A critical review on neonatal hyperbilirubinemia—an Ayurvedic perspective

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ABSTRACT

Neonatal hyperbilirubinemia is the elevation of the bilirubin level in the newborns blood, which results in yellowish staining of the skin and sclera of the newborn eyes by pigment of bile. It is due to the breakdown of RBC’s (which release bilirubin into the blood) and the immaturity of newborns liver (which cannot effectively metabolize the bilirubin and prepare it for excretion into the urine). Increased bilirubin production, reduced hepatic clearance and enhanced enterohepatic circulation are the sole causes of increased prevalence of jaundice in newborn. The science of Ayurveda is supposed to add a step in order to understand the pathophysiology of neonatal jaundice that have resemblance with clinical entity of kamala (jaundice) mentioned in Kashyapa Samhita. The concept of neonatal hyperbilirubinemia in Ayurveda can be understood in the context of Pittaja stanya dushti along with the physiological variations in the newborns leading to the raised level of unconjugated bilirubin. Therefore, the patho-physiology should be known by a pediatrician in Ayurveda based on the involvement of dosha, dhatu, mala and srotas. Hence, an attempt is made in this review to discuss about the hidden concept of pathology of neonatal jaundice described in Ayurveda. These findings to understand the concept of neonatal jaundice in Ayurveda add up to the Ayurvedic science that has been developed through ages.

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1. Introduction

Newborn have unique health issues and problem due to structural and functional immaturity of various body organs depending upon their gestational age and birth weight [1]. Jaundice is the most common abnormal finding in neonates. About 60% of term and 80% of preterm babies develop jaundice in the first week of life. Untreated severe hyperbilirubinemia often signifies a serious illness [2]. Unconjugated bilirubin can cross the blood brain barrier due to many factors. These include alterations in the bilirubin binding capacity of albumin and other proteins and disruption of the blood brain barrier due to underlying conditions like asphyxia, acidosis etc. It is due to physiological polycythemia, shorter lifespan of RBC (90 days vs 120 days in adults), limited hepatic uptake, conjugation and excretion of bilirubin due to transient deficiency of receptor proteins and UDGPT enzymes in newborn especially in premature.

It is also due to paucity of bacterial flora in the gut and over activity of beta glucuronidase enzyme in the newborn. In India, physiological jaundice, immaturity, blood group incompatibility, antenatal and postnatal infections, G-6PD deficiency and breastmilk jaundice are the causes of order of incidence of neonatal jaundice. Higher prevalence of jaundice is due to increased bilirubin production, reduced hepatic clearance and enhanced enterohepatic circulation in newborn. Increased bilirubin production can overwhelm the normal buffering capacity of the blood and result in the production of bilirubin acid, which is highly neurotoxic. It may cause transient encephalopathy and kernicterus which may progress over 24 h to 7 days [3].

The broad aim of this article is to provide a general outline on the description of neonatal hyperbilirubinemia from Ayurvedic perspective. This article reviews the available literature to understand the pathological changes and its manifestations in relation to neonatal hyperbilirubinemia through Ayurveda. It is written with an intention to create awareness and implement the principles mentioned in the ancient texts, suggesting an integrated approach in its management and treatment.
2. Analysis of neonatal hyperbilirubinemia in Ayurveda

By looking on to the signs and symptoms of the neonatal jaundice, it can be considered similar as that of the features of Kamala explained by Kashyapa Acharya in Kashyapa Samhita.

The Signs and symptoms of Kamala related to shishu (infant) are described in Vedana Adhaya, Sutrasthana, Kashyapa Samhita are considered to be an exclusive texts on pediatrics in Ayurveda. Vedana Adhaya is written by Vruddha Jeevaka after he prayed to Lord Kashyapa to explain the features an infant will show, when he is not able to express his pain, for the diagnosis of various diseases [4] (How a physician should know, only on the basis of clinical features, about various pains children's who cannot narrate the symptoms.)

