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INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/18600
DOI URL: <http://dx.doi.org/10.21474/IJAR01/18600>



RESEARCH ARTICLE

ASSOCIATION OF VITAMIN B12 DEFICIENCY AND MUCO-CUTANEOUS FINDINGS IN DERMATOLOGY: A CASE-CONTROL STUDY

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Manuscript Info

Manuscript History

Received: 26 February 2024
Final Accepted: 30 March 2024
Published: April 2024

Key words:-

Vitamin B12 Deficiency, Diffuse HAIR-FALL, Muco-Cutaneous Pigmentation, Graying of Hair, Glossitis

Abstract

Background: Vitamin b12 deficiency is considered a common nutritional deficiency in Indian population. Vitamin B12 deficiency related to hair and cutaneous features like hair-fall, and cutaneous pigmentation are not well described in literature.

Aim: To study serum vitamin b12 level in relation to diffuse hair-fall and muco-cutaneous pigmentation.

Study design: Case-control observational study

Materials and methods: Total 240 patients presented with diffuse hair-fall or muco-cutaneous pigmentation were taken as cases and screened for serum vitamin b12 level at tertiary health care centre. Other 240 patients of same age group presented with other dermatological conditions were taken as control. Also associated symptoms like weakness, malaise, numbness, tingling, paresthesia, burning sole, glossitis, angular cheilitis, angular stomatitis, aphthous stomatitis, graying of hair, mild memory impairment, irritability, psychosis, delusion of paresthesia, dementia and depression were noted in each patient.

Results: Out of 240 patient females: male ratio was 3.52:1. Vegetarian:non-vegetarian ratio was 3.36:1. Out of 240 patients 42% patient presented with hair fall, 33% with hyperpigmentation and 25% had both complain. Facial pigmentation in 20%, extra-facial in 15%, both (facial & extra-facial) in 45% of patients were noted. Mucosal pigmentation was present in 20%. Serum vitamin b12 level was low in 198 cases and 87 control. Hemoglobin level was low (<10 gm/dl) in 196 of cases and 127 of control. Amongst 240 cases weakness in 58, malaise in 22, numbness in 5, tingling in 15, paresthesia in 2, burning sole in 108, glossitis in 76, angular stomatitis in 13, aphthous ulcer in 31, graying of hair in 92, memory impairment in 18, irritation in 64, psychosis and delusion of paresthesia in 1, dementia in 8 patients were noted.

Conclusions: Vitamin B12 deficiency is not rare, but data are insufficient regarding its prevalence. In our study, 240 patients with diffuse hair fall and muco-cutaneous pigmentation as case group and 240 patients as control group were included. Among groups, vitamin b12 deficiency was found in 198 cases and 87 control. We found that there was significant association with vitamin b12 deficiency, diffuse hair fall and muco-cutaneous pigmentation as clinical markers for dermatologists.

Introduction:-

Vitamin b12 deficiency is common in Indian population, because of a greater number of vegetarian people.^[1] But data regarding vitamin B12 status in Indian population is limited. Two vitamins, vitamin B₁₂ and folic acid are essential for DNA biosynthesis. Megaloblastic anaemia occurs due to abnormal maturation of hematopoietic cells due to defective DNA synthesis.^[2] Deficiency of either of these vitamins results in asynchrony in the maturation of the nucleus and cytoplasm of rapidly regenerating cells.^[3]

There is very little Indian data regarding relationship between serum b12 and diffuse hair-fall, pre-mature greying as well as muco-cutaneous pigmentation.

Cutaneous features of vitamin B₁₂ deficiency are not well described in literature. The first description of hyperpigmentation in vitamin B₁₂ deficiency was described by Dr. Bramwell Cook.^[4] B12 deficiency is usually presents with skin hyperpigmentation, vitiligo, angular stomatitis, and hair changes.^[4] Here, we described relation between serum vitamin b12 level with diffuse hair-fall and muco-cutaneous pigmentation.

Materials and Methods:-**Study design:**

Observational case-control study

Sample size:

Case group: 240

Control group: 240

Inclusion criteria:

1. Patients of all age groups
2. All patients presented with diffuse hair-fall and muco-cutaneous pigmentation
3. Patients willing to give informed, written consent/assent for the study

Exclusion criteria:

1. Those who received blood transfusions within 1 month prior to presentation.
2. Those already on vitamin B₁₂ supplementations.

Study period:

6 months (July 2023 to Dec 2023)

Study protocol:

All patients presented with diffuse hairfall and muco-cutaneous pigmentation were enrolled in this study after informed consent as case group. 240 patients of same age group presented with other dermatological conditions were enrolled as control group after informed consent. Detailed clinical history including weakness, malaise, numbness, tingling, paresthesia, burning sole, glossitis, angular cheilitis, angular stomatitis, aphthous stomatitis, graying of hair, mild memory impairment, irritability, psychosis, delusion of paresthesia, dementia and depression were also noted in each patient. The history regarding blood transfusion, diet habit, drug and family history were noted according to predetermined proforma.

