Fertility And Pregnancy Outcomes In Congenital Uterine Anomalies

Meherin Majeed, MBBS, FCPS, Classified Specialist, Department of Obstetrics & Gynaecology, Combined Military Hospital (Adhoc),Kholahati, Parbatipur,Dinajpur, Bangladesh. drmeherinmajeed@gmail.com

Syed Naufel Mahmud, MBBS,MPH,MPhil, Assistant Director of Medical Services, Rangpur and Principal, Army Nursing College, Rangpur, Bangladesh.

For correspondence: Lt Col Meherin Majeed, Gynaecologist, Combined Military Hospital (Adhoc),Kholahati, Parbatipur,Dinajpur, Bangladesh. Cell: +8801722600477, email:drmeherinmajeed@gmail.com

Abstract:
Introduction : Congenital uterine anomalies (CUAs) are structural deviations of normal anatomy of uterus which results from maldevelopment of Mullerian ducts and are often discovered during infertility workout, investigating recurrent pregnancy loss and evaluating pregnancy complications .Management of CUAs is a challenge as complications ranging from preterm labour to uterine rupture are associated with it. **Objective:** To observe fertility and pregnancy outcomes in patient with uterine anomalies. **Material and methods:** This cross-sectional study enrolled all patients with uterine anomalies who were willing to conceive, reported with pregnancy and were incidentally diagnosed during the study period. Fertility and pregnancy outcomes were measured in ten patients of all groups. **Results:** One third cases were incidentally diagnosed during caesarean section. Bicornuate uterus was found in half of cases. 40**%** of patients had subfertility. Half of the subfertility patients got pregnant after ovulation induction. Early pregnancy loss was observed only in 25% of patients. Majority of patients had successful pregnancy outcome. Caesarean section was prevalent mode of delivery for all patients. **Conclusion:** High index of suspicion is required in order to diagnose CUAs especially in low resource setting. Diagnostic tools should be chosen considering its availability, cost effectiveness and appropriateness to individual. Counseling of women ensures positive fetomaternal outcome.

Keywords: Uterine anomaly, Recurrent pregnancy loss, Preterm birth, fertility.

I. Introduction:

Congenital uterine anomalies occur in varieties of forms as a consequence of abnormal genesis, fusion or canalization of the mullerian ducts during fetal development. Overall frequencies of reported cases are estimated 3%-5% in general population [1].Majority of cases remained completely asymptomatic [2].It is highly suspicious when patient presents with recurrent pregnancy loss and poor pregnancy outcomes. Certain gynecological conditions such as dysmenorrhea, dyspareunia and leucorrhoea were common among women with congenital uterine anomalies [3].Fertility and evolution of pregnancy depends on its type. Diagnosis of congenital uterine anomalies depends mainly on radiological and endoscopic evaluation rather than analysis of clinical features. Prenatal diagnosis is important to ensure proper care and prevent complications. There are no definite guidelines about the management & follow up of the pregnancy or selecting the mode of delivery as the incidence is very low.

II. Material and Methods

This cross-sectional study presents observation analysis of fertility and pregnancy outcome in patients with congenital uterine anomaly. Study underwent from January 2020 to January 2023 in a single hospital. Total ten cases of congenital uterine anomalies were detected during the study period. The American Society for Reproduction Medicine (ASRM 2021)classification for CUAs was used in this study. Three groups of patients enrolled in this study: A) Patients who were investigated for subfertility and found to had uterine anomalies (n=4). B)Patients who were pregnant and diagnosed to had uterine anomalies (n=3).C) Patients who had incidental diagnosis of uterine anomalies during caesarean section (n=3).

Group A: Patients with subfertility and uterine anomalies were diagnosed by hysterosalphingography, laparoscopy and laparotomy. Thereafter, observed for fertility and pregnancy out comes. They were treated with ovulation induction. Luteal phase oral progesterone support given to all four cases followed by oral and intramascular progesterone support to patients who conceived. Group B: Patients reported with pregnancy and uterine anomalies were diagnosed in early pregnancy by transabdominal ultrasound and transvaginal ultrasound. They were treated with oral progesterone from early pregnancy, Nifedipine 20mg daily from third trimester and steroid for lung maturity. Thereafter, their pregnancy outcomes were observed. Group C: Patients with uterine anomalies diagnosed incidentally

during caesarean section were inquired about their current and past obstetric history to correlate with pregnancy outcome. In each group, their obstetric records were analyzed to find out previous fertility and pregnancy outcome related to uterine anomalies. Fertility was assessed by ability to conceive spontaneously or after ovulation induction. Pregnancy outcomes were assessed by pregnancy loss, preterm birth, term birth, PROM, abruption placenta, malpresentation and mode of delivery. Neonatal outcomes were also included with pregnancy outcomes and observed by low birth weight, fetal growth retardation and perinatal mortality.

