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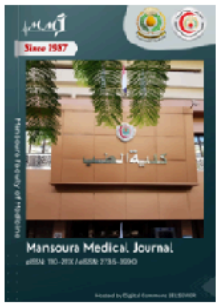

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Study of Indices Comprising Surrogate Markers of Vitamin D Deficiency

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Indices Comprising Surrogate Markers of Vitamin D Deficiency

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Abstract

Background: Vitamin D deficiency is one of the most common medical conditions in recent times. It is becoming endemic in many parts of the world because of insufficient UVB exposure, urbanization, pollution and traditional clothing preventing UVB reaching skin surface. As a result, wide prevalence of vitamin D deficiency is observed in many countries. **Objective**: to investigate markers of vitamin D deficiency applicable in large sectors of society at low cost. Methods: A cross sectional study was conducted on 80 healthy adults aged (20-60) ys. All patients were subjected to full history, thorough clinical examination, laboratory measurement of hemoglobin, serum creatinine, Ca (total & corrected total), phosphorus, magnesium, intact PTH (iPTH), 25 hydroxy vitamin D level. Five indices were calculated and attempt to correlate each of them to Vitamin D level were undertaken statistically. The indices are) :total Ca × PO4)/PTH, (ionied Ca++ × PO4)/PTH, (Ca × PO4 × Mg)/PTH, (Ca × PO4)/(PTH × 1/S.creatinine), PTH alone. Results: we classified volunteers into vitamin D Deficient (<20 ng/ml) and vitamin D non deficient (>20 ng/ml), on comparing variables between them: there was highly significant difference between both groups in total calcium , PTH , (Total calcium ×PO4) /PTH, (Ionized calcium × PO4) /PTH, (Total calcium ×PO4 × Mg) /PTH , and (Total Ca × PO4 ×Cr) /PTH.Conclusion: All indices suggested in our study are very close to each other as a predictive product so it is better to use the simplest and least costy one..

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INTRODUCTION

Vitamin D deficiency is one of the most common medical conditions in recent times. It is becoming endemic in many parts of the world because of insufficient UVB exposure, urbanization, pollution and traditional clothing preventing UVB reaching skin surface. As a result, wide prevalence of vitamin D deficiency is observed in many countries. Hypovitaminosis D is very common in Middle East & Africa and does not spare the pediatric age**[1]**. A large proportion of adolescent girls, up to 70% in Iran **[2],** 80% in Saudi Arabia **[3]** & 32% in Lebanese girls and between 9% and 12% in Lebanese adolescent boys **[1].** Studies from Saudi Arabia, Kuwait, United Arab Emirates, and Iran reveal that 10–60%of mothers and 40–80% of their neonates had undetectable low vitamin D levels (0–10 ng/mL) at delivery **[4**]. Pilot Studies about the prevalence of vitamin D in Egypt reveal that; the rate of hypovitaminosis - D in fertile females between (20-50) ys is 80% in Cairo (Matar, 2011) and 70% in port-Fouad **[5],** in old age between (60-70) ys the rate is more than 50% **[6]**and 90% in those over 75ys **[6]** and in pregnant females receiving vitamin D and calcium supplementation the rate is 50 % **[7].**

Hypovitaminosis- D is typically diagnosed by measuring the concentration of 25-hydroxyvitamin D (calcidiol) in blood, which is a precursor to the active form 1, 25-dihydroxyvitamin D (calcitriol).

The following presents the recent levels considered important in interpretation of 25-hydroxyvitamin D levels:

- Levels <30Nmol/L (<12ng/ml) associated with vitamin D deficiency, leading to rickets in children and osteomalacia in adults.
- Levels from 30-50 Nmol/L (12-20 ng/ml) are generally considered inadequate for bone and overall health in healthy individuals.
- Levels≥50 Nmol/L (≥20ng/ml) are generally considered adequate for bone and overall health in healthy individuals.
- Levels >125Nmol/L (>50ng/ml) are emerging evidence links potential adverse effects to such high levels, particularly > 150 Nmol/L (>60 ng/ml) **[8].**

Vitamin D deficiency is defined as a 25 (OH) D below 20 ng/ml (50 nmol/liter).Vitamin D insufficiency as a 25 (OH) D of 21–29 ng/ml (52.5–72.5) nmol/liter **[9].**

Aim of the work

A discrepancy exists between the cost of diagnosis of vitamin D deficiency and the cost of treatment. For example; measurement of 25 (OH) vitamin D costs about 500 - 600 EGP, on the other hand the cost of 1 injection of 200000 IU of vitamin D is 10 EGP. Because of the high prevalence of vitamin D deficiency and because of the high cost of diagnosis, surrogate markers

are needed to identify the individuals who need vitamin D supplements.

