ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 8, Issue, 05, pp.31963-31970, May, 2016

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

ROLE OF HYSTEROSCOPY IN DIAGNOSIS OF ASHERMAN'S SYNDROME – A RETROSPECTIVE STUDY

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ARTICLE INFO

Article History:
Received 10th February, 2016
Received in revised form
23rd March, 2016
Accepted 15th April, 2016
Published online 31st May, 2016

Key words:

Amenorrhea,
Asherman's,
Dysmenorrhea,
Hysteroscopy,
Hypomenorrhea,
Infertility.

ABSTRACT

Aim: To assess the significance of hysteroscopy in diagnosis of Asherman's syndrome in patients presenting with infertility, hypomenorrhea, secondary amenorrhea and dysmenorrhea.
Material and Method: This is a retrospective study conducted in the department of gynecological endoscopy at Manchanda's Endoscopic Centre, PSRI, Delhi, from March 2014 to March 2016. 230 patients between 18 to 50 years age group, who presented with complaints of infertility, hypomenorrhea, amenorrhea and dysmenorrhea were selected. All patients underwent hysteroscopy post-menstrually whenever feasible except in patients with amenorrhea. Patients with Asherman's syndrome were treated with adhesiolysis using scissors followed by insertion of intra uterine device in patients with moderate and severe Asherman's syndrome. They were given conjugated estrogen for 21 days followed by medroxyprogesterone acetate for 7 days.
Results: Total of 230 patients with above complaints were selected, of which 101 patients had Asherman's syndrome and 129 patients had other pathologies. Of the 101 patients, 45.5% (46 cases) presented with primary infertility, 32.7% (33 cases) with secondary infertility, 8.9% (9 cases) with secondary amenorrhea, 8.9% (9 cases) with hypomenorrhea and 4% (4 cases) with dysmenorrhea. The role of hysteroscopy in asherman's syndrome for patients presenting with infertility, amenorrhea and hypomenorrhea was found to be significant as proven by predictive value of less than 0.05.
Conclusion: Hysteroscopy plays a vital role in accurately assessing and classifying the pathology and is the gold standard method for diagnosis and management of asherman's syndrome.

Citation: Sravani Chithra, C.H., Rahul Manchanda, Nidhi Jain and Anshika Lekhi, 2016. "Role of hysteroscopy in diagnosis of Asherman's syndrome – A retrospective study", *International Journal of Current Research*, 8, (05), 31963-31970.

INTRODUCTION

Asherman's syndrome is an acquired uterine condition, characterized by the formation of adhesions or scar tissue inside the uterus and/or the cervix. Depending on the extent of the adhesions it can be classified as mild, moderate or severe.
It is a relatively rare condition but one which is being increasingly recognized nowadays with the wider use of hysteroscopy for the assessment of subfertile women. Asherman's syndrome (AS) or intrauterine adhesions (IUA's) are most commonly caused by infections or iatrogenic uterine trauma. This condition is suspected in women with a history of infertility and menstrual disturbances like amenorrhea or hypomenorrhoea not responsive to hormonal treatment (Allouc, 1999).

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Hysteroscopy has evolved from a diagnostic procedure into a therapeutic approach and plays an important role in the diagnosis and management of Asherman's syndrome (Sieglar *et al*., 1990). The objective of our study is to determine the significance of hysteroscopy in diagnosis of Asherman's syndrome in patients who presented with infertility, amenorrhea, hypomenorrhoea and dysmenorrhea.

MATERIALS AND METHODS

This study is a hospital based retrospective observational study over a period of two years from March 2014 to March 2016. It was conducted in the department of gynecological endoscopy at Manchanda's Endoscopic Centre, PSRI, Delhi. 230 patients between 18 to 50 years age group, who presented with complaints of infertility, hypomenorrhea, amenorrhea or dysmenorrhea were selected. All patients underwent hysteroscopy post-menstrually whenever feasible except in patients with amenorrhea.

