

Clinical and Reproductive Outcomes Following Hysteroscopic Adhesiolysis for Asherman Syndrome in an Asian Population

Dear Editor,

Women with Asherman syndrome present with menstrual abnormalities, subfertility or recurrent pregnancy loss, as a result of intrauterine adhesions.¹ There may be a geographical variation in the prevalence of Asherman syndrome due to varying incidence of genital infections and the different laws with regard to therapeutic and illegal abortions across the world.² The pathophysiology of Asherman syndrome is linked to the disruption of the basalis layer during intrauterine injury, in turn leading to endometrial sclerosis and adhesion formation.³ It is now recognised that Asherman syndrome may result from causes other than trauma to a gravid uterine cavity.⁴ The aims of our study were to elucidate the possible predisposing risk factors for Asherman syndrome in our population and to describe the clinical, reproductive and obstetrical outcomes following hysteroscopic adhesiolysis in our centre.

Materials and Methods

This is a retrospective case series analysis carried out in a tertiary women's hospital in Singapore. Approval from Institutional Review Board was obtained. Symptomatic women with hysteroscopically diagnosed intrauterine adhesions aged 45 years and below were included in our study. The demographics, predisposing factors and menstrual symptoms and reproductive outcomes following hysteroscopic adhesiolysis were recorded for 76 patients over a 2-year period. Hysteroscopic grading of intrauterine adhesions in our centre was done using a modified classification proposed by Yu et al based on that by the European Society of Gynaecological Endoscopy.⁵

Results

Table 1 shows the demographics of the 76 patients in our study. Seventy-one procedures classified as trauma to the gravid uterus were performed on 62 patients (Table 2), of which 23/71 (32.4%) were elective terminations of pregnancy (TOP) by suction curettage, 2/71 (2.81%) were curettage with blunt curette after medical mid-trimester TOP, 39/71 (54.9%) were dilatation and suction curettage secondary to missed or incomplete miscarriage and 7/71 (9.9%) were dilatation and curettage post-delivery secondary to retained products of conception. Fifty-one patients had only trauma to the gravid uterus while 11

Table 1. Patient Demographics

Patient Demographics (n = 76)	
Age	
Median age (years)	35 (24 – 45)
Ethnicity (n, [%])	
Chinese	54 (71.0)
Malay	10 (13.1)
Indian	6 (7.9)
Others	6 (7.9)
Parity (n, [%])	
Nulliparous	45 (59.2)
Multiparous	31 (40.7)

had an episode of trauma to the gravid uterus, in addition to other procedures at a different time. None of these 11 patients had a prior hysteroscopy and dilatation and curettage for endometrial pathology and 2 underwent transcervical resection of polyp; 16/62 (25.8%) patients were classified as having severe adhesions after trauma to the gravid uterus while only 1/10 (10%) patient presented with severe adhesions after predisposing factors that affected the non-gravid uterus. The 4 patients with no documented risk factors were all nulliparous and presented with primary subfertility. Only mild adhesions were found in them.

A total of 65.8% (56/76) of patients in our study had presented with subfertility, of which 4 had recurrent pregnancy loss (Table 3). Fifty-percent of patients presenting with subfertility had mild adhesions. In contrast, 60.8% of patients who presented with menstrual abnormalities had moderate to severe adhesions. Following treatment, there was a return of normal menses in 20/23 (87%) of patients presenting with menstrual abnormalities. Of the 56 patients who presented with subfertility, 9 were lost to follow-up for the 2-year period. Of the remaining 47 patients with intrauterine adhesions who presented with subfertility, 3 patients had other gynaecological conditions affecting fertility (adenomyosis, fibroids distorting the endometrial cavity and septate uterus) and were excluded from analysis of reproductive outcomes following hysteroscopic adhesiolysis (n = 44). Clinical pregnancy was achieved in 56.8% of patients (Table 4). However, while 83.8% in the

