

SUPPLEMENTARY NOTE

Disproportionate vitamin A deficiency in pregnant women of specific ethnicities in the United States and ethnic differences in allele frequencies of polymorphisms of vitamin A-related genes

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Table of Contents

The Bronx dataset2

- Supplementary Note Table 1: Demographic information of the participants2
- Supplementary Note Figure 1: Comparison of serum retinol and beta-carotene levels between non-Hispanic Black (AA) and Hispanic (His) in each time point..... 3

NHANES datasets4

- Supplementary Note Table 2: Demographic information of the participants in the NHANES datasets.....4
- Supplementary Note Table 3: Availabilities of poverty income ratio (PIR) in each ethnic group.....4
- Supplementary Note Table 4: Summary of weighted values in each ethnicity4
- Supplementary Note Table 5: Proportion of vitamin A deficient individuals in the dataset (age 17-80).....5
- Supplementary Note Table 6: Proportion of vitamin A deficient pregnant women5

Genetic variations of serum retinol related SNPs and ethnicity6

- Supplementary Note Figure 2: Permutation analysis of the deviation of MAF between different ethnic groups6

References7

The Bronx dataset

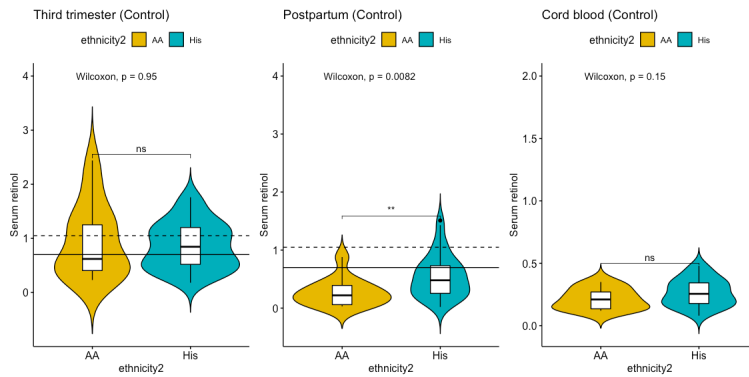
The original data was collected for testing the associations to post-bariatric surgery and vitamin A levels among pregnant women in the Bronx [1].

Supplementary Note Table 1: Demographic information of the participants

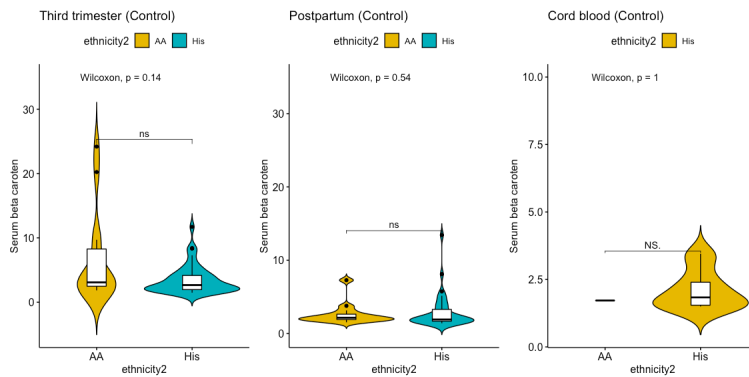
		non-Hispanic Black	Hispanic	Other	P-value
Total N (%)		15 (22.4)	44 (65.7)	8 (11.9)	
Age	Mean (SD)	29.0 (6.3)	29.8 (5.7)	33.3 (4.3)	0.252
Multipara	No	4 (26.7)	11 (25.0)	2 (28.6)	1
	Yes	11 (73.3)	33 (75.0)	5 (71.4)	
Education	High school	4 (28.6)	25 (61.0)	3 (42.9)	0.017
	College	4 (28.6)	13 (31.7)	4 (57.1)	
	<HS	6 (42.9)	3 (7.3)	0	
BMI (prepregnancy)	Mean (SD)	29.7 (6.7)	32.1 (6.7)	35.9 (12.0)	0.191
BMI (delivery)	Mean (SD)	34.4 (6.2)	36.6 (6.2)	39.4 (10.5)	0.257
Obese (prepregnancy)	NormalWeight	4 (26.7)	3 (7.0)	1 (14.3)	0.544
	OverWeight	3 (20.0)	13 (30.2)	1 (14.3)	
	ClassI obesity	4 (26.7)	15 (34.9)	2 (28.6)	
	ClassII obesity	4 (26.7)	12 (27.9)	3 (42.9)	
Gestational weight gain (GWG)	Mean (SD)	24.2 (9.5)	26.4 (19.6)	19.7 (15.1)	0.624
GWG recommended level	Below		5 (11.9)	2 (28.6)	0.112
	Above	15 (100.0)	37 (88.1)	5 (71.4)	
Delivery mode (C-section)	notCS	8 (53.3)	23 (53.5)	5 (71.4)	0.696
	CS	7 (46.7)	20 (46.5)	2 (28.6)	
Baby weight	Mean (SD)	2933.5 (439.8)	3093.6 (611.8)	3260.7 (807.2)	0.466
Large for gestational age	0	13 (100.0)	36 (97.3)	5 (83.3)	0.255
	1		1 (2.7)	1 (16.7)	
Vitamin A status	VAD	8 (53.3)	29 (65.9)	3 (37.5)	0.311
	VAS	7 (46.7)	15 (34.1)	5 (62.5)	
Serum retinol postpartum	Mean (SD)	0.2 (0.2)	0.6 (0.4)	0.7 (0.8)	0.053
Serum retinol cord blood	Mean (SD)	0.2 (0.1)	0.2 (0.1)	0.4 (0.1)	0.094
Serum beta carotene third trimester	Mean (SD)	6.5 (7.1)	3.6 (2.2)	5.5 (5.2)	0.063
Serum beta carotene postpartum	Mean (SD)	2.8 (1.7)	2.8 (2.3)	2.9 (1.2)	0.99
Serum beta carotene cord blood	Mean (SD)	1.7 (NA)	2.0 (0.6)	1.4 (0.1)	0.487

