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Research Article

Prevalence of Vitamin D Deficiency in Children with Inherited Ichthyosis: A Transversal Controlled Study

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Abstract

Introduction and Objective: Inherited ichthyosis constitutes a heterogeneous group of cornification disorders. Its healthcare management is a challenge for most specialists doctors in dermatology. The objective of this study was to determine the prevalence of vitamin D deficiency of patients suffering from inherited ichthyosis, and to identify the different factors associated with this deficiency.

Methodology: This was a cross sectional study performed in the University Hospital center at the dermatology department among two groups: patients with inherited ichthyosis and patients without this disease. Patients' clinical characteristics were collected. Serum concentration of 25-hydroxyvitamin D was determined among the two groups. Comparisons between the two groups conducted by bivariate analysis.

Results: A total of 46 patients were included in the study. The majority (84.8%) had serum 25-hydroxyvitamin D below the optimal level of 30 ng/mL. Among patients with inherited ichthyosis, 56.5% had a lamellar form, 39.1% had a vulgaris form and 01 case had netherton disease. The mean of serum level of 25-hydroxyvitamin D was lower at in patients with inherited ichthyosis 18.24 ± 10 ng/mL in comparison with control group 22.0 ± 15.0, (p = 0.19). The vulgaris ichthyosis form was mainly associated to ectropion (p = 0,02) and thick dander scales (p = 0.001).

Conclusion: The measure of vitamin D among patients with inherited ichthyosis was suboptimal. A supplementation in vitamin D is strongly recommended to this category of patients either severe ichthyosis or lamellar ichthyosis.

Keywords: *Inherited Ichthyosis; Vitamin D*

Background

Inherited or congenital ichthyosis is a collective name for a group cutaneous disorders of cornification. There may be an abnormal quality or quantity of scale produced, abnormal thickness of stratum corneum or abnormal keratinocyte kinetics, often associated with

skin inflammation [1]. Clinical presentation, pattern of inheritance, and laboratory evaluation may establish a precise diagnosis, which can assist in prognosis and genetic counseling.

The prevalence of inherited ichthyosis in Moroccan population is approximately 1/300,000. The major subtypes are ichthyosis vulgaris and lamellar ichthyosis, and congenital ichthyosis form erythroderma [2]. Ichthyosis vulgaris is the most common type of congenital ichthyosis, in an autosomal dominant genetic disorder. At birth, skin may appear normal and gradually it becomes dry, rough and scaly, usually before the age of one year. Involvement is generally mild and may vary greatly with climate and humidity. Congenital autosomal recessive ichthyosis usually presents at birth, often as a collodion baby. It can progress into any one of cornification disorders. Lamellar ichthyosis is characterized by large, dark, plate-like scales covering their skin on most of their body. Netherton's syndrome is an autosomal recessive disorder characterized by ichthyosis, a hair shaft abnormality and atopy. The ichthyosis may present at birth with erythroderma or in some cases a collodion presentation. Other type of ichthyosis congenital are congenital ichthyosis form erythroderma, epidermolytic hyperkeratosis, X-linked ichthyosis… The dry skin of ichthyosis can be treated by applying skin softening emollients. Lotions containing alpha-hydroxy acids, urea, or propylene glycol can also be effective. Skin barrier repair formulas containing ceramides or cholesterol may also improve scaling. Severe cases of ichthyosis may be treated systemically with oral synthetic retinoid.

In patients with ichthyosis, the barrier function of the skin is compromised and has a decreased the ability to protect against bacterial, chemical, and mechanical assault and to prevent trans epidermal water loss [3]. A little-known complication is the vitamin D deficiency. Solar ultraviolet B irradiation of skin accounts for approximately 90% of vitamin D. Only 10% is derived from dietary sources [4]. Vitamin D plays a vital role in the skin, the keratinocytes are not only a source of vitamin D, but also a responder to its active form. Away from the classical phosphocalcic effect of vitamin D, its role in the proper functioning of tissues and organs including the skin has been receiving an expanding interest. Vitamin D has an effect antiproliferative, prodifferentiative, antiapoptotic and immunomodulator in the skin. In many skin pathologies, it positively influences the evolution of certain inflammatory dermopathologies [5].

The most serious complications of vitamin D deficiency are hypocalcemia, hypophosphatemia, rickets, and osteomalacia. It is a well-identified risk factor for increased morbidity of children with inherited ichthyosis. The development of vitamin D deficiency in patients with inherited ichthyosis (CI) has recently been observed, yet exact cause of such association is not properly understood. To date, few studies have investigated serum vitamin D status in patients with inherited ichthyosis.