Table 2. Possible Aetiologies for the Development of Asherman Syndrome

Severity of Intrauterine Adhesions	Trauma to Gravid Uterus	Trauma to Gravid and Non-Gravid Uterus	Trauma to Non-Gravid Uterus	Uterine Mobiliser	Endometritis	No Obvious Cause Found
Mild, n = 35, (n [%])	22 (62.9)	4 (11.4)	2 (5.7)	1 (2.9)	2 (5.7)	4 (11.4)
Moderate, n = 24, (n [%])	17 (70.8)	3 (12.5)	3 (12.5)	1 (4.2)	0	0
Severe, n = 17, (n [%])	12 (70.6)	4 (23.5)	1 (5.9)	0	0	0
All stages, n = 76, (n [%])	51 (67.1)	11 (14.5)	6 (7.9)	2 (2.6)	2 (2.6)	4 (5.3)

Table 3. Presenting Symptoms of Patients with Asherman Syndrome

	Subfertility	Menstrual Abnormality	Subfertility & Menstrual Abnormality
Mild adhesions, n (%)	25/50 (50.0)	9/23 (39.1)	1/3 (33.3)
Moderate adhesions, n (%)	21/50 (42.0)	3/23 (13.0)	0/3 (0)
Severe adhesions, n (%)	4/50 (8.0)	11/23 (47.8)	2/3 (66.7)
All grades, n (%)	50 (65.8)	23 (30.2)	3 (3.9%)

Table 4. Severity of Intrauterine Adhesions and Reproductive Outcomes

Severity of Adhesions	Number of Patients	Clinical Pregnancy	Live Birth in Patients who Achieved Clinical Pregnancy
Mild	22	12/22 (54.5%)	10/12 (83.3%)
Moderate	17	9/17 (52.9%)	7/9 (77.8%)
Severe	5	4/5 (80%)	1/4 (25%)
Total	44	25/44 (56.8%)	18/25 (72%)

mild adhesions group with clinical pregnancies went on to have live births, only 25% achieved live births in the severe adhesions group. Rate of miscarriage was higher in the group with severe adhesions compared to the group with mild adhesions, odds ratio 15.00 (95% confidence interval 0.98 to 228.91, $P = 0.05$). For the 19 patients who achieved live births in our study population, 21% (4/19) had preterm deliveries while 5.3% (1/19) had abnormal placentation (placenta praevia major). Caesarean section rate was 63.2% (12/19) and there was intrauterine growth restriction in 5.3% (1/19).

Discussion

Trauma to the gravid uterus (81.6%) was the main predisposing factor for the development of Asherman syndrome in our study population. In 1982, Schenker and Margalioth reviewed 1856 cases of intrauterine adhesions and found that pregnancy was the dominating predisposing

factor in 90.8% of patients.⁴ More recent data, including 3 retrospective studies that included a total of 239 patients, found trauma to the gravid uterus to be the predisposing cause in 57.7% to 76.9% of patients with Asherman syndrome.¹ The endometrium is dependent on oestrogen for regeneration, and it is hypothesised that a low oestrogen status at the time of operation and postoperative period is a reason why the basal layer of the endometrium is more vulnerable after pregnancy to trauma.¹ Tan WH et al performed a randomised controlled trial on 82 women who had been treated with conservative management, medical evacuation, or surgical evacuation of retained products of conception after spontaneous abortion and found no cases of intrauterine adhesions in patients managed conservatively or by medical evacuation, whereas 2 cases (7.7%) of filmy intrauterine adhesions were detected in those managed by surgical evacuation.⁶

In our study population, 65.8% presented with subfertility and 30.3% presented with menstrual abnormalities. We found that the percentage of moderate to severe adhesions in the group presenting with menstrual abnormalities was higher than that in the group presenting with subfertility. Mild adhesions could possibly affect the microenvironment of the endometrium and lead to disruption in the maternal-fetal crosstalk in the complicated process of embryo implantation. Defective vascularisation of the regenerating endometrium in turn could lead to recurrent pregnancy loss.⁷ Amenorrhoea or hypomenorrhoea may be explained by more severe adhesions such as cervical adhesions blocking menstrual flow or fibrosis leading to destruction of the entire basal layer of the endometrium or that the small pockets of endometrium present have atrophied because of limited local exposure to sex steroids.⁸

