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Utility of Magnetic Resonance Imaging over Ultrasound in Evaluation of Mullerian Duct Anomalies

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ABSTRACT

Introduction: Mullerian duct anomalies (MDAs) are complex group of anomalies presenting with menstrual abnormalities and infertility. The diagnosis of MDAs and their proper classification is important from treatment point of view. Most of these anomalies are suspected on clinical ground and subjected to the radiological evaluation. Pelvic ultrasonography (USG) is a commonest screening modality in these patients. However, with time Magnetic Resonance Imaging (MRI) has become modality of choice in evaluation of these pathologies.

In this study we discuss the imaging features of MDAs, utility of USG and MRI in their diagnosis.

Materials and Methods: Total 20 patients who were clinically suspected of having MDAs were included in our study. All underwent MRI .Out of these, 17 patients were subjected to USG pelvis as primary investigation. Age of the patient ranges from 13 to 33 years(with mean age 20.7). Chief presenting complaints were pain in abdomen followed by primary amenorrhea. USG and MRI findings in all these patients were compared and classified accordingly.

Result- Most of the findings seen on USG were confirmed on MRI. MRI showed status of ovaries, location and thickness of Transvaginal septum and associated renal anomalies better than ultrasound. Because of better soft tissue resolution and better contrast, uterus, cervix and vagina were very well appreciated.

Conclusion- Because of its non-invasive nature, use of non-ionizing radiation and excellent soft tissue resolution, MRI has become the investigation of choice in clinically suspected cases of MDA. Accurate classification of MDA is important as it affects the treatment and for which MRI plays important role in diagnosis as well as classification.

Keywords: Magnetic resonance Imaging, Mullerian Duct Anomalies, Ultrasonography.

INTRODUCTION

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 two-thirds of the vagina which occurs between 6th to 11weeks[1]. Any Disruption of normal development of the mullerian ducts results in mullerian duct anomalies (MDAs) [1,2] .The ovaries and distal third of the vagina originate from the primitive yolk sac and sinovaginal bud, respectively. So MDAs are not associated with anomalies of the external genitalia, distal third of vagina or ovaries [2] . Diagnosis of MDAs is clinically important because of the highly associated risk of primary infertility, endometriosis, and miscarriage [3]. It has been

reported that, 15% of women complaining of recurrent miscarriages have MDAs [3]. MDAs are commonly associated with renal anomalies, with a reported prevalence of 30%–50%, including renal agenesis (most commonly unilateral agenesis), ectopia, hypoplasia, fusion, malrotation, and duplication [4-6]. Other congenital anomalies commonly associated with MDAs include those of the vertebral bodies (29%), viz. wedged or fused vertebral bodies and spina bifida (22%–23%), cardiac anomalies (14.5%) and syndromes such as Klippel-Feil syndrome (7%)[7,8].

Classification of these anomalies is of utmost importance as treatment varies with type of anomaly. MDA classification was given by Buttram and Gibbons[9] in 1979. The American Society for Reproductive Medicine has given a revised classification in 1988[10].

Imaging plays important role in diagnosis of particular MDA and hence guide the treatment. Ultrasonography (USG) of pelvic region is the primary modality of choice as it is readily available, inexpensive, less time consuming and does not use ionizing radiation. But disadvantages with USG are that it is a subjective modality. In young, unmarried patient, when we are doing USG pelvis per abdominally field-of-view restrictions, patient body built, and artifact from bowel gases hampers the proper visualization of pelvic structures. Transvaginal ultrasound (TVS) can be done in married; sexually active female with their consent, but still field of view restriction is a major limitation.

Hysterosalpingography (HSG) is commonly used as an initial procedure for evaluation of infertility. But only uterine cavity and fallopian tube patency can be seen in this procedure. Adnexal or other pelvic abnormality could not be assessed. And more over this invasive procedure cannot be done in young, unmarried patients.

So in these situations MR imaging is the modality of choice. MR imaging is a preferred imaging method, as it wonderfully delineates uterine cavity, adnexa and other pelvic organs and external contours[12].

In this study we discuss the utility of USG and MRI in evaluation of MDAs and their classification.

