Original Article

Prevalence and Pregnancy Outcome of Mullerian Anomalies in Infertile Women: A Retrospective Study

Bharti Joshi, Aayushi Kaushal, Vanita Suri, Shalini Gainder, Neelam Choudhary, Sunita Jamwal, Shruti Sharma

Department of Obstetrics and Gynaecology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Abstract

Background: Uterine anomalies arise if there is agenesis of one or two mullerian ducts, or absence of fusion or reabsorption of the septum between these ducts. The process may be partial or total and affect one or multiple parts of the tract. **Aims:** This study was done to assess the distribution of various types of mullerian anomalies in infertile women, their classification based on ESHRE and AFS, associated anomalies, types of diagnostic modalities used, surgical interventions done(if any), various types of infertility treatment used and their outcomes. **Setting and Design:** A retrospective analysis in a tertiary level hospital. **Materials and Methods:** This was a retrospective study in which the women found to have mullerian anomalies were recruited from infertility clinic from July 2019 to March 2020.They were classified according to ESHRE and AFS criteria and their records were analyzed after taking various factors like age, ovarian reserve, duration of infertility, treatment given , associated ovarian and tubal factors and pregnancy outcomes. **Statistical Analysis:** Analysis was performed in Excel. **Results:** There were 30 women with mullerian anomalies. Unicornuate uterus was most common anomaly .Four women required septoplasty in view of septate uterus. Five women had associated renal anomalies in form of shrunken kidney and ectopic kidney. Most of these women were considered for controlled ovarian stimulation followed by intrauterine insemination. In our study 16.6% women had successful pregnancy outcome. **Conclusion:** Mullerian anomalies continue to attract infertility specialist as they pose challenge in making clear diagnosis and its management as obstetrics outcomes are excellent after septum resection in women with septate uterus and conservative management in women with other anomalies. Proper work up of infertility and its management varies from case to case and associated factors like endometriosis, male factor, polycystic ovarian syndrome etc.

Keywords: *Infertility, Mullerian anomaly, pregnancy outcome*

Introduction

Uterine anomalies arise if there is agenesis of one or two Mullerian ducts, absence of fusion or reabsorption of the septum between these ducts. The process may be partial or total and affect one or multiple parts of the tract. Renal anomalies are often associated with uterine anomalies as there is close embryologic relationship between the development of the urinary and reproductive organ.[1,2] Uterine anomalies have been classified according to the American Fertility Society (AFS)/American Society for Reproductive Medicine (ASRM) and The European Society of Human Reproduction and Embryology (ESHRE)/The European Society for Gynaecological Endoscopy (ESGE) classifications systems. ASRM divides uterine malformations into seven main groups.[3] While AFS classification does not include vaginal anomalies and certain combined anomalies, ESHRE/ESGE classification is based on malformations of the uterine cervix and vagina and can even classify complex Mullerian anomalies.[4]

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Address for correspondence: Dr. Aayushi Kaushal, J.K. Hospital, Palm City, Attewali, Fatehgarh Sahib - 140 406, Punjab, India.
E-mail: kaushalaayushi@gmail.com

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Table 1: Number of women with Mullerian anomaly, mean age, type of infertility, modality for confirmation of diagnosis, any associated abnormalities, classification of Mullerian anomalies based on American Fertility Society and European Society of Human Reproduction and Embryology, required surgical interventions, infertility treatment and their outcomes

