Prenatal vitamin D supplementation and infant vitamin D status in Bangladesh

Nandita Perumal, Abdullah Al Mahmud, Abdullah H. Baqui, Daniel E. Roth

SUPPLEMENTAL MATERIAL

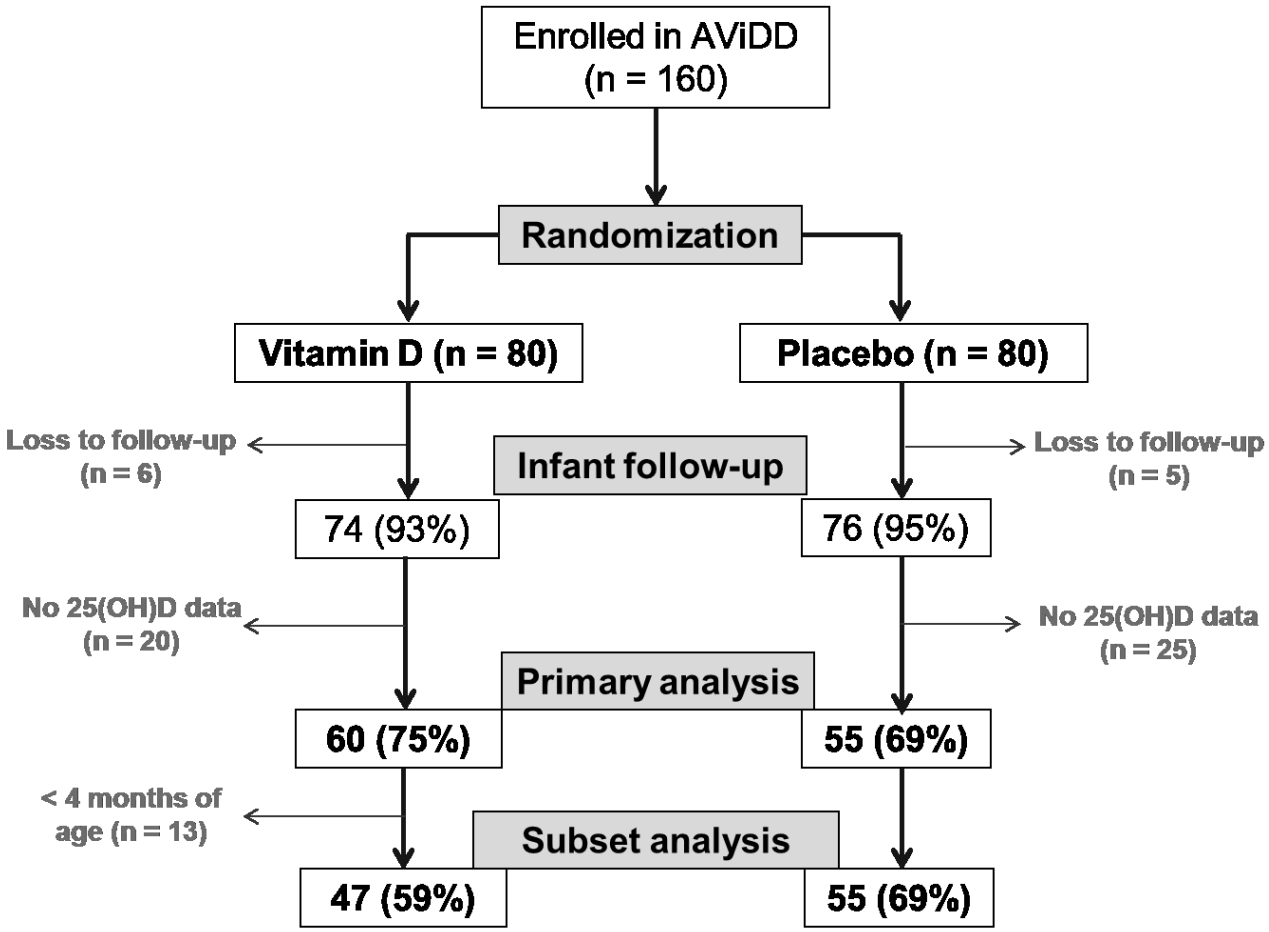
Public Health Nutrition

Table of Contents

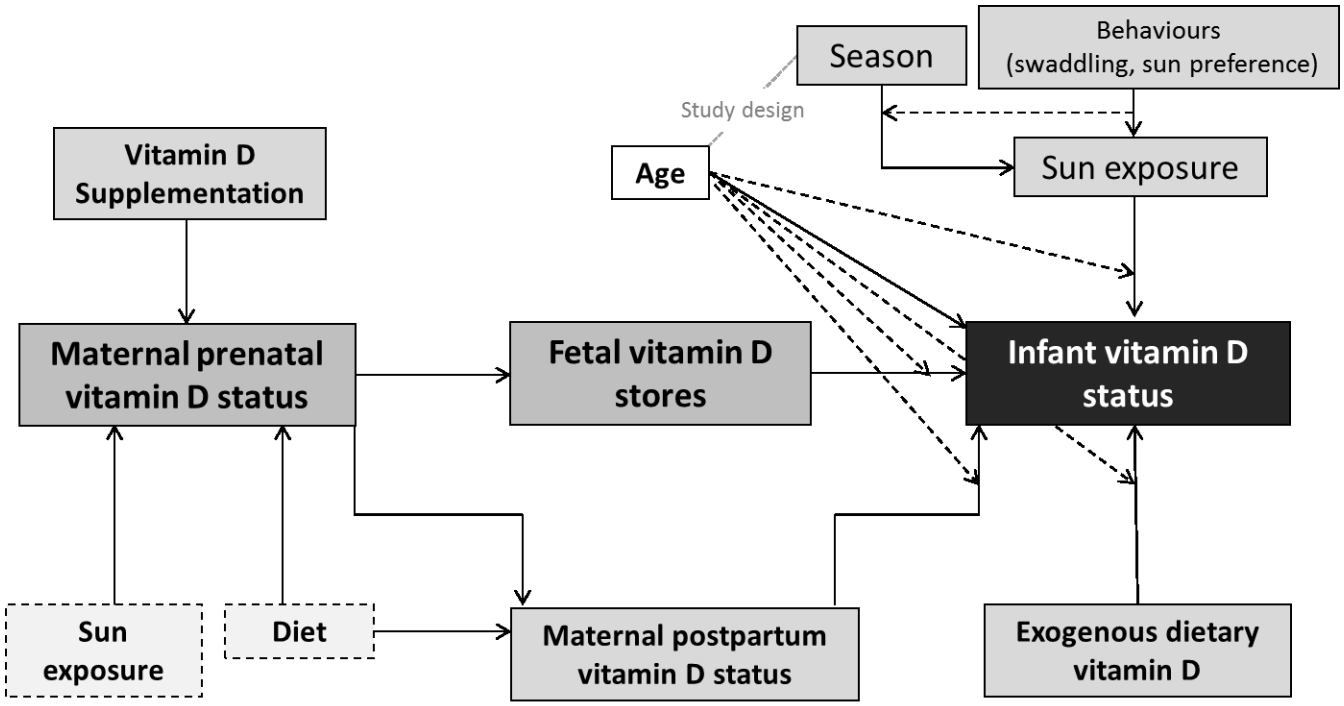
Supplemental Table 1: Maternal demographic, lifestyle and dietary characteristics, by supplementation group

Characteristic	Placebo (n=54)		Vitamin D[a]				
			All (n=60)		Subset (n=47)		
	%, Mean or Median[c]	*n*, SD or (min, max)	%, Mean or Median[c]	*n*, SD or (min, max)	%, Mean or Median[c]	*n*, SD or (min, max)	*P*[b]
Age, yrs	22.8	3.6	22.6	3.5	22.6	3.6	0.81
Marital status, n (%)							
Married	100	54	100	60	100	47	-
Level of education, n (%)							
Primary school incomplete (<8 yrs)	65	35	68	41	68	32	0.97
High school incomplete (≥8 to <12 yrs)	31	17	25	15	26	12	
High school complete (≥12 yrs)	4	2	7	4	6	3	
Primary occupation, n (%)							
Homemaker	94	51	87	52	87	41	1.00
Other	6	3	13	8	13	6	
Gravidity[d]	2	(1, 4)	1	(1, 5)	1	(1, 5)	0.89
Parity[e]	1	(0, 2)	0	(0, 4)	0	(0, 4)	0.89
Height, cm	150.0	5.3	150.4	± 5.1	150.7	4.9	0.38
Weight at enrolment, kg	51.6	8.5	52.5	± 8.4	52.9	9.1	0.48
Gestational age at enrollment, weeks	28.0	1.0	27.6	± 1.1[§]	27.6	1.1[§]	0.71
Season at enrolment[f]**, n (%)**							
August – November	61	33	60	36	68	32	0.02
December – January	39	21	40	24	32	15	
100% adherent with supplemental dose, n (%)	53	98	57	95	45	96	0.63