MATERIALS AND METHODS:

Informed consent was obtained from all patients who were part of this study. The cases were retrospectively as well as prospectively reviewed from our MRI database who underwent pelvic MRI at our institution between 2016 to 2018 for suspected mullerian anomalies. Total 20 patients were identified. The age of patients who underwent imaging ranged from 13 to 33 years with mean age of 20.7 years. There were11 adolescent (10-19 years as per WHO definition) and 9 adults. Four patients amongst the study group were already diagnosed as cases of mullerian anomaly and two of them had been treated / operated for the same. The chief complaints with which the patients presented were pain in abdomen (n=9), primary amenorrhea (n=4), infertility (n=2), menorrhagia with dysmenorrhea (n=1), irregular cycles (n=1), spotting per vagina (n=1). Two patients were diagnosed with mullerian anomaly during their first routine antenatal scan. Out of the nine patients who presented with pain in abdomen one patient also had history of primary amenorrhea, another had complains of cyclical pain and acute urinary retention, one had cyclical pain, one patient had difficulty in micturition and two patients had complains of dysmenorrhea. On local examination no vaginal orifice was seen in 5 patients and local bulge at vagina was seen in four patients. The uterus was bulky in 6 patients. On assessment of the secondary sexual characteristics amongst the adolescent patients, secondary sexual characteristics were underdeveloped in 2 patients, absent in one patient and normally developed in eight patients. Other associated anomalies were present in 4 patients. Two patients who were diagnosed as MRKH were operated for congenital inguinal hernia in the past. One patient had imperforate anus while other had short stature. Amongst the study group one patient had a family history of amenorrhea in her elder sister who responded to medical treatment. Other laboratory investigations were done by 5 patients which included karyotyping, hormonal assay (FSH, Oestrogen, TSH, prolactin, anti mullerian hormone), electrolyte assessment, CA 125. CECT abdomen and HSG was done in one patient outside where she was given bulky uterus with? Pyometra; hypoplastic left kidney with left megaureter on CECT abdomen and on HSG - bicornuate uterus with right terminal hydrosalpinx with cystic collection in left vagina communicating with cervical canal was given.

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Another patient had performed HSG which revealed bicornuate uterus.

USG was done as primary screening modality in 17 patients. USG was done using a MYLab 50 Esaote USG with colour doppler ultrasound machine with curvilinear (3.5-5 MHz) array transducer. The various ultrasound findings are as detailed in Table no 1.

MRI: All MRI studies were performed on 1.5 HD XT 16 channel 1.5T GE MRI machine using body coil. Dedicated pelvic MRI sequences were done in all patients using following sequences:

T1WI (TR -634, TE-10); (T-5mm,L-70.6mm), T2WI(TR-5225 ,TE-89.3);(T-3mm,L

56.4mm) ,STIR (TR-7400, TE-49);(T-7, L-52.4),Axial T1 fat sat +c (TR- 350, TE-4.2);(T-5, L-48.6),AXIAL 2D FIESTA FS BH (TR-3.9, TE-1.7) ; (T-9, L-107), COR 2D FS FIESTA (TR-4.1, TE-1.8);(T-6, L-42.4)

MRI contrast study was done in two patients, one with Herlyn-Werner-Wunderlich syndrome and other with transverse vaginal septum. In rest it was not needed. To delineate transverse vaginal septum jelly was used in two cases who were suspected to have transverse vaginal septum. The vaginal length was calculated in patients with MRKH. Abdomen was also screened in patients to look for other associated abdominal pathology. The various MRI findings are as detailed in Table 2.

Additional finding noted on CECT abdomen in a patient was mass lesion in region of head of pancreas, liver metastasis, sclerotic vertebral metastasis.

RESULTS: Our results revealed that most of our patients were in the adolescent age group (55%). The youngest patient aged 13 years and the oldest one with 33 years of age. The chief complaint was pain in abdomen (45%) followed by primary amenorrhea(20%) followed by infertility (10%).The uterus was not seen in 5 patients (25%), bicornuate uterus was present in 5 patients (25%), hypoplastic uterus was seen in 2 patients (10%) and uterus didelphys , septate , sub septate and arcuate uterus were seen in one patient each.