Variable	Number
Number of women with Mullerian anomaly	30
Mean age±SD (years)	29.46±2.71
Type of infertility	
Primary	24
Secondary	6
Diagnostic modality for confirmation	
Clinical examination+2D ultrasonography	3
Hysterosalpingography	2
3D ultrasonography	9
Magnetic resonance imaging	6
Diagnostic hysterolaparoscopy	10
Associated anomalies	
Shrunken kidney/ectopic kidney	5
Endometriosis/adenomyosis	4
Polycystic ovary syndrome	4
Male factor infertility	6
Classification according to AFS (class and subclass)	
Unicornuate	
2b	3
2c	7
Didelyphs	
III	5
Bicornuate	
IVa	2
IVb	3
Septate	
Vb	7
Arcuate	
VI	3
Classification according to ESHRE (class and subclass)	
Dysmorphic	
U1cC0V0	3
Septate	
U2aC0V0	7
Bicorporeal	
U3aC0V0	3
U3bC0V0	2
U3bC2V0	4
U3bC2V3	1
Hemiuterus	
U4aC0V0	5
U4bC0V0	4
U4bC0V3	1
Treatment modality	
Hysteroscopic resection of septum	4
Vaginal septum resection	3
Treatment for infertility	
Controlled ovarian stimulation + intrauterine insemination	28
In vitro fertilisation	2
Outcome	
Pregnancy	5
LSCS at term	3
Preterm LSCS	2

AFS: American Fertility Society, ESHRE: European Society of Human Reproduction and Embryology, SD: Standard deviation, 2D: Two-dimensional, 3D: Three-dimensional, LSCS: Lower segment caesarean section

Uterine anomalies are associated with higher obstetric complication risks, including recurrent pregnancy loss and preterm delivery, as well as higher perinatal morbidity and mortality. The association of primary infertility with uterine anomalies remains less clear. However, non-feasibility of fundal implantation in an abnormal uterus could lead to occurrence of lateral wall implantation or septal implantation. The subsequent alteration in vascular supply, myometrial and endometrial formation in this area, results in inadequate implantation. Many a times, Mullerian anomalies are accidently diagnosed in an infertile woman during her workup for infertility.[5]

Aims and objectives

This study was done to assess the distribution of various types of Mullerian anomalies in infertile women, their classification based on ESHRE, associated anomalies, types of diagnostic modalities used, surgical intervention done (if any), various types of infertility treatment used and their outcome.

Materials and Methods

This study was a retrospective analysis of infertile women with Mullerian anomalies conducted in the infertility clinic of a tertiary care hospital of Northern India. No sample size calculation was performed, and all cases identified from July 2019 to March 2020 were included. After taking clearance from the ethics committee (OBGYN/EC/185), data of all women during the above study period seeking infertility treatment and found to have Mullerian anomalies were collected and analysed. After taking informed written consent, these women were further evaluated clinically and radiologically to identify for type of associated anomalies. They were classified based on the AFS and ESHRE criteria. Infertility treatment was individualised after taking into consideration the type of Mullerian anomaly and other factors such as age,

ovarian reserve, duration of infertility, associated ovarian and tubal factors. Outcomes in the form of clinical pregnancy rates were noted.

Statistical analysis

The data were analysed in terms of prevalence of Mullerian anomalies and distribution of its types. Age is expressed as mean ± standard deviation. All other parameters are expressed as absolute numbers and percentages.

Results

Over a study period of 9 months, 600 women took treatment for infertility and 30 of them had Mullerian anomalies, thus making prevalence of 5%. Out of these 30 women, 22 women were diagnosed to have Mullerian anomalies after workup for infertility, and rest of the women were referred from outside with diagnosis of Mullerian anomalies and came for treatment purpose.