Detailed clinical examination including hair, nail, oral mucosa and skin were performed.

After informed consent, blood samples were drawn for serum vitamin b12, complete blood count, serum iron and ferritin level.

Statistical analysis:

Clinical features like hyperpigmentation and diffuse hair-fall etc., were expressed as percentage. Values are expressed as mean \pm SD for continuous variables.

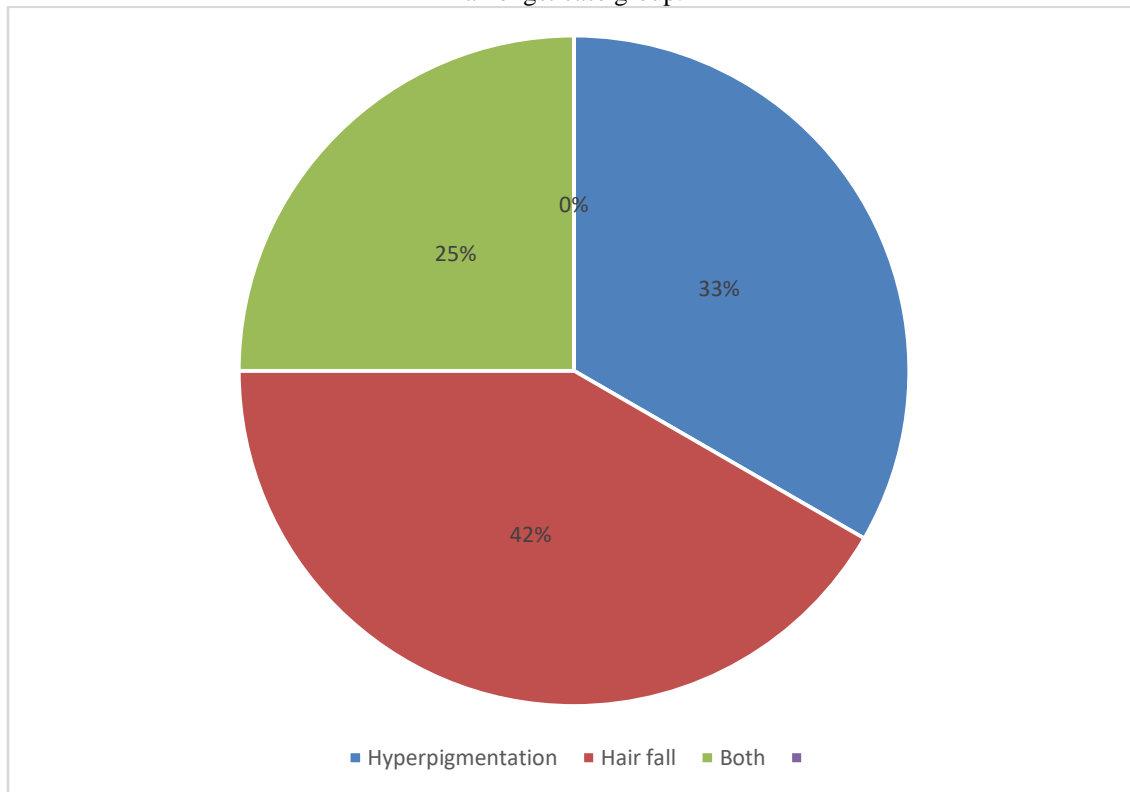
Results:-

Table 1:- Comparison of demographic data between cases and controls.

	Case	Control
Total No.	240	240
Male	53(22%)	53
Female	187(78%)	187
Age	35±20	33±20
Diet		
Vegetarian	185(77%)	164(68.3%)
Non-vegetarian	55(55%)	76(31.6%)