Hysterosalpingography was not done in our patients. Only imaging by ultrasonography was done as a routine for detection of pathologies and measure endometrial thickness. Hysteroscopy was carried out with the patient in the lithotomy position under general anaesthesia. After a bimanual examination, the speculum was placed and anterior lip of cervix was held by a valsellum to stabilize the uterus in most cases. Speculum was removed once procedure started. Vaginoscopic approach was performed in some patients. Hysteroscopy was done using office BETOCCHI hysteroscope, a 2.9 mm diameter, 30 degree telescope with an operative sheath. Cervical dilatation was not done. Normal saline was used as distending medium. The telescope was gently introduced through the cervix and advanced under direct vision through the endocervical canal into the cavity of the uterus. The distension fluid flow was regulated by a hysteromat. The uterine cavity was inspected and cornual ends were examined. Patients who were diagnosed with Asherman's syndrome were treated with adhesiolysis using 5 Fr scissors. In patients with suspicion of tuberculosis, biopsy was taken and sent for histopathology and TB-PCR. Postoperatively a multiload intra uterine device (IUD) without copper was introduced in patients with moderate and severe asherman's syndrome to prevent recurrence of adhesions. They were given conjugated estrogen for 21 days followed by medroxyprogesterone acetate for 7 days, in a dosage according to the severity of AS. (Table 1)

Patients were followed up after their menstrual cycle or symptomatically. We follow up our patients for second look after four weeks. IUD was removed and second look hysteroscopy was done in all patients with moderate and severe Asherman's syndrome. If adhesions were found, adhesiolysis was done. Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0. Categorical variables are presented as absolute numbers and percentage and were compared using Chi-squared test or Fisher's exact test as appropriate.

RESULTS

- Total of 230 patients with complaints of infertility, amenorrhea, hypomenorrhoea and dysmenorrhea were selected with an age distribution of 18 to 50 years.
- Out of 230 patients, 126 (54.8%) of them presented with primary infertility, 70 (30.4%) with secondary infertility, 13(5.7%) with secondary amenorrhea, 11(4.8%) with hypomenorrhea and 10(4.3%) presented with dysmenorrhea. (Table 2)
- Out of 230 patients, 101 patients had Asherman's syndrome and 129 patients had other pathologies like leiomyoma, polyp, adenomyosis, endometriosis and uterine anomalies.
- Among the 101 patients,51(50.5%) patients were in the age group of 10 to 30 years, 37 (36.6%) between 31 to 40 years and 13(12.9%) patients were between 41 to 50 years of age, with mean age group of 34 years.
- Of the 101 women with AS, 53 were nulliparous and 48 women were parous.
- Among the 48 parous women with AS, 23(47.9%) patients had a history of abortion and 19(36.6%) patients had history of previous caesarean section.
- Hysteroscopy finding showed asherman's syndrome in 101 patients of which 45.5% (46 cases) had presented with primary infertility, 32.7% (33 cases) with secondary infertility, 8.9% (9 cases) with secondary amenorrhea, 8.9% (9 cases) with hypomenorrhea and 4% (4 cases) with dysmenorrhea. (Table:3)

Table 1. Dosage of conjugated estrogen according to severity of as

Severity	Conjugated estrogen (21 days)	Medroxyprogesterone acetate (7 days)
Mild	0.625 mg twice a day	10 mg twice a day
Moderate	1.25 mg twice a day	10 mg twice a day
Severe	1.25 mg four times a day	10 mg twice a day

Table 2. Total number of patients with Asherman's syndrome and their hysteroscopy findings

Symptoms	Hysteroscopy findings				Total no. of Patients
	Grade of Ashermans Syndrome (n=101)			No. of patients without Asherman's syndrome (n=129)	
	Mild	Moderate	Severe		
Primary infertility	20	21	5	80	126
Secondary infertility	12	13	8	37	70
Secondary amenorrhea	2	4	3	4	13
Hypomenorrhea	1	5	3	2	11
Dysmenorrhea	3	1	0	6	10
Total	38	44	19	129	230

