

Reproductive Outcome in Women with Congenital Uterine Anomalies

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Abstract

Background: Mullerian duct malformations delineate a group of congenital anomalies that result from arrested development, or incomplete fusion of the mesonephric ducts. In many patients, uterine anomalies have been related with infertility, recurrent pregnancy loss, prematurity and other obstetric complications which increase perinatal morbidity and mortality rates, where as in others these malformations are asymptomatic and have normal reproductive performance.

Purpose: To determine the reproductive outcome in women with congenital uterine anomalies.

Design: Descriptive cross sectional survey.

Main Outcome Measures: Miscarriages, Preterm delivery, Ectopic pregnancy, Term delivery.

Material and Methods: A total of 1600 infertile women in the age group of 25 – 35 years were recruited in the outpatient department of Gynae and Obstetrics in Sharif Medical City Hospital from June, 2008 to June, 2009. The patients included in study were the women presenting with either primary or secondary infertility, bad obstetrical history, recurrent miscarriage, preterm deliveries, and ectopic pregnancies. Combined finding of trans-vaginal ultrasonography and hysterosalpingography were used to diagnose congenital uterine anomalies. 48 women were diagnosed with congenital uterine anomalies. Eight patients of primary infertility with uterine anomalies were excluded. The retrospective analysis of 40 cases with secondary infertility and uterine anomalies was done for

reproductive performance.

Results: Among 1600 infertile women, the average age of the study group was 30 years \pm SD 4.77. Forty eight patients were diagnosed with congenital uterine abnormalities. Among infertile population the most frequent uterine anomalies was bicornuate uterus (45.83%) followed by arcuate uterus (33.33%). The overall frequency of congenital uterine anomalies was 3%. Women with secondary infertility (83.3%) had higher frequency of mullerian duct anomalies in comparison to women with primary infertility (16.7%). In all these abnormalities, miscarriages (25%) and preterm delivery (22.5%) were quite common. ($P < .0750$). The reproductive potential of the bicornuate uterus showed a live birth rate of (67%) and, arcuate uterus of (42.8%). Unicornuate and Septate uterus were associated with poor obstetrical outcome.

Conclusion: Congenital uterine anomalies are relatively frequent among infertile population and are associated with higher miscarriages and preterm births but may be compatible with normal reproductive outcome.

Key Words: Uterine anomalies, preterm birth, miscarriages.

Introduction

The mullerian ducts are the primordial analogue of female genital tract. They differentiate to form the fallopian tubes, uterus, cervix and the superior aspect of vagina. A wide variety of malformations can occur when this system is disrupted. They range from uterine and vaginal agenesis to duplication of uterus and vagina to minor uterine cavity abnormalities.

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The importance of diagnosing uterine malformations lies in their association with miscarriage and infertility. Some mullerian defects can have normal reproductive outcome. The prevalence of major uterine anomalies is estimated to be 5% in general fertile population, 3% in infertile, and 5 – 10% in recurrent miscarriages.¹

These malformations affect negatively the reproductive performance of the uterus leading to increased incidence of abortions and preterm deliveries especially in women with unicornuate, bicornuate, didelphys and septate uteruses. This is seen clinically as an increased rate of primary infertility (failure to conceive) or more often as an increase rate of early pregnancy loss (impaired implantation and early development). Later in pregnancy, unsuspected uterine malformations may present as impaired intrauterine fetal growth due to abnormal placentation, or abnormal fetal positioning related to mechanical factors in the shape of the uterine cavity. Labour, delivery, and third stage problems may occur due to in – coordinate uterine muscular activity.^{2,3}

Patients with a bicornuate uterus and no extrauterine infertility issues usually have little difficulty in conceiving. Spontaneous abortion rates are reported to range from 28% to 35%. Premature birth rates range from 14% to 23%.⁴

The prevalence of septa in patients who have had recurrent spontaneous abortions (usually three or more) is well known, with reported spontaneous abortion rates ranging from 26% to 94% and the overall premature birth rates ranging from 9% to 33%.^{1,4}

