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DEVELOPMENTAL ABNORMALITIES OF MULLERIAN DUCT- A REVIEW

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ABSTRACT

The *beeja (sukra and artava rupa)* has chromosomes with genes representing the future organs to be developed. Any abnormality in the *beeja*, *beejabhaga*, *beejabhagaavayava* leads to various congenital abnormalities in foetus. Mullerian duct anomalies are one of the congenital abnormalities of the female reproductive tract resulting from failure in the development of the Mullerian ducts and their associated structures. Their cause has yet to be fully clarified, and it is currently believed to be multi factorial. Symptoms appear during adolescence or early adulthood, and affect the reproductive capacity of these women. When clinically suspected, investigations leading to diagnosis include imaging methods such as hysterosalpingography, ultrasonography and MRI. Mullerian duct anomalies consist of a wide range of defects that may vary from patient to patient. The aim is to understand the congential malformation of mullerian duct through *Ayurveda*.

Keywords: *Beeja*, *Beejabhaga*, Mullerian duct anomalies.

INTRODUCTION

The *beeja* and its component are the subtle form of the future organs and parts of the body and the particular parts consequently develop into the specific organs and parts. Acharyas states that if specific part of *beejabhaga avayava* is vitiated, it leads to the vitiation of that specific organs being generated from the part. *Vata dosha* also vitiated and hampers the development of reproductive organs. Some of the particular *beejabhaga* is responsible for formation of *garbhasaya* and artava, vitiation of these *beeja bhagas* lead to defective formation of the *garbhasaya* and *artava* in fetus. Different degrees of mullerian duct anomalies can be considered as defective formation of *garbhasaya* and *artava.*

Mullerian ducts are Paired ducts derived from intermediate mesoderm in females known as paramesonephric duct. Named after Johannes peter mullero -described them in 1830.

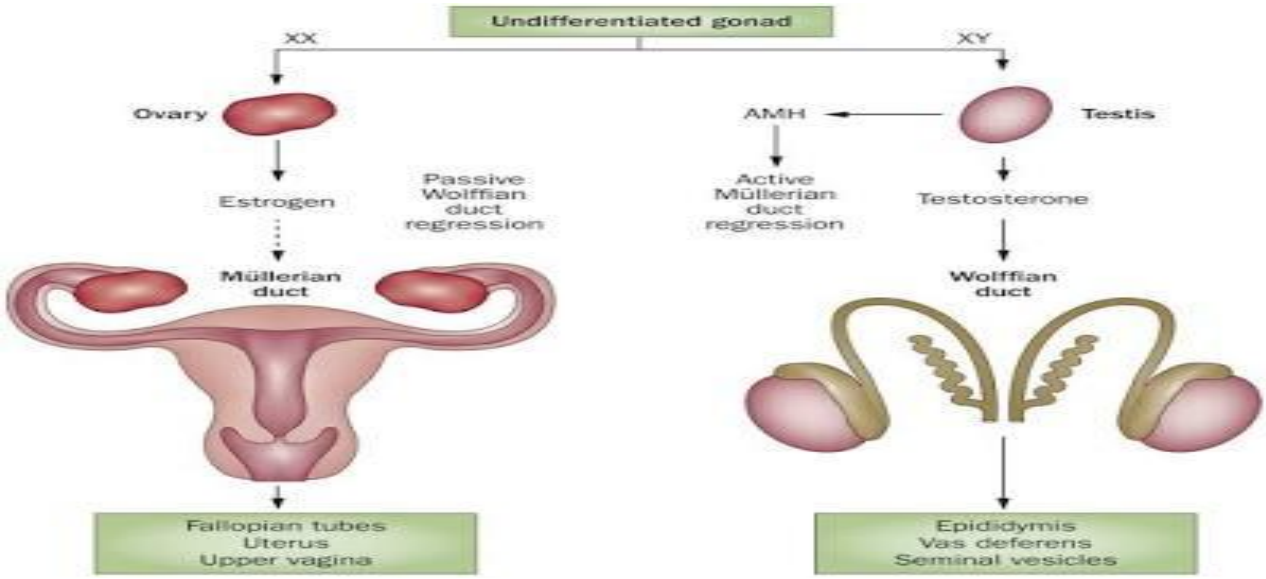
The mullerian ducts are paired embryologic structures that undergo fusion and resorption in utero to give rise to the uterus, fallopian tubes,

