International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Thanekar SS et al. Int J Reprod Contracept Obstet Gynecol. 2026 Aug;15(8):3201-3209
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20262556

Case Series

Tailored management for a diverse spectrum: lessons from seven Mullerian anomaly cases with varying clinical impact

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Received: 08 May 2026
Revised: 17 July 2026
Accepted: 18 July 2026

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ABSTRACT

Defects in the embryological developmental pathway led to Mullerian duct anomaly. The presentation of such anomalies ranges from being asymptomatic and incidental findings to severe dysmenorrhoea and heavy menstrual bleeding further affecting quality of life and reproductive outcome. Here, we presented case series of cases with mullerian anomalies visited B. J. Government Medical College and Sassoon hospital, Pune over the period of one year. All the case had varied clinical presentations of mullerian anomalies which were managed timely with good outcome Hence highlighting the fact that proper history elicitation & good imaging modality in association with high index of suspicion can lead to timely treatment and good outcome in terms of fertility and quality of life.

Keywords: Mullerian anomaly, Menorrhagia, Dysmenorrhoea, Infertility, Ultrasound, Magnetic resonance imaging

INTRODUCTION

Mullerian anomalies have origin in embryological period. At 6-8 week of gestational age, both mesonephric (Wolffian) and paramesonephric (Mullerian) ducts are present in pairs hence is known as ambisexual period of development. The internal genitalia have intrinsic tendency to feminize. When Y chromosome and functional testes are absent, wolffian system of ducts regresses & absent AMH (Antimullerian hormone) results into development of mullerian ducts into fallopian tubes, uterus, cervix and upper parts of vagina by 10 week of gestation.[1] Canalization to create uterine cavity, cervical canal and vagina completes by 22nd weeks of development. By 20th week uterine mucosa is fully developed into endometrium. So, formation, fusion and resorption are three critical processes in the development. The wolffian ducts make no direct contribution to the Müllerian ducts, but serve as a guide or migrational template.[2] Hence if wolffian duct does not form, mullerian duct also fails to develop. Consequently, renal system development is frequently associated with anomalies in development of uterus, cervix, fallopian tubes or vaginal upper portion.

The actual incidence and prevalence of mullerian anomalies in general population are missing owing to non-standardisation of classification systems, nonuniform diagnostic modalities and different study populations of women.[3] Grossly speaking, the frequency of anomalies is in decreasing order as septate (35%), bicornuate (26%), arcuate (18%), unicornuate (10%), didelphys (8%) and agenesis (3%). They are increasingly more common with infertile patients (8%) and in patients with recurrent pregnancy loss (13.3%). Highest incidence seen amongst individuals with history of both (23.5%).[4] The pathogenesis of RPL and preterm labour is attributed to reduced intrauterine volume, endometrial dysfunction and poor vascular supply. There are many proposed classification systems for mullerian anomalies. The one by American Fertility Society (AFS, 1988) was simplest and

most historical; but was unable to capture full array of complex anomalies.[5]

Further European Society of Human Reproduction and Embryology and European Society of Gynaecological Endoscopy proposed another classification (2013) where cervical and vaginal abnormalities were subclassified separately.[6] Also in 2021, American Society of Reproductive Medicine came up with latest classification having 9 categories.[7]

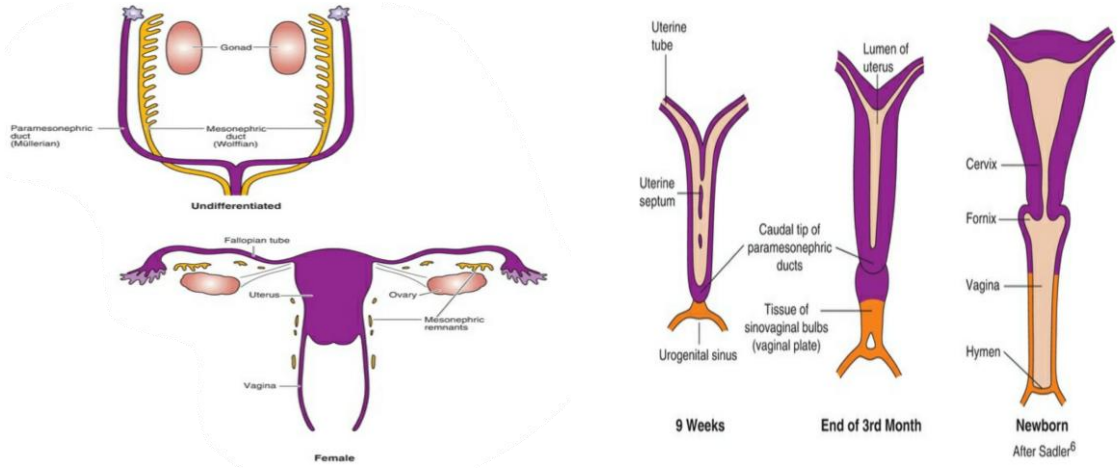

Figure 1: Mullerian system development.[1]