Data regarding the reproductive outcomes of patients with an arcuate uterus are extremely limited and widely disparate. In small studies, both poor and good obstetric outcomes have been reported, although an arcuate configuration is generally thought to be compatible with normal – term gestation, with a quoted delivery rate of 85%.⁵

A didelphys uterus is very rare anomaly and it can lead to a pregnancy failure. Spontaneous abortion rates are reported to range from 32% to 52% and premature birth rates range from 20% to 45%.¹⁻³

The aim of present study was to establish the frequency of congenital uterine anomalies in infertile population and to determine the reproductive performance of the different types of uterine malformations in women with secondary infertility.

Operational Definitions

Infertility

The couple who has not conceived after 12 months of contraceptive – free intercourse.

Primary Infertility

The couple who has never conceived.

Secondary Infertility

Difficulty in conceiving after already having conceived (and either carried the pregnancy to term, or had a miscarriage).

Miscarriage

Mean loss of embryo or fetus before 20th week of pregnancy.

Preterm Delivery

Birth of an infant before 37 completed weeks (259 days) of gestation.

Term Delivery

Birth of an infant between 37 completed weeks to 42 weeks of gestation.

Ectopic Pregnancy

A pregnancy that occur outside the uterus.

Live Birth

The birth of a newborn, irrespective of the duration of gestation, that exhibits any sign of life, such as respiration, heartbeat, umbilical pulsation, or movement of voluntary muscles.

Pregnancy Outcome

The results of conception and ensuing pregnancy like term deliveries (**Good outcome**), or miscarriages, preterm births and ectopic pregnancy (**Bad outcome**).

Material and Methods

This study was carried out in one year duration in the

department of Gynae and Obstetrics in Sharif Medical City Hospital from June, 2008 – June, 2009. A total of 1600 infertile patients were recruited in study group that were in the age group of 25 – 35 years. The patients included in study were the women presenting with either primary or secondary infertility, bad obstetrical history, recurrent abortions, preterm deliveries, and ectopic pregnancies using temporal sampling. It was a descriptive cross sectional survey.

All patients underwent detailed history regarding, menstrual pattern, duration of infertility, type of infertility, and obstetrical outcome. A detailed general physical, abdominal and pelvic examination was performed. Husband semen analysis was a pre-requisite for study group. All women underwent 2D transvaginal ultrasonography followed by hysterosalpingography.

A conventional B-mode two dimensional transvaginal ultrasonography was performed using 7.5 MHZ probe. The longitudinal axis of the uterus from isthmus to fundus was first defined. A series of parallel transverse sections was then done starting from the internal os to the top of uterine fundus. When there was any duplication or splitting of endometrial echoes, congenital anomalies were suspected.

All HSG were performed during the follicular phase of menstrual cycle. Fractionated technique under fluoroscopic guidance using iodinated water soluble contrast medium (urographin) was used. The initial

x-ray was taken after the injection of 3 – 4 ml of contrast material. 2 – 3 serial films were taken. Combined finding of ultrasonography and HSG were used to diagnose the uterine anomalies.

The following criteria's were included to differentiate between septate, bicornuate, arcuate and didelphys uterus.

Septate uterus (intercornual distance < 4 cm, intercornual angle < 60, and on USG indentation between horns absent).

Bicornuate uterus (intercornual distance > 4 cm, intercornual angle > 60%, and on USG indentation between the horns present).

Didelphys uterus (Horns widely splayed, 2 cervixes and cavities imaged and two widely splayed horns).

Arcuate uterus (concave fundal indentation with central point of indentation at an obtuse angle, external contour uniformly convex or with < 10 mm indentation).

Uterine anomalies were classified according to American fertility society into VII types (Fig. 1).

