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DIMINISHING OVARIAN RESERVE, AYURVEDIC MANAGEMENT - CONCEPTUAL STUDY

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ABSTRACT

Diminishing ovarian reserve refers to reduction of oocyte quantity, quality and reproductive potential. As per ESHRE & Bolognas criteria for DOR at least any of the two of the following should be present i.e. Age<38 years, abnormal ovarian reserve test, and poor response to previous stimulated cycle. The most appropriate correlation of DOR can be done with *Dathukshaya Vandya* explained in Haritha Samhita. Nowadays 10-30% of female infertility is due to DOR. In conventional system treatment options are limited. Adjuvant therapy with LH, DHEA and Growth hormones shows some benefit in oocyte yield, but long-term use may lead to conditions like breast ca, ovarian ca, endometriosis and fibroid uterus etc. Among ayurvedic clinical practitioners *rasayana chikitsa* followed by *shodhana* found to have promising results in management of DOR. The potential implication of our treatment protocol could be significant not only for the preservation of fertility status but also for the prevention of diverse spectrum of health problems.

Keywords: Diminishing ovarian reserve, *Dhatukshaya vandhya,* Reproductive potential

INTRODUCTION

Diminishing ovarian reserve (DOR) is a condition in which the ovary loses its normal reproductive potential, compromising fertility and causing early menopause. It refers to reduction of oocyte quantity, quality and reproductive potential[1]. As per ESHRE & Bolognas criteria for DOR at least any of the two of the following should be present i.e. Age<38 years, abnormal ovarian reserve test, and poor response to previous stimulated cycle[2]. 10-30% of female infertility is due to DOR[3]. The findings of ISEC survey highlight that on an average nearly 14% of Indian women menopauses between the ages of 29-34 years, one of the lowest thresholds in the word[4]. The most appropriate correlation of DOR can be done with *Dathukshaya Vandya*, one among 6 type of *vandya* explained in Haritha samhita[5]. It is due to depletion of *dhatus* or inadequate formation of *dhatus* leading to reduction in fertility potential and ultimately *anapathyatha*. Causes are extremely heterogeneous which are illustrated as follows[6]:

Table 1: Etiology of DOR

Autoimmune	Organ, non-organ specific auto antibodies bind to gonadotropins & receptors
Iatrogenic	Chemotherapy, Uterine artery embolization and ovarian drilling.
Infection	There is no direct evidence that infections cause DOR, but around 3.5% with DOR have history of infections like varicella, tuberculosis shigellosis, malaria and cytomegalovirus.
Oxidative stress	ROS-induced DNA damage potentially causes granulosa cell apoptosis, follicular atresia, chromosomal abnormalities and poor oocyte quality.
Environmental toxins	Endocrine disrupting chemicals (EDCs) eg Polycyclic aromatic hydrocarbons, tobacco.
Autosomal genes	FSH, LH Estrogen receptor mutations, and CYP19A1 mutation etc.
Chromosome defects	Monosomy e.g. Turner syndrome, Trisomy, Fragile X syndrome

Pathogenesis: Exact mechanism for development of DOR is obscure. It can be due to decrease in primordial follicle pool**,** accelerated atresia of follicles**,** defective maturation/recruitment of primordial follicles.

Clinical features: Primary or secondary infertility, menstrual irregularity, hot flushes, osteoporotic changes, vaginal dryness, dyspareunia, sleep disturbances, mood swings, cognitive errors, weight gain and uterine prolapse.

Table 2: Clinical categorization of DOR

Stage	**Menstrual cycle**	**Gonadotropin**	**Fertility**
Occult insufficiency	Normal	Normal	Reduced
Diminishing ovarian reserve	Shortened	Mild elevation	Reduced
Overt insufficiency	Amenorrhoea/ Oligomenorrhoea	Elevated	Reduced
Premature ovarian failure	Menopause	Elevated	Zero

Assessment: based on Basal AMH < 1.5 ng/dl, Basal FSH between 10 - 15 IU/ L, Basal Estradiol between 60 - 80 pg/ ml, Inhibin B < 400 pg/ ml, AFC< 10 (both ovaries)

Management: ovarian function cannot be restored by any proven therapeutic strategy. The primary goal of the treatment is to manage the hypoestrogenic state and fertility management by IVF. Stimulation with high doses of gonadotropins, GnRH analogues or antagonists are done.