III. RESULTS:

The study ascertained congenital uterine anomalies in ten patients which consisted of five bicornuate uterus (50%), two didelphys uterus (20%), two unicornuate uterus (20%) and one arcuate uterus (10%) Table I.

Types of CUAs	Number
Bicornuate	5 (50%)
Unicornuate	2 (20%)
Didelphys	2 (20%)
Arcuate	1 (10%)

Table I: Distribution of congenital uterine anomalies (n=10).

Three cases (30%) who were unaware of having any uterine anomaly during antenatal visit were diagnosed during caesarean section. During antenatal visit three cases (30%) were diagnosed by early ultrasonography. Another four cases (40%) were diagnosed during infertility workout (Table II).

Type	Early pregnancy USG	Infertility workout			Caesar-ean section
		HSG	Laparos-copy	Laparot-omy	
Bicorn-uate	2	2	1	0	
Unicor-nuate	0	0	0	0	2
Didelp-hys	1	0	0	1	
Arcuat-e	0	0	0	0	1
Total	3 (30%)	2(20%)	1(10%)	1(10%)	3 (30%)
		4 (40%)			

Table II: Method of diagnosis of congenital uterine anomalies (n=10)

Table III shows two primary subfertility and two secondary subfertility cases which is 40% of total cases. Two cases of bicornuate uterus with primary subfertility got pregnant after ovulation induction which represents 50% of subfertility patients (Table IV).

Type	Subfertility		No Subfertility
	Primary	Secondary	
Bicornuate	2	1	2
Unicornuate	0	0	2
Didelphyus	0	1	1
Arcuate	0	0	1
Total	2 (20%)	2 (20%)	6 (60%)
	4 (40%)		

Table III: Fertility in respective congenital uterine anomalies (n=10).

Type	Primary Subfertility	Secondary Subfertility
Bicornuate	2	0
Unicornuate	0	0
Didelphyus	0	0
Arcuate	0	0
Total	2 (50%)	0

Table IV: Fertility outcome (conception) in subfertiliy after ovulation induction in respective congenital uterine anomalies (n=4).

50% patients presented during their first pregnancy (primigravida) and 50% patients had previous one living child without history of previous miscarriage (Table V).Two bicornuate uterus with primary subfertility got pregnant for the first time after ovulation induction and got luteal phase progesterone support but unfortunately both ended with early pregnancy loss(25%).Prophylactic progesterone were continued in three early pregnancy with CUA patients and in one patient with history of preterm birth without knowing to have unicornuate uterus. One unicornuate uterus and one arcuate uterus patients were not diagnosed prior to caesarean section and didn't receive any prophylactic progesterone. Duration of current pregnancy was concluded with term delivery in five cases (62.5%) and preterm birth (12.5%) in only one acruate uterus.(Table VI and Table VII).Among the six patients who entered into second trimester, five patients (83.3%) experienced pregnancy complications (Table VIII).Among 5 term pregnancy birth three cases (60%) had birth weight between 2.6-3 kg and two cases (40 %)had birth weight 2.5 kg(Table IX).

Type	First pregnancy	Previous miscarriage	Living child term delivery	Living child preterm delivery
Bicornuate	3	0	2	0
Unicornuate	0	0	1	1
Didelphyus	1	0	1	0
Arcuate	1	0	0	0
Total	5 (50%)	0	4 (40%)	1(10%)
			5 (50%)	

Table V: Obstetric record of respective congenital uterine anomalies (n=10)

Type	Luteal phase	From early pregnancy	No support
Bicornuate	2	2	0
Unicornuate	0	1	1
Didelphys	0	1	0
Arcuate	0	0	1
Total	2 (25%)	4 (50%)	2 (25%)

Table VI: Progesterone support in current pregnancy in respective congenital uterine anomalies (n=8).

