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Management of female infertility presenting with low AMH and AFC count - A Case Study

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ABSTRACT

Diminishing ovarian reserve is the most important cause for poor ovarian response (POR). It is distinct from menopause and premature ovarian failure. It is often noted in women in their mid to late thirties and it may also affect younger females also. DOR is a common term refers to three different but related parameters like reduction in oocyte quantity, reduction in oocyte quality and reduction in oocyte reproductive potential. The AMH (Anti mullerian hormone) and AFC (antral follicular count) are the most reliable markers to assess the ovarian reserve. A lady aged 29 years came to my op, complaining of low AMH (1.2ng/ml) and AFC 3 on right ovary and 4 on left ovary. DOR can be done with *Dhatukshaya Vandya* explained in *Harita Samhita*.^[1] *Dhatukshaya Vandhya*, occurs due to depletion of *Dhatu*s or due to inadequate formation of *Dhatu*s, especially *Arthava* and *Sukradhatu* which in turn leads to reduction in fertility potential and ultimately *Anapathyatha*. *Agnideepana*, *Srothoshodhaka* and *Dhathuposhana* line of management was adopted and the patient got UPT positive on 10thfeb 2019 and delivered a healthy male baby on 20/10/2019.

Key words: AFC, Antral follicle count, AMH, Anti-Müllerian hormone, *Dhatukshaya vandhyatwa*.

INTRODUCTION

The AMH (Anti mullerian hormone) and AFC (antral follicular count) are the most reliable markers to assess the ovarian reserve. This ovarian reserve test predicts how well the ovaries are functioning at a certain point of time. The low AMH and AFC count are the indicators of poor ovarian reserve. Diminishing ovarian reserve is the most important cause for poor ovarian response (POR). It is distinct from menopause and premature ovarian failure. It is often noted in

women in their mid to late thirties and it may also affect younger females also. DOR is a common term refers to three different but related parameters like reduction in oocyte quantity, reduction in oocyte quality and reduction in oocyte reproductive potential. It occurs 1% of women worldwide. It is also unclear whether DOR represents a pathological condition resulting from abnormally rapid atresia in a normal pool of oocytes from normal atresia of an abnormally small pool of oocytes.^[2] Studies suggest that certain factors like Age, Exposure of Radiation therapy or Chemotherapy, Genetic abnormality (45X, FMR- Permutations), Smoking, Previous ovarian surgery like cystectomy or ovarian drilling done in PCOS management, uterine artery ligation, some Infections such as mumps, malaria, varicella, tuberculosis, cytomegalovirus, herpes simplex etc., Autoimmune disorders etc may contribute to DOR. Certain studies may also states that maternal nutritional status participates in programming growth, development, and function of the major foetal organ systems. Placental insufficiency impairs foetal development and reduces the number of primordial

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follicles in the ovaries of fetuses and neonates in humans (de Bruin et al., 1998).

From clinical features also DOR can be suspected. The most common clinical features include primary or secondary infertility, menstrual irregularity such as shortening of menstrual cycle length (MSL), which is the most common clinical feature of DOR. The shortening of MCL is due to the shortening of follicular phase, which is associated with decrease in inhibin B and increase in FSH, whereas in general the length of luteal phase is preserved. The mechanism behind in shortening of follicular phase is an earlier start of follicular growth (due to less inhibin as a result of low AFC).

CASE REPORT

Presenting complaint

A 29 years old married woman with her husband 34 years of age, consulted in OPD with a presenting concern of primary infertility since 5 years of married life. The patient is a school teacher (educated person), she herself presented that she is having an issue of low AMH. And male factor with normal seminal parameters.

