Studying the Reproductive Performance among Women with Congenital Uterine Anomalies. An observational descriptive study at Mansoura University Hospitals

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Running title: The reproductive outcome of uterine anomalies

Abstract

Background and aim: To study the pattern of congenital uterine anomalies and their impact on reproductive outcomes.

Methods: A Prospective clinical study included 100 women of childbearing age with reproductive failure either infertility, repeated miscarriage, or preterm birth, and diagnosed to have congenital uterine anomalies either inside or outside Mansoura university hospitals. Hysterosalpingogram (HSG), hysteroscope, and or laparoscope were performed to confirm the undiagnosed cases. The main outcome measure was reproductive complications among studied patients.

Results: The mean age (+SD) of the studied cases was 27.07 (+4.04) years, with the frequency of complaints as failure to conceive being recorded as the commonest (45%), 27 cases as primary while 18 as secondary infertility with a duration shorter in primary than secondary infertility (3.01± 1.1 vs 4.02± 1.2 respectively) followed by recurrent pregnancy loss (39%), preterm labor (13%), and lastly acute abdominal pain (3%). On the other hand, anomalies demonstrated according to their frequencies were arcuate uterus (35%), bicornuate unicolis uterus (17%), incomplete uterine septum (15%), complete uterine septum (9%), didelphys uterus (7%), uni-cornuate uterus with a rudimentary horn (6%) and without a horn (6%), complete uterine agenesis (4%) and lastly T-shaped uterus (1%). Ninety-one patients got pregnant after intervention but 21 ended by abortion, and 27 had preterm labor meanwhile the rest (43) passed fetal maturity despite some complications already occurred in about 65% of them including low birth weight (17) premature placental separation (8), and rupture uterus (3). All cases planned for delivery were delivered by Lower segment cesarean section.
**Conclusion:** There is a strong association between congenital uterine anomalies and adverse reproductive outcomes. The arcuate uterus was the commonest congenital uterine anomaly found in the study and this occurred mostly among women presenting with secondary infertility or recurrent pregnancy loss.

**Keywords:** Uterine anomalies; hysteroscopy; reproductive outcome.

**Synopsis:** There is a large variety of uterine anomalies among females with poor reproductive performance. Despite many patients may be detected during fertility workups but a remarkable number could present with poor pregnancy outcomes.

**Introduction**

Globally, congenital uterine anomalies (CUAs) are present in 1-10% of women and constitute 2-8% of infertile women and 5-30% of women with a history of miscarriage. This discrepancy in the prevalence rates is mostly related to the use of different diagnostic tests and the use of non-standardized classification systems to diagnose these anomalies [1]. Common categories of anomalies are agenesis, hypoplasia, uni-cornuate uterus, uterus didelphys, bicornuate uterus, septate uterus, arcuate uterus, and diethylstilbestrol-exposure related anomalies namely T-shaped uterus [2, 3].

Clinically CUAs may present by a variety of symptoms such as pelvic pain, prolonged or otherwise abnormal bleeding starting from the time of menarche, inability to conceive, recurrent pregnancy loss, or preterm birth. Consequently, these anomalies could be suspected in girls and women who present with one or more of these disorders [4]. Also, it could be suspected with ectopic pregnancies in primigravida, malpresentation, and intra-uterine growth restriction of unexplained etiology [4,5]. Imaging modalities are largely relied up on diagnosing and classifying uterine anomalies. Of these, the commonly used utilities are two-dimensional ultrasonography (2DUS), three-dimensional ultrasonography (3DUS), hysterosalpingography, saline infusion ultrasonography, and magnetic resonance imaging (MRI). A 3DUS proved to be highly accurate in diagnosing uterine anomalies and may be equivalent to MRI [2]. Even after management, patients with CUAs appeared to have increased morbidity and mortality both for the mother and fetus owing to the presence of pregnancy or labor-related problems [5]. This study was conducted to study the prevalence and patterns of CUAS and their association with reproductive outcomes.

**Patients and methods**

This observational prospective study had been carried out on 100 women of childbearing age with reproductive failure after confirming the presence of uterine anomalies. The patients were selected from those attending outpatient clinics at the fertility care unit and Obstetrics and Gynecology Department at Mansoura University Hospitals, Egypt from April 2020 to April 2022. The study protocol was approved by the Medical Research Committee of the Faculty of Medicine, Mansoura University (IRB Code No. MS.20.03.1059). Confidentiality and personal privacy were respected at all levels of the study. All women had written consent to participate after a verbal discussion about the role of the study and any patient who refused to share was withdrawn immediately. The collected data was not used for any other purpose.

