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Evaluation of Vitamin D status in patients with Atopic Dermatitis (Eczema) in Sulaimani Province, Kurdistan region, Iraq

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Abstract

Skin inflammation or atopic Dermatitis (AD) is a long-lasting, inflammatory skin condition which generally develops in early life. The aetiology is a complex disorder with genetics, barrier function, immunity, and environmental factors all playing key roles in disease progression. Since vitamin D has immunomodulatory properties and immunologic systems assume a job in the pathogenesis of atopic eczema. The point of the investigation is to correspond vitamin D focuses in patients who have skin inflammation with the clinical and natural elements. Questionnaire population-based study 60 patients and 50 healthy volunteers (control) with age between 17-60 years were used in this study for about 3 months. The diagnosis has based the prevalence and morphology of hand eczema in a patient with atopic dermatitis in 2006 and the blood samples were collected from each patient before filling the questionnaire form, then the level of vitamin D (VD) was measured. The mean estimation of serum vitamin D in AD was greatly of lower than the normal value, and there was a substantial difference found in the mean estimations of vitamin D between AD patients (18.51) and the controls (23.38) with *P value 0.001*, there is a significant distinction between patients with mild eczema and those with severe eczema, which could lead to a significant increase in vitamin D deficiency as eczema worsens, while there was no significant association among VD subgroups with age, and gender in AD patients. The results from this study indicated that VD is the main factor in the development of AD and its supplementation may help ameliorate medical signs of the disease.

Introduction

Skin inflammation or eczema also is known as atopic dermatitis (AD) is the most public cutaneous disease in industrialized countries [1]. Which is a common chronic skin inflammatory condition characterized clinically by pruritus, eczematous plaques, and a defective epidermal barrier [2]. That is impacted by hereditary and different elements including natural condition, disease, stress, and diet [3]. The universal increasing occurrence of AD is around 10%-20% in kids and 2-10% in grown-ups, and there has been an enduring increment in the course of recent decades [4]. Among other ecological components, vitamin D has been recommended as assuming a huge job in the improvement of hypersensitive skin sicknesses and explicitly in dermatitis [5, 6].

Vitamin D is a group of fat-soluble steroids known to acts as a pleiotropic hormone [4], that can be synthesized in the skin from ultraviolet radiation or absorbed through dietary intake.[7]

A current assessment has exhibited that vitamin D influences both natural and adaptive immune mechanisms, influences cell differentiation, and modulates proliferation and differentiation of keratinocytes s, and is related with keratinocyte creation of antimicrobial peptides [8]. Since these procedures are engaged with the pathogenesis of skin inflammation, the impact of vitamin D levels on this current condition's hazard

and seriousness appears to be a biologically reasonable theory. Numerous studies have endeavored to demonstrate this speculation however with conflicting results [9, 10, and 11].

Schauber and his coworker demonstrated that the active form of vitamin D [1,25(OH)2 D3] improved expression of antibacterial peptides, therefore stopped cutaneous infections [12]. Liu *et al.* presented a connection between vitamin D- mediated activation of Toll-like receptors, the creation of cathelicidin, and reduced sensitivity to bacterial infections. Vitamin D can encourage or inhibit keratinocyte differentiation [13].

In 2013, Mutgiand Koo published a review of the articles carefully extracted from those accessible up to January 2012, tending to the connection between nutrient D levels and the hazard or seriousness of AD and the helpful job of nutrient D substitution [14]. Most of assessed observational examinations exhibited a converse connection between vitamin D levels and the appearance and seriousness of skin inflammation in a portion subordinate way. Moreover, remedial preliminaries proposed that repletion of vitamin D is related with progress in AD seriousness and comparing serum vitamin D [15].

From that point forward, the quantity of concentrates that have examined the job of vitamin D in unfavorably susceptible skin illnesses has expanded essentially, and these investigations have shown all the more opposing outcomes, little is known about the complex effects of serum vitamin D on eczema in our geographical area.

