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Original Research Article

Nutritional dermatoses and its association with anemia and systemic illness

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ABSTRACT

Background: Mucocutaneous changes may be a "tell-tale" signs of multi nutrional deficiency including anemia. Some are very characteristic of a specific nutrient deficiency, while other signs may overlap and will reflect multiple deficiency states.
Methods: To scrutinize clinical signs of multi nutritional deficiencies accompanied with anemia, this observational clinical study of 75 patients (adult and adolescents) was undertaken. Patients were selected from out-patient and in-patient department (OPD and IPD) of dermatology as well as General Medicine ward including medical ICU. Relevant investigations were carried out whenever required. Detail clinical history of diet, tuberculosis as well as HIV disease, worm infestation, other co-morbid conditions and alcohol intake were taken. Clinical signs of nutritional deficiencies like of pellagra, kwashiorkor, beriberi, ariboflavinosis and other signs of avitaminosis and micronutrient deficiency were looked for in all such patients.
Results: Of 75 patients, 37 were male (M) and 38 female (F). One of the important findings was that one third patients were admitted in ICU and in 60 of 75 patients risk factors could be identified. Mental illness, ICU admission, elderly age, systemic illness and alcohol consumption were the predisposing factors. Iron deficiency anemia was the commonest anemia followed by dimorphic anemia with other multinutrional manifestations. Clinical signs which were observed due to multinutritional deficiency were of pellagra dermatosis, kwashiorkor, koilonychia with pale tongue and mucous membranes, angular cheilosis, hair changes of various types and other signs due to systemic involvement.
Conclusions: Anemia may be associated with other nutritional abnormality which is reflected in changes in the skin, mucous membrane, hairs and nails. Nutritional dermatosis and anemia can be part of systemic illness which maybe reflected as deficiency of multiple nutritive factors.

Keywords: Nutritional dermatosis, Pellagra, Anemia

INTRODUCTION

Malnutrition results from one or more basic nutrient deficiency. Mucocutaneous manifestations constitute important marker of malnutrition. Some signs are characteristic of a particular nutrient deficiency, however overlap and variable manifestations are found in multiple deficiency states.[1]

Though malnutrition problem is uncommon in developed nations, it is essential for clinicians to remain aware of them, as it can cause morbidity and mortality. Several patient populations are considered at risk for malnutrition like infants and children, patients having psychiatric problem, patients having perceived or real food allergy, patients receiving long-term tube-feeding and patients of cystic fibrosis.[2]

Anemia is considered to be an important health problem worldwide, especially developing countries like India.[3,4] Macronutrients as well as micronutrient deficiency due to dietary deficiency and other socio-demographic factors may give rise to malnutrition associated with nutritional anemia. Malnutrition associated anemia is common in poor, underprivileged and in rural community.[5,6] Acute malnutrition with severe anemia may require hospitalization and blood transfusion.[7]

Hospitalized and critical care unit patients especially patients that are from communities having inadequate resources are often found to have malnourishment.[8-10] They are found in 13-78% admitted to acute care settings.[10] Malnutrition detection tools are available to screen patients in many hospitals but are unreliable and requires further validation. Very obvious and noticeable changes of malnutrition are reflected on skin, mucous membrane, nails and hair which can be confirmed by relevant investigations.

METHODS

This observational study was done to scrutinize clinical signs of multi nutritional deficiencies accompanied with anemia.75 adult as well as adolescent patients (age> 12 years) were selected. This study was undertaken at two teaching hospitals of Gujarat. Study patients were included from Dhiraj Hospital, Piparia (Dist Vadodara) attached to SBKS Medical College from 2011 to 2017 and from V. S. Hospital, Ahmedabad from 2011 to 2014.These teaching hospitals cater services to patients coming from underprivileged group of the society. Patients having nutritional dermatosis and nutritional anemia were included in this study. Inclusion criteria were patients having mucocutaneous signs of nutritional dermatosis with hemoglobin level of less than 13 g/dl and 12 g/dl in male and female respectively. They were selected from indoor wards and OPD of Dermatology as well as General Medicine ward including Medical ICU. Infants, young pediatric age group patients (less than 12 years), pregnant women and patients having anemia due to hemolytic process were not included in this study. Detail socio-demographic and clinical details were noted. History in regards to diet, alcohol, worm infestation, chronic blood loss, tuberculosis, HIV disease, and food allergy and co morbid conditions was inquired. Obstetric and menstrual history was asked in female patients. Mental health examination was carried out in patients having psychiatric illness with malnutrition. Clinical signs of nutritional deficiencies like pellagra, kwashiorkor, beriberi, ariboflavinosis and other signs of avitaminosis as well as indicators of micronutrient deficiency were looked for in all such patients. Relevant investigations were carried out whenever required. Vitamin B12 level was done in patient having macrocytic and dimorphic anemia.

