International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Madhu Priya V et al. Int J Reprod Contracept Obstet Gynecol. 2025 Apr;14(4):1301-1306
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20250878

Case Series

A comparative study of the American Society for Reproductive Medicine and European Society of Human Reproduction and Embryology classification systems in the diagnosis and management of Müllerian anomalies: insights from a case series

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Received: 20 September 2024
Revised: 28 February 2025
Accepted: 01 March 2025

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ABSTRACT

Mullerian anomalies, congenital malformations of the female genital tract, arise from defective development, fusion, or resorption of Mullerian ducts and contribute to infertility, recurrent pregnancy loss, and primary amenorrhea. With a prevalence of 6.7% in the general population, accurate classification and diagnosis are crucial for effective management. This study compares the American Society for Reproductive Medicine (ASRM) and European Society of Human Reproduction and Embryology (ESHRE) classification systems using a prospective analysis of 12 cases. The ASRM's simplicity contrasts with the ESHRE's anatomical precision, but the latter struggles with complex anomalies. Findings reveal 41% of cases classified as hypoplastic uterus under ESHRE, with 25% remaining unclassifiable under ASRM. The study underscores the limitations of current systems in addressing complex anomalies involving vaginal and cervical deviations. It calls for a universal classification system integrating embryology, anatomy, and clinical insights for better diagnosis and treatment.

Keywords: Mullerian anomalies, ESHRE, ASRM

INTRODUCTION

Congenital malformations of the female genital tract are defined as deviations from normal anatomy due to embryological maldevelopment of Müllerian ducts such as non-development, defective vertical or lateral fusion, or resorption failure of the Müllerian ducts.[1] It contributes to primary amenorrhea, infertility, recurrent pregnancy loss, and poor pregnancy outcomes. Most Müllerian duct anomalies are associated with functioning ovaries, age-appropriate external genitalia, and a normal hormonal profile.[2] It has a prevalence of 6.7% in the general population, 7.3% in the infertile population, and 16.7% in the recurrent miscarriage population.[3]

A number of classification systems were proposed for Müllerian anomalies. The European Society of Human Reproduction and Embryology (ESHRE) and the European Society for Gynaecological Endoscopy (ESGE), along with the American Fertility Society (AFS), now termed the American Society of Reproductive Medicine (ASRM), are widely followed classifications.[4]

In 1988, ASRM classified Müllerian anomalies into seven categories based on anatomy. It grouped the uterine anomalies according to the failure of the Müllerian ducts to develop properly. The advantages of this classification system included its simplicity and recognizability. However, it does not classify vaginal, cervical, and complex anomalies.[5]

In 2013, the ESHRE classification was based primarily on anatomy, with embryology as the secondary characteristic in the design. Anomalies are classified progressively according to the degree of anatomical deviation and arranged in ascending order of severity. They proposed that this new classification is reproducible and allows anomalies to be described precisely, facilitating the development of management guidelines.[6] However, studies suggest that this classification still does not fully account for the complexity of combined uterine and vaginal anomalies.[7]

In 2021, the Müllerian anomaly classification (MAC2021) was published to update and expand ASRM 1988 and classifies Müllerian anomalies into nine categories that are not numbered like the old AFS-ASRM classification. It is an embryological and clinical system of classification.[8] Additionally, studies have shown an association between renal agenesis and Müllerian anomalies, highlighting the importance of a comprehensive diagnostic approach.[9] Further, advancements in 3D imaging techniques have improved diagnostic accuracy for complex anomalies, aiding in precise classification and management.[10]

In this short case series, we would like to present the cases using both ASRM classification and ESHRE classification and make an attempt to discuss the relative advantages and disadvantages of either, in day-to-day clinical practice.

This was a prospective observational study conducted in Department of Obstetrics and Gynecology over a 3-month duration. Non-pregnant patients aged 13 to 45 years were included. Those who had undergone prior surgeries for correction of Mullerian anomaly, who had attained menopause were excluded. Mullerian anomalies were detected in the process of investigation like hysterosalpingography, 2-dimensional ultrasonography or magnetic resonance imaging (MRI) for a specified problem, such as amenorrhea, dysmenorrhea, infertility or recurrent pregnancy loss. Each patient with Mullerian anomaly was classified using: ASRM classification, and ESHRE ESGE classification.