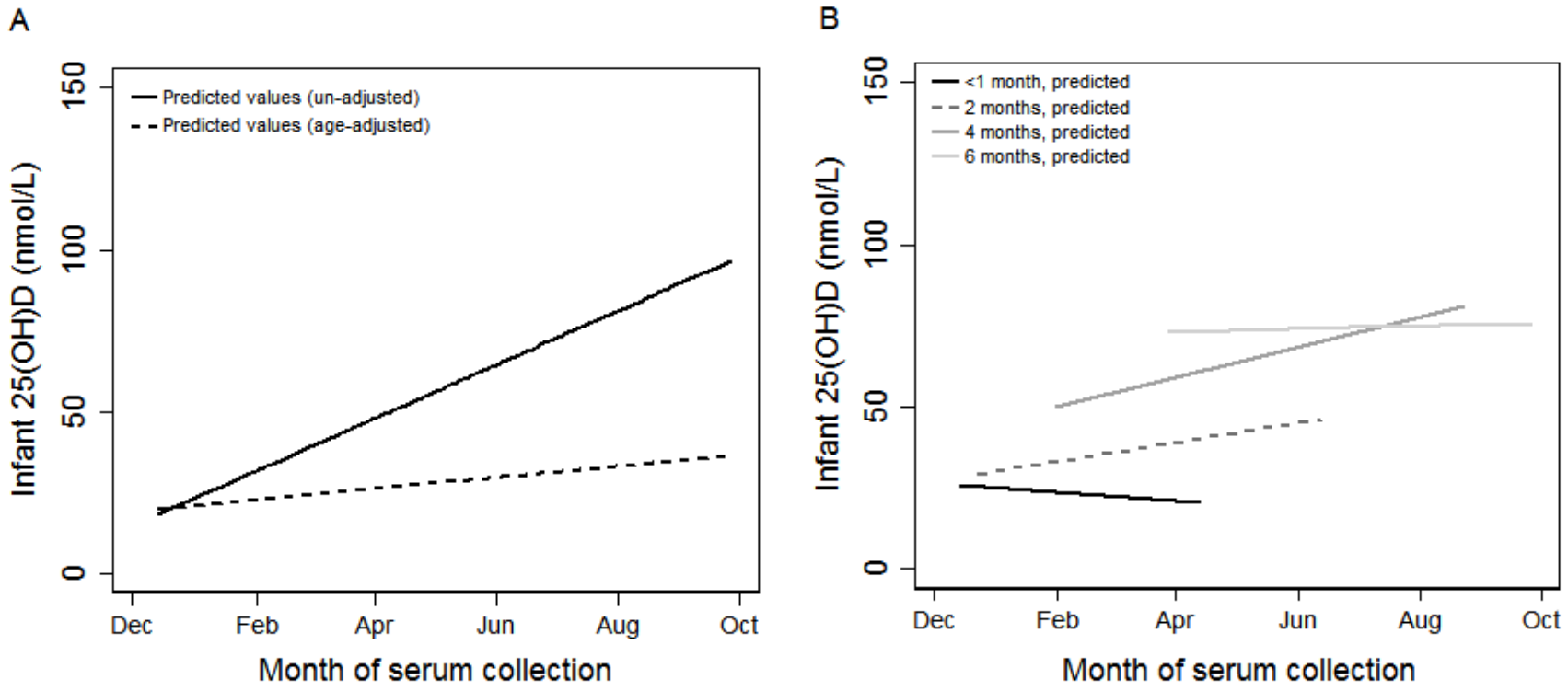
[a] The vitamin D 'All' group includes data for all participants (mothers) from whom any data on infant 25-hydroxyvitamin D (25(OH)D) were available; the 'Subset' excluded maternal data for n=13 infants who did not contribute 25(OH)D data beyond 4 months of age.
[b] P-value for differences between 'all' and 'subset' vitamin D groups.
[c] Median and range (min, max) reported for non-normally distributed variables: gravidity and parity.
[d] Gravidity defined as the number of times the participant was pregnant, including the pregnancy at the time of enrolment.
[e] Parity defined as the number of previous pregnancies carried to delivery.
[f] Participant enrollment occurred from August, 2010 to January, 2011.