The aim of the present study is to investigate the relation between prevalence of eczema and serum vitamin D level in sulaimani province.

Methods

Subjects

The study included 60 patients with eczema, including 22 female and 38 males, and 50 controls comprised of healthy volunteers having neither significant medical illness nor under medication for at least 3 month duration at the time of blood collection(25 female and 25 male) with age between (17-60) years.. The diagnosis was based on the prevalence and morphology of hand eczema in a patient with atopic dermatitis in 2006 and the occurrence of atopic dermatitis in north Europe: an international questionnaire study in [15].

Blood samples

The blood specimens were collected in the Dermatology Center of Skin Feeding in sulaimanya and in a private medical clinic.

Approximately 5-7 ml were collected directly under complete aseptic precautions in appropriate sterile vials by the venous arm, the blood allowed to clot at room temperature, then, samples centrifuged at 3000 xg for 10 minutes, With filling questionnaire form for each one. The questionnaire employed in the sampling campaign including the following parameter:

Subject NO., Name, gender, age, residency, smoker, weight, height, alcoholism, vegetarian, level of education, chronic diseases (hypertension, cholesterol, diabetes, heart disease, asthma, obesity, chronic kidney disease) family history, taken vitamin D and the duration of illness

Evaluation of Vitamin D[25 (OH) D3] concentration

The serum concentration of 25(OH)D3 was measured in (a private medical laboratory in sulaimanya) according to protocol of the Instruments, we add 5 micro ml of serum to the special tubes of instruments with reagents including calibrations and control obtained from 25 (OH) D3 determinations were under international control of the Vitamin D External Quality Assessment Scheme (DEQAS) with a certificate of Proficiency.

Vitamin D levels were based on the results of serum concentration of 25(OH)D3 and known as follows: deficiency <10 ng/ml (<50 nmol/l), insufficiency 10-29 ng/ml (52.5- 72.5 nmol/l) and recommended range 30-80 ng/ml (72.5-200 nmol/l)[16][17].

Results

The examples were comprised of 60 AD patients and 50 control group patients. Table 1 utilizing the SCORAD record, 19 cases (31.7%) with AD were classified as having a mild AD with value of

(24.23±7.01), 23 people (38.3%) were arranged as having a moderate disease with value of (17.54±2.05), and 18 people (30.0%) were ordered as having marked AD with value of (12.40±1.58).

Table 1: Frequency and severity of AD cases.

AD	SCORAD index		P-value
	Number %	Mean ±SD	
Mild	(19) 31.7%	24.23±7.01	
Moderate	(23) 38.3%	17.54±2.05	0.000
Severe	(18) 30.0%	12.40±1.58	

All the frequencies of eczema patients and their corresponding vitamin D status revealed in table (2) and both figures (1) and (2). This status was set to severe deficiency in those patients having their vitamin D below 7 ng/ml, and deficient for those who had a vitamin D in a range between 7 to 10 ng/ml. While it was set to insufficient if the value was between 10 to 29 ng/ml. Also, values from 30 to 100 were set to be sufficient above that was set to be toxic levels. Serum concentrations of 25(OH)D were found to be inadequate in 16 patients that had severe AD, while 24 and 14 cases where recorded as moderate and mild AD that had insufficient serum concentrations of 25(OH)D, whereas only 2 cases recorded in severe AD that had deficiency in VD serum level in comparison to the control group that 12 individual had sufficient level of VD while 38 persons had insufficient serum concentration of VD. The mean estimation of serum vitamin D in AD was a lot of lower than the normal value, and there was a substantial difference found in the mean estimations of vitamin D among AD and the controls (P=0.001).

Table 2: Vitamin D status frequency by eczema severity.