cervix and upper 3/5 of the vagina. Interruption of the normal development of the mullerian ducts can result in formation of mullerian duct anomalies (MDA). MDA are a broad and complex spectrum of abnormalities that are often associated with many gynaecological and obstetric complications. The prevalence of these anomalies ranges from 0.001 to 10% in the general population and from 8-10% in women with an adverse reproductive history[1]. The embryological development of the female reproductive system is closely related to the development of the urinary system, and anomalies in both systems may occur in up to 25% of these patients. Other associated malformations may affect the gastrointestinal tract (12%) or musculoskeletal system (10-12%) [2,3].

EMBRYOLOGY

At 5th week of intra uterine life primordial germs cells migrate from yolk sac via dorsal mesentry populate the posterior body wall. Induce the coelomic epithelium to form primitive sex cords. Sex cords proliferate and produce genital ridges. The sex cords surround the germ cells and will become ovarian follicle in female sertoli cells in males. At the end of 6 weeks of fetal life, primitive ducts will be formed which includes both mesonephric duct and paramesonephric ducts. After this point male and female phenotype diverges. The paramesonephric ducts are situated lateral to mesonephric duct. In the absence of hormonal (Testosterone and MIF) input these ducts will get close to each other. The two ducts are initially separated by a septum but later fuse to form the uterine canal. The united lower vertical parts form the uterovaginal canal. The unfused cranial part of each paramesonephric duct forms uterine tubes. The distal open end forms the abdominal ostium[4].

Picture 1: Embryology of Female Reproductive Organs



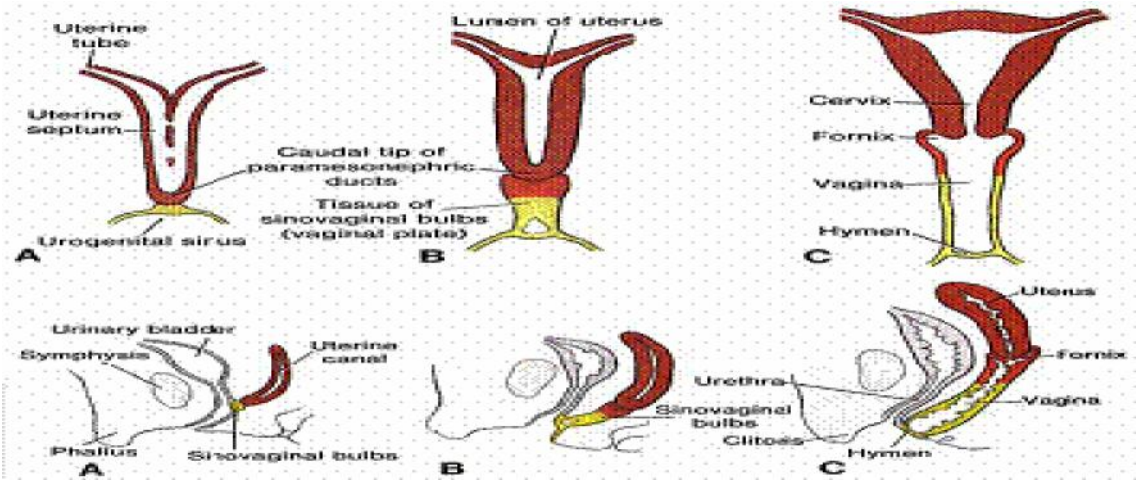
UNDESTANDING OF MULLERIAN DUCT ANOMALIES

To understand the origins of uterine and vaginal anomalies the process is typically related to

- Failure of mullerian duct to fuse at a particular point
- Failure of the tubes to fully descend to the urogenital sinus

Complete formation and differentiation of mullerian duct into female reproductive system depends on completion of 3 phases of development.

Picture 2: Differentiation of Mullerian Duct Into Female Reproductive System



A. Formation
B. Fusion
C. Septal resorption

Any defects in these three processes can lead to MDA.

FORMATION

- One or both mullerian duct may not develop fully – uterine agenesis or hypoplasia, unicornuate uterus.

FUSION-

- Lateral fusion – process during which lower segment of paired mullerian duct fuse. Improper fusion can lead to uterine didelphys, Bicornuate uterus, Arcuate uterus.
- Vertical fusion – fusion of ascending sinovaginal bulb with descending mullerian duct – Improper fusion can lead to Transverse vaginal septum.