History of presenting complaint

Patient attained menarche at the age of 14 years since menarche her cycles were regular. She had bleeding for 5-6 days and she was also having severe dysmenorrhoea during the 1st day of her cycle and she took some home remedies for the same. At the age of 24 years she married to a non-consanguineous man of age 31 year. The subject is well aware of fertile period and they were having adequate vaginal intercourse (3-4 /week). After 2 year they consulted allopathic hospital and investigations were carried out on both partners including semen analysis for the male partner, USG, follicular study and hormone assay including thyroid profile and prolactin were done for the lady. After an unsuccessful treatment 1 ½ year, she stopped the treatment for 8 months as she was having some depression issue. After 9 months again they decided to start treatment and consulted another allopathic gynaecologist and repeated a set of

investigations and also AFC (antral follicular count on day 2 of her cycles were 3 on right ovary and 4 on left ovary) done on 4/4/2018 and serum AMH test was found to be 1.2 ng/ml done on 5/4/2018 and she was advised to go for an IVF treatment. (the patient was financially not stable so they searched for other options and they came to my clinic on 6/8/2018 with the previous reports).

Personal history

- Appetite - good
- Bowel - constipated
- Micturition - 4-5 times/ day
- Sleep - disturbed
- Food - mixed diet
- Allergy - nil

Menstrual history

LMP - 26/7/18

Menarche - 14 years

Her cycles were regular and inter cycle duration was 28 days with 5-6 days of moderate bleeding and from 2016 onwards her cycles gradually shortened and duration reduced to 3 days and intermenstrual duration reduced was 24-26 day cycle and the amount of bleeding was also reduced remarkably (1-2 pad per day)

Sexual history

Adequate frequency of vaginal intercourse and the couples are well aware of the fertile period.

Diagnostic assessment

- Blood routine investigation was done and found to be normal
- TSH - 2.7 ng/ml and serum prolactin was 15ng /ml
- USG - showed normal anteverted uterus and both ovaries appear to be normal
- AFC - Rt side (3 follicles) and left side 4 follicles on 2nd day on menstrual cycle (i.e., on 4/4/2018)
- AMH - 1,2 ng/ml (on 5/4/2018)

Ashtasthana Pareeksha

Nadi	Vata Pittam
Mūtra	Prakristam
Mala	Vibhandham
Jihwa	Anupa-Liptham
Shabdham	Spashtam
Sparsham	Usnam
Druk	Avishesha
Akrithi	Krisham

Dashavidha Pareeksha

Prakriti	Vata Pitta
Vikrithi	Vata Pitta
Sara	-
Samhanana	Madhyama
Pramana	Madhyamam
Satmya	Katu, Amlarasam
Satva	Avara
Aharasakthi	Madhyama
Vyayamasakthi	Madhyamam
Vaya	Madhyama

Therapeutic Intervention

Vis it	Date	List of medicines with dosage	Consequence
1.	6/8/18	1) Ashtachooram 0-1tsp-0 with ½ tsp ghee 2) Saptasaramkashayam 4tsp-0-4tsp with ¼ glass of water 20min before	-

		food 3) Hinguwachadi tab (along with kashaya) 1-0-1	
2.	20/9/18	1) Sukumaramkashyam 4tsp-0-4tsp with ¼ glass of water 20min before food 2) Indukanthamghritam 1tsp-0-1tsp (6am and 6pm) 3) Bringarajasavam 30ml-0-30ml	Her cycles become normal. 28 day cycle 3-4 days of bleeding (On follicular study shows normal ovulation)
3.	28/10/18	1) Saptasramkashyam 4tsp o- 4tsp with ¼ glass of water before food 2) Sukumaramghritam 5ml -0- 0 (early morning along with the kashyam) 3) Kalyanakamkashyam as toyam	-
-	1/12/18	Sukumaramkashayam Lasuna Tab Kalyanakamkashyam	LMP - 13/11/2018
-	2/1/19	Chandraprabha Tab 1-0-1 Amyron tab 0-1-0 Abhyaristam 25ml -0- 25ml	LMP - 12/12/18
-	-	-	LMP- 11/1/19

Follow up and outcome

On 10th February 2019 UPT result was positive and on 17/2/2019 on USG single intra uterine gestational sac was seen and on 27/2/2019 Good FH seen she had followed *Masanumasika Ksheera Pakas* along with allopathic Ca+ and iron supplements and was under the supervision of allopathic gynaecologist. Her pregnancy was uneventful and she delivered a healthy male baby on 20/10/2019.

