

## ORIGINAL RESEARCH ARTICLE

# Severity of intrauterine adhesions and pregnancy success rates after treatment: Comparison of adhesions obtained from open myomectomy versus uterine curettage

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## Abstract

Intrauterine adhesions (IUA) are rare. A retrospective comparative study was conducted between January 1, 2015, and December 31, 2018. Group A comprised 117 women who developed IUAs after open myomectomy, while Group B comprised 113 women who developed IUAs following uterine trauma caused by uterine instrumentation after a termination of pregnancy (TOP) or spontaneous miscarriage. The IUA grade and pregnancy rates and outcomes were compared using the March classification system. All patients underwent hysteroscopic adhesiolysis. The adhesions tended to be more severe (45/117, 38.5%) in Group A than in Group B (29/113, 25.7%); however, this difference was not statistically significant (Chi-Square 5.047;  $p = .080$ ). The period of observation was 24 months from the last hysteroscopy. The pregnancy rate in Group A (26, 22.2%) was significantly lower than in Group B (46, 40.7%) (OR: 2.403, 95% CI: 1.352–4.271;  $p = .003$ ). Open myomectomy was the preceding aetiological factor in a greater proportion of women with IUA in our study. In cases where pregnancy is desired after open myomectomy, especially where the endometrial cavity is breached, postoperative hysteroscopy to exclude IUAs is recommended. (*Afr J Reprod Health* 2022; 26[12]: 90-96).

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**Keywords:** Asherman; intrauterine adhesions; hysteroscopy; myomectomy

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## Résumé

Les adhérences intra-utérines (IUA) sont rares. Une étude comparative rétrospective a été menée entre le 1er janvier 2015 et le 31 décembre 2018. Le groupe A comprenait 117 femmes ayant développé des AIU après une myomectomie ouverte, tandis que le groupe B comprenait 113 femmes ayant développé des AIU à la suite d'un traumatisme utérin causé par une instrumentation utérine après l'arrêt d'une grossesse (TOP) ou fausse couche spontanée. Le grade IUA et les taux de grossesse et les résultats ont été comparés à l'aide du système de classification de mars. Tous les patients ont eu une adhésiolyse hystéroscopique. Les adhérences avaient tendance à être plus sévères (45/117, 38,5 %) dans le groupe A que dans le groupe B (29/113, 25,7 %); cependant, cette différence n'était pas statistiquement significative (Chi-Square 5,047 ;  $p = 0,080$ ). La période d'observation était de 24 mois à partir de la dernière hystéroscopie. Le taux de grossesse dans le groupe A (26, 22,2 %) était significativement plus faible que dans le groupe B (46, 40,7 %) (OR : 2,403, IC à 95 % : 1,352–4,271 ;  $p = 0,003$ ). La myomectomie ouverte était le facteur étiologique précédent chez une plus grande proportion de femmes avec IUA dans notre étude. Dans les cas où une grossesse est souhaitée après une myomectomie ouverte, en particulier lorsque la cavité endométriale est percée, une hystéroscopie postopératoire pour exclure les IUA est recommandée. (*Afr J Reprod Health* 2022; 26[12]: 90-96).

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**Mots-clés:** Asherman; intrauterine adhesions; hysteroscopy; myomectomy

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## Introduction

Intrauterine adhesion (IUA) refers to the presence of scar tissue within the endometrial cavity. The presence of these scar tissues with associated symptoms, such as menstrual irregularities,

recurrent pregnancy loss, and infertility, is referred to as Asherman syndrome<sup>1</sup>. It has been suggested that cases in which IUA is accidentally found without any symptoms, should be referred to as “asymptomatic IUAs”<sup>2</sup>. This condition was first described by Henrich Fristch and later

characterized by Joseph Asherman in 1948<sup>3</sup>. All patients described by Asherman had histories of trauma to the uterine cavity following pregnancy. Some authors are of the opinion that the term Asherman syndrome should be restricted to cases where the cause of the IUA is pregnancy-related, as originally described by Asherman; others suggest otherwise<sup>4</sup>. The terms Asherman syndrome and IUA are therefore often used interchangeably. Other probable causes of IUAs include caesarean section, myomectomy, the use of B-Lynch compression sutures, infections (such as schistosomiasis and tuberculosis of the genital tract), and surgeries for Mullerian abnormalities<sup>5,6</sup>.

