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The Impact of Vitamin D Receptor Single Nucleotide Polymorphism on 1.25 (OH) Vitamin D3 and Bone Mineral Density in Egyptian Children with Beta-thalassemia

Eman AE Badr[1]*, Samah Ibrahim EL-Ghlban[2], Mahmoud Ahmed El-Hawy[3], Sara Hamdey Mohamed Elsaadany[2] and Ibrahim El Tantawy El Sayed[4]

[1]Department of Medical Biochemistry, Menoufia University, Egypt
[2]Department of Biochemistry, Menoufia University, Egypt
[3]Department of Pediatric, Menoufia University, Egypt
[4]Department of Organic and Medicinal Chemistry, Menoufia University, Egypt

Abstract

Background: Vitamin D Receptor (VDR) gene variation may associate with dysfunctions of vitamin D. The aim of this study is to evaluate VDR variation and its relation with Bone Mineral Density (BMD) values in Beta-thalassemia.

Methods: The children included in this study divided into two groups, 76 TM children, and 51 ages and sex matched healthy controls. All children subjected to full history taking, clinical examination. Liver and kidney functions, serum calcium, phosphorous, alkaline phosphatase and vitamin D levels measurement. BMD was determined. VDR rs2228570 SNP was assayed by real time PCR.

Results: There was a significant increase in phosphorus, alkaline phosphatase, frequency of the TT genotype and T allele of rs2228570 SNP of VDR and decrease in calcium, vitamin D levels and BMD in patients group. There was a significant increase of vitamin D levels and decrease in patients with TT genotype than both TC and CC. Also, There were significant increase in number and % of osteopenia and osteoporosis in patients group with TT genotype than both TC and CC ($p<0.001$).

Conclusion: TT genotype and T allele affect vitamin D level, function and associated with decrease BMD and high frequency of osteopenia and osteoporosis in children with Beta thalassemia.

Keywords: Polypeptide; Protein; Amino acid; Bone Mineral Density (BMD); Vitamin D

Introduction

Beta-thalassemia syndromes are a group of inherited disorders affects one or both of the beta-globin genes (chromosome 11) and characterized by a genetic deficiency in the synthesis of beta globin chains [1].

It may be associated with changes in the bone microarchitecture leads to low bone mineral density and high prevalence of fracture [2].

VDR is a nuclear transcription factor, that mediates the action of 1,25(OH)2D3, thus influencing calcium absorption, bone remodeling and mineralization rate [3].

VDR gene is located on chromosome 12q13.11 and consists of 14 exons. It has an extensive promoter region capable of generating multiple tissue-specific transcripts [4].

Its gene variation is highly associated with dysfunctions of vitamin D [5]. The SNP in the VDR gene can cause alteration in the structure of the VDR protein [6]. Moreover, some variation is strongly associated with different abilities of the VDR protein to bind Transcription Factor II B (TFIIB), leading to divergent gene transcription coupled with VDR [7].

FokI (rs2228570), is localized within the 5` end of the gene. It consists of a T>C variation at translation initiation codon (ATG) in exon 2 [8].

The Fok I VDR polymorphism described by diallelic (ATG/ACG) variant in exon 2 of the gene. This variation is located on the translation initiation leads to a three amino acid difference in VDR length between two alleles that may alters the function of the VDR protein [4].

The minor T allele leads to the production of the long 427 amino-acid VDR proteins with lower activity than the short 424 amino acids encoded by the major C allele. As the shorter polypeptide is of higher efficiency to couple with the transcription factor II B (TFIIB) and leads to a higher transcriptional rate of vitamin dependent genes [9].

The aim of this study is to detect VDR Single nucleotide polymorphism SNP and its possible association with vitamin D3 levels, DEXA scan and Bone Mineral Density (BMD) values in children with Beta-thalassemia (TM).

Subjects and Methods

Subjects

This study included 76 children with B-thalassemia (40 boys and 36 girls) who were selected from the attendants of the Pediatric Hematology Clinic, Menoufia University Hospital, Egypt with a mean age of 7.55 ± 4.24 years. They were on regular packed red cell transfusion.

