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Psychological Determinants In The Etiopathogenesis Of Pandu Roga: An Ayurvedic Review W.S.R. To Iron Deficiency Anemia

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ABSTRACT

Pandu Roga, as outlined in Ayurvedic literature, is a disorder presenting with pallor and systemic weakness, closely aligning with clinical features of iron deficiency anemia. Classical Ayurvedic sources attribute its pathogenesis to both physical and psychological factors. Notably, Acharya Charaka highlights *Chinta* (worry), *Bhaya* (fear), and *Shoka* (grief) as key psychological contributors. These factors are believed to impair the functioning of *Rasavaha* and *Raktavaha Srotas*, thereby disrupting the formation of *Rasa* and *Rakta Dhatus*. Contemporary biomedical research corroborates these insights by demonstrating that psychological stress can interfere with iron regulation, erythropoiesis, and inflammatory processes via hypothalamic-pituitary-adrenal (HPA) axis dysregulation. This review synthesizes classical Ayurvedic concepts with current scientific findings to explore the etiological role of mental stressors in Pandu Roga. Literature was gathered through systematic keyword searches including "iron deficiency," "psychological stress," "anemia," and "HPA axis," followed by evaluation of relevant studies. Results indicate that prolonged psychological stress negatively impacts iron homeostasis and hematopoiesis, potentially precipitating anemia. These findings support the inclusion of psychological assessment and management in the holistic treatment of Pandu Roga.

Keywords: *Pandu Roga, Iron Deficiency Anemia, Ayurveda, Chinta, Bhaya, Shoka, Rasavaha Srotas, Psychological Stress*

1. INTRODUCTION

Nidanas (etiological factors) are primary causes behind the manifestation of any disease, directly or indirectly. Ayurveda emphasizes the significance of understanding these causative factors not only for diagnosis but also for the prevention and management of diseases through their avoidance. Classical Ayurvedic texts, especially the *Charaka Samhita*, provide a comprehensive list of *Nidanas* for each disease and stage of pathogenesis [1].

In the context of *Pandu Roga*, which is considered to be analogous to iron deficiency anemia in modern medicine, *Acharya Charaka* outlines several physical and dietary *Nidanas*. Notably, he also identifies psychological factors such as *Kama* (excessive indulgence in sensual thoughts), *Krodha* (anger), *Chinta* (excessive worrying), *Bhaya* (fear), and *Shoka* (grief) as key contributors in the pathogenesis of Pandu [2]. Among these, *Chinta*, *Bhaya*, and *Shoka* are predominant and often interlinked, and are collectively associated with psychological stress (PS).

Modern biomedical literature suggests that chronic psychological stress influences iron metabolism, immune response, and hematopoietic function—factors directly linked to anemia development [3,4]. However, the Ayurvedic perspective on the psycho-pathophysiology of Pandu Roga remains underexplored in contemporary scientific literature. This review, therefore, aims to analyze the connection between the psychological *Nidanas* mentioned in Ayurveda and their possible correlation with mechanisms identified in modern research regarding iron deficiency anemia.

Review of Modern Scientific Literature and Research Findings

A comprehensive literature review was conducted using search engines such as Google Scholar, Bing, and biomedical databases like PubMed. The keywords used included *"psychological stress"*, *"anemia"*, *"iron metabolism"*, *"erythropoiesis"*, and *"iron deficiency anemia"*. Several relevant studies were identified that evaluated the potential role of psychological stress (PS) in the pathogenesis of anemia, particularly iron deficiency anemia (IDA).

A number of scientific studies highlight the adverse effects of chronic psychological stress on iron metabolism and erythropoiesis. One significant experimental study was conducted at the Department of Naval Medicine, Second Military Medical University, Shanghai. The research involved twenty male Sprague-Dawley rats, in which psychological stress was experimentally induced using a communication box—a method allowing visual, auditory, and olfactory exposure to stress without physical contact [5].

The findings demonstrated that the stress-exposed rats developed reduced serum iron levels and hemoglobin concentrations compared to the control group. Histological analysis of bone marrow samples showed impaired erythropoietic activity. The study concluded that chronic psychological stress significantly disrupts iron homeostasis and suppresses erythropoietic function, contributing to anemia [6].

These results correlate with the Ayurvedic view that persistent psychological factors such as *Chinta*, *Bhaya*, and *Shoka* may influence the body's internal systems, particularly *Rasa* and *Rakta Dhatu*, leading to clinical manifestations similar to those observed in iron deficiency anemia.

