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Research Article

A COMPREHENSIVE APPROACH TO THALASSEMIA IN AYURVEDA: A REVIEW

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¹Uganta Meena, ²Sudarshan Meena, ³V. K. Kori

¹Assisstant Professor, Department of Kaumarbhritya, Dhanwantari Ayurveda College, Koydam Mahi Sagar. ²Medical Officer, Department of medical and health community health canter Gangi, Dungarpur. ³Professor, Department of Kaumarbhritya, ITRA, Jamnagar.

Email - ¹ugantameena91@gmail.com

Abstract: Thalassemia is a genetic disorder that involves abnormal haemoglobin formation. While some mild forms of thalassemia might even go unnoticed and only cause mild anaemia and iron deficiency problems in patients, other more severe forms of thalassemia can even result in death. Individuals with thalassemia can get treatment according to the level of severity of their condition. The concept of thalassemia has not been directly mentioned as such, though the symptoms can be correlated with Beejadushtijanya pandu. All the relevant texts were explored, information was analysed and presented in an organised way. The review concluded that Beejadushtijanya pandu can be correlated with the varied conditions of thalassemia.

Key Words: Beejadushtijanya Pandu, thalassemia, blood transfusion, Aanuvanshika Pandu.

1. INTRODUCTION:

Thalassemia is the most transfused syndrome worldwide. Pre-screening of blood donors and testing of the blood reduce the risk of transmitting pathogens. Children with Thalassemia Major require repeated blood transfusions, which can lead to iron overload and the transmission of viruses such as HIV, HCV, and HBsAg, reducing their life expectancy. Inadequate transfusions, on the other hand, cause severe anaemia as well as overall weariness and debility.¹ Thalassemia is the most common hereditary blood disorder in the world, and its prevalence varies by population group. According to the World Health Organization (WHO), at least 6.5 percent of the world's population is a carrier of various inherited haemoglobin apathies. According to another WHO research, 3% of Bangladeshis are carriers of beta-thalassemia and 4% are carriers of HbE. In Bangladesh, more than 7000 children are born with thalassemia each year.²

Thalassemia is a genetic disorder that involves abnormal haemoglobin formation. Haemoglobin comprises of alpha and beta 'chains' which, in a patient with thalassemia, are faulty as a result of which the haemoglobin produced is faulty. In a patient with thalassemia, problems arise because there is a lack of healthy haemoglobin that the body requires for it to become properly oxygenated. A patient with thalassemia, not only has lower levels of haemoglobin present in his or her bloodstream but also lacks good quality haemoglobin. At the same time, the patient's body continues trying to produce more red blood cells and haemoglobin. However, since there is a genetic fault with the haemoglobin being produced in that individual's body, the new haemoglobin produced, causes further problems as an overproduction of unhealthy haemoglobin takes place. Individuals with thalassemia can be treated according to the level of severity of their condition. While some mild forms of thalassemia might even go unnoticed and only cause mild anaemia and iron deficiency problems in patients, other more severe forms of thalassemia can even result in death. Most commonly, however, regular blood transfusions are used to treat patients with thalassemia since blood transfusions allow for these individuals' bloodstreams to be flooded with adequate amounts of 'healthy' and normal haemoglobin. Blood disorders usually get their wide explanation under the broad umbrella of *Pandu* and hence present review work aims at establishing the extent of relationship in between Pandu and Thalassemia.

2. MATERIALS AND METHODS:

2.1. Materials:

Ayurvedic texts, as well as the data bases Google scholar, PubMed, Medline, AYUSH Research Portal, and Digital Helpline for Ayurveda Research Articles (DHARA), dissertation works from Ayurveda colleges, and studies available on Research Gate, were used to search for relevant literature.