There is a lack of prospective, randomised controlled trials on the treatment of Asherman's syndrome.⁹ Sharp dissection of adhesions minimises destruction of the endometrium.¹⁰ The use of electrosurgery is reserved for moderate to severe adhesions. Electrosurgery used in the lysis of adhesions include monopolar energy, bipolar (Versapoint), or Nd:YAG laser ablation. Zikopoulos et al found no difference with respect to reproductive outcome after adhesiolysis comparing monopolar to bipolar

electrosurgery.¹¹ In cases of severe adhesions, hysteroscopic lysis of adhesions was performed under ultrasonographic or laparoscopic guidance. Different methods of adhesiolysis for severe adhesions have been studied. McComb and Wagner described a simplified therapy of inserting a Pratt cervical dilator towards each cornua under laparoscopic guidance, converting the obliterated cavity into a uterine septum, which is then divided with hysteroscopic scissors.¹² The myometrial scoring technique in the management of severe Asherman syndrome was proposed by Protopapas A et al, and it involved making 4 mm deep longitudinal incisions on the myometrium with a resectoscope fitted with a knife electrode.¹³ Laparotomy as a last resort was offered only after 3-4 hysteroscopic failures in well counselled patients¹⁴ and was not utilised in any of the patients in our study. Ancillary treatment postprocedure has often been used, but varies according to surgeon preference. Insertion of a physical barrier between the uterine walls creating a separation between the endometrial layers after adhesiolysis, is hypothesised to prevent adhesion formation after surgery. Physical barriers include the loop intrauterine device and foley catheter. However to date, there have been no class I studies investigating the use of intrauterine device after hysteroscopic intrauterine adhesiolysis.¹⁰ Hormone therapy is another form of ancillary therapy. In 1964, Wood and Pena described regeneration of the endometrium with oestrogen therapy after surgical treatment of intrauterine adhesions. A new ancillary treatment recently introduced is adhesion barriers in the form of film or gel. A prospective, randomised, controlled study found that following hysteroscopic adhesiolysis, auto-cross link hyaluronic acid gel significantly reduced the development of intrauterine adhesions postoperatively.¹⁵

In a review of 36 articles that reported fertility and obstetric outcomes after hysteroscopic management, the pregnancy rate was approximately 63% and of women who conceived, the live birth rate was 75%.¹⁰ Our study reports a pregnancy rate of 56.8% and for those with a clinical pregnancy, 72% achieved live births. The group that had mild adhesions by hysteroscopic diagnosis achieved a higher live birth rate of 83.3% while those in the severe adhesions group achieved a live birth rate of 25%, despite pregnancy rates being more than 50% in each group. It is expected that with greater severity of the adhesions, there would be more endometrial fibrosis hindering successful implantation and even after adhesiolysis, there is a high rate of reformation of adhesions (20 to 65%).^{16,17} Patients with severe adhesions should be counselled regarding the prognosis and high miscarriage rates.

The obstetric complications rate reported in the group which achieved live birth was also high. Deans R and Abbott J reported 17 pregnancies out of 696 births complicated by

placental accreta and increta.¹⁰ Abnormal placentation is possible as the basalis layer of the endometrium has been disrupted in these women.⁹ They also reported an increased risk of premature delivery and uterine rupture.¹⁰ In our small group of 19 pregnancies posthysteroscopic adhesiolysis, 4 pregnancies (21%) were complicated by preterm delivery compared to the rate of preterm delivery of 13.6% in our centre.¹⁸ The caesarean section rate was 63.2% in our study group, which was higher than the caesarean section rates of our centre during that period (32.2% in 2010 and 33.8% in 2011).

We acknowledge the limitations of our study. It is retrospective in nature and consists of small numbers, with significant numbers lost to follow-up. No second look hysteroscopy was done to assess recurrence after treatment. The lack of a standardised pathway for the operative procedure also reduces the strength of our study.

Conclusion

The most common predisposing factor for developing Asherman syndrome in our population was trauma to the gravid uterus. The severity of adhesions has an impact on the prognosis of pregnancy outcomes. The importance of minimising, if not avoiding, the occurrence of endometrial injury post-TOP or post miscarriage, remains paramount. Efforts to reduce the number of unwanted pregnancies through effective contraception counselling, limiting instrumentation to the gravid uterus and the use of intrauterine adhesion barriers may help to prevent this rare but serious condition.

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