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Vitamin D deficiency among preschool children and its correlation with nutritional habits and sun exposure

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ABSTRACT

Introduction: Vitamin D deficiency is now being recognized as an epidemic worldwide. Recent accumulating data on the vitamin D status of Egyptians indicate a resurgence of its deficiency among otherwise healthy members.
Methods: a cross sectional study including 300 children of preschool age, with no rachitic manifestations, recruited from Aboulrich Children Hospital, Cairo University. 25 hydroxyvitamin D was measured by ELISA based technique, levels < 10ng/ml were considered deficient, levels of 10- 19.9ng/ml were considered insufficient and levels ≥ 20 ng/ml were considered sufficient.
Results:15% of children had sufficient levels of vitamin D, 27.3% had insufficient levels and 57.7% had deficient levels. The mean level of 25 hydroxyvitamin D in our study was 11.9 ng/ml ± 10.19 SD, ranging from 4.6 - 75.5 ng/ml.Vitamin D levels were significantly higher in children coming from rural areas (P < 0.001), levels were also much higher in children living in sunny areas (P = 0.005). Vitamin D deficiency was more common in the children who didn't receive vitamin D supplementation (P < 0.001).
Conclusion: Vitamin D deficiency is a common problem in Egyptian preschool children. Adequate sun exposure and vitamin D supplement are necessary in our community.

Keywords: 25 Hydroxyvitamin D, Sun exposure, Preschool children, Vitamin D deficiency.

Introduction

Vitamin D is unique among hormones because it can be made in the skin from exposure to sunlight. Vitamin D is popularly known as the sunshine vitamin ***(Holick, 2007)***.
In the last few years, knowledge about the relevance of vitamin D and its relationship to illnesses has extended beyond the skeletal system ***(Perez-Lopez et al., 2011)***. In addition to its main benefits on bone health, vitamin D has many other beneficial effects and its deficit has been associated with a great variety of diseases. Low vitamin D levels have been related to both acute and chronic illnesses ***(Abrams et al., 2013)*** such as: immune disorders, atopic diseases, respiratory infections and kidney diseases ***(Bozzetto et al., 2012)***.
In the Middle East, North African region and Arab gulf countries, a lack of population-based studies on vitamin D deficiency, as well as gaps in studies on infants, prepubertal children and adolescents hinder the development of region specific guidelines, and constitute a major obstacle impacting this chronic and most often subclinical diseases***(Ross et al., 2011)***.That said, accumulation of data on vitamin D status of Egyptians over the past two decades has indicated a resurgence of vitamin D deficiency among otherwise healthy members of population ***(Ross et al., 2011)***.
The aim of this work was to evaluate Vitamin D status in a sample of preschool Egyptian children, and to study its correlation with various variables including sunexposure, nutritional habits and Vitamin D supplementation.

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Subjects and Methods:

This study was conducted at Cairo University Children's Hospital; a hospital that occupies an advanced rank in the field of pediatrics and child-related surgery, providing great medical service for thousand of Egyptian children.

The study was approved by Cairo University's Pediatric department ethical committee, and informed consent was given by caregivers of the recruited children.

2.1 Patient population:

This cross-sectional study was conducted on 300 children recruited from the general outpatient clinics at Cairo University Children's Hospital (AboulRish), over a period of 1 year. Patients aged 24 to 72 months who were visiting the outpatient clinic for mild acute illnesses like upper respiratory tract infections or pharyngitis, were enrolled in the study. Patients suffering from chronic diseases, those with apparent rachitic manifestations or those on medications affecting Vitamin D levels were excluded from the study

2.2 Patient Evaluation

Complete nutritional and developmental history were obtained from all included patients. Nutritional history included type and duration of milk feeds (exclusive breastfeeding, artificial infant formulae or both in first six months of age), time and type of food introduction during weaning, as well as daily intake of vitamin D supplements. A 3- day food diary was obtained from each parent and was taken as an example of the child's average regular diet and used to calculate average daily intake of vitamin D units from food. Vitamin D intake from food was labeled adequate when above 200 IU/day and inadequate if below 200 IU/day, half the recommended daily dose for children (400 IU/day) as described by American Academy of Paediatrics***(Armstrong, 2009)*** as the main source of vitamin D is sunexposure.

