FERTILITY AND STERILITY

Vol. 40, No. 3, September 1983
Printed in U.S.A.

Primary infertility and uterine anomalies*

Pentti K. Heinonen, M.D.†
Paavo P. Pystynen, M.D.‡

University Central Hospital of Tampere and University of Tampere, Tampere, Finland

During a 20-year period, 19 (9.1%) of 208 patients with uterine anomalies had primary infertility. Women with unicornuate uteri had the highest (15%) incidence of primary infertility, which was found in the other groups of uterine anomalies in 7% to 13% of the patients. The cause of infertility was a nonuterine factor in 12 cases: hormonal (8), endometriosis (2), tubal (1), or male (1). The reason for infertility remained unknown or the patient conceived during investigation in five cases. Malformation of the uterus was considered the sole reason for infertility, and metroplasty was performed in two cases. During the follow-up period, 14 patients (74%) achieved pregnancy: 6 spontaneously, 3 after curettage, 2 after metroplasty, 1 after clomiphene treatment, 1 after hysterosalpingogram, and 1 after conservative endometriosis surgery. Four of five cases without pregnancy had a nonuterine factor as the cause of infertility, and in one case it may have been a uterine anomaly—a unicornuate uterus with a rudimentary horn. The results indicate that uterine anomalies are rarely the reason for infertility. Nonuterine causes of infertility must be ruled out before metroplasty is performed, as a last resort. Fertil Steril 40:311, 1983

The association between congenital uterine anomalies and repeated pregnancy loss and preterm labor is well known and well documented. Primary infertility is also connected with malformation of the uterus and has been mentioned in some reports as an indication for metroplasty,[1-10] although the duration of infertility, associated conditions, and additional operations or possible medical therapy have been less frequently described. In all, the etiologic relationship between primary infertility and the anomalous uterus is a controversial problem.

Received January 3, 1983; revised and accepted May 16, 1983.

*A preliminary report was presented at the Twenty-Second Congress of The Scandinavian Association of Obstetricians and Gynecologists, June 7 to 10, 1982, Helsinki, Finland.

†Reprint requests: Pentti K. Heinonen, M.D., Department of Obstetrics and Gynecology, University Central Hospital of Tampere, SF-33520 Tampere 52, Finland.

‡Department of Clinical Sciences, University of Tampere.

Tulandi et al.[11] reported that 23 (1.03%) of 2240 infertile women had uterine anomalies, 18 of 23 patients had primary infertility. The incidence of primary infertility among women with uterine anomalies has not been reported. The purpose of this study was to estimate the incidence of primary infertility, the causes of infertility, and pregnancy rates after different forms of treatment among women with uterine anomalies.

MATERIALS AND METHODS

A total of 228 women with uterine anomalies were evaluated from March 1962 to March 1982 at the Department of Obstetrics and Gynecology in the University Central Hospital of Tampere. The diagnostic methods used and the outcomes of pregnancies in the greater part of the present survey material have been described previously.[12] The diagnosed uterine anomalies were grouped according to the classification recently

Table 1. *Classsification of Uterine Anomalies and Distribution of Primary Infertility in 208 Patients*

Group	Uterine anomaly	No. patients	Primary infertility	
			No.	%
I	Uterine agenesis	20		
II	Unicornuate	20	3	15
III	Didelphic	24	2	8
IV	Bicornuate			
	A. Complete	8	1	13
	B. Partial	61	4	7
	C. Arcuate	23	3	13
V	Septate			
	A. Complete	27	2	7
	B. Incomplete (subseptate)	45	4	9
Total		208	19	9.1

proposed by Buttram and Gibbons.[13] This classification is based on the degree of failure of normal uterine development. Twenty patients with uterine agenesis (group I) had no reproductive potential and were therefore excluded from this study. The unicornuate uteri (group II) were not divided into subclasses, because 18 of 20 patients also had a rudimentary horn concomitant with the unicornuate uterus. No woman had been exposed to diethylstilbestrol in utero, and thus this series does not involve the T-shaped uterus related to the use of diethylstilbestrol.

With retrospective analysis, 19 (9.1%) of 208 potentially reproductive women with uterine anomalies had primary infertility. Table 1 shows that primary infertility was observed in 7% to 15% of patients in the different groups of uterine anomalies. The mean age of these patients was 28 years (range, 22 to 39 years). The duration of primary infertility ranged from 1 to 15 years (mean, 3.5 years).

Hysterosalpingography (HSG) had been performed in all cases. The uterine anomaly had also been confirmed in 16 cases during operative procedures, including 9 cases during laparotomy, 5 cases at the time of cesarean section, and 2 cases by laparoscopy.

