High rates of abnormalities in hysterosalpingography in couples with male factor infertility

G. Liberty[1], J. Hyman[2], S. Friedler[1], E.Y. Anteby[1], E.J. Margalioth[2]

[1]Department of Obstetrics and Gynecology Barzilai Medical Center, Ashkelon
[2]Department of Obstetrics and Gynecology, Shaare Zedek Medical Center, Jerusalem (Israel)

Summary

The rate of anatomical abnormalities in infertile couples with obvious male factor is unknown. For this purpose the authors retrospectively analyzed 376 hysterosalpingographies (HSG) of couples with severe male factor. Patients were subdivided into four groups according to the woman's age, and primary or secondary infertility: A - less than 35-years-old, primary infertility, B - less than 35-years-old, secondary infertility, C - 35-years-old or more, primary infertility, and D - 35-years-old or more, secondary infertility. Overall, abnormalities in HSG were demonstrated in 25.5% of the patients, and in 18, 21, 52, and 40 percent of patients in groups A, B, C and D, respectively. Age was found to be a significant independent risk factor ($p < 0.05$) while primary or secondary infertility was not. The adjusted odds ratio for woman who were 35-years-old or more to have any abnormalities in HSG were 3.7-fold greater (95% CI 2.2- 6.23), than women who were less than 35-years-old. In conclusion, relatively high rates of female mechanical abnormalities may be found even in infertile couples with obvious male factor and are significantly more prevalent in older women.

Key words: Hysterosalpingography; Male factor; Infertility; Mechanical factor; Age; Anatomical abnormalities.

Introduction

Evaluation of the reproductive tract in women is an integral part of the investigation of infertile couples. The rates of mechanical abnormalities among infertile women are variable in the different studies and range between 3% to 17% in the uterus, 18% to 37% in the tubes, and 4% to 25% in the pelvis [1-8]. Most of the studies did not report the relationship between the couple's background parameters and the pathologic findings. Kasby *et al.* found correlation between mechanical problems to history of pregnancy. He found tubal pathology in 18% of woman with primary infertility and as much as 30% in those with secondary infertility [3]. In addition, age may be possible factor for mechanical problems. It is well known that the existence of uterine fibroids and endometrial polyps are age-related, and that the cumulative potential exposures to pelvic insult events such as pelvic infection are higher as the woman becomes older [9, 10].

The basic evaluation of couples with infertility includes investigation of male factors, ovulation function, and mechanical problems. Hysterosalpingography (HSG) examination is common tool for the evaluation of the female reproductive tract. Its main advantage is the ability to demonstrate in one examination the uterine cavity, the tubes, and the female pelvis. Although the specificity and sensitivity are limited, it is an integral part of the evaluation of couples who suffer from infertility [7, 8]. However, it may be questionable whether it is justified sending women for mechanical evaluation in cases with clear male factor.

The goal of the present study was to evaluate the female mechanical status in cases where there was an obvious male cause for infertility. For this purpose the authors investigated retrospectively the HSG results of infertile couples with severe male factor. In addition they evaluated the relation between the women background parameters to the rate of mechanical abnormalities in the uterus, tubes, and pelvis. If there are considerable mechanical pathologies, it signifies that women mechanical evaluation should be done even in cases of male subfertility.

Materials and Methods

Over six consecutive years, 1,271 new couples were enrolled to the in vitro fertilization (IVF) clinic in Shaare Zedek Medical Center. The women underwent HSG for mechanical evaluation and the male partners underwent sperm analysis as a prerequisite for treatment. Only the couples with severe male factor were included in the current study population. Three hundred and seventy six males (30% of the total) were diagnosed as having severe male factor. The diagnosis was established following two sperm examinations taken at least six weeks apart. Severe male factor was diagnosed when the sperm concentration was less than five million/ml or if the total motile count was less than one million. HSG analysis was performed by an expert radiologist. Follicle stimulating hormone (FSH) higher than ten IU was diagnosed as "high". Any case of irregular vaginal bleeding, oligomenorrhea or polycystic ovarian syndrome (PCOS) was diagnosed as "dysovulation".

The authors retrospectively analyzed the HSG results of the women into four main groups:

- A (n = 196) – Women less than 35 years old with primary infertility,
- B (n = 86) – Women less than 35 years old with secondary infertility,

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Table 1. — Basal parameters in the different study groups.

