Reproductive Biology and Endocrinology

REVIEW

Open Access

Müllerian anomalies and endometriosis: associations and phenotypic variations

Surya Bhamidipaty-Pelosi[1,2†], Isaac Kyei-Barffour[3†], Marianna Volpert[4], Nora O'Neill[5], Alyssa Grimshaw[6], Lars Eriksson[7], Alla Vash-Margita[5] and Emanuele Pelosi[8,9*]

Abstract

Müllerian anomalies are congenital conditions characterized by the incomplete development of the female reproductive tract. Women affected by Müllerian anomalies often display additional malformations of the renal, skeletal, and cardiovascular system, and are at a higher risk for infertility and adverse pregnancy outcomes. Several Müllerian anomalies have been reported in association with endometriosis, but it is unclear if all classes or anatomical variations are associated with the disease. Most importantly, both Müllerian anomalies and endometriosis can manifest with a wide degree of variability, adding further complexity to their poorly defined relationship. Retrograde menstruation occurring in obstructive Müllerian anomalies is a well-accepted mechanism for the development of endometriosis. However, endometriosis can occur following surgical correction of the anomaly or in the absence of obstruction. This suggests that other mechanisms may be involved, although the specific pathogenesis remains elusive. This review provides a comprehensive summary of the current state of clinical research on endometriosis in Müllerian anomalies. This review also highlights research and knowledge gaps, informing the development of future experimental designs to address current limitations including heterogeneity of phenotypes, variable comorbidities, and lack of genetic information.

Keywords Müllerian anomalies, endometriosis, MRKH syndrome, unicornuate, OHVIRA, didelphys, bicornuate, septate

†Surya Bhamidipaty-Pelosi and Isaac Kyei-Barffour contributed equally to this work and share first authorship.

*Correspondence:
Emanuele Pelosi
epelosi@iu.edu
[1]Department of Clinical Pharmacology, Indiana University School of Medicine, Indianapolis, IN, USA
[2]Royal Brisbane and Women's Hospital, The University of Queensland, Brisbane, QLD, Australia
[3]Institute for Molecular Bioscience, The University of Queensland, Brisbane, QLD, Australia
[4]School of Biomedical Sciences, Queensland University of Technology, Brisbane, QLD, Australia
[5]Division of Pediatric and Adolescent Gynecology, Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine, New Haven, CT, USA
[6]Harvey Cushing/John Hay Whitney Medical Library, Yale University, New Haven, CT, USA
[7]Herston Health Sciences Library, The University of Queensland, Brisbane, QLD, Australia
[8]Centre for Clinical Research, The University of Queensland, Brisbane, QLD, Australia
[9]Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, IN, USA

Introduction

Müllerian anomalies are anatomical variations of the female reproductive tract resulting from the incomplete development of the Müllerian ducts [1]. During embryogenesis, the Müllerian (paramesonephric) ducts arise as an invagination of the coelomic epithelium, and elongate posteriorly parallel to the Wolffian (mesonephric) ducts until they fuse into a Y-shaped structure that forms the uterine primordium [2–4]. Resorption of the septum formed by the fusion of the two Müllerian ducts results in the formation of a single canal that will later develop into the uterine cavity [5]. At the site where the lower portions of the Müllerian ducts fuse with the medial wall of the Wolffian ducts, the Müllerian tubercle forms [6]. The subsequent cavitation of the Müllerian tubercle will result in the development of the primitive vagina, whose wall is formed by Wolffian duct cells and internally by Müllerian tubercle cells before proper epithelialization from the urogenital sinus occurs [4, 7, 8]. Disruption of any of these complex processes can lead to abnormalities of Müllerian tract structures. In addition, the development of the genital system is closely related to the urinary system as they both derive from the intermediate mesoderm [2]. Importantly, the Wolffian ducts are involved in the regulation of Müllerian duct development, while also providing a foundation for the formation of the metanephros (permanent kidneys) [4]. The metanephros are induced by the ureteral buds, which sprouts from the Wolffian ducts at the urogenital sinus. Therefore, anomalies of Wolffian duct development result in malformations of the urinary system in addition to the reproductive tract.

At the molecular level, several of the signaling pathways regulating Müllerian duct development are also involved in the development of other organs including the renal and skeletal systems, leading to additional concomitant congenital malformations [2, 9]. As a result, Müllerian anomalies occur with a wide range of clinical presentations, severities, and comorbidities including unilateral kidney agenesis, kidney dysplasia, and scoliosis. Müllerian anomalies are also associated with endometriosis, a disease characterized by the abnormal growth of endometrial-like tissue outside of the uterus. Like Müllerian anomalies, endometriosis has a multifactorial pathogenesis and shows high degree of phenotypic variability and severity [10, 11].

Several mechanisms have been proposed in the pathogenesis of endometriosis. One of the most accepted is Sampson's theory of retrograde menstruation, which suggests that during menstruation, some endometrial tissue moves through the oviducts into the peritoneal cavity causing endometriosis [12]. An alternative theory is coelomic metaplasia, postulating that because endometrium and peritoneum originate from the same embryonic coelomic epithelium, the peritoneal mesothelium can eventually transform into endometrium causing endometriosis [12]. Another mechanism involves Müllerian embryonic remnants, and suggests that Müllerian structures persisting from the time of embryonic development can adhere to the peritoneum and subsequently develop into endometriosis [12]. Each theory alone cannot explain the heterogeneity of endometriosis, sometimes occurring even within the same patients. Therefore, it is possible that multiple mechanisms are involved and it is likely that they are affected by genetic predisposition, immune status, and environmental factors.

The relationship between Müllerian anomalies and endometriosis is complex and unclear. High rates of endometriosis have been found in obstructive compared to non-obstructive Müllerian anomalies [13]. In addition, complete resorption of endometriosis has been reported following surgical removal of uterine rudiments or removal of obstruction [14–19]. These studies seem to support the retrograde menstruation mechanism. However, endometriosis has also been found in non-obstructive Müllerian malformations [13, 18, 20–23]. These reports refute retrograde menstruation and suggest the existence of alternative mechanisms including coelomic metaplasia or Müllerian remnants. To better characterize the heterogeneity of Müllerian conditions, their anatomical features, and their association with endometriosis, we performed an extensive search for studies on co-occurring Müllerian anomalies and endometriosis. We classified Müllerian anomalies into three main categories (agenesis, fusion, resorption) reflecting the embryological processes of Müllerian duct development, and discussed the involvement of mesonephric anomalies inducing Müllerian abnormalities [24]. Where available, we reported prevalence, phenotypic variations of the reproductive tract and other systems, and proposed pathogenic mechanisms.

Methods

An exhaustive search of the literature was conducted in Cochrane Library, Google Scholar, Ovid Embase, Ovid MEDLINE, PubMed, Scopus, and Web of Science Core Collection databases to find relevant articles published from the inception of each database. Databases were searched using a combination of keywords and controlled vocabulary for Müllerian anomalies and endometriosis, including "Müllerian anomalies", "uterine malformations", "female genitourinary malformations", "congenital malformations of the Müllerian ducts", "Mayer-Rokitansky-Küster-Hauser syndrome", "Müllerian aplasia", "unicornuate uterus", "bicornuate uterus", "vaginal atresia", "cervicovaginal atresia", "didelphys uterus", "Herlyn-Werner-Wunderlich syndrome", "obstructed-hemivagina-and-ipsilateral-renal-anomaly syndrome", "septate

uterus", "endometriosis", and "endometrioma". Studies were included if they reported Müllerian anomalies in combination with endometriosis in humans, and were written in English language. Case series and case-control studies with a minimum number of 10 patients were used to generate tables. Editorials, conference abstracts, reviews, and studies involving animals were excluded.

Agenesis anomalies

Combined uterovaginal agenesis

Bilateral Müllerian agenesis is also called Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, which occurs in 1:4500 women and is characterized by incomplete development of both Müllerian ducts. When isolated, this anomaly involves the Müllerian tubercle and ducts. However, when development of an entire urogenital ridge is affected, unilateral renal agenesis or malformation occurs [25]. Additional congenital abnormalities are also prevalent in MRKH syndrome (Table 1) [13, 25–32]. These comorbidities involve mostly the renal and skeletal system, and, like the reproductive tract, display variable phenotypes. The most common abnormality was unilateral renal agenesis, which was reported in roughly half of the studies with prevalence ranging from 4 to 66% of cases. Scoliosis was also observed and ranged from 12 to 25%. Other anomalies included horseshoe kidney, dysplastic kidney, ectopic kidney, spina bifida occulta, and bone malformations. Rarer were abnormalities of the cardiovascular system, which included septal defects and duplication of the inferior vena cava [27, 30, 31].

With the exception of Rosenberg et al., none of these studies stratified patients to distinguish endometriosis prevalence in cases of isolated agenesis versus agenesis of an entire urogenital ridge or mesonephric anomalies [25]. Overall, the association with endometriosis varied considerably among studies, ranging from ~2–68% (Table 1). In addition to phenotypic heterogeneity, a possible reason for these differences could be the approach in diagnostic evaluation as only few studies investigated the presence of a functional endometrium. When functioning endometrial tissue was confirmed, the prevalence of endometriosis was less variable, ranging from