One patient was diagnosed with Herlyn-Werner-Wunderlich syndrome which is a triad of uterine didelphys, obstructed hemivagina and ipsilateral renal agenesis [OHVIRA syndrome] i.e.; (obstructed hemivagina with ipsilateral renal anomaly). Transverse vaginal septum was very well delineated with ultrasound jelly and thickness and location of the transverse vaginal septum could be made out. Hematometra was present in five patients (25%) patients. Out of these five, four had hematocolpos and was secondary to transverse vaginal septum. Two patients were diagnosed with mullerian duct anomaly during their first routine antenatal scan. One patient had bicornuate uterus with pregnancy noted in the right horn and with a small left horn. Another patient had arcuate uterus with intrauterine gestational sac noted within.

Although the ovarian function is well preserved in patients with mullerian anomalies we did find certain variations in ovarian morphology and location. The bilateral ovaries were normal in 11 patients (55%). In four patients either one or both ovaries were ectopic in location (20%). Out of these four patients three patients were diagnosed with MRKH and one patient had hematometra with hematocolpos secondary to transverse vaginal septum.

The right ovary in one patient with MRKH was very small measuring 1 cc in volume and located adjacent to right iliacus muscle (lying anterior to right iliacus muscle along the right iliac blade). However the left ovary was normal in location with a volume of 4cc.

In another patient with MRKH in whom the ovaries were ectopically located the left ovary was located superficially medial to iliopsoas muscle just beneath the anterior abdominal wall with volume of 6cc. The right ovary was located high in the pelvis medial to right psoas muscle with volume of 9cc.

In the third patient diagnosed with MRKH the right ovarian volume was 2.3cc but was normal in location but the left ovary was 10cc in volume and was located superficially just beneath the anterior abdominal wall.

In other patient with hematometra and hematocolpos secondary to transverse vaginal septum the right ovary was located superficially along the right iliacus muscle beneath the anterior abdominal wall with approximate volume of 21cc. However the left ovary was normal in location and volume (8 cc).

In two patients with hypoplastic uterus right ovary was streak like and left ovary could not be seen

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(10%) on MRI. In two patients (10%) polycystic ovaries were present. Bilateral small ovaries (either one or both) were seen in three patients (15%). Unilateral renal agenesis with compensatory hypertrophy of other kidney was noted in two patients (10%). Out of these two patients one was diagnosed with MRKH and other was diagnosed with Herlyn-Werner-Wunderlich syndrome. In one patient with bicornuate uterus with collection in the left horn, the patient had right terminal hydrosalpinx and left megaureter. Hematosalpinx was present in two patients both had hematometra with hematocolpos secondary to transverse vaginal septum. The oldest patient who presented at age of 33 years with menorrhagia with dysmenorrhea was found to have bicornuate uterus with collection in the left horn with bulky cervix. However on clinical examination abdominal lump was palpable and CECT abdomen was done which revealed mass lesion in head of pancreas with liver metastasis and sclerotic vertebral metastasis and her CA -125 levels were raised and so chemotherapy was started.

Also the vaginal length was calculated in patients with MRKH with average vaginal length of 1.7 cm.

DISCUSSION:

In case of Mullerian Duct Anomalies (MDAs) developmental embryology is important as the stage at which interruption occurs will decide the type of anomaly.

Paired mullerian ducts undergo fusion and resorption in utero to give rise to the uterus, fallopian tubes, cervix and upper two-thirds of the vagina which occurs between 6^{th} to 11weeks.

In utero 6 weeks onwards the absence of mullerian-inhibiting factor in the female fetus promotes bidirectional growth of the paired mullerian ducts along the lateral aspect of the gonads in conjunction with simultaneous regression of the mesonephric ducts. Interruption of mullerian duct development during this period results in aplasia or hypoplasia of the vagina, cervix, or uterus[2].

Mullerian ducts get fused in the midline to form the uterovaginal primordium. Interruption of their fusion gives rise to bicornuate uterus and uterus didelphys[2].

