



ANATOMICAL OUTCOMES VERSUS CLINICAL OUTCOMES IN CASES OF ASHERMAN'S SYNDROME FOLLOWING HYSTEROSCOPIC ADHESIOLYSIS AND IUCD INSERTION : A HOSPITAL BASED COMPARATIVE STUDY

Gynaecology

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ABSTRACT

Background: Hysteroscopy has revolutionised the diagnosis and treatment of Asherman's syndrome the main challenges being not only correction of anatomical defect but also good outcome in terms of menstrual regularity and conception. The present study was undertaken to assess whether hysteroscopic anatomical correction of uterine cavity translated to a successful reproductive and clinical outcome.

Methods: All patients presenting with subfertility, menstrual disorders, recurrent pregnancy loss, and diagnosed with Asherman's syndrome on hysteroscopy were included in the study. These patients underwent laparohysteroscopy postmenstrually. Adhesiolysis followed by inert IUCD insertion was done. Patients were advised conjugated equine estrogens for 2 months. Second look hysteroscopy was done after two months of the index procedure, while third look hysteroscopy was done only in cases with reformed or persistent adhesions on second look hysteroscopy. All cases were followed for one year with clinical and radiological and hysteroscopic parameters.

Results: Of the 211 patients who were evaluated, 81 had Asherman syndrome. Of these 42% (n=34) had mild, 33% (n=27) moderate and 25% (n=20) had severe adhesions on hysteroscopy. Menstruation was restored in 78.5% (n=33) patients out of 42 patients & cumulative pregnancy rate of 47.4% was found. Out of 70 cases of infertility, 37 patients conceived spontaneously with a pregnancy rate of 52.85% and live birth rate of 29.4%. Spontaneous conceptions were maximum in the mild and moderate category.

Conclusions: Women who underwent hysteroscopic adhesiolysis showed significant improvement in anatomical, menstrual pattern and increased rates of conception as well as live birth rate per conception. Recurrence of intrauterine adhesions is an important consideration while performing adhesiolysis and adequate precautions must be taken

KEYWORDS

Asherman's syndrome, Hysteroscopy, IUCD

INTRODUCTION:

Asherman's syndrome is a sequel of injury to the endometrium subsequent to infections or previous uterine surgeries mostly postabortal curettage^{1,2}. It has a prevalence of 2.7% to 8.1% among general population. The prevalence in patients of infertility can be very high.^{3,4} The patients of intrauterine adhesions (IUA) generally present with amenorrhea or scanty menses, recurrent pregnancy loss & infertility or some are even asymptomatic⁵. Pregnancy after IUAs may be complicated by abortion, premature labour, placenta previa and placenta accreta^{5,6}. Historically, the use of hysterosalpingography (HSG) has been widespread in the diagnosis of IUA. Hysteroscopy has revolutionised the diagnosis and treatment of Asherman's syndrome².

In the past, many studies have been performed to evaluate reproductive and menstrual outcome after hysteroscopic adhesiolysis in Asherman's syndrome³⁻⁷ but the main challenges of hysteroscopic adhesiolysis involves not only correction of anatomical defect but also good functional outcome in terms of menstrual regularity and reproductive outcomes in terms of conception and pregnancy. Treatment includes not only excision of the dense adhesion bands, but also prevention of recurrence.^{5,6} Anatomical restoration to a normal uterine cavity by hysteroscopic adhesiolysis may not guarantee a good functional outcome as it depends on severity of adhesion, etiology as well as reformation of adhesion. The research question for the present study was whether anatomical correction of uterine cavity translated to a successful reproductive and clinical outcome.

MATERIALS & METHODS:

This prospective study was conducted in the Department of Obstetrics and Gynaecology, Teerthanker Mahaveer Medical College & Research Centre from April 2013 to May 2018. After obtaining clearance from the Institutional ethical board and taking informed consent, all patients diagnosed with Asherman's syndrome on HSG or TVS were included in the study. Patients with male factor infertility, ovulatory factors, tubal factors, acquired or congenital defects like fibroids, mullerian anomalies etc were excluded. Detailed history of all patients presenting to us with infertility, menstrual disturbances &

recurrent pregnancy failure was taken. A note was made regarding the age, duration of infertility, past menstrual cycles, past conception, history of uterine curettage and any uterine surgery. Routine blood investigations (including S.TSH, S.Prolactin, S.FSH), baseline transvaginal ultrasound (TVS), semen analysis.