Vitamin deficiency status			Eczema severity
Insufficient	Sufficient	Deficient	
16			Severe
24			Moderate
14			Mild
	2		Mild
		2	Severe
38			Healthy control
	12		Healthy control

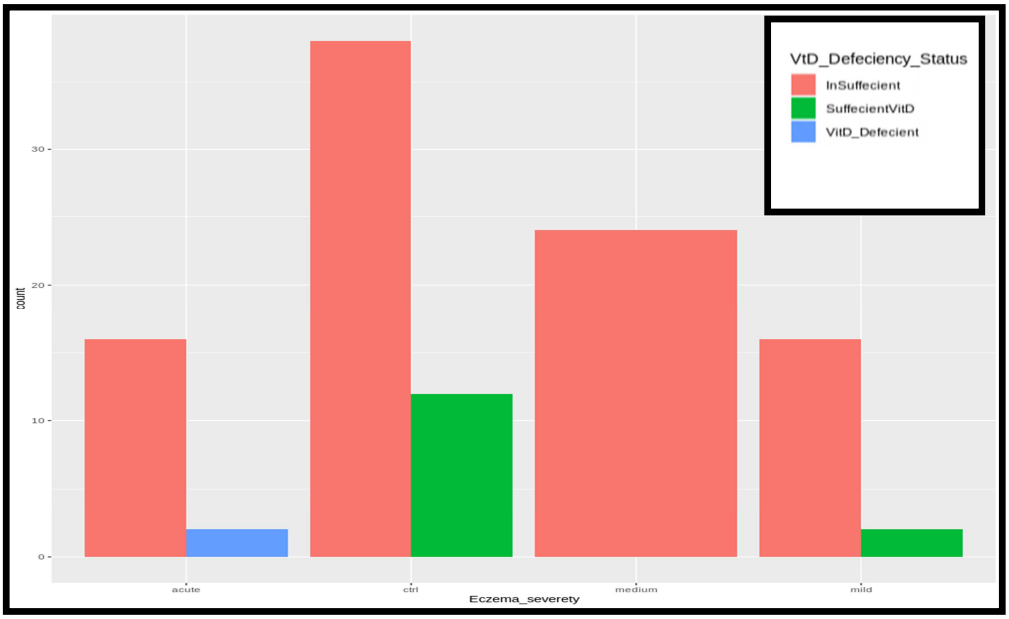

Figure 1: Column chart explains vit D deficiency status in eczema severity patients compared to control samples.

