AN ANALYSIS OF THE ROLE OF UTERINE MALFORMATIONS IN PRIMARY INFERTILITY – AN OBSERVATIONAL STUDY

A. Jayashree1, Udaya Kumar P.2, V. Padmaja1, L. Vinodini3, K. Sudha Rani4

1Assistant Professor, Department of Anatomy, Gandhi Medical College, Secunderabad, Telangana State, India; 2Assistant Professor, Department of Anatomy, Mamata Medical College, Khammam, Telangana State, India; 3Assistant Professor, Department of Anatomy, Gandhi Medical College, Secunderabad, Telangana State, India; 4Associate Professor, Department of Anatomy, Gandhi Medical College, Secunderabad, Telangana State, India.

ABSTRACT

Introduction: According to World Health Organization worldwide estimates 60-80 million couples suffer from infertility. Infertility or the inability of a female to conceive despite 12 months or more of unprotected coital exposure can be due to several factors including uterine anomalies, tubal anomalies, and hormonal imbalance among others.

Aims and Objectives: The scope of this study includes impact of Uterine Anomalies on primary infertility.

Materials and Methods: The study includes evaluation and investigation of 100 cases of infertile females and women with bad obstetric history over a period of 3 years from 2007 to 2009 in Gandhi Hospital, Secunderabad, Telangana. A detailed history for every complaint in all the cases was taken by the in charge gynaecologist.

Results: In the present study the bicornuate uterus predominates with 40% (4 cases out of 100). Septate uterus and uterus didelphys were observed in 2 cases each (20%), whereas arcuate uterus and unicornuate uterus were observed in 1 case each (10%).

Conclusion: It is pertinent to note that, a fairly high incidence of bicornuate uterus and uterus didelphys with poor reproductive outcome in the present study provokes a challenge in terms of management protocol on account of its morbidity and demands a meticulous antenatal surveillance. Considering the low socioeconomic and rural background in most of the cases in this study, it is worthwhile to investigate whether nutritional and environmental factors play a role in the genesis of the reproductive system.

Key Words: Uterine anomalies, Primary infertility, Bicornuate uterus, Uterus didelphys, Septate uterus, Arcuate uterus, Unicornuate uterus

INTRODUCTION

This study attempts to explain the much established linkage between Uterine Anomalies and Infertility. The scope of this study includes impact of these anomalies on primary infertility. Primary infertility in this study is taken to imply females who have never previously conceived.

Normal anatomy and development

The uterus is a hollow, pear shaped, thick-walled and muscular organ, normally situated in the lesser pelvis between the urinary bladder and the rectum. The uterus is divided into two main regions – the body – corpus uteri – forms the upper two thirds, and the cervix – cervix uteri - forms the lower third. The uterine tubes are attached to the upper part of the body of uterus with their ostia opening into the lumen [1].

Development

The mullerian (paramesonephric) ducts form a major part of the vagina, cervix and uterine body. The ducts begin to develop as a linear invagination of coelomic epithelium on the lateral aspect of the mesonephric ridge near its cranial end. The Mullerian duct consists of vertical cranial and caudal parts and an intermediate horizontal region.

The cranial part of the para mesonephric ducts forms the uterine tubes, and the original coelomic invagination remains as the pelvic opening of the tube. The caudal vertical parts of
the two ducts fuse with each other to form the uterovaginal primordium. This gives rise to the lower part of uterus and, as it enlarges, it takes in the horizontal parts to form the fundus and most of the body of the adult uterus. The stroma of the endometrium and the uterine musculature develop from the surrounding mesenchyme [2].

Failure of fusion of the two paramesonephric ducts can lead to a range of anomalies of the uterus with varying degree of septation and also contribute to anomalies of vaginal development.

**Classification of mullerian duct anomalies:**
The main groups of deformities arise from three embryological imperfections are discussed below.

1. Defective canalization of the vagina could lead to the formation of transverse vaginal septum or absence of the vagina itself.
2. Also possible is the unilateral maturation of Mullerian duct along with incomplete or total absence of development of opposite duct. The defects in such cases lead to upper urinary tract anomalies.
3. Absence or imperfect midline fusion of mullerian ducts: Total absence of fusion could lead to two independent uteri, vaginas and cervices. Uterine septum could be formed due to incomplete resorption of tissue between the fused mullerian ducts.

**MATERIALS & METHODS**

The study analyses the investigative observations procured from 100 cases of infertile women with bad obstetric history over a period of 3 years from 2007 to 2009 in Gandhi Hospital, Secunderabad, Andhra Pradesh. All cases were sourced from the hospital’s Gynaecology outpatient department. Prior informed consent was taken from the patient.

A detailed history for every complaint in all the cases was taken by the in charge gynaecologist. For those effected by primary infertility, details such as duration of married life, age of the couple, previous usage of contraception, duration of the couple living together, Previous history of expose to sexually transmitted diseases, history of tuberculosis, operations such as appendicitis and other illness, detailed menstrual history, history of abortions were taken. Patients were subjected to a detailed gynaecological and general examination.