Type	<12 weeks	12-28 wks	28-34 wks	34 -37 wks	>37wks
Bicornuate	2	0	0	0	2
Unicornuate	0	0	0	0	2
Didelphyus	0	0	0	0	1
Arcuate	0	0	1	0	0
Total	2 (25%)	0	1 (12.5%)	0	5 (62.5%)

Table VII: Current pregnancy duration in respective congenital uterine anomalies (n=8)

Type	Threat -ened preter -m labour	Concealed abruptio placenta	PPROM	PROM	Breech
Bicornuate	1	1	0	0	0
Unicornuate	1	0	0	0	1
Didelphyus	0	0	0	1	0
Arcuate	0	0	1	0	0
Total	2(33.3 %)	1(16.6%)	1(16.6 %)	1(16.6 %)	1(16.6%)

Table VIII: Complications encountered during 2nd and 3rd trimester of current pregnancy in respective congenital uterine anomalies (n=6)

Type	2.5 kg or less than 2.5 kg	2.6-3kg	>3 kg
Bicornuate	0	2	0
Unicornuate	1	1	0
Didelphyus	1	0	0
Total	2(40%)	3(60%)	0

Table IX: Birth weight of term current pregnancy in respective uterine anomalies (n=5)

IV. Discussion:

Congenital uterine anomalies was first reported by Cruveilher, Foerster and Von Rokitansky in the middle of 19th century [2].The actual prevalence of CUAs with reproductive failure remain unclear. Inheritance pattern in patients with uterine anomalies is most likely a polygenic mechanism and not inherited commonly in a dominant fashion [4].The mullerian ducts originate from the coelomic epithelium at 5 weeks of embryonic age and fuse with urogenital sinus at 8 weeks [5]. Initially the fusions of the ducts are incomplete with a persisting septum between the lumina. Later, the septum disappears to create a single cavity .The upper part of the cavity forms the lumen of the body and cervix of the uterus. The myometrium is derived from the surrounding mesenchyme [6].Mullerian ducts deformities can occur in different steps of embryogenesis : 1) Failure of one or more duct to develop (Agenesis, unicornuate uterus without rudimentary horn) 2) Failure of duct to canalize(unicornuate uterus with rudimentary horn) 3) Failure of fusion of the ducts(Didelphys uterus , bicornuate uterus) 4) Failure of resorption of mid line septum (septated uterus, arcuate uterus) [7].Agenesis of a mullerian duct is often associated with absence of an entire kidney on the ipsilateral side [8].

Latest classification system for female genitourinary congenital malformation (Mullerian anomalies classification 2021)was introduced by The American Society for Reproduction Medicine (ASRM) in 2021 based on similar elements of appearance, presentation and treatment which comprises into 7 main groups:1) Mullerian agenesis 2) Cervical agenesis 3) Unicorn uterus4) Didelphys uterus5) Bicornuate uterus6) Septated uterus7) Longitudinal vaginal septum 8) Transverse vaginal septum 9) complex anomalies [9]. Common congenital uterine anomalies are uterine septum, unicornuate uterus, bicornuate uterus and uterus didelphys [10].

Majority of the congenital uterine anomalies are asymptomatic and detected incidentally [2].The definitive diagnosis of these malformations are essentially para-clinical using ultrasonography, hysterosalpingography, sonohysterosalpingography ,MRI and even endoscopy. Each of these diagnostic tools has different accuracies with various pros and corns. Two dimensional ultrasound and hysterosalpingography have the lowest accuracy rates which would not warrant its diagnostic use. In contrast, sonohysterosalpingography has been shown highly accurate in diagnosis and classification of CUAs. Three dimensional ultrasonography is also very accurate diagnostic tool. MRI seems a relative sensitive diagnostic tool and could supplant invasive procedures. Many considers combined hysteroscopy and laparoscopy as gold standard as it allows direct visualization of internal and external contour [11] .Ultrasound allows simultaneous assessment of a urinary tract anomaly. Fibroid or other mass may sometimes be confused with mullerian anomalies in ultrasound. In this study, a patient presented with secondary subfertility and history of one term vaginal delivery. Her ultrasonoghaphy showed a pelvic mass and later laparotomy confirmed the diagnosis of didelphys uterus.