	Group	No (%)	Age (Y) ± SD	Infertility years	Children	High FSH (%)*	Dysovulation (%)*
Prim<35	A	196 (52)	26.4 ± 3.3	3.3 ± 2.3	0	1	16.8
Sec<35	B	86 (23)	29.7 ± 3.2	3.2 ± 1.8	1 ± 1.0	2.3	14
Prim>35	C	42 (11)	40.2 ± 5.2	5.2 ± 5.6	0	19	7.1
Sec>35	D	52 (14)	40.1 ± 4.7	4.7 ± 3.4	1.3 ± 1.6	7.7	5.8
Total		376 (100)	30.6 ± 3.7	3.7 ± 3.0	0.4 ± 0.9	4.3	13.6

* $p < 0.001$

Table 2. — The rate of abnormalities according to anatomical site, age, and infertility status.

6				Uterine*			Tubal**			Pelvic***			Any abnorm. in HSG‡
Male	Age	Infert. Type	Group	Congen.	Acquir.	Any uterine abnorm.	Unil. prox. occl.	Bilat. prox. occl.	Any tubal prox. 0ccl.	Hydro salpinx	Pelvic adhes.	Any pelvic abnorm.	
Severe Male Factor	less than 35 years old	PRIM.	A (196)	3.1	2.0	5.1	7.1	3.1	10.2	2.3	1.7	4.0	17.9
		SEC.	B (86)	5.8	2.3	8.1	7.0	2.3	9.3	2.5	2.5	5.1	20.9
	35 years old or more	PRIM.	C (42)	2.4	11.9	14.3	23.8	4.8	28.6	9.7	12.9	22.6	52.4
		SEC.	D (52)	7.7	5.8	13.5	13.5	0	13.5	6.5	13.0	19.6	40.4
TOTAL				4.3	3.7	8.0	9.8	2.7	12.5	3.6	4.0	8.1	25.5

*$p = 0.04$; ** $p = 0.026$; ***$p < 0.001$; ‡$p < 0.001$

- C (n = 42) – Women 35 years old or more with primary infertility,
- D (n = 52) – Women 35 years old or more with secondary infertility.

The analysis of reproductive tract abnormalities was classified according to three anatomical sites examined in HSG - the uterus, the fallopian tubes, and the pelvis:

- In the uterus: congenital uterine malformations, acquired abnormalities (polyps and/or adhesions and/or subserous fibroid) and 'any uterine abnormalities' (congenital or acquired).
- In the fallopian tubes: unilateral proximal occlusion, bilateral proximal occlusions, and 'any proximal occlusions'.
- In the pelvis: pelvic adhesions and 'any pelvic abnormalities'. Distal tubal occlusions/hydrosalpinx which express pelvic abnormality – were also included in this category.

Institutional Review Board of Shaare Zedek Medical Centre approved this study.

Statistical analysis

Statistical analysis included application of the t-test as well as the Mann-Whitney non-parametric test in order to compare quantitative variables between two independent groups. ANOVA was performed when quantitative variables were compared between more than two groups. The Pearson Chi-Square test and the Fisher's exact test were used for testing the association between two categorical variables. The Logistic Regression model was applied in order to assess simultaneously the significance of the effect of age group (age above or below 35 years old) and infertility group (primary or secondary) on five dichotomous outcome variables as follows: 'any uterine abnormalities', 'any proximal tubal occlusion', 'any pelvic abnormalities', 'any tubal and/or pelvic abnormalities', and 'any abnormalities in HSG'. Using this model, the adjusted odds ratio and its 95% confidence interval (CI) was calculated. All tests applied were two-tailed, and a significance level of 5% or less was considered statistically significant.

Results

The basal parameters of the study groups are summarized in Table 1. Seventy-five percent of the women were aged less than 35 years and 25% were older. The mean age in the younger groups was 26 ± 3 to 30 ± 3 years and in the older group 40 ± 5 years. Overall 63% of the women in the study population had primary infertility and 37% had secondary infertility. Dysovulation was apparent in more women younger than 35 years as compared with the older group (14-17% vs 6-7%) ($p < 0.001$), while the older group had a higher prevalence of high FSH levels (1% - 2% vs 8% - 19%) ($p < 0.001$, Table 1).

Overall some abnormality was found in 25.5% of the patients who underwent HSG. 'Any uterine abnormalities', 'any proximal tubal occlusion', and 'any pelvic abnormalities' were found in 8.0, 12.5, and 8.1 percent of the patients, respectively. (Table 2). Even in the younger women with primary infertility (group A) which was the specific subgroup with a lower expected rate of mechanical abnormalities, the authors found 'any abnormality in HSG' in 18% of patients (Table 2).

The authors did five different logistic regression models for 'any uterine abnormalities', 'any proximal tubal occlusion', 'any pelvic abnormalities', 'any tubal and/or pelvic abnormalities', and 'any abnormalities in HSG'. In all of them the authors found that age was an independent factor for the HSG abnormalities while infertility type (primary or secondary) was not ($p = 0.034$, $p = 0.005$, $p = 0.001$, $p < 0.001$, and $p < 0.001$, respectively).