DISCUSSION

The term “ovarian reserve” has traditionally been used to describe a woman’s reproductive potential—specifically, the number and quality of oocytes she

possesses. AMH is leading predictor of ovarian reserve. AMH, in contrast, is more reliable and varies very little throughout the cycle, and can therefore be measured at any time. Ovarian reserve defines the quantity and quality of the ovarian primordial follicular pool. When this occurs, conceiving becomes difficult for a woman as her ability to produce healthy eggs begins to diminish. The most appropriate correlation of DOR can be done with *Dhatukshaya Vandya* explained in *Haritasamhita*.^[3] *Dhatukshaya Vandhya*, occurs due to depletion of *Dhatus* or due to inadequate formation of *Dhatus*, especially *Arthava* and *Sukradhatu* which in turn leads to reduction in fertility potential and ultimately *Anapathyatha*.

In this case patient has an AMH level of 1.2 and her antral follicle count on USG shows 3 follicles on right side ovary and 4 follicles on left side. Low normal range of AMH blood level is 1.0-1.2 ng/ml in women under age 35. Patients at low and high risk for DOR, low AFC cut points of 3-4 total follicles (both ovaries combined) are highly specific for predicting poor ovarian response.

According to *Acharya Susruta* four factors essential for conception are *Ritu*, *Kshetra*, *Ambu*, and *Beeja*^[4]. When these factors are in *Avyapanna Avastha*, (normal state) conception is bound to occur. In *Ashtanga Sangraha* more importance is given to *Kshetra* and *Beeja*. In *Ashtanga Hrudhaya* in addition to the four essential factors of *Susruta*, *Sudhamargha*, *Anila (Apana Vata)* and *Hrudaya* is being included.^[5] Abnormalities in any one of this essential factor can cause *Vandhyatwa*.

In common all *Acharyas* mentioned *Beejaas* an important factor for conception. As per *Ayurveda* *Beeja* is *Sukra* and *Sonitha*. So here the *Beeja* the quantity and quality of oocyte is impaired. For both men and women, reproductive health depends on the health of the *Sukradhatu*, or reproductive tissue. *Sukradhatu* itself is created as part of a long chain of metabolic transformations, starting with the digestion of food and including the transformation of food to nutrient fluid, blood, muscle, fat, bone, bone marrow and finally, to *Sukra* tissue.^[6] Healthy *Sukradhatu*,

then, according to *Ayurveda*, depends on the health of all the other tissues in the body. If *Sukradhatu* does not get the proper nutrition which can happen due to poor digestion, lack of balanced diet results in *Vandhyatwa*. *Sukradhatu* can be described as the factor that nourishes both the male and female reproductive tissues and its secretions. In women the status of *Sukradhatu* is responsible for regulation of menstrual cycle and formation of ovum. Any deviation in *Sukradhatu* leads to pathogenesis. Function of the *Sukradhatu* is sustenance and nourishment of the body. This *Dhatu* is meant principally for reproduction.^[7] Reproduction is not local function of ovary to produce the ovum and fertilized ovum during sexual act. Therefore, support of this *Dhatu*, *Sukradharakala* is present all over the body.

Bhavaprakasa considered *Ritu* as most fertile reproductive period of a female.^[8] Age of female is important so here we can consider the impaired *Ritu* as the female partner is in her advanced age. Age is considered to be the principal factor in determining quality and quantity of ovarian reserve. The reduction of ovarian function with aging has been widely defined in term of progressive reduction of ovarian follicles and diminished capability to generate competent oocytes.

Ambu - Satmyaja and *Rasajabhavas* included under *Shadbhavas* and *Ambu* or nutrients, one of the four factors for conception come under this heading. Abnormal diet is the important cause of vitiation of *Doshas*, which if vitiated, influence fertilization by producing gynaecological disorders, diseases of *Vata*, chronic illness, *Udavarta* etc. *Ahara Dasha* causes vitiation of *Agni* and *Vata* in turn weakens the formation of - *Sukradhatu* inside our body which ultimately delay chances to conceive. Irregular diet habits like *Samasana* (combination of *Pathya* and *Apathyaahara*), *Vishama Asana* (untimely and inappropriate quantity of food) and *Adhyasana* (eating before digestion of food) and *Viruddhahara* (incompatible food) like junk foods, bakery items, fast food are considered as *Apathyas* (noncongenial) causing *dosha* vitiation

Acharya Vagbhata mentions *Hrudaya* as one of the essential factors of conception. Acharya Charaka mentions pleasant state of mind prime factor responsible for conception.^[9] Due to *Bhaya, Shoka, Krodha, Lajja, Manasika Bhavas, Vata* will be vitiated. So, it increases hypothalamic activity of CRH (corticotrophin releasing hormone) and further it inhibits normal GnRH pulsatile secretion and ultimately anovulatory cycles occur.