Between 9 and 12 weeks gestation, the fused mullerian ducts undergo reabsorption. Interruption of mullerian duct development during this phase gives rise to septate or arcuate MDA subtypes.

The ovaries and distal third of the vagina originate from the primitive yolk sac and sinovaginal bud, respectively. So MDAs are not associated with anomalies of the external genitalia, distal third of vagina or ovaries[2].

There is wide variation reported in the prevalence of the MDA ranging from1%-5% in the general population[12,13]. It accounts for about 13% -25% in women with recurrent pregnancy loss[12].

Most of the patients are of adolescent age group. In our study age ranges from 13 to 33 years (mean age 20.7 years).

The time of presentation of these anomalies will depend on the subtype. The anomaly like transverse vaginal septum will present early around the age of menarche as cyclical abdominal pain. Others like MRKH will present as primary infertility. Arcuate and subseptate uterus will present as recurrent abortions. In our study common presenting complaint was pain in abdomen (n=9) followed by primary amenorrhea (n=4) and primary infertility (n=2). Other lesser common presenting complaints were menorrhagia with dysmenorrhea (n=1), spotting per vagina (n=1), irregular menstrual cycles (n=1). Out of twenty patients, two patients were diagnosed as having MDA during their first antenatal scan.

One patient was diagnosed with Herlyn-Werner-Wunderlich syndrome which is a triad of uterine didelphys, obstructed right hemivagina associated with right hematometrocolpos and hematosalpinx causing compression over the urinary bladder and ipsilateral renal agenesis (OHVIRA syndrome) who presented to the emergency department with pain in abdomen and acute urinary retention. However she had normal menses through the unobstructed left uterine cavity (Fig 1).

Local examination in these patients was challenging as most of them are young and unmarried. In current study, no vaginal opening was seen in five patients, local bulge at the site of vaginal opening was seen in four patients, bulky uterus in six patients. In rest of the patients no obvious anomaly was seen externally. Out of eleven adolescent patients, secondary sexual

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characteristics were underdeveloped in two patients (one is of MRKH and other was of hypoplastic uterus with small ovaries), absent in one who had MRKH and normal in eight patients.

Clinical symptoms in these patients will direct towards the suspicion of MDAs and correct diagnosis of an anomaly (i.e. type) is the mainstay of treatment in these patients. So in these patients imaging plays very important role in screening and diagnosis.

Out of the available imaging modalities, USG pelvis is readily available, rapid, inexpensive, non-invasive and with no risk of radiation. Also in our study patients were subjected to ultrasound as the screening modality. It is frequently done in obstetric and gynaecological evaluation. Ideal time of doing USG pelvis is 8-10 days after menstruation, as endometrium in this phase of cycle is thin. In case of suspected MDA, USG should be done in latter part of the menstrual cycle, as the thick and highly echogenic appearance of the endometrium during this phase of cycle increases the chances of visualization of the MDAs[2]. However in our study, most of the scans were done on emergency basis.

Ultrasound facilitates the visualization of the uterine contour, length of the uterus, cervix, vagina, endometrial thickness, uterine morphology, endocervical canal, endomyometrial junction, uterine and cervical lesions, fallopian tube morphology, ovarian size, their location and morphology. Any adnexal abnormality can be seen depending upon the patients' built and bowel gases. In our study uterus was not seen on USG in 5(25%) patients, hypoplastic in 2 (10%), bicornuate in four (20%), arcuate in 1(5%). Hematometra was seen in five (25%) and hematocolpos in 4(20%). Out of the four patients with bicornuate uterus, two had collection in the left horn and one had pregnancy in the right horn. Both the ovaries were seen in 9 patients (45%), small sized ovary in 1(5%), single ovary is seen in 1(5%) and in 6 patients (30%) bilateral ovaries were not seen. Additional findings like unilateral renal agenesis (2), hematosalpinx (2), ascites (1), pleural effusion (1), echogenic kidney (1) and megaureter (1) were also noted.