Diagnostic modalities

Hysterosalpingography

It delineates the endometrial cavity but the limitation is external uterine contour cannot be outlined. Hence exact diagnosis becomes difficult (e.g., differentiating bicornuate from septate uterus).

Endovaginal ultrasound

Primary modality, sensitivity 93%, and specificity 100%. Timing of USG is late secretory phase of menstrual cycle so that good contrast is present between myometrium and endometrium.

3-dimensional ultrasound: fairly accurate

MRI pelvis

Gold standard for diagnosis with 98-100% accuracy.

Pregnancy losses with mullerian abnormalities usually occur in the second trimester; however, the presence of a uterine anomaly after repeated early losses deserves consideration of surgical repair. Septate uterus is the most common anomaly. Since septum resorption occurs only after urologic development is completed, prevalence of urinary track anomalies is not increased in women with septate uterus. Hysteroscopic septal resection improves fertility outcomes. An arcuate uterus is generally regarded as a normal variant and that residual septa measuring less than 1 cm in size have no adverse effect on pregnancy outcome.[8]

Bicornuate uterus is a fusion anomaly with single cervix. RPL ~30% and fetal loss ~10%. Strassman's metroplasty has good role in carefully selected patients. Since incidence of cervical incompetency is higher in association with bicornuate uterus, cervical cervical cerclage yields better result yields better result in terms of fetal survival rates.[9] Unicornuate uterus develops due to failure of development of one mullerian duct. It is usually associated with ipsilateral renal anomaly (~40%).[10] If there is presence of functional non communicating horn, it can lead to dysmenorrhoea, chronic chronic pelvic pain, endometriosis and sometimes ectopic pregnancy and hence need to be removed surgically. Reproductive outcomes are usually poor. Available evidence suggests that most pregnancies in women with unicornuate uteri are best managed expectantly with cervical cerclage reserved for those with previous second-trimester pregnancy losses or evidence of progressive cervical shortening.[11] No surgical procedure can enlarge unicornuate uterus.

Complete failure of fusion of mullerian ducts and normal differentiation of each to form cervix and to form cervix and hemiuterus lead to didelphys. It has slightly better reproductive outcomes because of improved collateral blood supply of each horn. In general, the only surgery indicated in women with uterine didelphys is the removal of an obstructing vaginal septum (75% prevalence).[12] Unification procedures are usually unnecessary and complicated but can rarely benefit some.[13]

Since DES is banned from 1971, it's rare to encounter DES related uterine anomalies (T shaped uterus, constriction rings, etc). Agenesis and hypoplasia have little reproductive potential depending on degree of hypoplasia and functional endometrium. Mutations in the AMH gene, located on chromosome 19p13.3, cause persistent Müllerian duct syndrome (PMDS), characterized by the presence of a uterus, fallopian tubes, and the upper part of the vagina in otherwise phenotypically normal males.[14] There can be various permutations and combinations in development defect in mullerian ducts. And can present with various clinical presentations. Muellerian duct anomalies encompass a wide spectrum of congenital malformations, and accurate imaging-based diagnosis is essential to guide their individualized management.[15]

CASE SERIES

Case 1

Acute abdomen in shock with UPT positive

A 26 yr old female, married for 6 years, gravida 2 para 1 death 1, unregistered unimmunized, presented in casualty with 4 months of amenorrhoea with severe anaemia, severe abdominal pain and multiple episodes of vomiting since 5 Hr and positive urine pregnancy test. Her obstetric history revealed previous one preterm vaginal delivery at home at 7th month of gestation which died on postnatal day one. From casualty she was admitted in ICU, started on started on inotropic support. After gynaecological opinion on examination, she was in hypovolaemic shock with signs suggestive of hemoperitoneum. On per vaginal examination, she had closed uneffaced cervix with forniceal tenderness. Diagnosis of ectopic pregnancy with hemoperitoneum was confirmed on ultrasonography. Patient was taken for emergency exploratory laparotomy after written informed consent and blood products arranged. Intraoperatively, there was ruptured left horn of unicornuate uterus (non-communicating functional) with foetus inside peritoneal cavity. 500 ml hemoperitoneum present along with 350 gm clots.