SEPTAL RESORPTION-

After fusion central septum persist later resorps to form single uterocervical cavity – if septal resorption fails to occur it will lead to Septate uterus.

Asymmetric obstructed disorders of uterus and vagina, as these tend to be associated with ipsilateral renal agenesis. Though there is no direct reference for mullerian duct anomalies in ayurveda, it can be considered under the broad heading of *beeja dusti* and *beeja bhaga dusti* mainly.

BEEJA DUSTI

Aggravated *vata* in mother affects *artava rupa beeja* during *garbhadana*. Due to abnormalities of *beeja*, *atma*, *karma*, *asaya*, *kala* and *ahara vihara*, the vitiated *doshas* produce abnormalities of fetus, affecting its appearance, *varna* and *indriyas*[5].Abnormalities in *beeja* leads to *yonivyapad* like *sandi yonivyapad*, *suchimuki yonivyapad.*

SANDI YONIVYAPAD

Acharya charaka says, due to abnormalities of *beeja (artava)* the uterus of the female is affected with *vata*. A woman with female phenotype having *beeja doshas* (chromosomal abnormalities) and suffering with deficient secondary sexual characters and un established reproductive functions like lack of menarche and menstruation should be considered under *sandi yonivayapad.*[6,7]

Sandi yonivyapad can be considered as Turner's syndrome (XO monosomy)

SUCHIMUKI YONIVYAPAD

Acharya charaka says, that when a pregnant woman consumes *vata* aggravating *ahara vihara*, this aggravated *vayu* due to its dryness vitiates *yoni* of female fetus, thus the orifice of *yoni* becomes very narrow. It can be considered as different grades of mullerian agenesis and dysgenesis.[8]

BEEJA BHAGA DUSHTI

Acharya Charaka has explained *garbhanga vikruti* depends upon the condition of *beeja*. Whatever part of the *beeja* is defective; the body part developing from that portion of *beeja* will be abnormal. *Beeja-bhaga* is responsible for formation of various organs. Vitiation of beeja-*bhaga* responsible for the formation of reproductive organ (uterus, fallopian tube, cervix and vagina) leads to defective formation that particular organ which exhibits congenital deformities of female genital organs leading to reproductive failure[9].

VANDHYA

The *beeja-bhaga* responsible for formation of *garbhashaya* is totally vitiated it leads to *vandhya. Vandhya* can be consider as different degrees of mullerian agenesis i.e. absence or incomplete development of mullerian ducts leading to complete absence of uterus, septate uterus, uterus didelphys, bicornuate uterus, unicornuate uterus, arcuate uterus[10,11].

MULLERIAN DUCT ANOMALIES

UTERINE ABNORMALITIES

CLASSIFICATION OF MULLERIAN ANOMALIES-

According to AFS[12]

CLASS I – Agenesis/hypoplasia ➢ Vaginal ➢ Cervical ➢ Fundal ➢ Tubal CLASS II – Unicornuate ➢ Communicating ➢ Non communicating ➢ No cavity ➢ No horn	CLASS III – Didelphys CLASS IV – Bicornuate ➢ Complete ➢ Partial CLASS V – Septate ➢ Complete ➢ Partial CLASS VI – Arcuate CLASS VII – DES related anomalies

INCIDENCE OF MDA[13]

Total mullerian duct anomalies – 3-4%

- Agenesis - 4%
- Unicornuate - 10%
- Uterine didelphys - 8%
- Bicornuate uterus - 26%

- Septate uterus - 35%
- Arcuate uterus - 18%

Class I (HYPOPLASIA/AGENESIS) includes entities such as uterine/cervical agenesis or hypoplasia. The most common form is the Mayer-Rokitansky-Kuster-Hauser syndrome, which is combined agenesis of the uterus, cervix, and upper portion of the vagina.

Class II (UNI-CORNUATE UTERUS) is the result of complete, or almost complete, arrest of development of one Mullerian duct. If the arrest is incomplete, as in 90% of patients, a rudimentary horn with or without functioning endometrium is present.

Class III (DIDELPHYS UTERUS) results from complete non-fusion of both Mullerian ducts. The individual horns are fully developed and almost normal in size. Two cervices are inevitably present.