***Corresponding author:** Eman AE Badr, Department of Medical Biochemistry, Faculty of Medicine, Menoufia University, Egypt, Tel: +201090365171; Fax: +20482181009; E-mail: ebadr2014@gmail.com

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Children with abnormal thyroid functions, abnormal renal functions, diabetes mellitus and serological evidence of hepatitis B or C were excluded from the study.

Fifty one (29 boys and 22 girls), age and sex matched healthy children were involved as a control group with a mean age of 8.31 ± 4.19 years.

The study was conducted between July December 2015 and July 2016. Informed consent was taken from the legal guardians of the included children before participation and ethical clearance from Faculty of Medicine, Menoufia University ethical committee was obtained.

Included patients were subjected to detailed history and thorough clinical examination with special emphasis on history of splenectomy, the presence of bone pain and the history bone fractures.

For each participant, body weight and height were measured by the standard methods with estimation of body mass index (BMI=Weight in kg/height in m^2).

Bone mineral density and DEXA scan: BMD evaluation was performed using dual energy X-ray absorptiometry (DXA) (Norland-XR-46, USA, version 3.9.6/2.3.1) at Lumbar Spines (LS) (L1-L4) and Femoral Neck (FN). The BMD, results were converted to age- and gender-specific Z scores based on the normative reference data for BMD in Egyptian children [10].

The diagnostic criteria for osteopenia/osteoporosis in the studied subjects will be characterized according to WHO classification using T-score (>-1: normal, -1 to -2.49: osteopenia and - 2.5 or less: osteoporosis).

Blood sampling

5 milliliters (ml) of blood samples were taken from each subject and divided into: two portion, one for complete blood count (CBC) and DNA extraction in EDTA tubes, while the other portion was put in a plain tube, left to clot for 30 min at room temperature, then subjected to centrifugation for 10 min at 4000 rotations per minute (RPM) and the serum obtained was put in aliquots, stored at -80°C until the time of assay of ALT, AST, urea, creatinine, calcium, phosphorus, alkaline phosphatase and vitamin D.

Assay methods

Complete blood picture was measured with Pentra-80 automated blood counter (ABX- France -Rue du Caducee- Paris Euromedecine-BP-7290.34184 Montpellier-Cedex 4.)

Liver function tests (SGOT, SGPT), Renal function tests (serum creatinine and blood urea) and alkaline phosphatase were analyzed on auto-analyzer (SYNCHRON CX5) from Beckman (Beckman, instrument Inc., Scientific Instrument Division, Fullerton, CA92634 - 3100). Quantitative colorimetric measurement of calcium [11] and phosphorus.

Determination of 1,25 (OH) vitamin D3 levels using commercial ELISA kits (Immunodiagnostic Systems Limited, Bolden, UK) [12].

VDR rs2228570 genotyping

Genomic DNA was extracted from whole blood using the Whole Blood Genomic DNA extraction Kit (Thermo Scientific, Vilnius, Lithuania). rs2228570 was genotyped using the TaqMan allelic discrimination Assay technique that detects variants of a single nucleic acid sequence. The actual quantity of target sequence is not determined. The allelic discrimination assay classifies unknown samples as follows: Homozygotes samples with only allele 1 or allele 2 or Heterozygotes samples with both alleles 1 and allele 2. Using the universal TaqMan Master Mix from Thermo scientific, the primers and TaqMan probes were designed by Applied Biosystems (Foster City, CA, USA) Life Technologies. The reaction mixture was prepared by mixing 10 ul of master mix, 1.25 ul of 20 x SNP assay kit contain primers and probes and 3.75 ul of DNAse-free water. For each unknown reaction, 5 ul of genomic DNA template was added and for the negative control reaction, 5 ul of DNAse-free water was added.

The cycling condition were set as follows: 50°C for 1 min Pre-PCR read, then 95°C for 10 min and 45 cycles of 95°C for 15 s, 60°C for 1 min (Post-PCR); using the 7500 Real-time PCR system (Applied Biosystems, Foster City, CA, USA). The genotyping appear in allelic discrimination plot in Figure 1.