Furthermore, the adjusted odds ratios for woman who were 35 years old or more to have 'any uterine abnormali-

ties', 'any proximal tubal occlusion', 'any pelvic abnormalities', 'any tubal and/or pelvic abnormalities', and 'any abnormalities in HSG' were 2.35 (95% CI 1.1 - 5.16), 2.58 (95% CI 1.33 - 5.01), 5.8 (95% CI 2.47 - 13.63), 2.74 (95% CI 1.57 - 4.78), and 3.7 (95% CI 2.2 - 6.23) fold greater, than women who were less than 35 years old, respectively.

Sixteen congenital uterine malformations (4.3%) were detected in the women in the study population. Of the malformations, ten were bicornuate/septate uterus, two unicornuate uterus, one uterus didelphis, and three T-shaped uterus. No differences were found between the different study groups (Table 2).

Discussion

In the present study the authors found a high rate of reproductive tract abnormalities, in spite of obvious male factor infertility. The discussion about the significance of each pathological finding in HSG on the female fertility status is beyond the scope of this study. However, all of the abnormalities that were assessed in this study may potentially have some impact on the management of infertile couples or at least on consideration for further mechanical evaluation [11-13]. This study focused on couples with an obvious 'non-female' cause of infertility. It does not mean that in this particular group, which probably requires IVF- intracytoplasmic sperm injection (IVF-ICSI), all the pathological findings in HSG are relevant. However it may be extrapolated to emphasize the importance of female reproductive tract evaluation in couples with less severe male factor, or couples without male factor infertility at all.

Surprisingly, even in the younger women (groups A and B) the authors found a relatively high rate (18% - 21%) of anatomical pathologies. However, female age was found to be an independent risk factor for mechanical problems. Women aged 35 years and older (groups C and D) had absolutely very high rates of mechanical abnormalities (40% - 50%). This finding together with the age relates lower ovarian reserve, may emphasize the importance of early anatomical evaluation in fertility assessment of older patients.

The overall prevalence of the HSG findings in the present study concurred with the range described in previous studies [1-6]. Krysiewicz *et al.* summarized a number of studies on female mechanical abnormalities in couples that underwent infertility evaluation [4]. There were similar rates of uterine/endometrial abnormalities in comparison to this study (2% - 5% vs 8%, respectively), but higher rates of tubal abnormalities (25% - 40% vs 17%, respectively) and peritoneal abnormalities (20% - 25% vs 7%, respectively).

In the present study the authors found that primary or secondary infertility has no correlation with abnormal findings in the female reproductive tract. Similar to their study results, Dhaliwal *et al.* found no significant correlation between the type of infertility and the HSG findings [2]. In contrast, Shokeir *et al.* prospectively evaluated 612 consecutive infertile women who underwent a complete fertility workup [14]. The abnormal hysteroscopic findings were higher in those with secondary than those with primary infertility. Behjatnia *et al.* compared hysteroscopic findings in 248 patients with primary infertility with those of 150 women with secondary infertility [15]. In his study, the prevalence of intrauterine synechiae was significantly higher in the latter group.

The acquired intrauterine abnormalities consist of subserosal fibroids, endometrial polyps and intrauterine adhesions. In the present study the authors found a higher rate of intrauterine abnormalities in the older women. The results confirm that the prevalence of uterine fibroids and endometrial polyps are age-related [9-10]. The authors also revealed a higher rate of pelvic adhesions and tubal occlusions in older women, which are usually caused by pelvic inflammatory disease (PID). The potential life exposure for PID is higher as the women is older [5]. The authors may have expected a higher rate of acquired intrauterine abnormalities in women with secondary infertility, given that Asherman's syndrome is frequently caused by infected abortion, curettage, and chorioamnionitis [4]. In the present study however, past pregnancy was not correlated with a higher rate of intrauterine abnormalities. The rate of congenital uterine malformations and the high rate of septate/bicornuate uterus in this group are similar to the findings in other studies [16-17].

In summary, in the present study it was demonstrated that female mechanical abnormalities are prevalent even where there is a clear 'non-female' infertility cause. Age is an independent risk factor for structural abnormalities while primary and secondary infertility are not. Mechanical evaluation seems to be prudent and should not be postponed, at least in infertile patients 35 years and older.

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Address reprint requests to:
G. LIBERTY, M.D.
Barzilai Medical Centre
Hahistadrout 3,
Ashkelon (Israel)
e-mail: liberg2@gmail.com