Management of congenital uterine anomalies prior to conception and after conception depends on its type and obstetric outcomes. Main aim of management is to prevent complications or manage complications for successful pregnancy outcomes. Surgical correction is

considered after correct diagnosis and ruling out other causes of infertility and recurrent pregnancy loss because a wrong surgery can end with poor fertility outcome. Studies showed impressive improvement of reproductive performance in bicornuate uterus after Strassman mertoplasty operation [12] and in septated uterus after hysteroscopic resection of septum[13].Cervical cerclage has been shown to be effective in preventing preterm births and should be considered for women with CUAs having history of cervical insufficiency, history of preterm birth or cervical shortening in current pregnancy [14].

Congenital uterine anomalies have been reported in 6.3% in the infertile population and 25-38% among the early miscarriage populations [1].None of unification defects (bicornuate uterus and didelphys uterus) lead to reduced fertility. Canalization defects (septated /subseptated uterus) lead to reduced fertility, increased miscarriage and preterm birth [15]. Prevalence of early pregnancy loss and late complications significantly higher in vascularized septum than those with non-vascularized septum [7].The exact cause of infertility in CUAs remain unclear. Women with rudimentary horns are at risk of developing endometriosis. Incompetent uterine and placental blood flow, uterine muscle insufficiency and cervical weakness causes pregnancy loss [16]. In our study subfertility was observed in three bicornuate uterus and one didelphys uterus.

Congenital uterine anomalies have been reported in 25-47% in women with preterm birth[1].Fox et al noted highest risk of preterm birth in female with unicornuate uterus (50%) followed by those with a bicornuate uterus (39.1%), didelphys uterus (33.3%),unrepaired septated 25%,repaired septated 16% and arcuate uterus (7%) [17]. Late pregnancy miscarriage and preterm birth is due to irregular contraction of uterus or reduced uterus capacity caused by unequal uterine shape [18].Hua M et al reported CUAs incidence 7% in preterm premature rupture of membrane (PPROM) and incidence 23.6% in Breech [10]. In our study only one primigravida patient with undiagnosed arcuate uterus had preterm delivery at 33 weeks for PPROM and diagnosed during caesarean section. One patient with undiagnosed unicornuate had first pregnancy preterm delivery at 34 weeks. She also had threatened preterm labour in current pregnancy. One primigravida patient with bicornuate uterus (communicating type) case had premature uterine contraction without cervical changes (Threatened preterm labour) at 34 weeks. They were managed for threated preterm labour by complete bed rest, progesterone support, nifedipine and finally delivered at term. One bicornuate uterus and one didelphys uterus patient reported for secondary subfertility but they had previous term delivery. So term delivery was observed in seven patients out of eight which accounts 87.5%.

One bicornuate uterus (partial type) presented with pain abdomen without per vaginal bleeding at 29 weeks. She was hemodynamically stable and ultrasonography showed concealed abruption of placenta. Hospitalization, clinical monitoring, progesterone support, nifedipine and measurement of retro-placental clot by serial ultrasound and delivered at term. .

A retrospective cohort study found higher rate of caesarean section due to malpresentation and previous caesarean section [19].All cases of our study underwent cesarean section. A study reported birth weight less than 10th percentile with didelphys uterus (50%), bicornuate uterus (28.3%), arcuate uterus (21%), unicornuate uterus (18.8%), repaired septated (12%) and unrepaired septated (6.2%) [17] . Our study recorded birth weigth 2.5 kg in term pregnancy with one didelphus uterus and one unicornuate uterus. Frequently occurred fetal congenital anomalies are nasal hypoplasia, omphalocele, limb deficiencies, teratomas and acardia-anencephaly [20]. In our study there were no low birth weight and no such fetal congenital anomalies.

V. Limitations:

This study has no control group and study population is very small. The duration of study was also short. Serial cervical length and fetal fibronectin were not assessed for prediction of preterm birth. Further detailed study is needed to assess the fertility and pregnancy outcome in CUAs.

VI. Conclusion:

Congenital uterine anomalies are a matter of concern in reproductive age as they are associated with poor fertility and adverse pregnancy outcome. Therefore, high index of suspicion is required in order to diagnose these anomalies especially in low resource setting. Diagnostic tools should be chosen considering its availability, cost effectiveness and appropriateness to individual. Counseling of women about prognosis, anticipation and preparedness to deal with known complications ensures positive fetomaternal outcome. Therefore, a nation wide register to reported cases is essential for improving pregnancy outcomes and fetal survival.