The consistency between symptoms, examination findings, radiological findings and diagnosis of the condition by both the systems were noted. For example, patients who have septate uterus, the presence of an indication for metroplasty on the basis of the two classifications were noted. After the diagnosis was made through previous clinical history, physical examination, imaging studies (USG and MRI) and diagnostic laparoscopy, they were classified and optimum management was formulated for individual cases.

CASE SERIES

Case 1

A 31 years old female with married life of 9 years came with recurrent 1st trimester pregnancy loss - with 3 spontaneous abortions at 2nd and 3rd month of amenorrhea. On examination, Abdomen was soft, no organomegaly. On per vagina, uterus was normal in size. Tanner staging of breast and pubic hair was stage 5.

Hormonal profiling was normal. Ultrasonography (USG) abdomen and pelvis showed bicornuate uterus, on diagnostic hysterolaparoscopy it was septate uterus and septal resection was done and classified as ESHRE U2b C0 V0 and ASRM class 5.

Case 2

A 25 years old female with married life of 8 years came with recurrent 1st trimester pregnancy loss - with 4 spontaneous abortions between 8-10 weeks of gestation. On examination, abdomen was soft, no organomegaly. On per vagina, uterus was normal in size. Tanner staging of breast and pubic hair was stage 5. Hormonal profiling was normal. USG abdomen and pelvis showed bicornuate uterus, on diagnostic hysterolaparoscopy it was partial septate uterus and septal resection was done. It was classified as ESHRE U2a C0 V0 and ASRM class 6.

Case 3

A 28 years old female with married life of 12 years came with recurrent 2nd trimester pregnancy loss - with 2 spontaneous abortions at 4th and 5th month of amenorrhea. On examination, abdomen was soft, no organomegaly. On per vagina, uterus was normal in size. Tanner staging of breast and pubic hair was stage 5. Hormonal profiling was normal. USG abdomen and pelvis showed bicornuate uterus and classified as ESHRE U3a C0 V0 and ASRM class 4.

Case 4

A 32 years old female came with primary infertility and married life of 10 years. On examination, Abdomen was soft, no organomegaly. On per vagina, uterus was normal in size. Tanner staging of breast and pubic hair was stage 5. Hormonal profiling was normal. Husband semen analysis was normal. USG abdomen and pelvis and HSG showed bicornuate uterus, however on diagnostic hysterolaparoscopy it was found to be septate uterus and septal resection was done, classified as ESHRE U2a C0 v0 and ASRM class 4.

Case 5

A 28 years old female came with primary infertility with no comorbidities and married life of 6 years. On examination, Abdomen was soft, no organomegaly. On per vagina, uterus was normal in size. Tanner staging of breast and pubic hair was stage 4. Hormonal profiling was normal. Husband semen analysis was normal. MRI abdomen and pelvis showed hypoplastic uterus classified as ESHRE U5a C0 v0 and ASRM class 1.

Case 6

A 22 years old female came with secondary infertility. On examination, abdomen was soft, no organomegaly. On per vagina, uterus was normal in size. Tanner staging of breast and pubic hair was stage 5. Hormonal profiling was normal.MRI abdomen and pelvis showed unicornuate uterus with non-communicating rudimentary horn. Classified as ESHRE U4a C0 v0 and ASRM class 2.

Case 7

A 14-year-old girl came with complaint of primary amenorrhea. On examination, breast and pubic hair showed tanner stage 4 development. On local examination, abdomen was soft and there was no organomegaly. MRI abdomen and pelvis showed hypoplastic uterus and cervix with normal bilateral ovaries and clear pouch of Douglas. It is classified as ESHRE U5a C4Vo and ASRM class 1. Patient was counselled and managed conservatively. Planned for vaginoplasty 6-months prior marriage.