Statistical Analysis

Results were collected, tabulated, statistically analyzed by IBM personal computer and statistical package SPSS version 11. Chi-square test (χ^2) and Fisher`s exact test: Were used to study association between two qualitative variables. Odds ratio, describe the probability that people who are exposed to a certain factor will have a disease compared to people who are not exposed to the factor. Student t-test used for comparison between two groups having quantitative variables. ANOVA (f) test is used for comparison between three or more groups having quantitative variables. Multiple regression analysis calculates the effects of risk factors as independent Odds ratios with the effects of other confounders removed. P-value <0.05 was considered statistically significant.

Results

The results of this study show a significant lower body weight, height

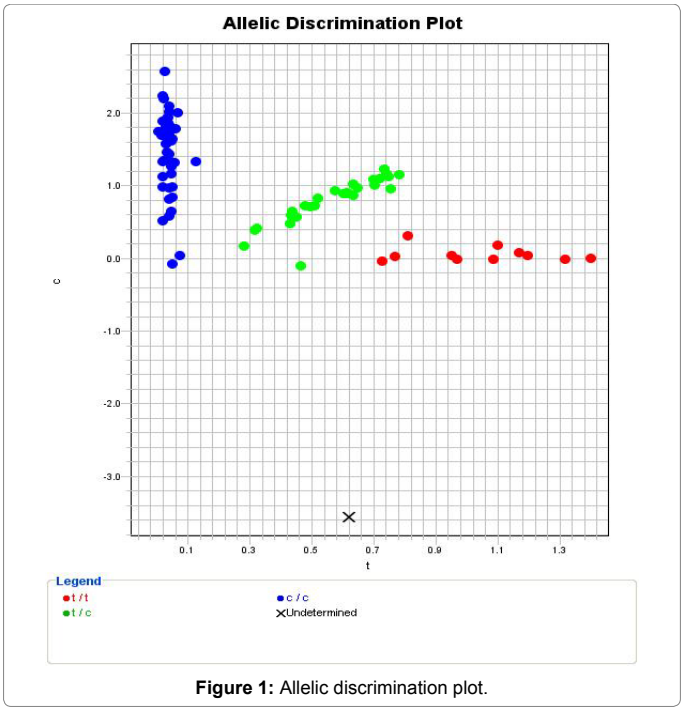

Figure 1: Allelic discrimination plot.

in children with β-thalassemia compared to the controls. Also, a significant difference in number and % of children has be done splenectomy operation in patients group compared to control (Table 1).

There was a significant increase in ALT, AST, phosphorus, alkaline phosphatase levels and WBCs count in β-thalassemia patients compared to control. While there was a significant decrease of calcium, vitamin D, hemoglobin levels, RBCs count DEXA scan and BMD (Table 2).

There was a significantly increased frequency of the TT genotype and T allele of rs2228570 SNP of VDR in patients group compared to controls (Table 3).

There was significant differences among TT, TC and CC types of rs2228570 genotypes of VDR as regard vitamin D levels, DEXA scan and BMD with TT genotype has significantly lower DEXA scan and BMD than both TC and CC ($p<0.05$). While there was a non significant difference as regard other parameters (Table 4).

There were significant differences among TT, TC and CC types of rs2228570 genotypes of VDR as regard number and % of osteopenia and osteoporosis in patients group with TT genotype has significantly higher rates of osteopenia and osteoporosis than both TC and CC ($p<0.001$) (Table 5).

According to The linear regression analysis rs2228570 genotypes of VDR and serum vitamin D level are two dependant factors (Table 6).

Discussion and Conclusion

β-thalassemia constitutes a major health problem in Egypt with an estimated carrier rate of 9-10% [13]. Osteoporosis may complicate iron overload diseases. Several studies support a role of osteoblast impairment in iron-related osteoporosis. A bone histomorphometry study in children and adolescents with β-thalassemia reported evidence of impaired osteoblast activity. A decrease in the bone formation rate (BFR) was found, but also defective mineralization associated with iron deposition on the mineralization front [14].