Nigeria, a country in West Africa, has one of the most restrictive abortion laws in the world. An estimated 1.25 million induced abortions were performed in 2012 alone, equivalent to 33 abortions per woman aged between 15 and 49 years<sup>7</sup>. Most of these abortions were unsafe, as they are performed by unskilled individuals and/or in environments lacking the minimum medical standards, with approximately 70% of cases undergoing dilatation and curettage<sup>8</sup>. As an African population, the prevalence of uterine fibroids is high<sup>9</sup>. Additionally, open myomectomy is often the treatment of choice in symptomatic women with multiple and/or large fibroids, still desirous of pregnancy<sup>10</sup>. This combination results in a high prevalence of IUAs or Asherman syndrome<sup>11</sup>.

Few published studies have highlighted the issue of IUAs following open myomectomy, and to the best of our knowledge, there are currently no published studies comparing IUAs secondary to curettage of a pregnant or recently pregnant uterus, with open myomectomy. We aimed to highlight the similarities and differences regarding the incidence, severity of adhesions of IUA, and treatment outcomes between the two aetiologies.

## Methods

This was a retrospective comparative study conducted between January 1, 2015, and December 31, 2018. The study was performed at a dedicated fertility and minimal access surgery centre, including women who presented for assisted reproduction. The centre provides fertility treatment to women up to the age of 56 years. The medical records of all 902 women who had hysteroscopies during the study period were

retrieved. Those included in the study were women with IUA and a previous history of open myomectomy or pregnancy-related uterine instrumentation performed before presentation at the centre. Uterine instrumentation included the evacuation of retained products of conception (ERPC) or termination of pregnancy (TOP), by manual vacuum aspiration (MVA) or dilatation and curettage (D&C). The inclusion criterion for Group A was IUA following open myomectomy, while that for Group B was a diagnosis of IUA following TOP or ERPC for incomplete spontaneous miscarriage. All postmenopausal women and six women lost to follow up as they could not be reached to ascertain their treatment outcome were excluded from the study.

A total of 117 women with IUAs following open myomectomy were compared for socio-demographic characteristics with 113 who developed IUAs following TOP or ERPC for incomplete spontaneous miscarriage. Clinical assessment was performed in the gynaecology clinic, and the biosocial and reproductive data were recorded. A transvaginal scan was performed to assess the endometrium, uterus, and ovaries for any pathology. Classification of the degree of IUA was performed during hysteroscopy, and the March classification system was used to grade the IUA<sup>12</sup>. This involved grading the adhesions as mild, moderate, and severe, depending on the adhesion density and extent of endometrial cavity involvement. In the mild category, adhesions are filmy, occupying less than one-quarter of the uterine cavity; ostia areas and upper fundus are minimally involved or clear. In the moderate category, one-fourth to three-fourths of the cavity is involved; ostia areas and upper fundus are partially involved, with no agglutination of the uterine walls. More than three-fourths of the uterine cavity is involved, for the severe grades with occlusion of both ostia areas and upper fundus, with agglutination of the uterine walls.

All patients underwent hysteroscopic adhesiolysis with a single, 5 mm, compact inflow and outflow channel (Richard Wolf, Knittlingen, Germany), including a 2.9 mm, 25-degree telescope, and 5F rigid hysteroscopy scissors<sup>13</sup>. Normal saline was used as the distension medium in all cases. Adhesiolysis began with the most distal adhesions, progressing proximally towards the fundus; centrally located adhesions were separated

before lateral adhesions, and the procedure was considered complete when an adequate cavity was successfully created.

An intrauterine Foley's catheter was inserted in all patients with moderate and severe IUA and left for 7 to 10 days. The balloon was inflated with 3 ml of sterile water to prevent adhesion recurrence in cases of moderate and severe IUA. A Foley balloon catheter was therefore placed after adhesiolysis in 172 (74.8%) patients, including 93 of 117 (79.5%) patients in Group A, and 79 of 113 (69.9%) in Group B (95% CI: 0.318–1.027;  $p = .6$ ). Oral antibiotics in the form of Doxycycline capsules (Doxycap®, Hovid Bhd, Ipoh, Malasia) 100mg twice daily and Metronidazole tablets (Unigyl®, Unique Pharmaceuticals Ltd, Sango Ota, Nigeria) 400mg every eight hours were prescribed for 7 days to prevent ascending infections. Hormonal therapy was used to promote endometrial regeneration; estradiol valerate (Progynova®, Bayer Plc, Reading, United Kingdom) 2 mg twice a day was prescribed for 28 days. A progesterone preparation (Primolut N®, Bayer Plc, Reading, United Kingdom) 5 mg thrice a day was added for 7 days, commencing 21 days from the start of estradiol valerate. Menstrual blood loss was estimated before and after hysteroscopy based on the duration of menstrual blood flow and the number of vaginal pads used. Postprocedural repeat Hysterosalpingography (HSG) or hysteroscopy was performed 4 to 8 weeks after the initial procedure in patients with moderate and severe IUA. Eighty nine patients in Group A subsequently had In-Vitro fertilization and embryo transfer (IVF-ET) treatment, with 21 pregnancies (23.6%), while 35 patients out of 78 in Group B (44.9%) achieved conception via IVF.

