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CONSTITUTIONAL DELAY IN FEMALES: A CONCEPTUAL STUDY

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ABSTRACT

Puberty is said to be delayed in a female when she has not achieved thelarche at the age of 13 years or has not attained menarche up to 16 years of age in presence of secondary sexual characters. Various factors are responsible for this. Besides chromosomal or genetic and anatomical causes, constitutional delay is one of the causes. Malnourishment may be responsible for this. Chromosomal and anatomic causes have limited scope of treatment, whereas constitutional delay resolves itself or requires supportive management. Improvement of general health can help in its treatment. Considering ayurvedic literature, the concept of delayed menarche is not described exactly, but if we go through areas of *Jataharini*, *Yonivyapad* or *Artava dushti* some conditions related to this can be found. Also, if we take into account the treatment prescribed, it can be applied.

Keywords: Puberty, delayed menarche, *Artava dushti*, etc.

INTRODUCTION

Puberty is an important phase of reproductive development of a female. Various neurological, physical and psychological changes occur around this time. The onset of menstruation, menarche, is an important component of this phase. Changes in the circulating levels of gonadotrophins are responsible for this. Throughout early childhood the levels of circulating gonadotropins continue to remain low, pituitary response to GnRH is minimal and secretion of GnRH from hypothalamus is supressed. The

transition to puberty is characterized by episodic LH secretion associated with the circadian sleep-wake cycle. The rise in LH values becomes 2–4 times higher during sleep as compared to the waking hours. This change is noted during the early phase of onset of puberty. Gradually, the levels of FSH begin to rise and reach a plateau at mid-puberty and the LH levels continue to rise even thereafter until late puberty. These effects are due to the rapidly maturing hypothalamic– pituitary relationship. The sequential changes occurring in the growing girl child indicate that the initial development begins with progressively increasing GnRH secretion, which leads to increased pituitary sensitivity and responsiveness to GnRH stimulation. This results in a rise in levels of circulating gonadotropins, which promote follicular development in the ovaries. The ovaries in response to the above stimulus produce oestrogens that act on the uterine endometrium to initiate proliferation and endometrial growth, a prelude to menarche. In time, the pulsatile secretion of GnRH is established followed by cyclic ovarian function and regular menstrual cycles. [1]

In addition to these changes, body weight also plays an important role in the establishment of menstrual cycle. In some females, despite having normal secondary sexual characteristics and no anatomical or endocrinal abnormalities, menstrual cycle is not established. For menstruation to occur, minimal fat should constitute 22% of body weight. Loss of weight >15% causes amenorrhoea. Leptin in the fat initiates gonadotropin-releasing hormone (GnRH) secretion. When weight reduction falls below required body fat, GnRH and gonadotropin secretions fail. Clinically, fasting, excessive exercise with or without purging and self-induced vomiting cause atrophy or non-development of breasts and amenorrhoea.[2] Constitutional delay is said to be present when secondary sexual characters are present, no anatomical or endocrine abnormality is present, still menstruation fails to occur. Generally, malnutrition, excessive exercise or anorexia nervosa is responsible for this. If serial sampling is carried out during a 24-h period these young women are found to have immature pulsatile release of GnRH. This is the sole reason for their constitutional delay. These young women will eventually menstruate spontaneously as the maturation process proceeds.[3] Considering family history, a sibling or parent may be present who was a "late bloomer". However functional hypogonadotropic hypogonadism is much more common in females. It usually develops secondary to condition that reduce total body fat which is commonly associated with anorexia nervosa or excessive exercise in females. Both involve a significant reduction in calories that also decreases the body's leptin concentration resulting in gonadotrophin deficiency. Decreased LH and FSH secretion combined with lower body fat depresses estrogen production and secretion, thus delaying puberty.[4] Constitutional delay is a common cause of primary amenorrhoea. Its diagnosis should be made only after excluding anatomical or chromosomal or endocrinal dysfunction. In addition to psychotherapy and improvement of nutritional status, hormonal treatment may be given to initiate and establish the endocrine axis.

Treatment

Though constitutional delay does not require treatment, it can have psychological effects. Oral contraceptives can also be given for one cycle for reassurance. Estrogen therapy can also be advised.