2. EXPERIMENTAL EVIDENCE LINKING PSYCHOLOGICAL STRESS WITH IRON DEFICIENCY ANEMIA

An elaborate experimental study conducted at the Department of Naval Medicine, Second Military Medical University, Shanghai explored the impact of psychological stress (PS) on iron metabolism and erythropoiesis in rats using a novel communication box model [7].

The setup involved two compartments, Room A and Room B, separated by a transparent acrylic divider. Room B had a metal grid floor through which rats were subjected to electrical shocks (90 V, 0.8 mA for 1 second, 60 times over 30 minutes). In contrast, rats in Room A were not physically shocked but were exposed to the distress responses (e.g., jumping, crying) of Room B rats. This model effectively induced psychological stress in Room A rats without physical harm [8].

On the 7th and 14th days, blood and bone marrow samples were collected for analysis. The stressed rats showed the following significant hematological and biochemical changes:

- **Femoral bone marrow iron** significantly reduced.
- **Serum iron (SI)** dropped by 28.6% (day 7) and 27.5% (day 14) ($P < 0.01$).
- **Hemoglobin (Hb)** levels declined by 10.0% and 12.8% respectively ($P < 0.01$).
- **Red blood cell (RBC)** count fell by 5.1% and 9.8% ($P < 0.05$, $P < 0.01$).
- **Mean corpuscular volume (MCV)** decreased by 1.7% and 7.3%.
- **Red cell distribution width (RDW)** increased by 10.7% and 22.5%.
- On day 14, **serum ferritin (SF)** and **erythropoietin (EPO)** decreased by 23.8% and 12.3%, while **transferrin receptor** levels increased by 31.5% [9].

Mechanistic Insight: The IL-6–Hepcidin Axis

A subsequent study conducted by another team from the same institution further confirmed these findings and delved into the pathophysiological mechanisms involved [10]. The researchers reported that psychological stress elevated hepatic iron concentration early (by day 3), even before any observable decline in Hb or RBC count, indicating altered iron distribution rather than deficiency in intake or absorption.

Importantly, the study highlighted activation of the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system, leading to increased interleukin-6 (IL-6) secretion. This in turn upregulated hepcidin, a key regulator that blocks iron export by downregulating ferroportin, the only known cellular iron exporter.

Further confirmation came from anti-IL-6 antibody experiments, which showed that inhibition of IL-6 prevented the hepcidin upregulation and hypoferremia, thus establishing the role of the IL-6–hepcidin–ferroportin pathway in stress-induced anemia [11].

These findings provide a modern physiological basis for the Ayurvedic assertion that psychological factors such as *Chinta*, *Bhaya*, and *Shoka* play a crucial role in the etiopathogenesis of Pandu Roga, corresponding to iron deficiency anemia.

Another study conducted at the same university corroborated these results and further elucidated the mechanism. It highlighted the role of the IL-6–hepcidin axis, activated by the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system, as a critical mediator of hypoferremia induced by PS. The study reported elevated hepatic iron storage and suppressed iron transport, with decreased serum iron observed as early as Day 3 of PS exposure. Anti-IL-6 antibody administration reversed hepcidin upregulation and restored normal iron distribution, confirming IL-6's role [12].

Additionally, a study from the University of Pittsburgh also reported that exposure to physical and psychological stressors significantly elevated plasma IL-6 levels, again implicating HPA axis activation as the underlying mechanism [13].

3. DISCUSSION

Although *Chinta* (worry), *Bhaya* (fear), and *Shoka* (grief) are recognized in Ayurveda as causative factors (*Nidana*) in the manifestation of *Pandu Roga*, the classical texts offer limited explicit details regarding their precise pathophysiological mechanisms. Nevertheless, scattered references provide crucial insights that help establish a conceptual framework linking psychological stress (PS) with *Pandu Roga*. Notably, *Atichintana* (excessive worry) is specifically mentioned as a cause for the vitiation of *Rasa Vaha Srotas*, the channels responsible for transporting *Rasa Dhatu*—the primary nutritive fluid formed after digestion. Given that *Pandu Roga* is categorized under *Rasa Pradoshaja Vikara* (disorders arising from vitiated *Rasa*), this highlights a foundational connection between psychological disturbances and the pathogenesis of *Pandu Roga*.

However, it is evident that multiple intermediary processes must exist between the initial psychological stimulus and the eventual pathological outcome. One such key intermediary is *Agni* (digestive/metabolic fire) vitiation. Classical Ayurvedic references suggest that even wholesome food, if consumed under emotional distress (grief, fear, anger, sorrow, or disturbed sleep), does not undergo proper digestion. This indicates that PS adversely affects *Agni*, thereby compromising digestion.