Intraoperatively, 2-pint packed cells and 4 fresh frozen plasma transfused. Postoperatively patient recovery was good. Her further line of management planned as USG and MRI after 6 weeks, contraception for one year and cervical encirclage in next pregnancy.

Case 2

IUD with failed D & E

A 31 yr old female, gravida 2 Abortion one with outside documented USG of intrauterine fetal demise of 13 weeks gestational age admitted for further management. Patient had no active complaint. On per vaginal examination, bulky uterus and os closed. Hence tablet misoprostol regimen started for cervical ripening and spontaneous expulsion of abortus but failed and hence planned for suction evacuation under anaesthesia in OT after proper consent. Suction evacuation was attempted but failed to retrieve products of conception and hence strongly suspected uterine anomalies. Urgent ultrasound repeated at our centre which revealed bicornunate uterus with right horn showing intrauterine fetal demise with no communication with Cervix and communicating left horn with cervix. Hence planned for exploratory laparotomy after written informed consent. Intraoperatively, methylene blue dye instilled through cervix. There was no spillage in abdominal cavity from either side. Incision taken over right horn showed methylene blue stained products of conception.

Provisional diagnosis was made as septate uterus with small communication with right horn which could not be negotiated in our could not be negotiated in our suction evacuation. Patient was advised MRI pelvis after 6 weeks Unfortunately, patient was lost to follow up as she went to her home town in another state.

Table 1: Case summaries.

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age (in years)	26	31	35	13	25	24	28
Obstetric score	G2P1D1	G2A1	P2L2	Nulligravida	A1	G3A2	Nulligravida
Presenting features	Acute abdomen with shock	Pregnancy loss	Dysmenorrhea Menorrhagia Anaemia Poor quality of life	Dysmenorrhea	Secondary infertility	Pregnancy loss	Dyspareunia
Diagnosis	Rupture of uterus – non communicating horn pregnancy	Non communicating horn pregnancy	Unclassified mullerian anomaly and	Endometriosis due to functional non communicatin	Subseptate uterus	T shaped uterus	Didelphys with vaginal septum

Continued.

Parameters	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
			endometriosis	g rudimentary horn			
Post treatment	Life Saving	Lost to follow up	Improved QOL	Complete relief	Successful pregnancy outcome	Lost to follow up	Complete relief

Case 3

Menorrhagia and dysmenorrhoea

A 35-year-old female, para 2 live 2 (2 FTVD) non-tubectomized brought by parents as abandoned brought by parents, abandoned by husband with complaint of chronic dysmenorrhoea & menorrhagia since 18 yr with malaise and weakness for 20 days in casualty with pain in abdomen. She had BMI of 17 with pallor. In her past history She gave history of twice blood transfusions (due to same complaints) and twice operative interventions. She had history of exploratory laparotomy 5 year back in view of right hematosalpinx for which salpingectomy was done. Her discharge card at that time mentioned intraop findings of arcuate uterus and right hematosalpinx. She had history of pain killer's intake multiple times over the counter due to severe dysmenorrhoea. She also had undergone hystero laparoscopy 3 years back for pain and was diagnosed as having bicornuate uterus with right rudimentary horn, right ovarian cyst and right ostia was not visualised at that time. Right ovarian cystectomy was done.

USG suggestive bicornuate uterus with thickened endometrium. After correction of anaemia patient was posted for Endometrial biopsy which showed endometrial hyperplasia without atypia. Endometrial TBPCR came negative. MRI pelvis was done which revealed bicornuate uterus with non-communicating right rudimentary horn with hematometra (1.8×1.9×3 cm) and ovarian haemorrhagic cyst.

She was started on inj. GnRH agonist and had some relief but refused to continue medical management. Hence after taking consent posted for hysterectomy. Intraoperative findings-uterus bulky 8 weeks with right sided chocolate cyst suggestive of endometriosis, absent right tube, normal left adnexae. Cut section of gross specimen revealed surprising findings of combination of bicornuate and septate with thick thick myometrial septum dividing two cavities, right cavity with small hematometra suggestive of functional endometrium and non-communicating with cervix and while left being communicating cavity. The finding confirmed on histopathology that intervening septum had myometrial tissue.