2.2. Methodology:

The methodology of understanding this disease has been mentioned in *Charaka Samhita* based on *Aaptopadesha Pramana*. The key points like *Prakopanama*, *Yonima*, *Utthanama*, *Aatmanama*, *Adhishthanama*, *Vedanama*, *Samsthanama*, *Shabda*, *Sparsha*, *Roopa*, *Rasa*, *Gandha*, *Upadravama*, *Vriddhi*, *Sthana*, *Kshaya*, *Udarkama*, *Namama*, *Yogama* and *Prateekarartha Pravritti* and *Nivritti* were considered to form a concrete base to formulate suitable regimen for this disease. The composite picture about this disease can be drawn considering above points, in the light of knowledge available in the modern medical discipline.

3. RESULTS:

3.1. Ayurveda and thalassemia major:

In Ayurvedic classics, genetically determined diseases come under Aadibalapravritta Kulaja Vyadhi and Sahaja Vyadhi and prognosis of these Vyadhi is said to be Asadhya in nature.

Genetical basis of various diseases were known to ancient *Acharya*, including their *Hetu* (cause) that is *Upatapti* of *Beeja*, *Beejabhaga*, *Beejabhagavayava*. They mentioned genetical basis for various diseases like *Arsha*, *Prameha*, *Kushtha* and so on. They also mentioned possible cause of *Beejadushti* (mutation) in the form of *Matru-Pitru Apachara*, *Daiva*, *Poorvakrita Ashubha Karma* and *Prakopa* of *Vatadi Dosha*. The last one appears to be almost rational. The role of above causative agents in causing mutation till date is a matter of investigation.

Whatever may be the nature and extent of *Upatapti* or *Beeja Dosha* ancient *Acharya* concentrated on the resultant variability or the Phenotypes They also used terms like *Upahatatva* and *Upatapti* to describe myriad of clinical consequences due to mutation. They also discussed the possible grave outcomes in the form of *Tridosha Prakopa*, *Vikrita Avayava* formation corresponding to biochemical abnormalities/functional abnormalities and structural defects. In case of Thalassemia, there is *Upatapti* of *Beejabhagavayava* in the *Beeja*, which is responsible for the formation of *Rakta Dhatu*, which can lead to *Lakshana* of *Tridosha Prakopa*. As the disease thalassemia is also consistent with life it can be considered as *Asadhya* in nature.

According to Acharya Chakrapanidatta, who quoted earlier, Rasa contributes to the formation of Rakta with parts of itself, which are the homologous of this Dhatu "Shonita Samanabhaga"- Rasa itself is not transmuted in to Dhaturupa Rakta. The remaining part of it assumes red color as it traverses through Rakta Sthana. Acharya Shivadas Sen likewise was quoted to have advanced the view that; Rasa Dhatu, in the course of its circulation, comes first in contact with the Rakta Sthana where, it is turned in to a substance resembling Rakta, in color and it then proceeds to nourish the Rakta Dhatu with substances which are homologous to this Dhatu. By the term Rakta Sthana is meant either the site where the Rakta is formed or stored or both. Charaka, Sushruta and Vagbhatta as Rakta Sthana already recognized Yakrit and Pleeha. In addition, all these authorities have described Yakrit and Pleeha as the Raktavaha Sroto Moolam (Root). The need to recognize the red bone marrow the Sarakta Meda also as an important Raktasthana was then emphasized.