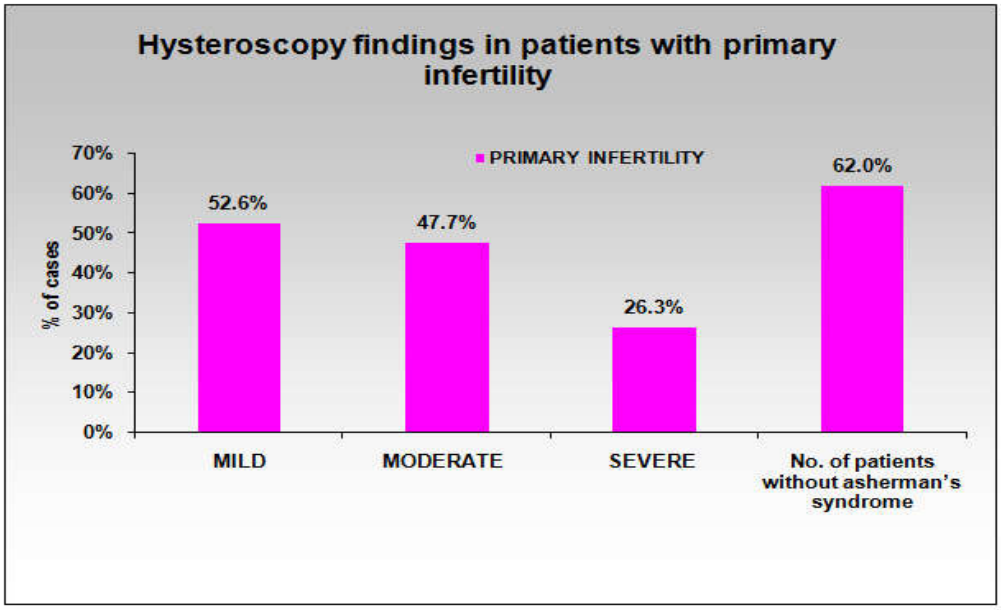
Table 3. Demographic profile of clinical presentations in Asherman's syndrome and their *P* values:

SYMPTOMS	ASHERMANS (n=101)	PERCENT	*P* value
Primary infertility	46	45.5%	*0.013*
Secondary infertility	33	32.7%	*0.514*
Secondary amenorrhea	9	8.9%	*0.043*
Hypomenorrhea	9	8.9%	*0.012*
Dysmenorrhea	4	4.0%	1

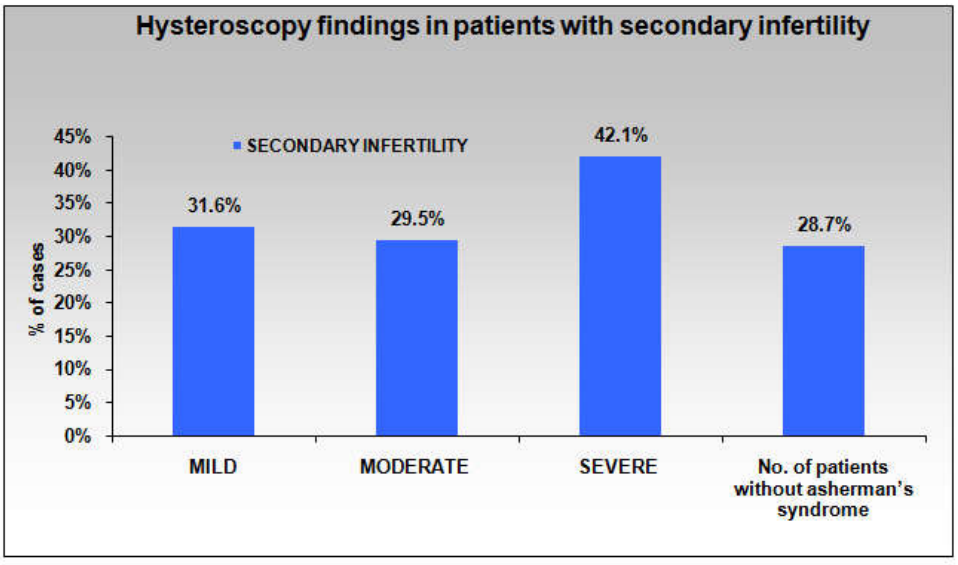
- Amongst the 46 cases of primary infertility with AS, 20 patients had mild, 21 had moderate and 5 had severe asherman's syndrome. (graph:1)
  Significant role of hysteroscopy was found in diagnosis of AS in patients with primary infertility, with P value of 0.013.
- Out of the 33 patients with secondary infertility with AS, 12 patients had mild, 13 had moderate and 8 had severe asherman's syndrome.(graph:2).