Table 1 Summary of studies on combined uterovaginal agenesis

Reference	Age (range, yrs)	Endometriosis prevalence (%)	Reproductive tract variations (*n*)	Additional malformations (*n*)
Rosenberg HK et al. 1986 [25]	5 days – 18 yrs	8.3 (1/12)	Uterine agenesis (1), rudimentary (1), bicornuate (3), didelphys (6), duplicated (1)	Renal agenesis (8), horseshoe kidney (1), crossed fused ectopia (1), mild hydronephrosis (1)
Olive DL and Henderson DY 1987 [26]	n/s	15.4 (2/13)	Mullerian agenesis/hypoplasia: vaginal (6), cervical (1), fundal (1), tubal (3), combined (9)	n/s
Uğur M et al. 1997 [13]	n/s	2.4 (1/42)	Mullerian agenesis/hypoplasia: vaginal (16), cervical (3), fundal (7), tubal (1), combined (34)	n/s
Wang Y et al. 2017 [27]	11–43	8.7 (8/92)	Uterine agenesis (20), unilateral rudimentary uterus (9), bilateral rudimentary uterus (63)	Renal agenesis (4), isolated pelvic kidney (3), unilateral pelvic kidney (1), unilateral dysplastic kidney (1), unilateral renal agenesis and dysplastic contralateral kidney and ureter (1); scoliosis (23), spina bifida occulta (6), lumbosacral transitional vertebral (6), vertebral deformation (2), bilateral ulnar clubhands (1), hexadactyly (1), rib malformations (1), talipes equinovarus (1); anal atresia (2), inguinal hernia (4), urogenital fistula (4), duplicated inferior vena cava (4), atrial septal defect (4)
Asaturova AV et al. 2020 [28]	20–24	40.4 (7/42)	n/s	n/s
Dabi Y et al. 2020 [29]	18.9 ± 4.8 (mean)	38.0 (8/21)	Bilateral uterine horns (20)	Urinary malformation (4), multiple malformations (1)
Wang Y et al. 2020 [30]	9–37	5.5 (11/201)	Bilateral rudiments (191), unilateral rudiments (3), uterine agenesis (7)	Renal agenesis (15), unilateral dysplastic kidney (4), horseshoe kidney (1), pelvic kidney (1), polycystic kidney (1), hydronephrosis (1); scoliosis (41), spinal bifida occulta (4), hemivertebra (6), rib malformation (1), scapula malformation (1), pelvic bone malformation (1), Klippel Feil syndrome (1), anal atresia (2), atrial septal defects (3), dextrocardia (1)
Tian W et al. 2021 [31]	5–26	67.6 (23/34)	Bilateral remnants (34)	Renal agenesis (8), scoliosis (4), limb malformations (3), anal atresia (3), cardiac malformations (3)
Steinmacher S et al. 2022 [32]	16–41	2.8 (9/319)	Bicornuate (5), gross uterine abnormalities without endometrium (4).	Pelvic kidney (2), double renal pelves (2), Abnormal vertebral development (2)

n/s = not specified

40 to 67% [25–27, 29–31]. In a study of 92 MRKH cases, 68.4% of patients presented with bilateral rudiments, whereas 9.7% had unilateral rudiments [27]. However, all unilateral rudimentary uteri showed the presence of endometrium compared to 22% of bilateral rudiments ($p<0.001$), and endometriosis was significantly more prevalent in unilateral compared to bilateral remnants (22% vs. 4%, $p<0.01$) [27]. In a separate study, the same group analyzed a total of 385 uterine rudiments from 201 patients with MRKH syndrome [30]. Using MRI, they classified the remnants into one-, two-, and three-layer differentiation stages (the latter being typical of a functional uterus). The authors found that endometriosis was present in 39.1% of patients with three-layer differentiation compared to 1.6% of the one- and two-layer differentiation class, consistent with a relationship between the degree of endometrial functionality and endometriosis.

Cervico-vaginal agenesis

Agenesis or atresia of the lower reproductive tract including cervix and vagina result from anomalies of the Müllerian tubercle [24, 33]. Typically, these cases are associated with a normal uterine morphology, but fusion or resorption defects may occur, resulting in upper tract anomalies such as didelphys or bicornuate uterus. In addition, segmentary atresia of one of the Müllerian ducts lead to unicornuate uterus presentations. Finally, as discussed above, developmental anomalies of the mesonephric duct are responsible for the co-occurrence of renal anomalies (Table 2) [34–45]. Unilateral renal agenesis was again the most reported comorbidity, which occurred in up to 37% of cases. Other anomalies were less frequent and included pelvic kidney, fused kidneys as well as scoliosis. Aside from Zhang et al., and Xu et al., who reported lower rates, endometriosis was generally highly associated with cervico-vaginal agenesis, ranging from 30 to 95% of cases (Table 2).

Retrograde menstruation is generally believed to be the main pathogenic mechanism for endometriosis in obstructive anomalies including cervico-vaginal agenesis and MRKH syndrome, and usually found in the form of endometriomas [14, 19, 26, 41, 46]. Song et al. reported that in a cohort of 52 patients with cervical atresia and endometriosis, the prevalence of endometriomas was 76% [38]. The authors argued that decreased peritoneal fluid movement due to the presence of the sigmoid colon

Table 2 Summary of studies on cervico-vaginal agenesis or atresia

Reference	Age (range, yrs)	Endometriosis prevalence (%)	Reproductive tract variations (*n*)	Additional malformations (*n*)
Uğur M et al. 1997 [13]	n/s	68.4 (13/19)	Mullerian agenesis/hypoplasia: vaginal (16), cervical (3), fundal (7), tubal (1), combined (34)	n/s
Deffarges JV et al. 2001 [34]	12–18	44.4 (8/18)	Unicornuate (2), hypoplastic (1), bilateral tubal agenesis (1)	Renal agenesis (1), ureteral duplicity (1), pelvic kidney (1)
Fedele L et al. 2008 [35]	12–17	58.3 (7/12)	Unicornuate (4)	Renal agenesis (2), Fallot tetralogy (1)
Kriplani A et al. 2012 [36]	12–19	85.7 (12/14)	Unicornuate (6)	Renal agenesis (5)
Kisku S et al. 2014 [37]	11–34	70.0 (14/20)	Didelphys (2)	Renal agenesis (1), cross renal fused ectopia (1), renal agenesis + rectovestibular fistula + segmental thoracolumbar spine scoliosis (1), rectovestibular fistula + ventricular septal defect + bilateral auditory anomalies (1)
Song X et al. 2016 [38]	10–20	54.2 (52/96)	Unicornuate (13), bicornutate (10)	Renal agenesis (9), pelvic kidney (1), horseshoe kidney (1), ectopic urethral orifice (1). Scoliosis (2), six finger malformation (1), sacral canal cyst (1)
Zhang H et al. 2017 [39]	10–18	13.3 (2/15)	Unicornuate (1), didelphys (4)	Renal agenesis (2), Scoliosis (2)
Xu S et al. 2019 [40]	15 days – 28 yrs	8.3 (1/12)	n/s	Ectopic kidney (1)
Kang J et al. 2020 [41]	12–19	80.0 (8/10)	Septate (1), bicorporeal (1)	Scoliosis (1)
Ding Y et al. 2021 [42]	16.42 ± 5.78 (mean)	60.5 (23/38)	Septate (2), bicorporeal (5), hemiuterus (8)	n/s
Pan HX et al. 2021 [43]	11–26	95.6 (22/23)	Septate (2), bicorporeal (2)	Duplex kidney (1). Lumbar/thoracic scoliosis (6), cervical curvature straight (1)
Regan L and Dewhurst J 2022 [44]	14–29	57.1 (8/14)	Bicornuate (5), gross uterine abnormalities without endometrium (4).	Pelvic kidney (2), double renal pelves (2), Abnormal vertebral development (2)
Candiani M et al. 2023 [45]	11–15	31.2 (5/16)	Unicornuate (5)	Renal agenesis (2)

n/s = not specified

on the left side could lead to left-sided cysts [38]. However, other studies reported absence of endometriosis in 32–40% of cases when a functioning endometrium was demonstrated, arguing that other factors were likely involved [26, 31].

The existence of other mechanisms is particularly relevant when absence of uterine tissue is suspected. In these instances, however, it is critical to achieve a definite diagnosis of the pathology. Acién reported a case of endometriosis in a woman with MRKH syndrome with complete agenesis of vagina and uterus and proposed the case as proof against the retrograde menstruation theory [18]. Interestingly, the authors later found a functional rudimentary horn in the same woman, confirming that retrograde menstruation was involved [47]. Although MRI is the primary non-invasive diagnostic choice for Müllerian anomalies, it does not demonstrate the presence of endometrial activity within Müllerian tissues [48]. Therefore, surgical/histological evidence must be attained prior to excluding retrograde menstruation. Importantly, reports of endometriosis in cases of confirmed uterine agenesis or following surgical correction of obstruction present evidence of coelomic metaplasia or other mechanisms [20, 21]. In a case series of congenital vaginal obstruction or agenesis, endometriosis was observed between 6 months to 5 years following surgical repair of the anomaly [22]. The authors suggested that although it was possible that prior endometriotic implants from retrograde menstruation may have remained active, coelomic metaplasia, lymphatic/vascular metastasis, immunologic deficiency, or genetic factors were the likely pathogenic mechanisms.

Transverse vaginal septum

Transverse or oblique vaginal septum is the result of segmentary atresia and failed canalization of the developing vagina [33]. The resulting partial or complete outflow obstruction is associated with a high rate of early endometriosis, seemingly supporting the pathogenic mechanism of retrograde menstruation. However, only case reports or small case series are present in the literature, making it difficult to assess prevalence rates [18, 19, 49, 50]. While none of seven women with transverse vaginal septum showed endometriosis in a report from Kapczuk et al., Deligeoroglou et al. presented a case series of seven adolescents with endometriosis and transverse or oblique vaginal septum [19, 49]. In the latter cohort, one patient had a bicornuate uterus, two had didelphys uterus, and congenital abnormalities of the urinary tract were present in six patients [49].

Unicornuate uterus

Unicornuate uterus results from lack or underdevelopment of one of the Müllerian ducts, and is estimated to represent about 10% of all uterine anomalies [46]. If the anomaly is isolated, both kidneys are present, whereas unicornuate uterus is associates with unilateral renal agenesis in cases of agenesis or hypoplasia of an entire urogenital ridge [33]. In the studies included, unicornuate uterus was often reported with renal anomalies, the most common being unilateral kidney agenesis (Table 3) [13, 26, 51–66]. Similar to MRKH syndrome, other malformations included horseshoe and ectopic kidney, but compared to MRKH, skeletal anomalies were less common.

Unicornuate uterus can present with or without a rudimentary horn, which may or may not be communicating with the contralateral horn. A non-communicating rudimentary horn was seen in the majority of patients, and these had higher risk of developing endometriosis and pelvic inflammatory disease [52]. Overall, the prevalence of endometriosis ranged from 5 to 62% (Table 3). As noted previously, this variability may be a reflection of lack of stratification according to clinical presentations and associated comorbidities. In general, lower prevalence was usually reported in studies that included higher numbers of patients with non-cavitated rudimentary horn or no horn [51, 54, 66]. Conversely, higher rates of endometriosis were seen in studies with larger proportions of communicating and non-communicating cavitated rudimentary horn [55, 63, 65]. After stratifying for the type of unicornuate uterus presentation, Piriyev and Römer histologically detected endometriosis in 87.5% of patients when endometrium was found in an obstructed rudimentary horn, compared to 25% when no active endometrium was present, and 66.7% in patients without a rudimentary horn [65]. Fedele et al. found that endometriosis was more prevalent in cases where the rudimentary horn was cavitated and non-communicating (57.2%) compared to communicating (33%), non-cavitated (42.1%), or when no horn was present (46.2%) [61]. In a retrospective cohort study of 326 women with unicornuate uterus compared to 326 controls, Tellum et al. found that the rate of endometriosis was significantly higher in the unicornuate uterus group (17.5% vs. 10.7%, $p=0.018$) [66]. Not surprisingly, the risk of developing endometriosis was higher in women with a functional rudimentary horn compared to those with unicornuate uterus but no functional horn [66].