MENARCHE IN AYURVEDA

The physiology of puberty or menarche has been narrated precisely in various *Samhitas.* The various changes occurring in the body and causes for these changes along with the resulting effects have been mentioned.

यथा च बालस्य जीर्णस्य । योषितश्चोनद्वादशातीतपण्चाशद्वर्षाया रजस्तनयादय इति ॥ (अ. स. शा. 1/21)[5] रसादेव स्त्रिया रक्त् रजः संज्ञ प्रवर्तते । तद वर्षाद द्वाद्शादूर्ध्व याति पंचाशतः क्षयम । आर्तव शोणित त्वाग्नेयम .... (सु. सू. 14/6) [6]

In description of menstrual cycle, the age of *Rajodarshana* or menarche is said to be twelve years. In females, *Raja* and *Stanya* before twelve years and after fifty years of age are not visible. *Acharya*

Shusruta states that the blood which is termed as *Raja* in females is evolved from *Ras dhatu*. Menstruation starts at the age of twelve years and stops permanently at 50 years of age. Its characteristic is *Agneya*. एव मासेन रसः शुक्रीभवति स्त्रीणा चार्तवम ॥ (सु. सू. 14/14)[7] *Acharya Sushruta* states that time period for *Artava* formation from *Rasa dhatu* is one month अष्टादशसहस्राणि संख्या (सु.सू. 14/15) [8] The *Ras dhatu* stays for about three thousand fifteen *kala* in each *dhatu*. In accordance with this, it takes one month time to convert *Ras dhatu* to *Artava* in females. रसात् स्तन्यं ततो रक्तम् (च. चि. 15/17) [9] According to *Acharya Charaka*, *Artava* is formed through *Rasa dhatu* by the action of *Dhatavagni*. रसादेव स्त्रिया रक्तं रजः संज्ञं प्रवर्त्तते। (सु. सू. 14/6)[10] According to opinion of *Acharya Sushruta, Rakta* is formed from *Rasa dhatu* which is termed as *Raja*. मासि मासि रजः स्त्रीणां रसजं स्त्रवति त्र्यहम् । (अ. हृ. शा. 1/7)[11] In females, *Raja* is produced from *Rasa dhatu* and is excreted every month for 3 days. रसात् आहाररसात् परिणमतो जात रसजमित्यत्र निर्दिष्टम् ..... ॥ (अ. हृ. शा. 1/7, अरूण.)[12]

Acharya *Arunadatta* has opined that this *Artava* is formed from *Ahararasa* and not from *Rasadhatu.* षोडशवर्षयोहि शोणितशुक्रयोर्मध्ये प्रभवतः । अर्वागपि यदाहारविशेषादारोग्याच्च पूर्णे भवत इति परिषत ॥ (का. शा. जाति/4)[13] *Acharya Kashyapa* has mentioned the age as 16 years at which *Shukra* and *Shonita* become capable of action. Further he says that this maturity can be achieved before the age of 16 years by the action of specific diet *(ahara)* and health condition *(arogya).* यथा च पुष्पमध्ये फलमनिर्वृत्त सुसूक्ष्ममस्ति न चोपलभ्यते..... ॥ (का. सं. शा. 5/4)[14]

Acharya Kashyapa states that as the fruit situated inside the flower, being unaccomplished and minute, cannot be procured, as the fire in spite of its presence in all woods cannot be obtained without efforts, similarly production of *Shonita* and *Shukra* in female and male respectively depend upon time and own deeds. परिपूर्णधातुशरीरास्तु यदा भवंति तदा विवेकजललोहितं मासे मासे प्रतिवेदयंति ॥ (भे. शा. 5/6)[15]

For the formation of *Artava, Acharya Bhela* believes that *Dhatuparampara* is one of the causative factors. हीनयोन्यास्तु बालायाः कायं गच्छति शोणितम । अथ पूर्णस्वभावायाः कायं योनि च गच्छति ॥ (का. स. खिल. 9/19)[16] *Acharya Kashyapa* states that *yoni* of girls is *heen* i.e., not developed; so, the blood circulates through whole body. After complete development, this blood flows through both body and *yoni*.