The presence of ovulation was assessed primarily by basal body temperature charting and with endometrial biopsy. Measurement of serum progesterone was also done in five cases with unclear ovulation or suspicion of luteal phase defect. Further evaluation of endocrine status, including determination of pituitary gonadotropins and adrenocortical and thyroid function parameters, was carried out whenever indicated by general or gynecologic examination. Tubal patency was investigated by HSG. Postcoital testing was performed in eight cases to assess the role of the cervical factor in infertility. The male factor in infertility was eliminated by semen analyses.

Metroplasty was performed in 21 patients in the total survey. Primary infertility was indicated in conjunction with requiring surgery in three cases. Two types of metroplasty were used for unification procedures: the wedge technique of Jones and Jones[14] in one case, and the median bivalving technique of Tompkins[15] in two cases.

RESULTS

Table 2 shows the reasons for primary infertility in the different groups of uterine anomalies. The "unknown factor" group consisted of cases in which all other causes of infertility had been excluded or where conception was achieved during the investigation.

UNICORNUATE UTERUS

Two of three patients with a unicornuate uterus also had a rudimentary horn. The first had pelvic endometriosis and conceived after conservative surgery, including resection of endome-

Table 2. *Reasons for Infertility in Women with Uterine Anomalies*

Group	Uterine anomaly	Nonuterine factor				Uterine factor	Unknown factor
		Hormonal	Endometriosis	Tubal	Male		
II	Unicornuate		1		1		1
III	Didelphic	2					
IV	Bicornuate						
	A. Complete	1					
	B. Partial	1	1			1	1
	C. Arcuate	1		1			1
V	Septate						
	A. Complete	2					
	B. Incomplete	1				1	2
Total		8	2	1	1	2	5

trial implants, but miscarried. In the second patient, no reason for infertility could be found. Laparoscopy showed a rudimentary horn but no endometriosis. Operative procedures were not undertaken, and she received no hormonal treatment. She did not conceive over the follow-up period of 3 years and was untraceable for further follow-up. A woman whose husband had oligospermia had a unicornuate uterus without a rudimentary horn confirmed by laparotomy. Uterine suspension was performed, but no other therapy was given. The husband's poor sperm was considered the reason for the couple's infertility.

DIDELPHIC UTERUS

Both women with a didelphic uterus had a longitudinal vaginal septum, and the anomalous uterus had been diagnosed before the patient attended the outpatient clinic. Both also had irregular menses, one of them irregular shedding of endometrium found by endometrial biopsy. She conceived without therapy. The other had "post-pill syndrome," and she achieved pregnancy 2 months after diagnostic curettage.

BICORNUATE UTERUS

The woman with a complete bicornuate uterus had anovulatory cycles. She received clomiphene treatment without success. One year after discontinuing hormonal therapy, she conceived spontaneously, but miscarried. One of four patients with a partial bicornuate uterus conceived after diagnostic curettage before any specific treatment. One woman had oligomenorrhea and no response after clomiphene treatment. The couple adopted a child after an infertile period of 15 years. The wife achieved pregnancy 1 year after the adoption without any treatment and delivered a viable infant. For two patients with a partial bicornuate uterus, plastic unification of the uterus was performed. The first had polycystic ovaries and pelvic endometriosis, which were considered the main reasons for infertility. The surgical procedures consisted of wedge resection of the ovaries, resection of endometrial implants, and metroplasty according to Jones and Jones.[14] The patient did not achieve pregnancy during a follow-up period of 6 years. The second woman underwent metroplasty according to Tompkins[15] after 1 year's infertility and conceived 1.5 years after surgery. This woman had a partial bicornuate uterus, although a small septum was also found. One of three women with an arcuate uterus conceived after diagnostic curettage before any reason for infertility could be demonstrated. The second woman had oligomenorrhea and became pregnant after ovulation induction by clomiphene. The third had bilateral tubal occlusions and did not conceive after salpingostomy.

SEPTATE UTERUS

Both women with a complete septate uterus had irregular menses. One of them conceived after HSG, and the other before any treatment. Also, two of four women with a subseptate uterus conceived without treatment before the cause of infertility was found. Tompkins metroplasty[15] was performed on the patient who had infertility of 2 years' duration. No additional operation was performed. This person conceived 1 year after the operation. Luteal phase defect and a poor postcoital test was found in one woman who received both clomiphene and human chorionic gonadotropin without success.

Table 3 summarizes the cases of five patients who did not conceive during the follow-up period. The reason for infertility was a nonuterine factor in four cases. Only in one case was the unicornuate uterus with a rudimentary horn possibly the main reason for infertility.

Table 4 shows that 14 patients (74%) conceived, and the first pregnancy ended in delivery in 10 cases (71%). During the follow-up period, the total number of pregnancies was 27; 10 of these (37%) miscarried. All infants were alive, and only two were premature. There were no ectopic pregnancies.

