Journal of Advances in Medicine and Medical Research

24(5): 1-13, 2017; Article no.JAMMR.37483
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Vitamin D Status and Contributing Factors in Patients Attending Three Polyclinics in Benghazi Libya

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Authors' contributions

This work was carried out in collaboration between all authors. Author MO designed and conducted the study, wrote the protocol, managed the literature search and wrote the first draft of the manuscript. Author FN performed study analyses, data reporting and tabulation and contributed to literature search. Authors MO, NN, MS and MA collected data and provided technical support in clinics. Authors FN, Manal Younis and Moftah Younis participated in the critical revision of the article. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2017/37483
Editor(s):
(1) Mustapha Diaf, Department of Biology, Faculty of Natural and Life Sciences, Djillali Liabes University, Algeria.
Reviewers:
(1) Lívia Garcia Bertolacci-Rocha, Universidade Federal de Goiás, Brasil.
(2) Susumu Inoue, Michigan State University College of Human Medicine, USA.
Complete Peer review History: http://www.sciencedomain.org/review-history/21765

Original Research Article

Received 19th October 2017
Accepted 31st October 2017
Published 6th November 2017

ABSTRACT

Background: About one billion people in the world suffer from vitamin D deficiency or insufficiency. The consequences of low vitamin D level include increased risk of some cancers, cardiovascular diseases, and type one diabetes, which makes it a crucial public health concern. In spite of the imperative role of sunlight in vitamin D synthesis, recent reports have shown that higher rates of hypovitaminosis in the sunniest areas of the world. Benghazi city is sunny most of the year; there is a lack of research on Vitamin D status in Libya.

Objective: The purpose of this paper was to investigate the status of Vitamin D and the contributing factors among patients attending three out patient clinics in Benghazi.

Design: Cross-sectional study with stratified random sampling technique was used to collect

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patients attending three outpatient clinics in Benghazi Libya between July 1st to September 30th 2016.
Participants/Setting: All Patients attending Alkiesh polyclinic, Alfohyaht polyclinic and Yakeen Health Center were approached. 287 participants were recruited, baseline information and serum 25(OH)D concentrations were provided by 184 subjects; participation rate of 64% (58.8% females and 5.9% males).
Statistical Analyses: Description and analysis of data were carried using SPSS version 21. Level of significance was set at p value < 0.05.
Results: Reported vitamin D deficiency was 76.1%, insufficiency was 15.2% and Vitamin D sufficiency was 8.7%. Age, gender, BMI, pregnancy, consumption of dietary supplements (calcium, vitamin D and multivitamin), history of vitamin D deficiency, consumption of milk and oily fish were the predicting factors of status of Vitamin D among Benghazi outpatients.
Conclusions: Vitamin D deficiency is common in this part of Libya especially among females and in the older age groups and calls for community based intervention and prevention strategies.

Keywords: Vitamin D; deficiency; insufficiency; Benghazi; factors.

1. INTRODUCTION

Vitamin D deficiency is considered to be one of the most common medical conditions worldwide [1]. The consequences of vitamin D deficiency (VDD) include poor bone development and ill health as well as increased risk of many common and serious diseases, including some common cancers, cardiovascular diseases, type one diabetes, autoimmune diseases, high blood pressure, and age-related cognitive decline, Parkinson's disease, multiple sclerosis and arthritis [1-3].

Vitamin D is present in two forms: ergocalciferol (vitamin D2) which is found in fungi and plants, and cholecalciferol (vitamin D3) from the sun [1]. Cutaneous synthesis of vitamin D3 relies on environmental factors (atmospheric conditions, geographic latitude/location, and season), behavioral factors (clothing, time spent outdoors, and use of sunscreen) as well as physiologic factors (skin type and age) [4]. Exogenous vitamin D can be obtained from fatty fish, supplements, and fortified foods such as margarine, yogurt and milk [5]. Serum concentrations of 25-hydroxyvitamin D (25(OH)D) is the best clinical indicator of vitamin D status available which reflects sun exposure, diet, and supplements [5,6].

Based on reports; about one billion people in the world suffer from vitamin D deficiency or insufficiency [1]. In spite of the imperative role of sunlight in vitamin D synthesis, recent reports have shown that higher rates of hypovitaminosis in the sunniest areas of the world, including the Middle East and Asian countries, such as Qatar, Saudi Arabia, United Arab Emirates, Iran Turkey, and India [7-12].

