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Original Research Paper

Ayurveda

CLASSICAL INSIGHTS OF B12 DEFICIENCY WITH RESPECT TO HEMOLYTIC ANEMIA AND RAKTAPITTA - A MICROSCOPIC APPROACH

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ABSTRACT

Background: Vitamin B12 deficiency disrupts DNA synthesis and erythropoiesis, often progressing to haemolytic anaemia through oxidative damage and red blood cell fragility. In Ayurveda, this aligns with Raktapitta (hemolytic disorders), a Pitta-dominant disorder marked by Raktadhatu (blood tissue) vitiation and spontaneous haemorrhages via impaired Raktavaha srotas (blood carrying channels). Integrating these views offers novel diagnostic insights. **Objective:** To elucidate microscopic correlations between B12 deficiency-induced haemolytic anaemia and classical Raktapitta (hemolytic disorders), promoting Ayurveda-biomedicine synergy for enhanced clinical management. **Methods:** Review of pathophysiological mechanisms, including homocysteine elevation, intramedullary/extramedullary haemolysis, and peripheral smear findings (e.g., hyper segmented neutrophils, fragmented erythrocytes). Ayurvedic texts analysed for Raktapitta (hemolytic disorders) aetiology, dosha involvement, and srotas dysfunction, alongside real-time microscopic images from clinical cases. **Results:** B12 shortfall triggers nuclear-cytoplasmic asynchrony, apoptosis, and elevated LDH/bilirubin, mirroring Raktapitta's blood tissue depletion and channel obstruction. Shared oxidative stress from hyperhomocysteinemia parallels Pitta aggravation, with low reticulocytes distinguishing it from other anaemias. **Conclusion:** Unifying microscopic haematology with Ayurvedic principles enables holistic detection via biomarkers and dosha assessment, advocating multidisciplinary interventions for better outcomes in haemolytic disorders.

KEYWORDS : Vitamin B12 Deficiency, Haemolytic Anaemia, Raktapitta, Ayurveda-Biomedicine Integration, Oxidative Stress; Homocysteine, Raktadhatu.

INTRODUCTION

Pathological view determines interconnected clinical association between vitamin B12 deficiency, hemolytic anemia an Raktapitta (hemolytic disorders) with deep implications for modern and contemporary medicine. Understanding their underlying correlations reveals a deeper microscope perspective, uniting genomics, biochemistry and classical concepts. Vitamin B12 also known as 'cobalamin' is a water soluble micro-nutrient crucial for synthesis of DNA, cellular maturation and maintaining neurological integrity.[1] Its absorption takes place in ileal mucosa of small intestine with the help of gastric intrinsic factor. B12 deficiency mainly causes due pernicious anemia an auto immune condition resulting destruction of gastric intrinsic factor, malabsorption, dietary insufficiency specifically in strict vegan and vegetarians.[2] Clinically B12 deficiency manifests as megaloblastic anemia – impaired DNA replication rapid divisions in bone marrow resulting in macrocytic picture on peripheral blood smear microscopy, pancytopenia, various neuropathies and psychological disturbances. Microscopic attributes include hyper segmented neutrophils, macrocytic RBC, nucleated RBCs on peripheral blood smear.[3] Pathophysiological homocysteine and methylmalonic acid accumulation secondarily to B12 deficiency leads to cell membrane damage resulting hemolysis – a process in which premature fragile erythrocytes are destroyed in bone marrow as well as in circulation. Hemolytic anemia is a condition where there is destruction of red blood cells is more than production - showing pallor, fatigue, jaundice, raised levels of lactate dehydrogenase (LDH) enzyme and indirect bilirubin.[4] The principal contributors to hemolysis are B12 deficiency, insufficient erythropoiesis, intramedullary hemolysis and oxidative stress aggravated by raised levels of homocysteine. Pancytopenia and reticulocytopenia differentiates hemolytic anemia from other thrombolytic micro-angiopathies.