With the advent of 3D ultrasound, anomalies leading to abnormal uterine contour viz. bicornuate, septate and arcuate uteri can be very well differentiated [15,16]. Despite all these, there are few limitation of USG in diagnosing MDAs and their accurate classifications. USG is mainly operator dependent imaging modality. It is highly reflected by patient built, bowel gases, uterine position, field of view and standard of machine used. As many patients of MDAs are young unmarried female, Transvaginal USG (TVS) cannot be done in them. In our study TVS was done in 6 patients (30%) and in rest not possible as they were young. In these patients localization of mullerian buds and ovaries with extrapelvic location is difficult to determine on USG[17].

Considering all these shortcomings of USG, MRI has become the imaging modality of choice in MDAs.

MRI because of its multiplanar imaging capability, better soft tissue resolution, high contrast and use of non-ionizing radiation is preferred in female pelvic imaging so as in MDAs. MR imaging gives better anatomic detail of both the internal uterine cavity and the external contour in cases of MDAs. Sagittal T2weighted sequences are particularly important as anatomy is best seen and it helps in determining the uterine abnormalities like agenesis, hypoplasia .For the purpose of MDA classification, oblique coronal T2-weighted images of the uterus are the most critical, since these are necessary for proper assessment of the uterine fundal contour[2]. Vaginal abnormalities like agenesis, atresia and septum are best seen on axial images. In cases of suspected vaginal septum, jelly can be introduced through the introitus to better delineate the septum, its location and thickness (Fig 2). In our study, 4 patients had transverse vaginal septum and out of them imaging after introducing jelly through introitus was done in 2 patients. Most of the uterine pathologies were very well seen on MRI as compared to USG. The contour abnormalities seen in nine patients (45%) were better appreciated on MRI. Transverse vaginal septum is better seen on MRI as compared to USG. Hematosalpinx seen in two patients in our study was distinctly seen on MRI. On MRI, ovaries were seen in all the patients as compared to USG which fails to demonstrate ovaries in six patients. Out of these six patients, two had streaky right ovary and left ovary was not seen on MRI, one had MRKH in whom the ovaries were visualized on MRI, and three had hematometra with hematocolpos out of which one had ectopically located ovary with bulky right ovary which was located high in pelvis and beneath the

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anterior abdominal wall and normal left ovary. So from this we can infer that MRI is better for ovarian location, size and morphology.

In our study, five patients were diagnosed with MRKH. Out of these one patient had right renal agenesis with compensatory hypertrophy of left kidney. In three patients with MRKH the ovaries were ectopic in location. It is important to calculate vaginal length in these patients as it is helpful in vaginal reconstruction. This is accurately possible with MRI. In our study average vaginal length was 1.7cm.

MRKHS accounts for approximately 15% of patients with primary amenorrhea and is second common cause of primary amenorrhea[18]. Recently MRKHS has been classified into two different forms:

Typical form (also called Rokitansky sequence, Type 1 or type A or isolated): Characterised by congenital absence of uterus and upper 2/3 of vagina with normal ovaries and fallopian tubes i.e.; only caudal part of mullerian duct is affected.

Atypical form /Type II / Type B/ MURCS (Mullerian Renal Cervical Somite)/ Genital renal ear syndrome: Associated with other anomalies including Renal anomalies (30-40% patients), Most common being unilateral renal agenesis; Vertebral anomalies (10%), Hearing defects, Ovarian cancers and rarely cardiac anomalies and anorectal malformations[18,19,20].

MRI helps localize ectopically located ovaries important in females undergoing fertility studies & egg harvesting[17] (Fig 3). In a phenotypic female with primary amenorrhea MRKH should be differentiated from testicular feminization syndrome which can be confirmed on MRI by presence of rudimentary testis and absent uterus and ovaries[21].

In our study most common MDA is class 1(35%) according to American society for reproductive medicine system (1988) classification i.e. uterine agenesis /hypoplasia which include 5 patient with uterine agenesis and 2 with hypoplastic uterus. This is followed by class IV (25%) i.e. Bicornuate uterus.

The sensitivity of ultrasound in our study is 100%, however specificity is 75%. In MRI Sensitivity and specificity is almost 100% which is not in consensus with study conducted by Krishna Pratap singh Sengar et al [22] who concluded that sensitivity of USG is less as compared to specificity. On USG in our study, the transverse vaginal septum and arcuate uterus were not clearly depicted which were better appreciated on MRI.