Infertility is often a presenting complaint in unicornuate uterus cases, and several studies included infertile women to evaluate if endometriosis was a possible factor [52, 57, 60, 66]. Fedele et al. reported endometriosis in 48.8% of 41 women with unicornuate uterus, the majority of whom were infertile patients [60]. Although the authors acknowledged that endometriosis could contribute to infertility, they found similar reproductive performances between women with and without

Table 3 Summary of studies on unicornuate uterus

Reference	Age (range, yrs)	Endometriosis prevalence (%)	Reproductive tract variations (*n*)	Additional malformations (*n*)
Buttram VC and Gibbons WE 1979 [51]	n/s	15.8 (3/19)	Non-communicating cavitated rudimentary horn (1), communicating cavitated rudimentary horn (6), non cavitated rudimentary horn (6), no horn (6)	Renal agenesis (1), crossed renal ectopy (1), moderate hydronephrosis (1)[d]
Heinonen PK 1983 [52]	16–79	20.0 (4/20)	Non-communicating cavitated rudimentary horn (7), non-communicating non-cavitated rudimentary horn (7), no horn (2), cavity in non-communicating rudimentary horn not determined (4)	Renal agenesis (5), pelvic kidney (3), horseshoe kidney (1)[b]
Heinonen PK 1983 [53]	n/s	5.0 (1/20)	n/s	n/s
Fedele L et al. 1987 [54]	n/s	14.3 (3/21)	Communicating rudimentary horn (1), non-communicating rudimentary horn (4), non-cavitated rudimentary horn (7), no horn (7)	Renal agenesis (3), renal ptosis (2), double renal pelvis (1), horseshoe kidney (1)[e]
Olive DL and Henderson DY 1987 [26]	n/s	30.0 (3/10)	Communicating rudimentary horn (1), non-communicating rudimentary horn (1), non-cavitated rudimentary horn (4), no horn (4)	n/s
Fedele L et al. 1990 [55]	14–33	60.0 (6/10)	Non-communicating rudimentary horn (10)	n/s
Donderwinkel PFJ et al. 1992 [56]	18–39	17.8 (8/45)	n/s	Renal agenesis (5), ectopic kidney (4), hypoplastic pyelum (2)[a]
Fedele L et al. 1992 [57]	n/s	55.0 (11/20)	Non-communicating cavitated rudimentary horn (11), non cavitated rudimentary horn (9)	n/s
Moutos DM et al. 1992 [58]	n/s	48.3 (14/29)	n/s	Renal agenesis (5), malrotated kidney (1), renal ptosis (1)[f]
Liu MM 1994 [59]	16–34	31.8 (7/22)	Non-communicating cavitated rudimentary horn (1), communicating cavitated rudimentary horn (1)	n/s
Fedele L et al. 1995 [60]	n/s	48.8 (20/41)	Communicating rudimentary horn (1), non-communicating rudimentary horn (8), non-cavitated rudimentary horn (19), no horn (13)	n/s
Fedele L et al. 1996 [61]	14–40	46.9 (23/49)	Communicating rudimentary horn (3), non-communicating rudimentary horn (14), non-cavitated rudimentary horn (19), no horn (13)	Renal agenesis (5), ectopic kidney (3), renal agenesis and contralateral ectopic kidney (1), double renal pelvis (2), horseshoe kidney (2), unilateral medullary sponge kidney (1)
Heinonen PK 1997 [62]	15–79	21.4 (9/42)	Non-communicating cavitated rudimentary horn (15), non-communicating non-cavitated rudimentary horn (15), no horn (7)	Renal agenesis (8), pelvic kidney (3), horseshoe kidney (1), renal malrotation (1); scoliosis (1), arthrogryposis (1), hypoplasia of radii (1), hemivertebra (1); auditory defects (2)[c]
Uğur M et al. 1997 [13]	n/s	23.1 (3/13)	Communicating rudimentary horn (4), non-communicating rudimentary horn (3), non-cavitated rudimentary horn (4), no horn (2)	n/s
Fedele L et al. 2005 [63]	14–26	50.0 (5/10)	Cavitated non-communicating rudimentary horn (10)	Renal agenesis (3)
Acién P and Acién M 2010 [64]	n/s	13.5 (5/37)	n/s	Renal agenesis (10); skeletal anomalies (5)

Table 3 (continued)

Reference	Age (range, yrs)	Endometriosis prevalence (%)	Reproductive tract variations (*n*)	Additional malformations (*n*)
Piriyev E and Römer T 2020 [65]	n/s	62.5 (10/16)	Rudimentary horn (13), no horn (3)	n/s
Tellum T et al. 2023 [66]	34.0 ± 9.5 (mean)	17.5 (57/326)	Communicating functional horn (4), non-communicating non-functional horn (126), non-communicating functional horn (88), no horn (108)	Renal agenesis (39), pelvic kidney (11), other urinary tract malformation (18), genetic syndrome (9), cloacal anomaly (6)

n/s = non specified

a Total number of malformations out of 35 intravenous pyelograms or ultrasound

b Total number of malformations out of 15 intravenous pyelograms performed

c Total number of malformations out of 34 intravenous pyelograms/renography/ultrasound

d Total number of malformations out of 13 intravenous pyelograms performed

e Total number of malformations out of 16 intravenous urographies

f Total number of malformations out of 12 intravenous pyelograms

endometriosis [60]. In a separate study that excluded patients with obstructive abnormalities, Fedele et al. compared infertile subjects with non-obstructive Müllerian abnormalities to infertile controls and found that the prevalence of endometriosis was significantly greater in unicornuate uterus compared to other Müllerian anomalies (55% vs. 28%, $p < 0.05$) [57].

Fusion anomalies

Obstructed hemivagina and ipsilateral renal anomaly

Obstructed hemivagina and ipsilateral renal anomaly (OHVIRA) syndrome, previously called Herlyn-Werner-Wunderlich (HWW) syndrome, is a complex anomaly characterized by uterine duplicity (didelphys, bicornuate, septate), obstructed hemivagina, and renal dysplasia ipsilateral to the hemivagina [67, 68]. This Müllerian disorder is induced by an associated Wolffian anomaly. The ureteral buds sprout from the opening of the Wolffian ducts in the urogenital sinus. Therefore, agenesis or developmental defects involving one of the mesonephric ducts would lead to absence of the ureteral bud, with consequent renal agenesis and blind ipsilateral hemivagina [69]. Like other Müllerian anomalies, significant variations of the uterine anatomy have been reported (Table 4) [19, 70–87]. Candiani et al. diagnosed didelphys uterus in 58% of patients, double uterus in 31%, and bicornuate in 11% [71]. In a cohort of 87 patients, the uterus was didelphys in 77% of cases, bicornuate in 11.5%, and septate bicollis in 11.5% [72]. Obstructed hemivagina was present in 95.4% of patients, whereas the remaining 4.5% had unilateral cervical atresia [72]. Similar findings were reported in a cohort of 51 patients, showing didelphys uterus in 78.4% of cases, complete septate in 17.6%, and bicornuate in 3.9% [84]. The renal anomaly usually presented as renal agenesis in postpubertal patients and multicystic dysplastic kidney in prepubertal patients [70, 73, 75, 77, 78, 82, 88, 89]. In patients with ages ranging 11–42 years, Fedele et al. reported ipsilateral renal agenesis in 95.4% of cases and ipsilateral hypoplastic kidney in 4.6%, although the authors did not provide a breakdown of ages [72]. Overall, laterality of the renal anomaly was reported in 564 patients, and showed that renal agenesis was right-sided in 341 cases (60.5%) and left-sided in 223 cases (39.5%). Additional associated malformations were rare, and included skeletal malformations, cervical aplasia, and unilateral vaginal agenesis [19, 78, 82].

The prevalence of endometriosis ranged from 3 to 60% (Table 4). However, the documentation of endometriosis was typically limited to patients who had undergone reparative laparoscopy or laparotomy and thus did not include all patients in the study cohorts, therefore underestimation of disease frequencies was possible [70, 71, 82, 83, 85]. Tong et al. and Zhu et al. both noted that patients with complete obstruction of the hemivagina were more likely to have endometriosis than those with incomplete obstruction [73, 77]. They hypothesized that complete obstruction led to a higher volume of retrograde flow compared to incomplete obstruction where blood could partly drain through the patent vaginal canal, supporting other reports [70, 78, 86, 88, 89]. These studies also pointed to a delayed diagnosis of both OHVIRA and endometriosis as contributing to more advanced endometriosis due to a longer duration of retrograde flow.

Didelphys uterus

Cohort studies of didelphys uterus were few, and showed endometriosis in 16.7–40% of cases (Table 5) [13, 26, 57]. None of these studies, however, mentioned additional variations of reproductive tract anatomy or the presence of associated congenital malformations. Therefore, it is not clear if all these cases were isolated Müllerian anomalies or some included mesonephric involvement.