Exclusion Criteria

Patients with Class I (have no reproductive potential) and VII with uterine were excluded from study as class I defects are more often seen in pediatric and endocrine clinics because of primary amenorrhea. In addi-

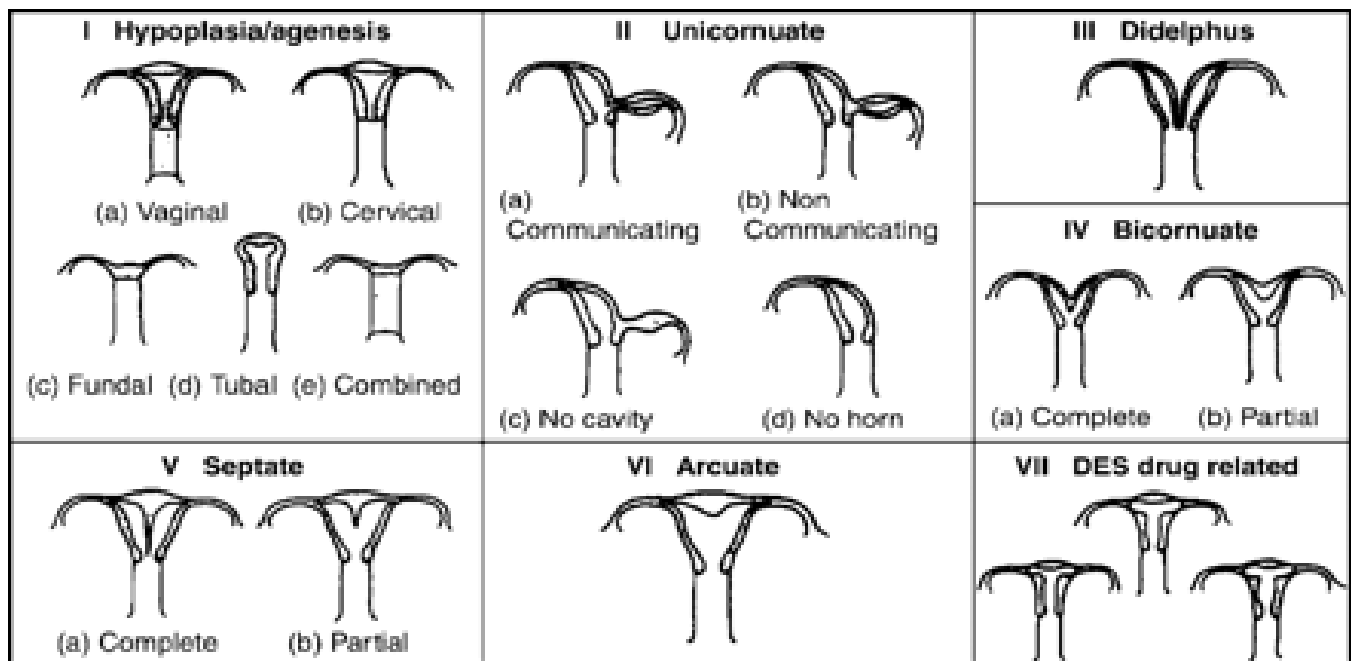


Figure 1: Classification of Congenital Uterine Anomalies.

tion, exposure to diethylstilbestrol (DES) was very seldom documented in the Pakistani population, but this observation is not relevant because it is an induced malformation dependent on the use of a medication in a given country. In addition patients in whom the cause of infertility was other than uterine anomalies were excluded. Eight patients with primary infertility having mullerian duct anomalies were excluded as they are sterile and never conceived.

Forty cases with secondary infertility and congenital uterine abnormalities were analyzed for reproductive performance i.e miscarriage, preterm birth, live birth, ectopic pregnancy (operational definitions).

The pregnancy outcome was observed as good (live births) and bad (miscarriages, preterm birth, and ectopic pregnancy). The data was analyzed using research Performa on computer using SPSS 11 applying “t” test for numerical data and Chi-square for nominal data. Data was analyzed regarding type of uterine anomalies and their reproductive performance. P value of <. 05 was considered as statistically significant.