2.1. Historical review

Rigveda: Rigveda in one of its hymn, mentioned prayer of Surya (Sun God) referring to the submission to remove Harimana ie; to remove yellowish pigmentation and make the complexion normal.

Atharvaveda: Ayurveda is the Upaveda of Atharvaveda. In Atharva-veda, Kamala was known by the name Harima — It is so because all the body parts become Haridravarna (yellowish) in Kamala vyadhi (jaundice). Atharvaveda suggest Surya kirana snana (exposure to sunlight) for Kamala as described in Suryakirtana chikitsa prakarana of Atharvaveda. Here sunlight function on the body to remove yellowish discoloration of the body as similar to that of phototherapy described in modern science for neonatal jaundice [5].

2.2. Disease review

Acharya Charaka has described the disease Kamala (jaundice) under the chapter of ‘Panduroga chikitsa upakarma’ [6]. Acharya mentioned different nidanas (causes), bheda (types), lakshanas (symptoms) and Chikitsa (treatment) for the disease. Kamala. Kamala related to Balaka (infant) is due to ingestion of Dushita Shanyya (vitiated breast milk) described in Charaka Samhita [7] and Madhava nidana [7] (Table 2).

In Ashtang Hridaya sutrasthana, disease Kamala is formed due to increased raktu dhata (blood plasma) [8] (Table 1).

There is a detail explanation of dronupushpi swarasa anjana (eye application) in kamala [9]. The above text also provided an explanation regarding stanya dushti (vitiating of breast milk) by various doshas (bodily humors) and their symptoms with management, where the author described Kamala as a symptom of pittaja stanya dushti (breast milk vitiated by Pitta). Under the same, Acharya explained the use of Guduchi, Shatavari, Patola patra, Nimba twak and Raktachandana processed with sharkara in pittaja stanya dushti to mother and child [9].

Acharya Kashyapa described the Lakshana of Kamala Vyadhi (symptoms of jaundice) related to balaka (infant) in Vedana Adhaya, Sutrasthana of Kasayapa Samhita. But the Nidana (causes), Sampat (pathogenesis) and Chikitsa (treatment) are not been mentioned in Kashyapa Samhita.

The symptomatology of Kamala is quite similar with jaundice of neonates, as this grantha (book) is uniquely described for Pediatrics. Kashyapacharya also described the disease as one of the lakshana’s of Revati graha [10]. The Revati graham has synonyms like Shasthi, Mukhandika. Acharya advised to worship shasthi maata on 6th day after birth of child (neonatal period). This make clear that it can affect the neonate by producing symptoms like Neonatal jaundice.

Virechana (purgation) has been considered as the best treatment according to Kashyapa in Pittaya Stanya dushti. For “Daungandhya Dasha” (a type of Pitta vitiated breast milk) use of Vishanika, Ajashringi, Triphala, Rajani, Vacha with cold water is indicated.

There are two references in classical texts of Ayurveda where the jaundice in newborn can be considered—

2.3. Stana dushti — a source for neonatal hyperbilirubinemia

Milk is defined as the essence of Rasa dhatu (plasma), which in turn depends on the diet and its assimilation in the mother. A navajata shishu (newborn) is dependent on to his mother for the food and nutrition. Therefore, breast milk if gets vitiated by the doshas (body humors), manifests various diseases as per the predominance of the doshas. The causes of vitiation of milk can be due to the defective dietetic intake in quality and quantity in the mother (Excessive use of snigdha (unctuous), abhishyanda (food which increases kapha) and guru (heavy) substances like paayasam or over intake of katu (spicy), amla (sour), lavana (salty) and kshara (alkali) substances) and also due to the defective eating habits and impaired digestion in mother [12]. Kashyapa describes number of grahas also to vitiate milk: Shakuni making the milk acrid and bitter and Pootana bring sweet and acrid taste in milk.