Table 4 Summary of studies on OHVIRA syndrome

Reference	Age (range, yrs)	Endometriosis prevalence (%)	Reproductive tract variations (*n*)	Additional malformations (*n*)
Stassart JP et al. 1992 [70]	6–26	46.7 (7/15)	n/s	Renal agenesis (15)
Candiani GB et al. 1997 [71]	9–36	27.8 (10/36)	Didelphys (21), double (11), bicornuate (4)	Renal agenesis (36)
Fedele L et al. 2013 [72]	11–42	13.8 (12/87)	Didelphys (67), septate bicollis (10), bicornuate (10)	Renal agenesis (83), dysplastic hypoplastic kidney (4)
Tong J et al. 2013 [73]	10–50	17.1 (12/70)	n/s	Renal agenesis (70)
Wang S et al. 2013 [74]	11–33	5.8 (3/52)	n/s	Renal agenesis (50), ectopic kidney (1), renal malformation (1)
Sabdia S et al. 2014 [75]	n/s	60.0 (6/10)	Cervical aplasia (2)	Renal agenesis (10)
Tong J et al. 2014 [76]	13–37	19.1 (18/94)	n/s	Renal agenesis (94)
Zhu L et al. 2015 [77]	12.86 ± 1.84 (mean, group 1) 21.68 ± 7.43 (mean, group 2)	20.2 (16/79)	Complete obstruction (24, group 1), incomplete obstruction (55, group 2)	Renal agenesis (79)
Kapczuk K et al. 2018 [78]	11–17	5.5 (1/18)	Didelphys (16), septate (2)	Renal agenesis (18). Scoliosis (1), scoliosis + lumbarization S1 + butterfly vertebra S2 (1)
Troncon JK et al. 2018 [79]	11–29	14.3 (2/14)	Didelphys (14)	Renal agenesis (14)
Dabi Y et al. 2020 [80]	16.6 ± 4.14 (mean)	16.4 (13/79)	Didelphys (79)	Renal aplasia (73), renal dysgenesis (2), renal duplicity (2)
Gungor Ugurlucan F et al. 2020 [81]	10–48	3.4 (1/29)	n/s	Renal agenesis (28), multicystic dysplastic kidney (1)
Kim YN et al. 2021 [82]	0–32	60.0 (6/10 who underwent laparoscopy in a cohort of 65 patients)	Didelphys (65)	Renal agenesis (34), multicystic dysplastic kidney (31)
Yi S et al. 2021 [83]	11–34	5.9 (1/17)	Complete septate uterus (17)	Renal agenesis (17)
Candiani GB et al. 2022 [84]	12–36	17.6 (9/51)	Didelphys (40), septate (9), bicornuate (2)	Renal agenesis (49), dysplastic kidney (2)
Zarfati A et al. 2022 [85]	0.5–15.7	3.6 (1/28)	Didelphys (28)	Renal agenesis (23), multicystic dysplastic kidney (5)
Zhang J et al. 2020 [86]	11–28	15.8 (3/19)	Cervical dysplasia (1)	Renal agenesis (19)
Zhang Y et al. 2022 [87]	13.13–23.34 (mean)	13.0 (6/46)	Didelphys (40), septate (6)	Renal agenesis (46)
Kapczuk K et al. 2023 [19]	11–17	43.5 (10/23)	Didelphys (23)	Renal agenesis (23); scoliosis (1)

n/s = non specified

Table 5 Summary of studies on didelphys uterus

Reference	Age (range, yrs)	Endometriosis prevalence (%)	Reproductive tract variations (*n*)	Additional malformations (*n*)
Uğur M et al. 1997 [13]	n/s	16.7 (2/12)	n/s	n/s
Olive DL and Henderson DY 1987 [26]	n/s	40.0 (4/10)	n/s	n/s
Fedele L et al. 1992 [57]	n/s	35.3 (6/17)	n/s	n/s

n/s = non specified

Heinonen retrospectively analyzed a cohort of 49 patients with didelphys uterus, including 8 with OHVIRA, and found endometriosis in 7 among the 45 women who underwent laparoscopy (16%) [90]. However, the author did not specify how many were didelphys or OHVIRA cases. Similarly, in a cohort of patients with didelphys uterus or OHVIRA, Moutos et al. reported a combined endometriosis prevalence of 8.7% (2/23) without providing further details [58]. Although retrograde menstruation was mentioned in some obstructive case reports, several authors proposed other mechanisms [90–94]. Heinonen reported that 9/49 (18%) cases had an obstructed hemivagina, but only 1 out of 9 cases (11%) had endometriosis, providing an argument against retrograde menstruation [90]. Hori et al. presented a case of ectopic endometriosis of the alimentary tract in a patient with didelphic uterus [94]. The patient did not show any ovarian disease, and the authors suggested that epithelial metaplasia or metastatic transplantation were likely responsible for the disease.

Bicornuate uterus

Similar to didelphys, bicornuate uterus results from the incomplete fusion of the Müllerian ducts during organogenesis. Case series of bicornuate uterus were also few, and showed a wide variation in endometriosis prevalence, ranging between 0% and 72.2% (Table 6) [13, 17, 53, 57, 65]. Most studies described the type of separation between the two uterine cavities (i.e. complete vs. partial), but only one reported the presence of additional malformations, which involved the renal system [17].

In a study where bicornuate and didelphic uterus were combined, Acién and Acién reported an endometriosis prevalence of 9.7% (12/123) [64]. Unilateral kidney agenesis was the most commonly reported anomaly associated with these conditions. The authors noted that subjects with bicornuate or didelphic uterus and renal agenesis were more likely to have endometriosis than those without renal anomalies (20.0% [9/45] vs. 3.8% [3/78], respectively) [64]. A retrospective analysis of 800 women with Müllerian anomalies in the restricted gene pool population of LaCrete (Canada) showed that bicornuate and unicornuate uterus were the most common (21.7% for both) uterine anomalies [95]. In this selected population, reproductive tract anomalies in general occurred 5.5 times more frequently than in the general population suggesting the existence of a genetic component [95]. The author also found some five cases of endometriosis and several associated renal malformations but did not report any statistics or clarify in which class of Müllerian anomalies they occurred.

Due to the limited number of studies, a causal or direct relationship between bicornuate uterus and endometriosis remains unclear [96, 97]. Few case reports described endometriosis in patients with hindered menstrual flow [98, 99]. However, several authors reported the type of endometriosis as scar endometriosis developing after past surgery [100–102]. This type of endometriosis usually occurs from the iatrogenic seeding of endometrial tissue following surgical procedures including exploratory laparoscopy, hysterectomy, or Cesarean section. In these cases, the concomitant Müllerian anomaly is unlikely to be directly associated with endometriosis.

Table 6 Summary of studies on bicornuate uterus

Reference	Age (range, yrs)	Endometriosis prevalence (%)	Reproductive tract variations (*n*)	Additional malformations (*n*)
Heinonen PK 1983 [53]	n/s	1.4 (1/69)	Complete (8), partial (61)	n/s
Fedele L et al. 1992 [57]	n/s	31.2 (10/32)	Complete (26), partial (6)	n/s
Creatsas G et al. 1994 [17]	11–19	0.0 (0/11)	Obstructed hemivagina (4), obstructed cervical os (3), rudimentary horn (4)	Renal agenesis (3), fused pelvic kidney (1)
Uğur M et al. 1997 [13]	n/s	17.2 (5/29)	Complete (12), partial (17)	n/s
Piriyev E and Römer T 2020 [65]	n/s	72.2 (13/18)	n/s	n/s

n/s = non specified

Resorption anomalies

Septate uterus

Septate uterus results from the incomplete resorption of the midline uterine septum after embryonic fusion of the Müllerian ducts. Complete septate uterus is associated with a septum extending to the cervix and sometimes, with a longitudinal vaginal septum, while partial uterine septum extends no further than the internal cervical os [9]. In the selected studies, partial septum was more represented than complete (941 cases vs. 482, respectively) (Table 7) [103–116]. However, very few studies described the presence of additional malformations. Comorbid congenital anomalies included renal agenesis, atrophic kidney, and ureter duplication [51, 64, 107]. Endometriosis rates were variable, ranging from 0 to 77.1%, and results were often conflicting. By comparing groups with and without septate uterus, Fedele et al., Uğur et al., and Demir et al. found no association between uterine septum and endometriosis [13, 57, 111]. Similarly, a retrospective Finnish study reported only a 3.3% rate of endometriosis in patients with complete septate uterus [107]. In contrast, a retrospective study by Nawroth et al. found endometriosis to be significantly more common in patients with partial or complete septate uterus compared to women with normal uterine cavities (25.8% vs. 15.2% endometriosis, respectively) [108]. Piriyev and Romer noted that in a cohort of 179 women with septate uterus, 92.6% of those with a complete septum had endometriosis versus 74.3% of patients with a partial septum [65].

Other studies used a different approach and investigated the rate of septate uterus among women with and without endometriosis. A prospective study from LaMonica et al. found that uterine septum was significantly more common in patients with histologically-confirmed endometriosis compared to those without (37% versus 27%, respectively) [114]. Consistent with these findings, a retrospective analysis by Matalliotakis et al. compared a group of 425 infertile patients with endometriosis to a control group of 200 women with tubal or male factor infertility and no endometriosis [117]. The endometriosis group contained 7 patients (1.6%) with septate uterus, while only 1 septate uterus (0.5%) was identified in the control group [117].

Table 7 Summary of studies on septate uterus

Reference	Age (range, yrs)	Endometriosis prevalence (%)	Reproductive tract variations (*n*)	Additional malformations (*n*)
Buttram VC et al. 1974 [103]	20–33	32.1 (9/28)	Complete (6), partial (22)	n/s
Buttram VC and Gibbons WE 1979 [51]	n/s	0.0 (0/67)	Complete (14), partial (53)	Duplication of collecting system (3), atrophic kidney (1)
Heinonen PK 1983 [53]	n/s	0.0 (0/72)	Complete (27), partial (45)	n/s
Olive DL and Henderson DY 1987 [26]	n/s	63.6 (7/11)	Complete (2), partial (9)	n/s
Fedele L et al. 1992 [57]	n/s	26.9 (31/115)	Complete (24), partial (91)	n/s
Fedele L et al. 1993 [104]	18–39	35.5 (11/31)	n/s	n/s
Haberal A et al. 1996 [105]	22–37	16.9 (10/59)	Complete (17), partial (42)	n/s
Uğur M et al. 1997 [13]	n/s	16.1 (10/62)	Complete (3), partial (59)	n/s
Grimbizis G et al. 1998 [106]	22–45	26.1 (12/46)	Complete (10), partial (36)	n/s
Heinonen PK 2006 [107]	14–46	3.3 (2/61)	Complete (61)	Renal agenesis (5), double ureter (6), obstructed hemivagina + renal agenesis (4)
Nawroth F et al. 2006 [108]	29.4 ± 4.7 years (mean)	25.8 (31/120)	Complete (24), partial (96)	n/s
Darwish AM et al. 2009 [109]	19–25	18.7 (6/32)	Complete (32)	No renal anomalies
Wang JH et al. 2009 [110]	22–39	12.0 (3/25)	Complete (25)	n/s
Acién P and Acién M 2010 [64]	n/s	5.8 (3/52)	Complete (26), partial (26)	Renal agenesis (1)
Demir B et al. 2010 [111]	26.9 ± 5.5 (mean)	9.8 (9/92)	Complete (39), partial (53)	n/s
Gergolet M et al. 2010 [112]	29.62 ± 4.5 (mean)	20.1 (36/179)	n/s	n/s
Galal AF et al. 2016 [113]	20–34	10.0 (5/50)[b]	Hypoplastic uterus (2)	n/s
LaMonica R et al. 2016 [114]	n/s[a]	37.0[b]	n/s	n/s
Sukur YE et al. 2018 [115]	n/s	13.0 (7/54)	Complete (54)	n/s
Piriyev E and Römer T 2020 [65]	n/s	77.1 (138/179)	Complete (27), partial (152)	n/s
Bean E et al. 2022 [23]	16–51	33.3 (4/12)	n/s	n/s
Chang Y et al. 2023 [116]	20–40	8.0 (28/348)	Complete (91), partial (257)	n/s

