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SERUM VITAMIN D LEVELS IN PREMATURE ANDROGENETIC ALOPECIA- A CASE -CONTROL STUDY.

Dr Shashikumar B M	Associate Professor, Dermatology, Venereology and Leprosy, Mandya institute of medical sciences
Dr Harish M R	Professor And Hod, Dermatology, Venereology and Leprosy, Mandya institute of medical sciences
Dr Deepadarshan K	Assistant Professor, Dermatology, Venereology and Leprosy Mandya institute of medical sciences
Dr Madhurya P K*	Postgraduate Cum Junior Resident, Dermatology, Venereology and Leprosy Mandya institute of medical sciences *Corresponding Author

ABSTRACT **Background:** Androgenetic alopecia is a hereditary, androgen-dependent disorder characterized by a gradual conversion of terminal hair into miniaturized hair and causes progressive hair loss. Studies have showed lowered vitamin D levels in patients with androgenetic alopecia, which also correlated to their severity. The purpose of this study is to determine the association and correlation of Serum vitamin D levels in premature onset of androgenetic alopecia **Methods and methodology:** A total of fifty males clinically diagnosed with androgenetic alopecia and fifty age matched healthy controls were recruited. Serum Vitamin D levels of the cases and controls obtained were assessed. The data was analysed statistically. **Results:** In this study the mean levels of serum vitamin D were significantly decreased in cases, compared to controls (13.90 vs. 28.4 nmol/L; $P \leq 0.001$). Eighty seven percent of the cases had deficiency of vitamin D (<25 nmol/L), while 13% had insufficient vitamin D levels (25-75 nmol/L). However, there was no correlation between severity of androgenetic alopecia and serum vitamin D levels. (P value =1.65). **Conclusion:** This study shows that majority of cases with early onset androgenetic alopecia had deficiency of vitamin D levels. However, there was no correlation between severity of androgenetic alopecia and serum vitamin D levels.

KEYWORDS : Alopecia; Vitamin D; Male pattern hair loss.

INTRODUCTION

Alopecia refers to the loss of hair from any part of the body. Scarring and non-scarring alopecia are the two primary subtypes. Alopecia areata (AA), androgenetic alopecia (AGA), telogen effluvium, traumatic alopecia, tinea capitis, and anagen effluvium are the six subtypes of scarring alopecia. [1]. Androgenetic alopecia is the most common type of progressive hair loss.[2] Androgenetic alopecia is a hereditary, androgen-dependent disorder characterized by a gradual conversion of terminal hair into miniaturized hair. [3] The two types of AGA are male pattern hair loss and female pattern hair loss. Although they both exhibit different patterns, they are the most prevalent types of baldness in both sexes. [4]. In males, AGA is categorised using the Norwood Hamilton scale. The typical course in men is described by the Hamilton categorization system as a receding frontal hairline, bitemporal hair loss, and vertex thinning. [5]. Premature androgenetic alopecia is described as androgenetic alopecia that appears to be at least stage 2 of Norwood Hamilton classification and appears before the age of 35.[6]

Vitamin D is a fat-soluble prohormone steroid that has endocrine, paracrine, and autocrine functions.[7] Vitamin D2 and vitamin D3 are the two main types. While vitamin D3 (cholecalciferol) is produced in humans' skin from 7-dehydrocholesterol and is also consumed in the diet through the consumption of animal-based foods, vitamin D2 (ergocalciferol) is primarily human made and added to food.[8] Keratinocytes, dendritic cells, macrophages, B and T lymphocytes, and two primary cell types in the hair follicle-epidermal keratinocytes and mesodermal dermal papilla cells, all express the vitamin D receptor (VDR). For the health of hair follicles, VDR is essential. Although it is not necessary for morphogenesis, its expression is necessary for normal postnatal hair follicle cycling, and its absence can prevent keratinocyte differentiation and disrupt the cycle.[9]

Since there are not many studies on role of vitamin D in premature onset androgenetic alopecia, we conducted this study to assess the levels of vitamin D3 in androgenetic alopecia with early onset.

