Optimising maternal nutrition

Investigating micronutrient deficiencies in women of childbearing age

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Developmental origins of health and disease – DoHAD (World Health Organisation)

Vitamin B12 – recommended daily intake 2.4mcg/day

**Natural food sources**
- Fish
- Chicken
- Meat
- Eggs
- Milk
- Yoghurt
- Cheese

**Fortified sources**
- Soya, rice, almond milks
- Vegetarian meat analogues
- Marmite
- “Vegetarian” vegemite
- Energy drinks
- Meal replacements
Risks from Maternal B12 Deficiency

- Increased risk NTD (Molloy et al, 2009; Ray et al., 2007)
- Impaired cognition/neurological deficit (Bhate et al., 2008)
  - Maternal/neonatal macrocytic anaemia
- Low birthweight and preterm delivery (Muthayya et al., 2006)
- Insulin resistance & low muscle mass in child...
- ...& increased risk of diabetes in adult life (Yajnik et al., 2008)
Prevalence of B12 deficiency

- Internationally – high rates of B12 deficiency in South Asian populations
- Insufficient NZ research
  - NZNS 2008/9 – average of 20% of population low in B12 (Devi et al. 2018)
  - 50% South Asian women low in B12 (Gammon et al., 2013)
- US study - around 30 – 40% of older adults B12 insufficient/deficient (Andres, 2004)
  - 60% of cases – due to food-bound cobalamin malabsorption
  - 15-20% due to pernicious anaemia – lack intrinsic factor
- US study - in younger adults – 39% insufficient/deficient (Tucker et al., 2000)
  - more likely to be due to insufficient dietary intake, malabsorption or medications that inhibit B12 absorption (Tucker et al., 2000).
- Prevalence increasing with more vegan/vegetarian/low-meat–eating diets
Contributors to B12 deficiency

• Poor or incomplete absorption of B12 from food
  • Food – bound cobalamin absorption
  • Pernicious anaemia- loss of intrinsic factor binding for B12 absorption
  • GI inflammatory conditions- Crohn’s, coeliac disease
  • GI infections – *H.Pylori*

• Inadequate dietary intake of B12
  • < RDI 2.4 mcg/day /2.6 mcg/day pregnancy
  • Low or non-meat eating dietary practices

• Medications that inhibit B12 absorption
  • e.g. Metformin, PPI
South Asian community perspectives on B12 deficiency - a qualitative descriptive study
South Asian community perspectives on B12 deficiency

Six community focus groups

One health professional focus group
Key findings health professional focus groups

- Lack of PHARMAC funded oral supplement
- Limited knowledge of B12 containing foods
- B12 deficiency only a problem if macrocytic anaemia or neurological deficits
- Poor specificity of serum B12 limits testing
- Perception that only IM B12 supplements effective
- Patients-IM B12 supplements as a “cure-all”
Key findings from South Asian Community

Being vegetarian integral to communal identity

- Being B12 deficient a common experience
- Struggling to make sense of why deficient
- Insufficient information or education
- Finding their own solutions to manage deficiency
- Wanting choices for managing deficiency
- Being B12 deficient a common experience
Pharmacological vs. physiological doses for B12 deficiency

• B12 deficiency due to malabsorption
  ➢ **Large pharmacological** doses of B12 (high dose oral B12 or B12 injections - 1000mcg x 3-5 doses)
  ➢ Enterohepatic recycling of B12 affected -1-2% still absorbed by passive diffusion
  ➢ Deficiency can become profound

• Low or non meat eaters at risk of B12 deficiency:
  ➢ Absorb B12 well
  ➢ **Require only physiological** oral dose supplement
  ➢ ??What is an appropriate dose?
  ➢ Oral B12 supplements - B12 not bound – easily absorbed even in lack of gastric acid
  ➢ Enterohepatic recycling of B12 intact
  ➢ Deficiency not profound
VitB12 study

- 6-month trial 63 South Asian women
- oral B12 supplementation 6 mcg
- vs placebo
- OR dietary advice
- Tested at baseline, 6 weeks, 3 months, 6 months
- Registered clinical trial: ACTRN12610000262000
VitB12 study - approx. 50% of South Asian women B12 insufficient/deficient (Mearns et al., 2014)
Response in B12 biomarkers to study treatments over 6 months (Mearns et al., 2014)

% change in serum B12 over 6 months

% change in holo TC over 6 months

\( p = 0.001 \)
Conclusions of VitB12 RCT

- Low vitamin B12 status common in sample population
- 6 mcg B12 supplement capsule effective treatment for increasing B12 biomarkers
- Adherence with supplements decreased over time – reduced efficacy of oral supplement
  - relook at dose and frequency
- B12 dietary advice: insignificant effect on increasing B12 intake or serum B12
  - relook at effective ways to increase B12 intake via dietary advice/support
Vitamin B12 Food Frequency Questionnaire

- Estimates vitamin B12 intake from dietary recall of foods consumed
Food frequency questionnaire (B12FFQ)

- 30 questions
- Included B12 containing food and beverages
- Recall of frequency and portion of foods eaten
- Approximated average B12 (mcg) consumed per day
- Compared with serum B12 and holoTC biomarkers
Relationship between B12 dietary intake and serum B12 biomarkers
Summary of B12 FFQ findings (Mearns & Rush, 2017)

