

# The role of imaging in the investigation of Asherman's syndrome

## Abstract

Asherman's syndrome has significant reproductive implications for patients. In most case series, the rate of fertility and full term birth directly correlates to extent of disease. However, there does not seem to be a connection between number of prior curettages, nor aetiology of adhesions in predicting outcome. Without a universally accepted classification system, comparison of research data and results for imaging modalities is difficult.

*Keywords:* Asherman syndrome, diagnostic imaging, intra-uterine adhesion, ultrasound

## Introduction

Intrauterine adhesions are known by many names including intrauterine synechiae, uterine atresia or endometrial sclerosis. In 1948, Joseph G Asherman described an organic amenorrhoea and inactive endometrium due to stenosis of the internal os of the cervix. He named it "Amenorrhoea Traumatica (Atretica)"<sup>1</sup>. Asherman's follow-up paper in 1950, "Traumatic Intra-uterine Adhesions", discussed uterine adhesions causing total obliteration of the cavity<sup>2</sup>. Today they are most often known by the eponymous name *Asherman's syndrome*.

The true incidence of Asherman's syndrome is unclear. Estimates range from 6–40% post dilatation and curettage<sup>3,4</sup>. The American Society for Reproductive Medicine (ASRM) estimates a frequency of 7% of secondary amenorrhoea<sup>5</sup>.

## Classification systems

Many classification systems have been proposed with no clear consensus. The European Society of Hysteroscopy (ESH) system distinguishes based on adhesion band thickness, tubal ostia patency and degree of uterine cavity obliteration. The American Society for Reproductive Medicine (ASRM) also takes menstrual pattern into account, potentially offering some prognostic information.

## Aetiology

Uterine adhesions are almost exclusively caused by injury to the basal layer of the endometrium. This most commonly occurs during uterine curettage for miscarriages, terminations or removal of retained products of conception. Stillman, *et al.*<sup>7</sup> discovered a significant association between mullerian duct abnormalities and Asherman's syndrome, possibly due to uterine abnormalities necessitating recurrent curettages. Evidence of association with caesarean section, myomectomy,

removal of septae and other intrauterine operations is also increasing.

Pituitary hypogonadotropism, and consequently a hypoestrogenic state, has been suggested to contribute to the severity of adhesions<sup>8</sup>.

While there is little evidence for association with infection, two organisms found commonly in third world countries have been reported. A retrospective series of intrauterine adhesions caused by genital tuberculosis was documented by Sharma, *et al.*<sup>9</sup> in 2008. A case report by Krowlikowski, *et al.*<sup>10</sup> described an amenorrhoeic Zulu woman with extensive uterine adhesions. Schistosomiasis was cultured from her ovarian biopsy.

## Diagnosis and imaging

By far the commonest presentations are amenorrhoea and infertility<sup>11</sup>.

A history of secondary menstrual anomalies following curettage of the pregnant uterus should always arouse suspicion<sup>12</sup>. The likeliest cause of secondary amenorrhoea in this age group is pregnancy and needs to be ruled out in the first instance. Other differentials include thyroid disease, prolactinoma, polycystic ovarian syndrome and premature ovarian failure<sup>13</sup>, all of which need to be excluded.

Hysteroscopy is the gold standard for diagnosis. It also has the added benefit of allowing simultaneous adhesiolytic treatment. However, with the risks of an invasive procedure under general anaesthetic, perforation of the uterus, long waiting lists and expense to our healthcare system, other imaging modalities should be considered for screening of uterine adhesions.

A literature search on diagnostic imaging of Asherman's syndrome and intrauterine adhesions or synechiae produced no randomised controlled trials, only case series and expert opinion.

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**Table 1:** European Society of Hysteroscopy (ESH).