	Group 1 (n=76) Mean± SD	Group 2 (n=51) Mean ± SD	t- test	P value
Age (years)	7.55 ± 4.24	8.31 ± 4.19	0.996	>0.05
Gender				
Male No % Female No %	40 52.6% 36 47.4%	29 56.9% 22 43.1%	χ^2 = 0.01	>0.05
Weight in kg	23.93 ± 11.73	28.76 ± 13.25	2.158	<0.05*
Height (cm)	115.68 ± 25.84	126.15 ± 25.54	2.249	<0.05*
BMI (kg/m^2)	16.93 ± 1.62	17.04 ± 2.87	0.236	>0.05
Splenectomy				
Positive No %	28 36.8%	00 00%	χ^2=24.10	<0.001*
Negative No %	48 63.2%	51 100%		

Table 1: Comparison between the studied groups regarding demographic and clinical data.

	Group 1 (n=76) Mean± SD	Group 2 (n=51) Mean ±SD	t- test	P value
AST (IU/L)	98.53 ± 100.89	28.07 ± 4.68	4.977	<0.001**
ALT (IU/L)	133.15 ± 283.20	28.11 ± 3.86	2.645	<0.01**
Creatinine (mg/dl)	0.69 ± 1.08	0.96 ± 0.7	1.064	>0.05
Urea (mg/dl)	31.88 ± 8.52	30.68 ± 5.81	0.873	>0.05
Calcium (mg/dl)	7.89 ± 0.97	9.54 ± 0.50	11.16	<0.001**
Phosphorus (mg/dl)	5.55 ± 0.75	4.78 ± 0.41	6.618	<0.001**
ALP (IU/L)	362.73 ± 85.32	96.01 ± 9.14	22.20	<0.001**
Vitamin D (ng/ml)	22.82 ± 19.15	37.43 ± 10.5	4.962	<0.001**
WBCs (×10^3/L)	22.82 ± 15.65	7.03 ± 2.44	4.377	<0.001**
RBCs (×10^6/L)	2.88 ± 0.69	4.76 ± 0.42	17.31	<0.001**
Hb (g/dl)	7.73 ± 1.82	11.72 ± 1.38	13.26	<0.001**
Z score	-2.49 ± 1.70	1.71 ± 0.54	11.2	<0.001**
BMD (g/cm^2)	0.85 ± 0.39	1.54 ± 0.50	8.740	<0.001**

ALP: Alkaline Phosphatase

Table 2: Comparison between the studied groups regarding laboratory data, DEXA scan and BMD.

	Group 1 (n=76) No. %	Group 2 (n=51) No. %	χ^2	P value	OR (CI 95%)
rs2228570 genotypes: T/T: No % T/C: No % C/C: No %	 10 13.2% 31 40.8% 35 46.1%	 03 5.8% 12 23.6% 36 70.6%	11.08	<0.01*	 OR1 1.77 (1.51-2.07) OR2 1.65 (0.77 – 3.52) Reference group
Allele frequency T allele C allele	 51 33.5% 101 66.5%	 15 14.7% 87 85.3%	3.27	<0.001*	 OR 2.92(1.53-5.57) Reference Allele

Table 3: Comparison between the studied groups regarding genotype and allele frequency.

	TT (n=10) Mean ± SD	TC (n=31) Mean ± SD	CC (n=35) Mean ± SD	ANOVA	P value
AST (IU/L)	95.70 ± 79.84	95.35 ± 96.29	102.17 ± 112.08	0.041	>0.05
ALT (IU/L)	105.80 ± 79.97	101.90 ± 104.73	168.65 ± 403.90	0.504	>0.05
Creatinine (mg/dl)	0.70 ± 0.48	0.90 ± 0.57	0.51 ± 0.50	1.061	>0.05
Urea (mg/dl)	32.80 ± 9.06	32.06 ± 7.49	31.45 ± 9.41	0.106	>0.05
Calcium (mg/dl)	8.00 ± 0.94	7.83 ± 0.93	7.91 ± 1.03	0.114	>0.05
Phosphorus (mg/dl)	5.4 ± 0.69	5.67 ± 0.83	5.48 ± 0.70	0.760	>0.05
ALP (IU/L)	364.20 ± 69.82	360.03 ± 86.40	364.71 ± 90.39	0.026	>0.05
Vitamin D (ng/ml)	30.10 ± 9.12	25.45 ± 7.48	17.29 ± 6.72	6.87	<0.01*
WBCs ($\times 10^3$/L)	20.7 ± 6.58	28.87 ± 5.63	18.08 ± 3.42	1.5	>0.05
RBCs ($\times 10^6$/L)	2.80 ± 0.78	2.96 ± 0.70	2.82 ± 0.66	0.40	>0.05
Hb (g/dl)	7.60 ± 2.06	7.96 ± 1.79	7.57 ± 1.80	0.415	>0.05
Platetets count ($\times 10^3$/L)	448.20 ± 217.5	475.25 ± 342.2	339.48 ± 186.95	2.282	>0.05
Z score	-2.81 ± 0.39	0.80 ± 1.26	1.17 ± 0.74	5.91	<0.05*
BMD (g/cm^2)	0.70 ± 0.31	0.83 ± 0.37	0.85 ± 0.42	3.9	<0.05*