For the purpose of the study, exclusive breastfeeding was defined as infants receiving only breastmilk for nutrition and no other liquids for the first 6 months of age; substitutive feeding was defined as infants receiving artificial formula only without breastfeeding; complementary feeding was defined as infants receiving breastfeeding followed by artificial formula to complete a feed; and supplementary feeding was defined as infants receiving both breastmilk and artificial formula for different feeds ***(World Health Organization, 2001).***

Food introduction was defined as 'optimal' when started between 4 to 6 months of age and 'suboptimal" if introduced before 4 months or after 6 months of age ***(Agostoni et al., 2008).*** Maternal knowledge about the importance of vitamin D as well as antenatal intake of vitamin D was assessed.

Sociodemographic data was collected such as urban/rural living, sunny environment of the living area & duration of child's daily sunlight exposure outdoors (minutes/day).

Full Anthropometric measurements including height (cm), weight (kg), head circumference (cm), and body mass index were analyzed and all growth parameters were plotted on WHO Z-score calculator. Developmental history of children was recorded and included mental, motor and dental milestones.

2.3 Patient Investigations:

Serum 25 hydroxyvitamin D was measured in all 300 children. The sample consisted of 2 ml blood obtained by venipuncture in a plain tube. Serum was separated by centrifugation and 25 hydroxyvitamin D was measured by ELISA technique using the DRG: HYBRID – XL 25- OH vitamin D apparatus. Levels of < 10ng/ml was considered deficient, levels between 10 and < 20 ng/ml were considered insufficient and level ≥ 20 were considered sufficient ***(IOM,2011***

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&Braegger et al.,2013). Based on these levels, patients were subcategorized into three groups and correlations were calculated with various factors.

2.4 Statistical Data

Data was analyzed using the Statistical Package For Social Science (SPSS) version 22: the following methods was employed: percentage distribution, range, means, ± standard deviation and correlation factor (r). The following tests were used: Chi-square test, One-way ANOVA test, independent T-test and Kruskal Wallis test. P values less than 0.05 was considered statistically significant and less than 0.001 was considered as highly significant.

Results

This study included 300 candidates (63% male, 37% females) ranging from 24-72 months of age with a median age of 48 months. Residences included 70.6 % from urban, 14.7% from suburban, and 14.7% from rural areas. Nutritional history showed 236 children were exclusively breastfed (78.7 %), 34 children were on substitutive formula feeding (11.3%), and 30 children received complementary or supplementary formula (10%). The mean age of food introduction was 6.7 ± 2.56 months SD; and mean vitamin D level for our study population was 11.9 +_10.19 ng/ml.

Demographically, correlation of sex showed no significant relationship with vitamin D serum levels. Areas of residence and bioavailability of sunny areas on the other hand showed a highly significant relationship with Vitamin D as regards to degree of urbanization (P value <0.001) (Table 2). Concerning nutritional data, there was no significant difference between serum vitamin D levels in terms of type of milk feeding nor time of food introduction (Table 2).

We recorded vitamin D intake in both dietary and supplements form. In terms of dietary vitamin D intake, a 3-day food recall showed a range of 10-333 IU/day of daily intake with a median of 131.5 (56-183) IU/day. In terms of adequacy, this translated into 56/300 children having received adequate dietary vitamin D, and 244/300 children having received inadequate amounts of Vitamin D. Surprisingly, adequacy of vitamin D units from diet did not reflect a significant correlation with mean serum levels of vitamin D (Table 2).

As for supplementation status, 128/300 (42.6%) children had received vitamin D supplementation in the amount of 250 - 2000 IU/day (484.58 IU/day) for an average of 4 (0.5-26) months. Vitamin D sufficiency was significantly prevalent between children receiving vitamin D supplementation while conversely vitamin D deficiency was prevalent in children who didn't receive supplementation. In the sufficient group 68.9% of children were receiving vitamin D, in the deficient group 59.9% didn't receive vitamin D, with a marked significant P value of <0.001 (Table 5).

