Association of Vitamin D Serum Concentration with Infection Outcomes for Children after Surgery

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Background

Vitamin D deficiency is a global health problem. Vitamin D may play a role the Immune System regulation Vitamin D insufficiency and deficiency has been associated with various disease states and lower health outcomes. In the adult population, higher vitamin D levels correlated with decreased odds of in-hospital morbidity and mortality. Some studies in infants and children are also exploring the effects of vitamin D insufficiency and type 1 diabetes mellitus as well as investigating the risk of developing of allergies and atopic diseases (1,2). Still, a significant gap exists in our understanding of the consequences of vitamin D insufficiency/deficiency in the pediatric population. Thus, we aimed to evaluate the association between vitamin D concentration and major in-hospital infection and length of hospital stay (LOS) in pediatric surgical patients.

Methods

With IRB approval we performed an EPIC search for all Children's Health patients from 2011 to 2015 where at least one 25-hydroxyvitamin D level was determined within the perioperative period (1 month pre- and post-surgery). Patients were included if they were less than 18 years of age and had underwent non-cardiac surgery. Patients were excluded if they did not receive general anesthesia, stayed less than one night in the hospital, had an American Society of Anesthesiologists Physical Status greater than 4, or underwent emergent surgery. Pertinent information including details of the surgery and relevant past medical history were collected for each patient to help analyze the data set and account for confounding factors (Table 1). In order to have access to a larger number of patients, this project was performed in collaboration with Cleveland Clinic (Cleveland, OH). The EPIC search provided us with 1600 patient charts from CMC or Children's Health-Plano, and 850 were screened and included into the study based on the criteria noted previously

Table 1

Table 1. Baseline and intraoperative characteristics for cardiac surgical patients (N = 816)

	Vitamin D level (ng/mL)					
Variable	**<13 (N = 182)**	**14-19 (N = 154)**	**20-25 (N = 162)**	**26-34 (N = 156)**	**>35 (N = 162)**	***P* Value [a]**
Age, yr	9 ± 6	10 ± 6	8 ± 6	7 ± 5	6 ± 6	<0.001 [b]
Gender (1), %	56	50	49	44	47	0.46
Race%						<0.001
African American	27	21	24	13	22	
Caucasian	23	42	39	53	40	
Hispanic/Latino	42	27	32	26	31	
Other	8	9	5	9	7	
Body mass index, kg/m^2	19 [16, 24]	18 [15,23]	18 [15,22]	16 [15, 19]	17 [15, 19]	<0.001 [c]
American Society of Anesthesiologists status, %						0.33
1	1	1	1	2	1	
2	19	19	27	26	19	
3	66	66	62	63	68	
4	14	14	11	8	12	
Vitamin D supplement within 1 month prior to surgery, %	34	44	36	34	40	0.31
Immunosuppressive treatment, %	35	34	24	21	19	<0.001
Atopic disease, %	5	6	9	9	5	0.30
Asthma, %	11	11	13	10	9	0.84
Dialysis, %	18	10	10	7	9	0.02
Human immunodeficiency Virus, %	1	0	0	0	0	0.48
Tuberculosis, %	1	0	0	0	0	0.48
History of malignancy, %	10	5	6	4	3	0.08
Chemo or radiation therapy, %	9	3	5	4	1	0.009
Hematologic / immunologic deficiency, %	5	4	4	4	3	0.86
Hypertension, %	12	10	9	10	12	0.88
Diabetes, %	2	2	2	2	2	>0.99
Procedure - %						
Abdominal	29	17	22	17	33	<0.001
Bone marrow biopsy	5	2	3	1	2	0.07
Central line	37	23	30	29	26	0.06
Dialysis	15	9	9	7	7	0.06
Endocrinology	3	6	11	4	4	0.01
Endoscopy	15	19	12	20	16	0.36
Esophagogastroduodenoscopy	11	13	9	15	12	0.44
Exams	12	6	8	8	7	0.45
Incision / excision	2	2	2	3	2	>0.99
Liver biopsy	10	1	2	2	1	<0.001
Lumbar puncture	5	5	4	4	0	0.08
Lung /chest wall	3	6	7	7	14	0.002
Neck/ear/eye	16	16	22	23	26	0.13
Neurological	2	3	4	3	1	0.4
Orthopedic	1	2	1	4	2	0.12
Other biopsy	1	1	2	2	2	0.8
Pain management	2	2	4	3	4	0.8
Rectal	14	17	9	16	9	0.08
Renal biopsy	14	16	9	11	6	0.04
Transplant	3	1	2	0	4	0.12
Urology	1	5	9	10	6	0.001
Month of procedure, %						0.10
Jan	10	8	12	15	10	
Feb	12	11	13	10	9	
Mar	10	12	9	8	12	
Apr	11	11	8	8	7	
May	6	8	4	4	5	
Jun	5	7	8	8	11	
Jul	5	3	6	10	12	
Aug	3	8	8	10	8	
Sep	9	8	7	6	9	
Oct	9	11	12	9	3	
Nov	7	4	6	6	7	
Dec	14	8	7	4	7	
Duration of procedure, minutes	82 [57, 148]	73 [52, 113]	74 [51, 126]	76 [54, 121]	78 [54, 120]	0.46 [c]