According to classical context, Raktapitta is a hemorrhagic disorder caused due to vitiation of Pitta dosha upon Rakta (blood) - characterized as pathological out flow of blood. Its etiology comprised of internal disturbances dietary and behavioral factors, underlying chronic infections. Vitiation of Raktadhatu (blood tissue) and due to increased Drava guna (fluidity quality) of vitiated Pitta - spontaneous bleeding from various opening is seen.[5] Raktapitta is also mentioned as Mahagada by Acharya Charaka due to its fatal and deteriorating nature. Raktapitta is classified on the basis of its out flow in 3 main types by Acharya Charaka as 1)Urdhwaga 2)Adhoga and 3)Tiryaka. Urdhwaga (upward) is mixed with Kapha dosha, Adhoga (downward) is mixed with Vata, Tiryaka (spread all over) is Tridoshaja. Microscopic and functional similarities shed a light on association between Raktapitta and hemolytic anemia in correspondence to B12 deficiency. Disturbed erythropoiesis, defects in cell maturation and increased cell fragility due to B12 deficiency parallels to classical concept of disrupted Raktadhatu integrity and abnormal bleeding.

Dysfunctional Raktavah srotas (blood carrying channels) leads to microangiopathic hemorrhages due to hemolysis and vascular complications are described in clinical hematology.[6] Comparative similarities can be drawn between oxidative stress mechanisms as hyper-homocystenemia found in b12 deficiency and vitiation of Raktadhatu (blood tissue) due to Pitta reflecting metabolic imbalance and tissue degeneration.

A comprehensive approach to early detection and management of this complex disorder can be made easy by correlating the ancient view to western biomedical lens, highlighting the importance of diverse viewpoints in clinical research.

Vitamin B12- Biological Functions and Metabolic Role

Re-methylation of homocysteine to methionine is catalyzed by methionyl synthase using methylcobalamine as a co-factor and regenerate tetrahydrofolate (THF) from 5-methyl-tetrahydrofolate.[7] Methionine is a universal methyl donor for Deoxy-ribonucleic acid (DNA) – Ribose nucleic acid (RNA) and lipid methylation and protein modification which regulates

the mechanism of gene expression and maintaining genomic stability methylation cascade gets disturbed due to B12 deficiency results in impaired gene expression related neuropathies and neuropsychiatric manifestations on an average 25% of vitamin B12 deficient individuals suffers peripheral neuropathy severe cares represented with irreversible myelopathy characterized by symmetric sensory loss, lower extremity weakness and perspective dysfunction.[8] Vitamin B12 act as enzyme mediating co-factor is synthesis of nucleotides responsible for erythroid all proliferation and maturation. Deficiency results in nuclear cytoplasmic asynchrony defective erythropoiesis and megaloblastic anemia.

Association to Ayurvedic Concepts

Vitamin B12 deficiency shows hematological disturbance correlating classical concepts of Raktadhatu-kshaya (depletion of blood tissue) reduced blood tissue responsible for nourishment, oxygenation and vitality. Cardinal symptoms of B12 deficiency are fatigue, weakness pallor associations with symptoms of Raktadhatu-kshaya (depletion of blood tissue) also neurological involvement as numbness, tingling, memory and balance dysfunction correlating Majjadhatu Dushti (nervous tissue vitiation) reflecting bone marrow and neurological tissue involvement.[9]

Jatharagni as a prime digestive fire responsible for digestion absorption and assimilation of food. Agnimandya as a main culprit to disease manifestation shows impaired absorption even if there is adequate dietary intake. This parallels with modern concept of intrinsic factor deficiency, gastrointestinal inflammation, enzyme deficiency hampering B12 absorption. Methionine cascade also relates the hierarchical pattern of tissue nourishment and energy production to support all Dhatwagni (tissue level digestive fire) function. Ojas is essence of all seven dhatu is formed after proper metabolism and sequential transformation responsible for immunity vitality, longevity and consciousness.[10] Disturbed nucleotide synthesis due to inadequate Vitamin B12 results in improper myelin formation. Depletion in hemoglobin production, affecting tissue level nourishment leading Ojas depletion thereby reduced body resistance and acceptance degeneration.