Vata is the most easily disturbed *Dosha*, which depletes *Sukradhatu*, causes functional defects in the egg and difficulties with implantation and is often responsible for infertility. Suppression of natural urges (*Vegadharana*) the normal physiological mechanism of body is disturbed and mainly *Vata Dosha* gets vitiated. Thus, *Vata* can also block healthy *rasa* flow to and from the uterus by constricting and causing spasms in channels like arteries and the cervical canal. However, infertility rarely involves only one *Dosha*. *Pitta Dosha* increases due to a lifestyle that is too competitive, and intense, as well as from a diet that is too spicy and hot. Patient preferred *Katu* and *Amla Rasa* food which may cause vitiation of *Pitta*. The patient had disturbed sleep. The hormones that trigger ovulation in women may be tied into the body's sleep-wake patterns. Sleep pattern is another major factor influencing health of an individual. According to *Charaka* keeping awake in night causes *Rukshata*(roughness) and causes increase in *Vata* and *Pitta Dosha*.^[10] Sleep is directly related to metabolism, reproductive health, and other physiological processes of the body.

Viprakrishta Nidana - Vata Pradhana Tridoshha Dhushti to *Matru* or *Pitru*beeja which causes *Beeja / Beejabaga / Beejabaga Avayava Dhushti* causes *Vandhya, Vartha, Trinaputrika*.

Samprapti

Due to *Nidanasevana* the *Jataragni* becomes *Vishamagni* leads to improper *Aharapachana* and leads to *Vathavrudhi, Pitta Dushti* and *Kapha Kshaya*. It causes improper formation of *Ahara rasa* and finally leads to *Rasa Dhatu Kshaya*. Depletion of *rasa Dhatu* results in *Arthava Kshaya* and *Utharotharadhatu*

Kshaya, ultimately it results *Vandhyatwam* and *Bala Kshayam*

Samprapthi Ghataka

- *Dosha - Vata, Pitta*
- *Vata - Apana, Samana, Vyanavayu*
- *Dhatu - Primarily Rasa Dhatu* and later stages *Sapthadhatu*
- *Upadhatu - Arthava*
- *Srotas - Rasavaha, Arthavavaha, Sukravaha*
- *Adhishtana - Yoni*
- *Marga - Abhyanthara*

Mode of action of drugs

There is inevitable metabolic dysfunction (*Dhatvagninasana*), out of which all *Saptadhatu*s are lost. Ultimately, deterioration of immunity (*Ojakshaya*) is evident. All *Dhatu*s get increased by the use of substances having similar properties and they get reduced by the use of those having opposite properties.

The process of stimulation of *Jataragni* is called *Deepana*. *Ashtachurna* is used for *Deepana*. *Pachana* does the digestion of *Ama* but not increases the *Agni*. Both *Deepana-Pachana* removes the *Sama Avastha* and detaches the vitiated *Doshas* which are adhered to *Srothases*. In this case *Hinguvachadichoorna* is used for *Deepanapachana*. The *Deepana* and *Pachana* property of *Hingu, Vacha, Vijaya* etc, help to attain *Amapachana* and *Koshtarookshana*. Improper diet intake can correlated with *Virudhaaharasevana* and prolonged intake will cause *Dhatuksheenatha* leading to *Vandhyatwa*. Due to *Nidanasevana* the *Jataragni* becomes *Vishamagni* leads to improper *Aharapachana* and leads to *Vathavrudhipitta Dushti* and *Kapha Kshaya*. It causes improper formation of *Ahara rasa* and finally leads to *rasa Dhatu Kshaya*. So correction of *Agni* is the important and initial step to be advocated.