Benghazi city is sunny most of the year [13]; the level of Vitamin D is expected to be adequate. There is a lack of research on Vitamin D status in Libya and to our knowledge this is the first study on Vitamin D status among Libyans. The present study investigated the status of Vitamin D and the associated risk factors among patients attending three out patient clinics.

2. METHODOLOGY

2.1 Study Population

A cross sectional study was designed to investigate Vitamin D status and contributing factors. Patients attending three outpatient clinics in Benghazi Libya were approached between July the 1st to September 30th 2016. Stratified random sampling technique was used and Benghazi was divided into three main areas according to Benghazi City Council. A random selection of clinics from each area was followed. (Alkiesh polyclinic, Alfohyaht and Yakeen Health Center), Alkiesh polyclinic, and Alfohyaht are public polyclincs. While Yakeen Health Center is a private outpatient clinic. Patients attended these three clinics for different medical specializations such as medicine, gynecology, minor surgery and dermatology. Exclusion criteria included the use of medications known to affect bone metabolism, such as seizure drugs phenobarbital, anti-tuberculosis drugs, cholesterol-lowering statin drugs, thiazide diuretics, anti retroviral drugs, and glucocorticoids. Data sets were excluded if any parameter investigated was not recorded. Subjects receiving treatment course for previously diagnosed VDD at the time of study or has received their last treatment less than one month before the study were excluded. All participants provided written informed consent. The University Ethics Committee and the Centre's administration approved the protocol.

2.2 Data Collection

Data was collected by trained researchers. To avoid subjective bias researcher underwent training sessions on interviewing skills, anthropometry taking and data coding and handling at Benghazi University. A small pilot study was conducted and 12 questionnaires were tested from 15th to 28th June 2016 to test questionnaire and feasibility of study methods.

Participants allocated into the research completed detailed interview based-questionnaires that included preliminary data on demographics, medical history, and food intake from major dietary vitamin D sources using short food frequency validated questionnaire [14]. The questionnaire included an assessment of calcium and vitamin D supplements (vitamin D, multivitamin, cod liver oil and calcium supplements). For the purpose of statistical analysis data considering history and food intake were coded into binary categories. Oily fish consumption (sardines, salmon, trout, tuna, herring, anchovies and mackerel) and butter consumption were reported as frequency of consumption per month, milk and yogurt consumption were reported as daily intakes. The questionnaire also included questions on history of previous diagnosis and treatment of Vitamin D deficiency. BMI (weight in kg/height in m2) was used to define weight status following standard techniques [15]. With subjects wearing light clothes and no shoes, weight was measured with SECA platform lever scale (Germany) recorded to the nearest 0.25 kg and height was measured using telescopic height rod attached to SECA scale and recorded to the nearest 0.5 cm.

2.3 Biochemistry

Vitamin D test was collected as part of routine investigation for all subjects. For the current analysis, vitamin D deficiency (VDD) was defined as 25-OHD values of ≤20 ng/ml, insufficiency at 21-29 ng/l; and sufficient serum 25-OHD level at ≥30 ng/ml [16]. Patients were divided into 3 diagnostic categories accordingly. To reduce bias of different vitamin D analysis techniques, ELISA was regarded as the accepted test, for being the most commonly used in Benghazi.

2.4 Statistical Analysis

All data was coded prior to being entered into a computer. Description and analysis of data were carried using SPSS version 21. We measured the proportion of subjects meeting predefined cut-points of serum 25(OH)D concentrations. Confidence intervals were set at 95%. Serum 25(OH)D was normally distributed. Chi-square t-test was performed to test the association of serum 25(OH)D with qualitative variables. A p-value of ≤ 0.05 was considered statistically significant. Multiple logistic regression investigated predictors of vitamin D deficiency (serum 25(OH)D of ≤20 ng/ml). Bivariate correlation was carried out to test the relationships between quantitative variables. Multiple regression model and adjustments for confounding factors were also conducted. Covariates included age, gender, body mass index (BMI), frequency of fish intake monthly, frequency of milk intake daily, vitamin D deficiency history, supplements consumption. trimesters for pregnant women. The goodness-of-fit of a model was assessed using Chi square test and multiple regression model.