Table 4: Comparison between rs2228570 genotypes regarding laboratory data, DEXA scan and BMD in patients group.

DEXA		Patients group			Total	Chi 2	P value
		TT	TC	CC			
Normal	Number	2	13	15	30	11.28	<0.05*
	%	20.0%	59.1%	71.4%	62.9%		
Osteopenia	Number	2	5	3	10		
	%	20.0%	11.4%	4.3%	8.1%		
Osteoporosis	Number	6	13	17	36		
	%	60.0%	29.5%	24.3%	29.0%		
Total	Number	10	31	35	76		
	%	100.0%	100.0%	100.0%	100.0%		

Table 5: Comparison of between rs2228570 genotypes according to Femoral T score by DEXA scan into normal, osteopenia and osteoporosis in patients group.

rs2228570[a]	B	Wald	Sig.	Odds ratio	95% Confidence Interval for Exp(B)	
					Lower bound	Upper bound
Intercept	-38.999-	0.910	0.340	-	-	-
Age	1.308	1.626	0.202	3.700	0.495	27.647
Weight	0.523	1.245	0.264	1.688	0.673	4.232
Height	-.396-	1.862	0.172	0.673	0.381	1.188
BMI	-1.095-	1.627	0.202	0.334	0.062	1.800
AST	-0.045-	3.547	0.060	0.956	0.913	1.002
ALT	-0.005-	1.436	0.231	0.995	0.987	1.003
Creatinine	-0.560-	0.258	0.611	0.571	0.066	4.953
Urea	0.239	2.329	0.127	1.270	0.934	1.728
Ca	2.798	2.792	0.095	16.419	.616	437.397
Ph	0.009	0.000	0.993	1.009	.154	6.591
ALK	0.035	2.915	0.088	1.035	.995	1.077
VitD	0.092	**4.104**	**0.043**	1.096	1.003	1.198
Dexa scan	-1.591-	2.203	0.138	0.204	0.025	1.665
BMD	-.966-	0.161	0.688	0.381	0.003	42.506
WBCs	0.040	1.008	0.315	1.040	0.963	1.124
RBCs	1.268	0.489	0.484	3.553	0.102	124.156
Hb	-.298-	0.179	0.672	0.742	0.187	2.948
PLT	0.003	0.801	0.371	1.003	0.997	1.009
MCV	0.155	0.410	0.522	1.168	0.726	1.878
MCH	-.174-	0.142	0.707	0.840	0.339	2.083
MCHC	0.477	1.002	0.317	1.612	0.633	4.106
Gender=Males	0.445	0.142	0.707	1.560	0.154	15.785
Splenectomy=Yes	-4.069-	1.939	0.164	0.017	5.565E-005	5.248

Table 6: The linear regression analysis of rs 2228570 genotyping.

VDR, a nuclear receptor that binds to the active form of vitamin D. VDR functions is influenced by gene polymorphisms, among which a start codon polymorphism (rs2228570) is the most frequently investigated polymorphisms in the VDR gene [15-17].

The calcium absorption depends on the action of calcitriol and the intestinal vitamin D receptor. So the regulation of VDR gene is most important in high efficiency of calcium absorption [18].

