



Patient Reported Menstrual and Obstetrical Outcomes Following Hysteroscopic Lysis of Adhesions for Asherman Syndrome at an American Hysteroscopic Office Practice

Citation

Morales, Blanca. 2020. Patient Reported Menstrual and Obstetrical Outcomes Following Hysteroscopic Lysis of Adhesions for Asherman Syndrome at an American Hysteroscopic Office Practice. Doctoral dissertation, Harvard Medical School.

Permanent link

<https://nrs.harvard.edu/URN-3:HUL.INSTREPOS:37364939>

Terms of Use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA>

Share Your Story

The Harvard community has made this article openly available.
Please share how this access benefits you. [Submit a story](#).

[Accessibility](#)

Scholarly Report submitted in partial fulfillment of the MD Degree at Harvard Medical School

Date: 01 March 2020

Student Name: Blanca Morales, BS

Scholarly Report Title: Patient Reported Menstrual and Obstetrical Outcomes Following Hysteroscopic Lysis of Adhesions for Asherman Syndrome at an American Hysteroscopic Office Practice

Mentor Name(s) and Affiliations: Peter Movilla, MD

Collaborators, with Affiliations: Joyce Wang¹, BS, Jennifer Wang¹, BS, Alexandria Williams, MD², Himabindyy Reddy², MD, Tammy Chen¹, BS, MPH, Jovana Tavcar³, MD, and Keith Isaacson³, MD

1-Harvard Medical School

2-Brigham and Women's/ Massachusetts General Hospital OB/GYN Residency Program

3-Newton Wellesley Hospital

Table of Contents

Abstract:3

Glossary of Abbreviations:4

Statement of Scholarly Project4

Manuscript.....5

Methods.....6

Results9

Discussion.....12

Figure 1: Newton Wellesley Hospital Asherman Syndrome Patient Distance Traveled For Care From Hometown Choropleth Map:16

Dates 01/01/2015- 03/01/201916

Figure 2: Asherman Syndrome Patient Contact Flow Chart17

Table 1. Patient Characteristics (All clinic patients) by March Classification18

Table 3. Presenting Menstrual Pattern by March Classification.....21

Table 4. Follow-up Menstrual Pattern for Patients that Presented with Amenorrhea by March Classification22

Table 5. Patient Reported Pregnancies Outcomes.....22

Table 6: Multivariable Analysis23

Table 7- Asherman Syndrome - Obstetrical Outcomes Literature Review Summary25

Supplemental Table 1. Patient Characteristics (Telephone Survey Completion)26

Supplemental Table 2. Telephone Survey Results for All Obstetrical Outcomes.....29

Citations:.....30

Abstract:

TITLE: Patient Reported Menstrual and Obstetrical Outcomes Following Hysteroscopic Lysis of Adhesions for Asherman Syndrome at an American Hysteroscopic Office Practice

Purpose: Asherman syndrome encompasses intrauterine scarring that results in menstrual and obstetrical irregularities. There has been a scarcity of publications regarding Asherman syndrome within the United States of America.

Methods: All patients meeting inclusion criteria were contacted via trained research assistants and invited to complete a telephone survey. Univariate and multivariate analysis was done on the three severity classifications of Asherman syndrome.

Results: The mean distance traveled per patient was 571.3 ± 849.1 miles (Median 205.0 miles). Among all of the Asherman syndrome patients treated in the clinic, 42.5% of had mild disease, 48.7% had moderate disease and only 8.7% had severe disease. Of the 355 clinic patients, 150 (42.3%) were successfully contacted and completed the telephone survey. Patients who completed the telephone survey were overall representative of the clinic population. On follow up of patients who presented with amenorrhea (absent flow, 38 patients), there was a significant difference in the rate of resolution of amenorrhea based on March classification with 93.7%, 85.0%, and 50.0% of mild, moderate, and severe Asherman syndrome. A total of 104 of the 127 patients reported ≥ 1 pregnancy following hysteroscopic treatment at our institution, for a 81.9% cumulative pregnancy rate amongst all Asherman syndrome patients completing the telephone survey. Amongst the total of 149 reported pregnancies, 46.3% (69 pregnancies) were categorized as "Preterm & Full Term Births", 38.9% (58 pregnancies) were categorized as "SAB/TAB/Ectopic", and 14.8% (22 pregnancies) were categorized as "Active Pregnancies". In multivariable analysis, March classification severity was not a predictor for ≥ 1 pregnancy or ≥ 1 live births when adjusted for potential confounders. March classification was a predictor of ≥ 1 miscarriage, specifically moderate Asherman syndrome patients demonstrating a lower rate of miscarriages when compared to mild Asherman syndrome patients (95% CI 0.1 - 0.8, P-value < 0.05).

