

**İnfertil Çiftin İlk Basamak Değerlendirmesinde Histerosalpingografi Rutin Herkese Mi Veya Seçilmiş Hastalara Mı Yapılmalı?****Should Hysterosalpingography Routinely Or Selectively Performed As A First Step In The Evaluation Of Infertile Couples?**

Sezcan MÜMÜŞOĞLU, Aslıhan YAZICIOĞLU, Özge Senem YÜCEL, Dila Zengin KASAPOĞLU, Gürkan BOZDAĞ

Hacettepe Üniversitesi Tıp Fakültesi, Kadın Hastalıkları ve Doğum Anabilim Dalı, Ankara, TÜRKİYE

**ABSTRACT**

**Aim:** Routine hysterosalpingography (HSG) in the evaluation of infertile couples is still a subject of discussion. Whereas some of the professional organizations recommend performing HSG to all patients, other authors recommend performing it selectively. We aimed to assess whether risk factors in medical history might predict the presence of tubal disease on HSG.

**Material and methods:** Five-hundred and fifty-three patients whom were assessed with HSG between January-2010 and December-2012 in Department of OBGYN, Hacettepe University were enrolled. Of them, images of 423 cases were sufficient for further evaluation. The pathologies those are observed with HSG were stratified according to the location as uterine, tubal, both tubal and uterine diseases. Meanwhile, all patients were questioned by telephone about Pelvic Inflammatory Disease (PID) symptoms and previous pelvic surgery.

**Results:** Of 423 women, no pathology was noticed in 47.8% of them (n= 202). We were able reach 208 of 423 subjects by phone and 48 (23.1%) of them had a history of previous PID attack. Among patients having significant symptoms for PID, while 50.0% had normal HSG, 33.3% had tubal-only, 8.3% had uterine-only, and 8.3% had both tubal and uterine diseases on HSG. Patients without a history of PID, the respective figures for normal, uterine-only, tubal-only and both uterine and tubal diseases were 50.0%, 17.8%, 27.5% and 5.0% on HSG (p > 0.05 for all comparisons). A presence of previous pelvic surgery was significantly more prevalent among the patients with abnormal HSG findings (42.3% vs. 28.8%, p=0.042) and it remained to be significant predictor for abnormal findings on HSG along with female age in the logistic regression analysis.

**Conclusion:** Even among patients who do not have risk factors for tubal disease, considerable amount of tubal pathology is still determined via HSG. Since some attacks remain subclinical, the underestimation of the prevalence of PID might be responsible for that conclusion. Therefore, only screening for risk factors related with tubal disease might not be ideal before deciding to perform uterine-tubal imaging or not. Whereas increasing female age and presence of previous pelvic surgery might be independent predictors for abnormal HSG findings.

**Keywords:** Tubal patency, PID, HSG, pelvic surgery, routinely

**Running title:** Previous medical history and tubal patency

**ÖZ**

**Amaç:** İnfertil çiftin değerlendirilmesinde rutin histerosalpingografi (HSG) yeri hala tartışma konusudur. Bazı dernekler bültenlerinde HSG'nin tüm hastalara rutin olarak yapılmasını önerirken buna karşın bazı yazarlarda seçilmiş hastalarda uygulanmasını önermektedir. Biz çalışmamızda kadının medikal öyküsündeki risk faktörlerinin HSG'de tubal patoloji varlığını öngörebilip öngöremeyeceğini araştırmayı amaçladık.

**Gereç ve Yöntemler:** Çalışmaya Ocak 2010 – Aralık 2012 tarihleri arasında Hacettepe Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Anabilim Dalında HSG çekilen 553 kadın dahil edildi. Bu HSG'lerin 423 tanesi ileri değerlendirme için uygun yeterlilikte bulundu. HSG'deki patolojiler yerine göre tubal, uterine ve hem tubal hem uterin patoloji şeklinde gruplandırıldı. Aynı zamanda çalışmaya dahil edilen bu hastalar telefon ile aranarak pelvik inflamatuvar hastalık (PID) ve geçirilmiş pelvik cerrahi yönünden sorgulandı.