Following criteria were adopted for diagnosing various types of anemia.[11-13] Iron deficiency anemia was considered if patients had microcytic hypochromic anemia on peripheral smear (PS) examination, serum iron (SI) less than 50, mean corpuscular volume less than 92fl and Srivastava and Mentzer index less than 3.8 and 13 respectively.[12,13] Serum iron-binding capacity (SIBC), serum ferritin and zinc protoporphyrin was additionally done, if indicated for diagnosis. Macrocytic anemia was considered when peripheral smear (PS) examination and MCV was suggestive was macrocytic/megaloblastic anemia (Normal MCV ranges 82-92 fl). Megaloblastic-Vit B12 or folate deficiency and non megaloblastic macrocytic anemia due to alcohol, liver disease and/ or hypothyroidism was considered on clinical as well as laboratory investigation evidences. High RDW/CV-SD and peripheral smear examination suggestive of dimorphic anemia was considered as an indicator of nutritional anemias.

RESULTS

Out of 75 patients of nutritional deficiency with nutritional anemia, 37 were male (M) and 38 were female (F). 10 (06M+04F) were of 12-18 years, 19 (07M+12F) were in 19-40 age group, 16 (06M+10F) were in 41-60 years and 30 (18M+12F) were above age of 60 years. Mild anemia (>10 g/dl) was present in 20 (26.67%), moderate (7-10 g/dl) in 42 (56.0%) and severe (<7 gm/dl) in 13 (17.33%) patients. Microcytic hypochromic anemia due to Iron deficiency anemia was present in 34 (45.33%) patients, dimorphic anemia in 18 (24.00%), megaloblastic in 08 (10.67%) and non megaloblastic macrocytic anemia in 15 (20.00%) patients respectively. Table 1 shows risk factors, systemic illness and co-morbidities which contributed to malnutrition and anemia. As shown in this table, only in 60 patients, cause of malnutrition could be identified. 106 risk factors were identified in 60 (30M+30F) patients of which 54 were in male and 52 were in female, average being 1.77 (1.8 in male and 1.73 in female). Table 2 shows predominant mucocutaneous changes found in the study. Illustration of 07 cases which shows various mucocutaneous signs are presented here. Following six salient points were abstracted.

Figure 1: Case 1- patient having iron deficiency anemia with kwashiorkor; pale skin & palpabral conjunctiva, silky hairs and flag sign.

Figure 2: Case 2- pellagra with iron deficiency anemia.

Figure 3: Case 3- Patient admitted in MICU. Patient had severe anorexia due to liver disorder. Pale and cracked lips and angular cheilosis, skin pigmentation and pale palmer creases, having jaundice and koilonychias.

Figure 4: Case 4- patient of anemia and hypoprotenemia with psychiatric illness.

Figure 5: Case 5- Severe anemia, angular cheilosis, hair on upper lip, with mulitinutrional deficiency in elderly patient.

Figure 6: Case 6- pellagra, anemia and neuropathy in patient taking alcohol.