1. Gynaecological Examination: Per speculum examination was performed to determine whether cervix was normal or conical with a pin point os, small, elongated, or infected. Also, bimanual examination was done to find out whether uterus was normal sized or ill developed or malformed. Position & mobility of uterus was established. Fornices were examined to make out palpable adnexal pathology, if any.
2. General Examination: A comprehensive general examination was done, which included the stature of the patient, nutritional status, examination of the heart and lungs, any enlargement of thyroid gland and cervical lymph nodes.

**Investigations:** In the Females – Complete blood picture, Blood Grouping & Typing, Erythrocyte Sedimentation Rate, Random Blood Sugar, X-Ray Chest, Venereal disease research laboratory test, dilation and curettage, Ultra Sonography of Pelvis and Hystero Salpingo-graphy. In the Males – Venereal disease research laboratory test, Semen Analysis.

From the above parameters, the information is collected and tabulated for the present study. The data under different investigative procedures like Hystero-salpingography, Ultrasonography, hysteroscopy, and laparoscopic findings were taken. Results were tabulated as per investigative procedures and compared with available literature.

**RESULTS**

The observations represent a total of 100 cases of primary infertility, between ages of 18 years and 35 years.

Table No. I and Figure No. 7 specify the type of anomalies observed, where the bicornuate uterus predominates with 40% (4 cases out of 100). Septate uterus and uterus didelphys were observed in 2 cases each (20%), whereas arcuate uterus and unicornuate uterus were observed in 1 case each (10%).

**DISCUSSION**

A large number of uterine anomalies are detected routinely in reproductive medicine as practiced in current times. This increase is attributed more to availability of better imaging techniques for the uterus rather than increases in prevalence of such anomalies in the general female population.

According to World Health Organization worldwide estimates 60-80 million couples suffer from infertility [3]. Infertility or the inability of a female to conceive despite 12 months or more of unprotected coital exposure can be due to several factors including uterine anomalies, tubal anomalies, and hormonal imbalance among others.

In all probability, arcuate uterus has the least impact on reproductive capacity. Infact, recurrent miscarriages are common in cases of uterine septum. Also, surgical correction of uterine septum is less morbid and easy. Excessive preterm delivery, retained placenta, malpresentation and miscarriage rates are characteristic in bicornuate uterus cases. This anomaly therefore requires extensive surgical repair. Re-evaluation of few studies has revealed that Didelphic uterus
impacts reproductive outcomes. Apart from high miscarriage rates and preterm deliveries, cases of didelphic uterus run the risk of Cesarean section for dystocia, and malpresentation. Poorest reproductive outcomes are observed in unicornuate uterus cases. High rates of ectopics, miscarriage, preterm delivery are therefore common in patients with a unicornuate uterus. Malpresentation, low live-birth rates, and Cesarean section for dystocia are the risks associated with unicornuate uterus [4].

Various authors have put forward explanations for the mechanism of reproductive failure in infertility. Disorganization of uterine stroma along with high intrauterine pressure caused by an enlarging fetus could lead to cervical incompetence and insufficient uterine expansion [5]. Additionally, poor vascular arrangement in the anomalous uterine fundus, will in turn fail to provide necessary support to the growing fetus. These conditions could lead to their loss in late first trimester and second trimester.

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.

In the present analysis of 100 infertility cases, Mullerian anomalies accounted for 10%. Bicornuate uterus (Figure No. 1) tops the list with 40% of total number of cases with Mullerian anomalies followed by the septate uterus (Figure No. 2) and uterus didelphys (Figure No. 3 and 4) with 20% each, while the arcuate uterus (Figure No. 5) and unicornuate (Figure No. 6) accounted for 10% each.

In a review by Saravelos S.H. in 2008 [6] uterine anomalies were found in 16.7% among those with recurrent miscarriages while it accounted for 13% as observed by Grigoris F. Grimbizis et. al. in 2001 [7]. Braun P. et. al., in 2005 [18] found the frequency of malformations to be 10% which tallies with the findings in the present study. Surprisingly the works of Pedro Acién in 1993 [11], Francisco Raga et. al. in 1997 [14], and Bruseo G.F. et. al 2001 [15] found the incidence to be 6%, 6.3% and 7.62%, respectively.

In the current study, bicornuate uterus takes the top slot with an incidence of 40% of total cases with anomalies. In a study reported by Grigoris F. Grimbizis et. al. in 2001 [7] the mean incidence of bicornuate uterus was 25% while it accounted for 13.6% in a retrospective study by Braun P. et. al. in 2005 [18]. Tulandi T. et. al. [8] in their evaluation of uterine anomalies in infertility in the year 1980 had 13 such cases, out of which 6 underwent metroplasty and 4 achieved term pregnancy after surgery. Pedro Acién’s [11] study in 1993 of 176 women found metroplasty and cerclage corrected infertility and increased live birth rate, but nevertheless found a poor pregnancy outcome. Pedro Acién and Maribel Acién in 2004 [12] also affirmed a higher reproductive loss, while in a study undertaken by A. M. Khalil et. al. in 1995 [13], it was observed that fetal wastage rate fell from a massive 93% prior to surgery to 16% after abdominal metroplasty was advocated for uterine unification. Operative outcome was not contemplated in the current study.

