Original Article

Role of Hysterosalpingography in Diagnosing Tubal Blockage – A Prospective Diagnostic Study

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Abstract

Background: Women with abnormal hysterosalpingography (HSG) are anxious regarding the presence of tubal pathology. It is important to know the predictive value of HSG and the need for subsequent laparoscopy following an abnormal report. In the era of assisted reproductive technology, the role of invasive testing such as diagnostic laparoscopy is being increasingly questioned due to its invasiveness and associated risks. There is a need to explore the positive predictive value (PPV) of HSG in detecting bilateral tubal block in our population as PPV changes with the prevalence of disease. **Aim:** The aim of this study was to evaluate the diagnostic accuracy of HSG in identifying tubal blockage in subfertile women. **Setting and Design:** This was a prospective diagnostic study conducted in the department of reproductive medicine and surgery in a university-level hospital. **Materials and Methods:** The study included 199 subfertile women who had undergone HSG earlier and were planned for laparoscopy from April 2017 to January 2021. Findings of HSG and laparoscopy were compared with HSG as index test and laparoscopy as reference test, and the outcomes analysed were PPV of HSG for a bilateral tubal block, bilateral hydrosalpinx, abnormal HSG (unilateral or bilateral tubal block) and agreement between HSG and diagnostic laparoscopy in detecting normal and abnormal findings. **Statistical Analysis:** Kappa statistics, Stuart–Maxwell tests of marginal homogeneity and prevalence-adjusted bias-adjusted kappa (PABAK) statistics were used. **Results:** The PPV for a bilateral block with HSG was 20.9% (95% CI: 13.7–29.7). The PPV of HSG for bilateral hydrosalpinx was 50.0% (95% CI: 6.8–93.2). PABAK was estimated to be 0.42 (95% CI: 0.30–0.55), suggestive of moderate agreement between the tests. Findings of laparoscopy in women with at least one patent tube in HSG showed that in 12.3% of cases, the management was likely to change due to the operative findings. **Conclusion:** The current study showed low PPV for bilateral tubal block diagnosed with HSG which translates into a need for further confirmation by laparoscopy. In one out of every eight women with at least one patent tube on HSG, performing laparoscopy changed the management.

Keywords: *Hydrosalpinx, hysterosalpingography, laparoscopy, positive predictive value, tubal block*

Introduction

Infertility is known to affect approximately one in six couples in the reproductive age group.[1] The burden

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of infertility is approximately 7%–9% in the developing regions across the world.[2] The aetiology of female infertility can be varied and is attributed to ovarian factors such as ovulatory dysfunction or diminished ovarian reserve, uterine or cervical factors and tubal and peritoneal factors. In low- and middle-income countries, tubal factor infertility is one of the common causes of infertility and tubal pathologies account for almost 30%–35% of infertility.[3]

There are numerous tests to detect tubal abnormalities, but hysterosalpingography (HSG) and diagnostic laparoscopy are the commonly used tests in contemporary practice. The HSG is often considered the first-line diagnostic test for assessing tubal patency, although laparoscopy is commonly viewed as the gold standard.[4] HSG has been reported to have a sensitivity of 53% and a specificity of 87% for any tubal pathology and 46% and 95% for bilateral tubal pathology.[5] Low sensitivity of HSG for identifying tubal pathology remains an important limitation. Nevertheless, HSG is still considered a first-line diagnostic test for assessing tubal patency since it is relatively inexpensive, less invasive and provides additional information on uterine cavity abnormalities.

Diagnostic laparoscopy is usually indicated in women with abnormal HSG and in women with clinical findings suggestive of pelvic pathologies such as pelvic inflammatory disease (PID) or endometriosis.[6] An earlier study evaluated the post-laparoscopy findings, performed following an abnormal HSG, and reported that amongst the bilateral tubal pathology cases diagnosed after HSG, the finding was confirmed in only 46% of the cases. Since there is a suboptimal correlation between HSG and diagnostic laparoscopy, the study suggested a definite role of laparoscopy as a follow-up for abnormal HSG.[7]

Laparoscopy is invasive, expensive and requires general anaesthesia. Risks with laparoscopy include infection, injury to the bowel and blood vessels.[8] In an era of *in vitro* fertilisation (IVF), which is a fairly low-risk procedure, if we can reach a diagnosis of the bilateral tubal block with certainty without performing laparoscopy by less invasive methods (e. g., HSG), this will be immensely beneficial for the women since surgical intervention is avoided.