Conclusions: We are the first group to investigate the impact of the March classification system on both pregnancy rate and live birth rate, and additionally perform a multivariate analysis to investigate for confounding variables.

Glossary of Abbreviations:

ART- Assisted Reproductive Technology

D&C- Dilatation and Curettage

D&E- Dilatation and Evacuation

ESGE- European Society of Gynecological Endoscopy

ESH- European Society of Hysteroscopy

ESHRE- European Society of Human Reproduction and Endocrinology

HCG- Human Chorionic Gonadotropin

SAB- Spontaneous Abortion

TAB- Term Abortion

Statement of Scholarly Project

The idea for this study was created by my mentor Dr. Peter Movilla as he has vast experience in the gynecological surgical arena. My participation included contacting patients to participate and complete the questionnaires regarding complications, menstrual and fertility outcomes following treatment for Asherman syndrome. The interviews were conducted over the phone. I was one of five research assistants that helped to collect data on the projected 355 patients. All research assistants entered their respective data on a secure site (RedCap). My specific project was to focus on menstrual and obstetrical patterns. Patients were classified by Asherman severity and menstrual flow pattern and amenorrhea rate was compared for pre and post treatment. For obstetrical outcomes, rate of pregnancy, live birth, term birth, spontaneous and term abortion and use of assisted reproductive technology was analyzed for patients before and after treatment. Statistical support was provided by a dedicated statistician. I was in charge of writing the introduction, results, and discussion. A novel aspect of this project was reporting on a large cohort of patients afflicted with a rather rare gynecological condition. In order to put our study into context a very comprehensive literature review was needed. I summarized the known studies in Table 7 of the paper. Currently, the manuscript is being reviewed by the senior mentor, Dr. Isaacson, and is pending submission into a high impact journal.

Introduction:

Intrauterine adhesions following uterine instrumentation was first described in 1894 by Heinrich Fritsch [1]. The compilation of symptoms encompassing amenorrhea, dysmenorrhea, infertility and recurrent pregnancy loss associated with intrauterine scarring was termed Asherman syndrome by Joseph G. Asherman in 1948 [1]. Asherman syndrome is diagnosed when a patient presents with irregular menstruation (oligomenorrhea, amenorrhea), pelvic pain (dysmenorrhea, non-cyclic pelvic pain), or subfertility (infertility, recurrent pregnancy loss) along with the identification of intrauterine adhesions confirmed by diagnostic hysteroscopy [2]. Alternative methods for identifying intrauterine adhesions include saline sonohysterogram, three-dimensional sonography, and magnetic resonance imaging, however diagnostic hysteroscopy remains the gold standard for confirmatory diagnosis [3].

The pathophysiology of Asherman syndrome is thought to be secondary to damage to the endometrial stratum basalis, a permanent endometrial layer that regenerates the endometrial stratum functionalis [4-6]. The functional layer becomes replaced by an epithelium monolayer that is not responsive to hormonal fluctuations, and results in endometrial fibrosis, synechia formation, calcification, ossification, defective vascularization, and nonfunctional glands [1,3]. States of infection or tissue hypoxia [1] and interventions such as postabortion and postpartum curettage [1-3, 5-7], evacuation of hydatidiform mole [1], cesarean section [6-8], surgical trauma [9-11], and uterine artery embolization [12] have been implicated in the development of Asherman syndrome. One theory is that low estrogen levels contribute to impaired regeneration of the endometrium in the immediate postpartum period, with loss of placental estrogen atop the initiation of breastfeeding, further inducing a hypoestrogenic state [1, 2, 13]. The incidence of intrauterine adhesion ranges from 6%-30% after intrauterine instrumentation with higher rates after postpartum intrauterine instrumentation [14-22].