DISCUSSION

The word *Vandhya*, derived from the root *"Vandha"* with *"yak"* suffix which means fruitless. As per Caraka *vandyatwa* is due to abnormality of *beejamsa* and factors which delays conception are *yoni pradosha, manaso abhitapa, asrug dosha, ahara-vihara dosha, akala yoga* and *bala samkshaya* etc[7]. Susrutha included *Vandhya* among *vimsathi yoni rogas*. Primary etiology for *vandhyathwam* and *arthavanasam* are injury of *arthavavaha srothas* and *nashtarthava* is consid-

ered as the *lakshana*. This can be considered with anovulatory menstrual cycle as seen in DOR. Kasyapa included *vandhyatw*a under *vatavyadhi* and opines when there is *sonitha garbhasaya beeja baga dushti* in *matrujabhava* the female progeny will be *vandha.*. From the broad references which are described in the classic's different stages of DOR can be inferred as following.

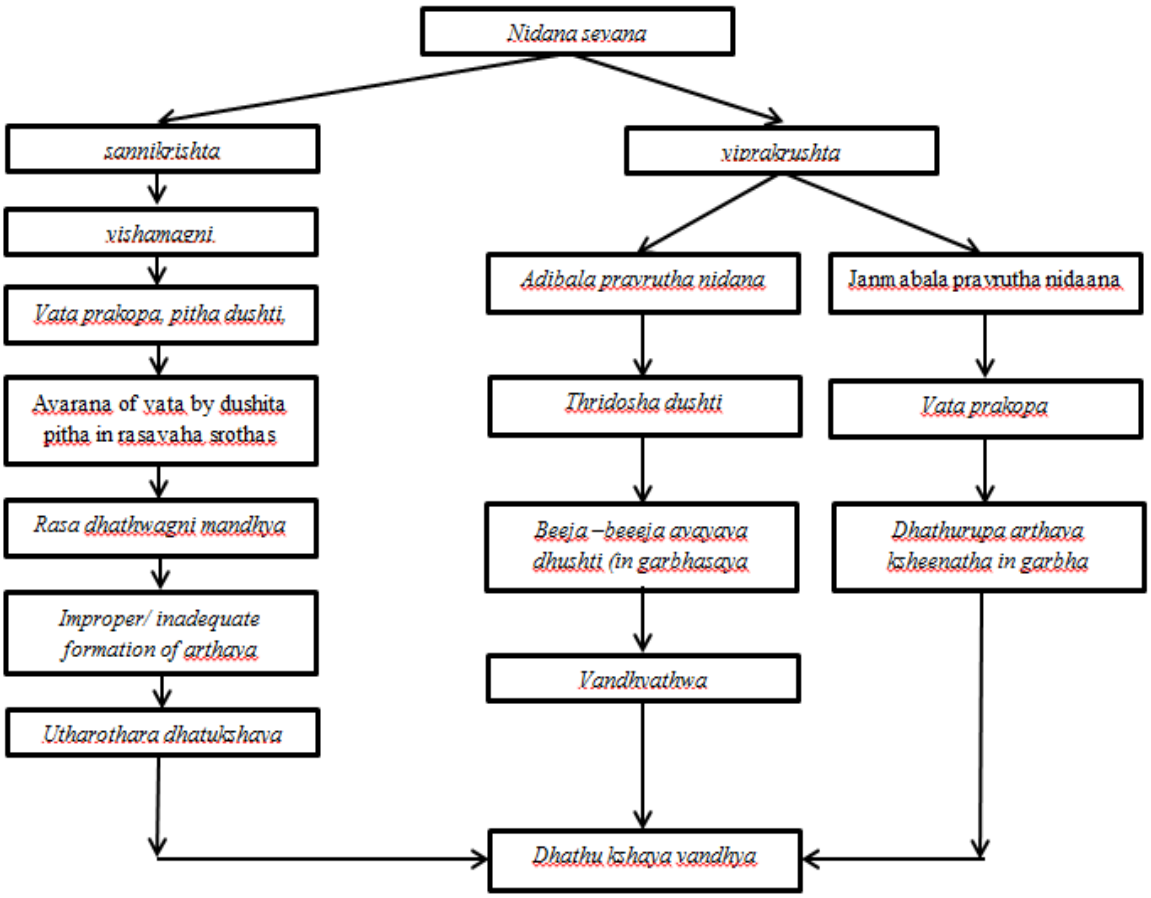
- *Rasakshaya, arthavakshaya – Purva rupa avastha*
- *Rasadhi saptha dhathu pariksheena- Vyadhyavastha*
- *Bala kshaya – Upadrava roopa vyadhi.*