3. RESULTS

Out of the 287 participants, baseline information and serum 25(OH)D concentrations were provided by 190 subjects; six subjects brought test by immune essay were excluded. 184 subjects provided test by ELISA giving an effective participation rate of 64% (58.8% females and 5.9% males). Out of 184 subjects; 90.8% were female, and 9.2% were male. The total mean age ± SD was 36.2 years ± 0.9 (37.4 ± 3.8 years for females and 29.2 ± 2.9 for males). Overall, the estimated prevalence of vitamin D deficiency (≤20 ng/ml) was 76.1%, insufficiency (21-29 ng/ml) was 15.2% and the proportion of the sample population with sufficient vitamin D concentrations (≥30 ng/ml) was 8.7% as shown in Table 1. Weighted mean serum 25(OH)D concentrations by gender was 15.4ng/ml (95% C.I 14.6-16.2) in males and 13.2 ng/ml (95% CI 12.5-13.9) in females, and by age group were 16.1ng/ml (95% CI 15.6-16.6) in those aged <20 years, 15.6 ng/ml (95% CI 14.8-16.4) in those aged 20-40 years and (13.9) ng/ml (95% CI 13.2-14.6) in those >40 years (Figs. 1, 2). The prevalence of vitamin D deficiency was higher among female and increased with age, adolescents less than 20 years showed the highest prevalence of sufficiency Vitamin D (serum 25(OH)D concentrations ≥30 ng/ml) as shown in Figs. 3 and 4. Mean serum 25(OH)D concentrations also differed (p≤0.05) by age, gender, BMI classification, pregnancy, consumption of dietary supplements (calcium, vitamin D supplements and multivitamin supplements), history of vitamin D deficiency, and consumption of milk and oily fish. Subjects' address and polyconic from where the subjects were recruited did not show statistical significance across vitamin D status (data not shown). Details on dietary intake of food rich with vitamin D and supplements, mean intake of vitamin D, nature of occupation, sun exposure and cultural and beauty beliefs and their effect of vitamin D status for the same sample will be described and discussed elsewhere in details. Correlation and Significant predictors of vitamin D deficiency are summarized in Table 2. In the full model, female gender (OR 2.86, CI 1.62-5.03), older age (OR 2.79, CI 1.32-4.65), and being obese (BMI≥30) (OR 2.19, CI 1.50-4.04) were associated with an increase in the odds of having serum 25(OH) D concentration ≤20 ng/ml (deficiency). Also, no daily consumption of milk (OR 2.34 CI 1.77-4.0), no monthly consumption of fish (OR 2.1, CI 1.52-5.06)), and history of Vitamin D deficiency (OR 1.22 CI 0659-2.44) were independently associated with an increase in the odds of vitamin D deficiency. On the other hand consumption of calcium or Vitamin D supplements predicted a decrease in vitamin deficiency odds (OR 0.526 CI 0.201-0.84, and OR 0.42 CI 0.27-0.54) respectively, women in early pregnancy had more chances of developing deficiency than latter stages of pregnancy (OR 0.32 CI 0.21-0.67). Almost half of normal subjects had no history of previous VDD diagnosis, while half of those with vitamin D deficiency or insufficiency had histories of VDD. Of those with previous history of VDD, almost half did not finish treatment course. All of insufficient and normal subjects with history of VDD had histories of undergoing VDD treatment.

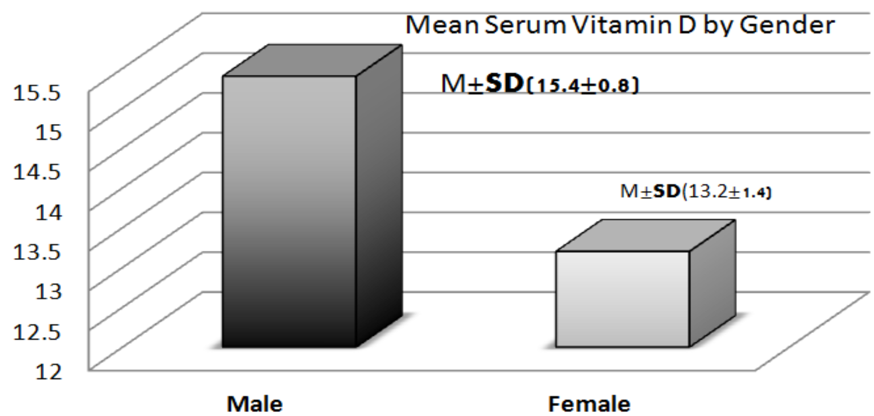

Fig. 1. Mean serum of Vitamin D by Gender among 287 patients participating in group data collection on Vitamin D status and contributing factors