Results

During the study period a total of 1600 infertile patients were recruited. Out of which 48 patients were diagnosed with uterine anomalies, rests have normal uteri. The average age of the study group was 30 years ± SD 4.77. The overall frequency of uterine anomalies in the study population was 3%. Among 48 patients, 8 patients were with primary infertility (16.7%) and 40 patients with secondary infertility (83.3%) (Fig. 2).

Regarding distribution of uterine anomalies in infertile study group, the most common uterine anomaly diagnosed was bicornuate uterus (45.83%) followed by arcuate uterus (33.33%), septate uterus (10.41%), didelphys (6.25%), and unicornuate (4.16%) uterus respectively (Fig. 3). Among patients with primary infertility, 8 patients (16.7%) have congenital uterine

anomalies, out of which 4 patients (50%) have bicornuate uterus, 2 patients (25%) have arcuate uterus, 1 septate (12.5%), and (112.5%) didelphys uterus (Fig. 4).

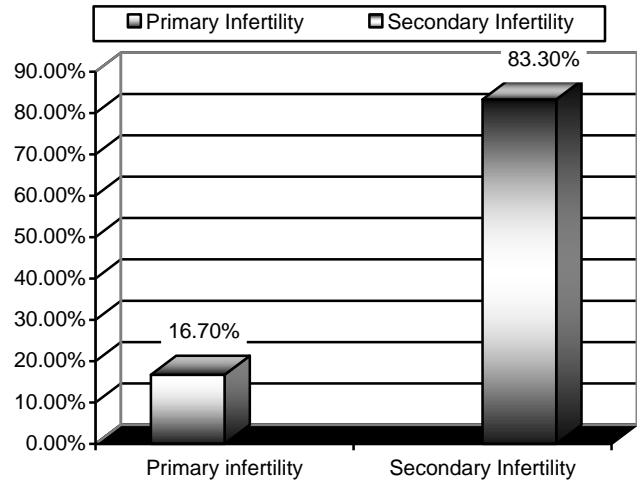


Figure 2: Frequency of Uterine Anomalies in Infertile Population.

The reproductive performance in 40 women with secondary infertility having congenital uterine anomalies was further analyzed for outcome (Table 1).

The total number of miscarriages in patient with uterine anomalies group was 10. The frequency of miscarriages was (25%), and preterm delivery rate was (22.5%) and term delivery rate of (47.5%) among women with congenital uterine anomalies. Ectopic pregnancy was observed in 2 patients (5%) in women with unicornuate and bicornuate uterus. The best pregnancy outcome was observed in bicornuate uterus with live birth rate of (67%). The worst pregnancy outcome was observed in unicornuate uterus and septate uterus with high rates of ectopic, preterm delivery and miscarriages (P <. 075).

Table 1: Reproductive Outcome of Women Secondary Infertility Having Congenital Uterine Anomalies N = 40.

Outcome	Bicornuate N = 18	Arcuate N = 14	Subseptate N = 4	Unicornuate N = 2	Didelphys N = 2	Total (%age) N = 40 (100.0%)
Miscarriage	2	4	2	1	1	10 (25%)
Ectopic pregnancy	1	0	0	1	0	2 (5%)
Preterm deliveries	3	4	2	0	0	9 (22.5%)
Term deliveries	12	6	0	0	1	19 (47.5%)

P value (.075)