There is evidence of excellent agreement between the clinical diagnosis of the subtype of the MDA and the MRI findings[23]. In our study MDA was suspected on clinical history, however on this classification of subtype is difficult for which MRI is the best modality of choice.

MRI had its own limitations, like it is expensive, time consuming study and not readily available.

Patients who presented with acute abdominal pain, had history of primary amenorrhea and who on local examination had vaginal bulge and on USG showed hematometra with hematocolpos were directly intervened. All these patients were excluded from our study so sample size in our study is less as compared to the studies in literature.

In our study which is done in central India, where most of the patients had poor socioeconomic background, lack of education and poor attention towards health, are reluctant to seek medical advice for their symptoms, this being another major reason for limitation of patients in our study.

Certain MDAs like MRKHS have significantly poor fertility outcomes and sexual function. The earlier the accurate diagnosis is made it can allow for earlier clinical intervention and psychological input. Family counselling can also be done. There are certain websites like www.MRKH.org and www.youngwomenshealth.org. to help the patients with MRKH and their families[21].

CONCLUSION:

Adequate bladder distension is key factor for visualization of uterus and pelvic structures on USG. TVS and 3Dimentional USG will help in identifying the contour abnormalities well. Still patient built, bowel gases, field of view and quality of machine are major limiting factor for USG. MRI eliminates all these limitations and gives clearer vision and details about anatomy and pathology. So we conclude that in suspected cases of MDAs, MRI is the imaging modality of choice for accurate diagnosis and its classification. Accurate classification of MDA is important as it affects the treatment and for which

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MRI plays important role in diagnosis as well as classification. If a MDA is encountered a radiologist should also look for other associated developmental anomalies.