1. Nutritional dermatosis may be accompanied with nutritional anemia wherein clinical signs may be related to skin, mucous membrane, hair and nails. Clinical signs were in form of pale tongue, pale palpaberal conjunctiva, band of multicolored hair

(Flag Sign) (Illustration case 1), in form of pellagrous dermatosis, (Illustration case 2), pedal edema signs of Kwashiorkor (Illustration case 1, 4 and 7), and others. Other presenting features of nutritional deficiency were feeling of fatigue, lassitude, dysthesias in form of pins and needle sensation, burning feet, numbness, hair fall, graying and change in the color as well as lusterless hairs, koilonychia and brittle nails, sore tongue and lips, mouth ulcers, change in texture of skin etc. Iron deficiency anemia patients had history of "Pica" (craving for non-nutritive substances), pagophagia (ice chewing), geophagia (eating clay or mud) (These patients had associated worm infestation) and other substances. Dysphagia related to Plummer–Vinson syndrome (PVS) was present in one patient. Other clinical signs which were associated with anemia were splenomegaly, tachycardia, koilonychia, pedal edema, pellagrous dermatitis, (Illustration case 2, 6), vitamin A deficiency, pernicious anemia, Kwashiorkor (Illustration case 1) and others.

2. Multiple nutritional deficiencies which coexisted with anemia were multifactorial. For example, a patient who presented with typical book picture of pellagrous dermatosis had moderate anemia because of iron deficiency (Illustration case 2).Thus niacin deficiency was associated with Iron Deficiency.

3. Anemia and nutritional deficiency could be a result of underlying Systemic illness or vice versa. We had three patients who were HIV positive. There were 4 patients who had associated pulmonary and/or systemic tuberculosis. Manifestations of anemia and multinutritional deficiency may prove to be a mirror of underlying systemic disorders and could thus help in its management. For example a patient presented with bald tongue and anemia had associated beriberi related neuropathy. One of the important findings was that half of the patients were having associated systemic illness. (Illustration case 3), Mental illness (Illustration case 4, 7), ICU admission (Illustration case 3), elderly age (Illustration case 5), alcohol consumption (Illustration case 6) and other risk factors (Table 1).

4. Anemia, adult kwashiorkor and psychological disturbances often associated together. Psychiatric manifestations could be both a cause and an effect. (Illustration case 7). Signs of systemic infections in form of cachexia and muscle wasting, “tell-tale” signs of psychiatric and eating disorder were present as clinical signs (Illustration case 4).

5. Hair changes of various types; about half of the patients who had anemia with multinutritional deficiency had hair changes. It was in form of colour change, premature graying, loss of luster, easy pluckability, thin and silky hair, dry and coarse hair, baldness, facial hairs in females etc.

6. Vitamin B12 deficiency was present in patients consuming vegetarian diet: In 4 patients documented vitamin B 12 deficiencies was found with macrocytosis. They had bald tongue and knuckle pigmentation.

Table 1: Shows risk factors, systemic illness and co-morbidities which contributed to malnutrition and anemia. (Some patients had more than one risk factor.)

	Risk Factor.	Male	Female	Total
1.	Alcohol	07	02	09
2.	Tuberculosis	04	02	06
3.	HIV	01	02	03
4.	Psychiatric illness	02	03	05
5.	Chronic diarrhea, worm infestation, giardiasis	03	04	07
6.	Internal malignancy	02	02	04
7.	ICU admission due to anemia, stroke, sepsis, GBS, surgical site infection, acute on chronic neurological problem, diabetic complications, acute on chronic liver condition, acute exacerbation of COPD, complication of malignancies, nutritional problems and others	13	11	24
8.	Chronic blood loss due to piles, mennorhagia, ulcerative colitis, NSAIDs and others	02	06	08
9.	Multiple pregnancy	00	04	04
10	Miscellanous: poor diet, food faddism	02	04	06
11	Elderly patients (>60 years)	18	12	30
	Total	54	52	106
	No cause identified	07	08	15
	Lacto-vegetarian food habit as premorbid diet	18	21	39

Table 2: Predominant mucocutaneous and nutritional dermatosis found with anemia.

