# MÜLLERIAN DUCT ANOMALIES- DIAGNOSTIC IMAGING IN PEDIATRIC AND ADOLESCENT POPULATION

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# ANOMALIJE MÜLLER-OVIH KANALA-DIJAGNOSTIČKI IMIDŽING U PEDIJATRIJSKOJ I ADOLESCENTNOJ POPULACIJI

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## ABSTRACT

*Müllerian duct anomalies (MDAs) are congenital entities that result from the non-development, defective vertical or lateral fusion, or the resorption failure of the Müllerian (paramesonephric) ducts. MDAs represent a more frequent entity than previously believed. Few recent meta-analyses reported a prevalence of 5.5 - 6.7%. MDAs are commonly associated with other anomalies, specially kidneys, so identification of both kidneys is important. In pediatric and adolescent population MDAs are discovered incidentally at patients observed for some other reason or because of the primary amenorrhea and low abdominal pain related to hematometra (colpos). Imaging is essential for a diagnosis, management, and reproductive counseling in patients with MDA. Patients suspected of having the MDA are often initially referred to pelvic ultrasonography (US). Field-of-view restrictions with US, patient body habitus and artifact from bowel gas may result in a request for the further MagneticRresonance Iimaging (MRI). Also US cannot help identify the type of the MDA. MRI is the imaging standard of reference because it is non-invasive, does not involve ionizing radiation, has a multiplanar capability, allows an excellent soft-tissue characterization, detailed delineation of the uterovaginal anatomy and accurate classification of the type of anomaly. This is especially true for young female patients, in whom the use of vaginal US probes is avoided. Establishing an accurate diagnosis is essential for planning treatment and management strategies. The surgical management of MDAs is specific to the type of malformation and may vary in a specific group.*

**Keywords**: *Müllerian Duct Anomaly, ultrasound, magnetic resonance imaginig*

## SAŽETAK

*Anomalije Müller-ovih kanala (MDA) su kongenitalni poremećaji koje nastaju usled nerazvijanja, oštećene vertikalne ili bočne fuzije ili neuspeha resorpcije Müller-ovih (paramezonefričnih) kanala. MDA predstavljaju češći entitet nego što se ranije verovalo. Nekoliko nedavnih meta-analiza prijavilo je prevalencu od 5,5 - 6,7%. MDA se obično povezuju sa drugim anomalijama, posebno bubrezima, tako da je identifikacija oba bubrega važna. Kod pedijatrijske i adolescentne MDA se otkrivaju slučajno kod pacijenata posmatranih iz nekog drugog razloga ili zbog primarne amenoreje i bola u donjem abdomenu koji su povezani sa hematometrom (kolposom). Imidžing je neophodan za dijagnostiku, lečenje i reproduktivno savetovanje kod pacijenata sa MDA. Pacijenti za koje se sumnja da imaju MDA često se u početku upućuju na ultrazvuk male karlice (US). Ograničenja vidnog polja kod US, konstitucija pacijenta i artefakti iz creva mogu usloviti potrebu za daljim magnetno rezonantnim imidžingom (MRI). Takođe US ne može pomoći u identifikaciji vrste MDA. MRI je referentni dijagnostički imidžing standard jer je neinvazivan, ne uključuje jonizujuće zračenje, ima multiplanarnu sposobnost, omogućava odličnu karakterizaciju mekog tkiva, detaljnu delineaciju uterovaginalne anatomije i tačnu klasifikaciju vrste anomalije. Ovo se posebno odnosi na mlade pacijentkinje, kod kojih se izbegava primena vaginalnih US sondi. Uspostavljanje tačne dijagnoze je neophodno za planiranje strategija lečenja i lečenja. Hirurški tretman MDA je specifičan za vrstu malformacije i može varirati u određenoj grupi.*

