Hysteroscopy is Gold standard in Uterine evaluation for Infertility, but HSG still has a place

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ABSTRACT

Background: Uterine abnormalities, congenital or acquired are implicated as causal factor in 10%-15% of infertile couples reporting for treatment. Hysteroscopy, hysterosalpingography (HSG), saline-infusion-sonography and USG are available for evaluation of uterine cavity. HSG helps in initial evaluation of a sub-fertile woman, but hysteroscopy is gold standard as it allows direct visualisation of intrauterine pathology and treatment in same-setting, if required. Aims and Objective: To describe hysteroscopic findings of infertile patients and compare the observations with their respective HSG findings. Materials and Methods: It’s a prospective analysis of 105 women with infertility who attended tertiary-care hospital during 18 months fulfilling pre-defined inclusion and exclusion criteria. All 105 infertility cases were evaluated with both HSG and hysteroscopy; observations were recorded and co-related with each other. Results: Among 105 cases, maximum (76.19%) were 25-35 years of age. The primary infertility accounted for 68.57% cases. Abnormal HSG findings observed in 19 cases (20%), most common being filling-defect. Hysteroscopy detected abnormalities in 39 cases (37.14%), commonest being endometrial polyp. Out of 39 cases of abnormal uterine cavity detected on hysteroscopy, only 19 were picked-up by HSG, rest 20 cases failed to be identified by HSG. The strength of agreement between hysteroscopy and HSG calculated is moderate (Kappa=0.505). Conclusion: As HSG had low false positivity (03%), high positive-predictive-value (90.48%) and negative-predictive-value (76.19%) and high specificity (96.96%) it is still considered as a first-choice screening method for uterine cavity. However, high false-negative-value (51.28%) of HSG makes hysteroscopy a better diagnostic test. HSG couldn’t differentiate endometrial polyp, adhesions and sub mucus fibroid, shown them as filling defect only.

Key words: HSG; hysteroscopy; USG, Uterine cavity; infertility

INTRODUCTION

Abnormal uterine cavity is present in 34-62% of infertile women. Among these, 10% to 15% of the couples seeking treatment for infertility has aetiology related to acquired or congenital uterine abnormalities.¹ Acquired uterine lesions, such as sub-mucosal myomas, uterine polyps, asherman syndrome etc. may cause difficulty in conception by interfering with proper embryo implantation and development. Congenital uterine malformations are also implicated in delaying natural conception.² Therefore, one of the fundamental steps of an infertility evaluation is to assess the morphology and regularity of the uterine cavity.³

For evaluation of uterine cavity of infertile women, various procedures available are: Hysteroscopy,
Hysterosalpingography (HSG), Saline Infusion Hysterosonography (SIS) and Ultrasound (USG). The World Health Organization (WHO) recommends hysterosalpingography (HSG) alone for infertile women evaluation while hysteroscopy is recommended only when clinical or other basic examinations (ultrasound, HSG) predict intrauterine pathology.

Traditionally, hysterosalpingography has been the most commonly used technique in the evaluation of the uterus and fallopian tubes in infertile women. The advantages of HSG include the ease of performance, safety, less time consuming and its cost effectiveness. The additional information on tubal status is quite vital. But as suggested by earlier studies, HSG may miss 30% to 40% of uterine cavity abnormalities. Given the high false-negative rate, and the inability to treat abnormal findings concurrent with diagnosis, HSG has significant limitations when evaluating the endometrial cavity.

Hysteroscopy has been proved to be the definitive method for evaluation of the uterine cavity and diagnosis of associated abnormalities in infertile couple work up as observed by many previous studies. Its reliability and safety as an office procedure has been documented widely in literature. Hysteroscopy has two main applications in infertile patients: to evaluate the cervix and uterine cavity revealing the nature and localization of endo-cavitary lesions; allows diagnosis of infectious, functional and organic abnormalities; guidance of the endometrial biopsies and histologic evaluation and even treatment of correctable abnormalities.

HSG, USG or dilatation and curettage are blind or indirect diagnostic or screening procedures whereas hysteroscopy offers direct visualisation of the uterine cavity which is a great advantage. Thus, hysteroscopy has been acknowledged as the gold standard procedure for uterine cavity exploration.

Based on the results of the previous studies, it appears that more than 30% of the women with normal HSG are found to have a uterine cavity pathology after diagnostic hysteroscopy, which can be an important contributing factor for infertility. These women may be unnecessarily evaluated or mistakenly treated, as their intrauterine pathology has been missed.

