Mullerian Anomalies diagnosis modern approaches

Chapidze I.[1], Kristesashvili J.[1]

Abstract

Background: Mullerian Anomalies are associated with such reproductive disorders as infertility, recurrent pregnancy losses, primary amenorrhea, and others. Accurate diagnosis is essential for determining a woman's reproductive prognosis and planning certain types of interventions. The internal and external uterine contours evaluation is the key to the exact diagnosis and treatment. The hysterolaparoscopic procedure is considered the gold standard for evaluating Mullerian Anomalies, but the method is costly and invasive. 2D ultrasound sonography is a good screening method, but the uterus is not evaluated in the coronal plane. MRI is an expensive method and is used for the evaluation of complex anomalies. 3D ultrasound is a fast, cheap, non-invasive, and informative method for evaluating Mullerian Anomalies.
Aim: To determine the effectiveness of 3D ultrasound in the diagnosis Mullerian Anomalies .
Methods: We aimed to observe literature data to review the current understanding of the role of 3D ultrasound in the diagnosis of Mullerian anomalies. For this purpose following electronic databases were searched: Pubmed, Crossref, Mendeley, and Elsevier.
Results: 90 articles were reviewed, and 43 of them attracted our attention due to their statistical significance and were analyzed and discussed in our article.
Conclusion: Based on the literature review, we can conclude that 3D ultrasonography is a cheap, fast, non-invasive method for evaluating Mullerian anomalies. It showed high diagnostic concordance with the MRI method, virtually identical images are obtained by 3D ultrasound. Diagnostic difficulties arise in the case of cervical and vaginal anomalies, as well as in complex anomalies. Up to this date, it remains as a challenge, the correct diagnosis of the unclassifiable forms of Mullerian anomalies and the subsequent selection of their treatment methods, which is the basis for future research. **(TCM-GMJ June 2024; 9 (1):P36-P42)**

Keywords: Mullerian anomalies; 2D ultrasound; 3D ultrasound function; MRI ; Hysterosalpingography; septate uterus, T-shaped uterus, unicornuate uterus.

Introduction

Woman's reproductive realization is a set of complex processes, which includes the sperm transportation processes, embryo implantation, fetal growth, and childbirth in a functionally and structurally normal uterus. A certain part of women with Mullerian anomalies have normal reproductive function, while another part has reproductive disorders. The process of embryogenesis includes the stages of differentiation, migration, fusion, and canalization of Mullerian ducts. At approximately 4 weeks of gestation, the primordial germ cells that form in the dorsal wall of the yolk sac migrate to the primitive gonads. The absence of Y chromosomes in female embryos leads to the formation of primordial follicles from primordial germ cells. Deficiency of testosterone and Anti Mullerian Hormone (AMH) in female fetuses leads to regression of Wolffian ducts and from the Mullerian ducts to form the fallopian tubes, the uterus, and the upper third of the vagina. Fused Mullerian ducts join the urogenital sinus below, which causes sinovaginal bulb endoderm proliferation, subsequently, it passes through the canalization stage and forms the upper third of the vagina by merging with the Mullerian ducts. Any deviation from these stages leads to the formation of different types of Mullerian Anomalies. The Mullerian ducts development is an independent process and is not related to the gonads development. Such women often have normal reproductive function. Mullerian Anomalies

From the [1]Iv. Javakhishvili Tbilisi State University, Faculty of Medicine, Department of Obstetrics–Gynecology-Reproductology, Tbilisi, Georgia.
Received March 15, 2024; accepted May 12 , 2024.
Address requests to: Chapidze Ia
E-mail: iachapidze253@gmail.com

are often associated with urinary system anomalies, which stipulates their investigation necessity [1,18,31].

There are three main phases in the Mullerian anomalies embryogenesis process. Either phase disruption causes Mullerian Anomalies with different variations.

Organogenesis phase – when one or both Mullerian ducts are incompletely developed, which causes such anomalies as uterine agenesis, bilateral or unilateral aplasia (unicornuate uterus)

Fusion phase – In this case, the Mullerian ducts' distal parts merge and form the uterus, cervix, and the upper third of the vagina. Incomplete fusion causes such anomalies as a uterus didelphys uterus and a bicornuate uterus

Resorption phase – As a result of Mullerian duct fusion, existing septum resorption leads to the formation of one cavity and one cervical canal. This process violation leads to the formation of a partial or complete septate uterus.