बालानामापि वयः परिणामाच्छुक्रप्रादुर्भावो भवति, रोमराज्यादयश्च विशेषा नारीणाम्। .... (सु. सू. 14/18)[17] आदिशब्दात् स्तन्यार्तवादयः..... । (सु. सू. 14/18; डल्हण टीका)[18]

For *Artavautpatti* there is a particular time period. According to *Acharya Shusruta*, with the lapse of time as the bud becomes flower and fragrance comes, similarly with the passage of time the child reaches to puberty, *Shukra* becomes visible and in females there is appearance of *Romaraji.*

While commenting upon this, *Dalhana* opines that *Artava* can be included here by using the word *Romarajiyadi*.

स्त्रीणां गर्भोपयोगि स्यादार्तवं सर्वसम्मतम । तासामपि बल वर्ण शुक्रं पुष्टि करोति हि ॥ (भा प्र पूर्व 3/188)[19] रजसि चोपचीयमाने शनैः शनैः स्तनगर्भाशययोन्याभिवृद्धिर्भवति ॥ (सु. सू. 14/18)[20] Also, one form of *Artava* in females is described as one that imparts *bala, varna, pushti*, hence it is considered as *Dhatu* similar to *Shukra dhatu* in males. According to *Dalhana*, this *dhatu rupa Artava* is responsible for *yoni, garbhasaya, stana vriddhi.* The detailed description of formation of *Artava* in texts shows that its formation solely depends on *Ras dhatu* which is produced from *Ahara ras*. Some have the opinion of it having produced from *Ras dhatu* since it is *updhatu* and some opine that it is produced directly from *Ahara ras*. *Bhav Prakash* has included *Artava* as eighth *dhatu.* This description shows that nutrition or food habits determine the formation of *Artava. Acharya Kashyap* has also stated that menstruation can occur before 16 years depending on the food habits. Though the onset of menstruation depends on age

and endocrine physiology, the importance of nutrition also plays an important role. The age of menarche has also been mentioned by the *Acharyas* as it is produced at a particular time. To achieve menarche, *Dhatuparipurnata* or proper formation of *Dhatus* is equally important which depends on the *Ahara*. The amount of body fat responsible for menarche depends on the nutritional status. So, *Dhatuparipurnata* can be considered as proper formation of all the *Dhatu*s including *Ras, Rakta, Maans* and *Meda* which ultimately depends on *Ahara Ras*. Also, one form of *Artava* is *Dhatu Roop* which is responsible for *Bala, Varna* and *Pushti* which means that *Artava* has direct relation to proper physical growth. It can be considered as the effect of oestrogen which causes fat deposition in the body around puberty. So, it can be concluded that Ayurveda texts also consider nutrition as an important aspect of menarche.

CONSTITUTIONAL DELAY IN AYURVEDA

Ayurvedic literature covers menstrual disorders under *Yonivyapada, Artava dushti* and *Jataharini*. Constitutional delay does not have any direct reference but some of the types indicate its possibility.

1) *Sushaka Rewati*

Acharya Kashyapa describes in this *Jataharini* that even after reaching the age of 16 years, menarche is not attained, and arms & hips are emaciated.

आषोड़शवर्षप्राप्ताया या स्त्री पुष्पं न पश्यति । प्रम्लानबाहुरकुचा तामाहुः शुष्करेवतीम् ॥ (का. सं. क. 6)[21]

The age of menarche is 12 years. In *Sushka Rewati* menstruation has not yet been established at the age of 16 years. Further emaciated arms and hips indicate malnourished status of the female. It may indicate primary amenorrhoea due to malnourishment.

2) *Vandhya Yonivyapad*

Acharya Sushruta states that *Artava* is not present in *Vandhya Yonivyapad*. *Dalhana* further states that breasts are present in *Vandhya.* वंध्या नष्ट आर्तवां विद्यात..... | (सु. सं. उ. ३८/१०)[22] Absence of *Artava* may indicate primary amenorrhea. The presence of breast development by *Dalhana* and differentiating it from *Shandi Yonivyapad* indicates normal secondary sexual characteristics in *Vandhya*.

3) *Arajaska Yonivyapad* *Acharya Charak* states that in *Arajaska Yonivyapad, Pitta* situated in *Yoni* & *Garbhasaya* vitiates *Rakta*, woman becomes extremely emaciated and discolored. *Chakrapani* has described amenorrhea as its symptom.