DISCUSSION

The prevalence of involuntary infertility is traditionally estimated at about 10% in a normal population. In this study, primary infertility was found in 9.1% of 208 patients with uterine anomalies. Musich and Behrman[9] reported that 3 (6.1%) of 49 patients with uterine anomalies had primary infertility as a primary clinical complaint. These findings indicate that uterine anomalies are not associated with a higher rate of primary infertility than that in a normal population.

Nickerson[16] found that 74% of 190 primary infertility patients had uterine anomalies diagnosed by HSG. Most cases were minor uterine anomalies such as a mildly or very mildly septate uterus. He concluded that there was a correlation

Table 3. *Patients with Uterine Anomalies Not Conceiving*

Group	Uterine anomaly	Reason for infertility	Treatment	Follow-up
				yr
II	Unicornuate	Male infertility	Uterine suspension	3
		Unknown (rudimentary horn?)	—	3
IV B.	Partial bicornuate	Polycystic ovaries, endometriosis	Wedge resection of ovaries, resection of endometriosis, metroplasty	6
C.	Arcuate	Bilateral tubal occlusion	Bilateral salpingostomy	2
V B.	Subseptate	Luteal phase defect, cervical factor?	Clomiphene and human chorionic gonadotropin	3

between an abnormal hysterographic contour and primary infertility, and that subtler anomalies were more often related to infertility than severe fusion defects. In the discussion section of the article, it was pointed out that hysterographic findings would probably be interpreted in most circles as normal.[16] In the present series comprising mostly major uterine anomalies, there were no findings to confirm a cause-and-effect relationship between uterine anomalies and primary infertility. Even the groups with minor anomalies such as arcuate and subseptate uteri had no higher incidence of primary infertility.

Irregular menses or a hormonal factor was the most common reason for infertility in the present study. Seven of eight patients achieved pregnancy during the follow-up period. One patient with a subseptate uterus had luteal phase defect and a poor postcoital test and no response after treatment. It may be that in this case the cause of infertility was multifactorial. Stampe Sørensen[17] reported that oligomenorrhea and amenorrhea are more common in infertile women with minor Müllerian anomalies than in infertile patients with normal uterine cavities. The author speculated that a defect in steroid receptor protein in the congenitally deformed uterus may explain the oligomenorrhea. In our series, oligomenorrhea was found in three patients, one with a partial bicornuate uterus, one with an arcuate uterus, and one with a septate uterus. Unfortunately, we have no data on oligomenorrhea in fertile women with uterine anomalies, but it seems likely that oligomenorrhea is no more common in such women.

Tulandi et al.[11] reported that 4 of 23 infertile patients achieved pregnancy while their cases were being investigated. In the present study, five patients had no discoverable reason for infertility, or they conceived before treatment. Four of them achieved pregnancy. These findings indicate that it may be subfertility that is associated with uterine anomalies. It may also be that a malformed uterus observed during preliminary investigation has more readily guided the patient to the infertility outpatient clinic for additional investigation.

The patients with unicornuate uteri had the highest (15%) frequency of primary infertility and the poorest pregnancy rate. The concomitant rudimentary horn is found in 90% of the unicornuate uteri. Pelvic endometriosis was observed in 20% of these patients during operative procedures.[18] Active endometrium of the rudimentary horn is the likely reason for endometriosis. Thus, this uterine anomaly may impair fertility. One patient with an unknown cause of infertility had this anomaly, and the role of the rudimentary horn remained, unfortunately, obscure. Removal of the rudimentary horn is preferred, although the rudimentary horn may be small and without functional endometrium.[18] Usually there is no communication between the rudimentary horn and the unicornuate uterus, and thus these patients have only one patent tube adjacent to a functional uterine cavity.

Infertility has been mentioned as being related to longitudinal vaginal septum, which is found mostly concomitant with a didelphic uterus and a

Table 4. *Reproductive Performance of Women with Uterine Anomalies*

Group	Uterine anomaly	No. patients	Conceived	Abortion	Delivery
II	Unicornuate	3	1	1	
III	Didelphic	2	2		2
IV	Bicornuate				
	A. Complete	1	1	1	
	B. Partial	4	3		3
	C. Arcuate	3	2		2
V	Septate				
	A. Complete	2	2	1	1
	B. Incomplete	4	3	1	2
Total		19	14	4	10

Table 5. *Primary Infertility as an Indication for Metroplasty*

Reference	Year	No. metroplasties	With primary infertility
Genell and Sjövall[1]	1959	59	13
White[2]	1960	11	3
Strassmann[3]	1966	26	8
Capraro et al.[4]	1968	14	0
Buttram et al.[5]	1974	28	7
Kaskarelis[6]	1975	62	5
Zourlas[7]	1975	13	2
Rock and Jones[8]	1977	43	0
Musich and Behrman[9]	1978	21	0
Mercer et al.[10]	1981	17	4
Total		294	42 (14.3%)

complete septate or bicornuate uterus.[19] In none of our cases was excision of the vaginal septum performed because of primary infertility, although in the total survey it was undertaken in three patients with secondary infertility.[19] However, the vaginal septum may cause dyspareunia and leukorrhea and may thus indirectly cause infertility. It should be noted that the vaginal septum found during speculum examination indicates investigation of the uterine cavity, because it is frequently found concomitant with a malformed uterus.[19]