Classification There are various classifications of Mullerian anomalies. The most frequently used is the classification developed by the American Fertility Society in 1988 (AFS). The advantage of this classification is its simplicity. In recent years, the disadvantage of this classification was considered that it does not reflect the cervix and vagina anomalies, and also could not be established accurate diagnostic criteria for evaluating complex anomalies. There is a wide spectrum of Mullerian anomalies, that are not correctly diagnosed or could not be diagnosed at all. Incorrect diagnosis leads to inappropriate treatment, unnecessary surgical interventions, and finally reproductive function disruption. In 2021 American Society of Reproductive Medicine created a new classification (ASRM) which is based on its predecessor (AFS) classification. The new classification takes into account cervical and vaginal anomalies and separates uterine anomalies into 9 categories: Mullerian agenesis, cervical agenesis, unicornuate uterus, uterus didelphys, bicornuate uterus, septate uterus, longitudinal vaginal septum, transverse vaginal septum, complex anomalies [2,13,19].

One of the most recent critical literature reviews discussed the shortcomings of the ASRM classification of Mullerian anomalies [6,29,33]. The review discusses the diagnostic dilemma that arises during the anomalies detection. According to the 2021 ASRM classification, an arcuate uterus is considered to be a uterus with a depth of internal indentation at < 10 mm and an angle of indentation > 90^0. However, if this angle is < 90^0, a diagnostic dilemma arises in the so-called "Grey Zone" when the uterus cannot be assigned to any specific category. The same can be said in the case of a septate uterus, in particular, according to the ASRM classification, a uterus with a depth of internal indentation > 10 mm and an angle < 90^0 is considered a septate uterus. However, when the angle of indentation is > 90 0, it is impossible to determine exactly which category the anomaly belongs to (Figure 1). The same article discusses different opinions of different authors regarding the new 2021 ASRM classification[6]. They ask the question of what kind of basis one of the important criteria of a septate uterus has changed[25]. Internal indentation depth > 15 mm known according to the 2016 ASRM classification. **Figure 1.**

The ESHRE/ESGE classification is based on the depth of indentation from the line connecting the endometrial horns and in the case of a septate uterus, it exceeds 50% of the wall thickness. In the case of a bicornuate uterus, the external fundal indentation exceeds 50% of the wall thickness [1]. It is also noteworthy that the new classifications have increased the number of misdiagnoses and excessive treatment interventions. (1) Different authors have different opinions about the working algorithm[7,8]. 3D ultrasonography is recommended in high–risk symptomatic patients, who undergo a routine ultrasound examination.

While, with the ESHRE/ESGE classification, the T-shaped uterus is subjectively diagnosed by some authors. In particular, it is based on a narrow uterine cavity due to the thickened lateral walls, without specifying definition. **Figure 2.**

Mullerian anomalies are associated with such complications as premature birth (up to 37 weeks), rupture of membranes, fetal malpresentation, and perinatal mortality. The risk of premature birth increases by the Mullerian anomaly types: septate uterus (31%), bicornuate uterus (39%), unicornuate uterus (43%), and uterus didelphys (56%) [4].

In the case of different types of Mullerian anomalies, the treatment methods are different. Surgical intervention can be performed in the case of unicornuate, didelphys, bicornuate, and partial septate uteruses, which significantly improves a woman's reproductive outputs [20,39].

Prevalence Mullerian anomalies prevalence varies widely among individual studies, which is supposedly due to the assessment of different population groups with different diagnostic methods. Based on two reliable studies, the Mullerian anomalies prevalence [1] in an unselected population is 5.5%, 8% in infertile women, and 13.3% in women with recurrent pregnancy loss. Based on other literature sources [4] Mullerian anomalies prevalence in the general population is 7%, in women with recurrent pregnancy loss and infertile women is 25%. Mullerian anomalies often present as complex anomalies involving the cervix, vagina, and urinary system. For infertile patients who need assisted reproductive technologies, such as insemination, it is important to detect Mullerian anomalies. According to the authors [5], special attention is paid to the incomplete septate uterus and the complete septate uterus that divides the cervical canal and is not clinically manifested. Information about these anomalies is important for clinicians, in particular, what type or subtype of Mullerian anomalies is diagnosed, which will help prevent obstetric and neonatal complications.

A septate uterus is considered the most common anomaly among Mullerian anomalies[4]. It accounts for 55% of Mullerian anomalies and is associated with first and second-trimester miscarriage, premature birth, and fetal malpresentation. Regarding this issue, different authors' opinions are various, because there is no definite consensus about diagnostic criteria. A septum uterus occurs at the 20th week of pregnancy due to the resorption process violation. The uterine septum may exist in a dif-

ferent form, in particular: a highly vascularized septum to an avascular fibrotic septum [40]. A vascular wall is a prerequisite for uterine contractions, that cause premature births and recurrent pregnancy loss. Fibrous, less vascularized septum interferes with the implantation process [4]. The septum presence implies histological changes in the endometrium. In particular, in this case, there is a low expression of HOXA10 genes and VEGF receptor genes, leading to a low number of endometrial glandular and ciliated cells. All this leads to the complications associated with the presence of a septate uterus [10].