**Ključne reči:** *anomalije Müller-ovih kanala, ultrazvuk, magnetna resonanca*

## ABREVIATIONS

**MDA** – Müllerian duct anomaly
**US** – Ultrasound
**MRI** – Magnetic resonance imaging
**DES** Diethylstilbestrol
**ASRM** – American Society of Reproductive Medicine
**AFS** – American Fertility Society
**ESHRE** – European Society of Human Reproduction and Embryology
**ESGE** – European Society for Gynaecological Endoscopy
**2D** – Two dimensional
**3D** – Three dimensional
**FSE** Fast Spin Echo
**SE** – Spin Echo
**SSFSE** – Single-Shot Fast Spin-Echo

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## INTRODUCTION

Müllerian Duct Anomalies (MDAs) are congenital entities that result from non-development, defective vertical or lateral fusion, or resorption failure of the Müllerian (paramesonephric) ducts (1). MDAs represent a more frequent entity than previously believed. The most of MDAs are asymptomatic, without any clinical relevance, but some types are associated with infertility and different gynecological and obstetric conditions.

## OBJECTIVE OF THE RESEARCH

Objective of this non – systematic review is to determine prevalence, clinical presentation and current diagnostic imaging standards od MDAs in pediatric and adolescent population.

## EMBRIOLOGY, PREVALENCE, CLASSIFICATION AND CLINICAL PRESENTATION OF MDAS

Müllerian ducts develop cephalocaudally from embryonal mesoderm to form the fallopian tubes, fusing distally to create the uterus, cervix, and cranial two-thirds of vagina (2). MDAs are not associated with anomalies of the external genitalia or ovarian development (3). Factors associated with MDAs are intrauterine and extrauterine elements, genetics, and teratogens (eg, diethylstilbestrol [DES], thalidomide). The genetics of Müllerian duct anomalies are complex. In general, they occur sporadically and most familial cases are multifactorial (4).

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 30% of these patients (1, 5). Strong consideration should be given to evaluating potential genital tract anomalies in females with antenatal or postnatal diagnoses of renal agenesis, ureteral ectopia, or a multicystic dysplastic kidney with or without associated hydrocolpos (6).

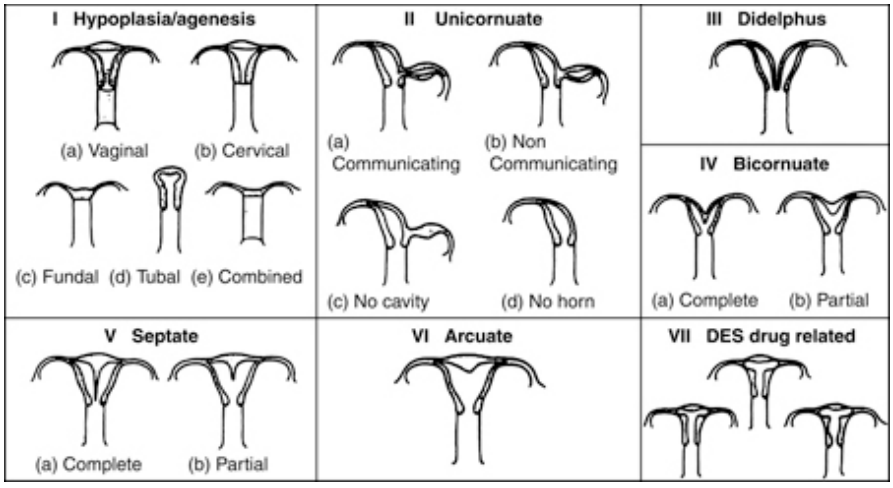
Other associated malformations may affect the gastrointestinal tract (12%), musculoskeletal system (10-12%) and cardiac system (6%) (3, 5, 7).

MDAs are most often found in women with a previous history of infertility and a repeated spontaneous abortion with the prevalence of 8-25% (1-4, 8). Previously reported prevalence in unselected populations ranged from 0.4% to 1%, but few recent meta-analyses reported a prevalence of 5.5 - 6.7% (2, 8). It should be noticed that term general population is not quite correct, as most of studies in this group included women being investigated for non-obstetric or fertility problems, such as the pelvic pain, abnormal bleeding, ovarian cancer screening and suspected pelvic pathology (4, 8). Also many anomalies remain unidentified as most of them are asymptomtic.