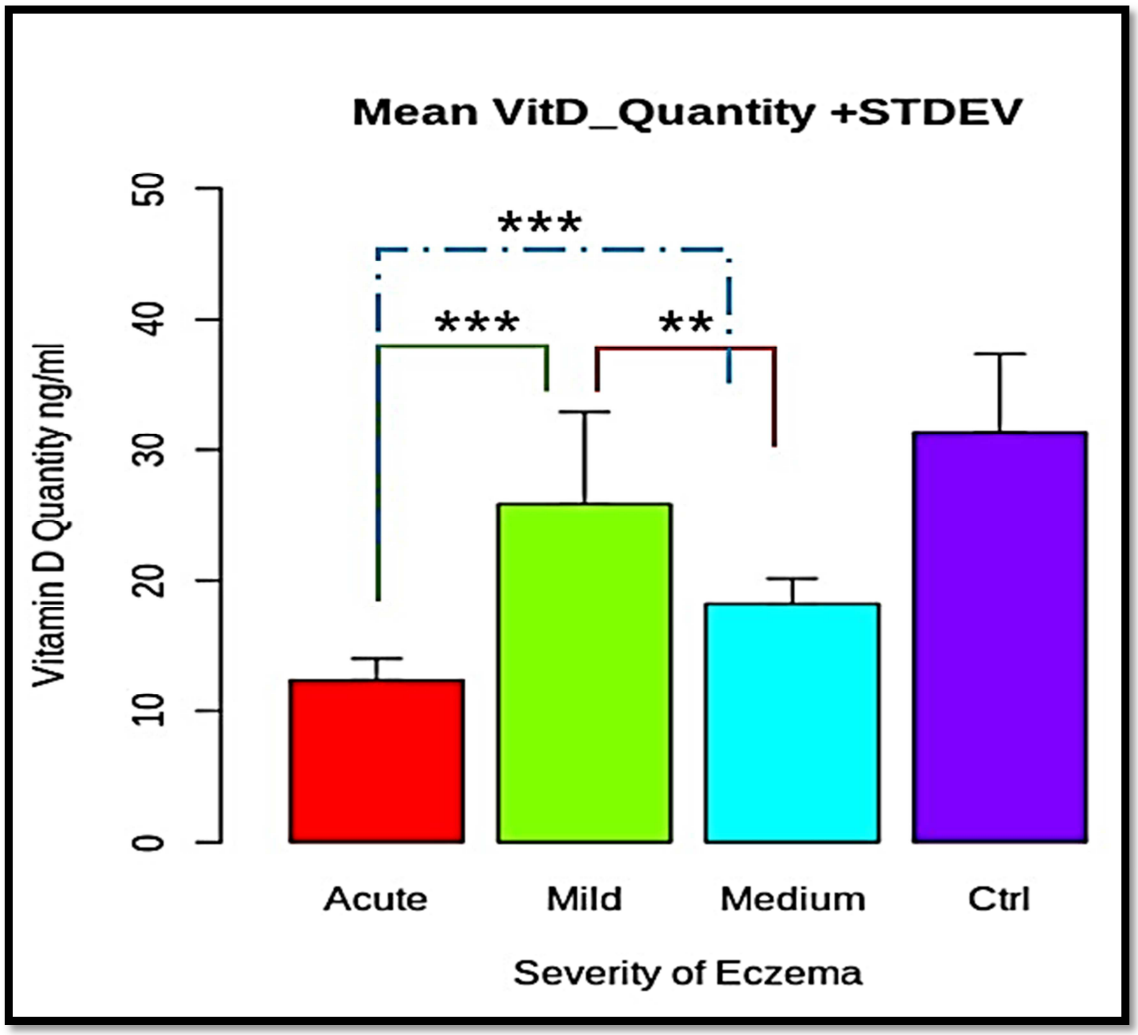

Figure 2: Bar plotof average vitamin D against severity subcategories of eczema patient and control sample sets.

Table 3 and figure 3, explains that there is a highly significant difference among the variables being studied for eczema patients (Acute or severe, mild, and medium or moderate) in terms of the vitamin D quantity of their samples by (*P=0.001*), and there is a significant distinction between patients with mild eczema and those with acute eczema, which could lead to a significant increase in vitamin D deficiency as eczema worsens.

Table 3: Descriptive summary statistics of the eczema patients' vitamin D quantity.

AcuteQuant	MildQuant	MediumQuant
Min. : 9.50	Min. :20.07	Min. :14.33
1st Qu.:11.37	1st Qu.:22.02	1st Qu.:16.07
Median :12.17	Median :23.44	Median :17.14
Mean :12.46	Mean :25.37	Mean :17.55
3rd Qu.:14.14	3rd Qu.:26.63	3rd Qu.:18.84
Max. :14.48	Max. :51.06	Max. :23.81