**Bulgular:** Değerlendirilen 423 kadın arasından %47.8'inde (n=202) herhangi bir patolojiye rastlanılmadı. Telefon ile yapılan ankete 423 hastanın 208 tanesi katıldı ve bunların 48 (%23.1) tanesinin hikayesinde geçirilmiş PID atağı saptandı. PID semptomları olan kadınların %50.0'sinin HSG'si normalken %33.3'ünün sadece tubal patoloji, %8.3'nün sadece uterin patolojisi ve %8.3'nün hem uterin hem tubal patolojisi vardı. PID semptomu olmayan hastalarda bu durum sırasıyla %50.0, 27.5%, %17.8 ve %5.0'idi ve tüm karşılaştırmalar istatistiksel olarak anlamsızdı. Diğer yandan anormal HSG'si olan kadınlar arasında geçirilmiş pelvik cerrahinin istatistiksel anlamlı olarak daha sık olduğu gözlemlendi ve lojistik regresyon analizinde de artan kadın yaşı ile birlikte geçirilmiş pelvik cerrahinin HSG'de

Yazışma Adresi/ Correspondence Address:  
Sezcan Mümüşoğlu  
Hacettepe Üniversitesi Kadın Hastalıkları ve Doğum Anabilim Dalı 06100, Sıhhiye / Ankara  
Tel/Phone: 05326404673  
Fax: 903213052315  
E-mail: sezcanmumusoglu@gmail.com

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anormal bulgular için bağımsız birer belirteç olduğu saptandı.

**Sonuç:** Medikal hikayesinde tubal hastalık yönünden risk faktörü olmayan kadınlar arasında bile HSG'de hala hafif sayılır derecede patolojiye rastlanılmaktadır. Bazı ataklar subklinik kalabileceğinden PID sıklığının azımsanması bu sonuçların nedeni olabilir. Bu nedenle uterin ve tubal görüntüleme yapıp yapılmayacağına sadece tubal hastalık ile ilgili risk faktörleri varlığına göre karar vermek ideal olmayabilir. Buna karşın ilerleyen kadın yaşı ve geçirilmiş pelvik cerrahinin varlığı da anormal HSG bulguları yönünden bağımsız belirteç olabilir.

**Anahtar kelimeler:** Tubal geçirgenlik, PID, HSG, pelvik cerrahi, rutin

## Introduction

It is estimated that 10–30% of infertile couples have a tubo-peritoneal factor as a cause of subfertility (1). As a consequence of this high prevalence, tubal patency testing is essential in the diagnostic fertility work-up.

There are various tests including hysterosalpingography (HSG), chlamydia antibodies (CAT), hysterosalpingo-contrast sonography (HSCoSy) to assess tubal patency, and laparoscopy (2). Of them, due to several advantages of technique, HSG is the most frequently preferred and recommended approach for the evaluation of tubal patency (2). Firstly, HSG can detect proximal and distal tubal occlusion and create a clear image of tubal architectural details (3). Secondly, HSG might allow evaluating the presence of fimbrial phimosis or peritubal adhesions when the escape of contrast is delayed or loculated (3, 4). Thirdly, it also provides information about the uterine cavity. Lastly, the main advantage of HSG is increasing spontaneous pregnancy chance after the procedure. This effect has been especially reported in women that tested with oil-based contrast media (5).

However, there are some disadvantages of HSG. Tubal/myometrial contractions may cause false diagnosis as a proximal tubal obstruction. Therefore, further evaluation may be required to exclude transient occlusion. The sensitivity and specificity of HSG, when compared with chromotubation under laparoscopy for the diagnosis of tubal patency, are 65% and 83%, respectively (6). Although, the low sensitivity of HSG in detecting tubal patency has limited the usage of procedure, the high specificity of HSG has made it a useful test to exclude tubal obstruction in the infertile women (6). In addition, it is an uncomfortable and painful procedure for many patients (7).