योनिगर्भाशायास्थं चेत पित्तं संदूषयेदस्रक | साअराजस्का मता काशर्यवैवणर्य जननीभृशम् || (च. चि. 30/17)[23]

अरजस्केति अनार्तवा || (च. चि. 30/ 17 चक्रपाणि टीका)[24]

Pitta is the predominant dosha in the *Rituchakra* of a female. The *Pitta* in the uterus and vagina when vitiates *Rakta* leads to absence of menstruation *(Arajaska).* The emaciated and discolored female is due to malnourishment and loss of body fat.

4) Nashtartava

When the vitiated *Doshas* obstruct the passage of menstrual flow, the *Artava* is not visible. Though it is present in the body but is not visible externally.

Acharya Vagbhatta also states that when *Vata* and *Kapha* Doshas obstruct the passage of *Artava*, it is not visible.

दोषेरावृतमार्गत्वादार्तव नश्यति स्त्रियाः। (सु. शा. 2/21) [25]

वातकफावृतमार्गाणां त्वप्रवर्तमान .... (अ. स. शा 1/13) [26]

This type of *Artava Dushti* may indicate Amenorrhoea due to any obstruction in the passage or may also indicate inactivation of neuroendocrine pathway resulting in Amenorrhoea.

5) Amenorrhoea due to emaciation

According to *Acharya Bhela*, though blood circulates in whole body for seven nights, if it is scanty, does not circulate in reproductive system and due to desiccations of *Artava* as well as body can result in absence of menstruation.

स एव आसप्तरात्रात सर्वसंचार. (भे. शा. 5/6) [27]

Acharya Bhela has mentioned that in emaciated women and due to less amount of *Artva*, it can result in amenorrhea.

TREATMENT

Treatment for *Sushka rewati Jataharini* and *Vandhya Yonivyapada* has not been given in particular. Management of other disorders is given as: *Arajaska Yonivyapad*

मृगाजाविवराहास्त्रिग्दध्यम्लफलसर्पिषा ॥ अरजस्का पिबेत सिद्ध जीवनीयैः पयोऽपि वा ॥ (च.चि.30/101)[28]

- Use of *Ghrita siddha* with *Rakta* of *Mriga* (deer), *Ajaa* (goat), *Aavi* (Sheep) & *Varah* (Hog) and *Amla Ras* fruits.
- Use of milk *siddha* with *Jivaniya Gana*.

Nashtartava[29]

- Use of *Basti*
- Use of food or drugs which increases *Pitta.*
- Use of *Lashun, Shatpushpa* and *Shatavari*
- *Matasya, Kulath, Kanji, Til, Mash, Sura, Gomutra, Takra, Dadhi*
- Use of *Krishna til Kwath* with *Gud* (Jaggery)
- Use of *Phalghrit* and *Brihatshatavarighrit*

The description of some of the drugs is given below-

1. TILA (SEASUMUM INDICUM)[30]

Rasa – Madhura, Guna - Guru, Snigdha, Virya – Ushna, Vipaka – Madhura, Doshaghnata – Vatashamaka, it has better action on *Rajorodha, Kastartava* etc, due to *Artavajanana* property. It is also *Balya* and *Vrishy*a due to *Snigdha guna.* Sesame seed has a high food value because of its higher contents of oil and protein. In addition, it has sufficient quantities of carbohydrates, fibre and minerals. It contains about Proteins 20-28%, Oil 48-55%, Sugars 14-16%, Fibre 6-8%, Minerals 5-7%. Sesame is a good source of minerals. The ash content ranges from 5-7%. It has 1% Ca, and 0.7% P. Calcium is mostly presented in the seed coat. The bioavailability of Ca is 65% as against 100% for CaCO3. Sesame is a good source of niacin, folic acid and tocopherols. The tocopherol level is 30-53 mg / 100 g. oil.