Methods

Recent years of technological progress have significantly improved the possibilities of ultrasound diagnostics**.** 3D/4D ultrasound research methods improvements have ensured an increase in the frequency of congenital uterus anomaly detection, which was not possible by 2D ultrasound [1]. Most women with Mullerian anomalies have normal reproductive output and are often discovered incidentally during routine examinations. Accurate diagnosis and correct classification of Mullerian anomalies make it possible to determine the women's reproductive prognosis and risks, certain types of interventions should also be planned [3]. The uterus' internal and external contours evaluation is the key to accurate Mullerian anomaly diagnosis and classification. The hysterolaparoscopic method is considered to be the gold standard for Mullerian anomaly evaluation. The disadvantage of this method is its invasiveness and high cost. MRI is an expensive method and its use is recommended to detect uterine complex anomalies. HSG evaluates only the inner contour of the uterus and cannot evaluate its outer contour. 3D/4D ultrasonography evaluates both the inner and outer contour of the uterus. The method is fast, cheap, highly informative, and noninvasive [1,3.27].

Hysterosalpingography is a good screening method for evaluating Mullerian anomalies, [1] although the outer contour of the uterus cannot be evaluated (Figure 3c). Differential diagnosis between bicornuate and septate uterus is based on the angle of divergence of the uterine horns. An angle less than 75º is considered a septate uterus, and an angle greater than 105º is considered a bicornuate uterus. It is also important to note that hysterosalpingography evaluates only that specific cavity, which is connected to the cervical canal, therefore, it is easy to miss the uterus rudimentary horn in the process of diagnosis. **2D transvaginal ultrasound** is a minimally invasive method (Figure3a). Septate, partial septate, bicornuate uterus, arcuate uterus may be suspected by 2D ultrasound, but exact differentiation cannot be made among them [42]. With 2D ultrasound, the outer contour of the uterus cannot be evaluated, the endometrium is evaluated only in longitudinal and transverse plane. 2D ultrasound is completely uninformative for evaluating certain types of unicornuate, T-shaped, and infantile uteri. **Figure 3.**

MRI examination is recommended to detect complex abnormalities(Figure 3d) [1,9,30]. Mullerian anomalies are often associated with congenital kidney anomalies. It is also not uncommon to have a diagnostic dilemma regarding a unicornuate uterus with rudiment when a connection between existing cavities is to be confirmed or excluded. MRI is informative to detect certain types of complex abnormalities of the vagina and cervical canal. MRI is 100% sensitive and specific in diagnosing Mullerian Duct Anomalies [43].

3D ultrasonography is now considered the gold standard for evaluating uterine abnormalities (Figure 3b) [1,23]. The advantage of the method is that the uterus is evaluated in the coronal plane and at the same time, both, its external and internal (endometrial) contours are evaluated. This creates the basis for accurate diagnosis of Mullerian anomalies and classification, and also to determine the diagnostic accuracy of 3D ultrasound in comparison with the hysterolaparoscopic and MRI methods. The diagnostic accuracy of the 3D ultrasound method is presented in the following way: sensitivity 97.6%, specificity 98.3%, and 99.4%, respectively[1,32,37]. 3D ultrasonography shows a high degree of concordance compared to the MRI method. Evaluation of the uterine cavity's outer contour and its base is done by both diagnostic methods and practically by an equal degree[9,22,41].

Results and discussion

3D ultrasonography allows differentiation between the arcuate, septate, and bicornuate uterus. However, some authors note the low diagnostic accuracy of this method in the case of uterus didelphys [11,16,28]. The differential diagnosis between the three types of Mullerian anomalies mentioned above is not always possible by 3D ultrasound and MRI methods. There are so-called intermediate, incomplete forms between septate and bicornuate uteruses, whose diagnosis is associated with certain difficulties [9]. For example, a septate uterus with a wide septum and a deep separation between the horns may be considered as a bicornuate uterus. Morphologically, the structure of the septum is similar to the myometrium, which characterizes the bicornuate uterus. In this case, Troiano's and McCarthy's formula is used for accurate diagnosis and the distance between the interostial line and fundal contour exceeds 5mm. There is also a rare form of the septate uterus, which has two cervixes and also a longitudinal vaginal septum [24,36]. This form also belongs to the unclassifiable forms of the septate uterus [38].