This anomaly does not fit in any of ASRM 2021 category. Hence can be included in 'unclassified'. Postoperatively patient visited outpatient and claimed significant improved quality of life and was happy.

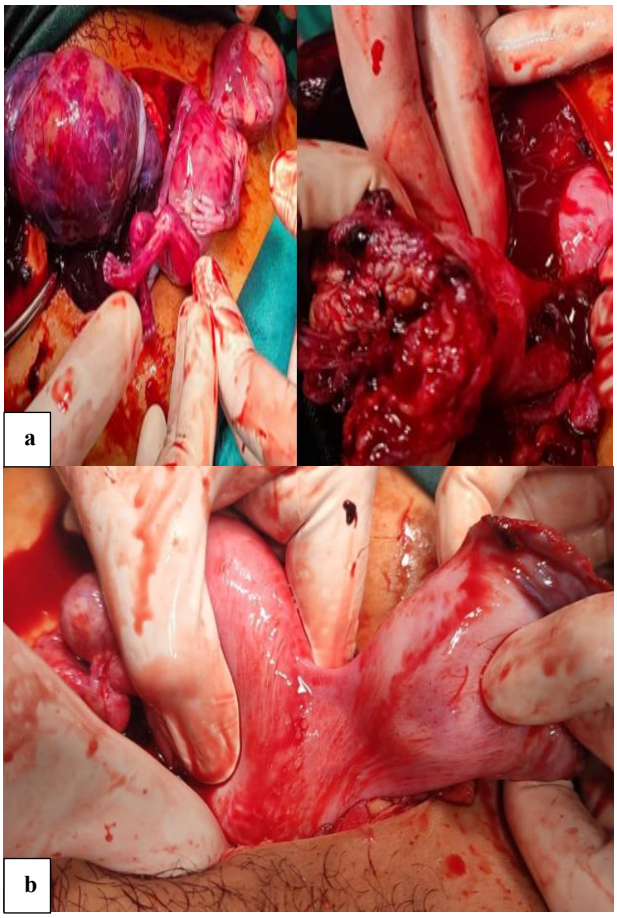

Figure 2: (a) foetus in situ and ruptured uterus with hemoperitoneum; (b) ruptured non-communicating functional left horn.

Case 4

Severe dysmenorrhoea since menarche

A 13-year-old girl, with severe dysmenorrhoea since menarche, not responding to pain killers came to OPD. Her 3 D USG done which showed a left tubo-ovarian lesion with multiple small endometriatic cysts in left ovary with left hydrosalpinx. Duplication anomaly of uterus with non-communicating rudimentary left horn with hematometra, single cervix and vagina in midline with diagnosis of ESHRE/ESGE U4aC0V0. She was posted for laparoscopic resection of left horn and ovarian cystectomy. Intraoperatively there was hemoperitoneum and bulky non communicating left horn and normal right horn.

Post operatively patient had relief of chief complaint.