It would appear from what has been stated above that the part of *Rasa* that is converted into a substance resembling *Rakta* is catalyzed as it were, by *Rasaagni*, yielding in the process of, a *Rakta* precursor substance that is *Asthayee (Poshaka) Rakta Dhatu*. This fraction together with the *Ranjaka Pitta* and the *Pachakamsha* leads to the production of *Dhaturupa Rakta*. The colorless *Rasa Dhatu* that appears to be red while in circulation then transports *Dhaturupa Rakta* from *Rakta Sthana*. It is for this reason that the circulating *Rasa Dhatu* is generally, spoken of as *Rakta*. In fact this fluid is *Rasa Dhatu* cum *Rakta Dhatu*. Obvious difference between the *Rasa Dhatu* and *Rakta Dhatu* is like the difference between plasma and erythrocyte on one hand and blood and lymph on the other. The corroborative evidences from the modern texts also support these views. During embryonic period the *Rakta Dhatu* (erythrocytes- primitive and nucleated) are formed in the Yolk Sac. The first blood islands appear in mesoderm surrounding the wall of the yolk sac at 3 weeks of development and slightly later in lateral plate mesoderm and other regions. These islands arise from mesoderm cells that are induced to form hemangioblasts, a common precursor for vessel and blood cell formation. Hemangioblasts are induced by Vascular Endothelial Growth Factor (VEGF), which is secreted by the surrounding mesoderm cells. Hemangioblasts in the center of blood islands from hematopoietic stem cells the precursor of all blood cells³.

Table 1.	Showing	Types of	Panduroga	given in	various	Avurvedic texts
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Samhita	Pandu description	Тур	es			
Charaka Samhita ⁴	Chikitsaasthana- Ch. 16	5-	Vataja,	Pittaja,	Kaphaja,	Sannipataja,
		Mria	dbhakshan	ajanya		
Sushruta Samhita ⁵	Uttaratantra- Ch. 44	4- V	ataja, Pitta	ija, Kaphaj	a, Sannipataj	a
Ashtanga Hridaya ⁶	Nidanasthana- Ch. 13	5-	Vataja,	Pittaja,	Kaphaja,	Sannipataja,



	Chikitsasthana- Ch. 16	Mridbhakshanajanya				
Ashtanga	Nidanasthana- Ch. 13	5- Vataja, Pittaja, Kaphaja, Sannipataja,				
Samgraha ⁷	Chikitsasthana- Ch. 18	Mridbhakshanajanya				
Kashyapa Samhita ⁸	Sutrasthana, Vedanadhyaya-	1- Panduroga				
	Ch. 25					
Harita Samhita ⁹	Trutiyasthana- Ch. 8	5- Vataja, Pittaja, Kaphaja, Sannipaataja,				
		Mridbhakshanajanya				
Bhavaprakasha ¹⁰	Madhyamakhanda- Ch. 8	5- Vataja, Pittaja, Kaphaja, Sannipataja,				
		Mridbhakshanajanya				

4. SAAMANYANIDAANA:

4.1. Following are the common etiological factors of Panduroga:

- Excessive intake of alkaline, sour, saline, hot and mutually contradictory food, unwholesome food, *Nishpava*, *Masha*, *Pinyaka* and *Tila Taila*
- Sleeping during day time, and exercise as well as sexual intercourse even before the food is not properly digested
- Improper administration of *Panchakarma* therapies and contravention of prescribed seasonal regimens (*Ritu Vaishamya*)
- Repression of natural urges
- Devoted to eating clay or salts
- Person with their mind afflicted with passion, worry, fear, anger and grief.

4.2. POORVA ROOPA

- Hridayaspandana (Palpitation)
- *Raukshya* (Ununctuousness)
- *Swedabhava* (Absence of sweating)
- Shrama (Fatigue)
- *Twak Sphotana* (Cracking of the skin)
- Shtheevana (More of spitting)
- *Gatrasada* (General debility)
- Mridbhakshana (Desire to eat mud)
- *Prekshanakootashotha* (Swelling of the eye socket)
- *Vit-mootra peetatva* (Yellowish colour of the faeces and urine)
- Avipaka (Improper digestion)

4.3. ROOPA (LAKSHANA)

- a) SAMAANYALAKSHANA
 - Karnakshweda (Tinnitus)
 - *Hatanala* (Repression of the power of digestion)
 - Daurbalya (Weakness)
 - *Sadana* (Prostration)
 - Annadwit (Aversion against food)
 - *Shrama* (Fatigue)
 - Bhrama (Giddiness)
 - *Gatrashoola* (Pain in the body)
 - Jwara (Fever)
 - Shwasa (Dyspnoea)
 - Gaurava (Heaviness)
 - Aruchi (Anorexia)
 - *Mrudita- Peedita- Unmathita Gatra* (Feels as if all the limbs of body are being kneaded, squeezed and churned)
 - *Shoonakshikoota* (Swelling of the orbital region)
 - *Harita* (Green complexion)
 - Sheernaloma (Falling of skin hair)