Grade	Description
1	Thin or filmy adhesions
2	Singular dense adhesion, patent tubal ostia
	Grade 2A – with occluding adhesions of interal cervical os
3	Multiple dense adhesions, unilateral obliteration of ostia
4	Extensive dense adhesions, partial occlusion of uterine cavity, both ostia occluded (partial)
5	Extensive endometrial scarring and fibrosis
	Grade 5A – with Gr1/Gr2 adhesions
	Grade 5B – with Gr3/Gr4 adhesions + amenorrhoea

**Table 2:** American Society for Reproductive Medicine (ASRM) classification of intrauterine adhesions.

Extent of cavity involved	< 1/3	1/3 – 2/3	> 2/3
	1	2	4
Type of adhesions	Filmy	Filmy-dense	Dense
	1	2	4
Menstrual pattern	Normal	Hypomenorrhoea	Amenorrhoea
	0	2	4

Ultrasound may be utilised with (sonohysterography) or without (standard) injection of sterile saline into the uterine cavity. Adhesions characteristically appear as “bridging bands” of tissue that distort the cavity. Filmy adhesions are described as thin, undulating membranes that are most easily seen on real time scanning<sup>14</sup>. Transvaginal ultrasound can also be useful in measuring the thickness of the endometrial lining.

Hysterosalpinography (HSG) is a commonly used first line investigation of uterine abnormalities and infertility. It involves injection of a radiopaque dye into the uterine cavity and x-ray evaluation the uterus and fallopian tubes. Adhesions are seen as filling defects that do not change with positioning.

A 1994 study by Raziel, *et al.* prospectively compared hysterosalpingogram and hysteroscopy for investigation of recurrent miscarriages. 106 patients suffering from recurrent miscarriages were studied. The sensitivity of HSG for detecting uterine abnormalities was 79%, with a false positive rate of 38%. This was especially prevalent in the intrauterine adhesions group. This result is frequently reproduced in the literature.

Salle, *et al.*<sup>15</sup> conducted a small retrospective study of 19 patients with suspected intrauterine adhesions in 1997. All patients underwent transvaginal ultrasound (TVS), sonohysterography (SHG) and hysterosalpingography (HSG) screening prior to hysteroscopic treatment of adhesions. TVS had poor sensitivity and specificity. SHG and HSG were both found to have a high sensitivity with complete correlation between the two imaging modalities.

In 2000, a prospective study of 65 infertile women by Soares, *et al.*<sup>16</sup> compared the same imaging modalities with hysteroscopy (gold standard) for diagnosis of uterine cavity diseases. The women were aged between 19 and 43 with 52.3% having primary infertility and 47.7% having secondary infertility. TVS failed to detect any cases of intrauterine adhesions, and in fact gave

three false positive diagnoses. HSG and SHG both returned a sensitivity of 75.0% and a positive predictive value of 50.0% and 42.9% respectively. SHG also yielded one more false positive result than HSG. Negative predictive value of both was 98.3%, with 95% confidence interval above 90. The authors attributed the false-positive results to possible misinterpretation of artefacts produced by air bubbles or cervical mucus injected into the uterine cavity. One complication of pelvic inflammatory disease was documented post SHG.

3D ultrasound allows for real time visualisation and provides more accurate assessment than traditional 2D ultrasound imaging.

A case series by Cohen, *et al.* studied 54 women with a primary diagnosis of Asherman's syndrome and compared 3D ultrasound to hysterosalpingogram for evaluation of diagnostic accuracy. Sensitivity was calculated using hysteroscopy as the gold standard. 100% of pre-operative 3D imaging was found to be consistent with hysteroscopy results in assessing severity of disease, compared to 66.7% for HSG. It provided a more precise map of intrauterine adhesions and also enabled differentiation between severe intrauterine disease and outflow tract obstruction.

Magnetic resonance imaging (MRI) has been suggested as a diagnostic tool<sup>18</sup>. Thus far, there is little evidence in the literature supporting the use of MRI with only three publications available.