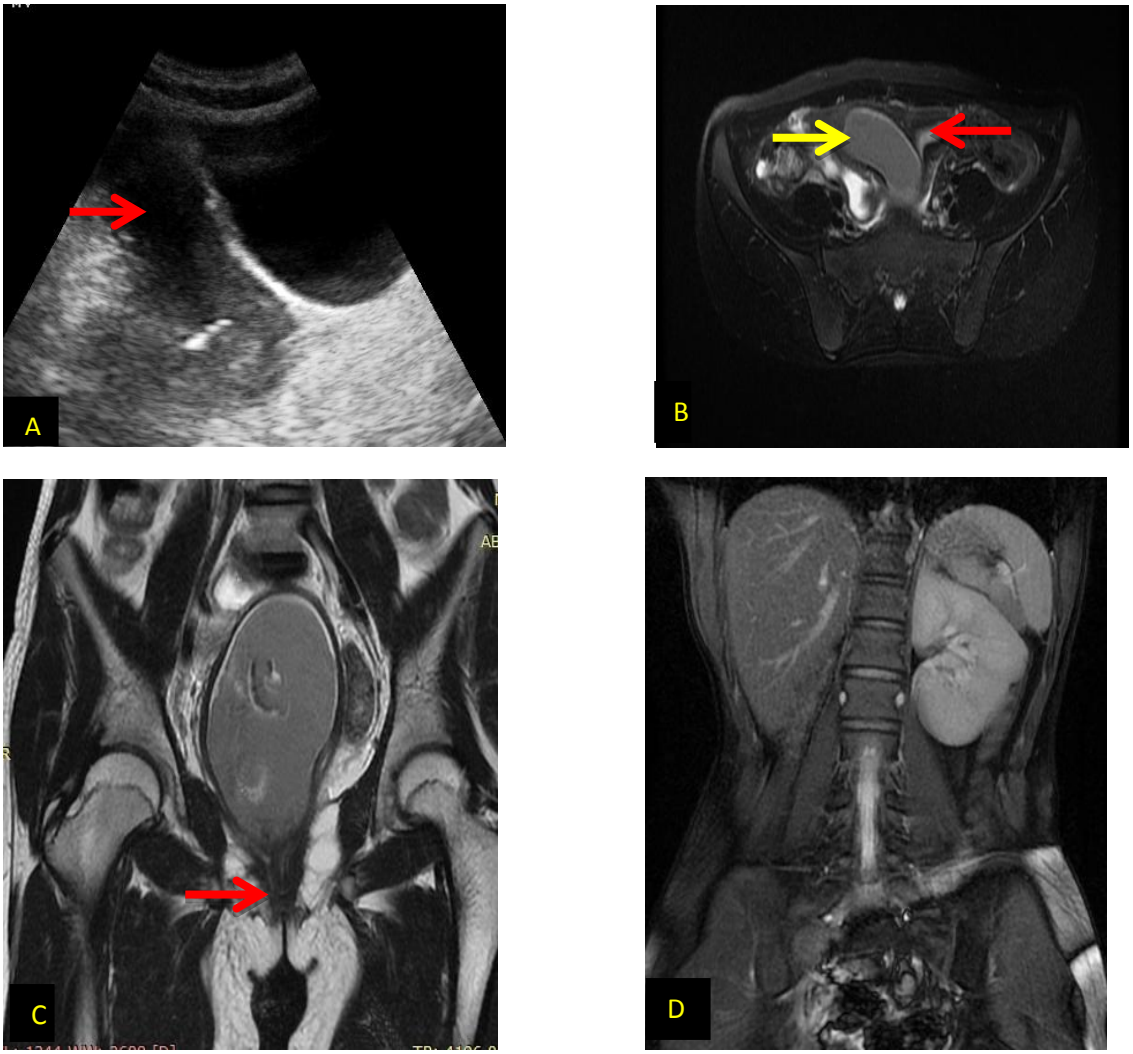

Fig.1. A.USG sagittal section images shows uterine cavity filled with hypoechoic collection (red arrow). B. Axial T2WI shows uterus didelphys. Right horn appears to be grossly distended and filled with a large homogenous altered signal intensity (yellow arrow) suggestive of hematometra. Left uterine horn appears normal in morphology (red arrow). C. COR T2WI shows linear transverse signal intensity area noted distal to the collection at the level of vagina. This represents Transverse Vaginal Septum (red arrow). D. Coronal T2 Fat suppressed Fiesta image shows right renal agenesis with mild compensatory hypertrophy of left kidney.

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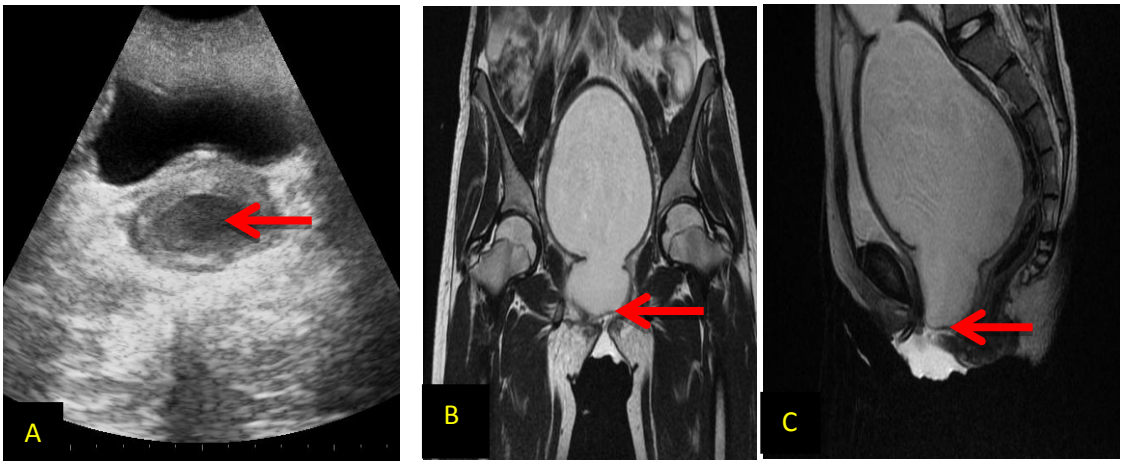

Fig.2. A. USG pelvis transverse images shows collection within the endometrial cavity suggesting hematometra(red arrow). B.CORT2WI with jelly in the introitus better delineates the transverse vaginal septum(red arrow) resulting in hematometra with hematocolpos. C. Mid Sagittal T2WI shows hematometra with hematocolpos with delineation of the transverse vaginal septum(red arrow).