Class IV (BI-CORNUATE UTERUS) results from partial non-fusion of the Mullerian ducts. The central myometrium may extend to the level of the internal cervical is (bi-cornuate unicollis) orexternal cervical is (bi-cornuate bicollis). The latter is distinguished from didelphys uterus because it demonstrates some degree of fusion between the 2 horns, while in classic didelphys uterus, the 2 horns and cervices are separated completely.

Class V (SEPTATE UTERUS) results from failure of resorption of the septum between the 2 uterine horns. The septum can be partial or complete, in which case it extends to the internal cervical is. The uterine fundus is typically convex but may be flat or slightly concave (<1 cm fundal cleft).

Class VI (ARCUATE UTERUS) has a single uterine cavity with a convex or flat uterine fundus, the endometrial cavity, which demonstrates a small fundal cleft or impression (>1.5 cm). Mild thickening of the midline fundal myometrium resulting in fundal cavity indentation but normal outer fundal contour.

Class VII (DIETHYLSTILBESTROL-RELATED ANOMALY) has occurred in several million women who were treated with diethylstilbestrol (DES), an estrogen analogue prescribed to prevent miscarriage from 1945-1971. Affected female fetuses have a variety of abnormal findings that include uterine hypoplasia and a T-shaped uterine cavity.

CLINICAL IMPLICATIONS

- Mullerian anomalies are frequently asymptomatic and are often missed in routine gynecological examinations. Nevertheless, a history of pelvic pain following the menarche, dysmenorrhea, primary amenorrhea and changes to menstrual flows may be present.
- Among the ductal differentiation malformations, vaginal agenesis presents with primary amenorrhea and dyspareunia. In cases of uteri with a functional endometrium, hematometra and hematocolpos are frequent findings.
- In unicornuate uterus if a rudimentary, noncommunicating uterine horn is present together with a functional endometrium, hematometra and sometimes hematosalpinges may be found.
- Uterine septum is generally an asymptomatic condition and is often only diagnosed when couples with a history of repeated miscarriage or infertility are undergoing investigation. Likewise, lateral fusion defects, which are responsible for uterus didelphys and bicornuate uterus.

- Anomalies resulting from failure in vertical fusion, such as cervical agenesis, transverse vaginal septum and imperforated hymen, are associated with primary amenorrhea, hematocolpos and hematometra.
- Mullerian malformations include decreased intraluminal volume, inadequate vascularization of regions such as the septum, presence of a medial wall or an unfused uterine horn and greater uterine contractility and irritability, thereby leading to miscarriages and premature deliveries.
-

CLINICAL DIAGNOSIS

Uterine anomalies are unnoticed until puberty in a majority of cases.

- At puberty- Few cases are typically discovered with subsequent menstrual abnormalities like primary amenorrhea, primary dysmenorrhea.
- At childbearing age- patients present with infertility or with unsuccessful pregnancy outcomes

These anomalies are not easily discovered on routine gynaecological exams, diagnose accidentally during imaging evaluation for another condition or during surgery.

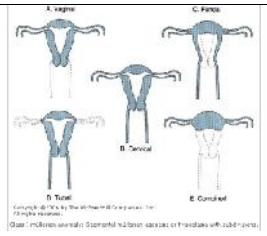
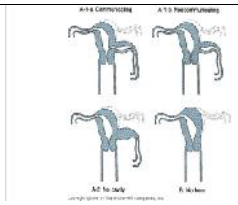
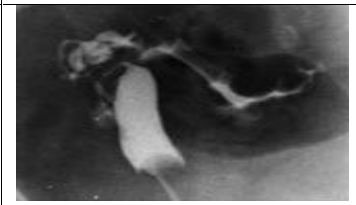
INVESTIGATIONS