2. Milk

Dugdh or milk is considered as wholesome in ayurveda and has no contraindications. It is indicated in a variety of disorders including *Yonirogas*. It is also considered *Balya, Vrishya* and *Rasayan.* [31] Casein is the principal protein, and it constitutes 80% of the total proteins present in milk. Milk protein contain all the essential amino acids in marked quantity and rich in lysine (07.5%), valine (08.4%), Isoleucine (08.5%) and leucine (11.3%). Milk fat contains numerous triglycerides and as many as 64 fatty acids. Mixed glycerides make up about 98% of milk fat. Lactose is the predominant sugar present in milk. Along with that free glucose and galactose are present in traces in fresh milk. Mineral composition of Cow's milk (per 100 gm)- Calcium 136.33 mg, Phosphorus 99.89 mg, Chloride 120 mg, Citrate 210 mg, Sulphate 16.52 mg, Sodium 43.12 mg, Potassium 131.98 mg, Magnesium 13.67 mg, Copper 20.00 mg, Zinc 1124 mg. Milk is also a good source of Vitamins such as Vitamin-A 1560 IU, Thiamine 0.42 mg, Riboflavin 1.57 mg, Nicotinic acid 0.85 mg, Vitamin-B6 0.48 mg, Pantothemic acid 3.50 mg, Biotin 35.00 µg, Folic Acid 2.30 µg, Vitamin-B12 5.60 µg, Vitamin-C 16 mg.[32]

3. SHATAVARI (Asparagus racemosus)[33]

Rasa: Tikta, Madhura; Guna: Guru, Snigdha; Veerya: Sheeta; Vipaka : Madhura; Prabhava : Rasayana; Doshagnata : Vatapittashamaka, *Asparagus racemosus* is used as general tonic and as an adaptogen in Ayurvedic system of medicine. *Shatavari* is prescribed for general debility diseases, chronic infections and inflammatory conditions. *Shatavari* when used for prolonged period in animals shows better weight gain. *Shatavari* contains phytoestrogen. In one of the studies *Shatavari*, an important ingredient of a poly herbal formulation was tested for its uterine tonic, activity. For this purpose, the parameters like estrogen and progesterone level and oxytocin like activities were evaluated. Administration of the formulation in normal and overectomized rats for 21 days showed an increase in dry and wet uterine weight. It also showed a marked increase in estrogen level but did not reveal any change in progesterone levels as compared with the controls.

4. ***Go- Ghrita*** [34]

Some of the properties of *Ghrit* are *Rasayan, Vrushya, Agnivardhaka, Rasavardhak, Balya, Ojavardhaka, Kantivardhak, Indriyabalavridhikar, Budhdhivardhak, Vayahsthapana, Unmadahara*, etc.

Chemical composition of Cow's ghee:

Triglycerides: 97.98%, Diglycerides: 0.25 -1.5%, Monoglycerides: 0.16 - 0.038%, Glyceryl esters:

0.011 - 0.015%, Free fatty acid: 0.1 - 0.44%, Phospholipids: 0.2 -1%, etc.

Fat soluble vitamins present are Vit. A: 2500 /100 gm, Vit. D : 8.5x 10.7 gm/100 gm, Vit. E: 24 x10.3gm/100gm, Vit.K : 1.0 x 10.4 gm /100 gm, *Ghrita* contains 8% lower saturated fatty acids, which makes it easily digestible. Due to having 4-5% linoleic acid, an essential fatty acid, it promotes proper growth of the human body. *Ghrita* also contains vitamin A, D, E and K.

In the process of evaluating the activities of natural compounds, it is found that when herbs are processed or mixed with *Ghrita*, their activity, utility and rate of absorption is potentiated. Thus, *Ghrita* in general and *Goghrita* in particular is one of the easily digestible and assailable foods which provides essential nutrients and critical antioxidants or free radical scavengers to human body for its protection and growth.

5. Kumari (Aloe vera)

Rasa: Madhur, Tikta; Guna: Laghu, Virya; Shita, Vipaka: Madhur, Doshghanta: Vata Kaphahara, in a study on female rats, 50, 100 and 200 mg/kg (three intervention groups) alcoholic extract of aloe vera was given for 10 days orally. Their extracted serum level of estrogen was significantly higher in the second and third interventional group. Thus, it can increase the estrogen levels and favour estrogen synthesis due to its phytoestrogens.[35]

6. Shatpushpa

In *Kashyapa Samhita*, it is indicated to be sweet, anabolic, strength provider, nutritional, improves complexion, initiator of *ritu*, improves quality of *yoni* and *shukra*, is of hot potency, suppresses *vata*, gives progeny and increases *virya.*[36] *Acharya* has stated that use of *Shatpushpa* is a boon for women having following disorders[37]- *Artavam na pashyanti* (amenorrhoea) or *pashyanti viphalam* (having menstruation but are not able to conceive), *atiprabhut* (menstruation in excessive amount or polymenorrhoea), *atyalpam* (very scanty menstruation), *atikrantam* (peri menopausal, menopausal), *anagatam* (delayed menarche) and several other conditions.