Objective of the Study

The objective of this study was to determine the prevalence of vitamin D deficiency in children with congenital ichthyosis, as against apparently healthy children.

Methods

It was a cross sectional study, conducted from 01st June 2022 to 01st December 2022 in the dermatology department at University Hospital Center Mohammed VI in Marrakesh, Morocco. This was conducted in accordance with the World Medical Association Declaration of Helsinki.

The study population is constituted by two groups; the first group included all the patients who had consulted at the dermatology department for inherited ichthyosis and had a previous serum vitamin D status. The second group included patients hospitalized in pediatric department for another health problem rather than inherited ichthyosis, thyroid, parathyroid, renal, or skin health problems and had a previous serum vitamin D status. The patients were selected based on a convenience sampling.

The inherited ichthyosis was diagnosed based on the Clinical presentation and pattern of inheritance. The serum 25(OH)D measurements performed in biochemistry laboratory at the same center. They were interpreted according to the Endocrine Society: 30 - 100 ng/

ml was assessed as normal, vitamin D insufficiency between 20 - 29 ng/ml and vitamin D deficiency (< 20 ng/ml). Data were collected using the patients' medical records including age, gender and serum vitamin D status for both groups. For the first group, more medical characteristics were gathered such as types of inherited ichthyosis, itching, hospitalization, treatment and complications.

The statistical analysis was performed by the statistical package for social sciences SPSS version 25. The qualitative variables were presented by effectives and percentage. The quantitative variables were reported by median and range. Fisher exact test and T-student test were used for comparison between the two groups. A p value under than 0.05 was considered statistically significant.

Results

46 patients were included in the present study. There was a majority of males (60.9%) with a median age of 04.5 years (0.16 - 20). The majority (84.8%) had serum 25-hydroxyvitamin D below the optimal level of 30 ng/mL with 19.6 in sufficiency, 43.5% in insufficiency, 47.9% in deficiency. The median age among patients with inherited ichthyosis was 3 years old (0.16 - 20) and the sex ratio male/female was at 2.28. In addition, 87% was below the optimal level of 25-hydroxyvitamin D. The mean of serum level of 25-hydroxyvitamin D was at 18.24 ± 10 ng/mL with in inherited ichthyosis and in control group (p = 0.19). More details are presented in table 1.

	Total **n (%)** **N = 46**	**Inherited ichthyosis group** **n (%)** **n = 23**	**Control group** **n (%)** **n = 23**	**P value**
Age	06.17 ± 05.45	04.60 ± 05.06	07.74 ± 08.00	-
Gender				0.183
Female	18 (39.1)	07 (38.9)	11 (61.1)	
Male	28 (60.9)	16 (57.1)	12 (42.9)	
Vitamin D status				-
Optimal	07 (15.2)	03 (42.9)	04 (57.1)	
Sufficiency	09 (19.6)	03 (33.3)	06 (66.7)	
Insufficiency	20 (43.5)	11 (55.0)	09 (45.0)	
Deficiency	10 (47.9)	06 (60.0)	04 (40.0)	
Vitamin D status				0.405
	20.15 ± 14.80	18.3 ± 14.7	22.0 ± 15.0	

Table 1: *Patients' sociodemographic characteristics and vitamin D status.*

Among patients with inherited ichthyosis, 56.5% had a lamellar form, 39.1% had a vulgaris form and 01 case had netherton disease. The dander scales were mainly thin in (60.9%). More than a half of patients had no erythema (60.9%) and no itching (65.2%). 65.2% had an ectropion. Moreover, oral retinoids were used as the main treatment in 52.2% of cases. The patient with netherton disease had a thin dander scale, an erythema, suffered from itching and had not an ectropion. Also, he is in insufficiency according to the classification of 25(OH). A bivariate analysis had identified that ichthyosis vulgaris form was mainly associated to ectropion (p = 0,02) and thick dander scales (p = 0.001). The mean of serum 25-hydroxyvitamin D was less among patients with lamellar ichthyosis form (19.71 ± 17.83) in comparison with patients with vulgaris ichthyosis form (17.28 ± 10.10). More details are presented in table 2.