In this study the calcium levels was significantly lower while phosphorus and alkaline phosphatase was significantly higher in TT genotypes than TC and CC genotypes.

Matched with this study of Sharla et al found that the *Fok*1 polymorphism at the VDR translation initiation site was significantly associated with BMD (p=0.02) and calcium absorption (p=0.04). Children who were CC homozygotes had a mean calcium absorption that was 41.5% greater than those who were TT homozygotes and 17% greater absorption than TC heterozygotes [19].

The outcomes of the present study revealed that Z score and BMD values are more lower in Beta-thalassemia children with TT genotypes of rs2228570 than others genotypes.

In accordance with these results Arai et al demonstrated that the BMD of the lumbar spine was 12.0% greater for CC homozygotes than for TT homozygotes in 110 healthy premenopausal Japanese women [20].

Also, Sharla et al found that BMD was 8.2% greater in the CC genotype than the TT genotype and 4.8% higher than the TC genotype [19].

Animal and human studies have shown that genes can affect bone density in various pathways focus on VDR gene and single point polymorphism in this gene is known to alter metabolic activity of the bone [21].

In the present study patients with TT genotype show higher levels of 1.25 (OH) vitamin D3 and lower BMD than other two genotypes of VDR rs2228570 SNP.

This may explained by that polymorphisms in the VDR gene have been shown to influence VDR mRNA and protein levels, which, in turn, may influence the function of VDR. So, need more vitamin D to do the same effect [22].

This matched with Arai et al who suggested that the extent of vitamin D-dependent transcriptional activation of a reporter construct was approximately 1.7-fold greater for the variant of the *Fok-I* (C-type) than for the T-type [20].

The study of Rieko et al demonstrated that the effect of the *Fok-I* genotype on the association with the serum 25(OH) D, where there were significant positive correlations between serum bone specific ALP and 25(OH)D concentrations in the CC type and TC type [23].

In the present study, a significant difference among TT, TC and CC types of rs2228570 genotypes of VDR as regard number and % of osteopenia and osteoporosis in patients group with TT genotype has significantly higher rates of osteopenia and osteoporosis than both TC and CC in β-thalassemia children group.

The most studies in this field were done on women and also on older ages. In more than 60% of the previous studies a significant association was found between the polymorphism Fok1 and osteoporosis [24].

Conclusion: It can be concluded that Fok1 SNP in VDR gene may affect bone mineral density BMD. Genetic variant TT genotype for VDR rs2228570 may consider as risk factors and predictor for osteoporosis in β-thalassemia children.

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Ethical Approval

Research Involving Human Participants: The study was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent, and the Ethics Committee of Faculty of Medicine, Menoufia University approved the study protocol.