Current treatments and management for Asherman syndrome are directed at removing and preventing recurrence of intrauterine adhesions with the goal of increasing the probability of a pregnancy and live birth, decreasing pelvic pain, and normalizing bothersome menstrual irregularities. Hysteroscopic adhesiolysis is currently the standard of care and performed under direct visualization with hysteroscopic scissors [1, 4, 7], and is preferred over electrosurgery to reduce the chance of uterine

perforation and recurrence of adhesions [23-25]. In patients with minimal to moderate Asherman syndrome, hysteroscopic lysis of adhesions can be performed as an outpatient procedure with no or minimal intravenous sedation [4, 26].

Following treatment of Asherman intrauterine adhesions via hysteroscopic adhesiolysis, there is a large variation in patients' reported obstetrical and menstrual outcomes, likely due to the heterogeneous patient population, marked variation in clinical treatment protocols, and unclear follow up times in reported publications.

The purpose of our research was to further understand the impact of intrauterine adhesions on menstrual cycle patterns and obstetrical outcomes when stratified by disease severity. In our gynecologic practice patients are categorized based on disease severity following the March classification system that utilizes the percentage of uterine cavity involvement with intrauterine adhesions to classify patients with either mild, moderate, or severe Asherman syndrome [27]. Although obstetrical and menstrual pattern outcomes have been reported in the literature on Asherman Syndrome patients, there is a paucity of data regarding these outcomes when stratified by all three disease severity categories with the March classification system. Additionally, from our literature review we could not identify a paper with more than one dozen patients with Asherman syndrome treated in the United States of America (USA) prior to 1988. As many technological advancements in both hysteroscopic management and assisted reproductive technology (ART) have occurred in the USA since that time period, we sought to investigate the current data on menstrual and obstetrical outcomes following hysteroscopic management of Asherman syndrome to better assist in patient counseling regarding at the time of diagnosis and designation of a March classification in an USA based gynecologic practice.

Methods

Study Population

Patients who underwent a diagnostic hysteroscopy and/or a hysteroscopy with lysis of intrauterine adhesions at the Center for Minimally Invasive Gynecologic Surgery at Newton Wellesley Hospital from 01/01/2015 to 03/01/2019 by one of the three gynecologic surgical providers within the practice were identified. These patients were first identified through our institution's electronic medical records via

the Research Patient Data Registry (RPDR) using the diagnosis code for Asherman syndrome, N85.6: Intrauterine synechiae (2018 ICD-10-CM Diagnosis Code), and the procedure codes for hysteroscopy, CPT Code: 58555 (Hysteroscopy, diagnostic), and/or CPT Code: 58559 (Hysteroscopy, with lysis of intrauterine adhesions). For completeness, all outpatient records from the Department of Minimally Invasive Gynecologic Surgery were also reviewed and checked with the list produced by the RPDR search of electronic medical records to ensure no patients were missed for evaluation during this defined timeframe. Evaluation of distance traveled per patient was calculated utilizing the web mapping service, Google Maps (Google; Menlo Park, CA) calculating the distance from the patients documented hometown to our institution location in Newton, Massachusetts, USA.

Surgical Management

Patients underwent both a transvaginal three-dimensional ultrasound and a diagnostic/therapeutic office hysteroscopy during their initial patient encounter. All intrauterine adhesions were completely lysed utilizing hysteroscopic scissors alone until normal uterine cavity anatomy was restored by one of three gynecologic surgical providers. All findings as well as a March classification of the disease severity were documented. Patients were then started on oral estradiol 2 milligrams twice daily for 30 days, followed by medroxyprogesterone acetate 10 milligrams daily for the last five days of this regimen to induce a withdrawal bleed. Patients were then seen between 2-3 weeks postoperatively and again at 6 weeks postoperatively for repeat office hysteroscopy and further lysis of adhesions if warranted. If patients demonstrated cervical canal adhesions, they then underwent serial cervical canal probing with an endometrial biopsy pipelle at two week intervals for a total of six weeks to prevent adhesion reformation within the cervical canal.

Chart Review/Survey administration

A retrospective review of the electronic health records identified patients perioperative characteristics, including age, gravidity, parity, gynecologic and menstrual history, past medical history, past surgical history, presumed etiology of intrauterine adhesions, previous treatment for intrauterine adhesions, hysteroscopic evaluation (March classification criteria utilized), and follow up plan. The March classification system is one of the most commonly utilized methods for stratifying patients based on disease severity. Patients are classified into one of three categories (mild, moderate or severe) based on

the degree of intrauterine adhesion involvement of the endometrial cavity and presence or absence of intrauterine adhesions at the tubal ostia identified by means of diagnostic hysteroscopy.