	Inherited ichthyosis group n (%) n = 23	Lamellar ichthyosis group n (%) n = 13	Ichthyosis vulgaris group n (%) n = 09	P value
Notion of collodion baby				0.305
Yes	13 (56.5)	06 (46.2)	06 (66.7)	
No	10 (43.5)	07 (53.8)	03 (33.3)	
Dander scales				0.001
Thick	09 (39.1)	09 (69.2)	00 (12.5)	
Thin	14 (60.9)	04 (30.8)	09 (100)	
Erythema				0.149
Yes	14 (60.9)	06 (46.2)	07 (77.8)	
No	09 (39.1)	07 (53.8)	02 (22.2)	
Itching				0.584
Yes	15 (65.2)	08 (61.5)	06 (66.7)	
No	08 (34.8)	05 (38.5)	03 (33.3)	
Ectropion				0.022
Yes	08 (34.8)	02 (15.4)	06 (66.7)	
No	15 (65.2)	11 (84.6)	03 (33.3)	
Oral retinoid				0.500
Yes	11 (47.8)	06 (46.2)	05 (55.6)	
No	12 (52.2)	07 (53.8)	04 (44.4)	
Vitamin D status				-
Optimal	03 (13.0)	01 (07.7)	02 (22.2)	
Sufficiency	03 (13.0)	01 (07.7)	02 (22.2)	
Insufficiency	11 (47.8)	08 (61.5)	02 (22.2)	
Deficiency	06 (26.1)	03 (23.1)	03 (33.3)	
Vitamin D status				0.700
	18.30 ± 14.70	15.26 ± 06.87	22.92 ± 21.97	

Table 2: *Associated factors to the types of inherited ichthyosis.*

Discussion

This study aimed to determine the prevalence of vitamin D deficiency in children with congenital ichthyosis, as against apparently healthy children. The majority (84.8%) had serum 25-hydroxyvitamin D below the optimal level of 30 ng/mL. Among patients with inherited ichthyosis, 56.5% had a lamellar form, 39.1% had a vulgaris form and 01 case had netherton disease. The mean of serum level of 25-hydroxyvitamin D was at 18.24 ± 10 ng/mL with in inherited ichthyosis and in control group (p = 0.19). The vulgaris ichthyosis form was mainly associated to ectropion (p = 0,02) and thick dander scales (p = 0.001).

In Europe few studies have investigated serum vitamin D status in patients with inherited ichthyosis. A recent study in Germany for 87 patients with inherited ichthyoses, and analyzed serum levels of 25-hydroxyvitamin D3 (25(OH)D3) and parathyroid hormone. The

vitamin D deficiency and insufficiency is highly prevalent in this study. Less than 10% of the patients had sufficient vitamin D levels [6]. A second study in France of 53 patients revealed that more than 80% of patients does not have an optimal vitamin D status [7].

The inherited ichthyosis characterized by generalized thick scaling may include alterations in epidermal cholesterol metabolism and difficulties in penetration of ultraviolet B, avoidance of sunlight to prevent sunburn and social stigma due to the abnormal scaling. Low vitamin D levels in these children are also because of consuming food low in vitamin D [4,8]. Oral retinoids are used to treat severe ichthyotic disorders in children, Shekhar reported that two children with ichthyosis disorders had developed deficiency of vitamin D after they were started on oral retinoids [9]. Recently, it has been reported that children with congenital ichthyosis with the pigmented skin types, are more prone to develop vitamin D deficiency [7].

Vitamin D may be considered as a sole alternative therapy in inherited ichthyosis congenital, the supplementation with stronger dose vitamin D followed by recommended daily allowance appears to be an effective form of therapy in the management of inherited ichthyosis with vitamin D deficiency. Sethuraman reported seven observations of an excellent clinical response with regard to skin scaling and stiffness in children with inherited ichthyosis after short-term high-dose vitamin D supplementation [10].

Based on our outcomes, we recommend a systematic supplementation to children with vitamin D deficiency with cholecalciferol 60,000 IU once a week for 4 weeks followed by monthly maintenance of 60,000 IU or daily maintenance of 400 IU for children and 600 IU for children above 1 year of age along with calcium supplementation [4].

A key strength of the present study was the comparison group of healthy children with vitamin D status, also that we included only children patients and controls and the well-described homogeneous patient group. The major limitation of this study is the small sample because the ichthyosis congenital is a rare disease. Moreover, considered as a developing country, there would be inequalities of access to healthcare due to poor socioeconomic status or because they live in far off places, ignorance by patients of complications of vitamin D deficiency and short-term study.

Conclusion

In summary, measurement of vitamin D levels should be recommended in patients with ichthyoses, especially for individuals with severe ichthyosis, the lamellar ichthyosis, and oral retinoids. This recommendation does not refer to distinct age groups. Treatment options proposed apart moisturizers, topical keratolytics and topical and systemic retinoids is recently systemic vitamin D analogues. Further studies are needed to confirm that vitamin D levels are a consequence of the cornification disorders or are related to its physiopathology.

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