References

1. Rachmilewitz EA, Giardina PJ (2011) How I treat thalassemia. Blood 118: 3479-3488.
2. Vogiatzi MG, Macklin EA, Fung EB, Cheung AM, Vichinsky E, et al. (2009) Bone disease in thalassemia: a frequent and still unresolved problem. J Bone Miner Res 24: 543-557.
3. Carlberg C, Molnar F (2006) Detailed molecular understanding of agonistic and antagonistic vitamin D receptor ligands. Curr Top Med Chem 6 :1243-1253.
4. Uitterlinden AG, Fang Y, Van Meurs JB, Pols HA, Van Leeuwen JP (2004) Genetics and biology of vitamin D receptor polymorphisms. Gene 338: 143-156.
5. Minghelli B, Oliveira R, Nunes C (2014) Non-specific low back pain in adolescents from the south of Portugal: prevalence and associated factors. J Orthop Sci 19: 883-892.
6. Mayer JE, Iatridis JC, Chan D, Qureshi SA, Gottesman O, (2013) Genetic polymorphisms associated with intervertebral disc degeneration. Spine J 13: 299-317.
7. Jurutka PW, Remus LS, Whitfield GK, Thompson PD, Hsieh JC, et al. (2000) The polymorphic N terminus in human vitamin D receptor isoforms influences transcriptional activity by modulating interaction with transcription factor IIB. Mol Endocrinol 14: 401-420.
8. Saijo T, Ito M, Takeda E, Huq AH, Naito E, et al. (1991) A unique mutation in the vitamin D receptor gene in three Japanese patients with vitamin D-dependent rickets type II: utility of single-strand conformation polymorphism analysis for heterozygous carrier detection. Am J Hum Genet 49: 668-673.
9. Costanzo P, Santini A, Fattore L, Novellino E, Ritieni A (2015) Toxicity of aflatoxin B1 towards the vitamin D receptor (VDR). Food Chem Toxicol 76: 77-79.
10. Zemel BS, Leonard MB, Kelly A, Lappe JM, Gilsanz V, et al. (2010) Height adjustment in assessing dual energy x-ray absorptiometry measurements of bone mass and density in children. J Clin Endocrinol Metab 95: 1265-1273.
11. Endres DB, Robert K (2006) Rude: Mineral and bone metabolism. Calcium, in, Tietz textbook of clinical chemistry and molecular diagnosis. In: Carl AB, Edward RA, David EB (eds.) Saunder (4th edn.), Chapter 46, pp: 1892-1904.
12. Hollis BW (2005) Circulating 25-hydroxyvitamin D levels indicative of vitamin D sufficiency: implications for establishing a new effective dietary intake recommendation for vitamin D. J Nutr 135: 317-322.
13. El-Beshlawy A, Kaddah N, Moustafa A, Mouktar G, Youssry I (2007) Screening for β-thalassaemia carriers in Egypt: significance of the osmotic fragility test. East Mediterr Health J 13: 780-786.
14. Mahachoklertwattana P, Sirikulchayanonta V, Chuansumrit A, Karnsombat P, Choubtum L, et al. (2003) Bone histomorphometry in children and adolescents with beta-thalassemia disease: ironassociated focal osteomalacia. J Clin Endocrinol Metab 88: 3966-3972.
15. Yin K, Agrawal DK (2014) Vitamin D and inflammatory diseases. J Inflamm Res 7: 69-87.
16. Wobke TK, Sorg BL, Steinhilber D (2014) Vitamin D in inflammatory diseases. Front Physiol 5: 244.
17. Alagarasu K, Honap T, Mulay AP, Bachal RV, Shah PS, et al. (2012) Association of vitamin D receptor gene polymorphisms with clinical outcomes of dengue virus infection. Hum Immunol 73: 1194-1199.
18. Xue Y, Fleet JC (2009) Intestinal vitamin D receptor is required for normal calcium and bone metabolism in mice. Gastroenterology 136: 1317-1327.

19. Ames SK, Ellis KJ, Gunn SK, Copeland KC, Abrams SA (1999) Vitamin D receptor gene *Fok*1 polymorphism predicts calcium absorption and bone mineral density in children. Journal of Bone and Mineral 14: 740-746.

20. Arai H, Miyamoto K, Taketani Y, Yamamoto H, Iemori Y, et al. (1997) A vitamin D receptor gene polymorphism in the translation initiation codon: effect on protein activity and relation to bone mineral density in Japanese women. J Bone Miner Res 12: 915-921.

21. Rizzoli R, Bonjour J, Ferrari S (2001) Osteoporosis, genetics and hormones. J Mol Endocrinol 26: 79-94.

22. Israni N, Goswami R, Kumar A, Rani R (2009) Interaction of vitamin D receptor with HLA DRB1 0301 in type 1 diabetes patients from North India. PLoS ONE 4: e8023.

23. Tanabe R, Kawamura Y, Tsugawa N, Haraikawa M, Sogabe N, et al. (2015) Effects of *Fok-I* polymorphism in vitamin D receptor gene on serum 25-hydroxyvitamin D, bone-specific alkaline phosphatase and calcaneal quantitative ultrasound parameters in young adults. Asia Pac J Clin Nutr 24: 329-335.

24. Mohammadi Z, Fayyazbakhsh F, Ebrahimi M, Amoli MM, Khashayar P, et al. (2014) Association between vitamin D receptor gene polymorphisms (Fok1 and Bsm1) and osteoporosis: a systematic review. Journal of Diabetes & Metabolic Disorders 13: 98.

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