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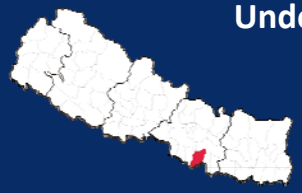

Underlying Vitamin A Status Affects the Association between Dark Green Leafy Vegetable Intake and Serum Retinol and β-Carotene Concentrations among Pregnant Women in Nepal

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INTRODUCTION

Vitamin A (VA) deficiency is prevalent among pregnant women in developing countries,[1] where VA is often derived from the bioconversion of the pro-vitamin A carotenoid, β-carotene (BC), in fruits and vegetables.[2,3] However, the efficiency of bioconversion of BC to VA is highly variable, which may relate in part to variation in VA status.[3-6]

We had a unique opportunity to assess differences in serum retinol with varied frequency of dark green leafy vegetable (DGLV) intake, known to be rich in BC, as a function of prior VA status in pregnant, Nepalese women. Different levels of VA status were achieved in women prior to dietary assessment by having been randomized to receive supplemental VA, BC or placebo (PL) on a weekly basis for months to years before evaluation, through their participation in a field trial assessing the impact of VA and BC supplementation during pregnancy on maternal and infant health and survival.[7]

OBJECTIVES

In this study, we aimed to:

1) **Determine the differences in circulating serum retinol (sROH) and serum β-carotene (sBC) concentrations by frequency of intake of dark green leafy vegetables (DGLV), and**

1) **Determine whether pre-existing VA and β-carotene status, achieved by random assignment, affects the association between frequency of DGLV intake and sROH and sBC in a population of rural, pregnant, Nepalese women.**

METHODS

- The study sample includes a subset of women enrolled in the NNIPS-2 trial who were assessed for biochemical nutritional status.[7] Women were randomized, by ward, to receive weekly capsules of VA [7000 µg retinol equivalents (RE), n=331], BC (42 mg, ~7000 µg RE, n=442) or placebo (PL, n=377) before, during and after pregnancy.[7]
- Blood samples were collected and risk factor surveys were administered at mid-pregnancy, following months to years of prior randomized supplementation; data include sROH and sBC concentrations (by HPLC), and DGLV intake (by a 7-day food frequency assessment) re-categorized as none, 1-6 times, and ≥7 times.
- Data analyses were performed using multiple linear regression (MLR), with a robust estimation of variance to adjust for clustering in the study design. All analyses were stratified by supplementation group.
- Models were adjusted for maternal age, gestational age, women's education, mid-upper arm circumference, and season of assessment.

RESULTS

Table 1. Characteristics of women during mid-pregnancy, by randomized supplementation group, NNIPS-2 Trial, Sarlahi, Nepal

Values are number and % unless otherwise stated

	Placebo (N=331)	β-carotene (N=442)	Vitamin A (N=377)
DGLV Intake in Previous Week:			
None	153 (46.2)	183 (41.4)	149 (39.5)
1-6 Times	167 (50.5)	241 (54.5)	221 (58.6)
≥7 Times	11 (3.3)	18 (4.1)	7 (1.9)
Maternal Characteristics:			
Vitamin A Deficiency (sROH <0.70 µmol/L)	68 (20.5)	67 (15.2)	17 (4.5)
Maternal Age (Years) Mean (SD)	24.3 (4.9)	24.2 (5.5)	23.8 (5.3)
Gestational Age (Weeks) Mean (SD)	19.5 (6.7)	19.4 (6.4)	19.2 (6.8)
MUAC			
<21.5cm	94 (28.4)	129 (29.2)	118 (31.3)
≥21.5 cm	237 (71.6)	313 (70.8)	259 (68.7)
Any Education*	38 (11.5)	86 (19.5)	54 (14.3)
Season of Interview:			
Winter	83 (25.1)	101 (22.9)	89 (23.6)
Pre-Monsoon	90 (27.2)	130 (29.4)	117 (31.0)
Monsoon	107 (32.3)	146 (33.0)	110 (29.2)
Peri-Harvest	51 (15.4)	65 (14.7)	61 (16.2)

*P < 0.05

Relationship between continuous variables and supplement groups were tested with ANOVA

Relationship between categorical variables and supplement groups were tested with X^2

Figure 1. Unadjusted mean serum β-carotene (A) and serum retinol (B) among women with increasing DGLV intake during mid-pregnancy, by randomized supplementation group, NNIPS-2 Trial, Sarlahi, Nepal

Error bars represent standard error of the mean; Dashed line represents marginal VA status (<1.05µmol/L)