One of the important causes of tubal pathology is PID. A diagnosis of PID is made in 1.6% of women aged 16–45 years attending their primary-care physician in the United Kingdom. The prevalence of PID is estimated to be between 3% and10% in India.[9] However, because most PIDs are asymptomatic, this figure underestimates the true prevalence. The prevalence of PID varies according to different regions, for example, tuberculosis, which is an important cause of PID, is more common in rural regions, and hence, it is likely that the prevalence of tubal factors may vary as well.[10] The prevalence of disease affects the predictive value of diagnostic tests, i.e., with an increase in the prevalence, the positive predictive value (PPV) of the test increases.

The diagnostic test parameters such as predictive value and agreement between the tests are more important from patients' perspectives, whereas sensitivity and specificity are of interest to clinicians.[11,12] Once a diagnostic test is performed, the predictive value (positive or negative) is of clinical importance in decision-making. Commonly, the infertile couples visit secondary/tertiary infertility centres with abnormal HSG reports, for opinion and/or further evaluation. Since there is a paucity of data on the exact prevalence of tubal factor infertility, the clinical decision is largely based on European and American guidelines. We decided to explore the PPV of HSG in diagnosing bilateral tubal block which will help in deciding the role of diagnostic laparoscopy in the Indian setting.

Materials and Methods

The current study was a prospective diagnostic study. It was conducted in the department of reproductive medicine and surgery in a university-level hospital from April 2017 to January 2021. The institutional review board approval was obtained prior to the beginning of the study (IRB no 10514, Date: 1 February 2017). The study was performed in accordance with the ethical standards laid down in the Declaration of Helsinki. Informed consent was obtained prior to the recruitment of the patients for the study.

The objectives of the study were (a) to estimate the PPV of bilateral tubal block and bilateral hydrosalpinx of HSG in comparison with diagnostic laparoscopy and (b) to estimate the agreement between HSG and laparoscopy for normal and abnormal findings.

Women with infertility who had undergone HSG earlier with radiological films available for interpretation and were planned for laparoscopy were invited to participate in the study. Those who were willing were included after obtaining written informed consent. Women with uterine anomalies and endometriotic cysts on ultrasonography or an obvious clinical event suggestive of severe PID or severe endometriosis were excluded from the study group. The HSG results were documented in the pro forma in terms of tubal patency or block (unilateral or bilateral) and presence

or absence of hydrosalpinx (unilateral or bilateral). The HSG films were reported by a radiologist and then reinterpreted by a trained reproductive medicine specialist prior to laparoscopy. Diagnostic laparoscopy was planned in women with abnormal HSG and in those with a suspicion of endometriosis or pelvic pathology. It was performed by experts in reproductive medicine, and operative findings documented in detail with pictures stored for future reference. All laparoscopy findings including the tubal patency, presence of hydrosalpinx, adhesions in the pelvic area and perihepatic area, endometriosis features and stage were documented. The HSG findings once interpreted and documented in the pro forma were not changed following laparoscopy.

The presence of 'disease' was defined as the presence of bilateral tubal block or bilateral hydrosalpinx on laparoscopy for calculating PPV for bilateral tubal block/hydrosalpinx. 'No disease' was defined as either both tube patent or at least one tube patent or no bilateral hydrosalpinx. Similarly, we defined 'disease' as the presence of unilateral or bilateral block on laparoscopy for calculating PPV for abnormal HSG (unilateral or bilateral block).

The primary outcome of the study was PPV of HSG for a bilateral tubal block with diagnostic laparoscopy as the reference test.