As per Susrutha *arthava kshaya* characterized by *yadochitha-kala-adarsana-alpatha* associated with *yonivedana* and Cakrapani comments *yoni vedana* is due to *yoni abhipuraka arthava kshaya* causing *vaataprakopa*. As per *Bela Samhitha* due to *sareera shosha* amount of *sonitha* reduces and thus *raja* will not be formed[8]. Haritha samhitha explains *vandyatha* due to *ajaatha rajas* due to *ahara-viharaja nidhanas* or *vyadhija*. This can be considered as reduction in reproductive potential manifested due to oxidative stress. If pregnant women involve in *apathya ahara vihara* e.g. *vega dharana, beeja dhushti* occurs causing *pariksheena* of *dhaturupa arthava* which originates during embryonic period. When *dhathu paripurnatha* is attained both production of *arthava* and development of *yoni* occurs. *Vandhyathwa* due to *beeja dhushti* are seen in *shanda, vartha* etc. conditions. It can be correlated with DOR seen in X –linked chromosomal abnormities. *Yonivyapath* and *ashta arthava dhushti* if not treated properly leads to *apooryamana dhathu uthpathi* (improper/inadequate formation of *dhathus*) and causing improper formation of *garbha sambhava samagri* and ultimately *anapathayatha* as per Susrutha Samhitha *bala* is the essence of *rasaadi saptha dhatu*[9]. As the disease progresses *upadrava avastha* manifests i.e. *sarva dhathu pariksheena*. This can be seen in patients undergoing chemotherapy etc. *Vandhyathwa* due to *aarthavavaha srothovigadha* can be correlated with DOR due to depletion of primordial follicles after ovarian drilling, uterine artery embolization etc.

Table 3: *Nidana* (Causative factors)

Sannikrushta nidaana[10]	***Viprakrushta nidaana***
Sangathabala pravrutha vyadhinidana, shatra vidha - Eg: ovarian surgery in endometriosis	*Adibala pravrutham – matrupitruja* Eg: chromosomal abnormalities
Kalabala pravrutha vyadhi nidana Avyapanna nidanas- Environmental pollution.	*Janmabala pravrutham- Rasajadouhrutha avamanajam* (Eg: exposure to Endocrine disrupting chemicals during pregnancy
Swabhavana balapravrutha vyadhi nidaana Akalaja jara due to improper *ahara vihaara*	
Daivabala pravrutha vyadhi nidana-Apatharpana eg: malnutrition, *upasarga* eg: Infections	
Doshabala pravrutha vyadhi nidanas- Mithyahara vihara - Eg: oxidative stress, EDCs	

Table 4: *Sampraptht* [11]



Chikithsa

In Ayurveda 3 types of *chikithsa* have been mentioned- *daiva vyapasraya, yukthi vyapasraya* and *saatwavajaya chikithsa*. The basic principle of *yukthi vyapasraya* is nourishment of dhosha which has been depleted, pacifying the vitiated and also elimination of the aggravated *dhosha*. *Panchakarma* is a unique approach of Ayurveda for internal purification of the body through which homeostasis can be maintained. It is done in 3 phases- *purvakarma (Deepana, pachana, snehana* and *swedana*), *Pradhana karma (vamana, virechana, asthapana- anuvasana vasthi* and *nasya-karma*), *paschath karma (samsarjana karma, rasayanadi karma, samana chikithsa)*. As per caraka samsodhana karma improves power of digestion, metabolism, and helps to attain healthy progeny. These concepts of are implied on the management of female infertility. *Sneha, swedana* followed by *panchakarma* and *utharavasthi* is the main treatment line for *vandhyathwa* by normalising the *dhoshas*.