Patients were contacted via telephone and invited to complete a scripted telephone survey. Verbal consent for participation was obtained and answers were recorded in a secure electronic database, *REDCap* (Research Electronic Data Capture). This study was approved by the Institutional Review Board at Newton Wellesley Hospital via the Partners Human Research Committee (PHRC), the Institutional Review Board (IRB) of Partners HealthCare: Protocol # 2018P002095.

Menstrual Outcomes

To assess menstrual outcomes following hysteroscopic lysis of adhesions for Asherman Syndrome, presenting menstrual pattern variables were compared to follow up menstrual patterns from the telephone survey. To more accurately evaluate the return of menses, we specifically looked at patients that presented with amenorrhea and their follow up menstrual patterns.

Obstetric Outcomes

The three different patient reported obstetrical outcomes of the study were number of pregnancies, number of miscarriages, and number of live births using data from the telephone survey. Each of the variables were used to construct dichotomous outcomes for pregnancy rate, miscarriage rate and live birth rate. Patients were either classified as having 0 or ≥ 1 pregnancies, 0 or ≥ 1 miscarriages, and 0 or ≥ 1 live births.

For patient reported obstetrical outcomes, pregnancy was defined as any positive urine and/or serum evidence of pregnancy via human chorionic gonadotropin (HCG) or any evidence of intrauterine pregnancy via abdominal and/or pelvic ultrasound. Miscarriage was defined as any pregnancy loss less than 24 weeks gestational age, excluding termination of pregnancy or ectopic pregnancy. Live birth was defined as any birth on or beyond 24 weeks gestational age.

Statistical Methods

Descriptive statistics were used to summarize the characteristics of the total clinic population and patients that completed the telephone survey. Bivariate analyses were formed to examine sample

differences across March Classification and telephone survey completion using the ANOVA *F*-test and unpaired *t*-tests for continuous variables and the χ^2 test for categorical variables.

Lastly, multivariable logistic regression analyses were performed to examine if March Classification was an independent indicator of obstetric outcomes after controlling for patient characteristics and medical and obstetrical/gynecological history. Due to the small sample size, we only focused on indicators of obstetric outcomes. In addition, we included all patient characteristics regardless of their statistical significance to ensure that observed associations were not confounded by these variables. All analyses were performed using the statistical software package SAS version 9.4.

Results

There were a total of 355 patients evaluated and treated for Asherman syndrome within the clinic during the study period. The mean patient age and gravidity were 35.5 years-old and 2.1 pregnancies respectively, with the most common indications for evaluation being infertility and menstrual irregularities at 66.0%, followed and 23.0% respectively (Table 1). These patients presented from a total of 41 different states within the USA and from 5 different countries; 233 patients (65.6%) presented from outside our institutions home state of Massachusetts, and 6 patients (1.7%) presented from outside of the USA (Figure 1). The mean distance traveled per patient was 571.3 ± 849.1 miles (Median 205.0 miles). Among all of the Asherman syndrome patients treated in the clinic, 42.5% of had mild disease, 48.7% had moderate disease and only 8.7% had severe disease when stratified by the March classification system (Table 1). Patients with severe Asherman syndrome were the most likely to report amenorrhea at 35.5%, while patients with moderate and mild Asherman syndrome reporting amenorrhea at only 23.1% and 15.9% respectively during their initial patient encounter (Table 1). The presumed etiology was significantly different amongst the three classification groups, with “D&C/D&E - Early Pregnancy Loss or Elective Termination” and “D&C/D&E – Postpartum” being the two most common presumed etiologies for both mild and moderate Asherman syndrome, while “D&C/D&E – Postpartum” and “Endometrial Ablation” accounted for the two most common presumed etiologies for severe Asherman syndrome (*p*-value <0.001). Similarly, the severe Asherman syndrome patients had overall the lowest mean number of previous miscarriages at 0.6 previous miscarriages (*p*-value <0.001) as well as the highest mean number of “D&C/D&E – Postpartum” at 0.4 postpartum uterine instrumentation procedures (*p*-value <0.05).