The period of observation was 24 months from the last hysteroscopy. Those who did not continue further care with the centre were called via telephone to get information about any subsequent pregnancy and outcome.

### **Data analysis**

Data was entered into excel spreadsheet and analysed using Excel Analyse-it® statistical software (Analyse-it software, Ltd. Leeds, United Kingdom, <https://.analyse-it.com>).

Categorical variables were compared between the 2 groups using the Chi square test. Level of statistical significance was set at  $p < 0.05$  (95% confidence interval). The outcome measures analysed were severity of intrauterine adhesions, post-procedural HSG or hysteroscopy findings, increase in menstrual flow, and achievement of pregnancy.

### **Ethical consideration**

Ethical clearance with number IRB/05-2019-005 was obtained from the research and ethical review committee of Gynscope Specialist Hospital. The procedure was explained to all the women, and a fully informed written consent was obtained from each of them.

## **Results**

### **Demographics**

Two hundred and thirty patients were included, aged 26–51 years, mean  $39.8 \pm 5.66$  (Table 1). Patients who underwent open myomectomy (Group A) and uterine instrumentation (Group B) were aged 28–51 years, mean  $\pm$  SD  $40.3 \pm 4.23$  and 26–49 years, mean  $\pm$  SD  $36.5 \pm 5.88$ , respectively (95% CI: 1.134 – 0.744;  $p = .129$ ). The parity of the patients was 0–2 (median, 0) in Group A and 0–3 (median, 0) in Group B. All patients were desirous of pregnancy; however, 121 (52.6%) presented with scanty menses (hypomenorrhoea), 29 (12.6%) had painful menses (dysmenorrhoea), 23 (10%) had recurrent miscarriages, and 18 (7.8%) had absent menses (amenorrhoea). The precipitating procedures were open myomectomy (Group A,  $n = 117$  [50.9%]), and uterine instrumentation (D&C or MVA; Group B,  $n = 113$  [49.1%]). All cases of IUA following open myomectomy had submucous fibroids.

### **Severity of adhesions**

The adhesion grades were mild, moderate, and severe in 62 (27.0%), 94 (40.9%), and 74 (32.2%) patients, respectively as shown in Table 2. The adhesions tended to be more severe (45/117, 38.5%) in Group A than in Group B (29/113, 25.7%); however, this difference was not statistically significant (Chi-Square 5.047;  $p = .080$ ).

**Table 1:** Age distribution of respondents

Age group	Myomectomy Group A n=117 f (%)	Instrumentation Group B n=113 f (%)	Total n=230 f (%)
26 – 35	14 (12.0)	31 (27.4)	45 (19.6)
36 – 45	90 (76.9)	63 (55.8)	153 (66.5)
≥ 46	13 (11.1)	19 (16.8)	32 (13.9)
Range	28 – 51	26 – 49	26 – 51
Mean (Std. Dev.)	40.3 (4.23)	39.5 (5.88)	39.8 (5.66)
Mean diff.	1.134		
t-stat.	1.522		
p-value	0.129		
95% C.I.	1.134 – 0.744		

**Table 2:** Severity of intrauterine adhesions

Severity of adhesions	Myomectomy Group A n=117 f (%)	Instrumentation Group B n=113 f (%)	Total N=230 f (%)
Mild	26 (22.2)	36 (31.9)	62 (27.0)
Moderate	46 (39.3)	48 (42.5)	94 (40.9)
Severe	45 (38.5)	29 (25.7)	74 (32.2)
Chi-Square	5.047		
P-value	0.080		

**Table 3:** HSG/Hysteroscopy findings in 90 patients

HSG/Hysteroscopy Findings	Group A (%)	Group B (%)	Total (%)
Normal	12 (27.3)	27 (58.7)	39 (43.3)
Mild	14 (31.8)	14 (30.4)	28 (31.1)
Moderate	9 (20.5)	3 (6.5)	12 (13.3)
Severe	7 (15.9)	2 (4.3)	9 (10.0)
Narrow cavity	2 (4.5)	0	2 (2.2)
Total (%)	44 (48.9)	46 (51.1)	90 (100)