• B12 FFQ a valid measure of dietary B12 intake
  \( r=0.55, p<0.001, 95\% \text{ CI } [0.34, 0.71] \)

• 44% of women had a dietary intake <RDI of 2.4 mcg B12/day

• Women who did not consume red meat were 2.2 and 2.8 times more likely to be B12 deficient or insufficient \( p=0.005, 95\% \text{ CI } [1.4, 5.9] \)
Nurses Nutrition Study

Micronutrient status and associations with dietary patterns
Ethnicity of study participants

67 female students age 18-45 years

- European n=40 (58%)
- Māori n=3 (4.3%)
- Pacific n=4 (5.8%)
- Asian n=11 (15.9%)
- South Asian n=6 (8.7%)
- Other n=3 (5.3%)
### NNS: Micronutrient biomarker status (n=67)

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Median (25&lt;sup&gt;th&lt;/sup&gt;/75&lt;sup&gt;th&lt;/sup&gt;)</th>
<th>Range Lower/Upper limit</th>
<th>n (%) low or deficient</th>
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<tbody>
<tr>
<td><strong>Hb</strong> Low&lt;115 g/L</td>
<td>135 (129/142)</td>
<td>104/166</td>
<td>5 (7.5%)</td>
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<tr>
<td><strong>MCV (f/L)</strong> Low &lt; 80 f/L</td>
<td>87 (85/90)</td>
<td>62/95</td>
<td>13 (19.4%)</td>
</tr>
<tr>
<td><strong>Serum ferritin (ug/L)</strong> Low &lt;20 ug/L</td>
<td>24 (12/28)</td>
<td>2/300</td>
<td>29 (43%)</td>
</tr>
<tr>
<td><strong>Serum vitamin B12 Low &lt;222pmol/L</strong></td>
<td>320 (237/407)</td>
<td>99/794</td>
<td>13 (19.4%)</td>
</tr>
<tr>
<td><strong>Serum folate (nmol/L)</strong> Low &lt;7nmol/L</td>
<td>26 (11/36)</td>
<td>6/45</td>
<td>1 (1.4%)</td>
</tr>
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Dietary practices

**Reported dietary practices:** Non meat-eating n=4 (6%), white meat-eating only n=5 (7.5%), red and white meat eating n=58 (86.5%)

**Factor analysis of dietary patterns**

Three dominant patterns in this group

- **Discretionary/junk:** deserts/sweets, snacks, takeaways, milk, pasta, starchy vegetables.

- **Flexitarian:** non starchy and starchy veges, fruit, nuts & seeds

- **Traditional:** all meats, dairy, eggs, bread and crackers, fruit
Analysis of dietary intake/patterns

• Significant associations
  • *Traditional pattern*—meat eating/dairy & eggs/bread pattern
    • More likely to be ferritin replete in this pattern (r = 0.26, p=0.035)
  • *Discretionary/junk food patterns* (r=-0.289, p=0.018)
    • More likely to be B12 deficient with this pattern

Regression and correlation analysis

• Only significant association
  • Serum B12 and servings of red meat/day (rho=0.38, p=0.003)
  • No association found between ethnicity and micronutrient deficiency
  • No association found between self-reported menstrual blood flow and ferritin
Challenges in screening for, preventing and managing B12 deficiency

- A more sensitive, specific and affordable test of B12 status needed
- Identifying and working with dietary ‘at-risk’ groups
- Treatment options appropriate for the cause of B12 deficiency
A more sensitive, specific and affordable test of B12 status needed for high risk

- Serum B12 – low specificity and sensitivity – especially in pregnancy (Morbak, 2007)
- HoloTC – reflects active B12 available for metabolism
  - Remains stable over pregnancy
- Testing for metabolites produced in B12 deficiency more accurate
  - Homocysteine and Methylmalonic acid (MMA) expensive and only tested in specialist laboratories
- Issues with transport of samples to specialist laboratories
  - MMA and Homocysteine
Future research – DBS-MMA testing

- Assistant Prof. Yvonne Lamers at the University of British Columbia (UBC) validated novel methods for testing DBS-MMA (Schroder et al., 2014)
- Convenient dried blood spot method (DBS) for sampling and tandem mass-spectrometry for testing.
- DBS-MMA measures methylmalonic acid (MMA), a metabolite specific to B12 deficiency.
- This DBS-MMA test has potential to aid more sensitive and reliable testing for B12 deficiency - complement the currently used serum B12 assay test.
- Proposed AUT project includes evaluation of DBS-MMA testing; cost, convenience, and sensitivity.
Summary

• Low B12 status is common in women of child bearing age – needs better recognition and prevention
• Align management of B12 deficiency with the contributors of deficiency
• Identify appropriate physiological oral B12 supplement dose
• More focus on dietary patterns for risk of deficiency
• MoH dietary guidelines - recommended food groups- discretionary/ junk eating patterns- increased risk of B12 deficiency.
• Better resources needed on sources of dietary B12 and when supplementation indicated
• More sensitive and specific tests needed to test for B12 deficiency
• PHARMAC funding of an oral B12 supplement
Thank you
Any Questions?
References