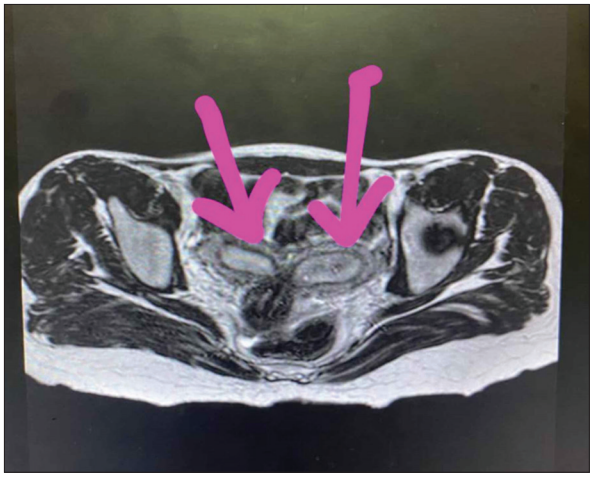

Figure 1: Axial T2-weighed image of didelyphs uterus by pink arrows

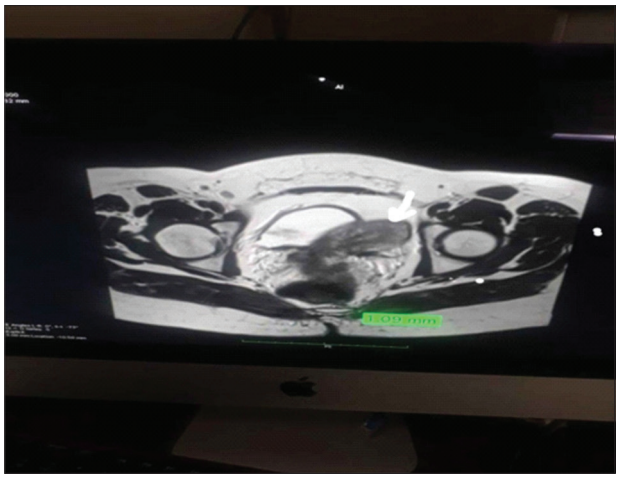

Figure 3: Axial T2-weighted image showing single uterine horn (marked by white arrow) suggestive of unicornuate uterus

Table 1 depicts the total number of women with Mullerian anomaly, their mean age, type of infertility, modality for confirmation of diagnosis, any associated abnormalities, classification of Mullerian anomalies based on American Fertility Society and European Society of Human Reproduction and Embryology, surgical interventions (required if any), infertility treatment and their outcomes

Age of the women ranged from 20 to 39 years, and most of them had primary infertility. Secondary infertility was present in 20% of women. The most common anomaly was unicornuate uterus [Figure 3] seen in ten women and five of these had associated tubal pathology, therefore required laparoscopy. Septate uterus was seen in seven women and four of them required hysteroscopic resection of septum under laparoscopic guidance. Out of five women with uterine didelyphs [Figure 1], two were variants of Herlyn–Werner–Wunderlich syndrome/obstructed hemivagina and ipsilateral renal anomaly (syndrome) which itself is a rare entity. Vaginal septum resection was done in these women.

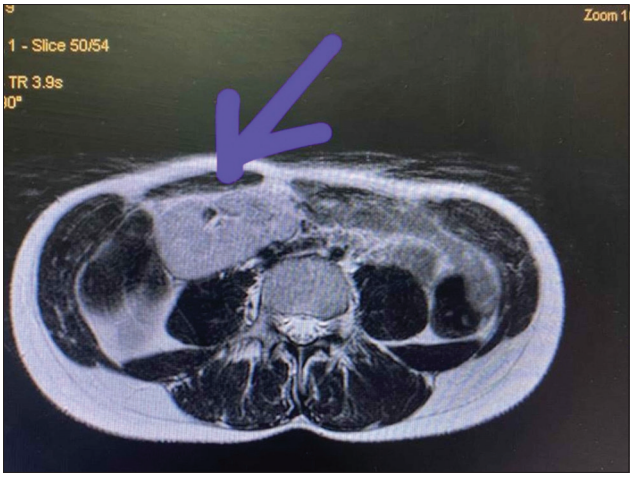

Figure 2: Axial T2-weighed image showing reniform structure (blue colour arrow) in the umbilical region with non-visualisation of kidney in the right renal fossa suggestive of ectopic kidney