We aim to investigate markers of vitamin D deficiency applicable in large sectors of society at low cost and find a vitamin D deficiency index to diagnose such a widely prevalent condition with reasonable cost benefit ratio.

Materials and methods

Our study was conducted on 80 healthy adults aged (20-60) ys (companions of inpatient and healthy hospital workers). Samples will be collected from participants in Cairo greater area.

The subjects were informed of the importance of vitamin D and the purpose of the study, responders who accepted to participate were included.

Exclusion criteria:

Including patients with chronic systemic diseases like: chronic liver disease, chronic kidney disease, congestive heart failure, chronic obstructive pulmonary disease & neurological disease. Also, Subjects on regular treatment with corticosteroids, antiepileptics and vitamin D supplements will be also excluded.

All participants will be subjected to the following: Full medical history taking with emphasis on sun exposure and dietary habits, medications and vitamin D supplements.General clinical examination, measuring BP, pulse, temp, Wt, Ht, BMI .Laboratory investigations performed on 8 - 12 hours fasting sample: Hb, S.creatinine, Ca (total & corrected total), phosphorus,Mg++ , intact PTH (iPTH) and 25 hydroxy vitamin D level by (ELISA). Five indices were calculated for each subject and attempt to correlate each of them to Vitamin D level were undertaken statistically.The indices are:(Ca × PO4)/PTH, (Ca++ × PO4)/PTH, (Ca × PO4 × Mg)/PTH, (Ca × PO4)/(PTH × 1/S.creatinine) and PTH alone.

Statistical analysis:

Data were analyzed using PASW(predictive analytics software) statistics 18 (first edition ISBN-13:978-0321725561,ISBN-10:0321725565). Description of the analyzed sample was done using the following tests:

- Mean (average): sum off all variables divided by total numbers of variables.
- Standard deviation (SD): the positive square root of variance.

Participants were classified into groups according to Vit-D level, gender and BMI and groups were compared using the following tests:

- Student t (t)
- Chi-Square (X2)
- Analysis of variance (ANOVA): an extension of z/t test which compares mean values for three or more groups simultaneously for one or more factors. So, this test used to compare quantitative data for more than 2 groups.

All quantitative data were correlated with each other using:

- Pearson correlation coefficient (r)

The significance of the test was determined according to the P value to be:

- Non-significant (NS) if $P > 0.05$.
- Significant (Sig) if $P \leq 0.05$.
- Highly significant (HS) if $P \leq 0.001$.

Significant relations were graphically represented by Pie and Scatter Graphs.

Data were analyzed using IBM© SPSS© Statistics version 23 (IBM© Corp., Armonk, NY, USA) and MedCalc© version 15 (MedCalc© Software bvba, Ostend, Belgium).

Normally distributed numerical variables were presented as mean and SD and inter-group differences were compared using the independent samples t test.

Categorical variables were presented as number and percentage and differences were compared using Fisher's exact test (for nominal data) or the chi-squared test for trend (for ordinal data).

Results:

Demographic, clinical and laboratory data for the whole study population are shown in Table (1).

On determining vitamin D status, there was 45% (36 volunteers) suffering from severe vitamin D deficiency (<12 ng/ml), 38.8% (31 volunteers) with vitamin D deficiency (12 to <20ng/ml), 15% (12 volunteers) vitamin D insufficiency (<30 ng/ml) and 1.2% (1 volunteer) vitamin D sufficient (>30 ng/ml). And according to Gender it was 36.3% for males (29 volunteers) and 63.7% for females (51 volunteers) (Table 2).