Pathophysiology of Hemolytic Anemia

Hemolytic anemia can be defined as destruction of red blood cells intra or extra vascularly resulted in decreased level of hemoglobin. There are many causes responsible for the condition one of them is vitamin B12 deficiency. Vitamin B12 act as cofactor in regeneration of tetrahydrofolate (THF) which is necessary for purine and thymidylate synthesis and DNA replication in erythroid and granulocytic precursor cells due to vitamin B12 deficiency erythroid precursors undergo S phase cell cycle arrest with ongoing cytoplasmic maturation results in nuclear cytoplasmic asynchrony, megaloblast containing cytoplasm and mature hemoglobin with enlarged nuclei and immature chromatin.[11] This dysplastic morphology leads to P53 mediated apoptosis of red blood cells before entering peripheral circulation. P53 is a protein responsible for prevention of cell division with damaged DNA by proliferation of cell with repaired DNA of by activation of self-destruction mechanism of cell (apoptosis).[12]

Hemolysis is of two types:

Intra Medullary13	Extra Medullary14
Ineffective erythropoiesis	Structural erythrocyte membrane defect
Dysmorphic, Megaloblastic erythroblasts destruction in bone marrow	Macroscopic erythrocytes
Increase levels of Lactate-dehydrogenase (LDH) and Indirect Bilirubin	Mechanical destruction occurs producing schistocytes
Lowered or normal reticulocyte count suggest bone marrow suppression	Polyacrylamide gel electrophoresis -Lacking spectrin bands diffuse faster migrating abnormal bands - suggest severe B12 deficiency. Raised MCV demonstrates extramedullary hemolysis.

Association of Ayurvedic Concept

A disease mentioned by Acharyas as Raktapitta (Hemolytic disorders) demonstrates spontaneous bleeding through natural openings of body without trauma. It is a hemorrhagic disorder arises due to vitiated Pitta causing contamination to Raktadhatu (blood tissue).[15] Hemolytic anemia and Raktapitta both share pathological association as blood tissue vitiation, erythrocyte dysfunction and blood loss .

Pathophysiology of Raktapitta explained by Acharya Charaka as follows[16]

Pittaprakopa (Aggravation of Pitta dosha)

(hyperacidity, excess hunger, heat sensation and emotional irritability)

Localization in blood tissue (Sthansamshraya)

(avergen to food, frequent and foul vomiting, burning sensation throughout body, sensation of smoke emanating from mouth and nostrils)

Rakta Vriddhi (Quantitative increase in blood tissue)

Pitta's Drava Guna (fluidity quality) and Pitta's heat & penetrating quality increase blood tissue quantitatively, blood tissue increases while other tissue undergoes depletion (Kshaya).

Raktavaha Srotobhishyand (Obstruction of blood channels)

Guru (heavy) and Abhishyandi (obstructing) qualities causes obstruction in blood channels and associated organs . Obstruction associated with

Kapha – affects upper body channels leading to bleeding from upward opening e.g. nostrils	Vata – affects lower body channels leading to bleeding from downward opening e.g. Blood in stool, urine

Obstructed channels build ups intravascular pressure. Accumulation of vitiated blood tissue proximally and nutritional deprivation seen in sequential body tissue.

Rakta Dushti (Contamination and functional disturbance of blood)

Prolonged presence of vitiated Pitta basically disturbs the composition and functions of normal blood tissue contaminate blood tissue fails to provide nutrition to other body tissue apart from this it carries destructive properties of Pitta which leads to thin , dry frothy blood of brownies red color and oiliness in blood. Along with Vata it causes tissue disintegration and Pitta causes liquification and kapha causes stagnation of oozing.

Rakta ksharana (Efflux of blood through bodily orifices)

Above pathophysiological progression manifest as spontaneous bleeding from natural body orifices. The bleeding is not as an effect of vascular rupture but as a result of excessive pressure. Due to quantitative increase in blood tissue with vitiated Pitta penetrating properties weakness the blood carrying channels overall combination leads to efflux of blood through orifices.

Microscopic Pictures of Peripheral Blood Smear Showing Classical Traits of Hemolytic Anemia with Vitamin B12 Deficiency

All images are clicked in real-time screening of patient at Central Clinical Laboratory of Dr. D. Y. Patil College of Ayurved, Hospital and Research Centre, Pimpri, Pune – 411018.

