

A review on role of psychological factors in the etiopathogenesis of *Pandu Roga* with reference to iron deficiency anemia

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Abstract

“*Pandu*” *Roga* is a disease entity described in Ayurveda which has clinical features similar to that of various types of anemia, in which there develops a pale-yellow discoloration on the skin. Besides the various etiological factors, *Acharya Charaka* has specially described some psychological causative factors among which *Chinta* (excessive worry), *Bhaya* (fear) and *Shoka* (grief) are three main factors, which play an important role in the pathogenesis of *Pandu Roga*. This paper aims to explore the scientific explanations for the above stated factors in the causation of *Pandu Roga* (anemia). Hence, a thorough search was made on the internet using the keywords anemia, psychological stress, anger, fear and some scientific studies were found on the concerned topic. It reveals that these factors disturb the process of iron distribution within the body and affects the process of erythropoiesis causing iron deficiency anemia.

Keywords: Anemia, Bhaya, Chinta, fear, grief, Pandu, psychological stress, Shoka, worry

Introduction

Nidanas (etiological factors) are the agents responsible for the causation of any disease – be it directly or indirectly. Ayurveda has laid down the importance of these etiological factors for both the causation of the disease and the treatment for the avoidance of the *Nidanas*. A list of various *Nidanas*^[1] have been given in the texts for every disease as well as for all stages of the pathogenesis.

In the chapter of *Pandu Roga*, *Acharya Charaka* has described various psychological etiological factors as *Kama* (excessive thinking about sex), *Krodha* (anger), *Chinta* (excessive worrying), *Bhaya* (fear) and *Shoka* (grief).^[1] However till now, no scientific study describing the mechanism of these factors in the causation of anemia has been reported. Hence, it was decided to study the three factors *Chinta*, *Bhaya* and *Shoka* which are collectively called as the main causes of psychological stress (PS) which in turn play a crucial role in the causation of various anemia and to observe the findings for any explanations.

Review of modern science literature and researches

A thorough search was made on the search engine Google, Bing and PubMed, regarding the topic using the keywords – role of PS in the causation of any anemia and its mechanisms.

Results

A few scientific studies were found describing the role of PS in the causation of iron deficiency anemia.

The first study^[2] (conducted in the Department of Naval Medicine, Second Military Medical University, Shanghai) performed in an animal model of twenty male Sprague-Dawley rats in whom PS was induced through a communication box.

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A communication box was divided into room A and room B with a transparent acrylic board, room A included ten little rooms with a plastic board-covered floor and room B included ten little rooms with a metal grid-exposed floor for electric insulation. Rats in room B were randomly given electrical shock 90 V, 0.8 mA for 1 s for 30 min, 60 times in total through the floor and exhibited no receptive stimulation-evoked responses, such as jumping up, defecation, and crying. Rats in room A were only exposed to the responses of rats in room B to establish PS model. On the 7th and the 14th day after administration, ten rats were executed and the rat blood and femoral bone marrow were collected for analysis of serum iron (SI), serum ferritin (SF), serum transferrin receptors, hemoglobin (Hb), red blood cell (RBC) count, RBC distribution width (RDW), mean corpuscular volume (MCV), serum erythropoietin (EPO) and bone marrow iron. Experimental data were statistically analyzed with SPSS 11.0. The data revealed that for rats analyzed on the 7th and 14th day in PS group, the following points were noted.

- Femoral bone marrow iron was significantly decreased
- SI was decreased by 28.6% ($P < 0.01$) and 27.5% ($P < 0.01$)
- Hb was decreased by 10.0% ($P < 0.01$) and 12.8% ($P < 0.01$)
- RBC count was decreased by 5.1% ($P < 0.05$) and 9.8% ($P < 0.01$)
- MCV was decreased by 1.7% ($P < 0.05$) and 7.3% ($P < 0.01$)
- RDW was increased by 10.7 and 22.5%
- SF, transferrin receptor and EPO showed no significant changes in comparison with controls after 7th day of administration, but SF and EPO were decreased by 23.8 and 12.3% while transferrin receptor increased by 31.5% after 14th day of administration.

Another study conducted at the same place but by other workers^[3] further confirmed the above findings and also described the mechanism responsible for it as the interleukin-6 (IL6) hepcidin axis. This study was also an experimental study in rats done in the same way as stated above through a communication box. The investigators found that the SI level was decreased after 3 day repeated PS exposure before the decline of red cell count and Hb (which decreased on 7th day). They also noticed elevated body iron stores in those rats as elevated hepatic iron concentration indicating that PS changed the iron distribution of the body and limited the transportation and utilization of iron. Only male rats were included in the study and standard diet was given to the rats to exclude the factors related to feeding loss and menstrual blood. The researchers also noticed increased IL6 after repeated PS exposure which was through the activation of the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system. They also observed the up-regulation of hepcidin and down-regulation of ferroportin through the Western blot technique after PS exposure.

The investigators further performed anti IL6 antibody experiments to examine whether the IL6-hepcidin axis was necessary for the development of hypoferrremia induced by PS. They found that anti-IL6 antibody inhibited the up-regulation

of hepcidin and down-regulation of ferroportin while also inhibiting liver and SI level changes.