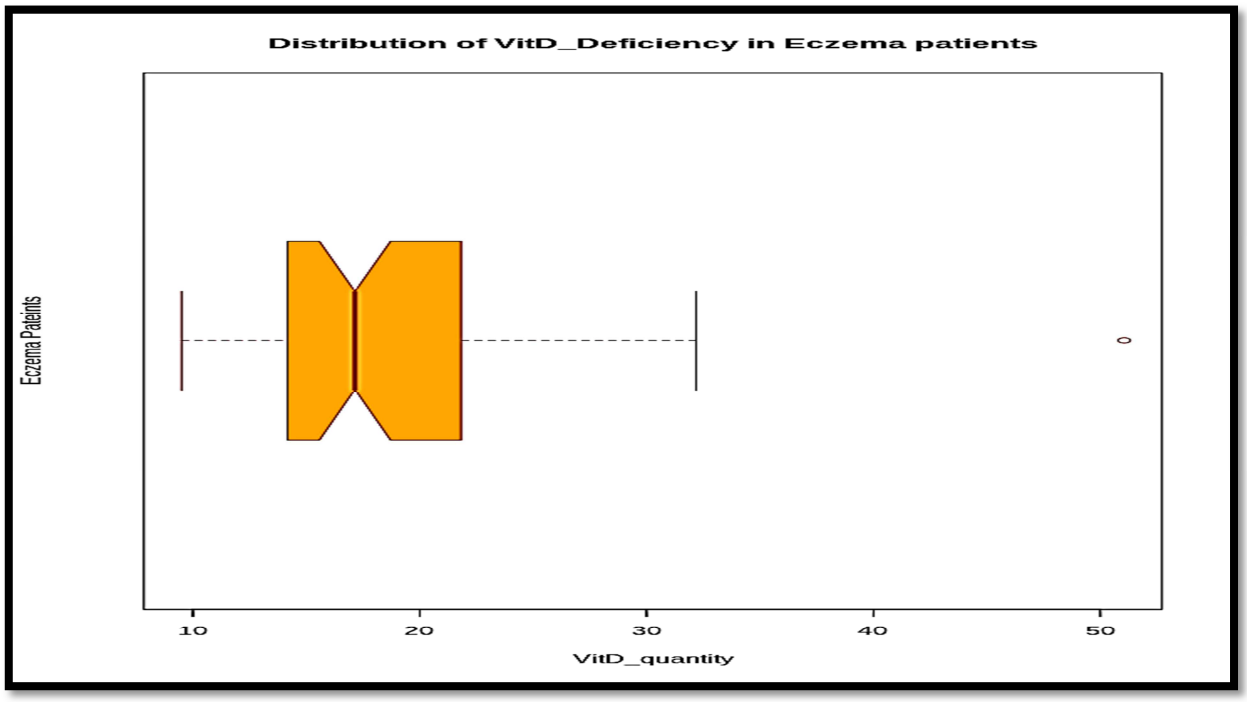

Figure 3: Boxplot displayed distribution of Vitamin D deficiency in Eczema patients.

Table 4 describes the relationship of all parameters with the VD group in all case study, the sex parameter in the VD group of (less than 20) 39 out of 63 male case study , the VD group of (20-30) 22 out of 63 case study and the VD group of (more than 30) 2 out of 63 case study with no significant association (*P=0.069*), this means that there is no association between the VD group and the gender parameter (Figure 4), then in the VD group (less than 20) 20 out of 32 case aged between (21-30), in the VD group (20-30) 10 out of 32 case study, and in the VD group (more than 30) 2 out of 32 case with no important association (*P=0.813*), this implies that no relationship exists between the VD group and the patient age parameter (Figure 5). Although there was an extremely important association between VD history and VD groups, for example the group of (less than 20) 58 out of 95 case study who had not previously taken VD, Whereas only 4 out of 15 cases had taken it before, in the VD group of (20-30) 32 out of 95 case study had not taken it before, while 7 out of 15 had taken VD before, finally, the VD group of (more than 30) 5 out of 95 case study had not taken it before, and only 4 out of 15 had taken it before, this stated a strong link between VD history and VD groups.

Table 4:Association between VD group and other parameters in all cases study.

		VD Group						**Total**		Chi-Square	P-Value
		Less than 20		between 20- 30		More than 30					
Gender	Male	39	62.9%	22	56.4%	2	22.2%	**63**	**57.3%**	5.333	0.069
	Female	23	37.1%	17	43.6%	7	77.8%	**47**	**42.7%**		
Age Group	Less than 20	2	3.2%	2	5.1%	1	11.1%	**5**	**4.5%**	4.460	0.813
	21-30	20	32.3%	10	25.6%	2	22.2%	**32**	**29.1%**		
	31-40	20	32.3%	13	33.3%	3	33.3%	**36**	**32.7%**		
	41-50	12	19.4%	11	28.2%	3	33.3%	**26**	**23.6%**		
	More than 51	8	12.9%	3	7.7%	0	0.0%	**11**	**10.0%**		
VD history	Non take it before	58	93.5%	32	82.1%	5	55.6%	**95**	**86.4%**	10.587	0.005
	Take it before	4	6.5%	7	17.9%	4	44.4%	**15**	**13.6%**		