Administration of *Saptasaramkashaya* along with *Deepanapachana* medicines is advised in the first visit. It cures *Agnimandya*.

Snehadravya is given after *Deepana-Pachana*. *Sapthadhatu*s are formed from the essence of *Sneha* (*Purusha is Snehasaara*). *Grita* preparation is lipid based have the potential to cross blood brain barrier and show beneficial effects on brain tissue. *Grita* is having *Madhura Rasa, Guru Snigdha Guna, Sitaviryam, Madhura Vipaka, And Vata Pitta Hara* properties. *Indukantamghritam* is *Bala Vardhanam* so the capacity of this *Grita* yoga to improve *Bala* is impregnated in this condition. As per *Susruthasamhita* *Bala* is the essence of *Rasadisapthadhatu* (*Rasadinaam sukraanthaanaam dhathunaam yath param tejaha*). When *Dhatu Kshaya* occurs it will lead to *Bala Kshaya*. *Bala Samkshaya* indicates reduced *Sahaja, Kalaja, Yukthikritha Bala*. It may be either due to *Ahara-Viharajanidhanas* or *Vyadhi*. All the *Yonivyapath* and *Arthavadushti* if not treated properly leads to improper/inadequate formation of *Dhatu*s and will result improper formation of *Garbha Sambhava Samagri* and leads to *Anapathayatha*.^[11]

Sukumaram Kasayam has *Rasayana* properties. *Rasayana* which has marked action on reproductive organs and also nourishes *Sukradhatu*. *Rasayana* nourishes the whole body and improves natural resistance against infection by increasing immunity power. It promotes the nutritional value of the *Rasa* which in term helps in obtaining the best qualities of *Dhatu*s and *Upadhathu*s such as *Arthava* which will cure *Vandhyatwa*.

Bringarajasavam cures *Dhatukshaya* and increases *Bala* as *Dhatukshaya* is the main event in the pathogenesis of *Vandhyatwa* here; this medicine plays an important role in *Samprapti Vigatana* of *Dhatukshaya Vandhya*. In the *Phalasaruti* of *Bringarajasava* it is mentioned as *Vandhayanam putrot bhavat*^[12] (gives progeny to infertile) and *Yogas* in *Arishtaasava* form are considered suitable for *Yonirogachikitsa*.

Patient is of *Avara Satwa* and very anxious. Psychological upset and resulting stress w alters the HPO axis or disrupts the function of hormones are thought to be the risk factors of DOR. Stress is also a root cause for the entire physiological disturbance as

stress stimuli causes the brain to release various neuro transmitters which can alter pulsatile function of GnRH which stimulate adrenal production of androgens and can disrupt the ovarian functions. In *Ayurvedic* view *Bhaya, Soka* and *Chintha* can vitiate *Vata* and this may hamper reproductive functions. *Kalyanakam Kashayam* is administered for the correction of *Doshadushti* due to disturbances in the *Manasikabhavas* as *Soumanasyam* is considered as the foremost thing among the *garbakarafactors*. *Kalyanakam Kashayam* corrects *Agni*, and it is *Balyam*. It is mentioned as *Aretasyaprajasi* and *Sreshtha* yoga for *Pumsavana*. After administering the medicines correcting *Agni, Doshadushti* and *Dhatukshaya*, administration of *Kalyanakam Kashayam*, a formulation best for *Pumsavana* is used for the purpose of *Garbhagrahana* and *Garbhasthapana*.

The women suffering from *Yoniroga* should follow diet which must normalise the vitiated *Dosha*. The diet and mode of life must be for the normal functions of *Vata* and for *Pitta*. As per *Kasyapa, Lasuna* is highly beneficial in *Vandhyatwa*. *Srotoshodhana* property of *Lasuna* helps in proper flow of *rasa* and nourishment of *Uttarottara Dhatu*. By *Balya, Brihmana* and *Rasayana* properties it act as *Dhatukashayahara* and *Vata Samana (Agyraoushada for Prabhanjanharam)* by *Vrishyaguna* it is *Sukrakara*.