2.4. Pittaja stana dushti-an origin to neonatal hyperbilirubinemia

Milk vitiated by Pitta either gets discolored (Vivarnata) or acquires a disagreeable fetid smell (Durgandha) with more waste metabolites or decomposed, as though, the milk is kept at room temperature for long time. “Acharya Charaka” stated- The diseases of children and that of adults are quite similar but the difference is only in the dosha dushta, which are in smaller quantity than that of the adult [12]. Hence, the disease will be reviewed as per Charaka’s description for adults in consideration for the neonates. In Ayurveda Pandu roga (anemia) and Kamala are described together [12]. Stage 1- Pandu (5 types of Pandu according to dosha pradhaananta (predominance of body humors) explained by Charakacharya).

In above mentioned conditions, or even without Pandu roga (anemia) when one indulges in Ateeva Pitvardhaka Ahara (food that causes Pitta vitiation), Kamala (jaundice) ensues in stage 2 (a) Vataja pandu with added Pitta produces Halemaka; (b) Pittaja pandu with added Pitta produces Kamala and (c) Kaphaja Pandu with added Pitta produces Kumbhakamala.

Table 1: Showing dhatu parinaama (tissue formation).

| Fuel | Dhatvagni | Prasada paka (essence) | Kitta paka (waste) |
|------|-----------|-----------------------|-------------------|
|       | Sthula bhaga | Sukshma bhaga |                      |
| Poshaka Rakta | Rasagni | Poshya Rakta | Rakta | Malrupa Kapha |
| Poshaka Rasa | Rasagni | Poshya Rasa | Rakta | Malrupa Pitta |
3. Etiopathogenesis

Severe depletion of ‘Ojas gunaah’ (essence) in body (like bala, varna, sneha etc.) leads to alpa rakta (anemia), alpa meda (loss of fat) and nissara (less essence) which in turn causes shithila indriya (weakness of the sense organs) [12]. Such child attains vaivarnata (discoloration) of skin like pandu (pallor), haridra (yellow), harita varna (green color). The depletion of ojo guna (essence of body) occurs due to 3 group of causes:

1. Group 1: Depression of RBC synthesis (dyshaemopoietic) due to excess intake of lavana, katu and Kashaya rasa (astringent taste)- can be considered in terms of dushta stanyaa paana (intake of vitiated milk) [13] and Pica/mud eating-cannot be considered in neonatal hyperbilirubinemia.

2. Group 2: Vitiation of Pitta pradhana doshas and dhatus (Pitta predominant body humors and tissues) leads to gauravam (heaviness) and shithilata (loosening) of that particular dhatu which further leads to depletion of ojo guna. Various metabolic and hemolytic causes are Maireyamadya sevana (alcohol intake) (cannot be considered in neonatal hyperbilirubinemia) and Daurgandhya stanyaa sevana (Pittaya stanyaa dushti).

3. Group 3: Various hemorrhagic conditions leads to rakta kshaya (depletion of blood)- cephalhematoma and sub-galeal hemorrhage in newborn can be considered. In conditions where there is depletion of ojoguna, if one indulges in Pittavardhaka ahara, Vayu through the ten dhnamenees (blood vessels) brings and lodges the pitta in twak (skin), mamsa (muscle) and rakta. This pitta burns these dhatus and produces different kamala (based on dosha). Thus kamala can occur in two ways: (a) Excessive Pitta in Pandu- Koshtashrira or Shashkhara kamala. (b) Without Pandu roga also as Pittolbana (due to increased Pitta).

Therefore, Kamala is Pitta dosha pradhanav vyadhi.