Moreover, hysteroscopy is useful in identifying endometrial lesions undetectable on HSG. This explains why many prefer hysteroscopy as a first line routine investigation for infertility patients regardless of guidelines.

In view of these we investigated if HSG can be replaced by the diagnostic hysteroscopy as a first line infertility investigation. The aim of the study was to describe the hysteroscopic findings in infertile patients, examine the role of diagnostic hysteroscopy in a basic infertility workup and to correlate the hysteroscopic uterine findings with normal and abnormal hysterosalpingographic findings.

**MATERIALS AND METHODS**

This prospective observational study was conducted in Department of Obstetrics and Gynaecology, ESI-PGIMS & ESIC, Medical College and Hospital & ODC(EZ) Joka, Kolkata from January 2015 to June 2016. The study protocol was approved by the ethical review committee of the institute and informed written consent was taken from all the participants. The patients attending gynaecology OPD with infertility were selected according to the following inclusion and exclusion criteria.

**Inclusion criteria**
1. Age 18-40 years.
3. Infertile women, primary and secondary.
4. Women with normal and abnormal hysterosalpingography unable to achieve pregnancy.
5. Infertile women with menstrual abnormality.

**Exclusion criteria**
1. Age<18 years and >40years.
2. Parous women who are not desirous of further pregnancy.
3. Unmarried women.
4. Women with husband having azoospermia.
5. Women with known uterovaginal abnormality like mullerianagenesis, transvaginal septum, hypoplastic uterus etc.
6. Morbid women like COPD, CVA, CHD, Cancer patients.

Although sample size calculated as per standard was n =96 but we took 105 to account for loss to follow up. After recording the detailed history and doing physical examination according to the pre structured proforma, patients were investigated for complete blood count, renal function tests, liver function tests and endocrine profile. The special investigations like husband semen analysis, hysterosalpingography and transabdominal USG of pelvis was routinely performed and documented. After getting informed written consent for the procedure, diagnostic hysteroscopy
was meticulously performed. Hysteroscopy was focused on pathologies like cervical polyp, uterine synechia, uterine polyp, submucous fibroid, septate uterus, congenital deformity etc. The patient's general condition, vitals were checked post procedure and kept under observation for any complications. A predesigned proforma was filled at the time of hysteroscopy with detailed record of hysteroscopic findings, which were later compared with hysterosalpingography reports. Data base was made in MS Excel and documented in a tabulated form. Appropriate statistical tests were applied as required. Kappa test (Altman, 1991) was used to find out any agreement between two diagnostic modalities. Descriptive statistics was used for demographic features.

**RESULTS**

Out of 105 patients, majority (76.19%) belonged to 25-35 years age group followed by >35-year age group with 14.29% women. Mean age of presentation was 29.95 years.

Most of the patients were nulliparous (68.57%) and parity one found in 29.52% of cases. In our study majority of the patients belonged to the middle class (67.62%) according to Modified Prasad’s classification (2014). Normal bleeding pattern was found in 65.71 % cases followed by oligomenorrhea in 26.67% women.

In our study majority of the patients (57.14%) reported less than 5 years of infertility. Mean duration of infertility was 4.74 years. 69 (65.71%) were diagnosed with primary infertility while 36 (34.29%) had secondary infertility.

In the present study, hysterosalpingography was carried out in all study subjects (n=105) for basic work up of infertility. The abnormal findings were documented in 20% (21/105) of cases. The most common abnormal finding on HSG was intrauterine filling defect in 33.33% women, followed by subseptate uterus (14.29%) and small uterine cavity (14.29%). Overall filling defect was found in 6.67% (7/105) of infertile patients.

Hysteroscopy was performed in all 105 infertile women. The most common indication for diagnostic hysteroscopy was as a part of an infertility workup (102 cases). Other indication included cases being part of a continuous workup before IVF treatment.

Hysteroscopy revealed a normal uterine cavity in 66/105 (62.86%) women and abnormal uterine cavity was found in 39/105 (37.14%) women. Among abnormal hysteroscopy 11 patients presented with congenital uterine cavity defect and 28 patients with acquired uterine lesion. Overall congenital uterine defect was found in 10.47% of infertile cases.

Hysteroscopy on basis of standardised magnified picture of uterine cavity identified endometrial polyps of different sizes in 8.57% patients, endometrial adhesion in 6.67% cases, subseptate uterus in 5.71%, septate uterus in 1.9%, cervical stenosis in 2.86%, cervical polyp in 4.76%, cornual fibrosis in 3.81%, unicorneate uterus in 0.95%, small cavity in 1.9%, atrophic endometrium in 0.95%, endometrial hyperplasia in 0.95%, submucous myoma in 1.9% cases and deformed cavity in 0.95% of cases. Among women with abnormal results, 12.82% showed more than one abnormality.