Another experimental study conducted on rats in the Department of Pathology,^[4] University of Pittsburgh School of Medicine, Pennsylvania, also had similar findings of elevation of plasma IL6 on exposure to physical and psychological stressors which they further related to the activation of HPA axis.

Discussion

Although *Chinta*, *Bhaya* and *Shoka* (PS) are described as etiological factors in the causation of *Pandu Roga* in Ayurveda^[5] but no detail about the exact mechanism of action and the pathological process has been made there. However, at certain places, some specific hints are obtained which clarify and elaborate the whole understanding about the topic.

An important aspect about the association between these psychological factors and *Pandu Roga* is a direct cause and effect relationship as excessive worry or stress (*Chintyaanam cha Atichintanaat*) has been described as the specific etiological factor for the vitiation of *Rasa Vaha Srotas*^[6] (channels carrying the first tissue element of the body formed from the digested nutrients) and *Pandu Roga* is a *Rasa Pradoshaja Vikara*.^[7,8]

Yet, it is clearly understood that certainly there must be several steps or processes between these two extreme points of cause and effect. These missing links are in the form of *Agni* vitiation. References are available in the texts which state that^[9-11] wholesome food taken even in the right quantity does not get digested properly if the individual is afflicted with grief, fear, anger, sorrow and inconvenient bed for sleep (meaning disturbed sleep) inferring thereby that these factors vitiate *Agni* and resultantly the digestion process.

In Ayurveda, the concept of digestion (*Pachana*) relates to the whole process of digestion, metabolism, absorption and assimilation in the body and depends on the proper functioning of the *Agni*.^[12] It is only after the digestion by *Jatharagni* and *Bhutagni* that the food substrate gets converted into a form suitable for use by our body tissues and gets converted into the respective tissue by the action of the respective *Dhatvagnis*.^[13] All these *Bhutagnis* and *Dhatvagnis* depend upon the main *Agni*, i.e., *Jatharagni* for their nourishment and strength. Vitiation of *Jatharagni* will also vitiate the other *Agnis* in due course of time and ultimately affect the status of tissues in the body.

Thus, this improper digestion might be related to any of the aspects stated above, resulting in the deficient production of *Rasa Dhatu* from *Adya Rasa Dhatu* (the fluid tissue of the body which contains the end products of digestion and metabolism and circulates it in the whole body for nourishing other body tissues) either quantity-wise or quality-wise (deficiency in the amount of nutrients present in it as result of digestion and absorption). This improper *Rasa Dhatu* further effects the

production of *Rakta Dhatu* (which is produced by the action of *Raktagni* on *Rasa Dhatu*)^[14] This could be the reason why the *Acharyas* have included *Pandu* in *Rasa Pradoshaja Vikaras* and described *Alpa Rakto* (decreased blood) as one of the main features of the disease along with *Panduta*.^[15]

Besides the above-stated processes, PS also has some other impacts on the body, for it is one of the factors responsible as an etiological agent for generalized debilitation of the body (*Samanya Kshaya Hetu*)^[16] as well as for decreased strength and immunity status of the body (*Oja Kshaya*).^[17] It is worthwhile mentioning here that in the disease *Pandu Roga* also, there is description of decrease in the qualities of the *Ojas* (*Ojo Guna Kshaya*)^[18] and absence of pure essence in all the body tissues (*Nihsaarata*).

Ayurveda states that the entity responsible for the intellectual capacities of the individual, enthusiasm, pride, the achievement of determined goals – all depends upon *Sadhaka Pitta*, which is located in the *Hridaya*.^[19] The pathogenesis of *Pandu Roga* also describes the involvement of *Hridyastha Pitta* in the disease pathogenesis.^[5] Hence, certainly, there is involvement of *Sadhaka Pitta* also by the effect of PS. It is also important to recall here that *Rasa Dhatu* is also the seat of *Pitta Dosha*.^[20] Hence, covering all the above-stated aspects regarding impact of PS, the following pathogenesis is proposed [Figure 1].

The scientific description provided by the studies quoted above specifies that the PS continued even for a small period of 7 – 14 days, changes iron distribution within the body and limits the transportation and utilization of iron; thereby causing a significant reduction of SI and bone marrow iron, significant inhibition of erythropoiesis process,^[21] and an increase in the body iron stores (as hepatic iron concentration increased).^[22] This process is mediated by the increased production of IL6 through the activation of the HPA axis and sympathetic nervous system. It is also to be noted here that the pituitary and the adrenal glands are capable of producing IL6,^[22] which may also function as a hormone to induce the production of acute phase proteins from the hepatocytes^[23] and to regulate the secretion of hormones from the hypothalamus as well as the pituitary

and adrenal glands.^[24,25] IL6 has been shown to stimulate the hepcidin expression *in vitro* and *in vivo*.^[26] which may be the mechanism responsible here also for the up regulation of hepcidin, collectively leading to the hypoferremia and hepatic iron storage.