Case 5

Secondary infertility

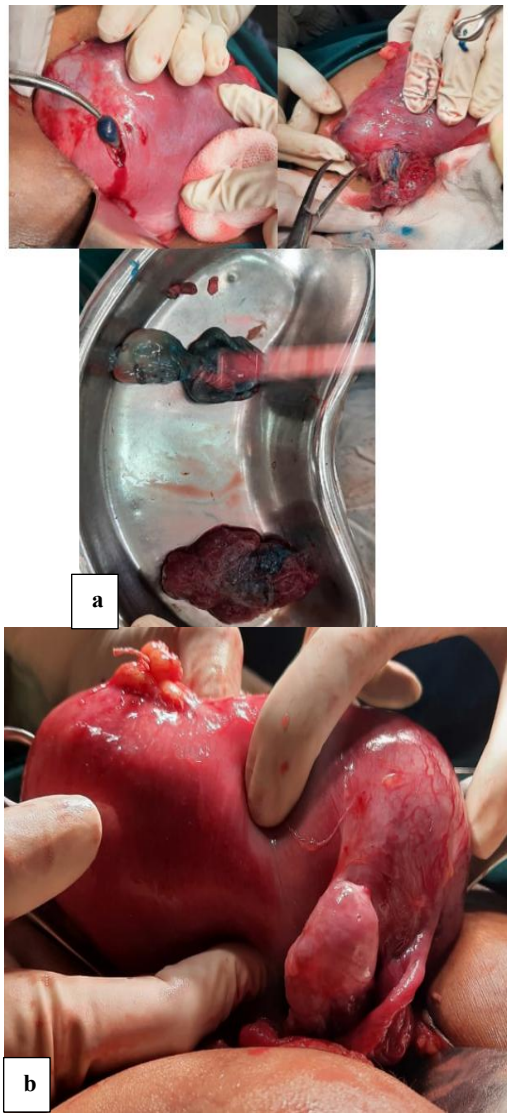

Figure 3: (a) methylene blue dye spillage in the amniotic sac hence stained products of conception; (b) uterus closed.

A 25-year-old female, married since 6 yr, abortion 1, secondary infertility since 3 years Hormonal profile and husband semen analysis were normal. Patient had regular menses. Her transvaginal ultrasound showed septate uterus with normal endometrial thickness, single cervix and single vagina. She was posted for hysterolaparoscopy and septal resection was done. Tubal patency was also confirmed.

Endometrial biopsy study revealed normal. Postoperatively, patient conceived and delivered healthy child by elective LSCS at term in the same institute.

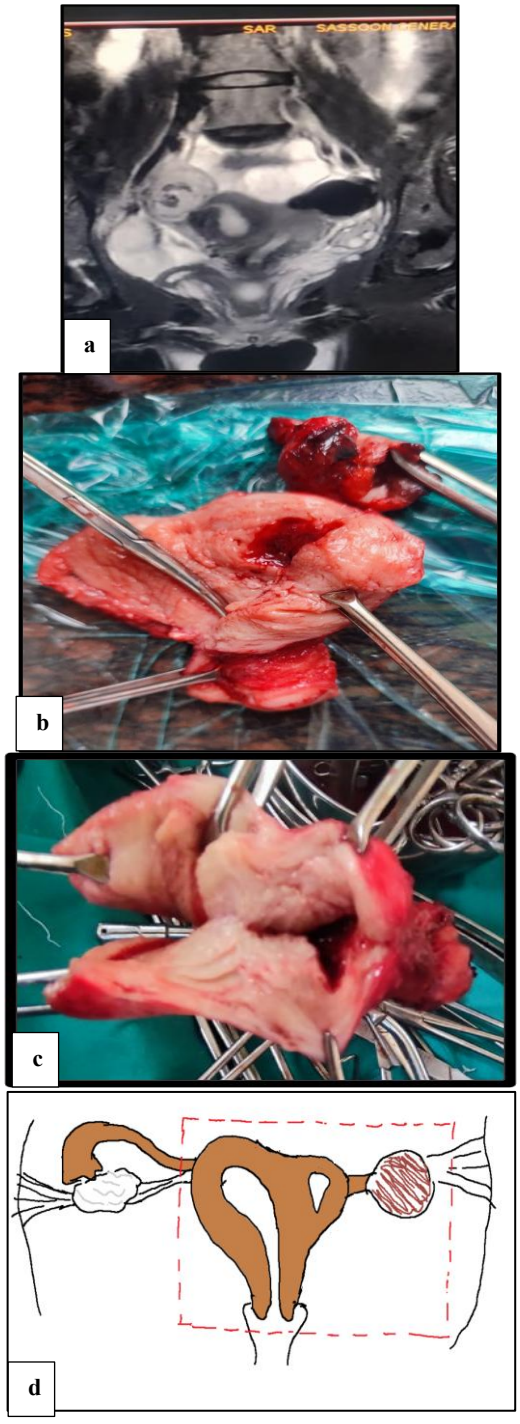

Figure 4: (a) T2-weighted MRI of the pelvis showing a bicornuate uterus with a non-communicating right rudimentary horn containing haematometra; (b) gross hysterectomy specimen; (c) cut section showing two endometrial cavities separated by a thick myometrial septum with haematometra in the right cavity; (d) coronal sketch of the bicornuate-septate uterus with the right ovarian endometriotic (chocolate) cyst.