One type of septate uterus, the non-communicating semi-cavity, was first described by Robert in 1969y [12], as a uterus-specific malformation (Figure 4). This disease is associated with a blind (closed) semi-cavity of the uterus, with unilateral hematometra, contralateral one-horned uterine cavity, and normal outer contour of the fundus. Robert's uterus is a very rare anomaly, which makes it difficult to diagnose. Correct diagnosis is essential to avoid such complications as recurrent pains since menarche, dysmenorrhea, endometriosis, infertility, and recurrent pregnancy losses. The first symptoms of this disease usually appear during menarche, when there is a functional endometrium in the closed cavity, which is the reason

for the development of hematometra and hematosalpinx. **Figure 4**.

A unicornuate uterus is a rare form of Mullerian anomalies and accounts for 2.4 – 13% of these anomalies, its prevalence ratio is 1:1000 (Figure 5) [14]. A unicornuate uterus may be presented alone or with a rudimentary horn, which may exist as a communicative and non-communicative rudiment. In the case of 75-90%, the rudimentary horn is non-communicating. The unicornuate uterus is characterized by such obstetric-gynecological complications as hematometra, endometriosis, and ectopic pregnancy [15,17,35]. 3D ultrasonography has increased the diagnostic accuracy of detecting this anomaly. **Figure 5.**

3D ultrasound is useful for detecting such rare anomalies as hypoplastic, atavistic, and infantile uteruses. Infantile and hypoplastic uteri have a long and narrow cervix, which is caused by the violation of their embryogenesis [3]. Meaker's index refers to the ratio of the uterus body to the cervix.

If this ratio is lower than 0.60, this uterus is considered hypoplastic, and if the ratio is 0.25, it is considered an infantile uterus. In the case of an atavistic uterus, the uterine cavity is star-shaped with asymmetrical horns

Conclusion

Based on the literature review, we can conclude that 3D ultrasonography is a cheap, fast, non-invasive method for evaluating Mullerian anomalies. It showed high diagnostic concordance with the MRI method, virtually identical images are obtained by 3D ultrasound. Diagnostic difficulties arise in the case of cervical and vaginal anomalies, as well as in complex anomalies. Up to this date, it remains as a challenge, the correct diagnosis of the unclassifiable forms of Mullerian anomalies and the subsequent selection of their treatment methods, which is the basis for future research.

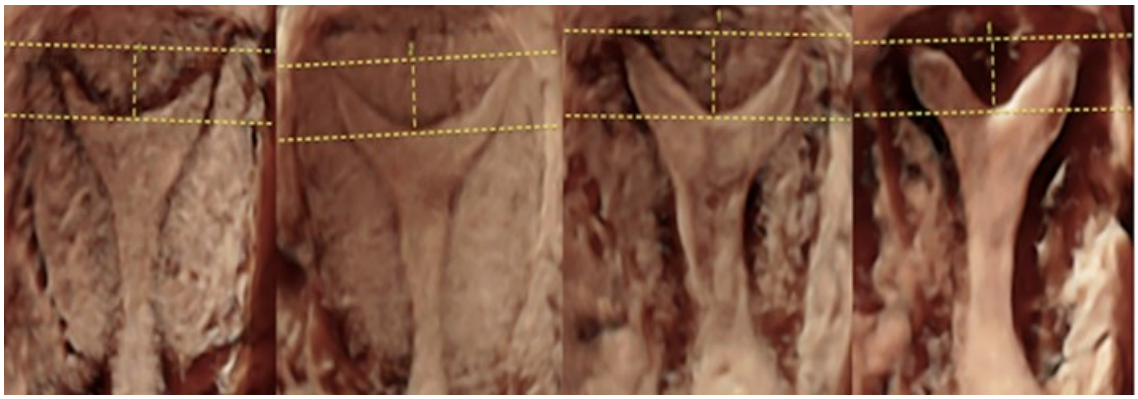

Figure 1. 3D ultrasound images illustrating uteri with internal indentation depth >10 to 15mm and indentation angle >90^0, which would be Mullerian anomalies unclassifiable forms