There were 20 abnormal findings on hysteroscopy which could not be diagnosed on HSG. 2 cases of abnormal HSG, hysteroscopy revealed normal cavity (Table 1). HSG could not differentiate endometrial polyp, adhesion, submucous myoma properly. It only depicted filling defect. But hysteroscopy could properly identify these conditions. Strength of agreement between hysteroscopy and hysterosalpingography was moderate (Kappa =0.50).

**DISCUSSION**

Traditionally, and even today, HSG has been the most commonly used test as first step in tubal and uterine factor evaluation in female infertility work up. Although it’s quite reliable for tubal patency but due to its low specificity and sensitivity in assessing the uterine cavity hysteroscopy is being resorted as first line. Hysteroscopy is an excellent tool for evaluating the uterine cavity. The feasibility and safety of hysteroscopy has improved dramatically, thanks to important progress made both in the techniques used in the procedure as well as in the technology.

<table>
<thead>
<tr>
<th>Table 1: Discrepancy between Hysteroscopy and HSG findings</th>
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<tbody>
<tr>
<td>Hysteroscopy (n=105)</td>
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<tr>
<td>----------------------</td>
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<tr>
<td>Abnormal Hysteroscopy (19)</td>
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<tr>
<td>Normal Hysteroscopy (64)</td>
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<tr>
<td>Normal (1)</td>
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<tr>
<td>Normal (1)</td>
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<tr>
<td>Endo Polyp (5)</td>
</tr>
<tr>
<td>Cervical Polyp (3)</td>
</tr>
<tr>
<td>Adhesions (5)</td>
</tr>
<tr>
<td>Ostium Fibrosis (2)</td>
</tr>
<tr>
<td>Atrophic Endometrium (1)</td>
</tr>
<tr>
<td>Hyperplastic Endometrium (1)</td>
</tr>
<tr>
<td>Cervical Stenosis (1)</td>
</tr>
<tr>
<td>Subseptate + Endometrial Polyp (1)</td>
</tr>
<tr>
<td>Adhesions + Ostium Fibrosis (1)</td>
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</table>

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In our study, maximum number of patients (76.19%) belonged to 25-35 years of age. Similar observations were made by Amiran et al.,10 Mali et al.,11 Sahu et al.,12 Wadhwa L et al.13 In this study 72 patients (68.57%) were nulliparous, 31 (29.52%) were of parity one and parity ≥2 was found in 1.90% patients. Where as in Koskas et al.1 study, nulliparity in 73.4% (409/557), parity one in 21.4% (119/557), and parity ≥2 in 5.2% (29/557) of cases was reported.

K. Mali et al.11 had reported 46% have normal menstrual cycle and 26% have oligomenorrhea, which was the most common menstrual abnormality found whereas same figures were 65.71% and 26.67% women respectively in our study. While polymenorrhagia and menorrhagia were present in 5(04.76%) and 3(02.86%) cases respectively.

Majority of the patients (57.14%) reported less than 5 years of infertility in the present study similar to finding of K. Mali et al.,11 while Amiran et al.10 reported <5-year infertility in almost 85% cases and Wadhwa L et al.13 reported mean infertility period of 5.65 ± 2.54 years. Amongst the infertility patients in our study, 69 (65.71%) was diagnosed with primary infertility and 36 (34.29%) with secondary infertility. In similar studies by Sahu et al.,12 Wadhwa et al.,11 Amiran et al.,10 Joseph A. Adedigba et al.14 found 70-75% cases were diagnosed with primary infertility and 25-30% with secondary infertility.

The most common indication for diagnostic hysteroscopy was as a part of an infertility workup (102 cases) that is comparable with Sahu et al.15 study where infertility was an indication in 224 cases (69.13%).

This study revealed a normal uterine cavity during hysteroscopy in 66 (62.86%) and abnormal uterine cavity in 39 (37.14%) cases. This was comparable to observation made by many studies. Sahu et al.,12 Mali et al.,11 Pansky et al.,1 Karayalcin et al.,15 who reported normal uterine cavity in 62-77% of infertile women and abnormal uterine cavity in 22-38%.