The P value was 0.514 which shows hysteroscopy has an insignificant role in diagnosis of AS in patients with secondary infertility, but 33 patients out of 70 with secondary infertility, i.e., 32.7% is significant enough a number to say that hysteroscopy is useful in diagnosis of AS in patients with secondary infertility.

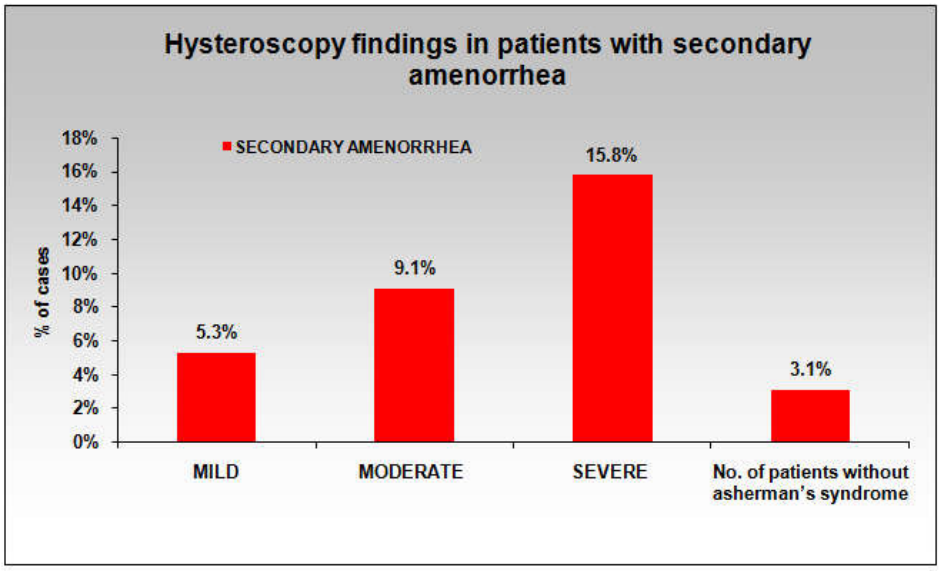
- Out of the 9 patients with secondary amenorrhea with AS, 2 patients had mild, 4 had moderate and 3 had severe asherman's syndrome. (graph:3) Significant role of hysteroscopy was found in diagnosis of AS in patients with secondary amenorrhea, with P value of 0.043.
- Amongst the 9 cases of hypomenorrhea with AS, 1 patients had mild, 5 had moderate and 3 had severe asherman's syndrome. (graph:4)Significant role of hysteroscopy was found in diagnosis of AS in patients with hypomenorrhea, with P value of 0.012.
- Amongst the 4 cases of dysmenorrhea with AS, 3 patients had mild, 1 had moderate and 0 had severe asherman's syndrome. (graph:5) Role of hysteroscopy in diagnosis of AS in patients with dysmenorrhea was insignificant, with P value of 1. Most of patients with dysmenorrhea had adenomyosis or endometriosis which are more common etiologies of dysmenorrhea.
- Biopsy for histopathology and TB-PCR were sent in 9 patients of which 5(4.9%) were proven to have endometrial tuberculosis.
- There were no complications during the procedure.