Concerning antenatal vitamin D intake, 115/300 (38.3%) mothers received vitamin D while pregnant, 185/300 mothers (61.7%) did not get any antenatal vitamin D intake, which reflected significantly on their children's vitamin D serum levels (p value = 0.001) (Table 2). Only 22/300 mothers were aware of the importance of giving their babies vitamin D as soon as possible after birth; however that knowledge did not reflect a significance on their children's' vitamin D mean serum levels (Table 2)

In terms of sun exposure, 70.7% of the study population live in sunny places, while 29.3% live in non-sunny, humid places; availability of sun at area of residence significantly affected vitamin D levels (p value = 0.005) (Table 2). In the sufficient group 82.8% of children were living in sunny places while in the deficient group 35.3% of children were living in non sunny places (p value = 0.026) (figure 2 & table 5). The median average duration of direct daily sun exposure was 30 minutes/day with a range of 5-360 min/day.There was a highly significant positive correlation between vitamin D level and duration of daily sunexposure (r = 0.156 and P value = 0.009) (Figure 3) .

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There was no significant difference in results of vitamin D levels between children with a history of normal versus delayed mental and motor development nor with dental development nor behavioral development (table 3). There was also no significant difference in vitamin D levels between children with or without recurrent acute infections (Table 3). Growth parameters based on WHO z scores also showed no significant correlations with vitamin D serum levels (Table 4)

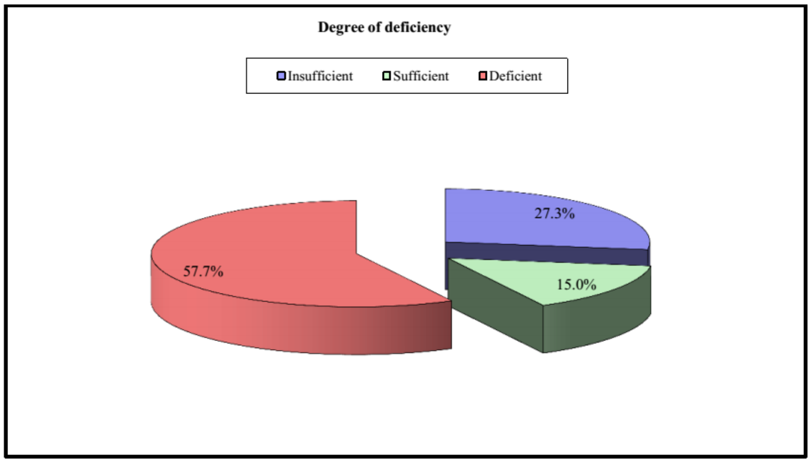

Figure (1): Percentage of children with vitamin D level sufficiency, insufficiency and deficiency.

In our study, serum Vitamin D levels were sufficient in 45/300 children (30.99 ± 12.42 ng/ml), insufficient in 82/300 children (14.16 ± 2.79 ng/ml), and deficient in 173/300 children (5.86 ± 1.7 ng/ml) averaging a mean serum level of 11.9 ± 10.19 ng/ml (4.6-75.5 ng/ml) for the entire study population. (Figure 1)

By correlation of vitamin D sufficiency to a number of factors: the study found that vitamin D sufficiency was more prevalent in children whose mothers took antenatal vitamin D and was also significantly related to residence in sunny places as well as to duration rather than amount of vitamin D supplementations (Table 5).

Table (1): Demographic and nutritional data of the studied population (n=300).

		No. = 300
Age (months)	Mean±SD	49.19±15.17
	Range	24–72
Gender	Female	111(37.0%)
	Male	189(63.0%)
Residence	Urban	212(70.7%)
	Suburban	44(14.7%)
	Rural	44(14.7%)
Breast feeding or formula	Exclusive Breastfeeding	236(78.7%)
	Substitutive formula	34(11.3%)
	Both (complementary and supplementary)	30(10.0%)

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Table(2): Correlations between serum levels of vitamin D (ng/ml) and various factors