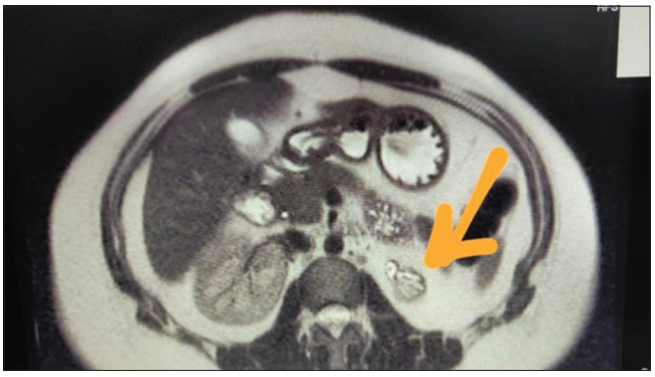

Figure 4: Axial T2-weighed image of the right shrunken kidney marked by yellow arrow

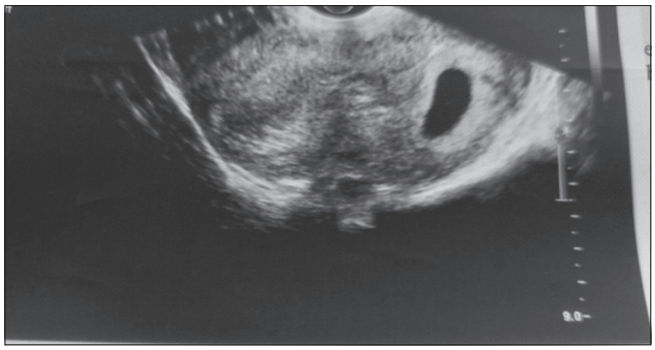

Figure 5: Early pregnancy showing gestational sac in the left horn of bicornuate uterus

Table 2: Comparison in prevalence between our study and previous studies

Prevalence	Percentage
Our study	5
Jayashree *et al*.[5]	10
Saravelos *et al*.[6]	7.3
Reyes-Muñoz *et al*.[7]	4.4
Attar and Amin[8]	4.1
Singh *et al*.[9]	8.13

Table 3: Comparison between most common anomaly between our study and previous studies

Study	Type of anomaly
Our study	Unicornuate uterus
Jayashree *et al*.[5]	Bicornuate uterus
Saravelos *et al*.[6]	Septate uterus
Reyes-Muñoz *et al*.[7]	Septate uterus
Singh *et al*.[9]	Septate uterus
Sayed *et al*.[10]	Arcuate uterus

Bicornuate uterus was seen in five and confirmed by magnetic resonance imaging and three-dimensional ultrasonography. There were associated renal anomalies in the form of shrunken kidney and ectopic kidney in five women [Figure 2 and 4]. According to the ESHRE classification, ten (33.3%) had hemiuterus uterus out of which eight had non-functional rudimentary horn and two had non-communicating functional horn. While septate uterus was diagnosed in seven women, bicorporeal uterus was diagnosed in ten women. Out of 30 women, five (16.6%) had bicorporeal uterus with normal double cervix (in AFS classification called uterine didelyphs) which was managed conservatively. Out of thirty women, seven required septoplasty/septum excision. Hysteroscopic resection of the septum was done in four 4 women in view of recurrent abortions, whereas the remaining, vaginal septum resection was done.

Two women were considered for *in vitro* fertilisation (IVF). One women among bicorporeal uterus required intrauterine insemination (IUI) with donor semen in view of obstructive azoospermia and not willing for sperm retrieval techniques. Five out of 30 women conceived after controlled ovarian stimulation (COS)+ IUI [Figure 5]. Two women who required IVF did not conceive in their fresh cycles and are planned for frozen embryo transfer. All five women required caesarean section as mode of termination of pregnancy. Preterm delivery had to be done in two women at 34 weeks due to PPROM and eclampsia.