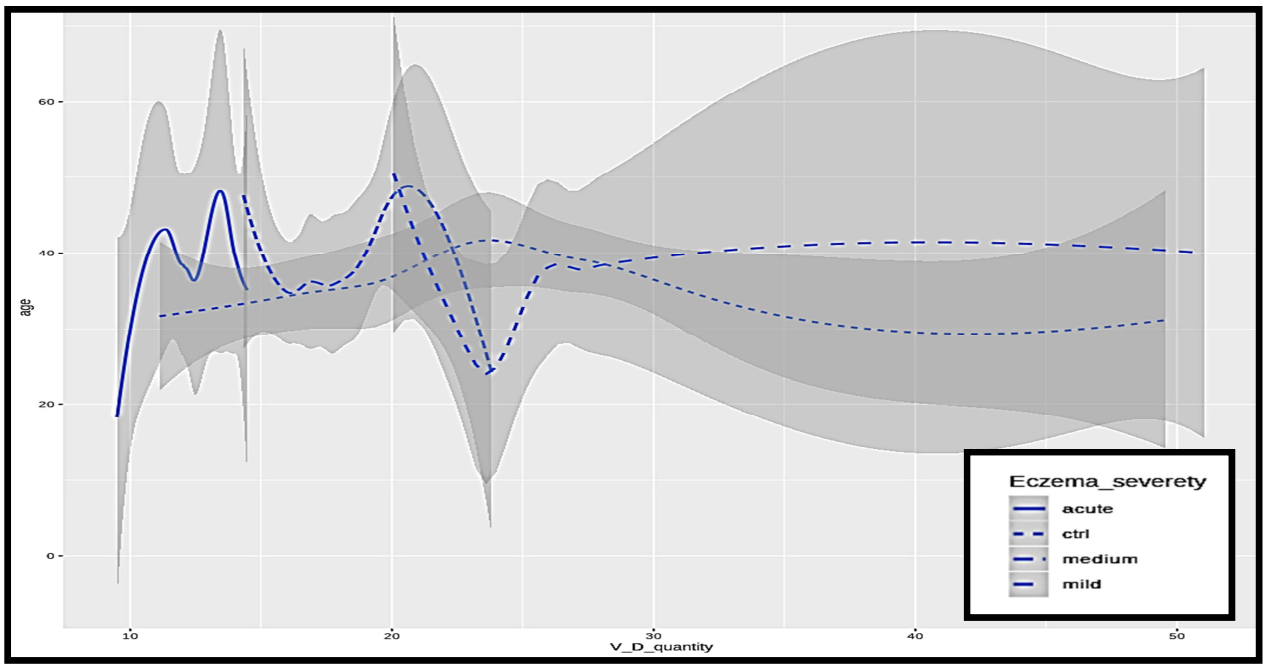

Figure 4: Shows variability in vitamin D quantity, and eczema severity status in different genders.