Prevalence in pediatric and adolescent population is not estimated, as MDAs are mostly asymptomatic in this population and most of the imaging reviews currently available in the references focus on the diagnosis of MDA in adults, so it is considered that prevalence in this population follows those found for general population (1, 2).

The most widely accepted method of categorizing MDAs is the American Society of Reproductive Medicine (ASRM) classification (former American Fertility Society (AFS)). This system organizes MDAs according to the major uterine anatomic defect and include 7 classes: hypoplasia/agenesis (vaginal, cervical, fundal, tubal, combined), unicournuate uterus (rudimentary horn with an endometrial cavity that communicates/does not communicates with the uterus, rudimentary horn with no endometrial cavity, no rudimentary horn), didelphys uterus, bicournuate uterus (complete/partial), septate uterus (complete/partial), arcuate uterus, DES drug-related (9).

**Figure 1.** Diagram from the American Fertility Society Classification of Müllerian Abnormalities (9).



There are some problems about the ASRM classification, as all of anomalies are not included (vaginal) neither combinations of two nor more anomalies. In children due to the small uterus it is hard to classify-for example for diagnosis of bicournuate uterus the external fundal cleft must measure at least 10 mm, but in prepubescent girls, the entire normal uterus may measure only 20 mm. Also arcuate uterus(class VI) has no clinical significance so it is a question that should be considered as normal variant and thus excluded from the classification system (2).

A new anatomy-based classification was established by the European Society of Human Reproduction and Embryology (ESHRE) and the European Society for Gynaecological Endoscopy (ESGE), classifying the anomalies according to the morphology of the uterus, cervix and vagina, independently (10, 11).

**Figure2.** ESHRE/EGRE classification of MDA (12)

| **Uterine anomaly** | | | **Cervical/ Vaginal anomaly** | |
|---|---|---|---|---|
| | Main class | **Sub-class** | **Co-existent class** | |
| U0 | Normal uterus | | C0 | Normal cervix |
| U1 | Dysmorphic uterus | a- T-shaped<br>b- infantile<br>c- other | C1 | Septate |
| | | | C1 | Double “normal“ |
| | | | C3 | Unilateral aplasia or dysplasia |
| U2 | Septate uterus | a-partial<br>b- complete | C4 | Aplasia or dysplasia |
| | | | V0 | Normal vagina |
| U3 | Bicorporeal uterus | a-Partial<br>b-complete<br>c- septate | V1 | Longitudinal non obstructing vaginal septum |
| | | | V2 | Longitudinal obstructing vaginal septum |
| U4 | Hemi uterus uterus | a-with/b-without rudimentary cavity | V3 | Transverse vaginal septum or imperforate hymen |
| U5 | Aplastic uterus | a-with/b-without rudimentary cavity | V4 | Vaginal aplasia |
| U6 | Unclassified uterus | | | |

The ESHRE and ESGE classification classifies 38 of the 39 congenital anomalies of the female genital tract, whereas the ASRM classification is not as comprehensive (10, 11).

But still the ASRM classification is most used at the moment.

Early identification of MDAs helps avoid prolonged symptomatic periods in young adolescents and the complications that may subsequently arise, such as hydronephrosis (mostly in obstructed anomalies), endometriosis, and infertility (1).

In the prepubertal pediatric population, MDAs are often asymptomatic and incidental findings on studies are obtained for other reasons (13). MDAs are frequently associated with abnormalities of the renal and axial skeletal systems (wedged or fused vertebral bodies and spina bifida), gastrointestinal and cardiac anomalies, and they are often the first encountered when patients are initially examined for associated conditions (1, 3, 4). MDAs are commonly associated with renal anomalies, with a reported prevalence 30-40% (1, 3). The most common is renal agenesis (most commonly unilateral agenesis), however ectopia, hypoplasia, fusion, malrotation, duplication and cystic renal dysplasia (1, 4).