Discussion

Mullerian anomalies arise due to abnormalities in formation, fusion or reabsorption of septum between Mullerian ducts.[1,2] There are obstetrical complications as well associated with these Mullerian anomalies.

This prevalence in infertile population is not much different from prevalence in general population which is estimated to be 6.7% in review by Saravelos *et al*.[6] The comparison of prevalence with other studies has been shown in Table 2. We did not estimate prevalence in general population as we collected data only from infertile women. Prevalence is much higher in women with recurrent miscarriages.

In our study, unicornuate uterus was the most common anomaly seen followed by the septate uterus. Four women required hysteroscopic resection of septum in view of septate uterus, and three required septum excision in view of transverse vaginal septum. Five women had associated renal anomalies in the form of shrunken kidney and ectopic kidney. Most of the women were considered for COS followed by IUI and two women underwent IVF. Successful pregnancy outcome was present in 16.6% of women in our study.

Among all Mullerian anomalies, unicornuate uterus was the most common one followed by septate uterus. Table 3 depicts that bicornuate uterus (40%) was the most common anomaly in infertile women in a study by Jayashree *et al*.,[5] whereas septate uterus came out to be most common anomaly in infertile women in a review by Saravelos *et al*.[6] and in the studies by Singh *et al*.[9] and Reyes-Munoz *et al*.[7] Another study by Sayed *et al*.[10] found out the presence of arcuate uterus as the most common anomaly. We could not find any specific reason for this higher incidence of unicornuate uterus in our study.

Renal anomaly was found in 16.6% of women out of which two were present in unicornaute uterus and one each in septate, bicornuate and didelyphs, whereas in a study done by Reyes-Munoz *et al*.,[7] renal anomalies were present in 2.8% of women. Renal

anomalies were present in 36% of women in study by Oppelt *et al*.,[11] which could be probably due to inclusion of all premenopausal women with Mullerian anomalies, whereas our study included only infertile women with Mullerian anomalies.

Out of thirty women, seven (23.3%) required intervention in the form of either hysteroscopic resection of septum or vaginal septum excision in view of transverse vaginal septum.

Stimulation protocols were decided upon age, duration of infertility, ovarian reserve, associated abnormalities such as endometriosis and polycystic ovarian syndrome (PCOS). Most of the women required COS followed by IUI. COS was done with either clomiphene citrate (CC), letrozole, CC/letrozole + gonadotropins or only gonadotropins depending upon age, ovarian reserve, body mass index or prior response. IVF was considered optimum in two women.

In our study, 16% of women had successful pregnancies and all of them conceived by means of COS followed by IUI in contrast to the studies by Reyes-Munoz *et al*.[7] and Singh *et al*.[9] in which 33% and 38.4% women had achieved pregnancy. Out of five pregnancies, two babies had to be delivered preterm at 34 weeks due to PPROM and eclampsia. Lower pregnancy rate in our study could be attributed to attrition of women due to onset of COVID pandemic, and moreover, maximum number of women had unicornuate uterus as Mullerian anomaly, whereas in the studies by Reyes-Munoz *et al*.[7] and Singh *et al*.,[9] maximum women had septate uterus which was corrected by septoplasty and pregnancy rates increase by 80% after septoplasty. None of the women had spontaneous conception in our study as there was another factor such as advancing age, decreased ovarian reserve and endometrioisis due to which fertility treatment was hastened.

Strengths and limitations

The strength of our study was homogeneity of study population as all women with infertility were taken. The main limitation was small sample size and short duration of study as further treatment of women could not be done due to onset of COVID pandemic.

Conclusion

Mullerian anomalies continue to attract an infertility specialist as they pose challenge in making clear diagnosis and its management as obstetrical outcomes are excellent after septum resection in women with septate uterus and conservative management in women with other anomalies. Proper workup of infertility and its management varies from case to case and associated factors such as endometriosis, male factor and PCOS.

Data availability statement

The data that support the findings of the study are available from the corresponding author, upon reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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