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Incidence of Mullerian defects in fertile and infertile women

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Although uterine anomalies have been reported in 0.1–2% of all women, in 4% of those with infertility and in up to 15% of those with recurrent abortion (March, 1990), their true incidence is not known. The more liberal use of hysterosalpingography and hysteroscopy, and the routine practice of ultrasonography, and more recently, transvaginal ultrasound scanning (TVS) and transvaginal three-dimensional ultrasound (TDU) have led to an apparent increase in the incidence and, currently, the figures cited above could be higher. In any case, there are no modern studies on the incidence of uterine anomalies in the general population, and those on fertile and infertile women, or with recurrent pregnancy loss (RPL), have reported conspicuously varied results. This variability in the reported incidence of uterine anomalies is due to the fact that it depends on the following variables: (i) the population studied (gynaecological patients, those referred for metroplasty, fertile, infertile or recurrent miscarriage women). In RPL patients, in whom the uterine malformations are more frequent, the incidence of anomalies depends on the inclusion criteria for RPL (two, three or more, late abortions, immature deliveries); (ii) the prospective or retrospective character of the investigation, directed search and physician interest and awareness to find or reject an uterine anomaly, because most of the uterine malformations are clinically silent; (iii) the diagnostic methods used. Hysterosalpingography (HSG) (and hysteroscopy) are the best general diagnostic tools for uterine anomalies, but they must be complemented with laparoscopy and/or others (magnetic resonance, pyelography) for a correct diagnosis in most classes of Mullerian anomalies. However, HSG and hysteroscopy are only indicated in infertility investigation, special clinical situations or suspected malformation. Currently, the routine transvaginal echography (TVS) evaluating the external shape of the uterus and, specifically, the presence of a median endouterine septum at any point along its longitudinal axis, is the best screening method (Nasri *et al.*, 1990). More recently, three-dimensional ultrasound has also shown its usefulness in a clinical setting to diagnose and classify Mullerian anomalies (Jurkovic *et al.*, 1995; Raga *et al.*, 1996); (iv) the classes included as congenital uterine anomalies in the different reported series. Hypoplastic, T-shaped, diethylstilbestrol-exposed women (DES)-related anomalies and arcuate uterus are frequently not included. In the present communication they are included as 'minor uterine anomalies' in spite of many cases causing frequent fertility problems (Acien, 1996). However, with the screening methods used (TVS) their identification may not be strainght forward, or (with HSG) many cases could be classified as normal or abnormal depending on the observer, apart from a dependance on exposure (Sorensen, 1981). Logically, the cases with Mullerian agenesis are excluded from the series where fertility problems are analysed; (v) the criteria and diagnostic tools used to classify the different types of uterine malformations clinically well recognized (e.g. subseptus–septate versus bicornuate uterus, or bicornis bicollis versus didelphys uterus), in spite of both following the American Fertility Society (AFS, 1988) classification of Mullerian anomalies, or the similar one from Buttram (Buttram and Gibbons, 1979; Buttram, 1983; Buttram and Reiter, 1985). We carefully observed the external shape of the uterus in laparoscopy, and if it had any visible depression on the middle part of the fundic uterine wall accompanied by an overall widening, it was classified as bicornuate uterus (Acien, 1993). Some of these cases are possibly classified as subseptus or septate uteri by other authors. Similarly, the distinction between arcuate and mildly subseptate or mildly bicornuate uterus is controvertial (Sorensen, 1981).

Taking into account the aforementioned considerations, in this communication we investigated the incidence of uterine anomalies based on the review of the literature and the analysis of our material. From this respect, we have studied: (i) women consulting for contraception or who were revised in the follow-up of contraceptive methods (pill, intrauterine device) during the last 3 years (June 93 to June 96) in the Institute of Gynecology 'Prof. P.Acien'. They were 241 women, 72 of whom had no previous pregnancies (single or married women); (ii) women consulting for recurrent abortion, subfertility or infertility during the same period, in both the Institute of Gynecology and the Infertility and Reproductive Endocrinology Unit of San Juan University Hospital. They were 259 women, 200 of whom suffered from infertility (Table I). All women in both series were examined by the author, one or more times, and TVS was routinely performed looking for uterine anomalies. An HSG and laparoscopy or laparotomy were also performed in the precise cases (HSG in the 75% of women with uterine anomaly detected by TVS, and laparoscopy or laparotomy in 28%). Also included was a series recently reported by the author, with regard to uterine anomalies and