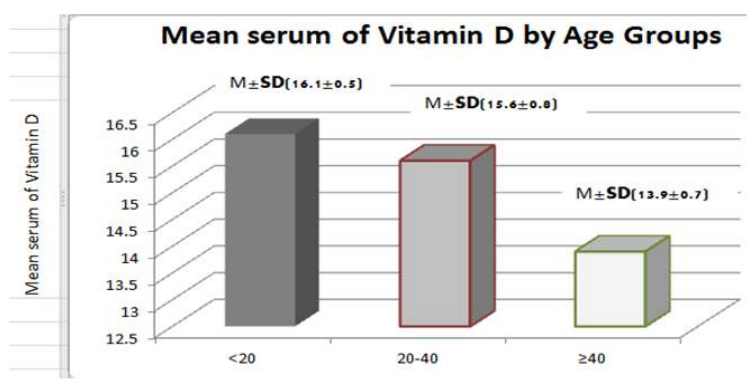

Fig. 2. Mean serum of Vitamin D by age among 287 patients participating in group data collection on Vitamin D status and contributing factors

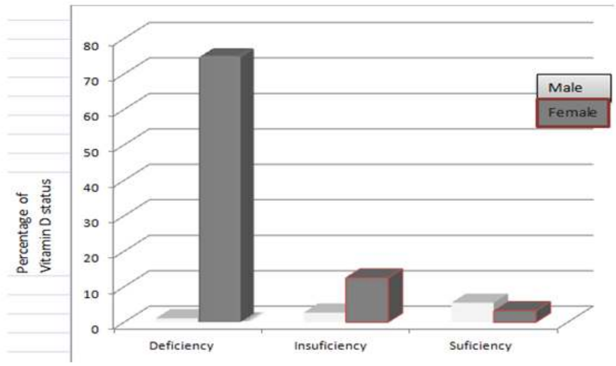

Fig. 3. Vitamin D statuses of 287 patients participating in group data collection on Vitamin D status and contributing factors

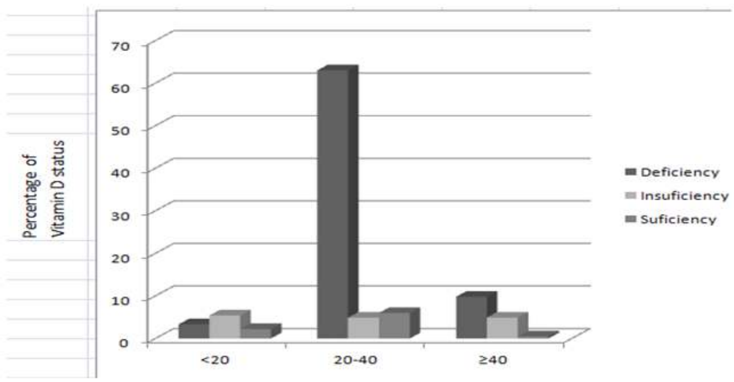

Fig. 4. Age and Vitamin D status of 287 patients participating in group data collection on Vitamin D status and contributing factors

Table 1. Demographics of 287 patients selected from 3 outpatient clinics in Benghazi participating in group data collection on vitamin D status and contributing factors

Variables	Male	Female	Total
Age (years)			
<20	3(1.1)	34(11.8)	37(12.9)
20-40	18(6.3)	153(53.3)	171(60)
≥41	8(2.8)	71(24.7)	79(27.5)
Mean ± SD	± 6.8	± 5.9	± 6.4
Pregnant			
No	29(10)	242(84.3)	261(94.4)
First Trimester	0	7(2.4)	7(2.4)
Second Trimester	0	3(1.1)	3(1.1)
Third Trimester	0	6(2.1)	6(2.1)
Single	15(5.2)	124(43.2)	139(48.5)
Married	14(4.8)	134(46.7)	148(51.5)
Education			
Illiterate/RW*	8(2.8)	1(0.3)	9(3.1)
Basic education	12(4.2)	37(12.9)	49(17.1)
Secondary/ university	8(2.8)	86(30)	94(32.5)
Master/PHD	0	135(47)	135(47)
Occupation			