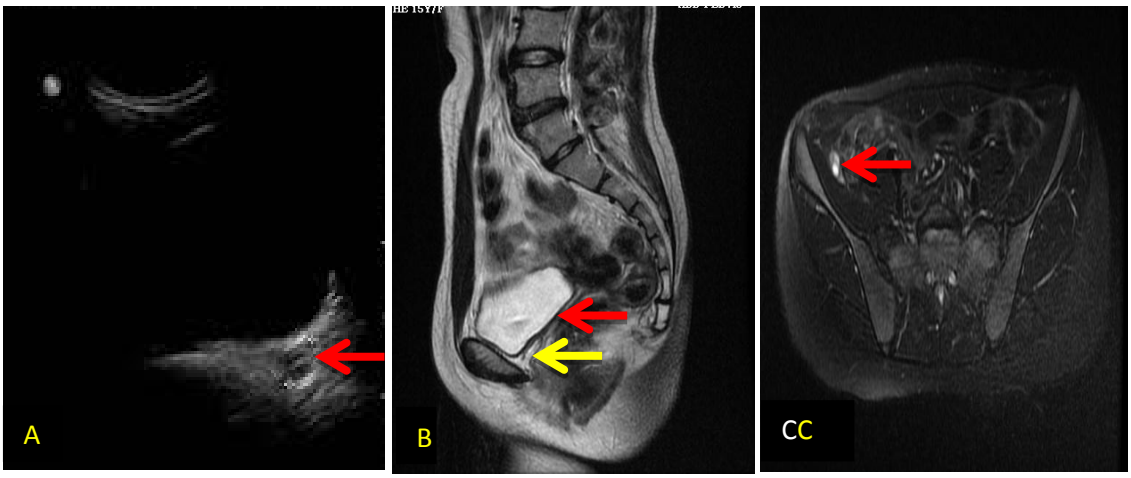

Fig 3. A. Transabdominal USG axial section shows left ovary (red arrow). Uterus & upper two third of vagina not visualized. Right ovary could not be visualized. B. Mid sagittal T2WI shows absence of uterus and upper two third of vagina between urinary bladder and rectum (red arrow). Blind ended lower one third of vagina is seen (yellow arrow).C. Axial T2 Fat suppressed image shows ectopically located right ovary (red arrow).

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TABLES:

Table 1- Ultrasound findings noted in patients with Mullerian Duct Anomalies:

ULTRASOUND Findings	No of patients
Non visualization of uterus	5
Hypoplastic uterus	2
Bicornuate uterus	4
Bicornuate uterus with collection in left horn	2
Bicornuate uterus with pregnancy in right horn	1
Hematometra	5
Hematocolpos	4
Arcuate uterus with gestational sac	0
Bilateral normal ovaries	9
Small ovaries (either one or both)	1
Single ovary visualized	1
Bilateral ovaries not visualized	6
Unilateral Renal agenesis with compensatory hypertrophy	2
Hematosalpinx	2
Ascites	1
Effusion	1
Echogenic kidneys	1
Megaureter	1
Mass lesion in head region of pancreas	1
Liver metastasis	1

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Table 2: MRI Findings noted in patients with Mullerian Duct Anomalies:

MRI Findings	No of patients
uterus not seen	5
Hypoplastic uterus	2
Hematometra	5
Hematocolpos	4
Septate uterus	1
Subseptate uterus	1
Bicornuate uterus	5
Uterus didelphys	1
Arcuate uterus with g. sac	1
Transverse vaginal septum	4
Normal ovaries	11
Ectopically located ovaries (either one or both)	4
Streak like right ovary , left ovary not visualized	2
Polycystic ovaries	2
Small ovaries (either one or bilateral)	3
Unilateral Renal agenesis with compensatory hypertrophy	2
Hematosalpinx	2
Hydrosalpinx	1
Megaureter	1

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