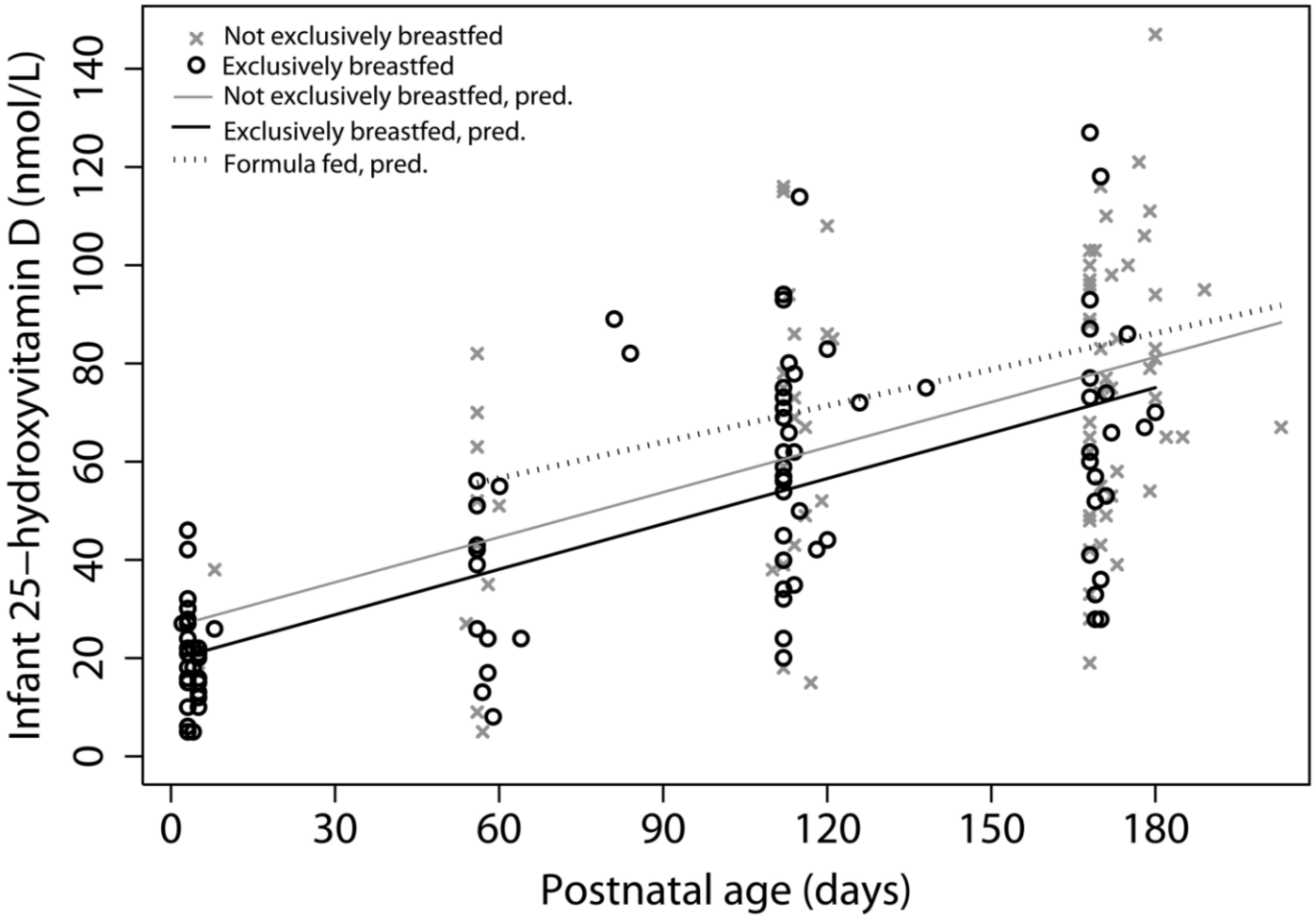
Supplemental Figure 1: **Flowchart of analytical sample**. 160 pregnant women were enrolled in the Antenatal Vitamin D in Dhaka (AViDD) trial and randomized to either the vitamin D or placebo groups. All available infant 25(OH)D data were used to assess the effect of prenatal maternal vitamin D supplementation on infant 25(OH)D up to 6 months of age ('Primary analysis'). A subset of infant 25(OH)D measurements from the vitamin D group and all available data from infants in the placebo group were used to assess the associations between postnatal factors and the rise in infant 25(OH)D with age ('Subset analysis'). The primary and subset analyses correspond to the primary and secondary aims of the study, respectively.