		Result of Vit D level (ng/ml) Mean±SD	Range	P-value
Gender	Female	13.26±10.65	4.60–75.50	0.075
	Male	11.09±9.85	4.60–59.70	
Residence	Urban	10.32±7.76	4.60–46.60	0.000
	Suburban	11.86±8.37	4.60–38.10	
	Rural	19.48±16.89	4.60–75.50	
Sun at residence	Not Sunny	9.35±6.79	4.60–34.90	0.005
	Sunny	12.95±11.15	4.60–75.50	
Type of milk Feeding	Breastfeeding	11.38 ± 9.01	4.60 – 54.80	0.241
	Substitutive formula	13.36 ± 11.33	4.60 – 54.80	
	Both	14.22 ± 16.04	4.60 – 75.50	
Time of food introduction	Non Optimal	10.50 ± 8.25	4.60 – 46.60	0.082
	Optimal	12.64 ± 11.05	4.60 – 75.50	
Average vitamin D intake/day (IU) from food	Not adequate	11.66 ± 10.09	4.60 – 75.50	0.403
	Adequate	12.92 ± 10.65	4.60 – 54.80	
Antenatal vitamin D intake	No	10.38±9.58	4.60–75.50	0.001
	Yes	14.33±10.70	4.60–54.80	
Maternal awareness of vitD	No	11.78±10.17	4.60–75.50	0.485
	Yes	13.35±10.64	4.60–38.10	

Table (3): Correlation of serum levels of vit D with developmental outcome and infections

		VitD Level (ng/ml) Mean±SD	Range	P-value
Motor development	Not delayed	11.94±10.36	4.60–75.50	0.796
	Delayed	11.40±8.33	4.60–28.60	
Mental development	Not delayed	11.86±10.20	4.60–75.50	0.408
	Delayed	–	–	
	Autistic features	17.85±8.56	11.80–23.90	
Dentition	Not delayed	11.99±10.33	4.60–75.50	0.546
	Delayed	10.62±8.29	4.60–28.60	
Recurrent acute infections	No	12.23±9.96	4.60–59.70	0.379
	Yes	11.09±10.73	4.60–75.50	

Table (4): Correlation of serum levels of vitamin D with growth parameters

		VitD Level (ng/ml) Mean±SD	Range	P-value
Height groups	Z-score<-2	8.93±5.78	4.60–19.20	0.463
	Z-scor(-2/+2)	12.06±10.40	4.60–75.50	
	Z-score>+2	13.70±0	13.70–13.70	
Weight groups	Z-score<-2	9.06±5.29	4.60–19.20	0.511
	Z-scor(-2-/+2)	11.96±10.35	4.60–75.50	
	Z-score>+2	15.99±7.28	9.08–23.60	
BMI groups	Z-score<-2	10.52±5.78	4.60–17.80	0.105
	Z-scor(-2/+2)	11.69±10.15	4.60–75.50	
	Z-score>+2	18.94±11.80	4.60–34.90	
Head circumference group	Z-score<-2	–	–	0.311

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Z-scor(-2/+2)	11.94±10.21	4.60–75.50
Z-score>+2	4.60±0.00	4.60–4.60

Table(5): Correlation between sufficiency of serum vitamin D level and various factors

		Sufficient		Insufficient		Deficient		P-value
		No.	%	No.	%	No.	%	
Antenatal vitamin D	No	16	35.6%	47	57.3%	122	70.5%	0.000
	Yes	29	64.4%	35	42.7%	51	29.5%	
Duration of vitamin D supplement intake (months)	Median(IQR)	6 (5-12)		4 (3-6)		3 (2-4)		0.000
	Range	2–26		1–12		0.5–18		
Amount of vitamin D supplement intake (IU/day)	Mean±SD	525.00±195.55		507.69±328.54		458.33±164.45		0.330
	Range	300–1000		400–2000		250–1500		
vitamin D supplementation in children	No	14 (31.1%)		55 (67.1%)		103 (59.9%)		0.000
	Yes	31 (68.9%)		27 (32.9%)		70 (40.1%)		
living place	Not Sunny	8 (17.8%)		19 (23.2%)		61 (35.3%)		0.026
	Sunny	37 (82.2%)		63 (76.8%)		112 (64.7%)		