In Ayurveda, *Agni* is not limited to gastrointestinal digestion; it encompasses the entire spectrum of digestion, metabolism, assimilation, and tissue formation . The conversion of ingested food into usable forms by *Jatharagni* (digestive fire), *Bhutagni* (elemental fire), and *Dhatvagni* (tissue-level fire) is fundamental to maintaining bodily health . All these subtypes of *Agni* are dependent on *Jatharagni*. Its vitiation leads to a cascade of dysfunction across the metabolic axis, ultimately resulting in defective tissue formation.

This impaired digestion results in suboptimal formation of *Rasa Dhatu*, either in terms of quantity or quality. Since *Rakta Dhatu* is formed from *Rasa Dhatu* through the action of *Raktagni* , compromised *Rasa Dhatu* directly affects the production of *Rakta Dhatu*. This is the probable reason classical texts describe *Pandu Roga* as a *Rasa Pradoshaja Vikara*, highlighting *Alpa Raktata* (reduced blood) and *Panduta* (pallor) as cardinal features .

Furthermore, psychological stress is also considered a general etiological factor (*Samanya Kshaya Hetu*) for bodily debility and is responsible for *Oja Kshaya* (loss of vitality and immunity) . Notably, *Pandu Roga* involves *Ojo Guna Kshaya* (loss of the qualities of *Ojas*) and *Nihsaarata* (lack of essence in all tissues).

Sadhaka Pitta, the subtype of *Pitta Dosha* located in the heart (*Hridaya*), governs intellectual faculties, enthusiasm, and mental endurance. Its involvement in the pathogenesis of *Pandu Roga* is evident as *Hridaya* is affected in the disease, thereby linking PS to the vitiation of *Sadhaka Pitta*. Also, *Rasa Dhatu* serves as a seat for *Pitta Dosha* , reinforcing the pathological correlation.

Recent scientific studies support this Ayurvedic understanding. PS maintained even for 7–14 days alters iron metabolism by inhibiting erythropoiesis, redistributing iron, and reducing serum iron and bone marrow iron levels. This effect is mediated by elevated interleukin-6 (IL-6) levels triggered by the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic stimulation. Notably, the pituitary and adrenal glands can produce IL-6, which then acts hormonally to induce hepatic acute-phase protein production and modulate hormonal secretions .

IL-6 also upregulates *hepcidin*, a key regulator of iron homeostasis, both in vitro and in vivo. The combined increase of IL-6 and *hepcidin* results in hypoferremia and hepatic iron sequestration, consistent with iron-deficiency anemia.

This modern understanding aligns closely with the Ayurvedic concept of *Pandu Roga* being a *Pitta Pradhana Vyadhi*. Since IL-6 and *hepcidin* act as inflammatory mediators and regulatory proteins, their activity parallels that of *Pitta Dosha*. As *Pitta* becomes vitiated and circulates via the *Srotasas*, it infiltrates *Rasa Dhatu*, initiating the disease process. Eventually, all tissues (*Dhatus*) may become involved, explaining the appearance of symptoms like *Nihsaarata*, *Ojo Kshaya*, reduced strength, and compromised immunity (*Bala/Oja*).

4. CONCLUSION

The present review provides a scientific rationale for the involvement of psychological factors such as *Chinta* (anxiety), *Shoka* (grief), and *Bhaya* (fear) in the etiopathogenesis of *Pandu Roga*. These factors, recognized in Ayurveda as significant contributors to disease, appear to affect iron metabolism through well-established mechanisms, including the suppression of erythropoiesis and reduction of serum and bone marrow iron levels. The role of inflammatory mediators—particularly interleukin-6 (IL-6) and hepcidin—in stress-induced anemia corresponds with the classical understanding of *Vata* and *Pitta* Dosha interactions in the progression of *Pandu Roga*. The inflammatory response triggered by psychological stress mirrors the physiological effects attributed to *Pitta Dosha*, thereby offering a potential bridge between Ayurvedic and modern biomedical perspectives. This integrative understanding supports the classical Ayurvedic *Samprapti* (pathogenesis) of *Pandu Roga*, particularly when triggered by emotional and psychological disturbances. However, further detailed experimental and clinical investigations are warranted to deepen our understanding of these psychoneuroimmunological pathways and their

relevance in Ayurvedic pathology.

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Conflicts of interest

None declared.

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