Of the 355 clinic patients, 150 (42.3%) were successfully contacted and completed the telephone survey. The mean follow-up period measured as the time from initial patient encounter to date of telephone survey was 825.9 days or 2.26 years. Of those patients contacted, 127 (84.7%) were attempting conception (Figure 2). There were no statistically significant differences in patient characteristics between the patients that completed the telephone survey when compared to those who did not complete the telephone survey, with the exception of a higher percentage of patients presenting with infertility (68.7% versus 62.9%) as their primary chief complaint amongst those that completed the telephone survey (Supplemental Table 1). Patients who completed the telephone survey were thus overall representative of the clinic population, and comprised of 40.6% patients presenting with mild Asherman syndrome, 52.7% with moderate Asherman syndrome and 6.7% with severe Asherman syndrome (Table 2). Amongst those patients attempting conception there was no statistical difference amongst in vitro fertilization utilization when stratified by March classification, with in vitro fertilization utilized by 52.7%, 53.0% and 33.3% ($p=0.645$) of patients with mild, moderate and severe Asherman syndrome respectively (Table 2).

Menstrual Results

The most common presenting menstrual pattern for mild Asherman syndrome was normal flow at 37.7%, for moderate Asherman syndrome light flow at 44.3%, and for severe Asherman syndrome light flow at 70.0%. The patient reported amenorrhea rate (absent flow) demonstrated no significant differences when stratified by March classification at 26.2%, 25.3%, and 20.0% respectively for mild, moderate, and severe Asherman syndrome (Table 3). On follow up of patients who presented with amenorrhea (absent flow, 38 patients), there was a significant difference in the rate of resolution of amenorrhea based on March classification with 93.7%, 85.0%, and 50.0% of mild, moderate, and severe Asherman syndrome patients respectively reporting resolution of their amenorrhea at the time of the telephone survey (Table 4).

Obstetrical Results

Amongst the 127 patients who had attempted conception at the time of the telephone survey, 43.3% had mild Asherman syndrome, 52.0% had moderate Asherman syndrome, and 4.7% had severe Asherman syndrome (Table 5, Patient Outcomes. All Patients Attempting Conception). A total of 104 of

the 127 patients reported ≥ 1 pregnancy following hysteroscopic treatment at our institution, for a 81.9% cumulative pregnancy rate amongst all Asherman syndrome patients completing the telephone survey. Although not statistically significant, there was a decreasing trend in pregnancy rate with increasing March classification severity at 85.5%, 80.3%, and 66.7% amongst patients with mild, moderate and severe Asherman syndrome respectively (p-value = 0.47). Miscarriage rate was greatest in the severe Asherman syndrome patient group 50.0% (p-value < 0.05). There was a total of 65 patients reporting a ≥ 1 live births, for a 51.2% cumulative live birth rate amongst all Asherman syndrome patients. There was no statistically significant difference or trend in live birth rate when stratified by March classification with 50.9%, 54.6%, and 16.7% live birth rate for mild, moderate and severe Asherman syndrome patients respectively (p-value = 0.21). Additionally, 22 patients were actively pregnant at the time of the telephone survey. Of the patients actively pregnant, 6 of these patients had already reported ≥ 1 previous live birth since hysteroscopic treatment for their Asherman syndrome at our institution, while 16 patients had reported no previous live births since hysteroscopic treatment for their Asherman syndrome at our institution.

There were a total of 149 pregnancies reported amongst those 104 patients who had reported ≥ 1 pregnancy following hysteroscopic treatment at our institution (Table 5, Pregnancy Outcomes. All Pregnancies). Amongst the total of 149 reported pregnancies, 46.3% (69 pregnancies) were categorized as “Preterm & Full Term Births”, 38.9% (58 pregnancies) were categorized as “SAB/TAB/Ectopic”, and 14.8% (22 pregnancies) were categorized as “Active Pregnancies”. “Preterm & Full Term Births” referring to any pregnancy resulting in delivery at or beyond 24 weeks gestational age. “SAB/TAB/Ectopic” referring to any pregnancy resulting in a pregnancy loss prior to 24 weeks gestational age, a termination of pregnancy at any gestational age, or an ectopic pregnancy at any gestational age. For complete details of all patient reported pregnancy outcomes based on March classification please see Supplemental Table 2: Telephone Survey Results for All Obstetrical Outcomes in supplementary tables section.