Variables	Male	Female	Total
No	5(1.7)	172(59.9)	177(61.6)
Employed	20(7)	75(26.1)	95(33.1)
Free works	4(1.4)	11(3.8)	15(5.3)
Nature of work			
Indoor	20(18.2)	80(72.7)	100(90.9)
Outdoor	9(8.2)	1(0.9)	10(9.1)
Address			
Urban	25(8.71)	245(85.37)	270(94.8)
Rural	4(1.39)	3(1.05)	17(5.2)
Smoking			
Yes	15(5.23)	0	15(5.23)
No	14(4.88)	258(90)	272(94.8)
Number of cigarettes			
1-3	6(40)	0	6(40)
5-7	5(33.33)	0	5(33.33)
8-10	4(26.6)	0	4(26.6)
Underweight	1(0.35)	12(4.18)	13(4.53)
Normal	11(3.83)	62(21.6)	73(25.44)
Overweight	8(2.79)	80(27.87)	81(28.22)
obese	9(3.14)	111(38.68)	120(41.81)
Chronic disease			
Yes	12(4.18)	65(22.65)	78(27.18)
No	17(5.92)	192(67.25)	209(72.82)
Chronic disease type			
Diabetes mellitus	5(6.4)	17(21.8)	22(28.2)
hypertension	6(7.7)	17(21.8)	23(29.5)
Gastrointestinal disorder	3(3.8)	7(9.0)	10(12.8)
Colitis	1(1.3)	11(14.1)	12(15.4)
Renal disease	0(0)	0(0.0)	0(0.0)
Liver disease	2(2.6)	1(1.3)	3(3.8)
Celiac disease	0(0.0)	8(10.3)	8(10.3)
History of vitamin D deficiency			
Yes	23(8.01)	176(61.32)	199(69.34)
No	6(2.09)	82(28.57)	88(30.66)
Milk intake[a s]			
Yes	29(10)	206(71.8)	235(81.9)
No	0	52(18.1)	52(18.1)
Fish intake[b F]			
Yes	14((4.8)	143(49.8)	157(54.7)
No	15(5.23)	115(40.07	130(45.3)
Butter intake[a z]			
Yes	27(9.3)	254(88.6)	281(97.9)
No	2(0.7)	4(1.4)	6(2.1)
Yogurt intake[a s]			
Yes	23(7.9)	222(77.5)	245(85.4)
No	6(2.1)	36(12.5)	42(14.6)
Calcium supplement			
Yes	7(2.4)	27(9.4)	34(11.9)
No	22(7.7)	231(80.5)	253(88.20
Omega 3 supplement			
Yes	8(2.8)	46(16)	54(18.8)
No	21(7.3)	212(73.9)	233(81.2)
Vitamin D supplement			
Yes	12(4.2)	56(19.5)	68(23.7)
No	17(5.9)	202(70.4)	219(76.3)

Variables	Male	Female	Total
Multivitamins supplement			
Yes	13(4.5)	45(15.7)	58(20.2)
No	16(5.6)	213(74.2)	229(79.8)
Vitamin D status			
<20 ng/ml	2(1.1)	138(75)	140(76.1)
21-29 ng/ml	5(2.7)	23(12.5)	28(15.2)
≥30 ng/ml	10(3.3)	6(3.3)	16(8.7)
Total	17(9.2)	167(90.8)	184(100)

[a] Daily Intake, [b] Monthly intake, [S] Serving size = 1 cup = 245 gm
[Z] Serving size= 1 tablespone = 14 gm
[F] Serving size= 1 Oz = 28 gm

Table 2. Correlation and Predictors of Serum 25(OH) at ≤20 ng/ml (Deficiency) in patients participating in group data collection on Vitamin D status and contributing factors