Summary statistics are presented as % of patients, mean ± SD, or median (Q1, Q3), respectively.
[a] Pearson's chi-squared test, unless specified; [b] ANOVA; and [c] Kruskal-Wallis ANOVA by ranks.

Table 2

Table 2. ***Primary analysis*** **–** Pairwise comparisons on postoperative infection among the five vitamin D quintiles using multivariable logistic regression models (N = 816)

Pairwise comparisons			
Vitamin D group (ng/mL)	**Vitamin D group (ng/mL)**	**OR [*] (99.5% CI) [†]**	**P[†]**
Vitamin D ≤ 13 (ng/mL)	Vitamin D 14-19 (ng/mL)	0.60 (0.15, 2.47)	0.31
	Vitamin D 20-25 (ng/mL)	0.91 (0.22, 3.87)	0.86
	Vitamin D 26-34 (ng/mL)	0.63 (0.15, 2.64)	0.36
	Vitamin D ≥35 (ng/mL)	0.33 (0.10, 1.16)	0.01
Vitamin D 14-19 (ng/mL)	Vitamin D 20-25 (ng/mL)	1.52 (0.35, 6.60)	0.43
	Vitamin D 26-34 (ng/mL)	1.05 (0.25, 4.40)	0.93
	Vitamin D ≥35 (ng/mL)	0.55 (0.16, 1.98)	0.19
Vitamin D 20-25 (ng/mL)	Vitamin D 26-34 (ng/mL)	0.69 (0.16, 2.96)	0.48
	Vitamin D ≥35 (ng/mL)	0.37 (0.10, 1.34)	0.03
Vitamin D 26-34 (ng/mL)	Vitamin D ≥35 (ng/mL)	0.53 (0.15, 1.85)	0.15

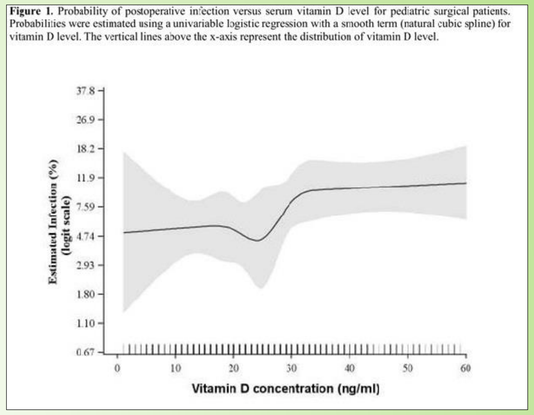
[‡] Observed incidences of infection were 5.5% (10 out of 182), 5.8% (9 out of 154), 4.9% (8 out of 162), 5.8% (9 out of 156), and 11.7% (19 out of 143) for patients with vitamin D level ≤ 13, 14-19, 20-25, 26-34, ≥35 ng/ml, respectively.

[*] We considered all the variables listed in the Table 1 to be included into the model via purposeful selection procedure [1]; age, gender, ASA status, atopic disease, dialysis, and month of surgery were retained in the final model.

[†] CIs are adjusted for multiple comparisons (a total of 10) using the Bonferroni correction, thus the significance criterion for each comparison was 0.005 (i.e., 0.05/10).

Figure 1

Figure 1. Probability of postoperative infection versus serum vitamin D level for pediatric surgical patients. Probabilities were estimated using a univariable logistic regression with a smooth term (natural cubic spline) for vitamin D level. The vertical lines above the x-axis represent the distribution of vitamin D level.



Results

The EPIC search provided us with 1600 patient charts from CMC or Children's Health-Plano, and 850 were included into the study after being screened. The incidence of infection were 5.5%, 5.8%, 4.9%, 5.8%, and 11.7% for patients with vitamin D level ≤13, 14-19, 20-25, 26-34, and ≥35 ng/ml, respectively. The odds of having infection did not differ significantly among the five vitamin D groups (Table 2). Secondly, no difference was found in LOS among the five vitamin D groups (p = 0.55).

Conclusion

Our analysis indicates that vitamin D level is not associated with infection or LOS in pediatric surgical patients. Other baseline and surgical factors have probably a stronger influence on in-hospital infection and LOS than vitamin D levels.

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References

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