Table 2
Showing lakshana (Clinical features) of different stages of Kamala

| Clinical features | Koshtashrira | Shashkhara | Halimaka | Kambha kamala | Lagharaka and Alasa | Panaki |
|------------------|--------------|------------|----------|---------------|---------------------|--------|
| Haridra Netra    | Yes          | Yes        | Yes      | No            | No                  | No     |
| Haridra Tvak     | Yes          | Yes        | No       | No            | No                  | No     |
| Haridra Nakha    | Yes          | No         | No       | No            | No                  | No     |
| Haridra Mukha    | Yes          | No         | No       | No            | No                  | No     |
| Haridra mutra    | No           | Yes        | No       | No            | No                  | No     |
| Rakta Peeta Mutra and Puresha | Yes | No       | No       | No            | No                  | No     |
| Sweta varcas     | No           | Yes        | No       | No            | No                  | No     |
| Tila -pishtanibha varcas | No | Yes       | No       | No            | No                  | No     |
| Krishna Peeta Puresha & Mutra | No | No       | Yes      | Yes           | No                  | No     |
| Jvra             | Yes          | No         | Yes      | No            | Yes                 | No     |
| Aruchi           | Yes          | No         | No       | Yes           | Yes                 | No     |
| Daha             | Yes          | No         | Yes      | No            | Yes                 | No     |
| Daurbalya        | Yes          | Yes        | No       | No            | Yes                 | No     |
| Shotha           | No           | No         | Yes      | No            | No                  | No     |
| Angamanda        | No           | No         | Yes      | No            | Yes                 | No     |
| Bhrama           | No           | Yes        | No       | Yes           | No                  | No     |
| Kshaya           | Yes          | Yes        | Yes      | No            | Yes                 | No     |
| Shrota           | No           | No         | No       | No            | No                  | Yes    |
| Sarakta Netra    | No           | No         | No       | Yes           | Yes                 | No     |
| Sarakta Puresha  | No           | No         | Yes      | No            | Yes                 | No     |
| Sarakta Mutra    | No           | No         | Yes      | No            | Yes                 | No     |
| Shwasa           | No           | No         | Yes      | No            | Yes                 | No     |

Koshtashrira kamala: Pandurogi (anemic) or by ingestion of Pittakara Ahara-Vihara leads to Pittaprapaka (excessive vitiation of Pitta). That Vitiated Pitta produces Vidaha (burning) of Mamsa (muscle tissues) and Rakta (blood). Vitiated Pitta gets accumulated in liver and then spread all over the body causing Bahupitta Kamala (hyperbilirubin) or koshtashrira Kamala [12]. In Koshtashrira Kamala, shakhashrira Kamala: Pandurogi (anemic) and or Pittolbana (having excessive Pitta) person who ingests Pittaja Ahara-Vihara, Pitta aggregates and produces kamala (jaundice). For this, specific causes like Dadhi sevana (curd) [14], Dushta stanyaa sevana (vitiated milk intake) [15], Raktavaha Strodotrushthi (vitiation of the blood channels), katurasa sevana (spicy food) [16] are mentioned.

In Koshtashrira Kamala, the excessive Pitta vridhi (increased pitta) due to all the above mentioned nidana (causes), produces abnormality in the Raktavaha srotas (blood channels) and Raktavaha srotomula (origin of blood channels), dusha dashyassamamurchan (pathogenesis) occurs in liver. Then ati pravritti (excessive flow) of pitta occurs through pitta vaha srotas (channels carrying Pitta) into the koshtha, resulting in the dark yellow coloration of urine and stool. Vitiated vata also causes ati-pravritti of pitta in Rasa-Rakta etc. Dhatu. So when this vridha pitta reaches the sites of the clinical manifestation of Kamala disease via Rasa-Rakta Dhatu, it produces yellow coloration just like that of Haridra (turmeric/yellow color) in these sites i.e. in eyes skin, face nail, urine etc. which is the cardinal signs of Kamala [17]. Nidana of Kamala explained by Acharya Charaka and Madhavakara as dashytha Stanyapanasa (intake of vitiated milk) by the baby which leads to navajata Kamala (neonatal hyperbilirubinemia). In modern science, it can be compared with the mechanism of pre hepatic jaundice or Haemolytic jaundice in which more bilirubin is found in blood due to excessive destruction of RBC and is not excreted adequately by liver resulting in hyperbilirubinemia responsible for various symptoms like yellow discoloration of eye, skin etc. Shashkhara kamala: Here, Vata and Kapha prakopa takes place due to ingestion of Kapha and Vata vitiating factors. When vitiated Vata get combines with vitiated Kapha, causing obstruction in biliary canaliculi, Pitta does not enters into the intestine and gets accumulated in liver. The excessive accumulation of Pitta in liver spreads all over the body except intestine, hence causing clay color stool i.e. Tilipishthanibhi Malapravritti (stools like sesame paste) and yellowish discoloration of Nakha (nails), Netra (eyes), Twak (skin), Mutra (urine). This is called as Shashkhara (at the periphery) or Rudhapatha Kamala (obstructive jaundice). In Shashkhara Kamala, the Koshthashrira Kamalapptas are Kapha and Vata vitiating factors like intake of food having predominantly Sheetu Gunan (cold), Guru guna, Madhura rasa (sweet), Rooksha guna (dry), Ativayayama (excessive exercise).
Vegadharana (suppressing natural urges) etc. In obstructive jaundice, same mechanism can be observed in which the bile ducts are obstructed by gall stone or other causes and bile is accumulated in liver, resulting in elevation of blood bilirubin level responsible for yellowness of eye, skin, mucous membrane and stool become clay colored due to lack of bile in the intestine. In Hepatocellular jaundice, when there is complete obstruction of all the bile canaliculi due to their compression by edematous hepatocytes, jaundice is produced just like shakhashrita Kamala. When there is incomplete obstruction or when all the bile canaliculi are not obstructed then it is produced like that of koshtashrita Kamala.