Table I. Incidence of congenital Müllerian anomalies in women consulting for contraception, in women with recurrent miscarriage or subfertility, and infertile patients. Values in parentheses are percentages

	No. women studied	Women with Müllerian anomalies[a]	Minor uterine anomalies[b]		Uterine malformations clinically well recognized					
			Hypoplastic	Arcuate	Subseptus	Septate	Bicornuate	Unicornuate	Didelphys	Total[c]
Women without previous pregnancy (single or married)	72	13 (18)[d]	1 (1.4)	8 (11.1)	2 (2.8)	1 (1.4)	1 (1.4)	0-	0-	4 (5.6)
Women with previous pregnancies and live newborns	131	9 (6.9)	3 (2.3)	4 (3.1)	0 (0)	0-	1 (0.8)	1 (0.8)	0-	2 (1.5)
Women with live newborns and some reproductive loss	38	4 (10.5)	1 (2.6)	1 (2.6)	0 (0)	1 (2.6)	1 (2.6)	0-	0-	2 (5.3)
Total for contraception	241	26 (10.8)[e]	5 (2.1)	13 (5.4)	2 (0.8)	2 (0.8)	3 (1.2)	1 (0.4)	0-	8 (3.3)
Recurrent miscarriage and subfertility (infertility and miscarriage)	59	15 (25.4)[e]	6 (10.2)	6 (10.2)	0-	0-	3 (5.1)	0-	0-	3 (5.1)
Infertile women	200	32 (16)	12 (6)	14 (7)	2 (1)	0-	1 (0.5)	2 (1)	1 (0.5)	6 (3)

[a]Diagnosis was made by transvaginal echography in all women, plus hysterosalpingography in 188 women (37,6%) (75% in uterine anomalies), and laparoscopy or laparotomy in 79 women (15.8%) (28% in uterine anomalies).
[b]Ten cases suggesting DES syndrome.
[c]No cases of bicornis–bicollis uterus.
[d]$P < 0.05$ with respect to previous pregnancies.
[e]$P > 0.05$ between women for contraception and recurrent miscarriage or subfertility.

Table II. Incidence of congenital Müllerian defects in the general population, various obstetric and gynaecological indications, and in fertile women: review of the literature. Values in parentheses are percentages

Reference	Population studied	No. women studied	No. Müllerian defects detected	Diagnostic methods	Minor Müllerian defects	Clear uterine malformations	Percentage uterine malformations
Dunselman, 1959	General	–	– (1,5)	–	–	–	–
Strassman, 1961	General	–	– (0.1)	–	–	–	–
Strassman, 1966	No specified	6.888	– (1.1–3.5)	HSG	–	–	–
Moore, 1941	All private patients	–	– (0.2)	–	–	–	–
Greiss and Mauzy, 1961	Women postpartum	–	– (3)	Manual exam	–	–	–
Green and Harris, 1976	Premature and abnormal deliveries in the total of deliveries	31.836	80 (0.25)	HSG/exam	–	–	–
Nasri *et al.*, 1990	Varied indications	300	8 (2.7)	Transvaginal echography	–	8	2.7
Maneschi *et al.*, 1995	Abnormal uterine bleeding	322	32 (10)	Hysteroscopy	21	11	3.4
Ashton *et al.*, 1988	Transcervical tubal sterilization	840	19 (2.3)	Hysteroscopy HSG	3	16	1.9
Simon *et al.*, 1991	Fertile, for tubal sterilization	679	22 (3.2)	Laparoscopy HSG	Excluded	22	3.2

HSG = hysterosalpingography.

recurrent miscarriage (Acién, 1996); not included were nine other cases with Müllerian agenesis (Rokitansky's syndrome).