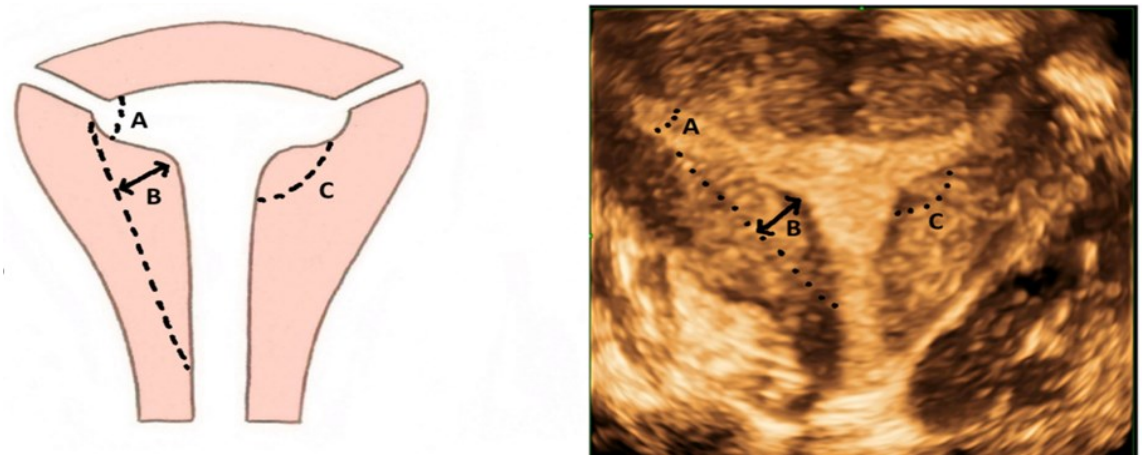

Figure 2. Congenital Uterine CUME (Group of Expert Anomalies) represented criteria for diagnosing T shaped uterus: the depth of the lateral indentation (b) > or equal to 7 mm, its angle (C) > or equal to 130^0, T angle (A) < 40^0

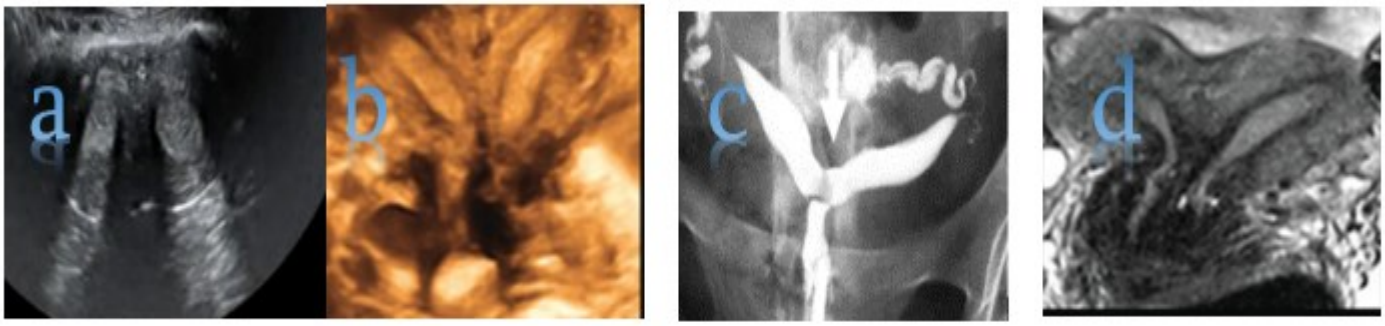

Figure 3. Bicornuate uterus with different imaging methods a. 2D ultrasound, b.3D ultrasound c.hysterosalpingography and d.MRI imaging

Figure 4. Robert's uterus is divided by an asymmetrical septum: Left closed semi-cavity with hematometra and right cavity similar to the unicornuate uterus. a. with 2D ultrasonography, b. 3D ultrasonography, c. HD-live

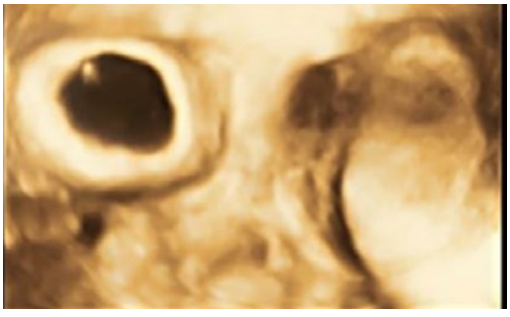

Figure 5. 3D configuration of the Unicornuate uterus and pregnant rudimentary horn