3.2. Physiology in relation to neonatal hyperbilirubinemia

Raktotapati (Erythropoiesis): Raka Dhatu (blood) is stated to be formed from Rasa Dhatu (plasma) through Dhatu Parinama karma (formation of body tissues). The Dhutaparinama, regular nourishment of the Dhatu of the body, comprise of two pakas [18]. (a) Prasada paka (nourishment)-Leads to production of 7 type of Prasada dhatu. (b) Kitta paka (waste)-Leads to production of kitta or mala of respective dhatu. Three factors participating in Parinama of Rasa dhatu to Raka dhatu, are Rasagni (fire of plasma), Raktaagni (fire of blood), and Kitta paka paka (waste). Rasagni acts on Ahara Rasa and leads to formation of Prasad (Rasi- and Raka dhatu respectively) and Kitta bhaga, i.e. Pitta (Ranjaka Pitta).

During the process of Dhutapurinama (transformation of the tissues), Dhutwagani (factors responsible for tissue transformation) leads to the formation of Rakta Dhatu (blood). All elements of blood, Rakta Dhatu, and Yakrita (liver): is the moola (site of origin). But ranjana karma (providing color) of Rakta is done by Ranjaka pitta situated in Yakrita (liver), Plaha (spleen), and Amashaya (stomach) produced from poshaka Rakta as a malarup [20]. As kamala (jaundice) is a Rakta pradoshaja vyadhi (disorder due to vitiation of blood) having Rakta vratro stroti vihara (vitiation in blood channels), so Yakrita (liver) and Pleheha (spleen) are also important factors involved in the samprapti (pathogenesis) of the disease Kamala.

Relation between Dosha (body humors) and Yakrut (liver): Pitta dosha is formed in Yakrita. It is the primary factor of Ranjaka Pitta. This is the factor involved for the formation of Rakta dhatu (blood) from Rasa dhatu (plasma). Therefore, here the hemolysis of the RBC’s can be considered giving rise to the production of bilirubin.

Relation between Dushya (body tissues) and Yakrut (liver): Yakrta is formed from Rakta Dhatu and it is the moola sthana of Rakta Vastus [21]. Formation of Rakta Dhatu takes place in Yakrita. According to the consideration of Acharya Sushruta and Vagbhata, the Yakrta is derived from the accha (pure) portion of the fetal blood [22]. Hence, the structure is soft, well organized and secretary in nature. It secretes Pachaka pitta that is stored in the Pittashaya (duodenum) or the gall bladder. The concentration of Pitta is very important. If the concentration alters, it leads to lot of diseases arising out of Agnivaishayamya (vitiation of digestive fire). Here, Yakrta can be compared with the organ Liver of the contemporary medicine.