Variables	Percentage of subjects			OR	CI
	Insufficient	Sufficient	Deficiency		
Gender*					
Female	25	16.6	58.4	2.8674 [a]	1.6217-
Male	21	52.9	26.1		5.0361
Age*					
<20	33.3	60.6	6.1	2.7931 [b]	1.3211-
20-40	42	41.1	16.9		4.6521
≥41	46	34.3	19.7		
Milk intake *					
Yes	17.1	53.6	29.3	2.3462	1.7706-
No	23.2	24.4	52.4		4.0118
BMI*					
Underweight	15.9	36.1	48	2.1995 [c]	1.1507-
Normal	20.7	30	49.3		4.0402
Overweight	22	24.6	53.4		
Obese	25	14	61		
Fish intake *					
Yes	16	55.1	28.9	2.1007	1.5237-
No	26	20.9	53.1		5.061
Calcium supplements *					
Yes	19.3	30	50.7	0.5263	0.2011-
No	23	21.3	55.7		0.8450
History of Vit D deficiency					
Yes	21	36.5	48.5	1.2243	0.6594-
No	15	30.3	50.6		2.440
Vitamin D* supplements					
Yes	16.3	37.6	46.1	0.4216	0.2711-
No	20.1	28.9	51		0.5413
Multivitamin supplements *					
Yes	15	36.5	48.5	0.4001	0.1989-
No	19.1	30.3	50.6		0.5124
Pregnancy*					
First trimester	19	20.7	60.3	0.3219 [d]	0.2136-
Second trimester	15	30	55		0.671
Third trimester	11.1	42	46.9		

[a] Compared to 1 in males, [b] Compared to 1 in <20 years, [c] Compared to 1 in BMI<24
[d] Compared to 1 in second and third trimester
$*p \le 0.05$

4. DISCUSSION

The results of this cross-sectional study in Benghazi, a sunny, second largest city in the east of Libya, located across the Mediterranean Sea (32.0948° N, 20.1879° E) [13], confirms the high prevalence of vitamin D deficiency (76.1.1%) and insufficiency (15.2%) among the population and an even higher prevalence among older age and females. The rates of vitamin D insufficiency/deficiency reported in this study despite living in (low attitude) are markedly higher than in many western countries. In Germany, Austria, Netherlands, Italy, in North Europe (Denmark, Finland, Ireland, and Poland), Canada, and United Kingdom prevalence of VDD range from 10-55.5% [17-23].

Despite living in one of the sunniest parts of the world; Benghazi shares the same vitamin D problem with some parts of the Africa, Asia and the Middle East [7], In Egypt [8] the estimated prevalence is (77%) deficiency and (15%) insufficiency, with 9% of population having adequate vitamin D level. In Qatar (83-91% of population are VDD) [9]. In Iran, and Tunisia (50.8%, 47.6%) of population have VDD [10,11]. In Saudi Arabia deficiency and insufficiency reached (67.8%) [12].

VDD is a worldwide problem and multifactorial in nature and not confined to specific geographical location [24]. In a recent systematic review which included 195 Studies from 44 countries worldwide, using the same cut-off points we used, 88·1% of the samples presented in the review had mean 25(OH)D values below 30 ng/ml, 37·3% had mean values below 20ng/ml [25].

We could not identify previous Libyan studies regarding vitamin D status in a similar setting to further interpret our findings; however, we highlight some contributing factors to the presented elevated VDD. Female gender was the single most predictor of vitamin D deficiency. Females were 2.8 more likely to develop Vitamin D deficiency than their counterparts. Though there are mixed literature results on gender differences [26]. This finding is comparable to others and can relate to cultural factors such as clothing styles that may impede vitamin D conversion in the skin [21,27-30]. The possible reduced outdoor activities and aggressive sun protection [31]. Also attitudes toward sun exposure, all of these factors are the scope of our research and results will be published in the near future.

Overweight and obesity represented 70% of the selected sample, which corresponds to previously estimated figures for Libyan and Benghazi city population [32-34]. Subjects' BMI>30 were found to have double the risk of low vitamin D level. Obesity has been described as a strong predictor for vitamin D deficiency [35, 36], and obese adults reportedly need at least two to three times more vitamin D to treat and prevent vitamin D deficiency [37,38]. A possible explanation is the sequestration of vitamin D as a fat-soluble micronutrient, in the adipose tissue [39-40]. Associations between BMI and vitamin D scores were confirmed in the Genetic Investigation of Anthropometric Traits (GIANT) consortium, each 1 kg/m^2 increase in BMI was accompanied with 1.15% lower 25(OH)D [41].