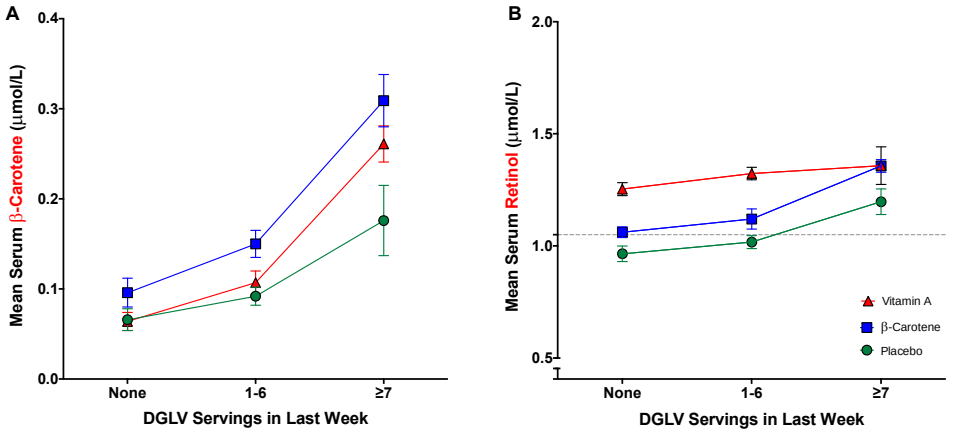

Table 2. Change in sBC and sROH concentrations (µmol/L) with increasing dark green leafy vegetable intake in women during mid-pregnancy, by randomized supplementation group, NNIPS-2 Trial, Sarlahi, Nepal

	Placebo N=331			β-carotene N-442			Vitamin A N=377		
Serum β-carotene§	Intercept	Coefficient (95% CI)	% Change (95% CI)	Intercept	Coefficient (95% CI)	% Change (95% CI)	Intercept	Coefficient (95% CI)	% Change (95% CI)
DGLV:	0.08			0.130			0.065		
None		REF	-		REF	-		REF	-
1-6		0.02 (-0.02, 0.07)	23% (-21, 91)		0.06 (0.00, 0.14)	44% (-1, 108)		0.04 (0.00, 0.09)	55% (-2, 145)
≥7		0.07 (-0.02, 0.29)	93% (-19, 362)		0.21 (0.07, 0.45)**	165% (56, 349)**		0.16 (0.08, 0.28)**	241% (117, 436)**
Serum Retinol§									
DGLV:	1.05			1.071			1.322		
None		REF	-		REF	-		REF	-
1-6		0.04 (-0.01, 0.17)	3% (-9, 17)		0.03 (-0.05, 0.10)	2.4% (-5, 10)		0.05 (-0.05, 0.14)	4% (-4, 11)
≥7		0.21 (0.06, 0.36)*	20% (6, 34)*		0.19 (0.09, 0.29)**	18% (8, 27)**		0.08 (-0.23, 0.34)	6% (-17, 29)

*P< 0.05; ** P ≤ 0.01

§ Models adjusted for maternal age, gestational age, MUAC, education, and season of assessment

KEY FINDINGS

Sample Characteristics:

- Women in each supplementation group were similar in dietary (DGLV) intake, nutritional status (MUAC), SES (education), and season of assessment (Table 1).
- However, as expected, the prevalence of VA deficiency (<0.70 µmol/L) was highest in women receiving PL (20.5%) and lowest in women receiving VA (4.5%), and BC recipients were in the middle (15.2%), indicating that ongoing supplementation was responsible for the observed differences in VA status (Table 1).

Differences in sBC by DGLV intake:

- sBC was higher with more frequent DGLV intake, significantly so for women eating DGLV ≥7x/week in the BC and VA groups (p<0.01; Fig 1A and Table 2).

Differences in sROH by DGLV intake:

- sROH did not change by DGLV intake in the VA recipient group (red line, Fig 1B). Among women supplemented with either BC or placebo, sROH rose with DGLV intake, significantly so for women eating DGLV ≥7x/week compared to non-consumers (Fig 1B and Table 2).

CONCLUSIONS

- The NNIPS-2 randomized design offered an opportunity to assess apparent effects of underlying VA status, achieved by PL, BC, or VA supplementation, on beta-carotene bioefficacy as a dietary source of VA, based on differences in sROH.
- BC from DGLV appeared more bioavailable, reflected by a dose-response increase in sBC with more frequent DGLV intake (assuming comparable portions eaten by groups).
- Frequent DGLV intake was associated with raised sROH among those with lower VA status (PL and BC groups); in contrast, frequent DGLV intake did not affect sROL of women with adequate VA status (VA group).
- The greatest differences in sBC and sROH were found among those consuming DGLV at least 7 times in the previous week, suggesting regular DGLV intake is most likely to raise serum retinol in groups with low VA status.

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