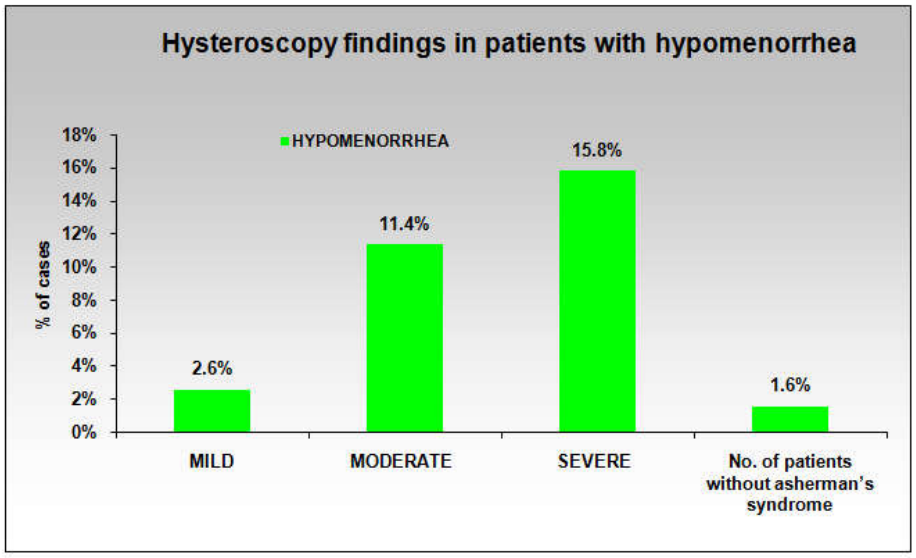
Graph 1. Hysteroscopy findings in patients with primary infertility



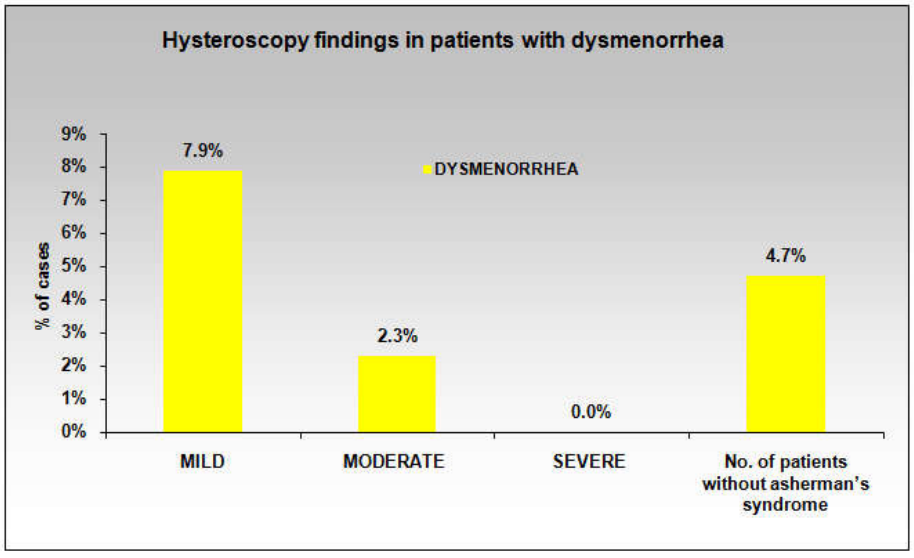
Graph 2. Hysteroscopy findings in patients with secondary infertility



Graph 3. Hysteroscopy findings in patients with secondary amenorrhea



Graph 4. Hysteroscopy findings in patients with hypomenorrhea



Graph 5. Hysteroscopy findings in patients with dysmenorrhea

DISCUSSION

Asherman's syndrome, named after Joseph Asherman, was a rare condition but in recent years is being increasingly recognized due to the wider use of hysteroscopy for the assessment of women with subfertility and menstrual disturbances. It is an acquired uterine condition, characterized by the formation of adhesions or scar tissue inside the uterus and cervix. The earliest reports of asherman's syndrome were made by Fritsch in 1894, Bass in 1927 and Stamer in 1946. The true prevalence of Asherman's syndrome is difficult to determine since IUA's can be entirely asymptomatic. It has been estimated to affect 1.5% of women undergoing hysterosalpingography, 5 and 39% of women with recurrent pregnancy loss and up to 40% of patients who have a history of surgical treatment for retained products of conception. In a recent prospective study by Malhotra *et al* involving 40 patients with AS who underwent hysteroscopic adhesiolysis for Asherman's syndrome in a tertiary level hospital concluded that a significant improvement in the endometrial thickness was observed post-adhesiolysis (Malhotra *et al*., 2012) Table 6. Thus accurate diagnosis and classification of AS becomes very important for proper management and to improve the endometrial receptivity and regeneration in order to treat infertility and alleviate menstrual symptoms.