- *Hataprabha* (Loss of lustre)
- Kopana (Irritable)
- Shishiradweshee (Dislikes cold)
- *Nidraalu* (Oversleep)
- *Stheevana* (More spitting)
- *Alpavaak* (Avoid speaking)
- *Pindikodweshtana* (Cramps in calf muscles)
- *Aarohana Aayase Kati-Uru-Paada Ruk Sadana* (While making efforts for climbing, pain and weakness in the lumber region, thighs and feet occurs).

In *Panduroga*, there is swelling around umbilicus, whiteness of eyes, deformity of nails, loss of appetite and swelling in the eye sockets. Child becomes apathetic and digestive capacity and desires for blood.

5. CONCEPT OF BEEJA, BEEJABHAGA AND BEEJABHAGAVAYAVA:

Table 2 : Showing Beeja, Beejabhaga, and Beejabhagavayava according to Charaka in the concept of Rakta Dhatu

Dinita					
Terms in classics ¹¹	Nearer terms in genetics				
Beeja	Sperm and Ovum				
Beejabhaga	Chromosomes				
Beejabhagavayava	Gene locus: Promoter region, Exons, Introns				

- **Beeja:** The Beeja from which the erythrocytes (*Rakta Dhatu*) develop can be traced back to hemangioblasts. Vascular Endothelial Growth Factor (VEGF) induces the mesodermal cells, from surrounding mesodermal cells to differentiate in to Hemangioblasts. These hemangioblasts forms blood islands in the wall of yolk sac. The hemangioblast at the center of these blood islands of the hemopoetic stem cells, which are the precursor of all the blood cells. The mesoderm arises from the zygote, which is the product of union of sperm and ovum through the process of fertilization. Thus, the concept of Beeja that is responsible for the formation of *Rakta Dhatu* should include sperm and ovum.
- *Beejabhaga:* The chromosome 16 and chromosome 11 can be taken as *Beejabhaga* that are accountable for the formation of *Rakta Dhatu*.
- Beejabhagavayava: The Beejabhagavayava (the gene locus) on the short arm of chromosome 16 also called as <u>α</u> gene cluster (30 kbp of DNA) and it consists have <u>α</u> and <u>ζ</u> genes and some pseudo genes. The <u>α</u> gene is duplicated on this chromosome; hence there are four copies of this gene on this chromosome. The Beejabhagavayava (the gene locus) located on chromosome 11p 15.6, also called as <u>β</u> gene cluster (50 kbp of DNA) includes the embryonic globin gene, epsilon (<u>ε</u>), the fetal globin gene (<u>γ</u>) and two adult globins genes, <u>δ</u> and <u>β</u> genes.

5.1. CONCEPT OF RANJAKA PITTA:

Acharya Sushruta indicated the location of Ranjaka Pitta in the Yakrita and Pleeha. It plays an important part in the formation of Rakta Dhatu. According to Acharya Charaka, Rasa is colorless and it gets colored red under the influence of heat of Pitta. Rasa becomes colored red while passing through Yakrita and Pleeha under the influence of the Tapa of Tejasa i.e. Ranjaka Pitta or Ranjakagni.

According to C. Dwarkanath, *Pitta* comprehends a large group of biochemical substances that take part in such important functions as digestion, metabolism, heat production, hemopoesis etc. and mentioned that the study of *Pitta* is in part, the study of enzymes, though some of the internal secretions of the body may also have to be considered in this connection. That the enzyme system as a whole and some of the hormones in part answers to the requirement of the *Pitta* can be deduced from a careful study of the function ascribed to the both. C. Dwarkanath has also given a beautiful methodology to search the substances included in the concept of *Pitta*. According to C. Dwarkanath the *Karma* (functions) and *Guna* ascribed to *Pitta* in its different aspects, should be considered and a systematic search should be carried out, to find out to which substances these functions and qualities refers.