No.	Nutritional dermatosis	Co-morbidities	No of patients (n=75) (%)
1.	Pellagra dermatosis	Anemia in all 9 (microcytic anemia and suggestion of Iron deficiency in 4, Dimorphic in 2, macrocytic in 3. Alcohol misuse in 5, HIV positive 1, 3 had Pulmonary tuberculosis of which one patient having tuberculosis was misusing alcohol.	09 (12%)
2.	Clinical signs and investigations suggestive of kwashiorkor	Psychiatric illness in 3,Nutrition and diet related in 3,HIV positive 2,Pulmonary Tuberculosis in 2 and no cause could be found in 1.	11 (14.67%)
3.	Knuckle pigmentation and bald tongue with macrocytic or dimorphic anemia and decreased Vitamin B 12 level	OPD patients, Chronic diarrhea	04 (5.33%)
4.	Koilonychia with pale tongue and mucous membranes (with Plummer–Vinson syndrome)	Worm infestation, chronic blood loss	05(01*) (6.67%) *= Plummer–Vinson syndrome (PVS)
5.	Angular cheilosis	Alcohol, OPD patients, ICU patients	06 (8%)
6.	Hair changes of various types change in colour, premature graying, loss of luster, high pluckability, thin and silky hair, coarse hair, hair loss and baldness	All group of patients	35 (46.67%)
7.	Miscellaneous and others	All group of patients	

Figure 7: Case 7- 30 yrs old housewife was diagnosed to have trichobezoar and was referred for pre-surgical management of malnutrition. She had serum Albumin of 2.2 g/dL, absolute lymphocyte count of1200, and enlarged liver and false appearance of well nourishment suggestive of Kwashiorkor. Photo shows frontal baldness, shiny skin and hairs, anemia and pedal edema.

DISCUSSION

Anemia with pellagra has been referred in old medical literature.[14,15] Anemia in association with pellagra was studied way back in the twenties and thirties and was area of interest at that time. In recent times, this type of data is not available. It may be because of improved nutrition and fortification of processed foods with niacin, prevalence has become less. It may be unappreciated cause which may remain under reported. as this problem is an integrated and multispecialty domain. A research article published by Spies and Chinn in 1935 had reviewed studies on anemia of endemic pellagra. This review contains citation of anemia and pellagra of the earlier studies done in twenties and thirties. Before this landmark study it was believed that anemia with pellagra is rare, is of mild degree and having low color index and of microcytic type. It can be interpreted that anemia with pellagra was of iron deficiency. Spies and Chinn reported that of their 30 alcoholic pellagrins (patient having pellagra), 63.3% had macrocytic anemia. Anemia in alcoholic pellagrins is thought because gastric mucosa dysfunction leading to pernicious anemia, inadequate intake of nutrients, liver dysfunction and due to malabsorption.[14,15] In our study we had 9 patients of anemia with pellagra, of which 4 (44.44%) had microcytic anemia which was suggestive of Iron deficiency. This was the type of anemia which was first noted in medical literature, as cited above. Dimorphic anemia was found in 2 (22.22%) while macrocytic anemia was noted in 3 of 9 patients (33.33%).It was mild in 2, moderate in 4 and severe in 3.

Pellagra dermatosis was present in 9 of our 75 patients. Pellagra is a multisystem nutritional disorder. Endemic pellagra occurs due to deficiency of nicotinic acid (niacin) (vitamin B_3) or its amino acid precursor

tryptophan. Pellagra was classified as endemic pellagra and those occurring due to alcohol were called as "pseudo pellagra", "pseudo-alcoholic pellagra" and "alcoholic pellagra", however relevance of this distinction does not have important clinical bearing. Of 9 patients having pellagra, 5 patients had alcohol related pellagra and one patient was HIV positive. This patient was referred to us by family physician with diagnosis of pellagra and was treated by him by niacin without much response. We found that this patient was HIV positive and had anemia. (Hb: 7.2 g/dL., MCV-100 fL, RDW-18, PS- S/O dimorphic anemia with low serum vitamin B12 and Iron levels. Patients were treated holistically with multivitamin preparation containing additionally folate and B12 and also iron supplements which improved his condition very fast. HIV positivity and multinutritional deficiency is reported in literature. Prevalence of HIV infection in patients with pellagra and pellagra-like erythemas are more common in asymptomatic HIV positive patients as compared to general population.[16] HIV infection decreases Intracellular nicotinamide adenine dinucleotide [NAD] –a niacin derivative.[17] One of the reason for HIV disease leading to pellagra can be postulated to be intracellular deficiency of niacin but our patient had hemoglobin of 7.2 gm% with macrocytosis and increased RDW, suggestive of multinutritional origin of dermatosis.