The secondary outcomes were (i) PPV of HSG for bilateral hydrosalpinx with diagnostic laparoscopy as a reference test, (ii) PPV of abnormal HSG (unilateral or bilateral tubal block) in comparison with diagnostic laparoscopy and (iii) agreement between HSG and diagnostic laparoscopy in detecting normal and abnormal findings.

Statistical analysis

The data were entered in EpiData software. The characteristics of the study participants were described using relative frequencies for categorical variables and means or medians with measures of spread for continuous variables. Kappa statistics were used to describe the overall agreement on either the unilateral or bilateral tubal blocks between HSG and laparoscopy. The Kappa statistic will be influenced by bias when there is an imbalance in the direction of disagreements. Stuart–Maxwell tests of marginal homogeneity were used to identify unidirectional bias between the HSG and laparoscopic responses. Prevalence-adjusted bias-adjusted kappa (PABAK) statistics and its 95% CI were calculated to account for the effect of bias and/or prevalence on kappa estimates.[13] The positive and negative predictive values on HSG in a bilateral tubal block and 95% confidence interval (CI) were estimated. Assuming a 41% PPV for HSG, the study would require a sample size of 200 with 6.8% absolute precision and 95% confidence.[5] All analyses were performed using STATA IC version 16 (Stata Corp, College Station, TX, USA).

Results

The planned sample size was 200, but one participant was inadvertently entered twice in the study database (detected during the analysis phase), which was later corrected, and hence, the final number of participants included in the analysis was 199.

The mean age of the included participants was 28.2 ± 3.5 years. The baseline characteristics are summarised in Table 1. Primary infertility was seen in 76.4% of the women, whereas 23.6% had secondary infertility. The median interval between HSG and laparoscopy was 2 years (interquartile range: 1–3). The HSG abnormalities were seen in 86% of the women, amongst which unilateral block was reported in 36% and bilateral block in 64%. Abnormal laparoscopy findings were reported in 31%. Amongst these, 56% had a unilateral block and 44% had a bilateral block [Table 1].

The PPV of bilateral block in HSG was 21% (95% CI: 13.7–29.7). The PPV of HSG showing bilateral hydrosalpinx was 50% (95% CI: 6.8–93.2). The

Table 1: Baseline characteristics of the study participants

Variables	*n*=199, *n* (%)
Age (years), mean±SD	28.2±3.5
Duration of infertility (years), median (IQR)	5 (3-7)
Infertility	
Primary	152 (76.4)
Secondary	47 (23.6)
Interval between HSG and laparoscopy (years), median (IQR)	2 (1-3)
HSG	
Normal	27 (13.6)
Abnormal	172 (86.4)
Abnormal HSG	
Unilateral bock	62 (36.0)
Bilateral block	110 (64.0)
Laparoscopy	
Normal	138 (69.4)
Abnormal	61 (30.7)
Abnormal laparoscopy	
Unilateral block	34 (55.7)
Bilateral block	27 (44.3)

HSG=Hysterosalpingography, SD=Standard deviation, IQR=Interquartile range

PPV of abnormal HSG (unilateral or bilateral block in HSG) was 32% (95% CI: 25.6–40.1) [Table 2].

The agreement between HSG and laparoscopic findings was categorised and presented as a bilateral block, unilateral block and normal findings in a 3 × 3 table [Table 3]. As there was bias in the off-diagonal cells due to the disagreement between the HSG and laparoscopy evaluation and the shift in the marginal distribution of the categories, the Cohen's kappa was found to be very low in our study. Hence, the PABAK was estimated to be 0.42 (95% CI: 0.30–0.55), suggesting moderate agreement between the tests.

In women who had a unilateral block (n = 62) on HSG, 21% had a unilateral block, 76% had normal findings and 3% had a bilateral block on laparoscopy. In women with bilateral patent tubes (n = 27) on HSG, 81.4% had similar findings, whereas 7% had a bilateral block and 11% had a unilateral block on laparoscopy.