Case 6

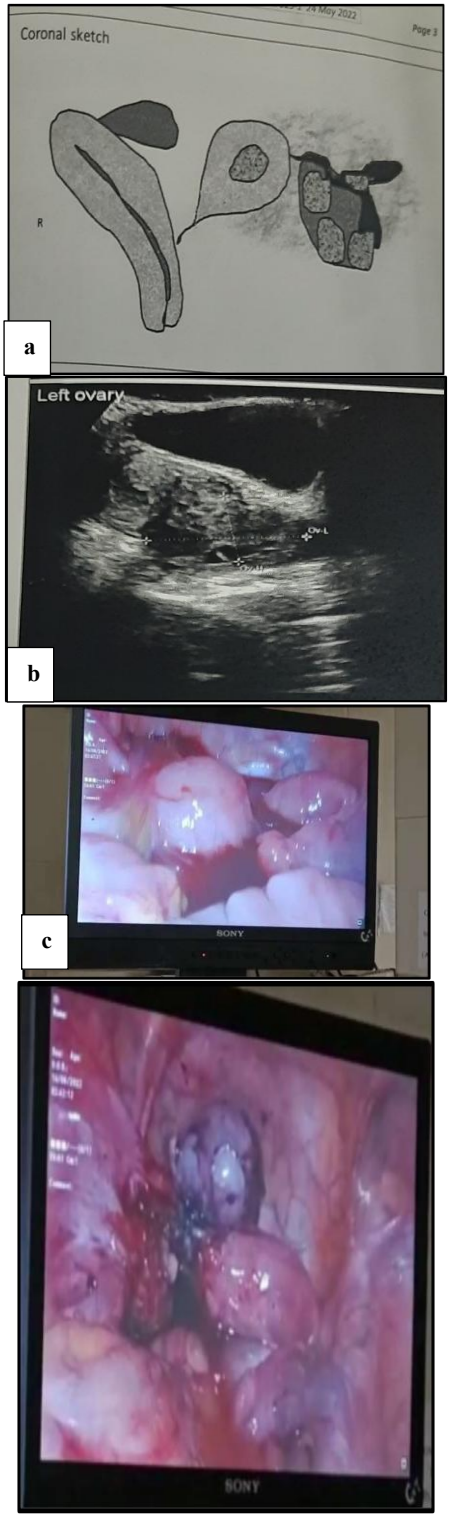

Figure 5: (a) coronal sketch depicting the uterine duplication anomaly with a non-communicating rudimentary left horn; (b) left adnexa on ultrasound showing endometriotic cysts; (c) laparoscopic view of the bulky non-communicating rudimentary left horn with left tubo-ovarian endometriotic cysts; (d) laparoscopic view during resection of the left horn with ovarian cystectomy.

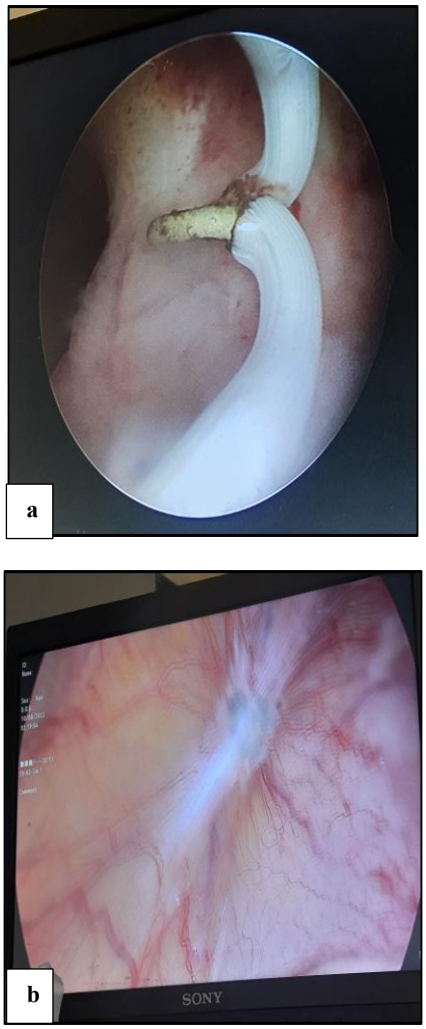

Figure 6: hysteroscopy - septum being resected and post septal resection.

Recurrent pregnancy loss

A 24-year-old female, gravida 3 abortion 2 (previous two 1st trimester abortions), with intrauterine fetal demise of 24 wk. with cervical os stitch in situ, received in labour room. She had USG suggestive of bicornuate uterus with fetal spalding sign present. On per speculum examination, longitudinal vaginal septum of 2 mm thickness and 4 cm length with single cervix and single vagina. Patient delivered 600 gm stillborn foetus vaginally. Intrapartum resection of septum done.