On correlating variables with vitamin D we found that there was very weak significant negative correlation with age (r=-0.046) (P=0.684), BMI (r=-0.163) (P=0.149) and total calcium (r=-0.039) (P=0.729), Moreover there was very weak significant positive with Hb (r=0.153) (P=0.176), S. createnin (r=0.142) (p=0.210) and magnesium (r=0.180) (P=0.111). Also there was weak significant negative correlation with Ionized Calcium (r=-0.212) (P=0.059) and PTH (r=-0.202) (P=0.072). There was also weak significant positive correlation with PO4 (r=0.301) (P=0.007). All indices was correlated weakly with vitamin D as follow: (Total calcium × PO4) /PTH (r=0.324) (P=0.003), (Ionized calcium × PO4) /PTH (r=0.305) (P=0.006), (Total calcium × PO4 × Mg) /PTH (r=0.372) (P=0.001) and (Total Ca × PO4 × Cr) /PTH (r=0.280) (P=0.012). Table (3)

According to vitamin D level we classified volunteers into vitamin D Deficient (<20 ng/ml) and vitamin D non-deficient (>20 ng/ml) and compared variables between them as shown in table (4). Highly significant differences between both groups in total calcium (P=0.048), PTH (P=0.004), (Total calcium ×PO4) /PTH (P=0.006), (Ionized calcium × PO4) /PTH (P=0.004), (Total calcium ×PO4 × Mg) /PTH (P=0.010), and (Total Ca × PO4 ×Cr) /PTH (P=0.030), but a non-significant correlation found between other variables.

Finally according to our study, we found that the cut-off value of each product suggesting >50% probability of vitamin D deficiency as follow:

- PTH > 44 pg/ml
- Total Ca × PO4/ PTH = <1
- Ca++ × PO4/ PTH = < 0.5
- Total ca × PO4 × Mg/PTH = < 3
- Total ca × PO4 × S.Creatinine/ PTH = < 0.

While the cut-off value of each product suggesting > 90% probability of vitamin D deficiency as follow:

- PTH > 59 pg/ml
- Total ca × PO4/ PTH = < 0.6
- Ca++ × PO4/ PTH = < 0.3
- Total ca × PO4 × Mg/PTH = < 1.25
- Total ca × PO4 × S. Creatinine/ PTH = < 0.3

Table (1): measured parameters of the study population

Percentiles							
Variable	Mean	SD	Minimum	Maximum	25th	50^{th}	75^{th}
Age (years)	29	9	21	58	24	25	34
BMI (kg/m2)	27.5	5.6	17.4	44.2	24.0	26.6	30.6
Hemoglobin (g/dl)	13.3	1.4	10.9	16.7	12.1	13.3	14.1
Creatinine (mg/dl)	0.6	0.2	0.4	1.1	0.5	0.5	0.7
Total calcium (mg/dl)	9.7	0.5	8.7	11.0	9.3	9.8	10.1
Ionized calcium (mg/dl)	4.79	0.25	4.07	5.49	4.64	4.78	4.94
Serum phosphate (mg/dl)	3.9	0.7	2.6	5.3	3.4	3.9	4.4
Serum magnesium (mg/dl)	2.1	0.2	1.7	2.5	2.0	2.1	2.2
PTH (pg/ml)	57.9	10.0	37.0	85.0	52.0	57.0	63.0
Vitamin D (ng/ml)	13.1	5.6	4.0	33.0	8.0	12.0	17.0
(Total calcium * PO4) /PTH	0.68	0.18	0.32	1.07	0.52	0.69	0.83
(Ionized calcium * PO4) /PTH	0.33	0.08	0.16	0.50	0.26	0.34	0.39
(Total calcium * PO4 * Mg) /PTH	1.42	0.40	0.62	2.57	1.11	1.44	1.73
(Total Ca * PO4 * Cr) /PTH	0.41	0.19	0.06	1.07	0.27	0.40	0.47

Table (2): Descriptive statistics for the whole study population: Qualitative statistics

Variable	N	%
Vitamin D level		
Normal	1	1.2%
Vitamin D insufficiency	12	15.0%
Vitamin D deficiency	31	38.8%
Severe Vitamin D deficiency	36	45.0%
Gender		
M	29	36.3%
F	51	63.7%

Table (3): Correlation between vitamin D level and other quantitative variables

Vitamin D		
Variable	R	p-value
Age	-.046	.684
BMI	-.163	.149
Hemoglobin	.153	.176
Serum creatinine	.142	.210
Total calcium	-.039	.729
Ionized calcium	-.212	.059
Serum phosphate	.301	.007
Serum magnesium	.180	.111
PTH	-.202	.072
(Total calcium * PO4) /PTH	.324	.003
(Ionized calcium * PO4) /PTH	.305	.006
(Total calcium * PO4 * Mg) /PTH	.372	.001
(Total Ca * PO4 * Cr) /PTH	.280	.012