There were 89 women who had bilateral or unilateral patent tubes in HSG. We recorded the additional information given by laparoscopy in these women to explore if the decision of laparoscopy changed the overall management. It was noted that 4% had a bilateral tubal block. The minimal, mild, moderate and severe endometrioses were found to be seen in 26%, 6%, 1% and 2% of women, respectively. Four (5%) women had peritubal adhesions [Table 4]. Overall, in 12% of women, the further management changed due to the operative findings (e.g., moderate/severe endometriosis, bilateral tubal block or pelvic adhesions).

The HSG abnormalities in relation to proximal and distal blocks were checked in laparoscopy, and the findings are described in Table 5.

Discussion

The current study showed that the PPV of HSG for the bilateral tubal block was low clearly indicating the limitation of HSG as a diagnostic test for tubal patency. The agreement between HSG and laparoscopy for unilateral tubal block, bilateral block and normal findings was suggestive of moderate agreement. A laparoscopy in women with HSG findings of unilateral or bilateral tubal patency resulted in a change in the treatment plan in one out of eight women.

A study by Mol *et al*. observed a PPV of 35.5% for bilateral tubal occlusion, whereas the retrospective study by Berker *et al*., in 264 women, reported a PPV of 67.5% for bilateral tubal block.[14,15] The differences in the PPV in these studies compared to our study can be explained by the fact that the prevalence of PID varies according to the geographic location and PPV is dependent on the disease prevalence.

The PPV for any tubal abnormality (either unilateral or bilateral tubal block) was also low in the current study. The studies by Mol *et al*. and Berker *et al*. reported PPVs of 50.1% and 54.6%, respectively, for any tubal abnormality.[14,15] These studies are in agreement with the current study suggesting an overall low PPV. Most of the evidence is in favour of going ahead with laparoscopy in women with abnormal HSG.[7,16]

The PPV for bilateral hydrosalpinx was 50%, which would again necessitate a laparoscopy to confirm the findings. This needs a cautious interpretation as the number of women who had a bilateral hydrosalpinx on HSG were low because these women would have been associated clinical findings or ultrasound findings suggestive of pelvic pathology and they would have undergone laparoscopy directly bypassing the HSG as recommended by ASRM and NICE guidelines.[6,17] A study by Ngowa *et al*. also showed a PPV for hydrosalpinx of 53.3% (95% CI: 39.1–67.1) similar to the present study.[18]

The findings in laparoscopy in women who had unilateral or bilateral patent tubes were documented to know the extra information the laparoscopy would give, which would have been missed by proceeding directly for further fertility treatment based on the HSG report. The management changed in a subset of women. The

Table 2: Positive predictive value of abnormal HSG findings in comparision to laparoscopy

PPV for bilateral tubal block	Disease (bilateral tubal block in laparoscopy)	No disease (no bilateral tubal block or only unilateral block)	Total	PPV (%) (95% CI)
HSG (bilateral block)	23	87	110	20.9 (13.7-29.7)
PPV for hydrosalpinx	**Disease (bilateral hydrosalpinx in laparoscopy)**	**No disease (no bilateral hydrosalpinx)**	**Total**	**PPV (%) (95% CI)**
HSG (bilateral hydrosalpinx)	2	2	4	50.0 (6.8-93.2)
PPV of abnormal HSG	**Disease (unilateral or bilateral block in laparoscopy)**	**No disease (bilateral patent tubes in laparoscopy)**	**Total**	**PPV (%) (95% CI)**
Abnormal HSG (unilateral or bilateral block)	56	116	172	32.5 (25.6-40.1)

HSG=Hysterosalpingography, CI=Confidence interval, PPV=Positive predictive value

meta-analysis by Swart *et al*. and also few other studies observed the poor reliability of HSG in diagnosing peritubal adhesions.[16,18,19] This is one of the main pitfalls in HSG as the endometriosis and tubal adhesions would be undetected and the treatment would have been incorrect, especially in women with moderate-to-severe endometriosis, and extensive tubal adhesions in whom IVF would be delayed due to the false reassurance by HSG.