Inclusion criteria were women of childbearing age with an evident history of reproductive failure including infertility, recurrent miscarriages, or recurrent preterm birth, and diagnosed to have CUAs confirmed by hysterosalpingography (HSG), hysteroscope, laparoscope, or MRI either before inclusion or confirmed by one or more of these investigations as a part of reproductive
failure work up in the place of the study. Every patient was subjected to a full history taking, demographic details, complaint, duration and type of infertility, and previous obstetric history. Systematic physical examination including general, abdominal, and local pelvic examination was done for all followed by one or more of the mentioned radiological investigations done by an expert radiologist for the detection of anomalies in those who were not diagnosed before. Combined laparoscopy and hysteroscopy were done by the same senior gynecologist for all selected cases under general anesthesia as a routine management step for assuring the diagnosis and surgical intervention when needed. All patients were followed up for 6 months to evaluate the improvement in their reproductive state. Those who proved to be pregnant were then followed up till the end of the journey of their pregnancies and the pregnancy data and outcome were verified. All patients’ demographic data and data gathered during the period of management and follow-up for pregnancy were collected and then subjected to statistical analysis.

**Statistical analysis and data interpretation**

Data was fed to the computer and analyzed using IBM SPSS version 22.0. (Armonk, NY: IBM Corp). Quantitative data were described by using numbers (%) and mean (SD) and then were analyzed by unpaired student t-test whilst nonparametric qualitative data were presented as numbers and percentages and then compared by chi-square (Χ²) or Fisher’s Exact test when appropriate. A two-tailed P value <0.05 was set as statistically significant.

**Results**

A total of 100 patients fulfilled the inclusion criteria of this prospective study. The Demographic parameters were given in table (1). It showed the mean age (SD) of the cases involved was 27.07± 4.04 while the anomalies demonstrated according to their frequencies were arcuate uterus (35%), bicornuate unicolis uterus (17%), incomplete uterine septum (15%), complete uterine septum (9%), didelphys uterus (7%), uni-cornuate uterus with a rudimentary horn (6%) and without a horn (6%), complete uterine agenesis (4%) and lastly T-shaped uterus (1%). On the other hand, the patients’ complaints were arranged as failure to conceive (45%), recurrent pregnancy loss (39%), preterm labor (13%), and acute abdominal pain (3%). In those who were infertile, 27 cases presented as primary and 18 cases as secondary infertility with the mean duration (SD) being shorter in primary than secondary type (3.01± 1.1 vs 4.02± 1.2 respectively). Looking at the pattern of menses, menarche didn’t occur in 4 cases (uterine agenesis) while the majority (87) had regular cycles, intermenstrual bleeding (irregular cycle) was the role in 7 cases and lastly, heavy frequent cycles [polymenorrhagia] was recorded in 2 cases only, table (1). Data from local examination and radiological as well as surgical investigations, namely hysteroscopy and laparoscopy, are represented also in the table (1). In 92 cases, local examination reported normal findings, however, double cervix was confirmed in 8 cases “all cases of uterus didelphys and 1 case of those who had complete uterine septum where the septum was extending to the external os”. Investigations done for cases involved in the study whether inside our hospitals or brought by the patients from the start were gathered and revealed that 2D-US diagnosed the type of anomaly only in 24 cases, while 60 cases were confirmed by 3D-US, and MRI used to confirm the cases of uterine agenesis (4). Despite HSG was done in 96 cases being a basic investigation in such cases but cannot rule out all types of anomalies except after confirmed by hysteroscopy [65 cases] or combined hysteroscopy and laparoscope [85 cases], table (1).
The relation between the patient’s complaints and the type of anomaly diagnosed was represented in table (2). The data showed that the arcuate uterus, bicornuate and unicornuate uterus, and uterine agenesis are the anomalies commonly associated with abortion, infertility, and menstrual abnormalities including amenorrhea that was set as the role in those with agenesis [p-values, 0.045, 0.007, 0.001, 0.001 respectively], table (2).

The reproductive outcome after intervention and pregnancy follow-up data were shown in table (3). Preterm birth was demonstrated in 27 cases but more in those having incomplete uterine septum (p-value 0.002) compared to other types. First and second-trimester abortion was the role in 21 cases and 6 cases occurred in those suffering from the arcuate uterus (p-value, 0.001). On the other hand, low birth weight was demonstrated in 17 cases, 9 of which from those with an incomplete uterine septum (p-value, 0.001). Also, these data reported a higher incidence of fetal malpresentation (15) and rupture uterus (3) with the arcuate uterus and unicornuate uterus with rudimentary horn (p-value, 0.001 in both). Premature placental separation was recorded in 8 cases, 5 of these are from those with an incomplete uterine septum, and 3 from cases of unicornuate uterus with a rudimentary horn (p-value, 0.001 in both). Rupture uterus occurred in 3 cases all of which had unicornuate uterus with rudimentary horn, table (3).

**Discussion**

This study established that CUAs are present and could not be discovered except late after marriage while the patient is seeking fertility or management of pregnancy complications.