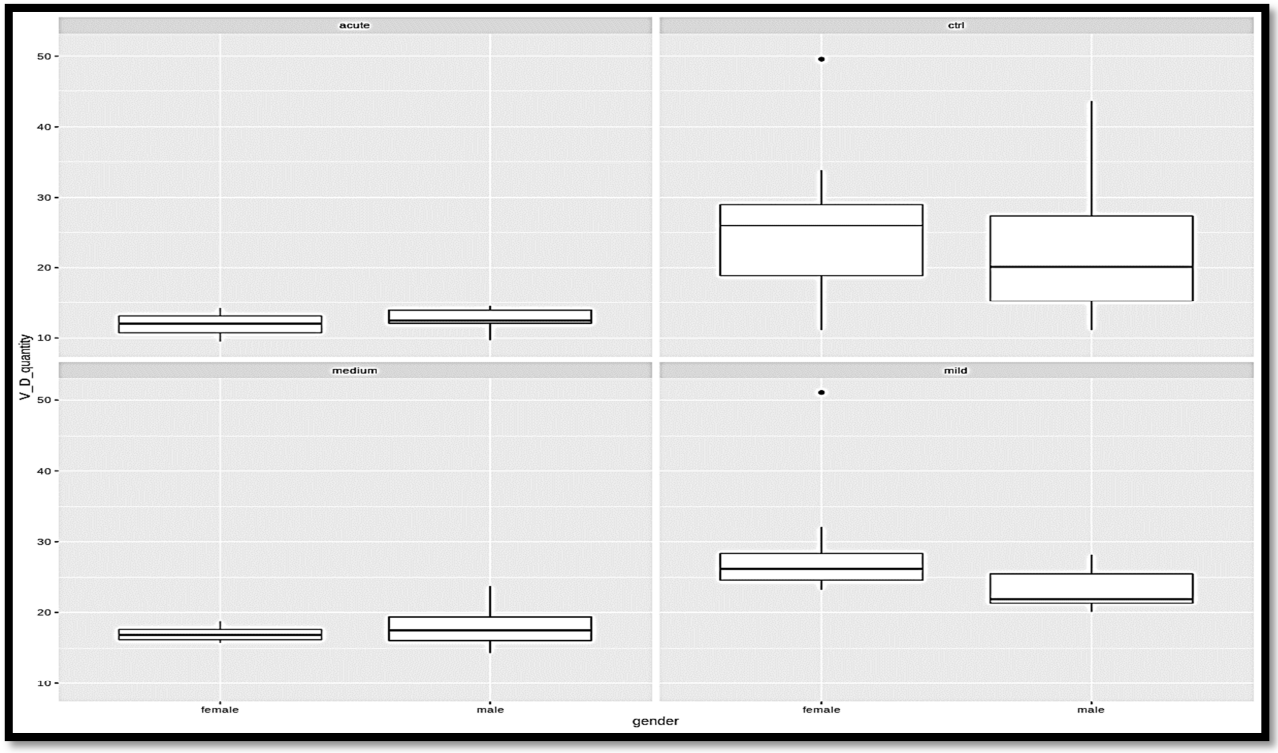

Figure 5: Shows vitamin D quantity in different age being categorized in accordance with eczema severity status.

Discussion

Vitamin D plays a major role in both the innate and the immune response [18]. It also plays a part in the skin's immune response, functions, and integrity [19]. The developing significance of vitamin D lack in atopic patients can be distinguished among the factors associated with the genesis of AD. Past studies appear, in connection to its classical role in calcium homeostasis, the effect of vitamin D in immunomodulation and cell differentiation, changing the nearby calcium balance and binding to nuclear receptors that control quality translation. It is additionally associated with antimicrobial peptide (AMP)

creation of keratinocytes. Vitamin D and its analogs seem to assume a developing role in disease management, for example, AD, psoriasis, vitiligo, skin inflammation, and rosacea [14].

In this study the difference in serum vitamin D levels and different sex patient was not statistically significant (table 4 and figure 4); however, in subgroup analysis, wefound (62.9%) among male gender of AD patients that had lower 25(OH)D concentration than female patients and matched controls. Similar results were recorded in New Zealand and Brazil, where middle-aged and older males had a greater 25(OH) D decrease compared to females [20, 21] particularly in the winter season. The explanation why in our results the 25(OH) D status was not statistically different, because small differences in serum 25(OH)D may not be clinically important, the association of categorical factors appears more relevant or our findings should be carefully interpreted, as the total amount of adult AD patients registered in our test was low and completed for short duration.