CONCLUSION

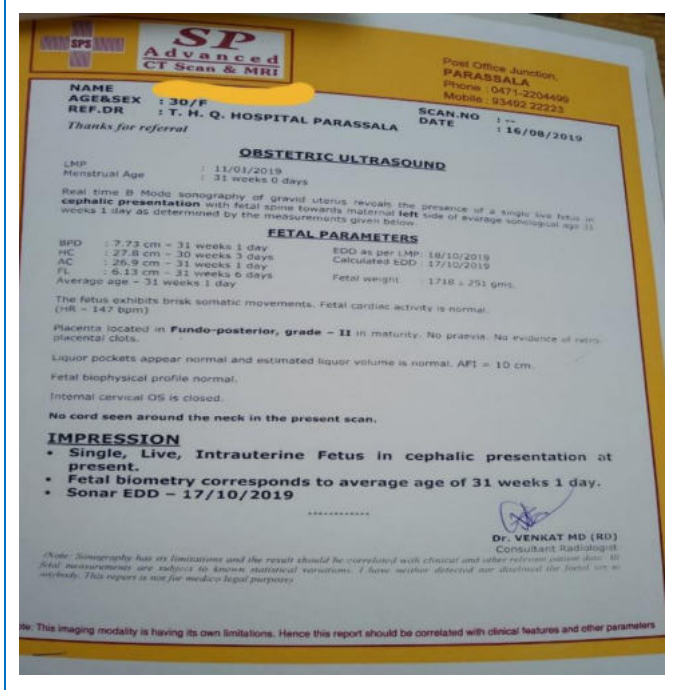
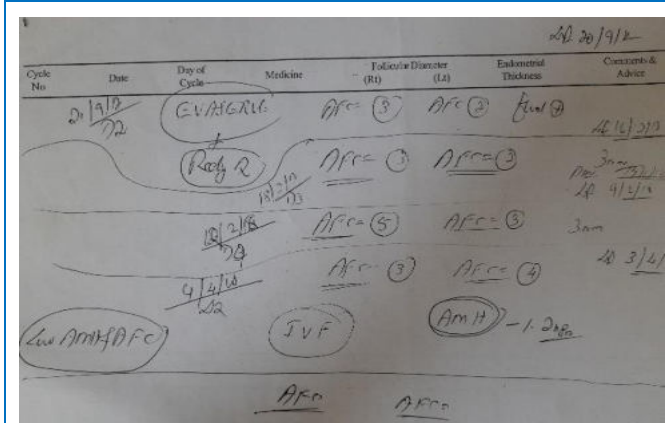
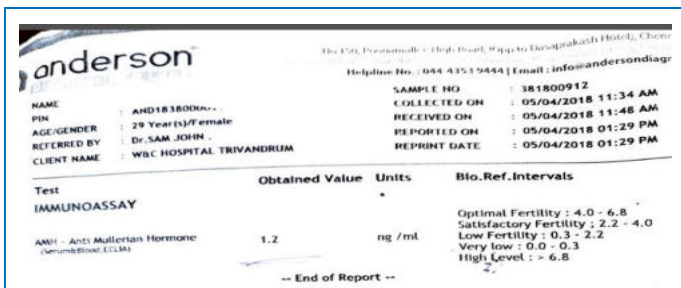
Infertility is becoming one of the major health concern in the present day life. The case reporting with DOR is increasing. The most appropriate correlation of DOR can be done with *Dhatukshaya Vandhya* explained in *Haritha Samhita*. *Dhatukshaya Vandhya*, is due to depletion of *Dhatu*s or due to inadequate formation of *Dhatu*s, especially *Arthava* and *Sukradhatu* which in turn leads to reduction in fertility potential and ultimately *Anapathyatha*.

Samana Chikitsa which normalises *Vata* and *Pitta*, promotes *Rasa Dhatu, Arthavaupadhatu, Sukradhatu* is highly beneficial in the treatment of DOR. Drugs having *Vrishyaguna, Rasayana* property will increases the reproductive potential. Management of DOR by

adopting the treatment concepts of *Dhatukshaya Vandhya* was effective. No treatments can slow ovarian aging and truly prevent diminished ovarian reserve. However, treatments opted for regularising the markers of ovarian reserve can improve the quality of ovum which may enhance the successful rate of conception and preventing associated health issues.

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