This increase of IL6 and hepcidin by the PS resulting in iron deficiency anemia through various mechanisms is quite consistent with the Ayurveda description pertaining to *Pandu Roga* and *Agni*. This also correlates to some extent to the description of Ayurveda pathogenesis of *Pandu Roga* (*Samprapti*) which states that *Pandu Roga* is a *Pitta Pradhana Vyadhi* (IL-6 and hepcidin are considered in the modern medical science as inflammatory mediators) and *Rasa Pradoshaja Vikara*. The above descriptions have clearly shown that *Rasa Dhatu* is getting affected here and is then causing *Pandu Roga*. The increase of IL6 and hepcidin which are regulatory proteins also acting as hormones is quite similar to the increase of *Pitta* (as they have functions similar to that of *Pitta*). This vitiated *Pitta* then circulates in the whole body by the channels of circulation or *Srotasa* getting lodged in the *Rasa Dhatu* and results in the manifestation of *Pandu Roga*. Initially, only the *Rasa-Vaha Srotasa* (channels) are involved, but later, all the tissues of the body and their channels might also be involved, that is why features such as *Nihsaarata* and *Ojo Kshaya Lakshanas* (features) are present in the patient, resulting in his/her decreased strength, work capacity and immunity status of the individual (described as *Bala/Oja* in Ayurveda).

Conclusion

The above-stated studies and the discussion reveals that the scientific explanation to the etiopathogenesis of *Chinta*, *Shoka* and *Bhaya* in the causation of *Pandu Roga*, i.e. to say that these factors cause iron deficiency anemia by causing a significant reduction of serum and bone marrow iron while also inhibiting the process of erythropoiesis. This study also reveals the involvement of inflammatory mediators such as IL6, hepcidin in the pathogenesis of *Pandu Roga* caused due to the above-stated factors of *Shoka* and *Bhaya*, which have been described to be *Vata* dominant. Earlier studies have already proven that the inflammatory mediators are very much similar to the *Pitta Dosha* of Ayurveda. Thus, the above study throws some light on the possible role of *pitta* in the pathogenesis of *Pandu Roga* and confirms the Ayurveda *Samprapti* also to some extent. However, still more studies are required to throw light on the other attributes of the pathogenesis of *Pandu Roga*.

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Conflicts of interest

There are no conflicts of interest.

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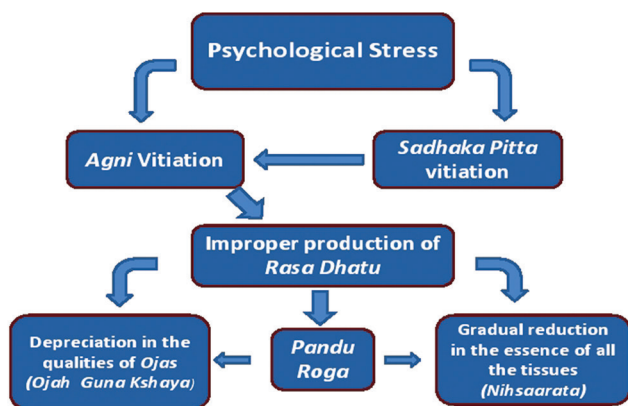


Figure 1: The pathogenesis of psychological stress in causing *Pandu Roga* and its effects in the body

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हिन्दी सारांश

पांडु रोग (लोह की कमी से होने वाले एनीमिया) की संप्राप्ति में मानसिक कारकों की भूमिका

पर एक समीक्षा

शालिनी राय, अनुकूल चन्द्रकर

पांडु रोग आयुर्वेद में वर्णित एक व्याधि है जिसका सादृश्य विभिन्न प्रकार के एनीमिया रोग से है जिसमें त्वचा पर पीले रंग की एक विकृत आभा परिलक्षित होती है। पांडु रोग में विभिन्न आहार एवं विहार परक निदानों के अतिरिक्त आचार्य चरक ने विशेष रूप से कुछ मानसिक कारणों का भी वर्णन किया है जिसमें अत्यधिक चिन्ता, भय और शोक (दुःख) तीन मुख्य कारण हैं जो पांडु रोग के रोगजनन में महत्वपूर्ण भूमिका निभाते हैं। प्रस्तुत शोध पत्र का उद्देश्य पांडु रोग (एनीमिया) के भिन्न-भिन्न प्रकारों में प्रयुक्त कारकों के लिए वैज्ञानिक आधार प्रतिस्थापित करना है। इसलिए उपरोक्त विषय से संबंधित कुंजी शब्दों यथा एनीमिया, मानसिक तनाव, क्रोध, डर इत्यादि का इस्तेमाल करने पर कुछ वैज्ञानिक शोध पत्र प्राप्त हुये, जिससे यह ज्ञात हुआ कि यह मानसिक कारण शरीर के भीतर लोह के वितरण की प्रक्रिया को तथा इरिथ्रोपोईसिस की प्रक्रिया को प्रभावित करते हैं जिससे लोह तत्त्व की कमी वाला एनीमिया रोग होता है।