Multivariable Analysis

We assessed March classification as an independent risk factor for pregnancy outcomes using multivariable analysis to control for several potential confounding variables such as patient age, gravidity, parity, presenting menstrual pattern, medical history, previous miscarriages, previous uterine instrumentation, and in vitro fertilization utilization (Table 6). March classification severity was not a

predictor for ≥ 1 pregnancy or ≥ 1 live births when adjusted for potential confounders. March classification was a predictor of ≥ 1 miscarriage, specifically moderate Asherman syndrome patients demonstrating a lower rate of miscarriages when compared to mild Asherman syndrome patients (95% CI 0.1 - 0.8, P-value < 0.05).

Discussion

Comprehensive evaluation and management of Asherman syndrome, including three dimensional pelvic sonography and advanced office hysteroscopic procedures, are essential for improving both the menstrual irregularities and fertility outcomes of patients diagnosed with this enigmatic disease. There has been a scarcity of publications regarding Asherman syndrome within the United States of America, with only three available studies identified through a comprehensive literature review published from institutions within the USA (Table 7), and none with a patient cohort of larger than a dozen since the year 1988. This lack of peer reviewed research into the disease may be reflective of the overall disparity in gynecologic surgical providers familiar with the disease entity around the nation who are comfortable in treating patients with a diagnosis of Asherman syndrome. We are the first publication to investigate the mean distance traveled per patient for evaluation and management of Asherman syndrome, demonstrating that patients are traveling great distances from both out-of-state and abroad to seek this thorough surgical care for their Asherman syndrome from high-volume gynecologic surgeons familiar with treating intrauterine adhesions and comfortable with advanced office-based hysteroscopic procedures. We recommended future research from the field of minimally invasive gynecologic surgeons focusing provider comfort with evaluation and management of Asherman syndrome, barriers to establishing advanced office based hysteroscopic practices, and lastly on the safety of office based hysteroscopic lysis of adhesions for treatment of Asherman syndrome.

One of the difficulties in investigating patient outcomes following treatment of Asherman syndrome is in the selection of the appropriate classification system for describing the intrauterine adhesions identified during hysteroscopy, with no one classification system solely validated with good predictive capabilities for either menstrual or obstetrical outcomes. There are several commonly utilized unvalidated classification systems reported in peer-reviewed publications including the March classification system, the American Fertility Society (AFS) classification of uterine adhesions, the European Society of Hysteroscopy (ESH) classification of intrauterine adhesions, the European Society of Gynecological

Endoscopy (ESGE) classification system of adhesions, and the European Society of Human Reproduction and Endocrinology (ESHRE) classification system. The variable nature of Asherman syndrome evaluation and management atop the numerous different unvalidated classification systems make it difficult to interpret any of the currently available literature on patient outcomes for the purpose of patient counseling. At our institution we have traditionally utilized the March classification system due to its focus on percentage of cavity involvement that allows for easy trending of scar reformation on follow-up hysteroscopy and its easily describable three tiered classification system that aids in patient and ancillary provider communication. In this series, we sought to investigate the predictive capabilities of the March classification system on both menstrual and obstetrical outcomes based on disease severity.

The rate of amenorrhea reported amongst all Asherman syndrome patients presenting initially for care has been described from 0.0%-100.0% [24, 28-38, 43], with only one paper reporting amenorrhea rate by disease severity via the AFS classification system at 0%, 2.6%, and 32.1% for mild, moderate, and severe disease, respectively [30]. Resolution of amenorrhea following treatment has been reported from 29.0 -100.0% [7, 23, 24, 28-30, 32-36, 39-41, 43, 44], and within our study was identified as 89.5% (34/38 patients with resolution of amenorrhea). We demonstrated that there was no significant difference in the initial amenorrhea rate amongst Asherman syndrome patients when stratified by March classification disease severity, thus patients reporting amenorrhea was not predictive of a patients final March classification following hysteroscopic evaluation of their intrauterine adhesions. We believe this may be due to the lack of menstrual history included in the March classification system, unlike the AFS classification system which does give significant weight on patient reported amenorrhea when calculating Asherman syndrome disease severity. Thus via the March classification it is possible for two patients two both report amenorrhea at initial consultation, although one patient has mild disease with focused adhesions in the lower uterine segment occluding the internal cervical os and all remaining cavity with functioning endometrium and the other patient having severe disease with significantly percentage of the intrauterine cavity affected by adhesions and thus majority of non-functioning endometrium. Our study validates this concept, as we did identify a significantly lower rate of resolution of amenorrhea based on increasing March classification disease severity, thus patients with severe disease having the lowest rate of menstruation returning. This supports the previously mentioned hypothesis that patients with mild disease and reported amenorrhea likely have a higher percentage of functioning endometrium than moderate and severe disease patients, with most of their adhesions

focused in the lower uterine segment that is amenable to hysteroscopic lysis of adhesions and return of menstruation.