**Table 4:** Outcome of pregnancy in 72 patients following treatment of intrauterine adhesions

Pregnancy outcome	Group A (%)	Group B (%)	Total (%)
Caesarean section	21 (80.8)	19 (41.3)	40 (55.6)
Spontaneous vaginal delivery	2 (7.7)	17 (37.0)	19 (26.4)
Miscarriage	2 (7.7)	7 (15.2)	9 (12.5)
Preterm birth	0	2 (4.3)	2 (2.8)
Ongoing pregnancy	1 (3.8)	0	1 (1.4)
Blighted ovum	0	1 (2.2)	1 (1.4)
Total (%)	26 (36.1)	46 (63.9)	72 (100)

### **Postprocedural HSG or hysteroscopy**

After adhesiolysis, 90 (39.1%) patients underwent HSG (n = 1) or hysteroscopy (n = 89), including 44 (37.6%) in Group A and 46 (40.7%) in Group B (OR: 1.139, 95% CI: 0.671–1.935; p = .630). While 12 or 27.3% of the patients in Group A had normal findings at second-look hysteroscopy, 27 or 58.7% in Group B had normal findings. In terms of severity, there were more severe adhesion

recurrences in Group A, compared to Group B, 7 (15.9%) and 2 (4.3%), respectively. The findings are summarized in Table 3.

### **Effect on menstrual flow**

Menses improved in 100/117 (85.5%) patients in Group A, and 102/113 (90.3%) in Group B (95% CI: 0.179 –0.194; p = .191). Overall, 202 (87.8%) patients demonstrated an increase in menstrual flow.

### **Pregnancy outcomes**

The time frame for pregnancy assessment was 24 months post hysteroscopic adhesiolysis. Overall, pregnancy was achieved in 72 (31.3%) of 230 patients; the pregnancy rate in Group A (26, 22.2%) was significantly lower than in Group B (46, 40.7%) (OR: 2.403, 95% CI: 1.352–4.271;  $p = .003$ ). Of the 72 pregnancies, 16 (22.2%) were spontaneous, while 56 (77.8%) occurred through IVF. Spontaneous pregnancies included 5 (4.3%) patients in Group A, and 11 (9.7%) in Group B, which was not statistically significant (OR 2.624, 95% CI: .895–7.695;  $p = .070$ ). The pregnancy outcomes of the 72 patients are summarized in Table 4.

### **Discussion**

IUA is generally considered a rare disease in most parts of the world, and as many patients remain largely asymptomatic, its true prevalence remains unknown<sup>2</sup>. Hooker *et al.*, reported a prevalence of 19.1% in 912 women who underwent hysteroscopic evaluation 12 months after a spontaneous miscarriage or surgical/medical expulsion of pregnancy<sup>14</sup>. Unfortunately, this condition is fairly common in developing countries, especially those with restrictive abortion laws, such as Nigeria<sup>11</sup>. This is manifested in this study, where 902 hysteroscopies were performed over a 4-year period; 230 (25.5%) of these were for IUAs.

Intrauterine adhesions are reportedly common following dilatation and curettage performed for elective TOP, missed or incomplete miscarriage, or treatment of retained placenta<sup>1,15</sup>; however, a greater proportion of women in our study (117, 50.9%) had an open myomectomy as the preceding aetiological factor before a diagnosis of IUA was made. This is important, as open myomectomy, especially where the endometrium is breached to remove submucosal fibroids, can lead to IUA<sup>16</sup>. There are rare cases of IUA following open myomectomy where the uterine cavity was not breached; tissue hypoxia was identified as a possible aetiology in such cases<sup>17</sup>. All the cases in our study had submucous fibroids, requiring a breach of the endometrial cavity. Our study population is of African descent where fibroids are fairly common with a reported lifetime risk of 80% by the age of 50 years<sup>18</sup>.

In a recent retrospective review, open myomectomy constituted 7.7% of all gynaecological surgeries performed at our centre<sup>9</sup>. The decision to exclude these patients from the present study was due to certain steps routinely taken to reduce the incidence of IUA, which would form the basis of another, ongoing study. A report from Southeast Nigeria observed that complicated caesarean sections and abdominal myomectomies were the major risk factors for severe IUA (42.1% and 26.3%, respectively) over an 18-month period<sup>16</sup>. The severity of IUA in our study was also higher in patients who underwent open myomectomy than in those who utilized uterine instrumentation for ERPC or TOP (45/117 (38.5%) vs 29/113 (25.7%), respectively). While this did not achieve statistical significance ( $p = .080$ ), it provides evidence of increased damage to the endometrium during open myomectomy.