Phytochemical constituents[38]

Phytochemical analysis of *Shatapushpa* revealed the presence of alkaloids, carbohydrates, tannins, triterpenoids, flavonoids and proteins in methanol extract. The presence of triterpenoids suggests their action of anabolism, weight promotion, rectification of *Agni* and diuretic.

Shatapushpa significantly showed the presence of flavonoids which are protective in action. These are considered as naturally dietary biologic response modifiers, disease preventing and health promoting. Its Steroidal presence indicates that this drug may have influence on the endocrine system. As these are precursors for synthesizing sex hormones, especially progesterone and estrogen. Carbohydrates found in *Shatapushpa* reflect its nutritive property.

7. Basti

In *Siddhisthana*, *Acharya Kashyapa* has given indications for *Anuvasana basti* which includes *Alpapushpa*, *Nashtapushpa* and *Nashtabeeja*[39]

Basti given through rectum reaches instantly into systemic circulation, thus has faster absorption and quick results. The *Basti dravyas* stimulates endogenous opioids which are usually present in GIT, these endogenous opioids influence GnRH release and thus regulate HPO axis and menstrual cycle. [40]

DISCUSSION

Delayed menarche or constitutional delay is not an uncommon problem. It may not be a potential health problem but may have several adverse consequences. A review study on potential medical and psychosocial issues in females with history of delayed puberty shows some long-term effects of delayed puberty. [41] Height and bone mineral density may be compromised and may cause higher risk for metabolic or cardiovascular disorders. Age at menarche may influence the risk of osteoporosis during both pre-menopausal and post-menopausal periods. The effect of pubertal timing on bone mass density has largely been attributed to differences in estrogen exposure. In one study of post-menopausal women, late menarche (>15 years) was associated with reduced BMD at the lumbar spine and femoral

neck when compared with BMD of women who underwent menarche before 15 years. Another study identifies women who had delayed menarche at 16 years or later and found that these women had an 80% increased risk of vertebral fracture in later adulthood compared with those with menarche before 16 years. Another study showed a 45% increase in risk of hip fracture in those with menarche at 15 years or later compared with those with menarche at 11 years or younger.

The high risk for cerebrovascular disease were observed for menarche at <10 years and at >17 years with 20% increase in risk for each group. A similar relationship was found with menarche >17 years associated with a 13% increase in risk for cerebrovascular disease and 7% increase in risk for hypertensive disease compared with menarche at 13 years.

All of these effects are thought to be due to the late exposure to estrogen hormone and other endocrine changes. It cannot be said that delayed menarche or delayed puberty is the only responsible factor in this, but it can be stated that it may have significant contribution in development of these conditions when combined with other factors.

Therefore, timely intervention in cases of delayed menarche is important. Estrogen therapy and contraceptive pills are one method. Upgradation of physical health is an important part of management. On the other hand, use of certain ayurvedic drugs and dietary improvements can also be used to achieve the aim of establishing menarche. Use of *Tila, Ghrita, Dugdh, Kumari, Shatavari, Shatpushpa*, etc can be implemented as they have high nutritional value with specific effect on reproductive physiology. These drugs can help in timely establishment of menstrual cycle and also promote general health.

CONCLUSION

Delayed menarche may appear as not a very big problem because in most cases it may be achieved spontaneously after some time. If all the other factors are excluded, low body weight and malnutrition are the responsible factors, which itself is a major threat. Ayurveda also considers the importance of age for menarche and pubertal growth. Along with improvement of nutrition, use of certain ayurvedic drugs and procedures may help in timely establishment of menarche. Also, these drugs may help improve overall physical and reproductive health of the female.

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