References

1. Jayaprakasan K, Ojha K. Diagnosis of Congenital Uterine Abnormalities: Practical Considerations. J Clin Med. 2022 Feb 25;11(5):1251. doi: 10.3390/jcm11051251. PMID: 35268343; PMCID: PMC8911320.
2. Pfeifer SM, Attaran M, Goldstein J, Lindheim SR, Petrozza JC, Rackow BW, Siegelman E, Troiano R, Winter T, Zuckerman A, Ramaiah SD. ASRM müllerian anomalies classification 2021. Fertil Steril. 2021 Nov;116(5):1238-1252. doi: 10.1016/j.fertnstert.2021.09.025. Erratum in: Fertil Steril. 2023 Jun;119(6):1088. PMID: 34756327.
3. Bonilla-Musoles F, Martin N, Esquembre MP, Caballero O, Castillo JC, Bonilla F Jr, Raga F, Machado L. Uterine Malformations: Diagnosis with 3D/4D Ultrasound. Donald School J Ultrasound Obstet Gynecol 2015;9(2):123-148.
4. Sugi MD, Penna R, Jha P, Põder L, Behr SC, Courtier J, Mok-Lin E, Rabban JT, Choi HH. Müllerian Duct Anomalies: Role in Fertility and Pregnancy. Radiographics. 2021 Oct;41(6):1857-1875. doi: 10.1148/rg.2021210022. PMID: 34597219.
5. Kim MA, Kim HS, Kim YH. Reproductive, Obstetric and Neonatal Outcomes in Women with Congenital Uterine Anomalies: A Systematic Review and Meta-Analysis. J Clin Med. 2021 Oct 20;10(21):4797. doi: 10.3390/jcm10214797. PMID: 34768344; PMCID: PMC8584292.
6. Ludwin A, Tudorache S, Martins WP. ASRM Müllerian Anomalies Classification 2021: a critical review. Ultrasound Obstet Gynecol. 2022 Jul;60(1):7-21. doi: 10.1002/uog.24905. Epub 2022 Jun 9. PMID: 35678250.
7. Khurana A. Recent Advances in 3D Assessment of Mullerian Anomalies. Donald School J Ultrasound Obstet Gynecol 2022;16(1):53-65.
8. Ludwin A, Ludwin I. Comparison of the ESHRE-ESGE and ASRM classifications of Müllerian duct anomalies in everyday practice. Hum Reprod. 2015 Mar;30(3):569-80. doi: 10.1093/humrep/deu344. Epub 2014 Dec 22. PMID: 25534461; PMCID: PMC4325671.
9. Cekdemir YE, Mutlu U, Acar D, Altay C, Secil M, Dogan OE. The accuracy of three-dimensional ultrasonography in the diagnosis of Müllerian duct anomalies and its concordance with magnetic resonance imaging. J Obstet Gynaecol. 2022 Jan;42(1):67-73. doi:.
10. JL, Carriles I, Cajas MB, Costa S, Fabra S, Cabrero M, Castro E, Tomaizeh A, Laza MV, Monroy A, Martinez I, Aguilar MI, Hernani E, Castellet C, Oliva A, Pascual MÁ, Guerriero S. Diagnostic Performance of Two-Dimensional Ultrasound, Two-Dimensional Sonohysterography and Three-Dimensional Ultrasound in the Diagnosis of Septate Uterus-A Systematic Review and Meta-Analysis. Diagnostics (Basel). 2023 Feb 20;13(4):807. doi: 10.3390/diagnostics13040807. PMID: 36832295; PMCID: PMC9955687.
11. Alcazar Luis Juan, Three-Dimensional Ultrasound in Gynecology: Current Status and Future Perspectives, Current Women`s Health Reviews 2005; 1 (1)
12. Deenadayal M, Günther 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 Mar 31;13(1):41-49. doi: 10.52054/FVVO.13.1.008. PMID: 33889860; PMCID: PMC8051191.
13. Di Spiezio Sardo A, Campo R, Gordts S, Spinelli M, Cosimato C, Tanos V, Brucker S, Li TC, Gergolet M, De Angelis C, Gianaroli L, Grimbizis G. The comprehensiveness of the ESHRE/ESGE classification of female genital tract congenital anomalies: a systematic review of cases not classified by the AFS system. Hum Reprod. 2015 May;30(5):1046-58. doi: 10.1093/humrep/dev061. Epub 2015 Mar 18. PMID: 25788565; PMCID: PMC4400201.
14. Roman, J. D., & Roman, J. D. (2021). Co-Existence of a Rudimentary Non-Communicating Horn with a Unicornuate Uterus in Association with 2 Components of the VACTERL Association: A Case Report. Case Reports in Obstetrics Gynecology and Reproductive, 1–4. https://doi.org/10.31487/j.crogr.2021.02.01
15. Obeidat RA, Aleshawi AJ, Tashtush NA, Alsarawi H. Unicornuate uterus with a rudimentary non-communicating cavitary horn in association with VACTERL association: case report. BMC Womens Health. 2019 May 30;19(1):71. doi: 10.1186/s12905-019-0768-4. PMID: 31146728; PMCID: PMC6543654.