Septate uterus accounted for 20% in the present study while it showed a higher incidence of 33.6% in a study undertaken by Francisco Raga et. al. in 1997 [14], and 35% was observed by Grigoris F. Grimbizis et. al. in 2001 [7]. According to Braun P. et. al. in 2005 [18] it was 24.3%, while Saravelos S.H. in his review in 2008 [6] found the dominance of septate uterus in infertile women.

Francisco Raga et. al. in 1997 [14] studied the impact of congenital Mullerian anomalies on women wanting to conceive, and they found that reproductive performance of the didelphys uterus was poor. Pui M.H. in 2004 [17] discussed the pros and cons of various diagnostic tools such as HSG, MRI, USG, hysteroscopy, and laparoscopy in management of anomalies. He inferred that diagnosis can be challenging, for instance complete uterine and vaginal septum can mimic uterus didelphys. Hence comprehensive evaluation has been mooted to pin point underlying anomaly. In the present study this malformation represents 20% of total anomalies.

The arcuate uterus gets listed for its 10% share in the current study. Francisco Raga et. al. in 1997 [14] reported an incidence of 32.8% whereas it accounted for a mean incidence of 20% in a study by Grigoris F. Grimbizis et. al. in 2001 [7], while a retrospective study by Braun P. et. al. in 2005 [18] took a high toll of 57.6%, which was reaffirmed by Saravelos S.H. in 2008 [6]. In 2002, Lin Paul et. al. [16] in their review opined that the arcuate uterus had minimal effect on reproduction, whereas Pedro Acien in 1993 [11] and again in 2004 with Maribel Acién [12] found greater reproductive loss in arcuate uterus when compared to septate.

Closely following with a parallel incidence of 10% is the unicornuate uterus in the current analysis. In 1983, Heinonen P.K. and Pystynen P.P.[10] found that the unicornuate uterus accounted for 15% while Braun P. et. al., in 2005 [18] accounted it for 4.5%. Penti K. Heinonen. et. al. in 1982 [9] observed that unicornuate uterus had a fetal survival rate of 40%.

**CONCLUSION**

It is pertinent to note that, despite being a known cause for many years now, mullerian anomalies continue to attract
academic interest and presents a formidable challenge for Obstetricians. Availability of better imaging techniques and associated therapeutic options has generated greater interest in this field. The current study has shown that bicornuate uterus accounted for 40% of the total number of patients with mullerian anomalies, while uterus didelphys and septate uterus accounted for 20% each. Unicornuate uterus and the arcuate uterus cornered 10% each. A fairly high incidence of bicornuate uterus and uterus didelphys with poor reproductive outcome in the present study provokes a challenge in terms of management protocol on account of its morbidity and demands a meticulous antenatal surveillance.

Considering the low socioeconomic and rural background in most of the cases in this study, it is worthwhile to investigate whether nutritional and environmental factors play a role in the genesis of the reproductive system.

**Competing Interests**
The authors declare that we have no competing interests

**Ethical Committee**
As this is only an observational study of the patients who attended the Gynaecology and Obstetrics outpatient department and underwent treatment later on, in the respective department, permission from ethical committee was not considered in the present study. But prior informed consent was taken from the patient in their own vernacular.

**Source of Funding**
This is a self funded study.

**ACKNOWLEDGEMENTS**
Authors thank Dr. Seema Madan, Professor and Head of the Department of Anatomy Dr. Ashok Kumar, Professor of the Department of Anatomy for precious suggestions and practical guidance during the study. Authors are indebted to the patients who consented to be included in the study.

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

**REFERENCES**
1. Susan Standring, PhD; Gray’s Anatomy, The Anatomical Basis of Clinical Practice; 40th ed.
Table 1: Showing various types of Uterine Anomalies in the Current Study (Total No. of Cases: 100)

<table>
<thead>
<tr>
<th>Type of Uterine Anomaly</th>
<th>Number of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bicornuate Uterus</td>
<td>4</td>
<td>40%</td>
</tr>
<tr>
<td>Septate Uterus</td>
<td>2</td>
<td>20%</td>
</tr>
<tr>
<td>Uterus Didelphys</td>
<td>2</td>
<td>20%</td>
</tr>
<tr>
<td>Arcuate Uterus</td>
<td>1</td>
<td>10%</td>
</tr>
<tr>
<td>Unicornuate Uterus</td>
<td>1</td>
<td>10%</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>100%</td>
</tr>
</tbody>
</table>

Figure 1: Showing Hystero-salpingography of Bicornuate uterus:

Figure 2: Showing 3D ultra sonography of septate uterus:

Figure 3: Showing Ultra sonography of Didelphys uterus:

Figure 4: Showing Hystero-salpingography of Didelphys uterus:

Figure 5: Showing Hysterosalpingography of arcuate uterus:
Jayashree et. al.: An analysis of the role of uterine malformations in primary infertility – An observational study

Figure 6: Showing Hystero-salpingography of unicormuate uterus:

Figure 7: Showing the graph of percentage in various types of Uterine Anomalies in the Current Study.