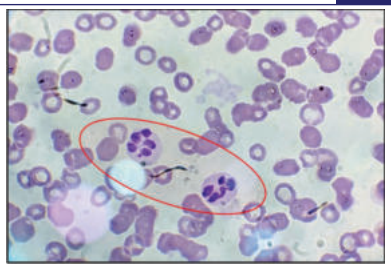

Fig 1. Hyper segmented Neutrophils

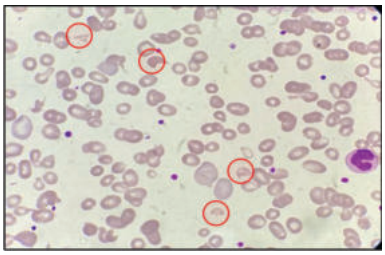

Fig 2. Fragmented Erythrocytes

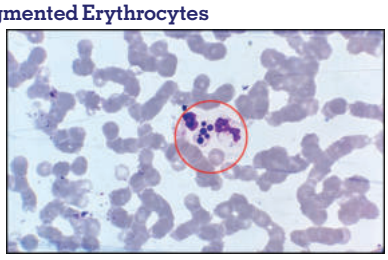

Fig 3. Apoptic Changes

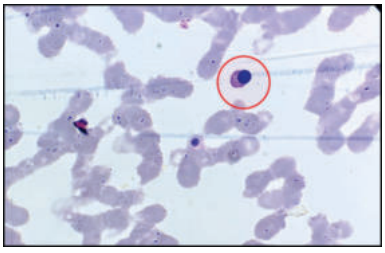

Fig 4. Nucleated Erythrocyte

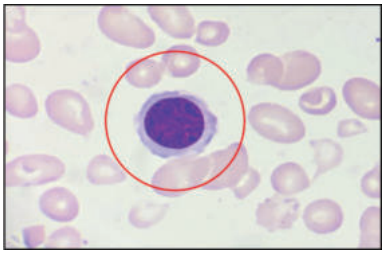

Fig 5. Polychromatic Erythroblast

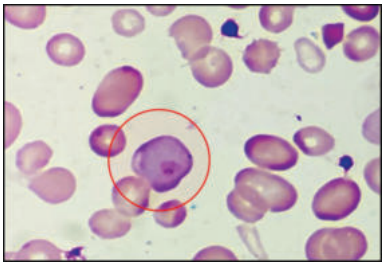

Fig 6. Reticulocyte

DISCUSSION

Vitamin B12 deficiency causes haemolytic anaemia by two mechanisms. Ineffective erythropoiesis causes intramedullary haemolysis. It results from defective DNA synthesis and nuclear cytoplasmic asynchrony, which leads to premature death of megaloblastic erythroid precursors in the bone marrow. Elevated methylmalonic acid and homocysteine are more sensitive metabolic markers of cobalamin deficiency because they accumulate when the vitamin is insufficient to support methionine re-methylation.[17] Therefore, hyperhomocysteinemia induces oxidative stress by lipid peroxidation and damage to the erythrocyte membrane, which leads to extramedullary haemolysis. In addition, intramedullary haemolysis is characterized by low haptoglobin levels, elevated lactate dehydrogenase, and indirect bilirubin, but reticulocytopenia is observed.

The classical pathophysiology conceptualizes this as Raktapitta (haemolytic disorders), which means Pitta-mediated vitiation of Raktadhatu (blood tissue) and Raktavah srotas (blood carrying chanels). The close link between the metabolic dysfunctions caused by vitamin B12 deficiency and the destabilization of Raktadhatu (blood tissue) suggests that they may be functionally correlated.

CONCLUSION

The deficiency of vitamin B12 and haemolytic anaemia have a close link to Raktapitta (haemolytic disorders), which shows that there are significant similarities in the pathophysiology of diseases between conventional medicine and contemporary sciences. The oxidative stress induced by homocysteine also has a similar effect on blood components as the Pitta aggravation in Raktadhatu (blood tissue). It is possible to integrate the analysis of haematological biomarkers with the assessment of Raktadhatu-kshaya (blood tissue depletion) and Raktavah srotas (blood carrying channels) dysfunctions.

Declarations

Ethics Approval and Consent to Participate

This work is a literature review that does not involve original human or animal experimentation. No institutional ethics committee approval was sought, as the study relied solely on analysis of published data and classical texts.

Consent for Publication

No patient-identifiable information or clinical images requiring consent appear in this manuscript. Images derive from de-identified peripheral blood smears captured during routine laboratory screening at the institution's central clinical facility.

Availability of Data and Materials

All data stem from publicly accessible peer-reviewed literature and Ayurvedic classical sources cited in the references. Microscopic images were obtained from institutional records; supplementary materials are available upon reasonable request to the corresponding author.

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