5.2. CONCEPT OF RAKTA DHATWAGNI:

The *Rakta Dhatwagni* is responsible for the synthesis of *Rakta* consuming the *Poshya Rakta Dhatu* from *Rasa* and it is further amenable for the maintenance of *Sthayee Rakta Dhatu*. Thus, various enzymes responsible for the synthesis of hemoglobin specifically the globin portion and membrane proteins, during different stages of maturation



of erythroid precursors should be included under this concept. Again after maturation the erythrocyte depends upon anaerobic glycolysis for energy. The erythrocytes have considerable repair capacity. The ATPs are utilized for the glucose consumption and maintenance of ionic composition, which in turn are responsible for the longevity of the RBCs. Further it can also reduce the met hemoglobin and oxidized glutathione, synthesize glutathione and reseal its membrane, if portion of it is lost.

5.3. FUNCTIONS OF RAKTA DHATU:

Rakta Dhatu is responsible for *Jeevana Karma. Rakta* is included in *Dasha Pranayatana*. It carries oxygen to all the tissues and thus maintains colour, strength, health, happiness and life itself. It strengthens muscular tissue and is responsible for maintaining optimum functions of skin and other sense organs. *Pitta*, i.e. the waste product of *Rakta*, is important for digestion. It also maintains life, complexion and nutrition of tissues. As blood is vital for existence, one must always take care to see that the volume as well as the quality of blood is well maintained.¹² *Acharya* Charaka has described the signs and symptoms of persons endowed with pure blood as, clarity of complexion, normal functioning of the sense organs, unobstructed digestion and activities, happiness, contentment and strength. Hereby, the *Rakta Dhatu* performs different *Karmas* like *Varna Prasadana*, *Asamshaya Sparsha Gyana*, *Dhatu Purana*, *Mamsa Poshana* and *Kshaya* or *Vriddhi* of the other *Dhatu*. These functions in turn results in *Deha Dharana* which is responsible for *Prananuvartana* on which depends the *Bala*, *Sukha*, *Aayushya* etc.

6. DISCUSSION AND CONCLUSION:

Samprapti (Etiopathogenesis) of this disease can be understood in the way that Pitta Pradhana Tridosha affect the functions of Raktavaha Srotasa and ultimately the process of formation of Rakta Dhatu is affected and produces Rakta Vikriti. Constant production of Vikrita Rakta Dhatu leads to various symptoms in the form of Tridoshajanya Pandu. There is no one to one correlation to Thalassemia with any type of Pandu. But by following the methodology mentioned by Acharya Charaka in Vimaanasthaana (Trividharogavisheshavigyaaneeya Adhyaaya), Thalassemia may be correlated to Tridoshajanya Panduroga and named as Beejadushtijanya Pandu, Kulaja or Aanuvanshika Pandu. Beejadushti is chief causative factor; Sarvashareera and Mana are the Adhishthaanas of the disease. Though, Thalassemia is Asadhya Vyadhi (incurable disease), prevention can be achieved through Atulyagotriya Vivaaha (nonconsanguineous marriage) as well as modern diagnostic techniques.

Thalassemia is not mentioned as such in Ayurveda but in both Thalassemia and *Pandu* the cardinal features appear to be the same that is *Pandutva*. Again, the genetical basis of this disease is well established. The terms *Kulaja*, *Aanuvanshika or Sahaja* are described in our classics to indicate the inheritable nature of the disease. Hereby, the name given to the disease thalassemia like *Kulaja Pandu / Aanuvanshika Pandu* seems to be appropriate to define this disease entity.

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