Table (4): R elation between Vitamin D deficiency and relevant factors

Vitamin D deficiency							
	No VitaminD deficiency (n=13)		**Vitamin D deficiency (n=67)**				
Variable	Mean	SD	Mean	SD	T	Df	p-value
Age (years)	31	11	29	8	0.690	78	0.493
BMI (kg/m2)	26.6	4.3	27.6	5.8	- 0.63	78	0.527
Hemoglobin (g/dl)	13.7	1.5	13.3	1.3	1.069	78	0.288
Creatinine (mg/dl)	0.7	0.2	0.6	0.1	1.678	13.703	0.116
Total calcium (mg/dl)	9.5	0.4	9.8	0.5	2.008-	78	0.048
Ionized calcium (mg/dl)	4.69	0.17	4.82	0.26	-1.688	78	0.095
Serum phosphate (mg/dl)	4.2	0.5	3.9	0.8	1.603	78	0.113
Serum magnesium (mg/dl)	2.1	0.2	2.1	0.2	0.147	78	0.883
PTH (pg/ml)	50.8	9.1	59.3	9.6	-2.953	78	0.004
(Total calcium * PO4) /PTH	0.80	0.12	0.66	0.18	2.802	78	0.006
(Ionized calcium * PO4) /PTH	0.40	0.06	0.32	0.08	2.983	78	0.004
(Total calcium * PO4 * Mg) /PTH	1.68	.25	1.37	0.40	2.641	78	0.010
(Total Ca * PO4 * Cr) /PTH	0.56	0.26	0.38	0.15	2.421	13.629	0.030

Discussion

Vitamin D deficiency and insufficiency is pandemic and is seen in essentially every country in the world. It has been estimated that more than one billion people worldwide are either vitamin D deficient or insufficient **[10] .**

Despite the abundance of sunshine in the Middle East, the region registers the highest rates of hypovitaminosis D worldwide **[11].** In Egyptian study, Vitamin D deficiency was found in 72.6% of the nursing group, 54% of the pregnant group, 72% of the childbearing age group, 39.5% of the elderly group, and 77.2% of the geriatric group. Vitamin D was significantly higher in non-veiled females [23 ng/dl] as compared to veiled females **[12].** In Europe vitamin D deficiency is a real problem as levels in the blood are low in 50% to70% of the population**[13]**, in the U.S., vitamin D status showed decline in 25 (OH) D levels by 20% in 2000-2004. National Health and Nutrition Examination Survey **(NHANES)** survey as compared with that done in 1988-1994 **[14].** The major causes are obesity, lifestyle changes, decreased milk consumption and increased use of sun protection **[15].**

Lack of awareness of the importance of this deficiency is crucial in individual and public health. The vitamin D deficiency pandemic increases the entire world's population risk of the most serious chronic illnesses including: deadly cancers, type 2 diabetes, heart disease, stroke, autoimmune diseases, asthma and infectious diseases, beside the skeletal consequences as muscle weakness, osteoporosis and increased risk of swaying and falling thus further increasing risk of fracture in the frail elderly with serious impact on quality of life and survival **[16].**

Although vitamin D deficiency is prevalent, measurement of serum 25 (OH) D levels is

expensive, so vitamin D testing is limited to those at risk for severe deficiency and universal screening is not supported **[17].**

A discrepancy exists between the cost of diagnosis of vitamin D deficiency and the cost of treatment. For example; measurement of 25 (OH) vitamin D costs about 500 - 600 EGP, on the other hand the cost of 1 injection of 200,000 IU of vitamin D is 5 EGP. Because of the high prevalence of vitamin D deficiency and because of the high cost of diagnosis, surrogate markers are needed to identify the individuals who need vitamin D supplements.

We aim to investigate markers of vitamin D deficiency applicable in large sectors of society at low cost and find a vitamin D deficiency index to diagnose such a widely prevalent condition with reasonable cost benefit ratio.

Our study was conducted on 80 healthy adults aged (20-60) years, selected from participants in Cairo (L=30). All subjects had no systemic disease, no regular treatment with corticosteroids or antiepileptics and not on vitamin D supplements.

Our study confirms that a large proportion of healthy people have low vitamin D level, as the prevalence of vitamin D deficiency in our study, was 83.8%, (67 subjects from the whole 80), and vitamin D insufficiency prevalence was 15%, (12 subjects from the whole 80), so about 98.8% was the prevalence of Hypovitaminosis D among healthy people according to our study. Which goes in line with similar Egyptian Studies that investigated the prevalence of vitamin D deficiency among healthy people in Egypt as **Matar M. [18**] who found that in fertile females between (20-50) ys the rate was 80% in Cairo, **Malak R. [19]** also found 99% the prevalence of Hypovitaminosis D among healthy people in Cairo, **EL-Dawoody A.[5]** also found 70% in port-Fouad.

