

## **Gael Mearns: Preventing Vitamin B12 deficiency in South Asian Women of child bearing age**

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Maternal nutrition during pregnancy and breastfeeding has long-term effects on the growth and development of offspring. Longitudinal studies in India provide evidence that maternal vitamin B12 deficiency in pregnancy is associated with increased insulin resistance and relative adiposity in the offspring, potentially increasing the risk for developing type 2 diabetes mellitus in later life. Vitamin B12 is an exclusive vitamin because it is only available naturally in foods of animal origin. In New Zealand, vitamin B12 deficiency is considered rare because of a predominantly meat-eating diet and it is mainly older adults with malabsorption of B12, and those with extremely strict vegetarian or vegan dietary practices who are assumed to be at risk. Consequently, public funding for vitamin B12 supplements, decisions on folic acid supplementation and food fortification, plus screening and management of vitamin B12 deficiency, are all orientated towards addressing vitamin B12 deficiency in older adults with vitamin B12 malabsorption.

Worldwide, there are high prevalence rates for noncommunicable disease (cardiovascular disease and type 2 diabetes mellitus) in the South Asian population, and evidence supporting a high prevalence of vitamin B12 deficiency related to dietary patterns that contain little or no meat. Phenotypic changes in response to maternal vitamin B12 deficiency may exacerbate the already high noncommunicable disease risk for subsequent generations of offspring. The South Asian population in New Zealand is growing rapidly, but there is little published information on the prevalence of vitamin B12 deficiency among South Asian women living in New Zealand. Health professionals need a better understanding of risk factors for vitamin B12 deficiency, including how to work with the South Asian community to effectively prevent deficiency, particularly in women preconception.

The aim of this vitamin B12 (VitB12) study was to explore ways to reduce vitamin B12 deficiency in Auckland based, South Asian women of childbearing age. The mixed methods community-based participatory research design involved enlisting a group of South Asian community members to guide and participate in the planning, conduct, and implementation of the focus group discussions and the randomised controlled trial components of the research, as well as subsequent dissemination of findings. Six focus group interviews with community members (five groups) and health professionals (one group), were recorded and thematically analysed. Key themes identified from the focus group interviews were dietary practices as integral to identity and belonging, managing B12 deficiency and study participation as a positive experience. The double blind, randomised controlled trial recruited 62 women of childbearing age, stratified by meat/non meat-eating dietary patterns, then randomly allocated to one of three treatment groups: vitamin B12 dietary advice, 6µg vitamin B12 supplement, or placebo capsule. Measurements were undertaken at baseline, two, then six months and included fasting blood for biomarkers of vitamin B12 status (serum B12 and holotranscobalamin), serum folate, glucose, insulin, lipids and a full blood count. Measures also included weight, height, body fat by single frequency hand to foot bioimpedance, and blood pressure. A 30-item, researcher-administered, food frequency questionnaire developed for this VitB12 study was used to assess reported dietary vitamin B12 intake at each time point.

Women in the study presented with metabolic risk factors for noncommunicable disease and gestational diabetes. Nearly 75% of women had total cholesterol and 50% low-density lipoprotein-cholesterol results that exceeded New Zealand National Heart Foundation recommended guidelines, and although body mass index was within recommended guidelines, all of the women were within the obesity range based on body fat percentage estimated using bioelectrical impedance (range 41 to 61%). Waist to hip ratio and waist to height ratio, two indices of central obesity, were borderline high.

At baseline, 48% of women were low in serum vitamin B12 (< 222 pmol/L), and 51% were low in holotranscobalamin (< 45 pmol/L). All had sufficient folate status. The food frequency questionnaire developed for the study was a valid estimate of dietary B12 intake, supported by a moderate positive correlation with serum B12 ( $r=0.50$ ,  $p < 0.001$ , 95 % CI [0.28, 0.67]) and holotranscobalamin ( $r=0.55$ ,  $p < 0.001$ , 95 % CI [0.34, 0.71]). The B12 FFQ demonstrated greater than 62% sensitivity and specificity for detecting low B12 biomarkers. Compared with women who ate meat (45%), those with non-meat-eating dietary practices (55%) were 2.2 (95% CI [1.4, 4.4]) times more likely to be low in serum B12 and 2.8 [1.4, 5.9] times more likely to be low in holoTC. Concurrently, 40% of women reported a dietary vitamin B12 intake less than the recommended daily intake of 2.4 µg/day. Women who ate no meat or white meat only were more likely to report an inadequate intake of dietary vitamin B12.

Over six months of the randomised controlled trial, the B12 supplement group treatment was associated with improvements that were substantial in both serum B12 (geometric mean increase of 30 %, 95 % CI

[11, 48]) and holotranscobalamin (42 % [12, 72]). A drop in supplement adherence over the latter four months of the study for participants in the B12 supplement group was detected, and was associated with less improvement. For the placebo group and dietary advice groups, over 6 months there was a trivial and insignificant change in both serum B12 and holoTC concentrations, with a small increase in the percentage of women low in serum B12, and no change in the percentage low in holoTC.

The evidence presented in this thesis confirms that in common with international studies, South Asian women of childbearing age living in Auckland, New Zealand, and in particular, women with vegetarian or low meat eating dietary preferences, are at high risk for B12 deficiency. Low dose oral vitamin B12 supplementation may be a beneficial strategy for preventing vitamin B12 deficiency in South Asian women prior to pregnancy. Future work could include investigating a prescription of a weekly B12 supplement dose rather than daily, and the effect of early screening before and during pregnancy for vitamin B12 insufficiency and deficiency. The vitamin B12 food frequency questionnaire developed for the VitB12 study has potential as a useful screening tool for inadequate dietary vitamin B12 intake.

This study has identified that South Asian women who eat little or no meat have a high prevalence of vitamin B12 deficiency, which could be ameliorated by oral supplementation. Promoting adherence to a low dose vitamin B12 supplementation or food fortification programme may be a beneficial strategy. In order to prevent or reduce life-course risks in offspring of women with vitamin B12 deficiency, the health literacy, policies, and practices of health professionals and communities must be informed by evidence.