Surgical technique:

- Patients were prepared for general anaesthesia.
- All patients underwent laparohysteroscopy post menstrually (except those with secondary amenorrhea) on day 5 to day 8 of the cycle.
- On hysteroscopy the severity of Asherman's syndrome was graded as mild, moderate or severe based on the AFS Classification 1988.
- The adhesions were cut with 5 french scissors followed by IUCD insertion.
- Adhesiolysis began inferiorly and proceeded towards the fundus until a panoramic view of the cavity was obtained and the ostia were visualized.
- In severe cases, the procedure was discontinued till fleshy pink myometrium was seen, even if ostia were not visualized.
- Endometrial biopsy was sent in all the cases and in patients with history of genital or extra genital tuberculosis. AFB culture and cartridge based nucleic acid amplification test (CBNAAT) was also performed in few selected cases where clinical suspicion of tuberculosis was high.
- The occurrence of any intra or postoperative complications was recorded.
- They were given antibiotics and discharged on the same day.

Post procedure protocol:

All patients were given conjugated equine estrogens for 21 days with medroxyprogesterone acetate on last 7 days of the cycle, for a total period of two months and IUCD was removed after one month of hysteroscopic adhesiolysis. 2nd look hysteroscopy was done after two months of index hysteroscopy to assess the anatomical outcomes of the procedure. Adhesiolysis was repeated in cases with persistent or recurrence of IUAs followed by inert IUCD insertion. Equine estrogen

and progesterone were given for 2 months as before. Cases where 2nd look hysteroscopy failed were offered 3rd look hysteroscopy.

Outcome assessment & follow up:

Regular follow up was done every 2 monthly. The patients were assessed by recording the details of changes in the menstrual flow, spontaneous conception and were subjected to TVS to assess the re-establishment of cavity. These patients were followed up further for spontaneous conception for two years.

Data analysis:

A simple description analysis was done in which the mean and mode were calculated for the continuous variables while the frequencies of the composite variable of interest were expressed as percentages and presented in tables. Statistical analysis was done using SPSS software 20.0. McNemar and Pearson Chi square test was performed for paired and unpaired samples, respectively to see the difference in menstrual pattern in pre-operative and post-operative patients as well as to see the difference in pregnancy rates in the two groups. $p < 0.05$ was considered significant.

RESULTS:

A total of 211 patients were evaluated during study period among them 123 cases were having Asherman's syndrome as confirmed on hysteroscopy. Out of these, 42 cases had simultaneous tuboperitoneal factors on laparo hysteroscopic evaluation hence they were excluded. This left us with 81 cases for the study.

The mean age was 29 yrs. Of the 81 cases, 3 patients had secondary amenorrhoea, 8 patients had recurrent pregnancy loss and 70 presented to us with infertility, of these 31 had primary infertility and 39 were having secondary infertility. Of the 81 patients 42 reported with menstrual complaints, of these 26 patients had hypomenorrhoea while 16 had amenorrhoea.

Table 1: Details of parity, etiological factors & clinical presentation of studied patients:

Parameter assessed	Number	Percentages
Age	28.4 -35years	
Parity	31	38.27%
Nulliparous	32	39.5%
Primiparous	18	22.2%
Multiparous		
Clinical presentation		
Infertility	70	86.41 %
• Primary	31	38.27 %
• Secondary	39	58.02 %
Menstrual pattern		
• Normal menses	39	48.148 %
• Hypomenorrhoea	26	32.09 %
• Amenorrhoea	16	19.75 %
Recurrent pregnancy loss	8	9.87 %
Risk factors associated with Asherman's Syndrome		
Curettage(total)	24	29.6 %
• Post partum	17	20.98 %
• Post abortal	5	6.1 %
• Post diagnostic	2	2.4 %
Post complicated caesarean	5	6.17%
Myomectomy	9	11.11%
PID	7	8.64%
Tuberculosis	5	6.17%

Infertility was the commonest complaint 86.41% followed by menstrual abnormalities was in 51.7% .Most important risk factor found was curettage 29.6% followed by myomectomy and pevic inflammatory disease.

Table 5: Reproductive outcome after adhesiolysis

Hysteroscopic finding	Number of cases	Spontaneous Conception	Spontaneous miscarriage	Preterm delivery	Term delivery	Live birth
Mild	34	19(55.28%)	4	2	13	15(48.3%)
Moderate	27	13(48.1%)	5	3	5	7((25.9%)
Severe	20	5 (25%)	3	1	1	1(5%)
Total	81	37(52.85%)	12	6	19	23(29.4%)

Table 2: Staging Of Asherman's As Per Afs Classification On 1st Hysteroscopic Evaluation

STAGING	NUMBER OF PATIENTS	PERCENTAGES
MILD	34	42%
MODERATE	27	33%
SEVERE	20	25%

Table 3: Evaluation On 2nd & 3rd Look Hysteroscopy

Procedure	Mild Cases Of Iuas	Moderate Cases Of Iuas	Severe Cases Of Iuas
Staging In 2 nd Look Hysteroscopy	Corrected normal cavity :34 no reformation of adhesions in all cases of mild adhesions	• Normal Corrected Cavity: 23(85.18%) • Reformation of Mild adhesions:3 • Moderate adhesions:1	• Normal Corrected Cavity: 5(25%) • Reformation of adhesions: 7 (35%) • Moderate adhesions: 5(25%) • Severe adhesions: 3(15%)
Staging On 3 rd Look Hysteroscopy	Not required	• Normal corrected: 3 • Reformation of mild filmy adhesions :1	• Normal corrected cavity:13 • Reformation of Mild IUAs:1 • Moderate IUAs:1
Complications Haemorrhage Perforation Recurrence	Nil	Nil 1	2 1 2