n/s = non specified

[a] women of reproductive age

[b] prevalence of septate uterus in endometriosis patients

In light of these observations, the association between septate uterus and endometriosis remains unclear. One contributing factor to the contradicting results may be that patients in the control populations typically had a significantly higher incidence of primary infertility compared to the septate uterus groups. Hence, it is possible that the prevalence of endometriosis may be overrepresented in the control populations. Another potential source of inconsistency is the evolving definition of septate uterus. For example, current ASRM guidelines require a septum length > 1 cm, whereas the previous 2016 ASRM classification defined fundal indentation > 1.5 cm as septate, and the American Fertility Society guidelines of 1988 did not provide measurable criteria [5, 118]. In contrast, the European Society of Human Reproduction and Embryology/ European Society for Gynaecological Endoscopy (ESHRE/ESGE) define complete septate uterus as a fundal indentation exceeding 50% of the uterine wall thickness and septa extending to the internal cervical os [119, 120]. These differences are likely to have contributed to inconsistent inclusion criteria across studies.

Table 8 Summary of studies on arcuate uterus

Reference	Age (range, yrs)	Endometriosis prevalence (%)	Reproductive tract variations (*n*)	Additional malformations (*n*)
Heinonen PK 1983 [53]	n/s	n/s	0.0 (0/23)	n/s
Fedele L et al. 1992 [57]	n/s	n/s	21.4 (3/14)	n/s
Piriyev E and Römer T 2020 [65]	n/s	n/s	77.6 (45/58)	n/s
Bean E et al. 2022 [23]	16–51	16–51	16.7 (2/12)	n/s

n/s = non specified

Arcuate uterus

There is currently limited data available about endometriosis in relation to arcuate uterus, which is defined by the ASRM as internal fundal indentation < 1 cm [9]. Uğur et al. found endometriosis in 3 of 9 women (33.3%) with arcuate uterus, whereas other case series found 3 and 2 patients with endometriosis in groups of 14 and 12 arcuate uterus respectively (Table 8) [13, 23, 57]. Perhaps more informative is a larger study by Piriyev and

Romer, which reported endometriosis in 48 of 55 patients (77.6%) [65].

Robert's uterus

Robert's uterus is a partially obstructive variant of septate uterus characterized by an asymmetric septum dividing the uterine cavity into a non-communicating hemicavity and a patent contralateral cavity. The external contour of the uterus and the urinary system are typically normal. Data on endometriosis in Robert's uterus are limited and none of the few case series available included more than five patients [121–123].

Discussion

Understanding how Müllerian anomalies arise and clinically present – including associated malformations and diseases – is critical to facilitate proper diagnosis and the development of effective management plans. Early detection could reduce the risk of endometriosis and facilitate the management of ancillary disorders of the renal or skeletal systems or complications related to subfertility and pregnancy. The first step in working up patients with cyclical pain and amenorrhea or dysmenorrhea for the diagnosis of Müllerian abnormalities is usually physical exam combined with pelvic ultrasonography [124]. Ultrasound is widely available and can be useful in detecting obstructive presentations, but is not the most reliable diagnostic method [124]. MRI is preferred as it shows up to 95% correlation with laparoscopic findings and is a valuable tool for the evaluation of associated complications [125]. However, although MRI is an efficient method for the diagnosis of Müllerian anomalies, it is not accurate to assess the presence of endometriosis [126]. Therefore, judicious use of laparoscopy may be necessary to reveal or manage other complications including endometriosis and ovarian tumors, in addition to guiding surgical reconstruction of upper genital tract structures [127, 128].

The risk of endometriosis for specific classes of Müllerian anomalies is still a matter of debate, and studies analyzing endometriosis in Müllerian anomalies showed a wide variability in prevalence. There are several possible explanations for the observed discrepancies. First, both Müllerian anomalies and endometriosis are complex, multifactorial conditions with variable phenotypic presentations that pose classification challenges for clinical analyses [9, 10]. When attempting to classify Müllerian anomalies, it would be important to consider the embryological events regulating the development of the genitourinary system to better correlate genital abnormalities with comorbid pathologies. For example, the involvement of Wolffian duct or mesonephric anomalies represent phenotypic classes that may have specific associations with endometriosis. However, lack of stratification of phenotypes was a significant limitation of the literature reviewed here. In addition, most papers did not report several details of endometriosis, including staging, type, and location of lesions. Similarly, past family history of genital malformations or endometriosis was rarely recorded or reported, further complicating assessment of causal or direct relationship.

Second, the etiology of Müllerian anomalies and endometriosis remain largely unknown. Familiar clustering showed that genetic factors play a significant role [2, 129]. However, the genetics of both disorders are characterized by heterogeneity, incomplete penetrance, and variable expressivity [130–132]. These challenges were rarely addressed among studies of concomitant Müllerian anomalies and endometriosis, and genetic analyses were rarely performed [133, 134]. Karyotyping analyses were almost exclusively limited to MRKH cases, with two studies identifying a 10:17 translocation and a ring 18 chromosome [25, 51]. For other anomalies, only two studies reported chromosomal investigations. Acién et al. identified an increased length of heterochromatin on the long arm of chromosome 9 (46,XX9qh+) in a woman with didelphys uterus, but the variant was considered "without clinical consequences" [135]. Fenn performed karyotyping in a patient with bicornuate uterus and found a mutation at chromosome 17q [98]. Although the author did not provide specific information on the chromosomal abnormality, they proposed it as possible cause for the susceptibility of endometriosis [98]. Notably, molecular genetic testing was not performed in any of the literature addressing concomitant Müllerian anomalies and endometriosis. Several genetic loci, including copy number and single nucleotide variants have been identified using microarray, genome sequencing, and GWAS in separate studies of MRKH syndrome or endometriosis [130–132, 136].

Interestingly, some of the genetic variants associated with endometriosis are also candidate variants for Müllerian anomalies, including WNT4, HOXA10, and HNF1B [130, 137–139]. Future genomic analyses in patients with both conditions may play a significant role in improving our understanding of the etiology and molecular mechanisms involved.

Finally, the complex cellular events responsible for endometriosis and their relationship with Müllerian anomalies remain unclear. In general, retrograde menstruation is widely accepted in obstructive anomalies, and it has also been proposed in cases where menstrual flow may be impaired but not completely obstructed, including septate and unicornuate uterus [23, 65, 105, 110–113]. However, when endometriosis ensues in cases of Müllerian agenesis, other mechanisms are more likely, including coelomic metaplasia, Müllerian remnants, and genetic predisposition [13, 18, 20–23]. A recent

meta-analysis tried to provide some clarity on these pathogenic drivers [140]. A significantly higher prevalence of endometriosis was found in obstructive versus non-obstructive anomalies, seemingly supporting the retrograde menstruation theory. However, the authors cautioned that other mechanisms may be involved since only half of patients with obstructive anomalies had coexistent endometriosis, and several confounding factors affected the comparison between the two groups, including age and surgical indications. The same study showed a lack of difference in endometriosis rates between women with non-obstructive anomalies versus no anomalies, an apparent argument against coelomic metaplasia or embryonic remnants. However, the authors pointed out that these mechanisms cannot be ruled out since the control group included women with infertility and pelvic pain, both associated with endometriosis [140]. This analysis further supports the observed lack of standardization in studies involving Müllerian anomalies and endometriosis.

In conclusion, the elucidation of the complex relationship between these two conditions hinges on improved experimental designs allowing better stratification and comparative analyses. Most importantly, as both conditions are heterogeneous, multifactorial, and affected by genetic, epigenetic, and environmental factors, the use of interdisciplinary approaches combining clinical investigations, molecular genetics, and population-based analyses become increasingly critical to understand cellular and molecular determinants, and develop better and more personalized management plans.

Acknowledgements
We thank Dr Miranda Margetts (Montana State University) and Dr Alexander Quinn (CSIRO) for help in screening papers.

Author contributions
EP: study conception. AG, LE: acquisition of literature. SBP, IKB, AG, AVM, EP: screening of literature. SBP, IKB, MV, AG, NON, AVM, EP: manuscript drafting and revision.

Funding
No external funding.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 5 November 2024 / Accepted: 13 December 2024
Published online: 19 December 2024