Like HIV, other chronic infections like tuberculosis may also interlinked with pellagra. There were 3 patients who had pellagra and pulmonary tuberculosis of which one had history of alcohol intake. In other 2, alcohol ingestion was not present. One patient who had pulmonary tuberculosis had Isoniazid induced neuropathy and was on Pyridoxine 50 mg twice a day. Despite this he had pellagra. Isoniazid induced pellagra despite pyridoxine supplementation was reported by Darvay et al.[18] Thus pellagra could be multifactorial and apart from niacin other factors like chronic infection, drugs like INH, alcohol, age may be contributing factor.

Nutritional deficiencies including anemia may be a result of psychological disturbances. They may not eat properly and so nutrition suffers. One of the patient who was admitted in medicine ward for anemia and adult kwashiorkor having pedal edema and frontal baldness (case 7). This patient was diagnosed to have trichobezoar. In this patient there was a vicious circle of psychological disturbance and not eating food properly with eating of own hairs which lead to anorexia, fullness of stomach and malabsorption and resulted in anemia as well as adult kwashiorkor. This patient had serum albumin below 2.8 g/dl, hair pluck ability and oedema, signs reported to diagnose kwashiorkor.[19] "Easy hair pluckability"- pulling a lock of hair from the top (not from the side or back) grasping with thumb and finger was present in this patient. In this patient "easy hair pluckability"- lead to complex phenomenon of teleophagia (hair eating) and formation of trichobezoar. One other patient in this study was admitted in MICU for primary nutritional deficiency had a pointer towards psychiatric problem in form of lock in her leg (bracelet locally called as a Zanzar).

Subtle skin and mucous membrane changes may give a clue to underlying systemic disease like skin pigmentation and shiny skin. Mucocutaneous manifestations associated with vitamin B12 deficiency are skin hyperpigmentation especially over knuckles, vitiligo, angular stomatitis, and hair changes. Mucocutaneous lesions predate other manifestations in Vitamin B12 deficiency.[20] Knuckle pigmentation with loss of tongue papillae leading to bald tongue with macrocytic and dimorphic anemia with decreased level of Vitamin B12 was present in 4 OPD patients, one of which had chronic diarrhea. Kannan et al, had reported 2 such cases.[20]

This study had 11 (14.67%) patients having clinical signs and investigations suggestive of kwashiorkor. Cause of kwashiorkor was psychiatric illness in 3, Nutrition and diet related in 3, HIV disease in 2 and, Pulmonary Tuberculosis in 2 and no cause could be found out in one patient. In our study, in 3 patients nutrition and diet seemed to be related to kwashiorkor and in other 3 it was related to other type of malnutrition. In one patient cause of kwashiorkor was not identified. Relation between diet and nutritional deficiencies and the etiology of kwashiorkor remains inscrutable in cross-sectional studies and longitudinal study research design may be needed for validity.[21] More than half of our patients (39 of 75) had lacto-vegetarian food (fruit, plant and dairy product) habit which is common in Gujarat state, however we were not certain about diet being the cause of multinutritional deficiency and/or vitamin B12 deficiency in this 39 patients and thus is not considered in risk factor table. HIV related cases of adult kwashiorkor and malnutrition is reported in literature. Striking cutaneous, hair, and nails changes are described.[22]

Skin manifestations in malnutrition and kwashiorkor have not been emphasized in the dermatologic literature. Dermatologists may play a vital role in diagnosis and management of these conditions.

CONCLUSION

Anemia may be associated with other nutritional abnormality which is reflected in changes in the skin, mucous membrane, hairs and nails. Nutritional Dermatosis and anemia can be part of systemic illness which maybe reflected as deficiency of multiple nutritive factors.

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