16. Wang L, Chen XJ, Liang JH, Zhang ZK, Cao TS, Zhang L. Preliminary application of three-dimensional printing in congenital uterine anomalies based on three-dimensional transvaginal ultrasonographic data. BMC Womens Health. 2022 Jul 14;22(1):290. doi: 10.1186/s12905-022-01873-0. PMID: 35836228; PMCID: PMC9284698.
17. Dhanawat J, Pape J, Stuhlmann-Laeisz C, Maass N, Freytag D, Gitas G, Alkatout I. Ectopic pregnancy in noncommunicating horn of unicornuate uterus: 3D-ultrasound and primary laparoscopic management. Clin Case Rep. 2021 May 24;9(5):e04261. doi: 10.1002/ccr3.4261. PMID: 34084520; PMCID: PMC8142796.
18. Lin PC, Bhatnagar KP, Nettleton GS, Nakajima ST. Female genital anomalies affecting reproduction. Fertil Steril. 2002 Nov;78(5):899-915. doi: 10.1016/s0015-0282(02)03368-x. PMID: 12413972.
19. 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 Jun;49(6):944-55. doi: 10.1016/s0015-0282(16)59942-7. PMID: 3371491.
20. 20. Passos IMPE, Britto RL. Diagnosis and treatment of müllerian malformations. Taiwan J Obstet Gynecol. 2020 Mar;59(2):183-188. doi: 10.1016/j.tjog.2020.01.003. PMID: 32127135.
21. Ludwin A, Coelho Neto MA, Ludwin I, Nastri CO, Costa W, Acién M, Alcazar JL, Benacerraf B, Condous G, DeCherney A, De Wilde RL, Diamond MP, Emanuel MH, Guerriero S, Hurd W, Levine D, Lindheim S, Pellicer A, Petraglia F, Saridogan E, Martins WP. Congenital Uterine Malformation by Experts (CUME): diagnostic criteria for T-shaped uterus. Ultrasound Obstet Gynecol. 2020 Jun;55(6):815-829. doi: 10.1002/uog.20845. Epub 2020 May 15. PMID: 31432589.
22. Groszmann YS, Benacerraf BR. Complete evaluation of anatomy and morphology of the infertile patient in a single visit; the modern infertility pelvic ultrasound examination. Fertil Steril. 2016 Jun;105(6):1381-93. doi: 10.1016/j.fertnstert.2016.03.026. Epub 2016 Apr 4. PMID: 27054310.
23. Ghi T, Casadio P, Kuleva M, Perrone AM, Savelli L, Giunchi S, Meriggiola MC, Gubbini G, Pilu G, Pelusi C, Pelusi G. Accuracy of three-dimensional ultrasound in diagnosis and classification of congenital uterine anomalies. Fertil Steril. 2009 Aug;92(2):808-13. doi: 10.1016/j.fertnstert.2008.05.086. Epub 2008 Aug 9. PMID: 18692833.
24. Brown SJ, Badawy SZ. A rare mullerian duct anomaly not included in the classification system by the american society for reproductive medicine. Case Rep Obstet Gynecol. 2013;2013:569480. doi: 10.1155/2013/569480. Epub 2013 Mar 21. PMID: 23573434; PMCID: PMC3618915.
25. Ludwin A, Ludwin I, Coelho Neto MA, Nastri CO, Bhagavath B, Lindheim SR, Martins WP. Septate uterus according to ESHRE/ESGE, ASRM and CUME definitions: association with infertility and miscarriage, cost and warnings for women and healthcare systems. Ultrasound Obstet Gynecol. 2019 Dec;54(6):800-814. doi: 10.1002/uog.20291. PMID: 30977223.
26. Coelho Neto MA, Ludwin A, Petraglia F, Martins WP. Definition, prevalence, clinical relevance and treatment of T-shaped uterus: systematic review. Ultrasound Obstet Gynecol. 2021 Mar;57(3):366-377. doi: 10.1002/uog.23108. PMID: 32898287.
27. Salim R, Woelfer B, Backos M, Regan L, Jurkovic D. Reproducibility of three-dimensional ultrasound diagnosis of congenital uterine anomalies. Ultrasound Obstet Gynecol. 2003 Jun;21(6):578-82. doi: 10.1002/uog.127. PMID: 12808675.
28. 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 Jun;91(6):2369-75. doi: 10.1016/j.fertnstert.2008.01.079. Epub 2008 Mar 25. PMID: 18367185.
29. Knez J, Saridogan E, Van Den Bosch T, Mavrelos D, Ambler G, Jurkovic D. ESHRE/ESGE female genital tract anomalies classification system-the potential impact of discarding arcuate uterus on clinical practice. Hum Reprod. 2018 Apr 1;33(4):600-606. doi: 10.1093/humrep/dey043. PMID: 29514262.