Close to 60% of participants showed their serum retinol levels lower than 1.05 $\mu\text{mol/L}$. While vitamin A sufficiency (VAS) females were slightly older than the vitamin A deficiency (VAD) women, all variables listed in this table were not significant, except serum retinol levels in the cord blood.

A. Serum retinol



B. Serum beta-carotene



Supplementary Note Figure 1: Comparison of serum retinol and beta-carotene levels between non-Hispanic Black and Hispanic pregnant women in each time point

We plotted serum retinol and serum beta-carotene levels in Third trimester and postpartum serum of the mother, and cord blood by the ethnic groups. No significant differences were observed except postpartum blood from the mother.

AA, non-Hispanic Black (African American); His, Hispanic; ns, not significant

NHANES datasets

The National Health and Nutrition Examination Survey (NHANES) data sets were downloaded from the website. We used 2001-2002, 2003-2004, 2005-2006 series. The vitamin D values were adjusted as the NHANES suggested.

Supplementary Note Table 2: Demographic information of the participants in the NHANES datasets

		Mexican American	Other Hispanic	NH White	NH Black	Other
Total N (%)		6127 (24.8)	860 (3.5)	10317 (41.7)	6381 (25.8)	1030 (4.2)
Gender	Male	2963 (48.4)	408 (47.4)	4998 (48.4)	3163 (49.6)	468 (45.4)
	Female	3164 (51.6)	452 (52.6)	5319 (51.6)	3218 (50.4)	562 (54.6)
Pregnancy Status at Exam	Yes	286 (11.2)	39 (10.3)	441 (11.9)	167 (6.4)	58 (12.8)
	No	2082 (81.6)	307 (81.2)	3034 (82.1)	2249 (85.9)	358 (78.9)
	Cannot ascertain	184 (7.2)	32 (8.5)	219 (5.9)	201 (7.7)	38 (8.4)

Supplementary Note Table 3: Availabilities of poverty income ratio (PIR) in each ethnic group

No PIR available	MexicanAmerican	OtherHispanic	NH_White	NH_Black	Other
No	5736	809	9813	6004	976
Yes	391	51	504	377	54

We have checked the number of entries that do not have poverty information. All groups have less than 10% (suggested threshold by CDC) of participants have NA in the PIR information. Therefore, we decided to analyze it as is.

Supplementary Note Table 4: Summary of weighted values in each ethnicity

	Age (years)	PIR	Vitamin D (nmol/L)	Serum retinol (µmol/L)
Mexican American	30.03 (0.50)	1.88 (0.05)	58.30 (0.92)	1.75 (0.01)
Other Hispanic	33.83 (0.75)	2.17 (0.11)	61.09 (1.28)	1.86 (0.03)
NH White	40.81 (0.41)	3.24 (0.06)	71.33 (0.73)	2.09 (0.01)
NH Black	34.85 (0.38)	2.19 (0.07)	46.26 (0.65)	1.74 (0.01)
Other	34.35 (0.80)	2.78 (0.09)	58.19 (1.18)	1.88 (0.02)

Since NHANES has a complex design, we followed the CDC's recommendation to perform the analysis with sample weight to see the distribution of age, PIR, serum vitamin D, and serum retinol. As we expected serum vitamin D and retinol levels of NH Black and Mexican Americans were lower than NH White.