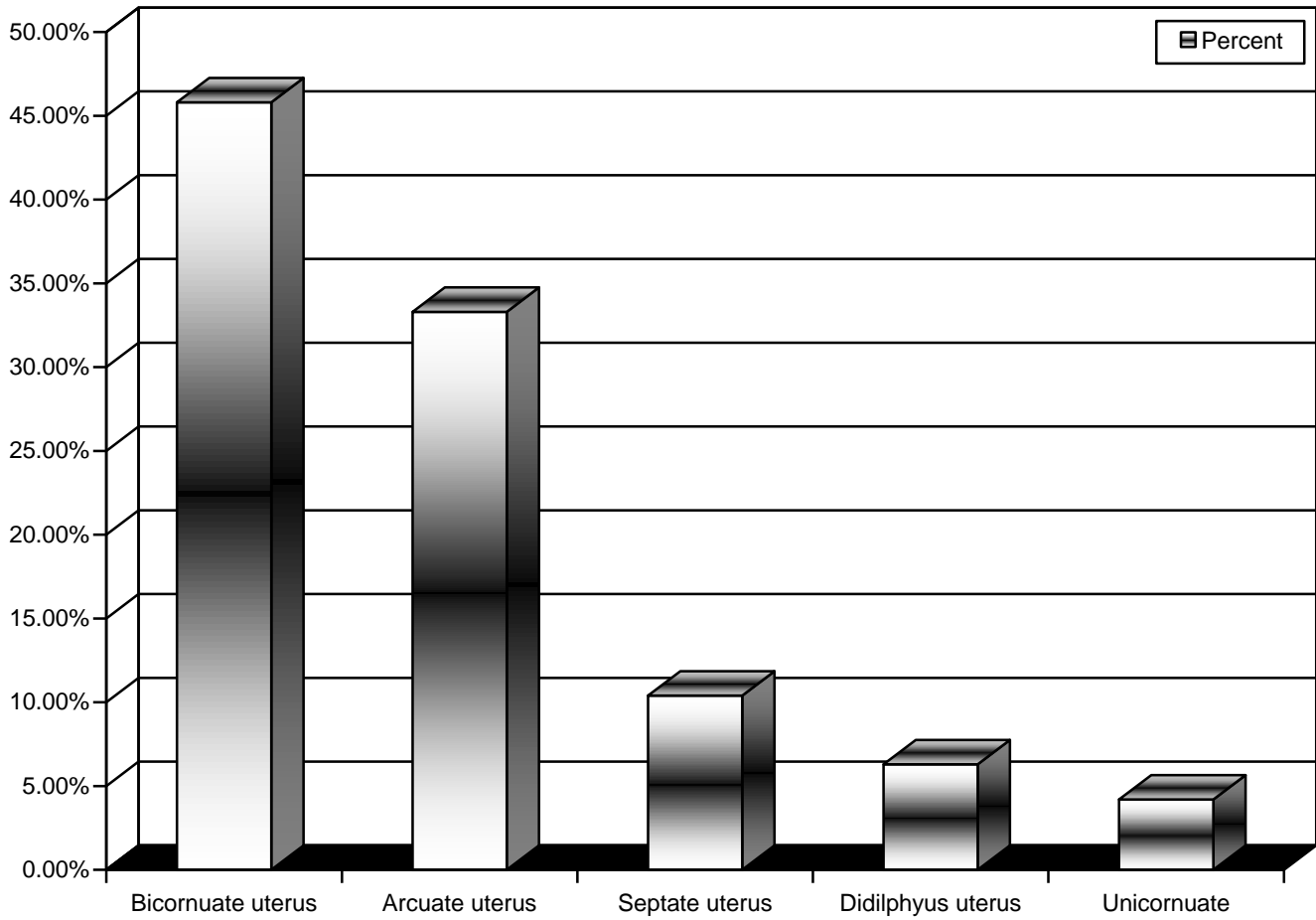


Figure 3: Distribution of Uterine Anomalies among Infertile Couple.

