Role of *Amlavetasa* (*Garcinia pedunculata* Roxb. ex Buch.-Ham.), an *Ayurvedic* drug in E-β Thalassaemia : A case study

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Thalassaemia has been recognized by the World Health Organization as an important inherited disorder which has an impact mainly on the populations of low income countries. The prevalence of variant haemoglobins varies considerably with geographic location and racial groups. Four hemoglobin variants, Hb S, Hb C, Hb E, and Hb D each affects millions worldwide and they represent a major public health problem in many areas of the world including South East Asia. However, in India, haemoglobin E-beta thalassemia is prevalent in Bengal and the North-eastern region, but relatively rare in the rest of the country. Genotype is responsible for almost one-half of all severe beta thalassemia worldwide characterized by marked clinical variability from asymptomatic anemia to a life-threatening disorder requiring regular blood transfusions from infancy life, iron chelation and management of secondary complications of iron overload. *Ayurveda* texts do not describe any disease similar to thalassemia. But considering the pathophysiology of disease in *Ayurveda*, it may be understood as a *Beejadoshajanya Pandu*. The following case study focuses on effect of *Amlavetasa* as a new adjuvent treatment on an 8-year-old girl having Hb E-β-thalassemia with several episodes of blood transfusions and increased serum ferritin level (2514 ng/mL) whose serum iron was marked down to significant level in due course of treatment. An effort was made with the hypothesis that *Amlavetasa* acts as an iron chelator in the management of β thalassemia (Hemoglobin E Disease) and improves the quality of life by increasing the gap of blood transfusion. Assessment was done on subjective and objective parameters after 6 months of treatment with follow up of two months.

**Keywords**: Hb E-beta Thalassaemia, *Amlavetasa*, *Ayurveda*, Iron chelation.

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Beta-thalassemias are a group of hereditary blood disorders characterized by anomalies in the synthesis of the beta chains of hemoglobin resulting in variable phenotypes ranging from severe anemia to clinically asymptomatic individuals. Thus, the affected individual may be symptomatic and transfusion dependent at an early age. Hemoglobin E trait is the third most common hemoglobin disorder in the world and the most frequent one in South east Asia, where its prevalence is estimated to be 30 %. Although it is associated with no morbidity, the offspring of individuals who carry this hemoglobin variant may exhibit hemoglobin E-β-thalassemia if the other parent has β-thalassemia trait and contributes that gene. This combination is the most common cause of transfusion-dependent thalassaemia in areas of South east Asia¹.

β-thalassemias are caused by point mutations or, more rarely, deletions in the beta globin gene on chromosome 11, leading to reduced (beta⁰) or absent (beta) synthesis of the beta chains of hemoglobin². Hemoglobin E (Hb E) disease is a mild, inherited blood disorder characterized by an abnormal form of hemoglobin, called hemoglobin E. People with this condition may have very mild anemia, but the condition typically does not cause any symptoms. It is inherited in an autosomal recessive manner and is caused by a mutation in the *HBB* gene³.

Pathophysiology of Hb E/β-thalassemia is related to many factors including reduced β chain synthesis resulting in globin chain imbalance, ineffective erythropoiesis, apoptosis, oxidative damage, and shortened red cell survival. Major genetic factors are responsible for its clinical heterogeneity ranging from essentially asymptomatic to severe transfusion-dependent life threatening condition. Interaction between Hb E and β-thalassemia alleles is the main determinant in pathophysiology⁴. The mutation that causes hemoglobin E disease primarily occurs in South east Asian populations, and rarely in Chinese

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populations. Most people with Hb E disease do not need any treatment. Hemoglobin E (Hb E) is estimated to affect at least one million people around the world. Carrier frequency of hemoglobin E/β-thalassemia (Hb E/β-thalassemia) is highest in South east Asia, reaching as high as 60% in parts of Thailand, Laos, and Cambodia. In the Indian subcontinent, highest frequency is observed in the North east regions, but relatively rare in rest of the country. Increasing migration of population from highly affected areas is resulting in rising prevalence in the South and other parts of India. Hb E/β-thalassemia is characterized by marked clinical diversity, phenotypic instability, and age-related changes in adaptation to anemia.