Pitta (Malarupi): Tejas (fire element) is present in the form of Agni, which is present in our body in the form of Pitta [23]. Manifestation of yellow color to body is due to Pitta vrudhdi which is due to tejo mahabhuta (fire element). Kamala is a disease which is due to Pitta vrudhdi. Hence, vitiation of pitta and agnivaishayamaya (impairment of digestive fire) affect each other and vice versa. Moolasthana of Rakta Dhatu strotas is Yakrta and Pleheha. Therefore, it can be understood that prasati of malaruppitita ( bile) takes place in Yakrita with the help of Raktaagni. Because of samana guna (same properties) of Pitta and Rakta, Pittare main along with Rakta in asrayashrayi bhava (association) [24]. When agnivaishayamya (impairment in the digestive fire) happens in the body, then it produces malarupi pitta in larger quantity which is stored in yakrita and circulated all over the body and gives vikruta varna (discoloration) to the body.

4. Clinical features of Kamala

4.1. Pathogenesis of neonatal hyperbilirubinemia in the view of Ayurveda

Due to the Nidana sevana (causative factors), Pitta pradhana tridosha (Pitta predominant body humor) gets aggravated, which in turn vititates the Rakta dhatu (due to ashraya ashrayi sambandha). After Rakta dhatu (blood) getting vitiated, the moola of Rakta dhatu i.e. Yakrut and Pleheha, also gets vitiated and therefore, the Rakta dhatu kshaya (decreased blood) takes place (both in quality and quantity-quality is maintained by the yakt by doing the ranjana karma which can be compared with the conjugation of the unconjugated bilirubin → gets hampered; Pleheha maintains the quantity of rakta dhatu which can be compared with the early lysis of the RBC’s). This leads to the shihilita (impairment) of the Rakta and Mamsa dhatu and therefore, the aggravated pitta due to atipravritti (excessive movement) and vimargamagana (movement in opposite direction), takes sthana samshraya (location) at tvak (skin), rakta (blood) and mamsa dhatu (muscle tissues) and manifest as Neonatal hyperbilirubinemia (Fig. 1).

Samprapti Chataka (factors responsible for pathogenesis) [25].

1. Dosha: Pitta

2. Dushya: Rakta, Mamsa

3. Adhishthana: Kostha (Mahasrotasa — Yakrit), Shakha (Raktadhi and tvacha)

4. Srotas: Rasavaha, Raktaavaha, Annavaha, Pureeshavaha

5. Srotodushthi: Atipravritti (excessive production), Sanga (obstruction), Vimargamagana (moves in opposite direction)- (In physiologic neonatal hyperbilirubinemia, atipravritti and vimargamagana can be considered whereas in pathologic neonatal hyperbilirubinemia, sanga, atipravritti and vimargamagana can be undertaken).

5. Prognosis

While describing the disease kamala of the Acharyas have mentioned its Sadyoha-Asadhyaya, whereas almost all the Acharyas have mentioned that negligence or improper management of Kamala leads to complications which can be taken as the conditions like kernericus, brain encephalopathy, chooro-athetoidal cerebral palsy in the contemporary science. Ayurvedic classics mentioned the following as the Asadhyaya lakshanas (untreatable symptoms) of kamala, indicating bad prognosis like Krishnapetcita mutra and shakrit (dark yellow colored urine and stool), Atishotha (edema), Raktaksita (redness of eye), Raktamutra (hematuria), Daha (burning sensation) Aruchi (loss of taste), Trishna (thirst/dehydration), Anaha (indigestion), Tandra (tiredness), Nashtaggni (loss of appetite), Nashta Sangya (unconsciousness) etc.

So, Kumbhha kamala can be compared with that of the Kernericus explained in modern science as the complication of neonatal hyperbilirubinemia.