- 2nd look hysteroscopy after 2 months of the first hysteroscopy was done in all patients to evaluate outcomes.
- It showed that 34 cases of mild adhesions had corrected normal uterine cavity. Of the 27 cases who had moderate adhesions, second look hysteroscopy revealed normal uterine cavity in 23 while mild adhesions in 3 and moderate adhesions in 1. So a success rate of 70.37% was found.
- Of the 20 cases with severe IUAs on 2nd look hysteroscopy, 5 patients(25%) had normal corrected endometrial cavity, 7 had mild, 5 had moderate & 3 had persistent severe IUAs.
- 3rd look hysteroscopy was done in 19 cases only i.e. those with persistent adhesions on 2nd look hysteroscopy.
- On 3rd look hysteroscopy 4 cases of index moderate IUAs with mild & moderate adhesions (on 2nd look hysteroscopy) had normal corrected uterine cavities except one case.
- While on 3rd look hysteroscopy of the 15 index cases having severe adhesions, all mild IUAs(7) had normal corrected uterine cavity. Among 5 cases of moderate adhesions only one had recurrence of adhesions and among 3 cases of persistent severe adhesions two had reformation of moderate adhesions (Table 3).

Table 4: Comparison Of Clinical Presentation Before And After Adhesiolysis

Clinical presentation	Before treatment	After treatment
Amenorrhoea	16(19.7%)	02(12.5%)
Hypomenorrhoea	26(32%)	07 (26.9%)
Normal menses	39(48.1%)	72
Recurrent pregnancy loss	8(8.1%)	02(25%)
Infertility	70(86.4%)	33(47.1%)

- There was marked clinical improvement following hysteroscopic adhesiolysis.
- Menstrual pattern was improved remarkably 78.5%
- Of the 70 patients with infertility, 37 showed spontaneous conception (52.85%).
- There was a successful pregnancy outcome in 6 cases of recurrent pregnancy loss with Asherman's syndrome.

Out of 70 cases of infertility, 37 patients conceived spontaneously with a pregnancy rate of 52.85% and live birth rate of 29.4%. Spontaneous conceptions were maximum in the mild and moderate category.

Table 6: Complications encountered during pregnancy

Complication during pregnancy	Number of patients	Percentage
Post partum haemorrhage	3	9.09%
Retained placenta	0	0%
Morbidly adherent Placenta	3	9.09%
Abortions	6	18.18%
Preterm delivery	8	24.24%

DISCUSSION:

In the present study, clinical outcomes in terms of pregnancy and restoration of normal regular menses following hysteroscopic adhesiolysis for Asherman's syndrome was studied and compared with anatomical restoration. Hysteroscopy at present time is the most effective method for diagnosis & staging of adhesions. It is a safe and more comprehensive technique, compared with blind curettage or hysterotomy as adhesiolysis is done directly under vision & only scar tissue is severed, sparing the normal endometrium¹⁰. In our study we found 42% cases (n= 34) with mild adhesions, 33% cases (n=27) had moderate adhesions & 25% patients (n=20) had severe intra uterine adhesions, as per the AFS classification. Ugboacha et al⁸ found that severe intrauterine adhesion accounted for 25% of IUAs and 11.9% of all infertility patients who had diagnostic hysteroscopies. They concluded in their study that severe IUAs are known to be associated with poor reproductive outcomes following surgery in terms of menstrual return, pregnancy rate and live birth rates 11,12 which is comparable to our study.

The demographic profile in terms of age is comparable to other studies

i.e. most of the patients were in the third decade.^{4,7} In our study patients of intrauterine adhesions presented with infertility or menstrual disturbances and recurrent miscarriages. Dan yu et al in 2008⁶ found 80.5% patients with secondary infertility while 18% with recurrent pregnancy loss. In our study infertility accounted 86.4% patients but secondary infertility was seen in 58.02% cases (n=39) while 41.98% had primary infertility. Recurrent pregnancy loss in 10.2% patients (n=8).

In our study we found post partum curettage as most important cause of intra uterine adhesions similar to previous studies.^{1,2} Ugboaja et al⁸ found myomectomies and previous caesarean section as most important etiological factor for development of severe intra uterine adhesions. Few studies from Indian subcontinent found history of tuberculosis in 67.8% of women with Asherman's syndrome⁹. In SAIMS case series post-partum curettage was seen in only 3.3% of patients. In many studies most of patients who had secondary amenorrhoea had tubercular etiology which has propensity to damage the basal layer of endometrium preventing its regeneration^{10,16}. In our study only 5 cases of genital tuberculosis were found which is different from other studies.