In Ayurveda it is a new clinical entity, and hence is termed as Anukta Vyadhi, which means ‘not told, unheard of’. According to Ayurvedic parlance thalassemia can be named as Beejadhustijanya Vikara. The Samhitas have not described any disease similar to thalassemia but when the pathophysiology and clinical features of the disease are examined under the lens of physiology and pathology concepts of Ayurveda, it may be understood as a Beejadoshajanya, Sahaja vyadhi, whose nomenclature may be correlated with Beejadushhtijanya Pandu. It is a Pitta pradhana tridoshaja disease, wherein the process of formation of Rakta dhatu is affected due to Sahaja karana, affecting the functions of Raktavaha srotasa and results in Raktavikriti.

Amlavetasa – Garcinia pedunculata Roxb. ex Buch.-Ham. of Guttiferae family (commonly known as Thaikal in Bengal) is an excellent cardiac stimulant, digestive and laxative used in Ayurved since 1500 BC. The principle chemical composition are pedunculol, garcinol, cambogin with the medicinal qualities as follows: amla rasa (sour taste), amla guna, laghu (light), rooksha (dryness), amla vipaka (undergoes sour taste conversion after digestion), ushna veerya (hot potency), effect on tridosha like it balances Kapha and Vata Dosha, increases Pitta Dosha. Its classical uses are in the treatment of cough, asthma, bronchitis, piles, intestinal worms, bloating, splenomegaly, anemia, heart diseases, anorexia, indigestion, constipation, abdominal pain due to digestion imbalance and bloating, for the treatment of epilepsy, toxic conditions, dysuria, ascites, malabsorption syndrome, etc. It is commonly found and harvested in North eastern states of India like Assam, Manipur and Shilong.

The main aim of such type of study is to provide a better quality of life and to reduce complication of blood transfusion and delay transfusion interval by Ayurvedic approach.

Case report

The following case study focuses on a 8-yr-old girl with OPD registration No. 6686/16-17; who reported to general out patient department of National Research Institute of Ayurvedic Drug Development, Bidhannagar, Kolkata, West Bengal with a chief complaint of jaundice, anemia, recurrent fever, generalized weakness, anorexia and fatigued for last few months.

Medical History: Revealed that she is a known case of Hb E-Beta Thalassemia by birth with repeated blood transfusions (17 total) and intermittent jaundice since she was 1.1 years old. Her parental screening revealed that father: Hb E trait and mother: Hb E-Homozygous. Her Haemoglobin Electrophoresis (Double band) shows, one band at Hb A/F region, another band at HbA2 region.

Physical examination reveals: The child was found to have growth retardation, thalassemic facies, splenomegaly and mild hepatomegaly with pallor (Figs 1-3), with evident icterus. First blood transfusion was at 18 months of life. Initial investigations of 2009-2010 showed Blood Group O (-Ve) and Hb of 6.1 g/dL, MCH of 17.4 pg, MCV of 57.7fl, PLT of 480x10^5/µL & RDW of 36.6 %. PS showed anisopoikilocytic RBCs, target cells with few nucleated RBCs and occasional fragmented cells. Hb Electrophoresis showed HbA0 = 2.6 %, HbF = 44.1 %, HbA2+E = 51.6 %. Patient had not undergone any Spleenectomy. Patient has no siblings too.

Before starting the treatment on 12.11.16, her CBC values as below:
- HB : 6.4 g/dL
- Ferritin Assay (By AIA 360): 875.2 ng/mL
- Bilirubin (total) : 2.17 mg/dL

Treatment regimen: Patient was given Amlavetas fruit pulp in the the dose of 10 g once daily to be taken at early morning on empty stomach for the regular use for 08 months. The fruits were soaked in.
the water and made into paste form. With this medication, the patient was not advised to follow any specific Pathya-Apathya during the scheduled treatment period.

**Results**

During the first follow up of 02 months it was noticed that the clinical symptoms like malaise, nausea, recurrent fever subsided except anemia. Meanwhile CBC was repeated on 13-01-17 revealed serum ferritin 311.12 ng/mL which has dropped down from previous value 875.2 ng/mL.

After 6 months of uninterrupted medication with Amlavetas, patient’s CBC values on 06-07-2017 were: HB: 5.6 g/dL, Serum Ferritin level (Chemiluminescent Immunoassay): 168.71 ng/mL and total Bilirubin: 4.4 mg/dL. Her family reported that she remained fine without transfusion for almost 02 months. She was receiving regularly Amlavetas fruit pulp as an adjuvant therapy during the course of treatment. Her body weight also increased from 17 kg to 20 kg during this treatment period (Table 1).

She was seen in every 02 month interval throughout the study for clinical examination and laboratory tests. A complete blood count, Serum iron, total iron binding capacity, ferritin, bilirubin were measured at 2 monthly intervals.