Supplemental Figure 2: **Conceptual model of the inter-relationships among pre- and postnatal factors associated with early infant 25-hydroxyvitamin D concentration in Bangladesh**. Solid lines represent proposed causal associations between infant 25-hydroxyvitamin D and maternal and infant variables. Dashed lines represent potential effect modification by age. Dashed boxes are variables for which the estimates were not quantified in regression analyses. In the present study, we considered random assignment to either maternal vitamin D or placebo supplementation to be the dominant prenatal determinant of maternal and early infant vitamin D status (aim #1). The rise in infant 25(OH)D with age was hypothesized to be caused by postnatal factors that were proximal to infant 25(OH)D (aim #2). Maternal vitamin D status was hypothesized to be associated with infant 25(OH)D through endowment of fetal stores (prenatal effect) and transfer via breastmilk (postpartum effect). Other potential exogenous dietary sources of vitamin D among infants included formula use and animal source foods (i.e., milk, eggs, meat and fish) or vitamin D-fortified complementary foods. The effect of season on infant vitamin D status was modelled using calendar day of serum collection, and was tested for evidence of effect modification by maternal preferences to expose infant to sunlight and swaddling practices when outdoors. The effects of distal maternal prenatal factors (e.g., maternal prenatal diet and sun exposure) on infant 25(OH)D were assumed to be mediated through maternal prenatal vitamin D status. For most of the causal associations hypothesized, we tested for evidence of interactions with age, given that effects of some maternal and infant pre- and postnatal variables would be expected to vary with age (e.g., the association between maternal prenatal 25(OH)D and infant 25(OH)D would be expected to diminish over the few several months of life). Season (calendar day) and age are shown to be associated with one another because of the study design (births occurred during only part of the year).



Supplemental Figure 3: Association between infant 25-hydroxyvitamin D concentration (25(OH)D) and calendar day of serum collection among a subset of observations uninfluenced by prenatal vitamin D supplementation. (A) The association between infant 25(OH)D (n=102; 187 observations) and calendar day in un-adjusted(P<0.001) and age-adjusted analysis (P=0.205). **(B)** Change in infant 25(OH)D by calendar day, stratified by age.



Supplemental Figure 4: Association between infant 25-hydroxyvitamin D concentration (25(OH)D) and age, stratified by feeding pattern: exclusive breastfed, not exclusively breastfed, and formula fed. The rise in infant 25(OH)D among infants who had been exclusively breastfed (n=65; 95 observations: 9.3 nmol/L per month, 95% CI 7.5 -11.1, *P*<0.001) was comparable (*P*=0.24) to the rise in 25(OH)D among infants who were reportedly formula-fed (n=50; 35 observations: 7.4 nmol/L per month, 95% CI 4.0-10.7, *P*<0.001). The association between infant 25(OH)D and not-exclusively breastfed overlapped with the association between not-formula fed and infant 25(OH)D (9.1 nmol/L per month, 95% CI 7.4-10.8, *P*<0.001), and therefore is not shown.