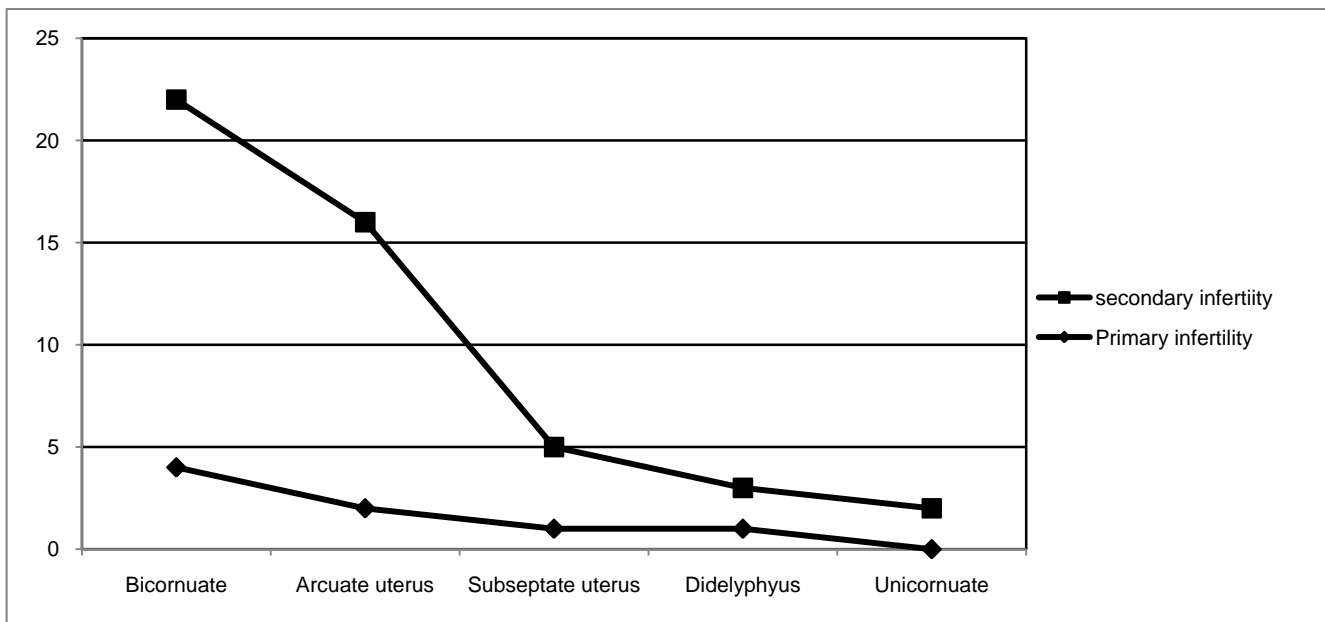


Figure 4: Distribution of Uterine Anomalies in Infertile Population = 48.

Discussion

Congenital uterine anomalies have always been a topic of considerable interest amongst Obstetricians and Gynecologists. Besides being mere anatomic curiosities, pregnancy in these patients may present with unusual and difficult obstetrical problems of which the most significant is recurrent pregnancy wastage. Though infrequent these uterine anomalies have now become sufficiently important to demand the attention of every practicing obstetrician.

The prevalence of uterine anomalies varies widely between 0.1 – 3.5 percent.³ The prevalence was higher among women with fertility problems as compared to general population. In our study the frequency of congenital uterine anomalies was 3% with 83.3% in women with secondary infertility and 16.7% in women with primary infertility. Raga (1995) reported that the overall frequency of uterine malformation was 4.0% comparable to our study.⁴

Women with primary infertility showed lowest frequency of uterine malformations and only eight of them (16.7%) presented with this problem. This disagrees with previous reports that have found a high incidence of uterine anomalies in patients with no obvious cause of primary infertility, but agrees with others who maintain that sterility in these women is generally caused by extrauterine factors, and in fact patients with congenital malformations undergoing in-vitro-fertilization and embryo transfer have good pregnancy rate.⁵

The bicornuate uterus results when two normally differentiated ducts partially fuse in the region of the fundus. Patients with bicornuate uterus have little difficulty in conception and live birth rate of 57 to 63% has been reported in literature. Spontaneous abortion rate varies from 25 – 35%, and preterm birth 14 – 23%. The most frequent congenital uterine abnormality identified in study group was bicornuate uterus (46%). It was found that bicornuate uterus was associated with better outcome with a term delivery rate of (67%), and miscarriage in 11% and, preterm births in 16%. The results are comparable to study by Rega et al with a term delivery rate of > 60%.⁴ Although this disagree with previous reports on a poor reproductive outcome associated with bicornuate uterus (Acien 1990, Green and Harris 1976).^{3,5}