The largest is a series of 4 case reports in 1995 by Bacelar, *et al.*<sup>17</sup> discussing the usefulness of MRI in patients with established adhesions where thorough hysteroscopic visualisation of the uterine cavity was not possible. Low signal intensity bands were seen on MRI, representing fibrous scar tissue. Dense adhesions and stenosis of the internal os limits the value of hysteroscopy in these cases. For therapeutic purposes, it is essential to establish healthy endometrial tissue still remains in the upper uterine cavity.



**Figure 1:** Echogenic foci visible within the endometrium.



**Figure 2:** SIS demonstrating intra-uterine adhesion.

### Case report

Our patient is a 37-year-old G4 P1 who was referred to a tertiary care imaging facility for investigation of secondary infertility. Of significance in her past history is a manual removal of the placenta, two first trimester miscarriages and an ectopic pregnancy.

Standard 2D pelvic images were obtained that revealed echogenic foci within the endometrium (Fig. 1). A saline infused sonohysterography (SIS) was also performed in view of this finding. Fig. 2 demonstrates the thin, undulating membranes suggesting the diagnosis of Asherman syndrome. This was confirmed on subsequent hysteroscopy.

### Reproductive implications

The most common presentation of Asherman's syndrome is secondary infertility. These patients are also at higher risk of recurrent miscarriage. In subsequent pregnancies second trimester loss, preterm delivery, incompetent cervix, uterine rupture and placenta accreta have all been reported.

Fertility post hysteroscopic lysis of adhesions is high if normal endometrial tissue is found, although gonadotropins, intrauterine insemination (IUI) or in vitro fertilisation (IVF) is sometimes necessary<sup>18</sup>.

A large case series of uterine adhesion treated with hysteroscopy was reported by Valle, *et al.*<sup>19</sup> in 1988; retrospective analysis of 187 patients treated over 10 years. All patients had endometrial trauma, except one who had acute endometritis. 23% had mild adhesions, 51.9% had moderate adhesions, 25.1% had severe adhesions according to ASRM criteria. 161 patients had adjuvant laparoscopy, 151 patients had an IUD placed intraoperatively, all patients received antibiotics, 171 patients received conjugated oestrogen and medroxyprogesterone acetate for at least one cycle.

Of these patients, 147 achieved pregnancy, 79.7% of whom carried to full term, 18.2% ended in spontaneous miscarriage and 2.1% of which were ectopic pregnancies.

In mild cases, the conception rate was 81.3%, but only 31.9%

in those with severe disease. No placenta accreta was reported. 21.6% of the moderate group and 48.9% of the severe group required repeat treatment.

### Conclusion

Asherman's syndrome has significant reproductive implications for patients. In most case series, the rate of fertility and full term birth directly correlates to extent of disease. However, there does not seem to be a connection between number of prior curettages, nor aetiology of adhesions in predicting outcome.<sup>18</sup>

Without a universally accepted classification system, comparison of research data and results for imaging modalities is difficult.

The high sensitivity of HSG has made it a useful screening tool for intrauterine abnormalities. Compared with hysteroscopy, HSG is a relative safe, cheaper and a less invasive test. However it can cause a great deal of patient discomfort and has the added disadvantage of ionising radiation exposure<sup>20</sup>. It also produces a high number of false positives and can overestimate the severity of disease.

Small studies and case reports suggest a similar rate or diagnostic superiority of SHG over HSG for identifying intrauterine adhesions. Most of the research has been conducted using 2D ultrasound. Larger studies need to be conducted to thoroughly assess the usefulness of SHG.

3D ultrasound can provide useful information on the location and extent of adhesions, therefore assisting with grading of severity. The benefit of which allows more accurate prediction of prognosis and fertility outcomes. This could possibly be done in combination with SHG to further improve diagnostic accuracy.

The continual improvement of high-resolution ultrasound together with simple infusion studies could make it potentially a very valuable tool in the assessment of these women. Consequences on fertility and possible complications in future pregnancy necessitate further research and publications.

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