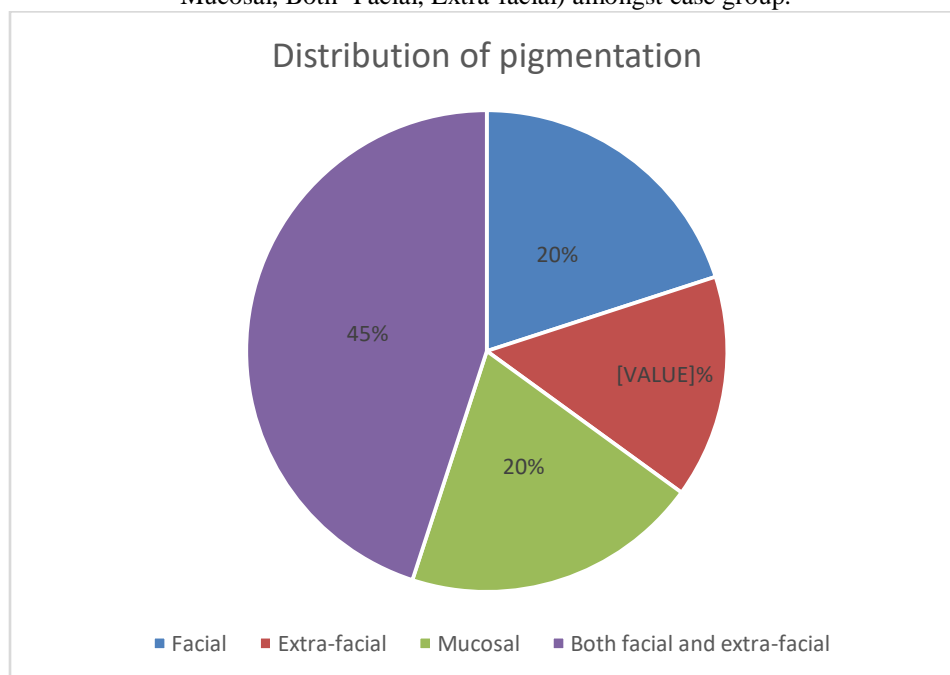
Out of 240 cases and controls, 53(22%) were male and 187(78%) were female in both groups. Females: Male ratio was 3.52:1 Mean age in cases group was 35±20 and in control group was 33 ± 20. Out of 240 cases, 185(77%) were Vegetarian and 55(55%) were non-vegetarian. Out of 240 control, 164(68.3%) were Vegetarian and 76(31.6%) were non-vegetarian. Vegetarian: non-vegetarian ratio was 3.36:1

Figure 1:- Pie chart showing % distribution of hair fall, hyperpigmentation and both (hair fall, hyperpigmentation) amongst case group.



Out of 240 patients 42% patient presented with hair fall, 33% with hyperpigmentation and 25% had both complain.

Figure 2:- Pie chart showing % distribution of hyperpigmentation over different body area (Facial, Extra-facial, Mucosal, Both- Facial, Extra-facial) amongst case group.



Out of 180 patient with pigmentation, facial pigmentation in 36 (20%), extra-facial in 27(15%), both (facial & extra-facial) in 81 (45%)of patients were noted. Mucosal pigmentation was present in 20%.

Table 2:- Showing correlation of other symptoms among case and control groups.

Other symptoms	Total number of cases with %		Total number of controls with %	
Weakness	58	24.16%	21	8.75%
Malaise	22	9.16%	8	3.33%
Numbness	5	2.08%	-	-
Tingling	15	6.25%	5	2.08%
Paresthesia	2	0.83%	-	-
Burning sole	108	45%	35	14.58%
Glossitis	76	31.66%	16	6.66%
Angular stomatitis	13	5.41%	2	0.83%
Aphthous ulcer	31	12.9%	4	1.66%
Graying of hair	92	38.33%	24	10%
Memory impairment	18	7.5%	4	1.66%
Irritation	64	26.66%	23	9.58%
Psychosis	1	0.41%	-	-
Delusion of paresthesia	1	0.41%	-	-
Dementia	8	3.33%	-	-

Amongst 240 cases weakness in 58 (24.16%), malaise in 22 (9.16%), numbness in 5 (2.08%), tingling in 15 (6.25%), paresthesia in 2 (0.83%), burning sole in 108 (45%), glossitis in 76 (31.66%), angular stomatitis in 13 (5.41%), aphthous ulcer in 31 (12.9%), graying of hair in 92 (38.33%), memory impairment in 18 (7.5%), irritation in 64(26.66%), psychosis and delusion of paresthesia in 1 (0.41%), dementia in 8 (3.33%) patients were noted.

Amongst 240 control weakness in 21(8.75%), malaise in 8(3.33%), tingling in 5(2.08%), burning sole in 35(14.58%), glossitis in 16(6.66%), angular stomatitis in 2(0.83), aphthous ulcer in 4(1.66%), graying of hair in 24(10%), memory impairment in 4(1.66%), irritation in 23(9.58%) were noted. There was no symptom of numbness, paresthesia, psychosis, delusion of paresthesia and dementia in control group.

Table 3:- Showing correlation of laboratory parameter between cases and controls.