References

1. Chandler TM, Machan LS, Cooperberg PL, Harris AC, Chang SD. Mullerian duct anomalies: from diagnosis to intervention. Br J Radiol. 2009;82(984):1034–42.
2. Kyei-Barffour I, Margetts M, Vash-Margita A, Pelosi E. The Embryological Landscape of Mayer-Rokitansky-Kuster-Hauser Syndrome: Genetics and Environmental Factors. Yale J Biol Med. 2021;94(4):657–72.
3. Sadler TW. Genital system. In: Gardner JN, editor. Medical Embryology. Baltimore, MD: Williams & Wilkins; 1990. pp. 270–80.
4. Acién P, Acién M. Malformations of the female genital tract and embryological bases. Curr Women's Health Rev. 2007;3:248–88.
5. Practice Committee of the American Society for Reproductive Medicine. Uterine septum: a guideline. Fertil Steril. 2016;106(3):530–40.
6. Acién P. Embryological observations on the female genital tract. Hum Reprod. 1992;7:437–45.
7. Sánchez-Ferrer ML, Acién MI, del Sánchez F, Mayol-Belda MJ, Acién P. Experimental contributions to the study of the embryology of the vagina. Hum Reprod. 2006;21:1623–8.
8. Georgas KM, Armstrong J, Keast JR, Larkins CE, McHugh KM, Southard-Smith EM, Cohn MJ, Batourina E, Dan H, Schneider K, Buehler DP, Wiese CB, Brennan J, Davies JA, Harding SD, Baldock RA, Little MH, Vezina CM, Mendelsohn C. An illustrated anatomical ontology of the developing mouse lower urogenital tract. Development. 2015;142(10):1893–908.
9. Pfeiffer SM, Attaran M, Goldstein J, Lindheim SR, Petrozza JC, Rackow BW, Siegelman E, Troiano R, Winter T, Zuckerman A, Ramaiah SD. ASRM mullerian anomalies classification 2021. Fertil Steril. 2021;116(5):1238–52.
10. Eskenazi B, Warner ML. Epidemiology of endometriosis. Obstet Gynecol Clin North Am. 1997;24(2):235–58.
11. Zondervan KT, Becker CM, Missmer SA, Endometriosis. N Engl J Med. 2020;382(13):1244–56.
12. Linden PJQ. Theories on the pathogenesis of endometriosis. Hum Reprod. 1996;11(3):53–65.
13. Uğur M, Turan C, Mungan T, Kuşçu E, Senöz S, Ağiş HT, Gökmen O. Endometriosis in association with müllerian anomalies. Gynecol Obstet Invest. 1995;40(4):261–4.
14. Sanfilippo JS, Wakim NG, Schikler KN, Yussman MA. Endometriosis in association with uterine anomaly. Am J Obsetet Gynecol. 1986;154(1):39–43.
15. Marsh CA, Will MA, Smorgick N, Quint EH, Hussain H, Smith YR. Uterine remnants and pelvic pain in females with Mayer-Rokitansky-Küster-Hauser syndrome. J Pediatr Adolesc Gynecol. 2013;26(3):199–202.
16. Deligeoroglou E, Iavazzo C, Sofoudis C, Kalampokas T, Creatsas G. Management of hematocolpos in adolescents with transverse vaginal septum. Arch Gynecol Obstet. 2012;285(4):1083–7.
17. Creatsas G, Cardamakis E, Hassan E, Deligeoroglou E, Salakos N, Aravantinos D. Congenital uterine anomalies with ob-structed cervix, hemivagina, or both during adolescence: report of 22 cases. J Gynecol Sur. 1994;10(3):159–67.
18. Acién P. Endometriosis and genital anomalies: some histogenetic aspects of external endometriosis. Gynecol Obstet Invest. 1986;22(2):102–7.
19. Kapczuk K, Zajączkowska W, Madziar K, Kędzia W. Endometriosis in Adolescents with Obstructive Anomalies of the Re-productive Tract. J Clin Med. 2023;12(5):2007.
20. Cho MK, Kim CH, Oh ST. Endometriosis in a patient with Rokitansky-Kuster-Hauser syndrome. J Obstet Gynaecol Res. 2009;35(5):994–6.
21. Mok-Lin EY, Wolfberg A, Hollinquist H, Laufer MR. Endometriosis in a patient with Mayer-Rokitansky-Küster-Hauser syndrome and complete uterine agenesis: evidence to support the theory of coelomic metaplasia. J Pediatr Adolesc Gynecol. 2010;23(1):e35–7.
22. Silveira SA, Laufer MR. Persistence of endometriosis after correction of an obstructed reproductive tract anomaly. J Pediatr Adolesc Gynecol. 2013;26(4):e93–94.
23. Bean E, Naftalin J, Horne A, Saridogan E, Cutner A, Jurkovic D. Prevalence of deep and ovarian endometriosis in early pregnancy: ultrasound diagnostic study. Ultrasound Obstet Gynecol. 2022;59(1):107–13.
24. Acién P, Acién M. Congenital uterine abnormalities. Encyclopedia of Reproduction (2nd edition), Academic Press. 2018, 113–120.
25. Rosenberg HK, Sherman NH, Tarry WF, Duckett JW, Snyder HM. Mayer-Rokitansky-Kuster-Hauser syndrome: US aid to diagnosis. Radiology. 1986;161(3):815–9.
26. Olive DL, Henderson DY. Endometriosis and Mullerian Anomalies. Obstet Gynecol. 1987;69(3 Pt 1):412–5.
27. Wang Y, Lu J, Zhu L, Sun Z, Jiang B, Feng F, Jin Z. Evaluation of Mayer-Rokitansky-Küster-Hauser syndrome with magnetic resonance imaging: Three

patterns of uterine remnants and related anatomical features and clinical settings. Eur Radiol. 2017;27(12):5215–24.
28. Asaturova AV, Faizullina NM, Bobkova MV, Arakelyan AS, Tregubova AV, Smolnova TY, Adamyan LV. Morphological features and the functional state of connective tissue of the uterine rudiments in reproductive age patients with Mayer–Rokitansky–Küster–Hauser syndrome. Clin Experimental Morphology. 2020;9(4):24–30.
29. Dabi Y, Canel V, Skalli D, Paniel BJ, Haddad B, Touboul C. Postoperative evaluation of chronic pain in patients with Mayer - Rokitansky - Küster - Hauser (MRKH) syndrome and uterine horn remnant: Experience of a tertiary referring gynaecological department. J Gynecol Obstet Hum Reprod. 2020;49(2):101655.
30. Wang Y, He YL, Yuan L, Yu JC, Xue HD, Jin ZY. Typical and atypical pelvic MRI characteristics of May-er-Rokitansky-Küster-Hauser syndrome: a comprehensive analysis of 201 patients. Eur Radiol. 2020;30:4014–22.
31. Tian W, Chen N, Liang Z, Song S, Wang Y, Ye Y, Duan J, Zhu L. Clinical features and management of endometriosis among patients with MRKH and functional uterine remnants. Gynecol Obstet Invest. 2021;86(6):518–24.
32. Steinmacher S, Bösmüller H, Granai M, Koch A, Brucker SY, Rall KK. Endometriosis in patients with Mayer-Rokitansky-Küster-Hauser-Syndrome-histological evaluation of uterus remnants and peritoneal lesions and comparison to samples from endometriosis patients without Mullerian anomaly. J Clin Med. 2022;11:6458.
33. Acién P, Acién MI. The history of female genital tract malformation classifications and proposal of an updated system. Hum Reprod Update. 2011;17:693–705.
34. Deffarges JV, Haddad B, Musset R, Paniel BJ. Utero-vaginal anastomosis in women with uterine cervix atresia: long-term follow-up and reproductive performance. A study of 18 cases. Hum Reprod. 2001;16(8):1722–5.
35. Fedele L, Bianchi S, Frontino G, Berlanda N, Montefusco S, Borruto F. Laparoscopically assisted uterovestibular anastomosis in patients with uterine cervix atresia and vaginal aplasia. Fertil Steril. 2008;89(1):212–6.
36. Kriplani A, Kachhawa G, Awasthi D, Kulshrestha V. Laparoscopic-assisted uterovaginal anastomosis in congenital atresia of uterine cervix: follow-up study. J Minim Invasive Gynecol. 2012;19(4):477–84.
37. Kisku S, Varghese L, Kekre A, Sen S, Karl S, Mathai J, Thomas RJ, Barla RK. Cervicovaginal atresia with hematometra: re-storing menstrual and sexual function by utero-coloneovaginoplasty. Pediatr Surg Int. 2014;30(10):1051–60.
38. Song X, Zhu L, Ding J, Xu T, Lang J. Clinical characteristics of congenital cervical atresia and associated endometriosis among 96 patients. Int J Gynaecol Obstet. 2016;134(3):252–5.
39. Zhang H, Qu H, Ning G, Cheng B, Jia F, Li X, Chen X. MRI in the evaluation of obstructive reproductive tract anomalies in paediatric patients. Clin Radiol. 2017; 72(7): 612.e7-612.e15.
40. Xu S, Zhang J, Wang S, Yang L, Qian J, Yue S, Zhu D, Yang L, Zhao L, Yang A, Li Y, Xue Q. MRI features and differential di-agnoses of congenital vaginal atresia. Gynecol Endocrinol. 2019;35(9):777–81.
41. Kang J, Zhu L, Zhang Y, Ma C, Ma Y. Postoperative Pelvic Abscess after Cervicovaginal Canalization for Congenital Cervical and Vaginal Agenesis: A Report of 4 Cases. J Pediatr Adolesc Gynecol. 2020;33(3):324–7.
42. Ding Y, Zhang X, Zhang Y, Shen F, Ding J, Hua K. Cervicovaginal reconstruction with small intestinal submucosa graft in congenital cervicovaginal atresia: A report of 38 cases. Eur J Obstet Gynecol Reprod Biol. 2021;267:49–55.
43. Pan HX, Luo GN, Qin CL. Laparoscopic uterovaginal anastomosis in patients with congenital cervicovaginal atresia: An institutional experience with 23 patients. Eur J Obstet Gynecol Reprod Biol. 2021;260:218–24.
44. Regan L, Dewrust J. Atresia of the cervix. Pediatr Adolesc Gynecol. 1985;3(1):83–102.
45. Candiani M, Vercellini P, Fedele F, Parma M, Salvatore S, Fedele L. Long-Term Follow-Up after Laparoscopic Uterovestibular Anastomosis in Patients with Cervical Atresia and Complete Absence of the Vagina. J Pediatr Adolesc Gynecol. 2023;36(1):72–8.
46. Kriplani A, Agarwal N. Hysteroscopic and laparoscopic guided miniaccess hemihysterectomy for non-communicating uterine horn. Arch Gynecol Obstet. 2001;265(3):162–4.
47. Acién P, Lioret M, Chehab H. Endometriosis in a patient with Rokitansky Kuster Hauser syndrome. Gynecol Obstet Invest. 1988;25(1):70–2.
48. Konrad L, Dietze R, Kudipudi PK, Horné F, Meinhold-Heerlein I. Endometriosis in MRKH cases as a proof for the coelomic metaplasia hypothesis? Reproduction. 2019;158(2):R41–7.
49. Deligeoroglou E, Makrakis E, Creatsas G. Obstruction of the Female Genital Tract Because of Vaginal Septum in Adolescence. J Gynecol Surg. 2001;17:49–56.
50. Özyer S, Uzunlar Ö, Özcan N, Yeşilyurt H, Karayalçin R, Sargin A, Mollamahmutoğlu L. Endometriomas in adolescents and young women. J Pediatr Adolesc Gynecol. 2013;26(3):176–9.
51. Buttram VC, Gibbons WE. Müllerian anomalies: a proposed classification. (An analysis of 144 cases). Fertil Steril. 1979;32(1):40–6.
52. Heinonen PK. Clinical implications of the unicornuate uterus with rudimentary horn. Int J Gynecol Obstet. 1983;21(2):145–50.
53. Heinonen PK, Pystynen PP. Primary infertility and uterine anomalies. Fertil Steril. 1983;40(3):311–6.
54. Fedele L, Zamberletti D, Vercellini P, Dorta M, Candiani GB. Reproductive performance of women with unicornuate uterus. Fertil Steril. 1987;47(3):416–9.
55. Fedele L, Marchini M, Baguoni A, Carinelli S, Zamberletti D, Candiani GB. Endometrium of cavitary rudimentary horns in unicornuate uteri. Obstet Gynecol. 1990;75(3 Pt 1):437–40.
56. Donderwinkel PFJ, Dörr JPJ, Willemsen WNP. The unicornuate uterus: clinical implications. Eur J Obstet Gynecol Reprod Biol. 1992;47(2):135–9.
57. Fedele L, Bianchi S, Di Nola G, Franchi D, Candiani GB. Endometriosis and nonobstructive müllerian anomalies. Obstet Gynecol. 1992;79(4):515–7.
58. Moutos DM, Damewood MD, Schlaff WD, Rock JA. A comparison of the reproductive outcome between women with a unicornuate uterus and women with a didelphic uterus. Fertil Steril. 1992;58(1):88–93.
59. Liu MM. Unicornuate uterus with rudimentary horn. Int J Gynaecol Obstet. 1994;44(2):149–53.
60. Fedele L, Bianchi S, Tozzi L, Marchini M, Busacca M. Fertility in women with unicornuate uterus. Br J Obstet Gynaecol. 1995;102(12):1007–9.
61. Fedele L, Bianchi S, Marchini M, Tozzi L, Vignali M. Anatomic features of 49 unicornuate uteri: gynecologic and urologic findings, associated disorders, and endometrial patterns. J Gynecol Surg. 1996;12:167–71.
62. Heinonen PK. Unicornuate uterus and rudimentary horn. Fertil Steril. 1997;68(2):224–30.
63. Fedele L, Bianchi S, Zanconato G, Berlanda N, Bergamini V. Laparoscopic removal of the cavitated noncommunicating ru-dimentary uterine horn: surgical aspects in 10 cases. Fertil Steril. 2005;83(2):432–6.
64. Acién P, Acién M. Unilateral renal agenesis and female genital tract pathologies. Acta Obstet Gynecol Scand. 2010;89(11):1424–31.
65. Piriyev E, Römer T. Coincidence of uterine malformations and endometriosis: a clinically relevant problem? Arch Gynecol Obstet. 2020;302(5):1237–41.
66. Tellum T, Bracco B, De Braud LV, Knez J, Ashton-Barnett R, Amin T, Chaggar P, Jurkovic P. Reproductive outcome in 326 women with unicornuate uterus. Ultrasound Obstet Gynecol. 2023;61(1):99–108.
67. Smith NA, Laufer MR. Obstructed hemivagina and ipsilateral renal anomaly (OHVIRA) syndrome: management and follow-up. Fertil Steril. 2007;87:918–22.
68. Gazárek F, Kudela M, Zenisek L, Nevrla F. Herlyn-Werner and Wunderlich syndromes. Zentralbl Gynakol. 1979;101:1411–5.
69. Acién P, Acién M. TThe presentation and management of complex female genital malformations. Hum Reprod Update. 2016;22:48–69.
70. Stassart JP, Nagel TC, Prem KA, Phipps WR. Uterus didelphys, obstructed hemivagina, and ipsilateral renal agenesis: the University of Minnesota experience. Fertil Steril. 1992;57(4):756–61.
71. Candiani GB, Fedele L, Candiani M. Double uterus, blind hemivagina, and ipsilateral renal agenesis: 36 cases and long-term follow-up. Obstet Gynecol. 1997;90(1):26–32.
72. Fedele L, Motta F, Frontino G, Restelli E, Bianchi S. Double uterus with obstructed hemivagina and ipsilateral renal agenesis: pelvic anatomic variants in 87 cases. Hum Reprod. 2013;28(6):1580–3.
73. Tong J, Zhu L, Lang J. Clinical characteristics of 70 patients with Herlyn-Werner-Wunderlich syndrome. Int J Gynaecol Obstet. 2013;121(2):173–5.
74. Wang S, Lang JH, Zhu L, Zhou HM. Duplicated uterus and hemivaginal or hemicervical atresia with ipsilateral renal agenesis: an institutional clinical series of 52 cases. Eur J Obstet Gynecol Reprod Biol. 2013;170(2):507–11.
75. Sabdia S, Sutton B, Kimble RMN. The obstructed hemivagina, ipsilateral renal anomaly, and uterine didelphys triad and the subsequent manifestation of cervical aplasia. J Pediatr Adolesc Gynecol. 2014;27(6):375–8.
76. Tong J, Zhu L, Chen N, Lang J. Endometriosis in association with Herlyn-Werner-Wunderlich syndrome. Fertil Steril. 2014;102(3):790–4.
77. Zhu L, Chen N, Tong JL, Wang W, Zhang L, Lang JH. New classification of Herlyn-Werner-Wunderlich syndrome. Chin Med J. 2015;128(2):222–5.

