± 1.64</td>
<td>5.39 ± 2.39</td>
<td>6.08 ± 2.53*</td>
</tr>
<tr>
<td>Vocabulary</td>
<td>10.20 ± 2.77</td>
<td>10.94 ± 4.63</td>
<td>12.51 ± 5.21*</td>
</tr>
<tr>
<td>Reading comprehension</td>
<td>3.20 ± 1.30</td>
<td>5.96 ± 4.52</td>
<td>7.68 ± 5.65**</td>
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</table>

Severe stunting <-3 SD Ht/age; stunting -3;-2SD Ht/age non-stunted >-2 SD Ht/age. Differences assessed with ANOVA; *p< 0.05; **p < 0.01; ***p < 0.005
Differences between iron-deficient and non-iron deficient children

<table>
<thead>
<tr>
<th>Country</th>
<th>Iron deficient N=</th>
<th>Not iron deficient N=</th>
<th>Visual Attention</th>
<th>RAVLT</th>
<th>Coding</th>
<th>Vocabulary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>17</td>
<td>141</td>
<td>41.06 ± 11.34</td>
<td>3.29</td>
<td>32.24 ± 8.63</td>
<td>18.41 ± 6.47</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>33.31 ± 11.04**</td>
</tr>
<tr>
<td>Indonesia</td>
<td>86</td>
<td>284</td>
<td>2.87 ± 1.63</td>
<td>3.35</td>
<td>4.08 ± 1.70</td>
<td>11.07 ± 5.22</td>
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<td>3.35 ± 1.85*</td>
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<td>4.08 ± 1.70</td>
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<td>4.08 ± 1.71*</td>
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<td></td>
<td>11.07 ± 5.22</td>
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<td></td>
<td></td>
<td></td>
<td>12.33 ± 5.00*</td>
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<td></td>
<td></td>
<td>6.07 ± 4.15</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>7.54 ± 5.70*</td>
</tr>
</tbody>
</table>

Iron deficiency defined as serum ferritin < 15 ug/L. Differences assessed with ANOVA; *p < 0.05; **p < 0.01; ***p < 0.005
Molecular mechanisms affected by dietary folate

- Vascular disease
- Redox buffer
- Folate dependent methionine biosynthesis lowers homocysteine, maintains biological methylations, and influences glutathione levels
- CpG methylation and gene expression
- Non-genomic biological methylations
- Folate dependent methylation of DNA regulates transcription
- Folate dependent biological methylations are numerous, and include biogenic amine synthesis, implicating folate in mood disorders
- Uracil misincorporation and DNA instability
- Folate is required for conversion of dUMP into dTMP. A low status can precipitate the misincorporation of uracil into DNA and may lead to cancer

- Cycling of folate for 1-carbon transfers needed in biosynthetic
- Food folate

DNA and RNA biosynthesis

Lucock, M. BMJ 2004;328:211-214
Genome damage

- Oxidative stress
- Nutrient deficiency
- Excess calories

- Strand breaks in DNA
- Chromosome malsegregation
- DNA hypomethylation
- Telomere shortening

Human cells with damaged & unstable genomes

Fenech, 2003
Cytokinesis-Block Micronucleus (CBMN) Cytome Assay

- Micronuclei - chromosome breakage and loss
- Nucleoplasmic bridges – DNA mis-repair, telomere end fusion
- Nuclear buds - gene amplification
- Necrosis
- Apoptosis

CBMN CYTOME ASSAY
CYTOKINESIS-BLOCK MICRONUCLEUS ASSAY
Cancer risk by sites for medium/high relative to low tertile micronucleus frequency

HUMN project

N = 6700, 63,000 PYs, 268 cancer cases,
All cancers RR = 1.67, P=0.002.

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Original Article

Determinants of child malnutrition during the 1999 economic crisis in selected poor areas of Indonesia

Saptawati Bardosono MD PhD, Soemilah Sastroamidjojo MD and Widjaja Lukito MD PhD

South East Asian Ministries of Education Organization Regional Center for Community Nutrition at the University of Indonesia, Jakarta, Indonesia
Findings (3): determinants of wasting

<table>
<thead>
<tr>
<th>Urban Poor Jakarta</th>
<th>Banggai</th>
<th>Alor-Rote</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purchasing power</td>
<td>Possession of KMS card</td>
<td>Purchasing power</td>
</tr>
<tr>
<td>Maternal and child care</td>
<td>Infectious diseases</td>
<td>Mother’s education</td>
</tr>
<tr>
<td>Infectious diseases</td>
<td></td>
<td>Maternal and child care</td>
</tr>
</tbody>
</table>

Height, Weight and BMI during Childhood in 286 Men and 185 Women who later Developed Type 2 Diabetes

A Z score of 0 corresponds to the mean value in the whole cohort; a Z score of 1 corresponds to a value of 1 SD above the mean. Solid line indicates height; dashed line indicates weight; dotted line indicates body mass index.
Refeeding Study on Children with Marasmus or Marasmic-Kwashiorkor

When children recovering from marasmus or marasmic-kwashiorkor had reached their expected weight-for-height, their bodies contained 25-37% of fat, with a mean value of 30%

Semistarvation and Refeeding Study

When body fat was 100% recovered, the recovery of muscle mass or fat-free-mass was less than 40%

Keys et al. 1950
Forgetting the evidence?

Forgetting the physiology of growth and development, eg bone lengthening processes??
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Total Nutritional Care at Various Life-cycle Stages

<table>
<thead>
<tr>
<th>Lifecycle stage</th>
<th>Nutritional care recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescents</td>
<td>Good hygiene and sanitation practices</td>
</tr>
<tr>
<td>Perinatal</td>
<td>Improved environment factors</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Sustainable and effective health and nutrition promotion</td>
</tr>
<tr>
<td>Infancy</td>
<td></td>
</tr>
<tr>
<td>Pre-school age</td>
<td></td>
</tr>
<tr>
<td>School age</td>
<td></td>
</tr>
</tbody>
</table>

- **Adolescent**
  - Pre-conception
  - Achieve appropriate body weight
  - Maintain balanced diet

- **Pre-school age**
  - Achieve appropriate weight gain
  - Appropriate exclusive breast-feeding
  - Introduce complementary foods

- **Infancy**
  - Achieve appropriate weight gain
  - Appropriate breast-feeding
  - Immunization

- **Pregnancy**
  - Achieve appropriate weight gain
  - Pre- and post-natal care
  - Immunization

- **Perinatal**
  - Achieve appropriate weight gain
  - Maintain balanced diet
  - School feeding program
  - Immunization (booster)

- **School age**
  - Achieve healthy body weight
  - Attending school health programs
  - Immunization

- **Macro-micronutrients**
  - Good hygiene and sanitation practices
  - Improved environment factors
  - Sustainable and effective health and nutrition promotion
Potential strategies to be considered: Operational level

- Penyeragaman terminologi
- Mengembangkan dan meningkatkan perinatal surveillance
- Penguatan nutritional surveillance system, terintegrasi dengan surveillance of infectious diseases
- Pengembangan dan revitalisasi ‘therapeutic feeding centers’ di masyarakat, primary health care and RS
- Mengembangkan program nutritional promotion yang efektif
- Inter-sectoral solution in developing sustainable school feeding programs
- Eradikasi neglected infectious diseases, like helminthiasis, filariasis and others
- Control dan minimkan persisting infectious diseases, seperti malaria, tuberculosis
Thank You

Terima Kasih