Laboratory parameter	Case	Control
Hemoglobin	8.46 ± 2.8 gm/dl	9.36 ± 2.5 gm/dl
Vitamin B12	102.71 ± 57.5 pg/ml	192.71 ± 62.5 pg/ml
MCV	108.16 ± 14.8 fl	94.16 ± 14.6 fl
S. Iron	43.4 ± 23.6 µg/dL	54.3 ± 22.5 µg/dL
S. Ferritin	18 ng/ml	20 ng/ml

The mean Haemoglobin level was 8.46 ± 2.8 gm/dl. Mean WBC count was 4.53 ± 2.5 × 10³ /mm³. Mean platelet count was 1.36 ± 1.2 × 10⁶ /mm³. The mean MCV was 108.16 ± 14.8 fl. The mean serum vitamin B₁₂ was 102.71 ± 57.5 pg/ml. Mean serum iron was 43.4 ± 23.6 µg/dL. Mean serum ferritin was 18 ng/ml.

In control group, mean haemoglobin level was 9.36 ± 2.5 gm/dl. The mean MCV was 94.16 ± 14.6 fl. The mean serum vitamin B₁₂ was 192.71 ± 62.5 pg/ml. Mean serum iron was 54.3 ± 22.5 µg/dL. Mean serum ferritin was 20 ng/ml.

Serum vitamin B12 levels are significantly associated with diffuse hair fall, pre-mature greying and muco-cutaneous pigmentation. {Odd's ratio=8.29(>1)}

Discussion:-

Vitamin B12 deficiency was first described by Cook in 1944 and later by Baker *et al.*, in 1963. Vitamin B12 (cobalamin) is a water-soluble vitamin. The main source for cobalamin is animal and dairy products. Currently, vitamin B12 deficiency was defined as a plasma concentration of <148 pmol/L (200 pg/ml) and marginal status defined as a concentration of 148-221 pmol/L.^[5] Vitamin B₁₂ deficiency affects all age groups, mainly affects hematologic, gastrointestinal, and nervous systems. Other involved systems include the cardiovascular, skeletal, skin and hair.

Inadequate intake, low consumption of animal-source foods, pernicious anemia (low intrinsic factor) in younger adults and food bound cobalamin malabsorption due to gastric atrophy in older persons are the main causes of low serum vitamin B12.^[5,6]

The common cutaneous and systemic features are hair-fall, muco-cutaneous pigmentation, weakness, malaise, numbness, tingling, paresthesia, burning sole, glossitis, angular cheilitis, angular stomatitis, aphthous stomatitis, graying of hair, mild memory impairment, irritability, psychosis, delusion of paresthesia, dementia and depression.

Hyperpigmentation of extremities mainly over the dorsum of the hands and feet, with enhanced pigmentation over the inter-phalangeal joints and terminal phalanges and pigmentation of oral mucosa are characteristic of vitamin B12 deficiency.

Histological study done by James *et al.*, from the hyper pigmented area showed irregular epidermal atrophy, absence of basal orientation of epidermal cells, patchy pigmentation of the lower epidermis, and numerous pigment-laden macrophages in the upper dermis and increase of melanin in the basal layer.

Vitamin B12 deficiency causes decrease in intracellular reduction potential that eventually leads to oxidation of the reduced glutathione and decrease in GSH/GSSG ratio. The epidermal melanocytes are stimulated to produce melanin because tyrosinase inhibiting effect of GSH has been diminished.^[7] So, the main mechanism of hyper pigmentation due to vitamin B12 deficiency are A) Deficiency of vitamin B12 decreases the level of reduced glutathione, which activate tyrosinase and thus leads to transfer to melanosomes and increase pigmentation. 2) Defect in the melanin transfer, resulting in pigmentary incontinence.^[8]

Vitamin B12 helps in DNA formation and enables cell replication which needed for hair to grow from hair follicles. It also aids in red blood cell formation that carries nutrients and oxygen to the scalp and hair follicles. That's why, in vitamin B12 deficiency, cell proliferation slows down, which leads to reduced hair growth and blood supply to hair roots.

An important clinical presentation found in this study was hyperpigmentation of the extremities, particularly of the knuckles(extra-facial), perioral and periorbital (Extra-facial) hyperpigmentation found in 15% and 20% respectively. This is a relatively consistent finding so that the index of suspicion rises significantly in those patients with knuckle, periorbital and perioral hyperpigmentation. There was also found mucosal pigmentation in 20%.

There was diffuse hair fall with vitamin b12 deficiency found in 42%. Also, hair changes like greying of hair with vitamin b12 deficiency found in 38.33%.

This study noted particularly the muco-cutaneous and hair changes, as it was a very consistent finding.

Conclusion:-

The dermatologist should have enough knowledge to identify b12 deficiency related mucocutaneous manifestations. As in our study it is proven that vitamin b12 deficiency is majorly associated with cutaneous and mucosal pigmentation with associated symptoms. There are several causes of diffuse hair-fall, one of them is vitamin b12 deficiency, that proven in this study.

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