Raso AA., et al [20], Rahman SA., et al [21], Arya V, Bhambri R., et al [22] and Fuleihan GE and Deeb M.[23] have documented hypovitaminosis D in people living in countries with abundant sunshine Reasons attributed are, indoor activities with inadequate sun exposure, improper duration and timing of sun exposure, poor dietary intake and genetic factors .

This reflects the magnitude of the problem we are facing in our community and practically makes us in need for searching for the most sensitive surrogate marker for vitamin D deficiency diagnosis.

As regard PTH as a surrogate marker for vitamin D deficiency we found that there is significant statistical difference between Vitamin D deficient group (<20 ng/ml) and vitamin D insufficient non-deficient (>20ng/ml) in PTH (p-value=0.004), and on correlating PTH with vitamin D a negative significant correlation found (r=-0.2) (P-value=0.072), with predictive value 85%. These results are in agreement with those of **Malak R. [19], Sunil K et al [24], Adami S., et al [25], Sai J ., et al [26]** and **Aloia et al [27]** who found a negative correlation between iPTH and 25 (OH) D at serum 25 (OH) D concentrations <30 ng/ml.

They also found that for every increase in serum 25 (OH) D of 1 ng/ml, there was a 1.03 pg/ml decrease in serum iPTH level after adjustments made for gender, race, age, total calcium intake and duration of calcium intake. This relationship was not observed at 25 (OH) D levels ≥30 ng/ml.

Zhao LJ., et al [28] and **Brot C., et al [29]** noted that hypovitaminosis D may co-exist with a blunted PTH response so not all patients with hypovitaminosis D develop secondary hyperparathyroidism.

The mechanism underlying the blunted PTH response is unclear but may be related to magnesium (Mg) deficiency according to **Sahota O., et al [30].**

As regard gender and its effect on 25-OHD, we found no significant statistical difference between male and female vitamin D levels (p-value = 0.355).

These results are in agreement with those of **Malak R. [19**] who found no significant statistical difference between males and females in PTH (p-value = 0.1) or vitamin D levels (p-value = 0.1).

There is a controversy between studies as regard gender and its effect on 25-OHD relation. **Arabi A., et al [31**] found that 25-OHD levels were lower in females than males ($p<0.05$), While **Atli T, Gullu S, Uysal AR., et al [32]** reported higher 25-OHD levels in men compared to women throughout the year.

This interesting phenomenon may be due to differences in adiposity between men and women with the same BMI **[33].** On average, men have 10-15% less fat content than women with the same BMI **[33].** Thus, in men, less vitamin D will be stored in fat tissue after cutaneous synthesis and more will stay in the blood **[34].**

As regard BMI and its effect on 25-OHD, our study showed that no statistical significance found between BMI and vitamin D levels (p-value = 0.149), and very weak negative correlation between BMI and vitamin D (r=-0.163). Which goes in line with **Nasri H & Rafieian-Kopaei M[35]** who found that no significant association between vitamin D level and BMI (p = 0.307).

As regard other bone biochemical markers that would reflect vitamin D status and could be used as surrogate markers for vitamin D like; total calcium, ionized calcium and phosphate, our results showed significant statistical difference between Vitamin D deficient group and vitamin D non-deficient in total calcium (p-value=0.048), and no significant statistical difference between ionized calcium (p-value=0.095), and phosphate (p-value=0.113), while on correlating them to vitamin D levels, there was no significant correlation between vitamin D and total calcium (p-value=0.729), ionized calcium (p-value=0.059) but there was significant positive correlation between phosphate and vitamin D (P-value=0.007) according to our results.

This was in partial agreement with **Singh SK ., et al [36]** who found that there was no

correlation between vitamin D insufficiency and plasma calcium, or phosphate levels.

Singh SK ., et al [36] also reported that plasma calcium and phosphate testing cannot detect vitamin D insufficiency**. Srinath R, Swaminathan S & Ramalingam C [37]** also found that an excellent correlation (r=0.999, t=138.62 and p= <0.0001) was obtained between calcium/vitamin D3 to ionized calcium/Vitamin D3. This could be explained by the known physiological action of vitamin D on calcium and phosphorous.