The agreement kappa statistic in the study by Mol *et al*. was also 0.42 (95% CI: 0.37–0.48) suggesting a moderate agreement which is similar to the present study.[14] The strength of the present study is that it is a prospective study. It helps to guide the clinician in developing countries, where the tubal factor infertility accounts for 30%–35% of the cases. Due to the low PPV of an abnormal HSG, it necessitates an additional laparoscopy to confirm or refute the findings.[20]

Table 3: Agreement between hysterosalpingography and laparoscopic findings

HSG findings	Laparoscopic findings			
	Bilateral block	Unilateral block	Normal	Total
Bilateral block	23	18	69	110
Unilateral block	2	13	47	62
Normal	2	3	22	27
Total	27	34	138	199

Percentage of observed agreement=29.2%, PABAK and 95% CI: 0.42 (0.30-0.55). HSG=Hysterosalpingography, PABAK=prevalence-adjusted bias-adjusted kappa, CI=Confidence interval

Table 4: Findings in laparoscopy in cases of bilateral or unilateral patent tubes in hysterosalpingography

	Bilateral or unilateral patent tubes in HSG (*n*=89)
Bilateral block	4 (4.5)
Minimal endometriosis	23 (25.8)
Mild endometriosis	5 (5.6)
Moderate endometriosis	1 (1.1)
Severe endometriosis	2 (2.2)
Peritubal adhesions	4 (4.5)

HSG=Hysterosalpingography

The limitations of the current study are that the sensitivity and specificity of HSG could not be calculated, which would have been more informative. We focussed on the PPV and not on the common parameters of diagnostic accuracy outcomes such as sensitivity and specificity as we wished to address the patient-related query about the next step of management in a tertiary level fertility clinic. From a patient perspective, PPV and NPV are more relevant outcomes, especially when the diagnostic test has already been performed. The other limitation was that we recruited only the women who presented to us at a tertiary care level, which would have led to selection bias. Another limitation was that the HSG interpretation is operator-dependent, which would have also led to bias. For the women with normal HSG, the interval between HSG and laparoscopy was longer (more than a year) in some women, who are likely to present with acquired pathology in due course such as PID or endometriosis which would have been picked by laparoscopy done at a much later date and would lead to a lowered agreement between the tests, as HSG was done before the acquired health condition.

Conclusion

The current study found low PPV for the bilateral tubal block diagnosed with HSG which translates into a need for further confirmation by laparoscopy. In one out of every eight women with unilateral or bilateral patent tubes, performing laparoscopy changed the management.

Overall, in Indian setting, while there is a definite role of performing laparoscopy following abnormal HSG, the benefit of performing laparoscopy seems to be lower in women with documented tubal patency following HSG. Further studies need to explore the cost-effectiveness of performing laparoscopy in women with documented tubal patency on HSG.

Data availability

The data that support the findings of this study can be shared on request, subject to regulatory permission from the corresponding author.

Table 5: Agreement of hysterosalpingography findings with laparoscopy in relation to site of block

	Laparoscopy						
HSG	Unilateral proximal	Unilateral distal	Bilateral proximal	Bilateral distal	One proximal and one distal	Normal	Total
Unilateral proximal	2 (5.8)	3 (8.8)	1 (2.9)	0	1 (2.9)	27 (79.4)	34
Unilateral distal	2 (7.1)	6 (21.4)	0	0	0	20 (71.4)	28
Bilateral proximal	5 (8.9)	1 (1.8)	11 (19.6)	2 (3.5)	0	37 (66.0)	56
Bilateral distal	2 (5.7)	4 (11.4)	0	4 (11.4)	0	25 (71.4)	35
One proximal and one distal	3 (15.7)	3 (15.7)	3 (15.7)	1 (5.26)	2 (10.5)	7 (36.8)	19

HSG=Hysterosalpingography

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Conflicts of interest

Dr. Mohan S Kamath is the Deputy Editor for Journal of Human Reproductive Sciences. However, for the current manuscript, he was not involved in the editorial decisions or blind peer review process. The other authors have no conflict of interest.

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