Another technique to assess tubal patency is HSCoSy. In this procedure, contrast media is injected from cervix while conventional ultrasound is being done simultaneously. HyCoSy provides better images of the uterus, tubes, and adnexa through injection of echogenic contrast media. It is easily and quickly performed at minimal cost and also well-tolerated by patients (8). According to a meta-analysis that consists of 428 infertile women in the three studies, sensitivity and specificity of HyCoSy compared to chromotubation test under laparoscopy were 93.3% and 89.7%, respectively (9). In that context, Maheux et al. suggested that HyCoSy should replace HSG in the initial work-up of sub-fertile couples (10).

Chlamydia trachomatis IgG antibody testing is a simple, inexpensive, and non-invasive test for predicting the presence of tubal pathology. According to a meta-analysis, the sensitivity of chlamydia antibody test in the diagnosis of tubal pathology is comparable to the sensitivity of HSG in the diagnosis of tubal occlusion (11). If CAT test is negative; the likelihood of tubal pathology is low and there is no need for further assessment. However, if CAT test is positive, it is more complicated to evaluate due to a possibility of cross-reactivity with chlamydia pneumonia (12). Moreover, positive test results cannot be

able to differentiate the past and present infections. Plus, it does not indicate whether chlamydia infection caused tubal damage (13). Therefore, if a positive CAT result exists then further assessment should be performed in order to assess tubal patency (14).

Among these three methods, HSG has been recommended as a standard test to assess tubal patency in the latest ASRM committee opinion (2). Moreover, according to the RCOG guidelines, HSG is suggesting as a screening test for tubal patency even in low-risk women for tubal pathology (15). However, routine HSG test in the evaluation of infertile couples is still a subject of discussion due to infection risk and lack of comfort during the procedure. Whereas some of the authors recommend performing HSG to all patients (2), the other authors recommend performing it in a selected population (16). In this study, we aimed to assess whether risk factors in medical history are sufficient or not to predict the presence of tubal pathologies on HSG.

## Material and Methods

This work was conducted at Hacettepe University School of Medicine in the Reproductive Endocrinology and Infertility Unit. A total of 553 patients who admitted with a complaint of infertility between 2010 and 2012 were enrolled. The HSG images of those patients were retrospectively evaluated from the computer database by a single physician in order to avoid inter-observer variability and by an expert gynecologist in order to avoid intra-observer variability. Among 553 patients 130 with defective image series were excluded from the study remaining 423 patients had sufficient images of HSG for the evaluation. Of them, 208 patients were available and they accepted to join the telephone survey. The questionnaire was applied to these patients that was about baseline characteristics of the patients, previous history of the Pelvic Inflammatory Disease (PID) symptoms and previous pelvic surgery. A patient, who has admitted to hospital with pelvic pain and vaginal discharge regardless of the presence of fever and has been being treated with antibiotics, was considered as a patient with previous PID attack.

HSG images were evaluated for uterine, tubal, both uterine and tubal pathologies and the results were classified in the same way. HSG images with the absence of intrauterine abnormalities, a bilateral tubal spill of the contrast medium without hydrosalpinx and absence of pooling in the diffusion were considered as normal.

Institutional review board of Hacettepe University approved the study protocol. All the statistical calculations were performed with the Statistical Package for Social Sciences (SPSS) for Windows (SPSS version 17.0; SPSS Inc., Chicago, IL) statistical software package. Differences were considered significant at the level of  $p < 0.05$ . In logistic regression model female age, secondary infertility, previous intra uterine device (IUD) use, previous pelvic surgery, and previous PID attack were studied as predictors.

## Results

The mean female age of the all patients was  $30.8 \pm 5.9$  and duration of infertility was  $4.0 \pm 3.6$  years. Of 423 women, no pathology was noticed in 47.8% of them (n= 202).