6. Treatment

There is no direct reference of Navajata Kamala chikitsa (neonatal hyperbilirubinemia) in Ayurveda, but, as the nidana for navajata kamala is considered to be pittaja stanya dushthi, which is consumed by the baby, pittaja stanya dushti chikitsa is taken as the line of treatment. Generally correction of vitiated milk brings forth normalcy in the child in mild cases. In severe cases, the child can be...
administered medicine depending on the vitiated dosha. Sushruta in chikitsa sthana advocates induction of vomiting to the mother irrespective of the vitiated dosha in milk. Charaka though advocates induction of both vomiting and purging in chikitsa sthana 30th chapter, advises one or more of the four means of commingling i.e. of Vamana (vomiting therapy), Virechana (purgation therapy), Asthapana and Anuvasana (enema therapy), depending on the doshas vitirated [12]. Thus, the principles of treatment of vitiated milk disorder can be classified as follows:

6.1. In mother

General measures taken are (a) Extirpation of the vitiated humor by induction of vomiting irrespective of the Dosha with oral use of the decoction of Nимba with honey and Pippali as advised by Sushruta [12]. (b) Pathya Bhогana [26]. (c) Internal medication to the mother [27] consists of combination of different drugs selected from among the groups of Dosha shaman (dosha pacifying) drugs, Stanyta vishodhana drugs (which treats the vitiated breast milk), Stanyta vardhana (which increases the breast milk formation) drugs.

Specific measures are described in the form of local application to the breasts, in various types of milk vitiations, along with internal medication. In cases of distasteful milk, the mother is made to drink the paste of Draksha, Madhupaka, Sariva and Ksheerakakoli in water. A paste made of Panchakola and Kulaththa is applied on the breasts which when dries off is washed out and the existing milk is removed with a breast pump. The milk that flows later is pure and can be safely given to the infant [12]. Foamy milk can be purified by making the mother take the paste of Patha, Naagara and Moorva in water. The existing milk in breasts is taken out after applying a paste of Anjanam, Shunthi, Devadaru and Priyangu to the mammary glands. Alternatively, Kirata, Guduchi and Shunthi can be used as decoction for oral use and the paste of Yava, Godhuma and Sarshapa for external use. Non-unctuous milk can be corrected by giving to mother, the decoction of Stanyas hodhaka drugs according to availability and by the application of a poultice made of Panchamoola and Jeelaneeya drugs. As usual, the poultice when dries is washed off and the milk is extracted. The milk that accumulates further, becomes pure for the infant to feed. When milk becomes discolored with Pitta, the mother is given with the paste of Yash-timadhu, Draksha, Payasya and Sindhuvara in cold water to drink and a poultice of Draksha and Yashthi is applied over the mammary glands. Repeated extraction of milk after the poultice gets dried and when washed off, brings normal color to the milk. Deodorization of disagreeable odor in milk is achieved by oral administration of either the paste of Vishanika, Ajashringi, Triphala, Rajani and Vacha in water; or the powder of Abhaya and Trikatu in Manjishtha, Shleshmataka and Chandana or Usheera applied to the breasts in similar fashion makes the milk free from disagreeable smell [12]. Excessive viscosity can be removed by oral administration of paste of Duru, Musta and Patha to which Saindhava is added. Slimy milk can be made good by oral use of Takarisha or of Abhaya, Vacha, Musta, Shunthi and Patha. A poultice made of Vidari, Bilva and yashti is applied to the mammary glands in both the conditions and milk is removed [12]. Heavy milk can be made light by oral use of either the decoction of Trayaman, Amrita, Nimba, Patola and Triphala or the paste of Pippalimoola, Chavya, Chittrak and Shunti. A poultice made by Bala, Shunthi and Moorva or of Prishnaparni and Payasya applied to the breasts and washed after it becomes dry makes the milk light [12].