Repeat 3D USG after 6 wk. was suggestive of partially bicornuate uterus with widely delivering horns giving endometrium a wide arcuate almost T like shape. No uterine septum.

Planned for MRI after 3 months for confirmation of diagnosis and later hysterolaproscopy and if required-lateral metroplasty. Unfortunately, patient is yet to follow up. Here, point to note is that USG in antenatal period might not be a good option to diagnose mullerian anomaly.

Case 7

Dyspareunia

A 28-year-old female, married since 2 yr, with dyspareunia. The couple had not consummated the marriage. On per vaginal examination, longitudinal vaginal septum with double cervices noticed.

In such cases just a thorough vaginal inspection sufficient to find out the cause of dyspareunia and treat.

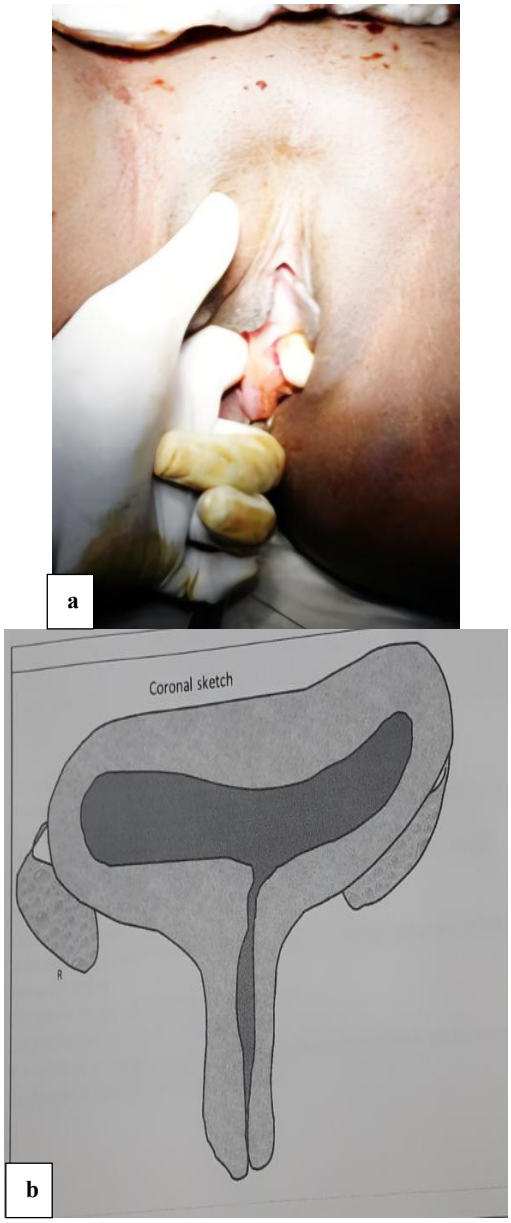

Figure 7: (a) per-speculum examination showing the longitudinal vaginal septum (2 mm thick, 4 cm long) with a single cervix, during intrapartum septal resection; (b) coronal sketch given by the radiologist.