78. Kapczuk K, Friebe Z, Iwaniec K, Kędzia W. Obstructive Müllerian Anomalies in Menstruating Adolescent Girls: A Report of 22 Cases. J Pediatr Adolesc Gynecol. 2018;31(3):252–7.
79. Troncon JK, Rosa-E-Silva JC, Miranda R, Candido-Dos-Reis FJ, Poli-Neto OB, Nogueira AA. Diagnosis and Treatment in a Tertiary Hospital of a Series of Complex Genital Malformations Corresponding to Double Uterus with Obstructed Hemi-vagina and Ipsilateral Renal Agenesis. Int J Reprod Med. 2018; 2018: 3806856.
80. Dabi Y, Dray G, Allanche M, Skalli D, Paniel BJ, Haddad B, Touboul C. Fertility and pregnancy outcomes in patients with bicorporeal uterus and blind hemivagina: 20 years of experience in a tertiary referral gynaecological department. J Gynecol Obstet Hum Reprod. 2020;49(3):101651.
81. Gungor Ugurlucan F, Dural O, Yasa C, Kirpinar G, Akhan SE. Diagnosis, management, and outcome of obstructed hemivagina and ipsilateral renal agenesis (OHVIRA syndrome): Is there a correlation between MRI findings and outcome? Clin Imaging. 2020;59(2):172–8.
82. Kim YN, Han JH, Lee YS, Lee I, Han SW, Seo SK, Yun BH. Comparison between prepubertal and postpubertal patients with obstructed hemivagina and ipsilateral renal anomaly syndrome. J Pediatr Urol. 2021; 17(5): 652.e1-652.e7.
83. Yi S, Jiang J. Clinical characteristics and management of patients with complete septate uterus, double cervix, obstructed hemivagina, and ipsilateral renal agenesis. J Obstet Gynaecol Res. 2021;47(4):1497–501.
84. Candiani M, Vercellini P, Ferrero-Caroggio C, Fedele F, Salvatore S, Fedele L. Conservative treatment of Her-lyn-Werner-Wunderlich syndrome: Analysis and long-term follow-up of 51 cases. Eur J Obstet Gynecol Reprod Biol. 2022;275:84–90.
85. Zarfati A, Lucchetti MC. OHVIRA (Obstructed Hemivagina and Ipsilateral Renal Anomaly or Herlyn-Werner-Wunderlich syndrome): Is it time for age-specific management? J Pediatr Surg. 2022;57(11):696–701.
86. Zhang J, Xu S, Yang L, Songhong Y. MRI image features and differential diagnoses of Herlyn-Werner-Wunderlich syndrome. Gynecol Endocrinol. 2020;36(6):484–8.
87. Zhang Y, Liu Q. Diagnosis and treatment of 46 patients with oblique vaginal septum syndrome. J Obstet Gynaecol. 2022;42(8):3731–6.
88. Kudela G, Wiernik A, Drosdzol-Cop A, Machnikowska-Sokołowska M, Gawlik A, Hyla-Klekot L, Gruszczyńska K, Koszutski T. Multiple variants of obstructed hemivagina and ipsilateral renal anomaly (OHVIRA) syndrome - one clinical center case series and the systematic review of 734 cases. J Pediatr Urol. 2021;17(5):e6531–9.
89. Bolonduro O, Akinpeloye A, Abuzeid O, Ashraf M, Abuzeid MI. Herlyn–Werner–Wunderlich Syndrome: Presentation and Surgical Management Options for Five Cases. J Gynecol Surg. 2015;31(1):46–51.
90. Heinonen PK. Clinical implications of the didelphic uterus: long-term follow-up of 49 cases. Eur J Obstet Gynecol Reprod Biol. 2000;91(2):183–90.
91. Hanton EM, Malkasian GD Jr, Dockerty MB, Pratt JH. Endometriosis associated with complete or partial obstruction of menstrual egress. Report of 7 cases. Obstet Gynecol. 1966;28(5):626–9.
92. Biljić-Erski IR, Vasiljević M, Rakić S, Džatić-Smiljković O, Mihajlović S. Uterus didelphys associated with ovarian endome-triosis in an infertile patient. Vojnosanit Pregl. 2019;76(7):749–52.
93. Leverton JC. A significant case of uterus didelphys solidus with gynastresia, adenonyosis, and pelvic endometriosis. Obstet Gynecol. 1953;1(6):681–8.
94. Hori T, Harada H, Yamamoto M, Yamada M, Yazawa T, Sasaki B, Tani M, Katsura H, Sato A, Sasaki Y, Yamamoto H. Ectopic endometriosis, menstruation, and acute appendicitis: A thought-provoking case. Int J Surg Case Rep. 2021;80:105605.
95. Ismail SR. Frequency of Uterine Malformation among Women in a Restricted Gene Pool Community: A retrospective cross-sectional study in La Crete, Canada. Sultan Qaboos Univ Med J. 2007;7(2):123–32.
96. Raga F, Bauset C, Remohi J, Bonilla-Musoles F, Simon C, Pellicer A. Reproductive impact of congenital Mullerian anomalies. Hum Reprod. 1997;12(10):2277–81.
97. Papp Z, Mezei G, Gávai M, Hupuczi P, Urbancsek J. Reproductive performance after transabdominal metroplasty: a review of 157 consecutive cases. J Reprod Med. 2006;51(7):544–52.
98. Fenn DJ. Endometriosis stage: IV associated with a bicornuate uterus: A rare case report. Res J Pharm Biol Chem Sci. 2014;5(6):556–9.
99. Mahboubi S, Rostain A. Computed tomography finding in Mayer-Rokitansky-Kuster-Hauser syndrome associated with endometriosis: A case report. J Comput Tomogr. 1987;11(3):301–2.
100. Chauhan V, Pujani M, Singh K, Chawla R, Ahuja R. Scar Endometriosis with Rudimentary Horn: An Unusual and Elucidative Report of a Case Diagnosed on Histopathology and Immunohistochemistry. J Midlife Health. 2017;8(4):196–9.
101. Baird D, Klepeiss S, Wehler A, Harkins G, Anderson B. Umbilical endometriosis in a woman with bicornuate uterus. Skinmed. 2012;10(4):248–50.
102. Pisat S, Tas B, van Herendael B. Laparoscopic Strassman's metroplasty for bicornuate uterus. Gynecol Surg. 2009;6:153–8.
103. Buttram VC Jr., Zanotti L, Acosta AA, Vanderheyden JS, Besch PK, Franklin RR. Surgical correction of the septate uterus. Fertil Steril. 1974;25(4):373–9.
104. Fedele L, Arcaini L, Parazzini F, Vercellini P, Di Nola G. Reproductive prognosis after hysteroscopic metroplasty in 102 women: life-table analysis. Fertil Steril. 1993;59(4):768–72.
105. Haberal A, Batioglu A, Uğur M. Hysteroscopic Treatment of Septate Uterus. J Gynecol Surg. 1996; 12:241–246.
106. Grimbizis G, Camus M, Clasen K, Tournaye H, De Munck L, Devroey P. Hysteroscopic septum resection in patients with recurrent abortions or infertility. Hum Reprod. 1998;13(5):1188–93.
107. Heinonen PK. Complete septate uterus with longitudinal vaginal septum. Fertil Steril. 2006;85(3):700–5.
108. Nawroth F, Rahimi G, Nawroth C, Foth D, Ludwig M, Schmidt T. Is there an association between septate uterus and endo-metriosis? Hum Reprod. 2006;21(2):542–4.
109. Darwish AM, Elsaman AM. Extended resectoscopic versus sequential cold knife-resectoscopic excision of the unclassified complete uterocervicovaginal septum: a randomized trial. Fertil Steril. 2009;92(2):722–6.
110. Wang JH, Xu KH, Lin J, ChenXZ. Hysteroscopic septum resection of complete septate uterus with cervical duplication, sparing the double cervix in patients with recurrent spontaneous abortions or infertility. Fertil Steril. 2009;91(6):2643–9.
111. Demir B, Dilbaz B, Karadag B, Duraker R, Akkurt O, Kocak M, Goktolga U. Coexistence of endometriosis and uterine septum in patients with abortion or infertility. J Obstet Gynaecol Res. 2011;37(11):1596–600.
112. Gergolet M, Gianaroli L, Kenda Suster N, Verdenik I, Magli MC, Gordts S. Possible role of endometriosis in the aetiology of spontaneous miscarriage in patients with septate uterus. Reprod Biomed Online. 2010;21(4):581–5.
113. Galal AF. Should hysteroscopy be combined with laparoscopy in endometriosis associated infertility? Reprodução Cli-matério. 2016;31(2):63–7.
114. LaMonica R, Pinto J, Luciano D, Lyapis A, Luciano A. Incidence of Septate Uterus in Reproductive-Aged Women With and Without Endometriosis. J Minim Invasive Gynecol. 2016;23(4):610–3.
115. Sukur YE, Yakistiran B, Ozmen B, Sonmezer M, Berker B, Atabekoglu C. Hysteroscopic corrections for complete septate and T-shaped uteri have similar surgical and reproductive outcome. Reprod Sci. 2018;25(12):1649–54.
116. Chang Y, Shen M, Wang S, Guo Z, Duan H. Reproductive outcomes and risk factors of women with septate uterus after hysteroscopic metroplasty. Front Endocrinol. 2023;14:1063774.
117. Matalliotakis IM, Goumenou AG, Matalliotakis M, Arici A. Uterine Anomalies in Women with Endometriosis. J Endometr. 2010;2(4):213–7.
118. The American Fertility. Society classifications of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Müllerian anomalies and intrauterine adhesions. Fertil Steril. 1988;49(6):944–55.
119. Grimbizis GF, Gordts S, Di Spiezio Sardo A, Brucker S, De Angelis C, Gergolet M, Li TC, Tanos V, Brölmann H, Gianaroli L, Camp R. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. Hum Reprod. 2013;28(8):2032–44.
120. Grimbizis GF, Di Spiezio Sardo A, Saravelos SH, Gordts S, Exacoustos C, Van Schoubroeck D, Bermejo C, Amso NA, Nargund G, Timmerman D, Athanasiadis A, Brucker S, De Angelis C, Gergolet M, Li TC, Tanos V, Tarlatzis B, Farquharson R, Gianaroli L, Campo R. The Thessaloniki ESHRE/ESGE consensus on diagnosis of female genital anomalies. Hum Reprod. 2016;31(1):2–7.
121. Ballabh S, Simon B, Ebenezer ED, John RA, Chandramohan A. Imaging features of Robert's uterus: Case series of a rare Mullerian duct anomaly. Trop Doct. 2021;51(4):553–60.
122. Deenadayal M, Gunther V, Alkatout I, Freytag D, Deenadayal-Mettler A, Deenadayal Tolani A, Sinha R, Mettler L. Critical Role of 3D ultrasound in the diagnosis and management of Robert's uterus: a single-centre case series and a review. Facts Views Vis Obgyn. 2021;13(1):41–9.
123. Ramesh B, Chaithra TM, Desai H, Ghanti R, Daksh S. Management of Robert's uterus by combined hysteroscopic and laparoscopic management: a clinical pearl. Gynecol Surg. 2016;13:521–42.
124. Management of Acute Obstructive Uterovaginal Anomalies. ACOG Committee Opinion, Number 779. Obstet Gynecol. 2019;133(6):e363–71.