The resumption of menses was seen in 78.5% of patients in our study which is comparable to other studies which show that more than 85% of patients resumed normal periods after adhesiolysis^{3,5,10, 11}. We found that the rate of reformation of adhesions was higher in patients with originally severe adhesions & though patients started having scanty periods the trilaminar pattern of endometrium in luteal phase was not seen in all cases^{5,14}. Studies which analyzed endometrial thickness and Doppler blood flows in patients with Asherman's syndrome after adhesiolysis found that although there was an improvement in the endometrial thickness but the vascularity did not improve. This indicates that even if the surgery provides a desired anatomical result, normal endometrial function is not guaranteed.^{5,10,14}

Name & year of study	Type of study	Number of cases	Etiological Factor	Chief presenting complaint	Adjunctive measure for prevention of adhesiolysis	Menstrual outcome	Reproductive outcome	Complication
J.O.Ugboaja et al 2017 [8]	Prospective study	19 out of 76 severe IUA'S	Myomectomies (26.3%) & complicated caesarean sections (42.1%)	Amenorrhea with infertility 68.4% Dysmenorrhea & cyclical abdominal pain (10.8 & 31.6%)				2 cases (10.5%)
IU Takai et al 1997-2006 [15]	Retrospective study	81	61.5% pregnancy associated curettage & caesarean section or puerperal infection	59% in third decade 79.5% with secondary infertility Infertility & hypomenorrhea 55.1%	Adhesiolysis & folleys catheter insertion with estrogen & progestin therapy	37.2%	32.1% pregnancy rate	
S. Bhandari et al 2015 [16]	Prospective study	60	53.3% no etiological factor	Hypomenorrhea 53.3%	IUCD estrogen & progesterone	45% menstrual improvement	52.2% pregnancy rate 43.4% live birth rate	
Nari yamamoto et al 1997-2012 [17]	Retrospective study	27		Infertility, hypomenorrhea	IUCD and estrogen progestin		56.2% Mean interval of conception- 8.7 +- 4.9 months	
Roy et al [9]	Retrospective adhesiolysis	89				70.6%	40.4%	2 uterine perforation
Dan yu et al 1998-2007 [6]	Retrospective adhesiolysis	85	42.4% termination of pregnancy 7.1% post partial curettage	Infertility and hypomenorrhea	IUCD & estrogen	74.2%	45.9% pregnancy rate 64.3 live birth rate 20.5% miscarriage rate	9% uterine perforation 3 patients with false channels

Conception occurred in 58.25% of our patients & live birth in 29.4%. It was also noted that successful pregnancy outcome was associated with the severity of adhesions as more patients conceived who had mild Asherman's syndrome at initial diagnosis. These findings are similar to previous studies reported in literature^{3,9,10,14}. It also signifies that restoration of anatomical defect does not restore functionality of the endometrium in case of severe adhesions.

In a study by **Dan Yu et al**⁶ hysteroscopic adhesiolysis achieved successful anatomical restoration in 57.8% to 97.5% of cases. In our study 96.29% (n=78) patients had restored anatomical cavity. They reported adhesion reformation (3.1 to 23.5%) as a major limitation to achieve success of the treatment which warranted repeat procedures.

Roy et al⁹ found that improvement in conception was 44.3% in those who had improved menstrual pattern compared to only 10% conception rate who continued to have amenorrhea after treatment. These findings were also similar to other previous reports^{3,4} and clearly reflect that endometrial function (as reflected by menstrual pattern) after hysteroscopic adhesiolysis is an important factor in determining the reproductive outcome.

In concordance with previous reports^{5,7}, conception rate was lower in patients who had recurrence of adhesions. This could be explained by the fact that reformation of intrauterine adhesion and concomitant endometrial atrophy are potential problems that may limit the success of hysteroscopic adhesiolysis.

According to **Zikopoulos et al**¹⁸, an overall cumulative delivery rate of 64.7% is expected within 2 years after the operation in patients with no additional infertility factors who attempt to conceive naturally. Their live birth rate is higher than that mentioned by others probably because of longer follow-up period.

CONCLUSION

Women who underwent hysteroscopic adhesiolysis showed significant improvement in the menstrual pattern and increased rates of conception as well as live birth rate per conception. Recurrence of intrauterine adhesions is an important consideration while performing adhesiolysis and adequate precautions must be taken. The use of repeat procedures and adhesion prevention strategies are needed. Also, a meta-analysis, taking into considerations all the research conducted in Indian subcontinent about this syndrome is required to achieve a better understanding of this disease.

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