The process of stimulation of *jaataragni* is called *deepana* and *pachana* does the digestion of *ama*[12]. It removes the *sama avastha* and detaches the vitiated *dhoshas* adhered to *arthavavaha srothasas*. *Udwarthana* does the *meda pravilayana* and *kaphaharana*. *Snehana* is the first line of management in *vaataja rogas* which is done after *deepana- pachana*. *Saptha dhathus* are formed from the essence of *sneha* thus proper *snehana* does *jaataragni vrudhi, koshta visudhi*, formation of *prathyagra dhathu, bala* and *varna* also increases life span. *Svedana karma* does the *vilayana* of *sneha uthklishta dhoshas* and *doshas* moves towards *koshta*[13]. *Sodhanakarma* are the methods through which vitiated *dhoshas* from *koshta* are expelled out the body. *Vamana* is main treatment for *kaphaja vikaras* e.g. *nashtarthava* (where *vata* get *avrutha* by *kapha*), *anapathyatha* due to *meda kapha*

dhushti etc. conditions. *Virechana karma* has direct effect on *agnisthana*. It pacifies the vitiated *kapha* and *vatadosha* and removes vitiated *pitta.* Kasyapa opines through *virechana beeja karmukatha* can be attained[14]. Reproductive organs are situated in *katisthana* which is *sthana* of *apanvayu*. Action of *vasti* is predominantly on *vatadosha* and *pakvashaya*. It is indicated in *alparaja* and *anarthava* conditions especially *yapanna vasthi* indicated in infertility[15]. *Uttarvasti* done after *panchakarma* facilitates drug administration into uterus, normalises *vata* and *garbhava samagris* are properly formed. *Rasayana* does *vayasthapana*. *ayushkara*, *medhakara and urjaskara* etc. It enhances immunity, delays aging process and improves quality of life. *Dhosha* wise management are given in the table 4.

Table 5: *Dhosha* wise management

	Vata dosha	*Pitha dhosha*	*Kapha dhosha*	*Tridosham*
Deepana Pachana	*Gandharvahasthadi ks Chiravilwadi ks*	*Guluchyadi ks Drakshadi ks*	*Amruthotharam ks Ashta churnam*	*Dadimashtakam Churnam Vilangathandulam ch*
Abhyanga	*Kottanchukkadi tailam*	*Chandanadi thaila*	*Chinchadi thaila*	*Lakshadi tailam*
Sneha pana	*Sukumaram ghritha*	*Thikthaka ghritha*	*Aragwadammaha thikthaka ghrtham*	*Dathradi gritham*
Virechana	*Gandarvahastha thaila*	*Avipathi churnam*	*hingutrgunam*	*Misraka sneham*
Utharavasthi	*Vidharyadi ghrtham*	*Thikthakam ghritha*	*Kethakimoooladi*	*Phalasarpis*
Rasayanam	*Abhayamalaka Vidharyaadi rasayanam*	*Drakshadi lehyam Amruthaprasam*	*Dasamoolaharitaki sukumararasayana*	*Chyavana prasam Kadali rasayanam*

Pathya- Apathya[16]

S*ura, asava, arishta, lasuna rasa*, milk and meat soup should be consumed daily in appropriate quantity. Food prepared with *yava, seedhu*, powder of *pippali* and *harithaki* are beneficial. In *aarthava kshaya agneya dravyas* like *tila, masha, sura* and *suktha* can be advised. *Ahara- vihara* causing *agnidhushti* such as *adhyasana, vishamasana, athichintha, divaswapna,ratri jagarana*, and *virudha ahara* should be avoided.

CONCLUSION

In current conservative management, the treatment options for DOR are limited. Ayurvedic management is significant not only for the preservation of fertility status but also for the prevention of diverse spectrum of health problems that emerge in women after depletion of ovarian reserve. Successful implication will be momentous in the management of DOR also it will project Ayurveda into the mainstream treatment.

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