Etiology: The causes for developing intrauterine adhesions are,iatrogenic factors like dilatation and curettage (40%), caesarean sections and myomectomies or infections like pelvic inflammatory disease and tuberculosis. In 1948 Asherman listed the etiology of the condition as curettage after delivery, miscarriage, or a molar pregnancy, or after manual removal of the placenta or uterine packing. He also extended the condition to include partial or complete obliteration of the uterine cavity secondary to trauma to the uterine body (Asherman, 1948; Adam Magos, 2002). Schenker and Margalioth in a study published in 1982, evaluated 1856 cases of AS confirming that women who underwent uterine curettage were at high risk of developing intrauterine adhesions. Curettage after a miscarriage had the highest association with AS in 1237 (66.6%) out of 1856 cases (Schenker and Margalioth, 1982). Taskin, *et al* observed IUA in 31.3% of patients undergoing hysteroscopy for a single uterine myoma, with an increase to 45.5% in patients diagnosed with multiple myoma prior to hysteroscopy (Taskin *et al*., 2000). Roge P *et al* in their study found that the risk of Asherman's syndrome from Cesarean section is estimated at approximately 2% to 2.8% (Roge *et al*., 1996). In our patients, out of 48(44.03%)parous women with Asherman's syndrome, 23 patients (47.9%) had history of abortion and 19 (36.6%) patients had history of previous caesarean section. Mycobacterium tuberculosis could also involve the genital tract resulting in severe IUA. In addition, genital tuberculosis seems to be associated with recurrence of IUA and poor prognosis (Bukulmez *et al*., 1999). Schistosoma species, have also been implicated in the development of AS, and it has been suggested that schistosomiasis infection should be ruled out in parts of the world where it is endemic (Krolikowski *et al*., 1995). In our study out of 9 patients who were suspected to have endometrial tuberculosis, 5 patients (4.9%) were proven to have the same by TB-PCR and histopathology.

Presenting symptoms: Patients usually present with secondary amenorrhea, hypomenorrhea, infertility, recurrent pregnancy loss or dysmenorrhea.

Diagnosis: Asherman's syndrome should be suspected in every woman presenting with menstrual problems and infertility with history of curettage or other intrauterine surgery. The diagnosis of asherman's syndrome cannot be made by physical examination, as it fails to reveal any abnormalities (Netter *et al*., 1956). It can be diagnosed by various other modalities like transcervical sounding, HSG, transvaginal ultrasonograghy, sonohysterography, 3D ultrasonograghy and hysteroscopy.

Transcervical sounding of the uterus may reveal cervical obstruction at or near the level of the internal os but the endometrial adhesions are not revealed (Jones, 1964). Historically, hysterosalpingography (HSG) has represented a cost-effective method to assess tubal patency in women who suffer from infertility. Usually, AS is characterized by filling defects described as homogeneous opacity surrounded by sharp edges.In severe cases, the uterine cavity appears completely distorted and narrowed, and ostial occlusion may also be evident. HSG has a sensitivity of 75% to 81% with high false positive rate of 39%, thus limiting its use in diagnosis of AS (Roma *et al*., 2004). Transvaginal ultrasound has a high compliance. The ultrasound image of AS is characterized by an echo dense pattern with difficult visualization of endometrium interrupted by one or more translucent cyst like areas. Although, the diagnostic accuracy of ultrasound has been reported to be low, it allows visualization of the uterine cavity when a complete obstruction of the cervix precludes HSG findings (Soares *et al*., 2000).

The use of saline infusion during the sonohysterography(SHG) was investigated in a retrospective study involving 149 cases with intrauterine anomalies where Acholonu *et al*. demonstrated a significant difference in general accuracy (50.3% in HSG group and 81.8% in SHG group) (Acholonu *et al*., 2011). Data regarding the value of three-dimensional (3D) ultrasound in the detection of intrauterine adhesions are limited. Preliminary data in 2003 showed a specificity of 45% in diagnosis of AS (Sylvestre *et al*., 2003). Magnetic resonance imaging (MRI) can be helpful as a supplementary diagnostic tool, especially when the adhesions involve the endocervix. IUA's are visualized as low signal intensity on T2 weighed-image inside the uterus (Bacelar *et al*., 1995). Despite the above developments, hysteroscopy remains the gold standard in the assessment of AS.Hysteroscopy is the diaSgnostic modality that accurately confirms the extent and morphological characteristics of adhesions, and the quality of the endometrium.