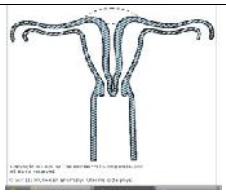
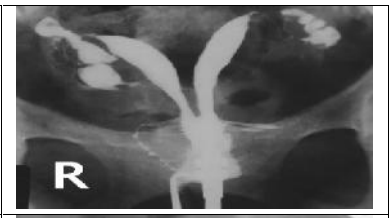
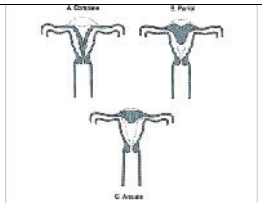
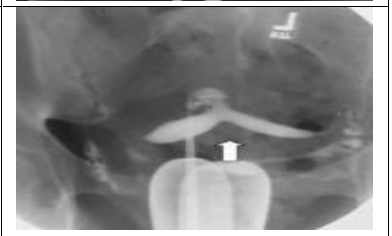
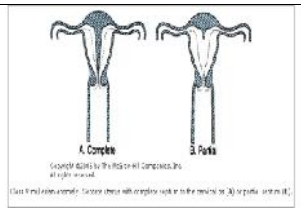
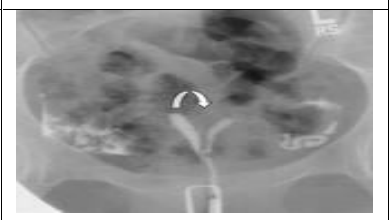
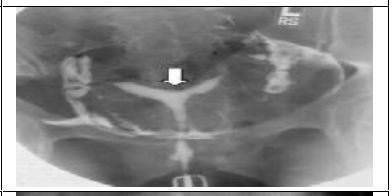
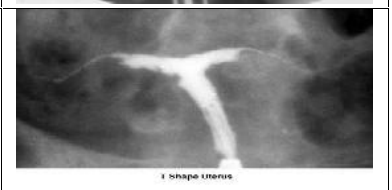
Hysterosalpingography (HSG) is the method used to evaluate the cervical canal, uterine cavity and Fallopian tubes. Its efficacy in diagnosing anomalies is debatable and varies according to the specific type of malformation

Three-Dimensional Ultrasonography (3D-USG)has shown high specificity and sensitivity in evaluations on all uterine anomalies, including Mullerian malformation

MRI- it provides high resolution images of the uterine body, fundus and internal structures.

Table 1: Mullerian Duct Anomalies With Imaging And Findings

Classification	Anatomical Representation	Imaging Findings	Imaging
AGENESIS/ HYPOPLASIA		• Absence of the cervix / uterus with a blind-ending vagina. • In uterine agenesis, no uterine tissue is present. • In uterine hypoplasia, the endometrial cavity is small with intercornual distance < 2cm	
UNICORNUATE UTERUS		• Banana shaped uterine cavity. • Full development of single uterine horn • A normal appearing cervix	

UTERUS DIDELPHYS		• 2 uterine horn with cervix and vagina	
BICORNUATE UTERUS		• Two uterine cavity with single cervix	
SEPTATE UTERUS		• Uterine cavity with septum	
ARCUATE UTERUS		• A single uterine cavity with a broad saddle shaped indentation at the uterine fundus	
DES- RELATED ANOMALIES		• T- shaped uterus	

VARTA

The *beeja-bhaga* responsible for formation of both *garbhashaya* and *artava* is vitiated it leads to *varta*, who is having only external feminine characters in abundance but not female[14].

Varta can be considering as intersexuality with a female phenotype as in testicular feminisation syndrome, triple X chromosome.

DISCUSSION

In Ayurveda description of *beeja, beejabhaga, beejabhagaavayava* which probably resemble pronucles of gametes chromosomes and gene. Vitiation of *dosha* affects beeja, *beejabhaga, beejabhagaavayava*. *Beeja dusti* and *beejabhaga dusti* are main cause for *garbha vikriti* and *yoni vyapad*. *Garbha vikriti* is one of the *ashubha bhava* of pregnancy. Developmental anomalies of the mullerian duct system represent some of the most fascinating disorders that obstetricians and gynecologists encounter. They range from uterine and vaginal agenesis to

duplication of the uterus and vagina to minor uterine cavity abnormalities. These abnormalities in minor form can be asymptomatic but when gross anomalies are present, may have a grave impact on health of a woman. Establishing an accurate diagnosis is essential for planning treatment and management strategies. *Nidana parivarjana, rajaswala paricharya, garbhadhana vidhi, garbini paricharya* and normalcy of *doshas* are having the prime importance in prevention of *garbha vikriti.*

CONCLUSION

Beeja, beejabhaga, beejabhagaavayava dusti, directly correlated Mullerian duct anomalies. Mullerian duct developmental abnormalities can affect the normal physiology of a woman ranging from amenorrhoea to abortions.Hence a depth knowledge of these abnormalities is very much essential which will further pave a way to diagnosis and treatment.

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