Age was directly associated with the prevalence of VDD and inversely associated with serum levels. Our findings suggest that the increase in age is associated with a 2.7 fold increase in vitamin D deficiency. This observation is supported by various reports demonstrating lower vitamin D serum concentrations with increased age, and higher insufficiency / deficiency rates in the older age group [25,31]. One potential explanation for this pattern could be that children/adolescents from this region (Middle East/Africa) generally spend more time outdoors compared with the other age groups (e.g. indoor working by the adult population [42]. Younger age groups in our study had better BMI status and the observed inverse relationship between obesity and age in our study may be partially responsible for this age-related difference in vitamin D levels. Another potential explanation for this pattern is the observation that younger age groups were found to be more likely to consume milk compared to the older age groups; which is consistent with other studies [43,44].

Pregnant women are at high risk for vitamin D deficiency during first and second trimester due to the increased demands for fetal growth and skeleton development [45]. A high prevalence of vitamin D deficiency was observed in early pregnancy in our study, corresponding to other studies and highlights the importance of targeting this high risk group for intervention and treatment measures [45-49].

Low consumption of milk and fish, not consuming Vitamin D, and multivitamin supplements were predictive factors of low vitamin D levels in our study. Lack of consumption of vitamin D-rich foods in addition to the lack of vitamin D supplementation have been shown to be one of the main risk factors to the paradoxically much higher prevalence of VDD [50,51], especially in countries with sunny climates, such as Saudi Arabia [52], Egypt [53], Oman [54], United Arab Emirates [55] and Jordan [30].

Presence of a history of vitamin D deficiency was associated with an increase in the odds of vitamin D deficiency at the present study (OR=1.22). This has been shown elsewhere; prevalence of vitamin D status is estimated to increase to 40-80% among people with history of vitamin D deficiency [56]. In short, this can be attributed to the the destruction in VD receptors resulting from VDD and the manifestly decreased intestinal calcium absorption (60% decrease) in adults who had history of VDD, as well as the complex metabolism of vitamin D in the human body resulting from previous deficiency [56,57]. Furthermore, the present study showed that there is a general negligence among patients regarding treatment compliance, almost half of those with previous VDD did not finish their prescribed treatment course by their physician, as compared to patients in the sufficient or insufficient group with previous history of VDD. This highlights the importance of community based awareness programs which has shown effectivity in reducing prevalence rate [58,59].

It seems that factors, such as style of clothing, air pollution, skin pigmentation, and lack of routine enrichment of foods with vitamin D in Libya, could also be contributing factors for the findings of our study [60]. We did assess dietary vitamin D intake, duration of exposure to sunlight, and cultural effect and these will be presented in our future work.

We realize that the observational and cross-sectional design, with single measurement of Vitamin D level and in one season are limitations of our study. Another limitation is the unequal gender distribution of males and females and the proportionally large presentation from middle age group that resulted from random sampling approach. Nevertheless, this could be attributed to the greater willingness among females to use health services, and to report health problems [61,62]. It has been reported previously in Benghazi [63], that females are more frequent users of health centers than their counterparts.

Our limited resources have hindered the assessment of serum Parathyroid hormone levels which could also affect Vitamin D level [55]. Furthermore, our sample was selected from patients attending out patient clinics for regular visits and check ups to GPs and this could affect the generality of results. Finally, differences of as much as 33% have been reported when laboratories using different methods have measured 25(OH)D [64]. We therefore recognize that caution is appropriate when comparing absolute values from our results with those of others. (However, directional changes and proportional differences would not be affected by such methodological differences).

5. CONCLUSION

This study demonstrates that Vitamin D deficiency is common in this part of Libya especially among females and in the older age groups. Continued efforts to improve status of Vitamin D are needed, coupled with intensive educational and awareness programs to increase the population's knowledge on this widespread epidemic. Furthermore, larger scale studies are needed to assess the contribution of different modifiable and non-modifiable factors to the problem.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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