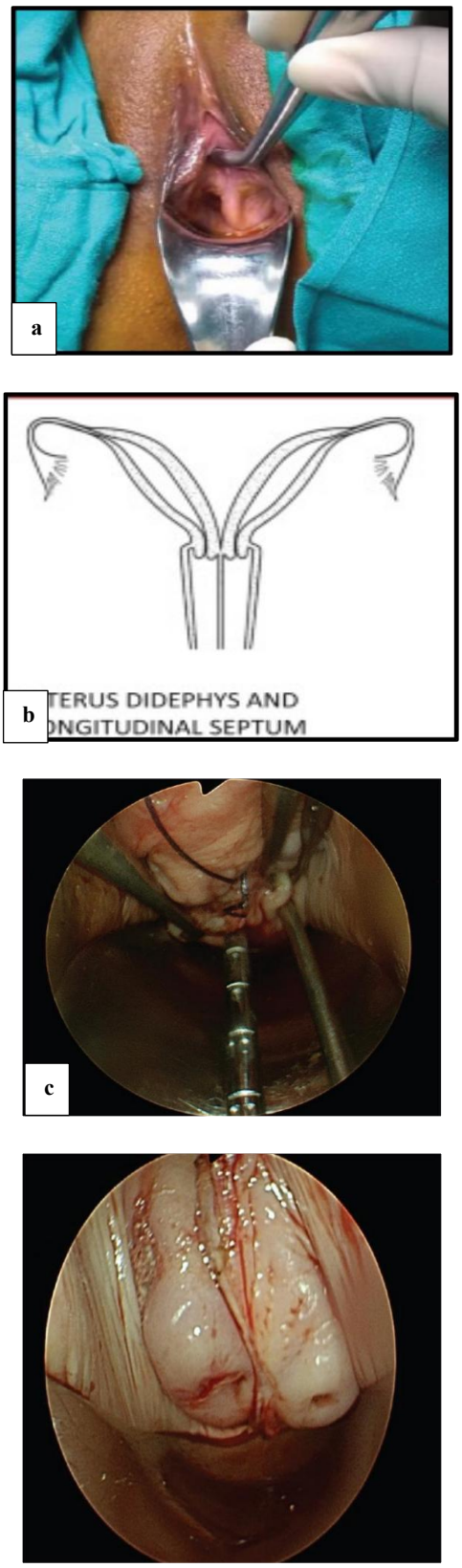

Figure 8: (a) USG revealed uterine didelphys with double vagina and vaginal septum; (b) under anaesthesia vaginal septal resection done; (c) after 6 weeks.

DISCUSSION

The exact incidence & prevalence of mullerian anomalies is difficult to estimate. especially if patient is asymptomatic, the incidence cannot be identified. In a systematic review by Chan et al where almost 90000 females were included, the prevalence was 5.5 and 8 percent, respectively, in unselected population & in patients with infertility (primary or secondary).[16] The prevalence was increased in those with history of RPL (12.3%) and a history of RPL and infertility (24.5%). In another case report of 22 patients by Kapczuk et al retrospectively obstructive Mullerian anomalies were diagnosed in menstruating adolescent girls. In that series four patients had undergone unnecessary surgical interventions due to misdiagnosis, while 2 patients had serious complications like pyoperitoneum and vesicovaginal fistula because of ruptured pyocolpos.[17] Similar to our cases, there are many case series including, by Arleo et al and multiple case reports including by Shirota et al, Dunn et al, Acien et al in which complex mullerian anomalies were described, none of them fitted into current classification systems.[18-21] In a retrospective case series of 110 patients at university hospital by Mazouni et al circumstances leading to diagnoses of mullerian anomalies were studied. This study shows that only 40% cases were diagnosed before hospitalization and mean time between first ultrasound and diagnosis in a specialized department was 6.7 months.[22] Moharana et al and Choudhary et al and others in their case report underlines the need for continued research to improve diagnostic accuracy and therapeutic approaches for such complex anatomical variations.[23] Also, there is need to maintain a registry where all such cases can be notified and registered for better guide to early diagnosis and tailored management to reduce all types of morbidities and complications.

CONCLUSION

Müllerian duct anomalies represent a diverse group of congenital conditions with variable clinical presentations. Early diagnosis using advanced imaging techniques is essential for appropriate classification and management. Despite the numerous classifications, the wide range of Müllerian anomalies is still largely unknown and confusing, not only to obstetrician-gynaecologists and the respective subspecialists, but also to providers including radiologists, paediatricians, specialists in adolescent and emergency medicine, and paediatric general and urologic surgeons, who may encounter patients with these anomalies. This is primarily due to the relative rarity of Müllerian anomalies and the limited exposure of these providers to patients with a Müllerian anomaly during training or practice. Consequently, individuals may endure a delay in diagnosis for weeks, months, and even years; may undergo inappropriate or inadequate surgical intervention(s); and may have persistent issues including chronic pain and/or loss of reproductive function as a result. Many may feel abnormal and may experience anxiety and depression, sexual dysfunction, and low self-esteem. Beyond the psychological effects, there are treatment-specific effects on quality of life that are important to consider. Appropriate medical and surgical management provides the opportunity to optimize gynaecologic and reproductive outcomes and concomitantly reduce the burden of comorbid conditions.

Individualized treatment strategies can significantly improve reproductive and symptomatic outcomes. A multidisciplinary approach and awareness of associated systemic anomalies are critical for optimal patient care.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Thanekar SS, Kale TP. Tailored management for a diverse spectrum: lessons from seven Mullerian anomaly cases with varying clinical impact. Int J Reprod Contracept Obstet Gynecol 2026;15:3201-9.