The onset of menses can prompt more clinical symptoms. The patient will be presented with primary amenorrhea or severe cyclic abdominal pain secondary to obstructed uterine drainage (hematometra/colpos) associated with the uteral agenesis/hypoplasia (1, 13).

In adolescent, in case of the unicornuate uterus with noncommunicating accessory horns that have an endometrial cavity hematometra development and there is also an increased risk of developing endometriosis, which usually resolves after excision of the horn.

Impaired fertility and obstetric complications such as the spontaneous abortion, malpresentation, intrauterine growth retardation and preterm delivery (14). Unicornuate uterus is associated with the poorest fetal survival among all Müllerian Anomalies (4). Septate uterus has the worst obstetric outcome of all Müllerian Duct Anomalies, with a high abortion and pregnancy complication rates compared to the bicornuate uterus (15).

## DIAGNOSTIC IMAGING

Imaging plays an essential role in MDAs diagnosis and treatment planning.

In pediatric and adolescent population most commonly used are ultrasound (US) and magnetic resonance imaging (MRI) as noninvasive, without ionizing radiation and with a high accuracy in MDAs identification and classification. A key component of MDAs characterization is the external uterine fundal contour, which is well observed using both US and MRI (3).

### US

In younger patients ultrasound is the preferred modality due to the excellent visualization, the dynamic nature of the examination modality, lack of ionizing radiation and sedation risks, and comparatively lower cost (1).

Field-of-view restrictions with US, patient body habitus, and artifact from bowel gas may result in a request for further imaging with MR imaging. Image quality for all US techniques is highly operator dependent.

Most commonly is used transabdominal two-dimensional (2D) imaging, ideally through a distended bladder, but offers reduced sensitivity and specificity because of the increased distance from the uterus and, often, intervening bowel (16).

In pubertal patients it may be advantageous to perform the scan during the latter part of the menstrual cycle, as the thick and a highly echogenic appearance of the endometrium during this time may accentuate visualization of the MDA (3).

More recently, three-dimensional (3D) US of the uterus has been reported to improve depiction of the external fundal contour. With the advent of 3D techniques, US may have the future potential to match the capabilities of MR imaging (10, 11). Reports have shown that three-dimensional ultrasound scan has a high sensitivity and specificity, as high as 100% in diagnosing uterine anomalies (8).

2D endovaginal sonography is very useful but limited because of persistent hymen in most of pediatric and adolescent population or because discomfort of young patients. Endosvaginal ultrasonography allows a more detailed analysis of the endometrium, uterine cavity and cervix. The specificity of this examination ranges from 85 to 92% (14).

Also transperineal/rectal US can be used for an assesment of some MDAs, but it is not in common use.

### MRI

MDAs are often diagnosed with US, but further investigation is necessary to define the MDA type and to assess whether intervention is required. At present, magnetic resonance (MR) imaging is the study of choice because of its high accuracy (95-100%), detailed delineation of the uterovaginal anatomy, ability to details both the uterine cavity and external contours, noninvasiveness, and lack of ionizing radiation (5). This is especially true for pediatric patients, in whom the use of vaginal US probes is avoided (1, 6, 8).

For the diagnosis of most anomalies, next sequences are sufficient:

- Sagittal T2 FSE (without fat-saturation pulse) images. This sequence is useful for determining anterior versus retroverted uterus and to set up subsequent oblique scans along the long and short axes of the uterine fundus.
- Oblique long-axis T2 FSE (without fat-saturation pulse) images are similar to sagittal T2 FSE sequences but obtained along the long axis of the uterus (perpendicular to the sagittal plane, usually a slightly oblique coronal). This plane is ideal for visualization of the uterine cavity and uterine fundal contour.
- Oblique short-axis T2 FSE (without fat-saturation pulse) images are perpendicular to the long axis and sagittal planes (usually oblique axial), providing short-axis (target) views of the uterine cavity useful for visualizing a transverse septum if present.
- Axial fat-suppressed T1 spin-echo (SE) images are also obtained to evaluate for the presence of blood products in cases of obstruction and hemato (metro) colpos.
- Coronal T2 single-shot fast spin-echo (SSFSE) images of the kidneys, ureters, and pelvis provide good localized and survey views of kidneys and ureters. This sequence is important because of the high incidence of associated renal anomalies (up to 50%), including agenesis, kidney duplication, or pelvic kidney.
- Axial T1 SE (without fat-saturation pulse) images. Fat signal is useful to delineate pelvic structures (1, 3,14).