The arcuate uterus is a simple change in the uterine cavity shape with no external dimpling. Data regarding arcuate uterus was extremely limited and widely disputed. The term delivery rate of 85% has been

quoted. In our study the second commonest uterine abnormality was arcuate uterus (33.33%) with live birth rate of (43%), abortion (28%), and preterm birth (28.5%). This agrees with results of Acein in which arcuate uterus is associated with poor survival and abortion rate.³

The septate uterus results from the failure of resorption of the medial segment of the Mullerian duct. Septate uterus is associated with abortion rate of 26 – 94%, preterm birth (9 – 33%) and term delivery rate varies from 10 – 75%. In our study the abortion and preterm birth rate both were 50% comparable to study by Green Haris, Heinone and Woelfer B, Salim in which the Septate uterus is associated with poor outcome.⁵⁻⁷ Recurrent pregnancy loss in these patients was attributed to the fibrous and avascular nature of the septum. Reproductive outcome has been shown to improve after resection of the septum with reported decrease in spontaneous abortion rate from 88% to 6% after metroplasty.

The unicornuate uterus results from normal differentiation of only one Mullerian duct. In our study the worst pregnancy outcome was in unicornuate uterus with 50% abortion and 50% ectopic pregnancy. Ectopic pregnancy was in rudimentary horn.⁶ These findings are comparable to study by Munire E. AKAR et al where the reproductive performance of women with unicornuate uterus was poor, with a live birth rate of only 29.2%, prematurity rate of 44%, miscarriage rate of 29%, and an ectopic pregnancy rate of 4%. The worst pregnancy outcome observed in septate and unicornuate uterus suggests that some form of corrective measures should be done in order to improve the chances of live birth like cervical cerclage, and metroplasty in women suffering from this uterine anomalies.⁸

The didelphys uterus results from complete failure of the Mullerian ducts to fuse in the midline. The frequency of didelphyus in infertile population was (6%). In our study (6.3%) patients have didelphyus uterus. In didelphys uterus spontaneous abortion rate ranges from 32 – 52%, term delivery rate of 41 – 64%. In our study the abortion rate was 50% with term delivery rate of 50%.¹¹

Ectopic pregnancy was observed in 2 patients with an overall prevalence of 5%.

The frequency of abortion and preterm birth in our study was 25% and 22.5% respectively (P value .075). According to literature, the pregnancy loss has been higher than general population though the rates vary from study to study (Table 2).

Table 2: Rate of Pregnancy Loss in Literature.

Rate of Pregnancy Loss		
Study	Spontaneous Abortion	Preterm Delivery
Raga et al ⁴	28%	30%
Michalas, et al ⁹	36%	22%
Stein et al ¹⁰	14%	25%
Heinonen et al ⁶	29%	23%

These results confirm earlier reports that patients with uterine malformations have higher rates of reproductive loss, preterm delivery, that increase obstetric intervention and perinatal mortality but the results are not statistically significant ($P < .075$) and require large clinical trial in Pakistan.

Limitation and Further Studies

The limitation in this study was that we did not use 3 – D sonography for all patients; we should utilize it, as it is accurate than other modalities but less sensitive in the presence of fibroids. Moreover, we did not send all the women to perform the special procedures such as MR, hysteroscopy, and Laparoscopy. We could miss many uterine malformations by using TVS and HSG alone. Future studies should focus on the distributions and the percentages of each anomaly and correlate them with the general population.

Conclusion

Uterine anomalies are relatively frequent among infertile women. There is association between congenital uterine anomalies and adverse reproductive outcome but mullerian defects can permit normal delivery. The reproductive performance of the unicornuate and Septate uteri was poor, while that of the bicornuate uteri was better than expected.

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