The uterine unification procedure is usually performed on women with septate or bicornuate uteri. Table 5 shows that primary infertility has been considered an indication for metroplasty in 42 (14.3%) of 294 cases collected from the literature. In only three surveys[4, 8, 9] was no unification procedure indicated by primary infertility. Genell and Sjövall[1] reported 13 patients who underwent metroplasty for primary infertility of 1 to 12 years' duration. However, seven patients had additional procedures performed, such as liberation of adhesions, tubal surgery, or myomectomy. Of these 13 patients, 5 conceived postoperatively. In the total survey collected from the literature, 15 patients underwent additional operative procedures with metroplasty, mostly tubal surgery. There is in most cases no information as to the duration of infertility, associated conditions such as endometriosis, adhesions, a tubal factor, or additional operative procedures, which renders the role of metroplasty difficult to assess. In the present study, two patients underwent metroplasty when extrauterine causes of infertility had been excluded. Both achieved pregnancy after operation. It may be speculated that the "test of time" should be equally successful, since the duration of infertility was relatively short in both cases, 1 and 2 years. In all, it is difficult to see how primary infertility can be caused by a uterine anomaly. On the other hand, if a nonuterine factor of infertility is found, as it most often is, and this calls for operative procedures by laparotomy, it may be prudent to perform metroplasty as well, because uterine anomalies are associated with repeated pregnancy wastage.

In conclusion, our results confirm the view that uterine anomalies alone are rarely associated with primary infertility. A patient who has a malformed uterus and who complains of primary infertility should at first be subjected to a thorough investigation to exclude other nonuterine causes of infertility. If there is no other reason for infertility, metroplasty may be performed as a last resort.

REFERENCES

1. Genell S, Sjövall A: The Strassmann operation: results obtained in 58 cases. Acta Obstet Gynecol Scand 38:477, 1959
2. White MM: Uteroplasty in infertility. Proc R Soc Med 53:1006, 1960
3. Strassmann EO: Fertility and unification of double uterus. Fertil Steril 17:165, 1966
4. Capraro VJ, Chuang JT, Randall CL: Improved fetal salvage after metroplasty. Obstet Gynecol 31:97, 1968
5. Buttram VC Jr, Zanotti L, Acosta AA, Vanderheyden JS, Besch PK, Franklin RR: Surgical correction of the septate uterus. Fertil Steril 25:373, 1974
6. Kaskarelis DB: Metroplasties. Acta Eur Fertil 6:287, 1975
7. Zourlas PA: Surgical treatment of malformations of the uterus. Surg Gynecol Obstet 141:57, 1975
8. Rock JA, Jones HW Jr: The clinical management of the double uterus. Fertil Steril 28:798, 1977
9. Musich JR, Behrman SJ: Obstetric outcome before and after metroplasty in women with uterine anomalies. Obstet Gynecol 52:63, 1978
10. Mercer CA, Long WN, Thompson JD: Uterine unification, indications and technique. Clin Obstet Gynecol 24:1199, 1981
11. Tulandi T, Arronet GH, McInnes RA: Arcuate and bicornuate uterine anomalies and infertility. Fertil Steril 34:362, 1980
12. Heinonen PK, Saarikoski S, Pystynen P: Reproductive performance of women with uterine anomalies. Acta Obstet Gynecol Scand 61:157, 1982
13. Buttram VC Jr, Gibbons WE: Müllerian anomalies: a proposed classification (an analysis of 144 cases). Fertil Steril 32:40, 1979
14. Jones HW Jr, Jones GES: Double uterus as an etiological factor of repeated abortion, indication for surgical repair. Am J Obstet Gynecol 65:325, 1953
15. Tompkins P: Comments on the bicornuate uterus and twinning. Surg Clin North Am 42:1049, 1962

16. Nickerson CW: Infertility and uterine contour. Am J Obstet Gynecol 129:268, 1977
17. Stampe Sørensen S: Minor Müllerian anomalies and oligomenorrhea in infertile women. Am J Obstet Gynecol 140:636, 1981
18. Heinonen PK: Clinical implications of the unicornuate uterus with rudimentary horn. Int J Gynaecol Obstet 21:145, 1983
19. Heinonen PK: Longitudinal vaginal septum. Eur J Obstet Gynaecol Reprod Biol 13:253, 1982