Acknowledgement:

Our sincere thanks and acknowledgement to all patients enrolled in this study for their kind cooperation and all staffs of department of Obstetric & Gynaecology, Anaesthesiology and Paediatrics for tireless effort to manage all cases.

Reference:

1) F. Raga, C. Bauset, J. Remohi, et al. Reproductive impact of congenital Mullerian anomalies. Hum Reprod.1997;12:2277-81.

2) K. Jayaprakasan , K. Ojha. Diagnosis of Congenital Uterine Anomalies :Practical Consideration.J Clin Med. 2022 March;11(5):1251

3) P.K. Heinonen. Uterus didelphys:a report of 26 cases .Eur J Obstet Gynecol Reprod Biol.1984 July;17(5):345-50.

4) J.C. Petrozza, M.R.Gray, A.J.Davis, R.H. Reindollar RH. Congenital absence of the uterus and

vagina is not commonly transmitted as a dominant genetic trait: outcomes of surrogate pregnancies. Fertil Steril .1997;67(2):387-9
5) American Fertility Society classification of Mullerian Anomalies (1988). Fertility and Sterility .49:944-955
6) D. Madhavi. Bicornuate Uterus –A Case Report.Anat Physiol .2012;2:109.
7) S. Kupesic. Clinical implications of sonographic detection of uterine anomalies for reproductive outcome. Ultrasound Obstet Gynecol 2001 Oct 1;18 (4):387-400.
8) J.A. Rock, L.L Breech. Surgery for anomalies of mullerian ducts. In: J.A.Rock, H.W. Jones III, editors. Telinde's Operative Gynaecology 10th ed. Philadelphia: Lippincott Williams and Wilkins; 2011.
9) S.M. Pefeifer, M. Attaran, J. Goldstein et al. ASRM mullerian anomalies classification (2021). Fertil and Steril. 2021 Nov116 (5)1238-1252
10) M.Hua, A.O.Odibo, R.E.Longman, et al. Congenital uterine anomalies and adverse pregnancy outcomes. Am J Obstet Gynecol. 2011; 205(6):558.
11) S.H. Saravelos,K.A.Cocksedge and T. Li. Prevalence and diagnosis of congenital uterine anomalies in women with reproductive failure : a critical appraisal. Hum Reprod Upadate. 2008 Sept-Oct; 14(5):.415-429.
12) D.E.Lolis , M.Paschopoulos,G.Makrydimas, et al. Reproductive outcome after starssmanmetroplasty in Women with a Bicornuate Uterus .J Reprod Med .2005 May;50(5):297-301
13) H.A.Homer, T.C.Li, I.D. Cooke.The Septated Uterus: A review of management and reproductive outcome. Fertil and Steril. 2000 Jan;73(1):1-14.
14) D.E. Reichman, M.R.Laufer. Congenital uterine anomalies affecting reproduction. Best Practice and Research Clinical Obstet Gynaecol .2010 April;24(2):193-208
15) Y.Y.Chan, K.Jayaprakasan, A. Tan, et al. Reproductive outcomes in women with congenital uterine anomalies: a systematic review. Ultrasound Obstet Gynecol .2011 Oct;38(4):371-82
16) H.Hosseinirad, P.Yadegri, F.M.Falahieh et al. The impact of Congenital Uterine Anomalies on pregnancy and Fertility, a literature review .JBRA Assist Reprod. 2021 Oct-Dec;25 (4): 608-616
17) N.S.Fox, A.S. Roman, E.M.Stern, et al.Type of congenital uterine anomaly and adverse pregnancy outcome. J Matern Fetal Neonatal Med. 2014 Jun;27 (9):949-53.
18) S. Choudhary, P. Jelly, P.Mahala. Successful outcome of pregnancy in bicornuate uterus: a case report. Int J Reprod Contracept Obstet Gynecol. 2019 .Oct ;8 (10): 4086-4089.
19) L. Hierch, E.Yeoshoua, H. Miremberg, et al. The association between mullerian anomalies and short term pregnancy outcome .Journal of Maternal Fetal Neonatal Medicine.2016; 29 (16):2573-8
20) M.L. Martinez–Frias, E. Bermejo, E. Rodriguez-pinilla, J.L.Frias. Congenital uterine anomalies In the offspring of mothers with a bicornuate uterus. Pediatrics. 1998; 101 (4) :E10.