There is no statistically significant difference between primary and secondary infertility women with respect to uterine cavity abnormality as was observed by Sahu et al.12 and Pansky et al.1

The hysteroscopic findings reported by various studies are mentioned in Table 2. Most common abnormal hysteroscopic finding was endometrial polyp in many studies. Shokeir16 observed such lesions to be more prevalent in the unexplained infertility, role being unclear, although improved reproductive outcomes were reported after polypectomy. Thus, logical to propose surgical treatment of all endometrial polyps as it may enhance fertility.

In our study no significant difference was found in the rate of intrauterine adhesions comparing the patients with primary versus secondary infertility, in spite of the known relationship between secondary infertility and the existence of adhesions, being mostly the result of uterine curettage for postpartum or post abortion residua. In our study we found 6.67% women with intrauterine adhesion and most other studies reported in 3-7% cases.

We find uterine septum in 1.90% of cases and sub-septum in 5.71% of cases. Similar study carried out by Pansky et al.1 found uterine septum in 5.47% of cases. Hysteroscopic septum resection improves pregnancy outcome by removing an unfavourable implantation site and improving endometrial function, probably through re-vascularization of the uterine fundus.

In our study, deformed cavity was found in 0.95% of cases where as Sahu et al.15 reported it in 3.71% of cases. Koskas et al.3 found deformed cavity due to intramural fibroid in 3.1% of cases. The reported incidence of myomas in infertile women without any obvious cause of infertility is estimated to be between 1% and 2.4%. In the current study, submucous myomas were diagnosed in 1.90% of patients with infertility. Submucous and intramural myomas distort the cavity, impairing implantation and pregnancy rates in women undergoing IVF. Hysteroscopy not only diagnose these pathologies accurately, but also enables optimal assessment and treatment.

In our study, abnormal hysterosalpingography was found in 20% (21/105) of cases, same in Wadhwa et al.13 was found in 22.85% (24/105) women and in Panda et al.17 study in 23.6% women. While normal uterine cavity was found in 123 (49.2%) cases in study by Onwuchekwa et al.18 and in 63(69.2%) as reported by Hafizi et al.18 The most common abnormal findings on HSG were filling defect 7/105 (6.67), followed by subseptate in 3 and small cavity in 3 women, arcuate, bicornuate in one woman in the present study. Wadhwa et al.13 too reported common abnormality as filling defects in 15 (14.28%) women followed by congenital uterine anomaly in five women, bicornuate uterus in four, and arcuate uterus in one woman whereas uterine filling defects were seen in 78 (31.2%) cases in Onwuchekwa et al.19 study. Panda et al.17 too observed filling defect as most common in 10.8% followed by irregular cavity in 7.64%, bicornuate uterus in 5.73%, arcuate uterus in 1.27% and small cavity in 2.54%.
In our study among 39 cases of abnormal hysteroscopy only 19 cases HSG could diagnose as abnormal and rest of the 20 cases were diagnosed as normal uterine cavity. Two cases of abnormal HSG, hysteroscopy shows normal uterine cavity. Similar study by Roma et al. reported hysteroscopic examination of the 37 patients with normal findings on HSG showed six to have uterine cavity abnormalities including three cases of endometrial polyps, two cases of endometrial hyperplasia, and one submucosal myoma. In 15 of the 41 patients depicted on HSG as having endo-cavitary abnormalities, hysteroscopy revealed no abnormality.

The diagnostic accuracy of HSG taking hysteroscopy as gold standard in various studies is documented in Table 3. The sensitivity ranges from 21- 91 % but maximum lies between 38-45 %. The specificity varied between 78.57%-96.9% in these studies.

In our study, the strength of agreement between hysteroscopy and hysterosalpingography is moderate (Kappa =0.505) while the same in Panda et al. study was fair (kvalue=0.302) and in Ahmed et al. study ranged from moderate to good (K=0.49-0.79). Hafizi L et al. and Taskin et al. reported an agreement rate of 68.9% between the two.

Diagnostic hysteroscopy allows complete, accurate identification of intrauterine abnormalities that might negatively affect endometrial receptivity and implantation. The information derived from hysteroscopy helps the physician to institute appropriate therapy, and by doing so improve conception rates over shorter intervals. In view of all of the above, many authors believe that uterine and endometrial integrity should be evaluated primarily by hysteroscopy in the infertile/IVF treated population.

While Phillips et al. observed no single modality provided accurate identification of all different pathologies. Complete work up of women with infertility may include all modalities, given the unique information obtained from each. HSG is superior for evaluation of tubal pathologies and endometrial pathologies are best identified with hysteroscopy.