MATERIALS AND METHODS

A case control study was conducted from July 2021 to February 2022 in the outpatient department of at Mandya Institute of Medical Sciences, Mandya. The objectives were to determine the Serum vitamin D levels in premature onset of androgenetic alopecia and to determine the correlation between severity of androgenetic alopecia and vitamin D deficiency.

Age-matched groups of fifty male cases of androgenetic alopecia under 35 years and fifty male healthy controls were recruited. An informed consent was obtained and ethical committee clearance was obtained prior to commencement of study. Inclusion criteria included male patients with age less than or equal to 35 years with a clinical diagnosis of androgenetic alopecia. Exclusion criteria included other causes of alopecia -alopecia areata, Stage 1 androgenetic alopecia(based on Hamilton-Norwood classification) trichotillomania, tinea capitis, traction alopecia, participants with clinical evidence of hyperandrogenemia like acne, seborrhea, intake of drugs that can alter serum vitamin D levels-systemic corticosteroids, antiepileptic drugs, cholesterol lowering drugs, malabsorption disorders, nutritional deficiencies, kidney, liver, bone diseases.

Patient's demographic data and relevant history was taken at baseline. The diagnosis of androgenetic alopecia was made based on clinical findings. Patients were graded as stage I-VII based on the Hamilton Norwood scale.

Type I-Absence of bilateral recessions along the anterior border in the frontoparietal region.Type II-anterior border of the hairline in the frontoparietal region has triangular areas of recession,which tend to be symmetrical and extend no further posteriorly than a point 3cm anterior to a line drawn in a coronal plane between the external auditory meatus. Type III-

borderline cases are listed separately as type III which also included scalps in which classification is rendered inaccurate due to scars, lateral asymmetry in denudation, unusual types of sparseness and thinning of the hair, and other factors.

Type IV-There are deep frontotemporal recessions, usually symmetrical, and are either bare or very sparsely covered by hair.Type V-extensive frontoparietal and frontal recessions with a sparseness or absence of hair on the crown.

Type VI- the tonsural region of alopecia remains separated from more anteriorly located areas of denudation by a laterally-directed bar of scalp in which the hair is only slightly sparse. An island of hair lies in the midline anterior to this laterally-directed hairy bridge.Type VII-horseshoe-shaped area of sparse hair or of denudation is unbroken by any well-haired, laterally-directed bridge of scalp.

Serum Vitamin D levels of the cases obtained were assessed. The values were interpreted as follows.
Deficient: <25nmol/L
Insufficient:25-75nmol/L
Sufficient:76-250nmol/L.

Data collected were entered in MS excel spreadsheet and analysed statistically by appropriate tests on SPSS software version. Descriptive statistics like proportion, mean, standard deviation, etc. was used. Tests to detect significant difference or association like T test, chi square test, etc was used. P value <0.05 is considered significant.

RESULTS

A total of fifty cases were recruited and analyzed. All were males. The mean age of the cases 21.56 ±3.43 years. Range of age was 18 to 34 years. The mean age of onset of androgenetic alopecia is 20.34±2.44 years. Average duration of Androgenetic alopecia was 28.78±16.19 months.

The majority of cases had grade 5 (50.9%) androgenetic alopecia, followed by grade 4(24.9%), grade 6(14.4%), grade 3(9.8%). The initial site of thinning of hair loss is temporal scalp in 78% of cases, frontal scalp in 13% of cases, vertex in 9% of cases.

Majority of cases (49%) showed moderate rate of progression of hair loss, while 34% of patients showed a gradual onset.17% of cases showed rapid progression of hair loss. A positive family history was present in 44% of cases. Associated premature canities was seen in 25% of patients. The mean levels of serum vitamin D were decreased in cases (13.90 nmol/L).