The surprising age difference in our study(table 4 and figure 5) showed no significant association between VD subgroups across all ages, we found a high mean of patient in less than 30 years age of male gender with the VD group of (less than 20), while its serum 25(OH)D concentration lower than those of the controls. Rather than our discoveries, Chiu et al found that vitamin D was not corresponded with the seriousness of AD yet it had a significant relationship with age younger than 3 years and even older, in which, the older the patient, the lower the serum 25(OH)D level [22]. Also, disagreements to the other study documented that older people consume more oily fish with elevated levels of vitamin D or most of them take supplements of vitamin D and calcium to avoid osteoporosis [23, 24], because most of Kurdish older patients do not eat fish regularly while they took the vitamin D and calcium supplements.

In table 4, the results showed considerable decreasing number in AD patients who taken vitamins D supplement, and showed significant relation between taking VD as supplement before gotten AD disease and decreasing the rate of the AD which was consistent with other hypothesis proved that the adverse association between the 25(OH)D serum level could have an impact on the enhancement of AD patients and suggest a possible reverse relation between the consumption of vitamin D and the incidence of AD diseases [25]. Additionally through a postal questionnaire, the aggregate rate of AD, at 6 years old were researched in 123 children. AD was increasingly predominant in the group with the highest intake of vitamin D3, paying little mind to family ancestry of AD [10].

In our investigation we found a profoundly huge connection between serum levels of 25(OH)D and AD disease severity as assessed by the SCORAD index in contrast with the control group (table 1 and figure 1). Adequate level of 25(OH) D were distinguished in the patients with mild disease than in those with moderate and severe disease, correspondingly. In accordance with many observational studies, including meta-analysis, have shown that serum vitamin D levels are smaller in adults and children with AD relative to controls, and the relation between vitamin D deficiency and atopic eczema risk has been reported [26, 27]. It has been noted in the literature that the concentration of 25(OH)D in patients with AD was considerably smaller than in control groups [28, 29]. A nutritional study comparing AD (n=132) patients with healthy controls (n=132) showed that AD patients had reduced dietary consumption of vitamin D than the control group [30].In addition, it was noted in large population-based research that there is an enhanced probability of developing AD in people with either deficient or inadequate concentrations of vitamin D [31].

In this investigation, we established that vitamin D levels were significantly lesser in moderate and severe AD compared with mild AD This finding is the same as El Taieb et al, which reported an adverse correlation between vitamin D and AD severity [25].Conversely, the association of 25(OH)D with AD (table 3 and figure 2).is controversial, especially in adult patients. As in the research by Peroni et al, which discovered an adverse correlation between 25(OH)D serum concentrations and AD severity [32].Other research, however, found no statistically significant variations in adult and AD levels of serum vitamin D [3,33]. A large-scale cohort study involving adult Koreans discovered that AD was correlated with reduced serum concentrations of 25(OH)D [34]. On the other hand, a Danish cohort study discovered that serum level 25(OH)D was not associated with adult AD and other allergic diseases [35].According to the Korean hypothesis, there is an increased possibility of vitamin D insufficiency due to elevated autonomy living and increased sunscreen use

decreased outdoor activity and absence of vitamin D-fortified food intake [36].In addition, Hata*et al*, after an oral vitamin D supplementation course, discovered enhanced cathelicidin (antimicrobial peptides) in skin biopsies in patients with atopic eczema. Increasing the synthesis of vitamin D and improving the concentrations of vitamin D in the serum could assist reinforce inherent defense obstacles to avoid skin infections that cause inflammation of the skin in AD [37].

Conclusion

In this investigation, we found that vitamin D levels were essentially lower in moderate and severe AD compared with mild AD, and there is an exceptionally significant connection between serum levels of 25(OH)D and AD disease severity as assessed by the SCORAD record in contrast with the control group; Sufficient degree of 25(OH)D were distinguished in the patients with mild disease than in those with moderate and severe disease.

Insufficiency of vitamin D in the overall adult Kurdish population is correlated with an enhanced risk of atopic dermatitis. Further investigation is required for the role of vitamin D in pathogenesis and management of atopic dermatitis in adults.

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