Further systematic review and meta-analysis by Di Spiezio Sardo et al. and Cochrane Database of Systematic Reviews 2019 (Kamath et al.) reported that robust and high-quality RCTs are still needed before hysteroscopy can be regarded as a first-line procedure in all infertile women, especially during the basal clinical assessment of the couple, when assisted reproductive treatment is not indicated yet.

The NICE guidelines on fertility assessment and treatment state that women should not be offered hysteroscopy on its own as part of the initial investigation unless clinically indicated, because the effectiveness of this technique on

### Table 2: Hysteroscopic findings as reported by various studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>Endometrial polyp (%)</th>
<th>Cervical polyp (%)</th>
<th>Cervical stenosis (%)</th>
<th>Endometrial adhesion (%)</th>
<th>Sub-mucous myoma (%)</th>
<th>Cornual fibrosis (%)</th>
<th>Septum (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wadhwa et al.</td>
<td>4.67</td>
<td>4.67</td>
<td>9.34</td>
<td>10.25</td>
<td></td>
<td></td>
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<tr>
<td>Amirian et al.</td>
<td>15.5</td>
<td>6.8</td>
<td>1.0</td>
<td>5.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hafizi L et al.</td>
<td>20.9</td>
<td>14.3</td>
<td>0</td>
<td>7.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panda et al.</td>
<td>6.3</td>
<td>2</td>
<td>12</td>
<td>7.5</td>
<td>8.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sahu et al.</td>
<td>0.62</td>
<td>1.54</td>
<td>6.48</td>
<td>8.95</td>
<td>3.08</td>
<td></td>
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<tr>
<td>Karayalcin et al.</td>
<td>7.7</td>
<td>0.5</td>
<td>0.1</td>
<td>3.8</td>
<td>5.2</td>
<td></td>
<td></td>
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<tr>
<td>Koskas et al.</td>
<td>9.7</td>
<td>2.3</td>
<td>1.8</td>
<td>0.35</td>
<td>0.7</td>
<td></td>
<td></td>
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<tr>
<td>Pansky et al.</td>
<td>5.9</td>
<td>1.36</td>
<td>3.65</td>
<td>2.23</td>
<td>5.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Our study</td>
<td>8.57</td>
<td>4.76</td>
<td>2.86</td>
<td>3.81</td>
<td>7.61 (septate+ sub-septum)</td>
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</tbody>
</table>

### Table 3: Diagnostic accuracy of HSG taking Hysteroscopy as gold standard

<table>
<thead>
<tr>
<th>Statistical Interpretation of HSG with Hysteroscopy as Gold standard</th>
<th>SENSITIVITY %</th>
<th>SPECIFICITY %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>48.72</td>
<td>96.97</td>
<td>90.48</td>
<td>76.19</td>
</tr>
<tr>
<td>Wadhwa et al.</td>
<td>44.83</td>
<td>86.67</td>
<td>56.52</td>
<td>80.25</td>
</tr>
<tr>
<td>Hafizi L et al.</td>
<td>38.78</td>
<td>78.57</td>
<td>67.86</td>
<td>52.38</td>
</tr>
<tr>
<td>Panda et al.</td>
<td>42.3</td>
<td>85.7</td>
<td>59.45</td>
<td>75</td>
</tr>
<tr>
<td>Amirian et al.</td>
<td>44.8</td>
<td>86.6</td>
<td>56.5</td>
<td>80.2</td>
</tr>
<tr>
<td>Taskin et al.</td>
<td>21.5</td>
<td>83.76</td>
<td>55.26</td>
<td>70.75</td>
</tr>
<tr>
<td>Ahmed et al.</td>
<td>90.8</td>
<td>96.5</td>
<td></td>
<td></td>
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</tbody>
</table>
improving reproductive outcome has not been established (NICE, 2013).

So, we can conclude that hysteroscopy is simple, safe, valuable procedure and has been proved as gold standard for evaluation of uterine cavity in infertility patients but still HSG in spite of its limitations has its own place in the initial work up of these women in view of low-cost, less time consuming, easy to interpret, widespread availability and technically less demanding.

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REFERENCES

24. Spiezzo Sardo AD, Di Carlo C, Minozzi S, Spinelli M, Pistotti V,
Bajaj, et al.: Hysteroscopy is gold standard in uterine evaluation for infertility, but HSG still has a place

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Author’s contribution:
MB-Interpreted the results, review of literature and manuscript preparation; RR-Concept of the study, coordination, review of literature and manuscript preparation; MR-Concept and design of the study; prepared first draft of manuscript; JRC-Critical revision of the manuscript.

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