It can be performed in an office setting with less discomfort than a blind HSG. Hysteroscopy also makes immediate treatment possible.

According to AAGL guidelines (AAGL, 2010):

- Hysteroscopy is the most accurate method for diagnosis of IUAs and should be the investigation of choice when available. Level B.

- If hysteroscopy is not available, HSG and hysterosonography are reasonable alternatives.

Classification: It is very important to classify and grade AS as accurately as possible since it helps us decide the mode of management and follow up. The extent and severity of adhesions can be noted using various classifications. The classifications include:

- Toeff and Ballas (1978) were the first authors who tried to classify AS on the basis of hysterosalpingographic findings (Toaff, 1978).
- March *et al.* grading system (1978) gave the first hysteroscopic classification of AS (March *et al*., 1978).

Table 4. March *et al*. grading system

Classification	Condition
Mild	Flimsy adhesions occupying less than $1/4^{th}$ of uterine cavity. Ostial areas and fundal region minimally involved or clear.
Moderate	$1/4^{th}$ to $3/4^{th}$ of cavity involved. Ostial areas and upper fundus involved. No agglutination of uterine walls.
Severe	$>3/4^{th}$ cavity involved. Occlusion of both ostia and upper fundus. Agglutination of uterine walls.

- Valle and Sciarra's classification (1988)
- American Fertility Society classification (1988) is the most widely used system which took into account the extent of the disease, menstrual pattern and the morphological feature of the adhesions.
- Europian society for hysteroscopy classification.(1989)
- Donnez and Nisolle classification (1994)

AAGL guidelines for classification (AAGL, 2010):

- Intrauterine adhesions should be classified because this is prognostic for fertility outcome. Level B.
- The various classification systems make comparison between studies difficult to interpret. This may reflect inherent deficiencies in each of the classification systems. Consequently, it is currently not possible to endorse any specific system. Level C.

At our institution we use the Manchanda's Endoscopic Centre classification of Asherman's syndrome. This is a very simple classification to quickly and accurately grade the Asherman's syndrome.(table:6) From the results in our study it has been proven that hysteroscopy is the gold standard and plays a significant role in diagnosis and classification of Asherman's syndrome in patients presenting with infertility and menstrual disturbances.

Treatment: The aims to treating a patient with intrauterine adhesions are, to restore the size and shape of the uterine cavity, normal endometrial function and to treat the symptoms. According to AAGL guidelines, "surgery is the criterion standard in management of Asherman's syndrome, and there is no role for medical treatment." (AAGL, 2010) Hysteroscopic treatment enables lysis of IUAs under direct vision and with magnification (Duffy *et al*., 1992). In case of mild adhesions the Adhesiolysis can be achieved by blunt dissection using only the tip of the hysteroscope. The more lateral the adhesions are, and greater their density, the more difficult becomes the dissection and the greater the risk of complications such as perforation. In a study by March *et al* on sixty-six patients with Asherman's syndrome complete lysis of adhesions was accomplished during the initial hysteroscopy on an outpatient basis under local anaesthesia in 65 patients. Uterine perforation occurred in two patients. The extent of the intrauterine adhesions correlated with the patients' presenting menstrual patterns. After the surgery 98 per cent had normal spontaneous menses. Seven of these patients conceived and the pregnancies were uncomplicated (March *et al*., 1978). In our study we had no complications and all the patients (100%) with amenorrhea and hypomenorrhea resumed mensus after surgery. Different Hysteroscopic techniques have been described for adhesiolysis. We have used office hysteroscope with 5 Fr scissors for adhesiolysis in our patient, which is a mechanical method with an advantage of precise cutting and less damage to the endometrium and cervical dilatation is not required. Resectoscope with monopolar or bipolar probe can also be used.