**Discussion**

Ayurveda has different holistic view while treating any disease. Etiopathogenesis and clinical features of thalassemia have got maximum resemblance with Beejadushtijanya Pandu. It is a Pitta pradhana tridosha disease. So it can be interpreted by the application of methodology described by Acharya Charaka in Vimanasthana in context of Anukta Vyadhi.

Because the hemoglobin in RBCs is an iron rich protein, regular blood transfusions can lead to a build up of iron in the blood. The excess iron of the transfused blood starts depositing in various organs and tissues. Consequently such organs and tissue get damaged and suspected to be failing in its functioning. Liver of the patient is also seen affected after several transfusion therapies due to over iron deposition. This condition is called iron overload. It

<table>
<thead>
<tr>
<th>Investigation parameters</th>
<th>Before treatment (11/11/16)</th>
<th>After treatment (13/01/17)</th>
<th>After treatment (09/07/17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>4.4 g/dL</td>
<td>5.6 g/dL</td>
<td>5.6 g/dL</td>
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<tr>
<td>Serum Ferritine</td>
<td>875.2 ng/mL</td>
<td>311.12 ng/mL</td>
<td>168.71 ng/dL</td>
</tr>
<tr>
<td>Serum Bilirubin</td>
<td>2.17 mg/dL</td>
<td>4.5 mg/dL</td>
<td>4.4 mg/dL</td>
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damages the liver, heart, and other parts of the body. To prevent this damage, iron chelation therapy is needed to remove excess iron from the body.

In the present study, Amlavetas is given with the hypothesis that it might have potential iron chelating activity and would contribute to the reduction in S. Ferritin. After 6 months uninterrupted treatment patient’s serum iron level decreased upto 168.71µg/dL, but no relevant changes in hemoglobin and bilirubin parameters. Her body weight measured 20.71kg which was markedly increased from 17 kg. After treatment spleen measurement was 2.5 cm whereas it was palpable up to 4 cm per abdomen initially. Above all receiving Amlavetas adjutently improved her associated symptoms such as nausea, fever, weakness, whole bodyache, etc.

To combat the burden of hemoglobinopathies in India, there is an urgent need for the prenatal diagnosis of thalassemia. Hemoglobin E-beta thalassemia patients are treated with life long blood transfusion for every 15 to 30 days along with iron chelation therapy. Apart from the psychosocial and emotional trauma, thalassemia also poses a huge financial burden for the family. The costs of chelation for removing excessive iron and for Blood transfusion is closed to ₹ 10,000/- to 15,000/- per month which can be prohibitive for families with limited means. Normal growth of Thalassemia children during the first 10 yrs of life depends on the maintenance of haemoglobin levels above 8.5 g /dL; during this period hypoxia may be the main factor retarding growth and the maintenance of Hb levels together with adequate iron chelation therapy makes the Beta thalassemia patients indistinguishable. Though Blood transfusion is ideal procedure to maintain haemoglobin g % and to save life of thalasaemic patient; now a days parallel approaches are being adopted to correct the resulting haemoglobin and iron imbalance, in an endeavor to move beyond the life long red blood cell transfusion, iron chelation and splenectomy, which impose high costs on healthcare systems. Administration of indigenous drugs help to avoid recurrent transfusion, minimizing the clinical findings and increase the hemoglobin g % in blood picture. The patients of thalassemia must be given moral support, they should be accepted by the society with open arms.

In conclusion our findings provided that present study inferring that this OPD based case had received more than 16 transfusions and her spleen was enlarged more than 4 cm. But after receiving Amlavetas fruit pulp as the enlargement of spleen was gradually reduced (upto 2.5 cm), most of the complaints like fever, weakness, and pain in extremities, lack of thrive even the body weight was gradually improving during the course of treatment.

**Conclusion**

This case study revealed the success of Ayurvedic medication, without any adverse effect. Amlavetas is used with the hypothesis as an iron chelating agent as the fruit pulp helps to decrease iron overload from body, normalize iron metabolism, prolong RBCs life span, relieve signs and symptoms of the disease, increase Blood transfusion interval. All these factors increase the expectancy of good life as well as improve quality of life of thalassemic patient.

However, large scale clinical studies would be more confirmatory. Attempt of prescribing Amlavetas fruit pulp as an adjuvant to Thalassemic patient would improve the overall quality of life and increase the gap of blood transfusion.

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**References**