The mean levels of serum vitamin D were significantly decreased in cases, compared to controls (13.90 vs. 28.4 nmol/L; $P \leq 0.001$). Eighty seven percent of the cases had deficiency of vitamin D (<25 nmol/L), while 13% had insufficient vitamin D levels (25-75 nmol/L).However there was no correlation between severity of androgenetic alopecia and serum vitamin D levels. (P value =1.65)

DISCUSSION

By controlling the growth cycle and the development of mature anagen hair, and enabling stem cells in the bulge to replicate, the vitamin D receptor appears to play a significant role in hair follicle cycling. Such an expression was found to be necessary for maintaining the normal hair cycle.

Additionally, it has been demonstrated that vitamin D3 concentration as high as possible is necessary to prevent ageing and hair loss and that a lack of vitamin D receptors reduces epidermal differentiation and hair follicle growth.[10]

Kondrakhina et al. investigated the plasma content of vitamins and trace elements in a cross-sectional study. Patients with AGA were discovered to be lacking in all trace minerals and vitamins, including vitamin D. [11]. In order to assess the serum vitamin D levels in Chinese patients with various kinds of alopecia, including AGA, Jun Zhao et al. conducted case-control research. Male AGA was shown to be statistically correlated with low serum vitamin D levels (P=0.0005). [12].

In a Turkish study conducted by Gulbahar Sarac et al., a correlation was again found between AGA, telogen effluvium, and low serum vitamin D[13].

According to a study by Daroach et al., alopecia areata is associated with a downregulation of vitamin D receptors. The greater prevalence of hair cycle issues in vitamin D-deficient people points to vitamin D's critical role in maintaining the hair cycle. [14] In this study it was found that majority of cases had deficiency of vitamin D levels (87%). This is an important finding that may advance our understanding of the pathophysiology of androgenetic alopecia in patients with an early onset.

To fully understand the role of vitamin D in the development of hair loss, additional research on the expression of vitamin D receptors in male pattern hair loss patients with adequate serum vitamin D levels is advised. Further studies are required with a large control population is essential to further corroborate the above findings.

Our study's limitations include small sample size, the inability to measure the levels of vitamin D receptors, and VDR gene variations.

CONCLUSION

Our study shows that majority of cases with early onset androgenetic alopecia had deficiency of vitamin D levels (87%) while 13% had insufficient vitamin D levels (25-75 nmol/L). However there was no correlation between severity of androgenetic alopecia and serum vitamin D levels (P value =1.65). Hence, vitamin D levels should be assessed in AGA patients. Additionally, patients with AGA who are vitamin D deficient may be considered for vitamin D supplements.

Table 1: Baseline characteristics of males with premature onset androgenetic alopecia.

Parameter	Number of cases
Mean age at onset(in years)	20.34±2.44
Mean duration of disease(in months)	28.78±16.19
Mean age of cases(in years)	21.56±3.43
Initial site of hair loss	
Frontal	7(13%)
Temporal	37(78%)
Vertex	6(9%)
Family History	22(44%)
Grade of alopecia	
Grade 5	25 (50.9%)
Grade 4	13(24.9%)
Grade 6	7(14.4%)
Grade 3	5(9.8%)
Grade 7	0(0%)

Table 2: Percentage of cases with vitamin D deficiency and severity grading

Grading of alopecia	Percentage of cases with vitamin D deficiency
Grade 4	27.2%
Grade 5	25.6%
Grade 3	19.4%
Grade 6	14.8%

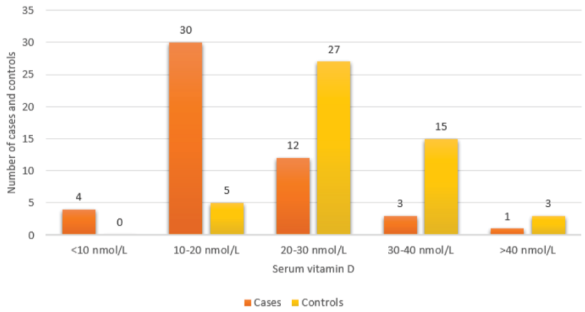

Figure 1: Serum vitamin D levels in cases and controls.

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