Post operative management and follow up

One of the challenges with Asherman's syndrome is that once the scar tissue is removed, it frequently returns. Techniques used to prevent recurrence of IUA's include the use of estrogen post-procedure, repeat office hysteroscopies to break up scar tissue as it forms, and placement of an intra uterine device or a foley's catheter. Insertion of an intrauterine device (IUD) provides a physical barrier between the uterine walls, separating the endometrial layers after lysis of IUAs. We place a multiload intra uterine device without copper post adhesiolysis and give our patients conjugated estrogen of 21 days followed by medroxyprogesterone acetate 10 mg BD for 7 days to improve endometrial regeneration and prevent recurrence.(Table 1)

As per the AAGL guidelines (AAGL, 2010)

- Because of the suppressive or inflammatory effect on the endometrium, neither progestin-releasing nor copper or T-shaped IUDs should be used after surgical division of intrauterine adhesions. (Grade C)
- Postoperative hormone treatment using estrogen, with or without a progestin, may reduce recurrence of IUAs. (Grade B)

Polishuk *et al* in their study examined the use of the IUD after hysteroscopic adhesiolysis by and concluded that IUD could be applied after hysteroscopic adhesiolysis to avoid regeneration of IUAs. Placement of an IUD to maintain the uterine cavity is safe and effective in ensuring the return of normal menstruation and later pregnancies with minimal complications (Polishuk, 1976). Myers *et al*. proposed a prolonged preoperative and a postoperative treatment with estrogens in 12 subjects with severe amenorrhea. All women resumed a normal menstrual pattern and six of them become pregnant (Myers and Hurst, 2012). March *et al*. suggested a treatment with micronized oestradiol, 2 mg twice daily for 30–60 days and medroxyprogesterone acetate 10 mg per day at last 5 days of oestrogen therapy Presently, there is no clear consensus about follow up management.

Table 5. American Fertility Society Classification

Extent of cavity involved	< one third 1	One third to two third 2	>Two thirds 4
Type of adhesions	Flimsy	Flimsy and dense	Dense
	1	2	4
Menstrual pattern	Normal	Hypomenorrhea	Amenorrhea
	0	2	4
Prognostic classification			
Stage I (mild)	**1-4**		
Stage II (moderate)	**5-8**		
Stage III (severe)	**9-12**		

Table 6. MEC Classification

MEC (Manchanda's Endoscopic Centre) Classification of Asherman's Syndrome		
GRADE 1	Mild	Less than 1/3rd of uterine cavity obliterated (flimsy / dense adhesions)
GRADE 2	Moderate	1/3rd to 2/3rd of uterine cavity obliterated (flimsy / dense adhesions)
GRADE 3	Severe	More than 2/3rd of uterine cavity obliterated (flimsy / dense adhesions)

Usually, post-treatment assessment of the uterine cavity is recommended one-two months after the initial surgery. Valle and Sciarra reported a 50% and 21.6% of recurrence in severe and moderate AS respectively (Valle and Sciaara, 1988). Timely recognition of any recurrence of adhesions is essential to provide the best prognosis; therefore it may be necessary to repeat surgery. Hysteroscopy remains the only method which allows an accurate estimation of adhesion recurrence and it is the most commonly used in clinical practice. Of course, it also allows further in office adhesiolysis. Regardless of the surgical intervention used, reassessment of the uterine cavity is necessary. We reassess our patients after four weeks.

Conclusion

The main objective of treatment in AS is to restore the volume and shape of the uterine cavity to normal and to facilitate communication between the cavity and both the cervical canal and the fallopian tubes. For proper management to be administered, accurate diagnosis is very important. In our study we can see that out of 196 patients with infertility, 79 patients (49%) were diagnosed with Asherman's syndrome and out of 25 patients with menstrual disturbances i.e., hypomenorrhea and amenorrhea,18 (72%) patients had asherman's syndrome. Thus proving that hysteroscopy plays a vital role and is the gold standard method in diagnosis and classification of asherman's syndrome thus aiding in its treatment.

Acknowledgement

I express my sincere gratitude to Dr.Rahul Manchanda, (HOD, Manchanda's Endoscopic Centre) whose guidance and suggestions have contributed immensely to the evolution of ideas on this subject. I am also thankful to my co-fellows (Manchanda's Endoscopic Centre), husband (Dr.Gopalakrishnan) and my family for their input, suggestions and constant support.

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