Case 8

A 13-year-old girl came with complaint of primary amenorrhea and cyclic pain abdomen since 8 months. Breast and pubic hair showed tanner stage 4 development. On local examination, abdomen was soft and there was no organomegaly. A mass could be felt in vagina on per rectal examination. Ultrasound revealed bicornuate uterus with a mass of 7×2×3 cm in the vaginal suggestive of haematocolpos, normal bilateral ovaries and clear pouch of douglas with absent right kidney. MRI revealed uterine didelphys and, hematocolpos of size 41×36×26 mm. A diagnosis of OHVIRA (obstructed hemivagina with renal agenesis) syndrome was made. The dilated right hemivagina was drained and the septum was excised followed by reanastomosis of the vaginal edges. The patient is under regular follow up.

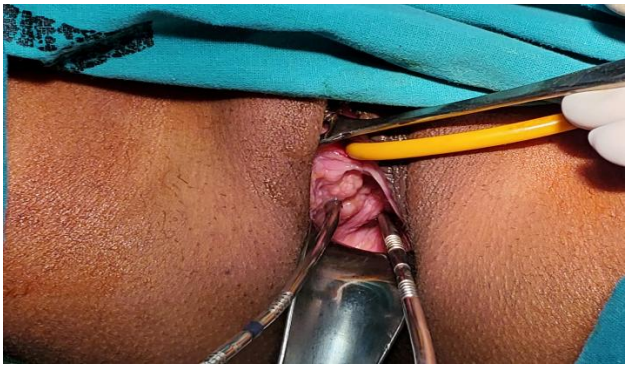

Figure 1: Didelphys with bicollis.

Case 9

17-year-old girl presented with primary amenorrhea and chronic pelvic pain since 4 months. she had normal secondary sexual characters. Examination revealed longitudinal vaginal septum of about 3-4 cm and horizontal septum and cervix was not visible through the vagina. MRI abdomen pelvis reported it as Mullerian duct anomaly (class III) with uterine didelphys, one hypoplastic cervix, two separate vaginal canal with intervening longitudinal and horizontal septum, small left ovary and right hematosalpinx. She was managed with abdomino perineal approach with vaginal septum resection and utero-cervical anastomosis.

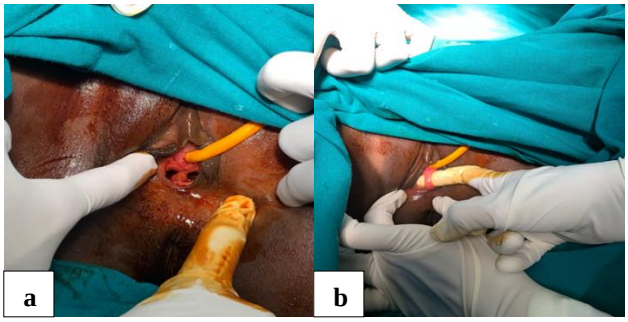

Figure 2 (a and b): Longitudinal vaginal septum.

Figure 3: Didelphys uterus.

Case 10

A 14-year-old girl presented with cyclical lower abdominal pain every 1 month for 2 years and primary amenorrhea. Secondary sexual characters were well developed. On examination external genitalia appeared to be normal. The patient had blind vaginal pouch. MRI abdomen and pelvis revealed a collection of 5×4 cm in endometrial cavity with cervical and vaginal stenosis. Both ovaries and kidneys were normal. She underwent hematometra drainage and vaginoplasty.

Case 11

An 18-year-old girl was admitted in gynecology ward with complains of primary amenorrhea cyclical pain for 4-5 days for 3 years. On examination, external genitalia appeared to be normal. The patient had blind vaginal pouch. On per rectal examination, a cystic mass was felt in the vagina. Ultrasound revealed a heteroechoic collection of size 4×3.4 cm cm in the endometrial cavity. MRI of pelvis revealed a hypolplastic uterus with a normal myometrium. A well-defined collection of 4×3.4 cm was

noted in vagina. Both the ovaries and kidneys were normal. Patient was operated for excision of the transverse vaginal septum followed by reanastomosis of the vaginal edges. Post operatively regular vaginal dilatation was done, and the patient was symptomatically better and has menstrual cycles.