Table (6): Correlation between sufficiency of vitamin D and mental, motor& dental development

		Sufficient		Insufficient		Deficient		P-value
		No.	%	No.	%	No.	%	
Motor development	Normal	39	86.7%	79	96.3%	156	90.2%	0.127
	Delayed	6	13.3%	3	3.7%	17	9.8%	
Mental development	Normal	44	97.8%	81	98.8%	173	100.0%	0.204
	Autisticfeatures	1	2.2%	1	1.2%	0	0.0%	
Dentition	Normal	41	91.1%	79	96.3%	158	91.3%	0.325
	Delayed	4	8.9%	3	3.7%	15	8.7%	

Table (7): Correlation betweensufficiency of vitamin D and growth parameters.

		Sufficient No. = 45	Insufficient No. = 82	Deficient No. = 173	P-value
Height	Mean±SD	97.70 ± 8.80	101.48 ± 10.36	99.42 ± 9.25	0.083
	Range	83 – 114	77 – 127.5	78 – 120	
Z-score Height	Median(IQR)	-1 (-1.38 - -0.64)	-0.97 (-1.44 - -0.26)	-0.95 (-1.52 - -0.28)	0.869
	Range	-1.95 – 0.67	-3.52 – 2.34	-3.51 – 1.92	
Height groups	Z-score < -2	0 (0.0%)	6 (7.3%)	11 (6.4%)	0.201
	Z-score (-2 /+ 2)	45 (100.0%)	75 (91.5%)	162 (93.6%)	
	Z-score > +2	0 (0.0%)	1 (1.2%)	0 (0.0%)	
Weight (kg)	Mean±SD	15.24 ± 3.02	16.00 ± 3.31	15.31 ± 2.96	0.208
	Range	10.5 – 23	9.8 – 28	9 – 27.5	
Weight Z-score	Median(IQR)	-0.6 (-1.03 – 0.23)	-0.5 (-1.08 – 0.2)	-0.6 (-1.19 - -0.202)	0.428
	Range	-1.7 – 2.08	-3.08 – 2.03	-2.8 – 2.09	
Weight groups	Z-score < -2	0 (0.0%)	4 (4.9%)	7 (4.0%)	0.539
	Z-score (-2/+ 2)	44 (97.8%)	77 (93.9%)	165 (95.4%)	

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	Z-score > +2	1 (2.2%)	1 (1.2%)	1 (.6%)	
BMI	Mean±SD Range	15.90 ± 1.74 13.8 – 21.8	15.47 ± 1.56 12 – 20	15.41 ± 1.45 12.8 – 23.5	0.153
BMI Z-score	Median(IQR) Range	-0.1 (-0.48 - 1) -1.4 – 3.6	-0.01 (-0.64 - 0.69) -2.64 – 2.51	-0.18 (-0.74 – 0.49) -2.2 – 4.33	0.300
BMI groups	Z-score < -2 Z-score (-2 /+ 2) Z-score > +2	0 (0.0%) 41 (91.1%) 4 (8.9%)	3 (3.7%) 77 (93.9%) 2 (2.4%)	2 (1.2%) 168 (97.1%) 3 (1.7%)	0.053
Head circumference (cm)	Mean±SD Range	49.22 ± 1.11 47 – 52	49.63 ± 1.54 46 – 53	49.67 ± 1.54 46 – 54	0.195
Z-score	Median(IQR) Range	-0.18 (-0.68 – 0.38) -1.43 – 1.05	-0.16 (-0.68 - 0.47) -1.68 – 1.81	-0.19 (-0.64 - 0.33) -1.83 – 3.14	0.836
Head circumference	Z-score (-2 /+2) Z-score > +2	45 (100.0%) 0 (0.0%)	82 (100.0%) 0 (0.0%)	171 (98.8%) 2 (1.2%)	0.478