Incidence of Müllerian defects in the general population

There are few studies analysing the incidence of uterine anomalies in the general population of women, and to our knowledge, none of them in the last 30 years. In the literature (Buttram and Reiter, 1985; Coll *et al.*, 1988; others) there are references to papers by Strassman (1961) with an incidence of 0.1%, or by Dunselman (1959) with an incidence of 1.5%, although the diagnostic methods used were not stated. Strassman (1966), who found Müllerian defects in 1.1–3.5% of 6888 women with hysterography, did not specify the studied population, either (Buttram and Reiter, 1985). Instead of representing the general population they seem to be gynaecological cases consulting because of specific symptoms and in this way Moore (1941) found uterine anomalies in 0.2% of all his private practice patients. These cases were collected using the diagnostic methods of that time and, in most cases, comprised only a physical examination (Table II).

If we consider that young women without a previous pregnancy who consult for contraception (generally pill) could be representative of the general population of menstruating

Table III. Incidence of congenital Müllerian defects in women with recurrent pregnancy loss (RPL) or infertility (I): review of the literature. Values in parentheses are percentages

Reference	Population studied	No. women studied	No. Müllerian defects detected	Diagnostic methods	Minor Müllerian defects	Clear uterine malformations	Percentage uterine malformations
Tho *et al.*, 1979	RPL	100	14 (14)	HSG	4 (CI)	10	10
Harger *et al.*, 1983	RPL	155	19 (12.3)	HSG/hysteroscopy	10	9	5.8
Coulam, 1986	RPL	110	11 (10)	HSG	–	11	10
Makino *et al.*, 1992a	RPL	1200	188 (15.7)	HSG	–	–	–
Makino *et al.*, 1992b	RPL	1000	147 (14.7)	HSG	95	52	5.2
Hatasaka, 1994	RPL	158	(6)	Complete study of RPL	–	–	6
Raziel *et al.*, 1994	RPL	106	19 (18)	HSG/hysteroscopy	–	–	–
Clifford *et al.*, 1994	RPL	500	9 (1.8)	HSG/echo	–	9	1.8
Jurkovic *et al.*, 1995	RPL	61	12 (19.7)	HSG/echo–TDU	9	3	4.9
Acien, 1996	RPL	189	71 (37.6)	HSG/others	33	38	20.1
Tulandi *et al.*, 1980	I	2240	23 (1.03)	HSG	7	16	0.7
Sorensen, 1981	I	134	32 (23.9)	HSG	29	3	2.2
Raga *et al.*, 1996	I	42	12 (26.2)	Echo–TDU HSG, lap	–	–	–

[a]Minor Müllerian defects include arcuate, T-shaped and hypoplastic uterus.
CI = cervical insufficience; TDU = tridimensional ultrasound; HSG = hysterosalpingography; echo = echography; lap = laparoscopy.

Table IV. Fertility and reproductive losses before studying the existence of uterine anomalies. Values in parentheses are percentages

	Women with a normal uterus	Minor uterine anomalies	Uterine malformations
Total no. women with pregnancies	227	23	6
No. women with:			
Early abortions	77 (33.9)	10 (43.5)	3 (50)
Ectopic pregnancy	9 (4)	3 (13)	0 (0)
Late abortions	7 (3.1)[a]	4 (17.4)	1 (16.7)
Inmature deliveries	3 (1.3)	2 (8.7)	1 (16.7)
Premature deliveries	5 (2.2)	1 (4.3)	1 (16.7)
Breech presentation	9 (4)	0 (0)	1 (16.7)
Normal delivery at term	190 (83.7)[b]	12 (52.2)	2 (33.3)
Live newborns	194 (85.5)[b]	12 (52.2)	4 (66.6)

[a]Significant difference between normal uterus and uterine anomalies ($P < 0.05$).
[b]Significant difference between normal uterus and uterine anomalies ($P < 0.001$).

women (we do not known if they will be fertile or infertile in the future, although cases with Müllerian agenesis or gonadal disgenesis would be excluded), in those women we found a possible uterine anomaly (chiefly an arcuate uterus) in 18%. However, there were still 5.6% (4/72) with a clinically well recognized uterine malformation. Therefore, the incidence of Müllerian defects in the general population of women in our area must be ⩾5%.