It is important to observe next structures:

1. Uterus:
    - Size: Uterine length normally measures from 1cm in pediatrics to 9cm in reproductive women and the uterine body to cervix ratio is 1:1 in pediatrics to 2:1 in reproductive women (in sagittal plane).
    - Inter-cornual distance is normally from 2-4cm (in the oblique long-axis images).
    - External fundal contour is normally convex (best detected in long-axis oblique images).
    - Zonal anatomy is the differentiation between the high-signal-intensity endometrium, the low-intensity junctional zone (inner myometrium), and the intermediate-intensity outer myometrium, as depicted in T2-weighted images. It is normally seen in the reproductive age group.
    - Uterine septum: Evaluating its presence, its signal intensity and extent.
    - Inter-cornual angle: the angle between the most medial aspects of the two uterine hemi cavities.
    - Obstruction: Distended blood-filled uterus/cervix and in extreme cases blood-filled fallopian tubes.

2. Vagina
   - The direction and extent of a vaginal septum and the obstruction site of a blood-filled vagina, if present.
3. Ovaries
   - Both ovaries should be identified. And any associated lesions such as endometriosis noted.
4. Associated pelvic lesions or renal anomalies (15, 17)

## CLASS I - AGENESIS/HYPOPLASIA

The most common form is the Mayer-Rokitansky-Kuster-Hauser syndrome. This consists of a combined agenesis of the uterus, cervix and upper portion of the vagina.

Ultrasonographic findings can add support to the clinical findings suggesting the absence of uterus and fallopian tubes in the presence of normal ovaries, but evaluation of a uterine remnant may be difficult with US owing to the limited acoustic window and generally small uterus in pediatric population (4, 14). In uterine agenesis, no identifiable uterine tissue is noted. Partial agenesis of Müllerian Duct derivatives also can be visualized. In uterine hypoplasia, the endometrial cavity is small, with a reduced intercornual distance (< 2 cm).

MRI is important for differentiating between the uterine agenesis and hypoplasia, both of which can best be assessed on sagittal images. However, vaginal agenesis is best characterized on axial images. In uterine hypoplasia, an abnormal low-signal-intensity myometrium is typically seen on T2-weighted images, with or without an endometrial layer. When a functional remnant is present, poorly differentiated zonal anatomy, reduced endometrial and myometrial width are seen (1, 3, 14).

## CLASS II - UNICORNUATE UTERUS

Ultrasound is useful for identifying rudimentary horns and isreliable for determining whether the horn is communicating. Unicornuate uterus is suspected when a small, rounded uterus is identified in the lateral aspect of the pelvis. If present, a rudimentary horn can be observed as a soft-tissue mass with echogenicity to that of myometrium. If obstructed, a rudimentary horn with functioning endometrium may present as a complex hemorrhagic cystic structure, with high intensity on T1-weighted images.

MRI reveals a slender, laterally deviated banana-shaped uterus. Only 1 fallopian tube is identified. The zonal anatomy is normal, though the uterine volume is reduced. The accessory horn can appear solid because it is not opacified when endometrium is absent. It is located adjacent to the main uterine cavity. It can also be observed as a soft tissue mass. When endometrium is present, a small cavity can be detected; this may or may not communicate with the main endometrial cavity (1, 3, 14).

## CLASS III - DIDELPHYS UTERUS

In didelphys uterus US shows 2 separate normal-sized uteri and cervices that are seen. The 2 uterine horns are usually widely splayed, and endometrial and myometrial zonal widths are preserved. Vaginal septa are most commonly associated with this type and may result in the hematometrocolpos.