Case 12

Similar to case 10, an 18-year-old girl presented with cyclical lower abdominal pain every 1-2 months for 4 years and primary amenorrhea. Secondary sexual characters were well developed. On examination a firm, non-tender pelvic mass of size 12-weeks size with restricted mobility was felt per abdomen. Imperforate hymen with a bulge was seen on local examination of vagina. Ultrasound revealed a collection of 6×4.7 cm in endometrial cavity. Both ovaries and kidneys were normal. With the diagnosis of imperforate hymen, a cruciate incision was given on the centre of bulge. Drainage of hematometra was done followed by eversion of margins. Postoperatively the patient is having regular menstrual cycles.

These are summarized in Table 1.

Table 1: Cases.

Case, age (years)	Clinical picture	Imaging	Anamoly with ESHRE and ASRM classification	Treatment
Case 1, **31**	Recurrent T1 pregnancy loss A3, and abdomen	USG: bicornuate uterus	Complete septate uterus, ESHRE: U2B C0 V0, ASRM: class 5	DHL with septal resection
Case 2, **25**	Recurrent T1 pregnancy loss - A4	USG: bicornuate uterus	Partial septate uterus, ESHRE: U2A C0 V0, ASRM: class 6	DHL with septal resection
Case 3, **28**	Recurrent T2 pregnancy loss A2	USG: bicornuate uterus	Bicornuate uterus, ESHRE: U3A C0 V0, ASRM: class 4	Conservative
Case 4, 32	Primary infertility	USG: bicornuate uterus, HSG: bicornuate uterus	Septate uterus ESHRE: U2A C0 V0, ASRM: class 4	DHL with septal resection
Case 5, **28**	Primary infertility	USG and MRI: hypoplastic uterus	Hypoplastic uterus, ESHRE: U5A C0 V0, ASRM: class 1	Conservative
Case 6, **22**	Secondary infertility A1	USG: unicornuate uterus, MRI: unicornuate uterus with non-communicating rudimentary horn	Unicornuate uterus with non-communicating rudimentary horn, ESHRE: U4A C0 V0, ASRM: class 2	Conservative
Case 7, **14**	Primary amenorrhea	MRI: hypoplastic uterus and cervix	Hypoplastic uterus and cervix, ESHRE: U5A C4V0, ASRM: class 1	Conservative (planned for vaginoplasty 6m prior marriage)
Case 8, **13**	Primary amenorrhea	MRI: bulky uterus with uterine didelphys; hematometra and hematocolpus; absent right kidney	OHVIRA syndrome, complex	Diagnostic laparoscopy with right hematopyo salphinx excision with right cervix canalisation with adhesiolysis
Case 9, **17**	Primary amenorrhea	Uterine didelphys, hypoplastic cervix, 2 vaginal canals with longitudinal and horizontal septum with right hematosalphinx	Complex	Septal resection with uterovaginal anastamosis
Case 10, **14**	Primary amenorrhea cyclic pain abdomen	MRI: vaginal and cervical stenosis; hematometra	Complex	Hematometra drainage with vaginoplasty
Case 11, **19**	Primary amenorrhea	MRI: hypoplastic uterus with transverse vaginal septum	ESHRE: U5A, ASRM: class 1	Resection of transverse vaginal septum and vaginal reanastamosis

Continued.

Case, age (years)	Clinical picture	Imaging	Anamoly with ESHRE and ASRM classification	Treatment
Case 12, 18	Primary amenorrhea	USG: hypoplastic uterus with imperforate hymen	ESHRE: U5A, ASRM: class 1	Incision and drainage

DISCUSSION

The most common age group was 14-19 years (50%), comparable to Banerjee et al. In literature, the average age at diagnosis of Müllerian anomalies is reported to be from 10-18 years.[11]

Primary amenorrhea (50%) was the most common complaint among the adolescent age group, while the women of reproductive age presented with recurrent pregnancy loss (25%).[2] Similar findings were reported by Vyas et al, who found primary amenorrhea to be the most common symptom in a study conducted in India in 2018.[3] In the early adolescent group, with complaints of primary amenorrhea, the most common anomaly was hypoplastic uterus (41%), followed by imperforate hymen and transverse vaginal septum.