30. Al Najar MS, Al Ryalat NT, Sadaqah JS, Husami RY, Alzoubi KH. MRI Evaluation of Mullerian Duct Anomalies: Practical Classification by the New ASRM System. J Multidiscip Healthc. 2022 Nov 9;15:2579-2589. doi: 10.2147/JMDH.S386936. PMID: 36388626; PMCID: PMC9659481.
31. Hassan MA, Lavery SA, Trew GH. Congenital uterine anomalies and their impact on fertility. Womens Health (Lond). 2010 May;6(3):443-61. doi: 10.2217/whe.10.19. PMID: 20426609.
32. Bohiltea, R. E., Clotea, E., Dima, V., Varlas, V., Bacalbasa, N., & Pelinescu Onciul, D. (2021). 3D ultrasound in the diagnosis of uterine anomalies. Romanian Medical Journal, 68(S6), 32–36.
33. Chan YY, Jayaprakasan K, Tan A, Thornton JG, Coomarasamy A, Raine-Fenning NJ. Reproductive outcomes in women with congenital uterine anomalies: a systematic review. Ultrasound Obstet Gynecol. 2011 Oct;38(4):371-82. doi: 10.1002/uog.10056. PMID: 21830244.
34. Ludwin A, Martins WP, Nastri CO, Ludwin I, Coelho Neto MA, Leitão VM, Acién M, Alcazar JL, Benacerraf B, Condous G, De Wilde RL, Emanuel MH, Gibbons W, Guerriero S, Hurd WW, Levine D, Lindheim S, Pellicer A, Petraglia F, Saridogan E. Congenital Uterine Malformation by Experts (CUME): better criteria for distinguishing between normal/arcuate and septate uterus? Ultrasound Obstet Gynecol. 2018 Jan;51(1):101-109. doi: 10.1002/uog.18923. Erratum in: Ultrasound Obstet Gynecol. 2018 Feb;51(2):282. PMID: 29024135.
35. Reichman D, Laufer MR, Robinson BK. Pregnancy outcomes in unicornuate uteri: a review. Fertil Steril. 2009 May;91(5):1886-94. doi: 10.1016/j.fertnstert.2008.02.163. Epub 2008 Apr 25. Erratum in: Fertil Steril. 2015 Jun;103(6):1615-8. PMID: 18439594.
36. Duffy DA, Nulsen J, Maier D, Schmidt D, Benadiva C. Septate uterus with cervical duplication: a full-term delivery after resection of a vaginal septum. Fertil Steril. 2004 Apr;81(4):1125-6. doi: 10.1016/j.fertnstert.2003.12.015. PMID: 15066474.
37. Raga F, Bonilla-Musoles F, Blanes J, Osborne NG. Congenital Müllerian anomalies: diagnostic accuracy of three-dimensional ultrasound. Fertil Steril. 1996 Mar;65(3):523-8. doi: 10.1016/s0015-0282(16)58147-3. PMID: 8774280.
38. Chang AS, Siegel CL, Moley KH, Ratts VS, Odem RR. Septate uterus with cervical duplication and longitudinal vaginal septum: a report of five new cases. Fertil Steril. 2004 Apr;81(4):1133-6. doi: 10.1016/j.fertnstert.2003.08.051. PMID: 15066477.
39. Grimbizis GF, Camus M, Tarlatzis BC, Bontis JN, Devroey P. Clinical implications of uterine malformations and hysteroscopic treatment results. Hum Reprod Update. 2001 Mar-Apr;7(2):161-74. doi: 10.1093/humupd/7.2.161. PMID: 11284660.
40. Saravelos SH, Cocksedge KA, Li TC. Prevalence and diagnosis of congenital uterine anomalies in women with reproductive failure: a critical appraisal. Hum Reprod Update. 2008 Sep-Oct;14(5):415-29. doi: 10.1093/humupd/dmn018. Epub 2008 Jun 6. PMID: 18539641.
41. Pan HX, Liu P, Duan H, Li PF, Chen RL, Tang L, Luo GN, Chen CL. Using 3D MRI can potentially enhance the ability of trained surgeons to more precisely diag-

nose Mullerian duct anomalies compared to MR alone. Eur J Obstet Gynecol Reprod Biol. 2018 Sep;228:313-318. doi: 10.1016/j.ejogrb.2018.07.007. Epub 2018 Jul 9. PMID: 30075412.
42. Caliskan E, Ozkan S, Cakiroglu Y, Sarisoy HT, Corakci A, Ozeren S. Diagnostic accuracy of real-time 3D sonography in the diagnosis of congenital Mullerian anomalies in high-risk patients with respect to the phase of the menstrual cycle. J Clin Ultrasound. 2010 Mar-Apr;38(3):123-7. doi: 10.1002/jcu.20662. PMID: 20091695.
43. Meenakshi, G., Smita, G., Vikas, V., & R.P, K. (2016). Role of 2d Ultrasound, 3d Ultrasound And Mri in The Diagnosis of Mullerian Duct Anomalies. IOSR Journal of Dental and Medical Sciences, 15(09), 64–68.