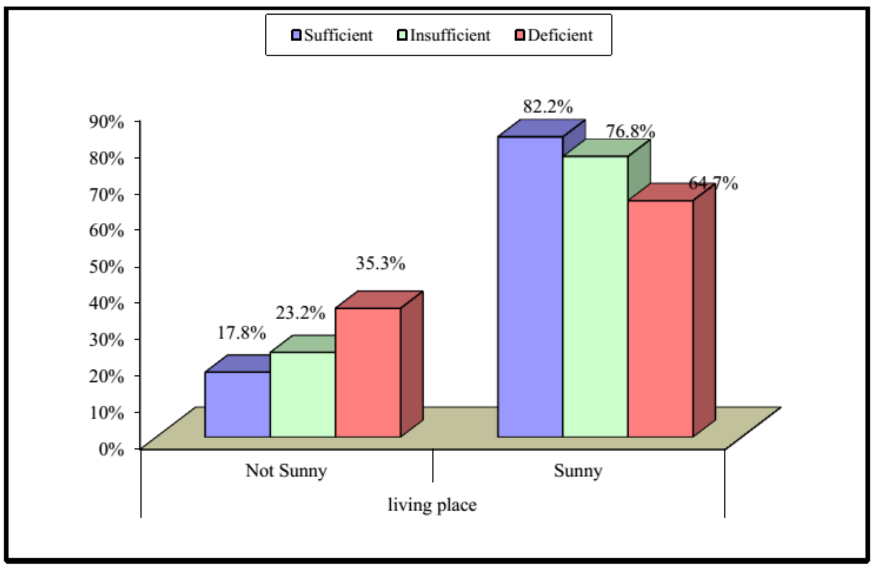

Figure (2): Percentage of children living in sunny places

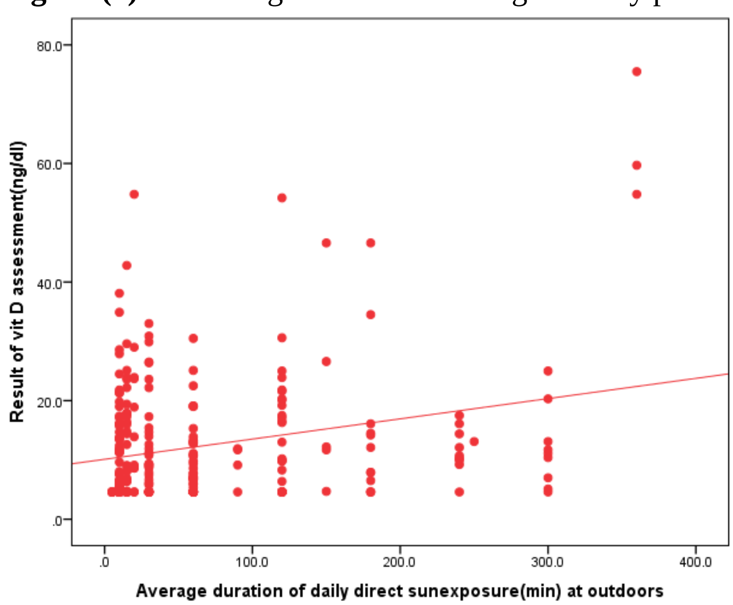

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Figure (3): Vitamin D correlation with duration of daily sunexposure (P=0.009)

Discussions

This is a cross sectional study involving 300 healthy Egyptian children of preschool age, screened for serum 25 (OH) vitamin D levels.

Comparison with other studies was challenging in view of the variability in the 25 hydroxyvitamin D cut-off values in the literature. Unlike other vitamins, the vitamin D concentration in blood varies cyclically over the course of the year in relation to genetic (gender, ethnicity, polymorphisms) and environmental factors (sunlight exposure, diet, food-related or direct vitamin D supplementation, skin pigmentation), furthermore the high intra- and inter-laboratory variability may lead to incorrect vitamin D deficiency/insufficiency diagnosis. This is why many reviews discuss the main factors that influence the variability of vitamin D concentrations and whether a centile curve, individually calculated by a theoretical equation considering such factors, might be better suited than a fixed limit to assess abnormal vitamin D concentrations in otherwise healthy subjects ***(Ferrari et al., 2017).***

In our study 57.7% of patients had vitamin D deficiency, which is comparable to ***(Mansour and Elhadidi, 2012)*** a study that measured vitamin D level in 510 healthy Saudi Arabian children aged 4-15 years old, where only 13.72% had normal level of vitamin D (> 20 ng/ml) and the mean value of vitamin D level was 13.07 ± 7.81 ng/ml. These findings reflect a prevalence of vitamin D deficiency in the school age group of children.