The most common anomaly seen in the reproductive age group was septate uterus (25%), which is comparable to Grimbizis et al who reported a 35% prevalence of septate uterus in their study.[4]

The most common diagnosis was hypoplastic uterus (41%), followed by septate (25%) and complex (25%) anomalies according to the ESHRE classification. However, 25% of the cases could not be classified according to the ASRM classification as they were complex anomalies with coexisting cervical and vaginal anomalies.

In the current study, all patients were evaluated for other anomalies. However, only one patient was found to have an associated renal anomaly (8%). According to the work done by Li et al the association between renal and Müllerian agenesis is around 29%.[8]

There was an interesting case of uterine didelphys, one hypoplastic cervix, and two separate vaginal canals with intervening longitudinal and horizontal septum with a small ovary and right hematosalpinx, which was classified as a complex anomaly by ESHRE. Our study was comparable with Ludwin et al, who concluded that ASRM criteria failed to classify this complex anomaly as it primarily focused on uterine anomalies, excluding those of the vagina and cervix.[9]

A case report by Kumar et al on complex Müllerian anomalies concluded that there should be an integrated clinico-radiological classification scheme and familiarity with rare and complex anomalies for appropriate diagnosis and management of Müllerian duct anomalies.[7]

There was a case classified as partial septate uterus according to ESHRE, which defines a septate uterus (class U2) as a uterus with a normal fundal external contour and a depression in the midline >50% of the uterine wall thickness. This class is subdivided into two subclasses: class U2a (partial septate uterus, where the lower edge of the septum does not reach the level of the internal cervical os) and class U2b (complete septate uterus, where the lower edge of the septum reaches the level of the internal cervical os).

However, according to ASRM, it was classified as an arcuate uterus, which was confirmed on diagnostic hysterolaparoscopy. This suggests that the new classification of ESHRE/ESGE leads to an increased frequency of diagnosing a septate uterus, making more cases eligible for hysteroscopic metroplasty. Similar studies by Youm et al and Ludwin et al also concluded that the ESHRE–ESGE criteria should not be used to diagnose and manage septate uterus.[12]

CONCLUSION

Among the 12 patients with an average age of 23 years the most common presenting complaint was primary amenorrhea (50%) followed by cyclic pain abdomen (30%) and recurrent pregnancy loss (23%). The most common diagnosis was hypoplastic uterus (41%) followed by septate (25%) and complex (25%) anomalies according to ESHRE classification. However, they couldn't be classified according to ASRM classification as they were complex anomalies with coexisting cervical and vaginal anomalies. One case was classified as partial septate uterus according to ESHRE was reclassified as arcuate uterus by ASRM classification. One case (8%) was associated with renal anomalies.

Mullerian anomalies are morphologically diverse group of anomalies which require meticulous examination and imaging studies to reach the diagnosis with precision.

ESHRE classification though applicable in larger way than the old ASRM classification, still has many lacunae such as It required referring to a chart for interpretation of the class assigned to a patient. It did not cover complex anomalies. It included a class in which to put all anomalies that did not fit in the classification system, which was admitting that it was an incomplete classification system.

Also, none of the classification systems describe anomalies of the cloaca and urogenital sinus, and associated anomalies.

Hence, further studies are needed to design new classification system which is comprehensive, accurate in definition of abnormal anatomy and pathology, unambiguous, simple to use and interpret.

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

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Cite this article as: Madhu Priya V, Peethambaran P, Datti SN. A comparative study of the American Society for Reproductive Medicine and European Society of Human Reproduction and Embryology classification systems in the diagnosis and management of Müllerian anomalies: insights from a case series. Int J Reprod Contracept Obstet Gynecol 2025;14:1301-6.