While some CUAs are proven to be asymptomatic and pass with normal reproductive outcomes but others proved to be associated with adverse effects [6]. The results of the current study proved that the mean age of the patients involved was 27.07±4.04 years and despite this appears slightly higher in developing countries like ours but comes in accordance with data proved by Nisha et al 2020. [7] and Cahen-Peretz et al 2019. [8] and contrary to the findings published earlier by Vyas et al. [9] who reported that the majority of CUAs related to gynecological cases were observed at 19.03 years. This discrepancy could be explained, according to the author’s opinion, by the fact that some of the patients involved in our study might deny their pre-marriage complaints or knowledge about the presence of an anomaly and that they discovered this during the course of the management plan for infertility or obstetric complications. It is unlogic and unbelievable for example for those who had uterine agenesis (4) to be discovered only after marriage not complaining before from amenorrhea.

Forty-five cases of the studied patients in this research complained of infertility but 72.2% of them had secondary infertility compared to 27.8% who had primary infertility. This finding comes in disagreement with the results revealed by some authors who proved primary infertility higher than secondary infertility in patients with CUAs [7, 10, 11]. Again, the authors can give an explanation of this by the fact that all patients who had any type of uterine anomaly during the period of the study were involved, and a large proportion of them was found to have an arcuate uterus (35) which manifests commonly by obstetric complications rather than fertility problems.

As mentioned, the results of this study convinced that the arcuate uterus was the most frequent anomaly (35%) followed by bicornuate unicollis (17%), and the least was a T-shaped uterus (1%). These findings are similar to that proved by some national and international researchers [10, 18, 22] but contrary to some other authors who stated in their work that a septate uterus came out to be the most common anomaly [7, 19, 20] and to those who assured the unicornuate uterus to be the
highest followed by septate uterus [21]. For explaining this, according to our insight, some of the previous authors [19-21] investigated uterine anomalies in infertile women only, but we included infertile women and those coming with obstetric complications.

The most frequent complaint in patients explored by this study was a failure to conceive (45%) followed by recurrent pregnancy loss (39%), preterm labor (13%), and lastly acute abdominal pain (3%). However, this comes in contrast to the study published by Raj and Chavan 2019 [13] who showed dysmenorrhea as the commonest gynecological complaint followed by abnormal uterine bleeding, and then chronic pelvic pain in patients with CUAs. In the patients of this study, the mean (SD) duration of primary infertility appeared shorter in those with primary than secondary type (3.01 ± 1.1 vs 4.02 ± 1.2 respectively) and this agreed with the report of Ajayi et al 2015. [12].

The findings described from this study showed a statistically significant relationship between the patients’ complaints and the type of anomaly present as those with uterus didylphus complained mainly of recurrent pregnancy loss, those with unicornuate uterus with rudimentary horn complained of acute abdominal pain and recurrent pregnancy loss while 80% of cases in whom incomplete septum was proved, failed conception was the main presentation. Also, in all cases of the complete uterine septum, the main presentation was a failure to conceive meanwhile those with arcuate uterus had a higher rate of recurrent pregnancy loss and preterm labor, and rarely presented with infertility or acute lower abdominal pain. These findings come in association with the data described before [13, 23] that studied the patterns of recurrent pregnancy losses and their correlations with CUAs. Interestingly and surprising to us, Chan et al 2011,[24] reported no difference in pregnancy rates when compared to women with CUAs and those with normal uteri.

After the intervention, obstetric-related problems were documented in nearly all cases (91) of the studied group after excluding 4 cases of uterine agenesis, no hope for fertility, and 5 cases who did not cope for follow-up. Of these pregnant and followed-up women, 27 cases had preterm labor, 21 cases had abortions, 17 cases had low birth weight, 15 cases had an abnormal fetal presentation, 8 cases had a placental abruption, and lastly 3 cases were urgently undergone laparotomy on rupture uterus. Similar findings were established by many other investigators [5, 14-17, 22, 24]. Here, the authors can state that these variable obstetric outcomes could be resorted to the associated abnormal uterine cavity, disturbed uterine vasculature, or endometrial receptivity that is commonly found in an animalized uterus.

In some previously published data, CUAs were reported to increase the risk for cesarean delivery by more than 13-fold [8, 17]. They explained that higher rates of cesarean section were mainly due to malpresentation and previous cesarean delivery, while other indications observed were non-progressive labor or non-reassuring fetal heart rate tracing were less common in the exposed group [8, 17]. A fact also proved in this work, as all delivered cases were by lower segment cesarean section except 3 cases that were subjected to urgent laparotomy for rupture uterus, and all had unicornuate uteri with rudimentary horns.

Certainly, this study had some shortcomings, namely the wide variables of CUAs involved as this brought an unequal number in each group and made specifying a certain obstetric complication to a specific anomaly difficult. Also, the lack of presenting data for the maternal and neonatal outcomes. Lastly, this study is a unicentric one that investigated some populations in one locality of the country, so the authors recombed for further multicenter study for obtaining more convenient results.
Conclusion

there is strong evidence of poor reproductive outcomes and many obstetric complications in women with CUAs and canalization defects. Therefore, it is so beneficial for obstetricians and gynecologists to be notified of the potential problems that are actually increased depending on the type and severity of anomaly discovered.

References


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