6.2. In child

In mild cases, no treatment to the child is required and hence Sushruta and Agnivesha do not advocate treatment for the child normally when vitiated milk is sucked. The ailment becomes corrected with the treatment of the mother alone. However, Vaghbhat gives description of treatment to the child and this should be applied when humors get vitiated more. When milk becomes vitiated with Vayu, the child is given the powder or ghee prepared
of Rasna, Ajamoda, Sarala and Devadaru to which sugar may be added [28]. In Pittaja milk disorder, the decoction of Amrita, Abheeru, Patola, Nimba, Chandana and Sariva can be given to both, the mother and the child [29]. After applying the paste of Raathapushpa to the nipple and areola, the child is made to suck it without being washed to bring forth an easy emetic effect in cases of vitiation of milk by Kaphadosha [12].

6.2.1. Anulomana and Mruduvirechana

In Kamala vyadhi, Virechana is the main treatment. In Pittaja vikara also, the main principle of treatment is Virechana. Acharyas mentioned anulomana (correcting the direction of Vata) and Mrudu virechaka drugs for virechana karma in Kamala and Pittaja Vikaara. In Balaka, Virechana like Panchakarma is contra-indicated but Mruduvirechana (mild purgative therapy) and Anulamana karma are mentioned [30]. The following formulations mentioned under the disease Kamala (Jaundice) as mentioned in classics can be tried in newborns in an appropriate and palatable form (Table 3).

7. Role of MRP 2 molecule and mode of action of drugs

The pharmaceutical action of the ayurvedic drugs can be understood in two ways i.e. increasing the uptake of the unconjugated bilirubin for its conjugation by the hepatocytes, enhancing the transportation of the conjugated bilirubin to the intestine and then the excretion of the conjugated bilirubin [31]. The increase in the uptake, conjugation and its transport can be understood by the role of MRP 2 molecule. The multi-drug resistance protein MRP2 is an ATP-binding cassette transporter playing an important role in detoxification by transporting a wide range of compounds, especially conjugates of lipophilic substances with glutathione, glucuronate and sulfate, which are collectively known as phase II products of biotransformation. In addition, MRP2 can also transport uncharged compounds in cotransport with glutathione, and thus can modulate the pharmacokinetics of many drugs. For the excretion of the conjugated bilirubin, the rechaka (purgative) property of the drug helps to prevent the rise of serum bilirubin level. The above mentioned drugs for the treatment of Kamala act upon the uptake of unconjugated bilirubin by the hepatocytes, stimulating the MRP 2 protein molecule for the quick transport of the conjugated bilirubin for its excretion by the rechaka property. The drugs by their Pittahara and rasayana (rejuvenative) property help in reducing the formation of malarupi Pitta (bile) and also in the regeneration of the yakrut (hepatocytes) for its uptake. The antioxidant, antimicrobial and immunomodulatory property of the drugs help in scavenging the free radical stress, thereby, prevent the rise in the level of bilirubin.

8. Conclusion

The concept of neonatal hyperbilirubinemia in Ayurveda can be understood in the context of Pittaja stanyas dushti along with the physiological variations in the newborns leading to the raised level of unconjugated bilirubin. Therefore, the patho-physiology should be known by a pediatrician in Ayurveda based on the involvement of dosha, dhatu, mala and srotas. The standard treatment principle mentioned in the contemporary science as phototherapy has its own side-effects [32]. Therefore, Ayurvedic pediatricians should bring forth formulations to prevent the rise of bilirubin to an extent to cause complications like kernicterus etc.

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Table 3

Showing Shama naushadhis in Kamala vyadhi.

| Single drugs                                | Compound drugs:                           |
|---------------------------------------------|------------------------------------------|
| Amrita Swarasa                              | A. Churna: Navayasa Churna                |
| Bhumibhandamaik Svarasa                     | B. Kwatha: Daryyadi lehya                 |
| Daraubhandira Svarasa                       | C. Avaleha: Triphaladi Avalehya          |
| Nimbapatra Svarasa                          | D. Rasoukhadthi: Vidangadi Loha          |
|                                             | E. Chritas: Kalyanaka Chrita             |

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