A total of 208 patients have participated to the study and accepted to take the questionnaire. Demographic characteristics of these patients are depicted in Table 1. Patients with any abnormal HSG findings were significantly older than patients with normal HSG findings ( $32.0 \pm 6.3$  vs.  $29.4 \pm 5.1$ ,  $p=0.027$ ). Secondary infertility, gravida, parity, previous ectopic pregnancy, duration of infertility, and previous IUD use were comparable among the patients with abnormal and normal HSG findings (Table 1). However, in patients with abnormal HSG findings presence of previous pelvic surgery (42.3% vs. 28.8%,  $p=0.042$ ) was significantly higher. When subgroups of pelvic surgeries were compared, although ovarian cystectomy and tubal surgery was higher in-patient with abnormal HSG findings, it failed to reach statistical significance differences (Table 1).

**Table 1 :** Patient characteristics

|                                         | Patients with normal HSG findings<br>n= 104 | Patients with abnormal HSG findings<br>n= 104 | P     |
|-----------------------------------------|---------------------------------------------|-----------------------------------------------|-------|
| Age, year                               | $29.4 \pm 5.1$                              | $32.0 \pm 6.3$                                | 0.02  |
| Secondary infertility                   | 59 (64.3%)                                  | 75 (72.1%)                                    | NS    |
| Gravida                                 | 1 (3)                                       | 1 (2)                                         | NS    |
| Parity                                  | 1 (3)                                       | 1 (1)                                         | NS    |
| D&C                                     | 0 (1)                                       | 0 (1)                                         | NS    |
| Previous ectopic pregnancy              | 0 (0)                                       | 0 (1)                                         | NS    |
| Duration of infertility (years)         | 3 (3.3)                                     | 4 (4)                                         | NS    |
| Previous intra-uterine device use (IUD) | 5 (4.8%)                                    | 4 (3.8%)                                      | NS    |
| Previous pelvic surgery                 | 30 (28.8%)                                  | 44 (42.3%)                                    | 0.042 |
| C-section                               | 15 (14.4%)                                  | 18 (17.3%)                                    | NS    |
| Appendectomy                            | 6 (5.8%)                                    | 6 (5.8%)                                      | NS    |
| Ovarian cystectomy                      | 4 (3.8%)                                    | 9 (8.6%)                                      | NS    |
| Tubal surgery                           | 0 (0%)                                      | 5 (4.8%)                                      | NS    |
| Other abdominal surgeries               | 5 (4.8%)                                    | 6 (5.8%)                                      | NS    |

Descriptive were defined as means  $\pm$  standard deviation or median (inter-quartile range)

NS: non-significant

Based on questionnaire, the frequencies of PID related symptoms among the participants were as follows; vaginal discharge (75/208; 36%), severe pelvic pain (51/208; 24.5%) and fever accompanied by pelvic pain (20/208; 9.6%). A total of 48 (23.1%) patients among 208 patients were considered as pa-

tients with previous PID attack. There were no statistical significant differences among the patients with previous PID attack and without previous PID attack in terms of HSG findings (Table 2). Approximately three quarters of women (80/104; 76.9%) with an abnormal HSG finding had no history of PID (Table 2).

**Table 2 :** HSG results of the patients in terms of previous PID attack

| HSG results                 | Previous PID attack |        |          |        | P  |
|-----------------------------|---------------------|--------|----------|--------|----|
|                             | Negative            |        | Positive |        |    |
|                             | n=160               | (%)    | n=48     | (%)    |    |
| Normal findings             | 80                  | (50.0) | 24       | (50.0) | NS |
| Uterine pathology           | 28                  | (17.5) | 4        | (8.3)  | NS |
| Tubal pathology             | 44                  | (27.5) | 16       | (33.3) | NS |
| Uterine and tubal pathology | 8                   | (5.0)  | 4        | (8.3)  | NS |

Among patients with pathologic HSG findings; 37 of them had unilateral, 7 of them had bilateral intramural block; 15 of them had unilateral, 4 of them had bilateral mid-tubal pathology; 56 of them had unilateral, 17 of them had bilateral distal tubal pathology; 38 of them had bilateral and 7 of them had unilateral adnexal collection.