MRI reveals 2 widely separated uterine horns, and 2 cervices are typically identified. The intercornual angle is >60°. The zonal anatomy is preserved within each hemiuterus. Obstructions are represented by variable dilation of the vaginal component and diminished endometrial dilation (1, 3, 14).

## CLASS IV- BICORNUATE UTERUS

US may demonstrate 2 uterine cavities with a normal endometrium. The most important imaging finding is a concave fundus with a fundal cleft greater than 1 cm. When the apex of the fundal contour is below or less than 5 mm above a line drawn between the tubal ostia, the uterus is bicornuate (3). This has been shown to be a reliable means of distinguishing bicornuate from septate uteri. An increased intercornual distance (>4 cm) may be observed. The cleft is visualized best on oblique coronal images in the plane of the long axis of the uterus. The septum separating the 2 horns demonstrates echogenicity identical to that of myometrium. The inferior portion of the septum may be fibrous (1, 14).

On MRI, 2 uterine bodies and a single or double cervix characterize the bicornuate uterus. The intercornual distance is increased to >105°. The myometrial tissue that separates the 2 horns has a signal intensity identical to that of the myometrium. The inferior portion of the septum (extending for a variable length inferiorly) may be fibrous, with low T1 and T2 signal intensity (1, 3).

## CLASS V - SEPTATE UTERUS

US may demonstrate a convex or flattened fundal contour. When the apex of the fundal contour is more than 5 mm above a line drawn between the tubal ostia, the uterus is septate (3). The intercornual distance usually is normal or decreased (< 4 cm), and each uterine cavity is usually small. The septum may be composed of muscle or fibrous tissue and may be complete or partial.

MRI provides excellent tissue characterization and helps in reliably differentiating a septate uterus from a bicornuate uterus. MRI reveals low signal intensity for the septum, a normal fundal contour with outward fundal convexity (1).

## CLASS VI - ARCUATE UTERUS

US may detect the abnormality, but typically, it is not clinically significant because the arcuate uterus has no significant negative effects on pregnancy outcome.

MRI findings show convex or flat external uterine contour. The indentation is broad and smooth. The signal intensity is myometrial in composition. A subtle associated indentation in the course of the arcuate vessels is sometimes detected, suggesting aberrant vascularity within the fundal myometrium. Normal zonal anatomy is evident (1, 3).

## CLASS VII - DES RELATED

This class has almost only historical interest as prescription of DES was stopped in the 1970s

US may detect the abnormality as the uterine hypoplasia. At MR imaging, the hypoplastic uterus is seen to have an abnormal T-shaped endometrial configuration (1, 3).

## VAGINAL SEPTUM ANOMALIES

## CLASS I - TRANSVERSE SEPTUM

A transverse vaginal septum divides the vagina into two segments and in most situations resulting in outlet tract obstruction. Hematocolpos can be detected at US. MRI helps determine the thickness of the vaginal septum. Identification of the cervix on MRI is crucial for differentiating a high septum from congenital absence of the cervix (1, 7).

## CLASS II - LONGITUDINAL SEPTUM

Patients may experience difficulty with sexual intercourse or vaginal delivery. US usually do not detect longitudinal septum. MRI can depict a vaginal septum as a thin, low-signal-intensity structure that is best visualized in the coronal or axial plan. T2- weighted images are ideal for differentiating the low-signal-intensity septum from the surrounding high-signal-intensity vaginal mucosa and secretions (1, 7).

## CONCLUSION

MDAs represent wide spectrum of genital anomalies, with prevalence not correctly estimated, but higher than previously believed. This fact might be at least partly related to the availability of noninvasive and accurate diagnostic imaging. In pediatric and adolescent population most of the MDAa are asymptomatic but with potential complications in later years especially as the infertility. Early diagnosis and correct classification are crucial for planning adequate surgical treatment when it's necessary. US represents a widely available method that can point to existence with great certainty for the MDA. Imaging gold standard in pediatric and adolescent population is the MRI, which allows correct classification and has a high positive correlation with surgical findings. In cases that do not fulfill all criteria it is much more important to correctly describe all observed structures than classify the MDA type.

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