On the other hand, **Peacey SR [38]** found that a border-line positive correlation was found between 25-OHD and calcium (r=0.22 to 0.42); (P=0.05).

Srinath R, Swaminathan S & Ramalingam C [37] also found that an excellent correlation (r=0.999, t=138.62 and p= <0.0001) was obtained between calcium/vitamin D3 to ionized calcium/VitaminD3. This could be explained by the known physiological action of vitamin D on calcium and phosphorous.

As regard PTH, total calcium, ionized calcium and phosphorous together as surrogate markers for vitamin D to detect vitamin D status, our study revealed that no significant correlation between PTH and total calcium (p-value=0.57), ionized calcium (p-value=0.667). Several studies done to prove this relationship with diverse results; **Tahrani AA., et al [39]** reported that routine bone profiles and PTH levels are insensitive and should not be used for screening for vitamin D status. However, they may provide value in assessing severity.

While **Brot C., et al [29]** and **Malberti F, Farina M & Imbasciati E [40]** found significant correlation between PTH and ionized calcium, **Mayer GP & Hurst JG. [41]** demonstrated the inverse relationship between serum calcium and PTH.

As regard gender and its relation with vitamin D level, we found no significant statistical difference between gender and vitamin D levels (p-value = 0.355). We found that vitamin D levels were lower in females than males.

This was in agreement with **Arabi A., et al [31]** who found that vitamin D levels were lower in females than males. While, **Atli T, Gullu S, Uysal AR., et al [32]** reported higher 25-OHD levels and lower PTH in men compared to women throughout the year .

As regard indices that suggested in our study we found that all indices was correlated strongly with statistically significant correlation with vitamin D as follow: (Total calcium × PO4) /PTH (r=0.324) (P=0.003), (Ionized calcium × PO4) /PTH (r=0.305) (P=0.006), (Total calcium × PO4 × Mg) /PTH (r=0.372) (P=0.001) and (Total Ca × PO4 × Cr) /PTH (r=0.280) (P=0.012). Our results showed significant statistical difference between Vitamin D deficient group and vitamin D non deficient with (Total Calcium ×PO4) /PTH (P=0.005), with predictive value 82.5%, (Ionized calcium × PO4) /PTH (P=0.003), with predictive value 82.5%, (Total calcium × PO4 × Mg) /PTH

(P=0.010), with predictive value 82.5%, (Total calcium × PO4 × creatinine) /PTH (P=0.003), with predictive value 86.25%.

Our results revealed that, PTH can be used as surrogate marker for vitamin D to reflect its status (hyperparathyroidism despite normal calcium and creatinine) after taking into consideration the blunted PTH response that may coexist with Hypovitaminosis D due to Mg deficiency. In conclusion Age and BMI also should be taken into consideration as they can modulate PTH/25 (OH) D relationship. All indices that suggested in our study are very close to each other as a predictive product so it's better to use the simplest and the least costly one.

The mathematical index with the strongest statistical correlation predicting a vitamin D level <20 ng/ml was (PTH) (p=0.002) and (Total calcium × PO4 × Mg)/PTH) (0.01)

Thus we propose a wider adoption of these models which includes the variables affected by vitaminD level.

The cost of measurement of total calcium, PO4, Mg and PTH about 200 -250 EGP. As compared to the current cost of measurement of 25OH vitamin D (currently about 650 EGP) would represents 60% savings in the diagnostic cost. Hence, we propose these models as local cost index for case of wide prevalence and cheap with limitations in our study: our study was conducted on healthy volunteers. Confounding conditions interfers with predictive value of our models include hypoparathyroidism primary or tertiary, hyperparathyroidism, hyperphosphatemia and hypercalcemia of chronic kidney disease, familial hypocalcemic hypercalceuria and malignancy associated hypercalcemia.

Further studies are needed to explore the predictive value of our proposed model (s) in presence of disease condition outlined above.

In conclusion, in absence of the disease condition outlined above, our indices can serve as a surrogate marker to predict vitamin D deficiency and justify the institution of treatment.

Conclusion: PTH can be used as surrogate marker for vitamin D to reflect its status (hyperparathyroidism despite normal calcium and creatinine) after taking into consideration the blunted PTH response that may coexist with Hypovitaminosis D due to Mg deficiency. The mathematical index with the strongest statistical correlation predicting a vitamin D level <20 ng/ml was (PTH) and (Total Calcium*PO4*Creatinine/PTH). Thus we propose a wider adoption of these models which includes the variables affected by vitaminD level.

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