Incidence of Müllerian defects in fertile women

Green and Harris (1976) carried out physical examinations and HSG 6–8 weeks *post-partum* in 31 836 patients with premature labour or abnormal fetal presentation found 80 cases with an uterine anomaly (0.25%). However, later studies on fertile women for tubal sterilization found a higher incidence (Table II). Ashton *et al.* (1988) observed 2.3% (1.9% if the cases with arcuate uterus are excluded) of uterine anomalies in 840 women, with hysteroscopy and HSG, and Simon *et al.* (1991) found 3.2% of uterine malformations (minor classes excluded) in 679 women with laparoscopy for tubal sterilization and then HSG.

In 169 fertile women consulting for contraception (pill or intrauterine device), we have found 7.7% of uterine anomalies, although only 2.4% had evident uterine malformations (minor classes excluded). This incidence was higher when the women had some reproductive loss among the obstetric antecedents (see Table I).

In other gynaecological indications, 2.7% of uterine malformations have been observed with TVS (Nasri *et al.*, 1990), and 10% with hysteroscopy (but 3.4% if the minor classes are excluded) (Maneschi *et al.*, 1995). Therefore, ~3% of fertile women have an uterine malformation, but this figure is higher if the minor uterine anomalies are included.

Incidence of Müllerian defects in infertile women

This incidence is quite similar to that observed in fertile women, at least with respect to clear uterine malformations. It agrees with previous references pointing out that the frequency of infertility is not significantly increased in uterine malformations (Acien, 1993). There seem to be more cases of 'minor Müllerian anomalies' related to infertility. Tulandi *et al.* (1980) found Müllerian defects in only 1% of 2240 infertile women by HSG, while Sorensen (1981) observed an incidence of 23.9%, although only 2.2% had major uterine malformations. Also Raga *et al.* (1996) observed Müllerian defects in 26.2% of 42 infertile women by transvaginal TDU, although it is possible that this was a selected group of patients (Table III). In 200 infertile women in our study population, we found uterine anomalies in 16%, but only 3% were evident uterine malformations, without significant differences from those women consulting for contraception (see Table I). Some authors (Ugur *et al.*, 1995) have found a higher incidence of polycystic ovarian disease in women with uterine malformations, but we found no such relationship.

Table V. Distribution of Müllerian defects in different publications

Reference	No. Müllerian defects studied	Diagnostic methods	Arcuate %	Subseptus %	Septate %	Bicornuate %	Bicornis Bicollis %	Didelphys %	Unicornuate %	Agenesis[a] %
Semmens, 1962										
Personal cases	56	–	3.6	–	–	48.2	44.6	–	1.8	1.8
Review	500	–	5	–	–	52.2	40	–	2.8	–
Exalto and Eskes, 1978	25	Echo/lap	4	24	16	20	20	–	12	–
Musich and Behrman, 1978	41	HSG	7.3	–	34.1	29.3	–	26.8	2.4	–
Heinonen *et al.*, 1982	182	Varied	11	18.1	10.4	29.7	2.7	11.5	7.1	9.3
Rock and Schlaff, 1985:										
Blair	57	–	30	14	1.7	36.8	14	3.5	–	–
Frenton and Singh	77	–	9.1	6.5	7.8	32.5	6.5	40.2	–	–
Baker *et al.*	127	–	0.8	4.7	4.7	46.5	1.6	39.3	3.2	–
Philpott and Ross	41	–	19.5	12.2	4.9	48.8	–	12.2	2.4	–
McGregor	16	–	37.5	18.7	–	43.7	–	–	–	–
Way	12	–	–	41.6	–	58.3	–	–	–	–
Stein and March, 1990	150	Varied	6	–	30	39.3	–	16.7	8	–
Kovacevic *et al.*, 1990	127	HSG	59.8	–	15	21.2	–	0.8	3.1	–
Ugar *et al.*, 1995	120[b]	Echography	7.5	50.8	–	21.7	–	9.2	10.8	–
Acien, 1996	240[c]	HSG/others	27.1	7.9	9.2	27.9	8.3	7.1	12.1	4[d]
Mean % malformations	–	–	15.2	13.2	8.9	37.1	9.2	11.1	4.4	–

Echo/lap = echography/laparoscopy; HSG = hysterosalpingography.
[a]The publications reported obstetric complications and did not include the cases with agenesis.
[b]A further 47 cases were hypoplastic uteri.
[c]A further 36 cases were hypoplastic uteri/DES syndrome.
[d]Corresponding to nine cases of agenesis that were not included in the paper.

