VITAMIN D RECEPTOR PROMOTER METHYLATION STATUS IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSIS

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Introduction

Systemic lupus erythematosus (SLE), is a systemic autoimmune disease, can cause chronic inflammation and damage in several tissues and organs.

Vitamin D, as a steroid hormone, exhibits regulatory effects on growth, proliferation, apoptosis and function of the immune system cells. Vitamin D is associated with pathophysiology of SLE.

The discovery of vitamin D receptor expression by cells of the immune system has spurred more research on the immunomodulatory properties of vitamin D over the past decade.

Vitamin D deficiency is highly prevalent in SLE patients due to the avoidance of sunshine, photoprotection, renal insufficiency and the use of medications such as glucocorticoids, anticonvulsants which alter the metabolism of vitamin D or down regulate the functions of the vitamin D receptor.

The human VDR gene is located inchromosome 12 and contains 14 exons and spans approximately 75 kb. The promoter of the VDR gene is embedded in a GC-rich island with five binding motifs for the transcription factors. The transcriptional activity of VDR could be affected also by epigenetic mechanisms such as DNA methylation which regulate gene expression and chromatin structure.

Aim of the work

The aim of the present work is to study the methylation status of VDR gene promoter and serum levels of 25-hydroxyvitamin D (25(OH)2D) and their clinical significance in patients with pediatric systemic lupus erythematosus.

Subjects and Methods

SUBJECTS

The Study will be conducted on 2 groups:

Group I: 40 patients with pediatric Systemic Lupus Erythematosus.

Group II:40 age and sex matched controls.

The study will be conducted on patients presenting to Alexandria University Children Hospital.

METHODS

All the patients included in the study will be subjected to the following:

* Full history taking. * Complete Physical examination.

* Laboratory investigations:

- Complete Blood Count.
- Serum Urea, Creatinine.
- Serum Calcium and phosphorus.
- Alkaline phosphatase.
- C-reactive protein.
- Serum albumin.
- Liver enzymes (ALT, AST).
- Anti nuclear antibody ANA titre and pattern.
- Anti double strand DNA (Anti dsDNA).
- Complement (C3).
- Systemic Lupus Erythematosis Disease Activity Index (SLEDAI) will be recorded.
- Measurement of vitamin D (25(OH)2D) by Enzyme Linked Flourescent Assay (ELFA) technique.
- Vitamin D Receptor Methylation Assay by Quantitative Methylation specific PCR (qMS-PCR).

Results

The current study included 80 patient presenting to Alexandria university children hospital. They are 2 groups, the patient group include 9 males and 31 females while control group include 16 males and 24 females.

In the studied cases vitamin D status shown in the table:

Table 1: Comparison between the two studied groups according to Vitamin D

	Patient (n = 40)		Control (n = 40)		Test of Sig.	p
	No.	%	No.	%		
Vitamin-D status						
Deficiency	12	30.0	0	0.0	χ^2= 29.490*	<0.001*
Insufficiency	14	35.0	3	7.5		
Sufficiency	14	35.0	37	92.5		
Vitamin D level						
Min. – Max.	2.01 – 26.56		14.80 – 52.50		U= 106.0*	<0.001*
Median (IQR)	17.26 (8.10 – 20.45)		27.05(24.05 – 31.10)			

Table 2: And the Comparison between the two studied groups according to % methylation

% methylation	Patient (n = 40)	Control (n = 40)	U	p
Min. – Max.	0.0 – 86.45	0.0 – 23.95	520.5*	0.007*
Mean ± SD.	16.43 ± 15.88	7.91 ± 5.64		
Median (IQR)	9.75 (7.50 – 26.26)	7.80 (3.23 – 9.03)		

IQR: Inter quartile range SD: Standard deviation U: Mann Whitney test

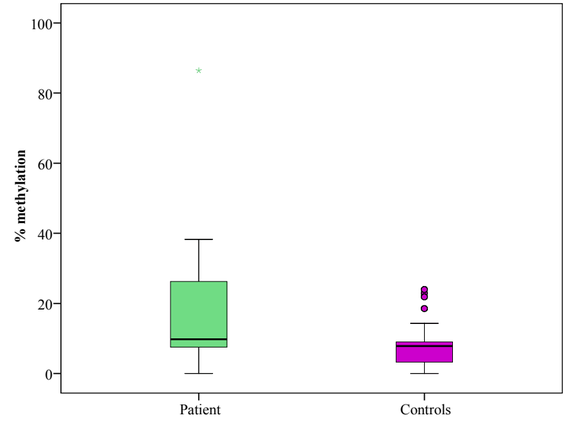

Figure 1: Comparison between the two studied groups according to % methylation

Conclusion

Gene promoter methylation status is negatively correlated with vit D serum level and associated with clinical flare in pediatric patient with SLE.