125. Preibsch H, Rall K, Wietek BM, Brucker SY, Staebler A, Claussen CD, Siegmann-Luz KC. Clinical value of magnetic resonance imaging in patients with Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome: diagnosis of associated malformations, uterine rudiments and intrauterine endometrium. Eur Radiol. 2014;24(7):1621–7.
126. Zurawin RK, Dietrich JE, Heard MJ, Edwards CL. Didelphic uterus and obstructed hemivagina with renal agenesis: case report and review of the literature. J Pediatr Adolesc Gynecol. 2004;17(2):137–41.
127. Htay WT, Huang KG, Yu HH. Ovarian teratoma and peritoneal endometriosis in a woman with Mayer–Rokitansky–Kuster–Hauser syndrome. J Endometr Pelvic Pain Disorders. 2019;11(1):45–8.
128. Li MH, Zhang ZY. Laparoscopically assisted biomaterial graft for reconstruction in congenital atresia of vagina and cervix. Fertil Steril. 2013;100(6):1784–7.
129. Saha R, Pettersson HJ, Svedberg P, Olovsson M, Bergqvist A, Marions L, Tornvall P, Kuja-Halkola R. Heritability of endometriosis. Fertil Steril. 2015;104(4):947–52.
130. Thomson E, Tran M, Robevska G, Ayers K, van der Bergen J, Gopalakrishnan Bhaskaran P, Haan E, Cereghini S, Vash-Margita A, Margetts M, Hensley A, Nguyen Q, Sinclair A, Koopman P, Pelosi E. Functional genomics analysis identifies loss of HNF1B function as a cause of Mayer-Rokitansky-Küster-Hauser syndrome. Hum Mol Genet. 2023;32(6):1032–47.
131. Backhouse B, Hanna C, Robevska G, van den Bergen J, Pelosi E, Simons C, Koopman P, Juniarto AZ, Grover S, Faradz S, Sinclair A, Ayers K, Tiong YT. Identification of candidate genes for Mayer-Rokitansky-Küster-Hauser syndrome using genomic ap-proaches. Sex Dev. 2019;13:26–34.
132. Borghese B, Zondervan KT, Abrao MS, Chapron C, Vaiman D. Recent insights on the genetics and epigenetics of endometriosis. Clin Genet. 2017;91(2):254–64.
133. Jacquinet A, Millar D, Lehman A. Etiologies of uterine malformations. Am J Med Genet A. 2016;170(8):2141–72.
134. Hansen KA, Eyster KM. Genetics and genomics of endometriosis. Clin Obstet Gynecol. 2010;53(2):403–12.
135. Acién P, Acién M, Sánchez-Ferrer ML. Müllerian anomalies without a classification: from the didelphys-unicollis uterus to the bicervical uterus with or without septate vagina. Fertil Steril. 2009;91(6):2369–75.
136. Rahmioglu N, Mortlock S, Ghiasi M, Møller PL, Stefansdottir L, Galarneau G, Turman C, Danning R, Law MH, Sapkota Y, et al. The genetic basis of endometriosis and comorbidity with other pain and inflammatory conditions. Nat Genet. 2023;55(3):423–36.
137. Philibert P, Biason-Lauber A, Gueorguieva I, Stuckens C, Pienkowski C, et al. Molecular analysis of WNT4 gene in four adolescent girls with mullerian duct abnormality and hyperandrogenism (atypical Mayer-Rokitansky-Küster-Hauser syndrome). Fertil Steril. 2011;95:2683–6.
138. Ekici AB, Strissel PL, Oppelt PG, Renner SP, Brucker S, Beckmann MW, Strick R. HOXA10 and HOXA13 sequence variations in human female genital malformations including congenital absence of the uterus and vagina. Gene. 2013;518(2):267–72.
139. Mortlock S, Corona RI, Kho PF, Pharoah P, Seo JH, Freedman ML, Gayther SA, Siedhoff MT, Rogers PAW, Leuchter R, et al. A multi-level investigation of the genetic relationship between endometriosis and ovarian cancer histotypes. Cell Rep Med. 2022;3(3):100542.
140. Vercellini P, Salmeri N, Somigliana E, Piccini M, Caprara F, Viganò P, De Matteis S. Müllerian anomalies and endometriosis as potential explanatory models for the retrograde menstruation/implantation and the embryonic remnants/celomic metaplasia pathogenic theories: a systematic review and meta-analysis. Hum Reprod. 2024;10:deae086.

Publisher's note