Supplementary Note Table 5: Proportion of vitamin A deficient individuals in the dataset (age 17-80)

		Both male and female					Male					Female				
		Mexican American	Other Hispanic	NH White	NH Black	Other	Mexican American	Other Hispanic	NH White	NH Black	Other	Mexican American	Other Hispanic	NH White	NH Black	Other
Total N (%)		3684 (22.9)	580 (3.6)	7377 (45.9)	3778 (23.5)	651 (4.1)	1782 (22.9)	268 (3.5)	3573 (46.0)	1853 (23.9)	291 (3.7)	1902 (22.9)	312 (3.8)	3804 (45.8)	1925 (23.2)	360 (4.3)
Vitamin A deficiency	Yes	111 (3.2)	24 (4.4)	94 (1.3)	194 (5.7)	23 (3.9)	16 (1.0)	4 (1.6)	16 (0.5)	41 (2.4)	7 (2.6)	95 (5.3)	20 (6.9)	78 (2.2)	153 (8.8)	16 (5.0)
	No	3354 (96.8)	519 (95.6)	6886 (98.7)	3225 (94.3)	571 (96.1)	1656 (99.0)	249 (98.4)	3387 (99.5)	1647 (97.6)	264 (97.4)	1698 (94.7)	270 (93.1)	3499 (97.8)	1578 (91.2)	307 (95.0)

Women tends to have higher proportion of vitamin A deficiency compared to male in all race.

Supplementary Note Table 6: Proportion of vitamin A deficient pregnant women

		Mexican American	Other Hispanic	NH White	NH Black	Other
Total N (%)		276 (28.6)	38 (3.9)	435 (45.0)	160 (16.6)	57 (5.9)
Vitamin A deficiency	Yes	39 (14.9)	11 (29.7)	44 (10.9)	47 (32.0)	6 (12.0)
	No	222 (85.1)	26 (70.3)	358 (89.1)	100 (68.0)	44 (88.0)

We observed high prevalence rate of VAD in NH Black followed by other Hispanic (including Latin Americans with Afro-Caribbean ancestry) which is concordant to what Hanson et al. reported [2].

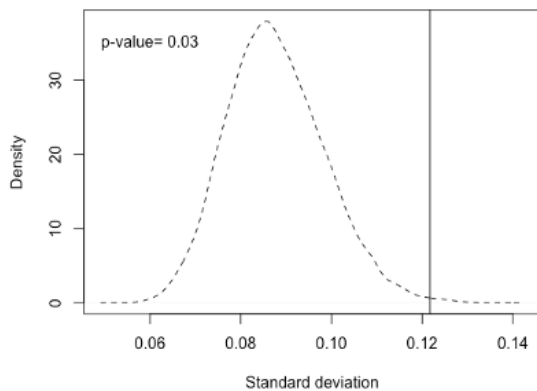
Genetic variations of serum retinol related SNPs and ethnicity

Borel and Desmarchelier listed 42 SNPs associated with fasting blood vitamin A concentration or vitamin A bioavailability on their 2017 Nutrients review [3]. Of those, 39 SNPs have the dbGAP accession numbers. I downloaded the frequency information of those SNPs from <https://www.ncbi.nlm.nih.gov/snp/>. We calculated if these SNPs also have high alle-frequency variations, we calculated the deviations of reference allele frequency differences between each ethnic group (Average 0.121 (95% CI: 0.105, 0.138)).

To perform a permutation test to see if the obtained deviations were higher than by chance, we obtained SNPs (75281370 SNPs) information with allele frequencies (fileformat=VCFv4.1 fileDate=20190817) from the 1000 genome database. We removed following SNPs from the analysis:

1. The minor allele frequency (MAF) was not reported.
2. The MAF is less than 0.33.
3. More than one variant is recorded.

We, then, calculated the deviation of the MAF of each SNPs (6025429 SNPs) between different ethnic groups, and performed a permutation test (n=1,000).



Supplementary Note Figure 2: Permutation analysis of the deviation of MAF between different ethnic groups

We plotted the averaged distribution of standard deviation of MAF of randomly selected 39 SNPs from 6025429 SNPs for 1000 times with a dashed line. The vertical line indicates the mean value of vitamin A related SNPs (0.121). The result suggests that deviation of the allele frequencies of the serum retinol related SNPs among different ethnicities is significantly larger than that of randomly selected SNPs (p-value=0.03).

References

- 1 Garretto, D. *et al.* (2019) Vitamin A and β -carotene in pregnant and breastfeeding post-bariatric women in an urban population. *J Perinat Med* 47, 183–189
- 2 Hanson, C. *et al.* (2016) Serum retinol concentrations, race, and socioeconomic status in of women of childbearing age in the united states. *Nutrients* 8,
- 3 Borel, P. and Desmarchelier, C. (2017) Genetic Variations Associated with Vitamin A Status and Vitamin A Bioavailability. *Nutrients* 9,