Incidence of Müllerian defects in women with recurrent miscarriage

In this group of patients uterine anomalies are diagnosed more frequently, the incidence being 1.8–37.6% (see Table III). However, clear uterine malformations have been reported in 1.8–20.1% of cases. This higher incidence has been found by us (Acien, 1996), but it is necessary to point out that: (i) cases of late abortion and immature delivery, in which the incidence of uterine malformations is higher (43%), were included, and (ii) that incidence was 14.7% considering only cases with complete study for RPL and including arcuate uterus. In all, 36% of the uterine malformations had an associated cervical insufficiency. The conclusions were that the uterine malformations, specially arcuate and bicornuate uterus, are observed in more than 15% of patients with RPL, and even more frequently when late abortions or immature deliveries are included. But these findings were also related to cervical incompetence that is frequently associated with uterine malformation. In other cases of congenital uterine anomalies with early abortions, these were more probably caused by other associated factors (e.g. luteal insufficiency, immunological) that seem to be more common in patients with Müllerian anomaly.

In the 59 cases of recurrent miscarriage or subfertility analysed in Table I, uterine anomalies comprised 25.4%, including hypoplastic and arcuate uterus, but only 5.1% if these minor anomalies were excluded.

From a different viewpoint, patients with Müllerian defects have miscarriges among their obstetric antecedents more frequently than women with a normal uterus (56 versus 21.4%; Acien, 1996). In Table IV it can be seen that in the 500 cases of fertile and infertile women analysed in Table I, the women with uterine anomalies had antecedents of reproductive losses significantly more frequently than women with a normal uterus, and therefore, a lower percentage of live newborns.

Therefore, either directly or indirectly, Müllerian defects are a cause of miscarriage, and the incidence of Müllerian defects among women with recurrent abortions is increased compared with fertile women. That incidence seems to be ~25% although clear uterine malformations (excluded hypoplasic and arcuate uterus) are observed in only 5–10% of cases (and >25% in cases with late abortions and/or immature deliveries).

Distribution of Müllerian defects

Table V shows this distribution in different reported series, and the mean percentage among them, for each type of uterine anomaly. The class most frequently diagnosed was bicornis–unicollis uterus (37%), followed by arcuate (15%), subseptate (13%), didelphys (11%), bicornis–bicollis (9%), complete septate (9%), and unicornuate uterus (4.4%). The frequency of Müllerian agenesis was ~4%.

Conclusions

From the review of the literature and our own cases, we can conclude that if the minor uterine anomalies (hypoplastic, arcuate uterus) are included, the incidence of Müllerian defects varies currently between 7–8% of the normal fertile population and >25% of women with recurrent miscarriage. However, clear uterine malformations are observed in 5% of the general population, in 2–3% of fertile women, in 3% of infertile women, and in 5–10% of patients with recurrent miscarriage, being >25% in cases with late abortions and immature deliveries. The uterine malformation most frequently diagnosed is the bicornuate uterus, although particularly in patients with

abortions, minor uterine anomalies are probably diagnosed more frequently.

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Results of conventional and hysteroscopic surgery

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Mullerian anomalies usually come to medical attention when they become problematic and require treatment. Most of these complications require surgical correction. The most commonly presenting anomaly is the double uterus which can be the source of recurrent abortion and preterm deliveries. The Strassman, Jones and Tompkins metroplasties have been shown to greatly improve the rate of successful deliveries in these patients. Hysteroscopic metroplasty, using either scissors, resectoscope or laser is now the recommended treatment for most septate uteri