In logistic regression model significant predictors of the abnormal HSG findings were only female age and previous pelvic surgery (Table 3),

**Table 3 :** Logistic regression analysis for independent predictor of abnormal HSG findings

|                          | Odds ratio | 95% Confidence Interval | P     |
|--------------------------|------------|-------------------------|-------|
| Female age               | 1.093      | 1.013 – 1.178           | 0.021 |
| Secondary infertility    | 0.882      | 0.351 – 2.215           | 0.789 |
| Previous PID attack      | 0.973      | 0.486 – 1.947           | 0.938 |
| Previous IUD use         | 0.615      | 0.139 – 2.724           | 0.522 |
| Previous pelvic surgery* | 1.577      | 1.089 – 2.282           | 0.016 |

\* Considered as a dichotomous variable, presence or absence of pelvic surgery

whereas secondary infertility, presence of previous PID attack, and previous IUD use were not.

## Discussion

In this study, we evaluated the association between the risk factors in medical history in the context of tubal damage and HSG findings. According to our results, the risk factors such as vaginal discharge, severe pelvic pain accompanied by fever, a previous IUD using history were not related to abnormal findings on HSG. Importantly, three quartiles of subfertile women with abnormal HSG findings had no PID related risk factors in their medical history. However increasing female age and presence of any previous pelvic surgery seem to be independent predictors for abnormal HSG findings.

There are various studies recommending tubal patency testing selectively, especially in patients with some risk factors: Coppus et al. suggested to use decision rules to express a woman's probability of severe tubal pathology at the couple's first consultation (17). They aim to select women for tubal testing

more efficiently. It is well known that PID is the main cause of tubal infertility (18). Nevertheless, women who give no history of the disease end up with tubal factor infertility, which has been apparently induced by past episodes of PID (19). There might be silent attacks of PID causing tubal infertility that we should take into account. Also, it was confirmed by a systematic review that risk factors such as a history of PID, complicated appendicitis, ectopic pregnancy and pelvic surgery are indicators for tuba-peritoneal pathology. Based on the available data in the literature, laparoscopy might be recommended in the first step with the presence of risk factors for tubal damage in medical history, and guidelines recommend using HSG as a screening tool for patients with no co-morbidities (15, 20).

It is a known fact that risk factors in medical history such as PID increase the possibility of tubal damage (21). Rozewicki et al. reported that patients with a medical history included inflammatory processes had pathological signs on HSG more frequently when compared to the inflammatory-free ones (21). However, patients without risk factors had also pathological findings on HSG. Although the numbers of pathological cases are higher in the patients with inflammatory processes, nevertheless, identifying patients with previous PID symptoms can recognize severe tubal pathology. On the other hand, decision-making based on the patient's medical history would probably cause underestimation of the tubal pathology. We should bear in mind that the patient without any risk factors on their medical history but having abnormal findings on HSG. We reported that half of the patient without any risk factors for PID had abnormal finding on HSG evaluation. It is clear that medical history, especially PID related symptom query, has not have sensitivity or specificity to predict the tubal pathological on HSG.

Retrospective design and failure to reach all of the patients were the major limitations of this study. The differences between groups may come forth from the non-responsiveness rate of the patients.

Even among patients who do not have risk factors for tubal disease, considerable amount of tubal pathology is still determined via HSG. Since some attacks remain subclinical, the underestimation of the prevalence of PID might be responsible for that conclusion. Therefore, only screening for risk factors related with tubal disease is not ideal before deciding to perform uterine-tubal imaging or not. Whereas increasing female age and presence of previous pelvic surgery might be independent predictors for abnormal findings on HSG. Nevertheless, we can conclude that tubal patency testing might not be offered selectively based on the previous PID history in order to avoid underestimation of tubal damage.

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