In a prospective, descriptive audit study, Conforti *et al.*, found that 50% of women who underwent open myomectomy subsequently developed IUA, confirmed by hysteroscopy, three months after the initial surgery<sup>11</sup>. They did not observe any statistically significant difference regarding the rate of IUA, irrespective of whether the endometrial cavity was breached; however, their sample size was relatively small.

Although the true incidence of IUA following TOP or instrumentation for ERPC is unknown, it is well documented that an increase in the time interval between the death of a fetus and evacuation of the products of conception, as well as the number of procedures performed to evacuate the fetus, all increase the risk of IUA<sup>19</sup>. There is an estimated 16% risk after one dilatation and curettage, increasing to 32% after three or more attempts at intrauterine ERPC<sup>19</sup>. The surgical method for ERPC also determines the rate of IUA. While dilatation and curettage are more likely to increase the rate and severity of IUA compared with MVA<sup>20</sup> we, unfortunately, did not document the method used, or the number of times the patients underwent ERPC.

Following hysteroscopic adhesiolysis, a total of 90 patients (39.1%) underwent either second-look hysteroscopy ( $n = 89$ ) or HSG ( $n = 1$ ), performed 4–8 weeks after the initial procedure. Xu *et al.*, recently demonstrated that early second-look hysteroscopic examinations within 2 months may increase cumulative pregnancy and live birth

rates<sup>21</sup>. There was no statistically significant difference between the two groups regarding the number of patients who underwent second-look hysteroscopy or HSG ( $p = .630$ ); the remaining patients either could not afford a second-look hysteroscopy or HSG, or spontaneously achieved conception. The inability of some of the patients to undergo a second-look hysteroscopy constituted one of the limitations of this study.

Overall, 39 (43.3%) patients had normal findings following hysteroscopic adhesiolysis, while mild cases of IUAs were detected in 28 patients (31.1%). Severe cases reduced from 32.2% to 10.0% posttreatment, with Group A still comprising a greater number than Group B (seven (15.9%) vs. two (4.3%), respectively). This is not surprising, since higher adhesion grades as observed in our patients are known to suggest a higher likelihood of spontaneous recurrence of adhesions<sup>4</sup>.

An 87.8% overall improvement in menstrual flow was observed; 85.5% and 90.3% of the patients in Group A and Group B exhibited improved menstrual flow, respectively. A study in Netherlands reported a 97.8% increase in menstrual flow; however, the aetiology of IUAs in the study was pregnancy-related in 96.3% of cases<sup>4</sup>.

Pregnancy was achieved in 72 (31.3%) of the 230 patients within 2 years of the initial hysteroscopic treatment. Women who developed IUAs following open myomectomy (Group A) exhibited significantly lower pregnancy rates than their counterparts in Group B (26 (22.2%) versus 46 (40.7%) patients, respectively;  $p = .003$ ). However, we are unable to conclude if the difference in pregnancy rates was due to the IUA, as other causes of infertility were not extracted from the case records for comparison. An overall conception rate of 40.4% following hysteroscopic adhesiolysis using a monopolar electrode knife for the separation of adhesions was reported in another study<sup>22</sup>. A recent meta-analysis of randomized controlled trials compared cold scissors and electrocautery<sup>23</sup>. The study concluded that cold scissors was more efficient than cautery at preventing IUA recurrence, increasing menstrual flow, reducing intraoperative blood loss, and shortening the operation time. Part of the strength of our study is that all the cases were performed using cold scissors by a single operator with over 15 years experience, thereby eliminating inter-operator error.

More patients underwent caesarean sections in Group A (80.8%) than in Group B (41.3%), which may be due to the fear of subsequent uterine rupture during labour in patients with a previous myomectomy, particularly when the endometrial cavity is breached<sup>24</sup>. Recent reports have demonstrated that the risk of uterine rupture during labour following open myomectomy is between 0.4% and 1.7%<sup>25,26</sup>; however, the true risk remains unknown.

Only two women (2.8%), both with uterine instrumentation prior to developing IUAs, experienced preterm delivery; none of the patients in the myomectomy group experienced preterm deliveries. We were unable to comment on the occurrence of morbidly adherent placentas in women, as half of the deliveries took place at other facilities; however, none of the patients who delivered at our facility exhibited a morbidly adherent placenta.

## Conclusion

Open myomectomy was the preceding aetiological factor in a greater proportion of women with IUA in our study. It also appears to be a prominent cause of severe IUAs compared with adhesions caused by pregnancy-related instrumentation of the uterine cavity. In cases where pregnancy remains desirous after open myomectomy, especially where the endometrial cavity is breached, postoperative hysteroscopy to exclude IUAs is, therefore, recommended.

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