Our result differed from ***Abu Shady et al. (2016)*** another Egyptian study which included 200 children with higher age group (9-11 years old) where only 11.5% had deficient vitamin D (<20 ng/ml). This may be explained by the differing age group in this study compared to ours; schoolchildren usually have better sunexposure and spend more time outdoors than their peers of the preschool age.

In our study, similar to that by ***Zhao et al.(2015)***we detected no significant difference in vitamin D status between genders. Other studies however, showed a prevalence of vitamin D deficiency related to gender. One such study ***Abu Shady et al. (2016)***, performed on school children aging (9-11 years), showed that females were 10.3 times more likely to have vitamin D deficiency than males.

This vitamin D level difference between genders in Middle Eastern studies have been thought to be the result of certain cultural factors related to the female sex, such as, concealing clothes and reduced outdoor activity which in turn reduces sunexposure. Despite our study being in the middle East as well, we may not have shown that gender prevalence since our population was of a much younger age, and these aforementioned cultural factors mostly apply to girls at the pubertal age. Another theory for this gender-dependent relation may be due to regulation by sex hormones, particularly estradiol and estrogens in the synthesis and metabolism of vitamin D ***(Aarskog et al., 1983).*** And since these factors are commonly absent in preschool children that would explain the absence of significant vitamin D level difference between girls and boys in our study.

Vitamin D supplementation showed significant correlation with mean serum vitamin D levels in our patients. These results are similar to those found in other studies such as ***Mallet et al. (2014)***, ***Mansbach et al. (2009)***.

As for effect of urbanization on vitamin D level, children from rural areas had significantly higher level of vitamin D in comparison with children from suburban and urban areas. Sun exposure and duration of time spent outdoors during daytime also showed a significant effect on vitamin D level in our patients.These results have similarities to a few other studies. A Saudi

Arabian study by ***Mansour and Elhadidi(2012)*** also detected significant direct correlation between vitamin D level and BSA exposed to sunlight and duration of sunexposure. In Kuwaiti study by ***Alyahya(2017)*** showed vitamin D level was significantly lower in the group that reported no sunexposure. In ***Abu Shady et al.(2016)***another Egyptian study, results detected significant positive correlation between hours of sunexposure / week and vitamin D level.

Vitamins deficiency may not always reflect anthropometric measurements; Hidden Hunger according to WHO is the lack of vitamins and minerals that occurs when the quality of food people eat does not meet their nutrient requirements, the food is deficient in micronutrients such as the vitamins and minerals that they need for their growth and development. Our study reflected this theory in that vitamin D deficiency was not significantly correlated to any abnormalities in weight and height.This is similar to ***Chowdhury et al. (2017)***, an Indian study where vitamin D level was measured for 960 children with age 12 to 36 month old, their physical and neurodevelopmental growth were also assessed at a 6 month interval, and concluded that there was no difference between vitamin D deficient and non deficient children regarding these parameters and that vitamin D deficiency was not associated with any significant change in the physical growth parameters including weight for age, height for age and weight for height on Z score curves.

Limitations of this study

Mayhave been the lack of further genetic studies for our study population. Recently, several large-scale genome-wide associations studies (GWAS), have identified associations of GC, NADSYN1/DHCR7, CYP2R1, CYP24A1, VDR, SEC23A and AMDHD1 with serum levels of vitamin D ***(Jiang et al., 2019).***

The seasonal variability at time of sample collection was also not accounted for.

Conclusion

Highprevalence of vitamin D deficiency and insufficiency in apparently healthy preschool Egyptian children was observed in this study. A lack of community awareness and a deficiency in supplementation of vitamin D within vulnerable groups such as preschool children, pregnant and lactating mothers, in addition to inadequate daily sun exposure are among the important risk factors contributing to vitamin D deficiency in this study.

Conflict of interest

No conflict of interest.

Acknowledgment

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