The pregnancy rate amongst all Asherman syndrome patients attempting conception following hysteroscopic treatment varies in the reported literature from 32.1 - 85.0 % with a cumulative pregnancy rate of 56.2% (1467/2609 patients)(Table 7), although the definition of pregnancy is absent in a many of these studies [1, 7, 23, 24, 28, 30-41, 43, 45-47]. Additionally the definition of live birth rate varies amongst the published literature, but when defined as the total number of patients with ≥ 1 live birth following treatment of Asherman syndrome divided by the total number of patients attempting conception following treatment of Asherman syndrome, then the live birth rate ranges from 14.3 - 78.0% with a cumulative rate of 36.8% (960/2609 patients)(Table 7). Thus, in our clinical practice, following hysteroscopic treatment of all of our patients presenting with Asherman syndrome, our cumulative pregnancy rate and live birth rate of 81.9% and 51.2% respectively are both higher than the cumulative average from our literature review. Additionally, there are currently 22 patients who were actively pregnant at the time of the telephone survey, with 16 of these patients not yet having a live birth since treatment of their Asherman syndrome, 6 patients actively pregnant with already ≥ 1 live birth. Thus if all of these 16 patients were to go on to carry out their pregnancies to viability and deliver a live birth, our cumulative live birth rate would jump up from 51.2% (65/127 patients) up to 63.8% (81/127 patients).

Interestingly, we noted that there was not a significant difference in the pregnancy rate with increasing disease severity. We believe this may be due to both the similar pregnancy rates amongst both the mild and moderate Asherman syndrome patients (85.5% versus 80.3% respectively) as well as the low number of patients in the cohort completing the telephone survey with severe Asherman syndrome. Similarly we demonstrated that there was no statistically significant difference in live birth rate when stratified by March classification, again we believe owing to the similar live birth rates between the mild and moderate Asherman syndrome patients (50.9% versus 54.6% respectively). In both cases, severe Asherman syndrome patients did appear to have appreciably lower pregnancy rate and live birth rates at 66.7% and 16.7% respectively. The inability of the March classification system disease severity to predict pregnancy rate and live birth rate were further demonstrated with the multivariate analysis after accounting for confounder factors such as patient age and utilization of ART. The similarity in the pregnancy rate between both mild and moderate Asherman syndrome, atop the appreciably worse

obstetrical outcomes for patients with severe Asherman syndrome infers that the prognostic counseling for patients regarding obstetrical outcomes following treatment of Asherman syndrome should truly be more in a binary fashion than a three tiered system, with mild and moderate Asherman syndrome patients counseled with a similar prognosis versus severe Asherman syndrome patients to be counseled with a separate more modest prognosis.

Some advantages of our study include the large cohort of patients from multiple gynecologic surgical providers experienced in treating patients with Asherman syndrome. We are also the first group to investigate the impact of the March classification system on both pregnancy rate and live birth rate, and additionally perform a multivariate analysis to investigate for confounding variables. Some limitations of this study include its retrospective nature, with only 42.3% of all clinic patients able to be contacted and complete telephone survey, and the large distance and variation in practice of patient follow up following our hysteroscopic management of their Asherman syndrome owing to the large distances patients traveled for our care.

In addition, the previously mentioned recommended research activities we encourage our colleagues in minimally invasive gynecologic surgery to investigate their own clinical outcomes following hysteroscopic treatment of Asherman syndrome. We would recommend future research focusing on identifying additional confounders outside of the traditionally measured characteristics (age, gravidity, etc) that may additionally impact obstetrical outcomes in patients with Asherman syndrome such as adenomyosis, endometriosis, intrauterine insemination utilization, in vitro fertilization utilization, embryo quality, and pre-embryo transfer endometrial thickness measurements, with the ultimate goal of creating a prediction model and clinical calculator that can be utilized to input patient characteristics and ART utilization and display a predicted clinical pregnancy rate and live birth rate for patient counseling and personalized patient treatment planning.

Figure 1: Newton Wellesley Hospital Asherman Syndrome Patient Distance Traveled For Care From Hometown Choropleth Map:
 Dates 01/01/2015- 03/01/2019

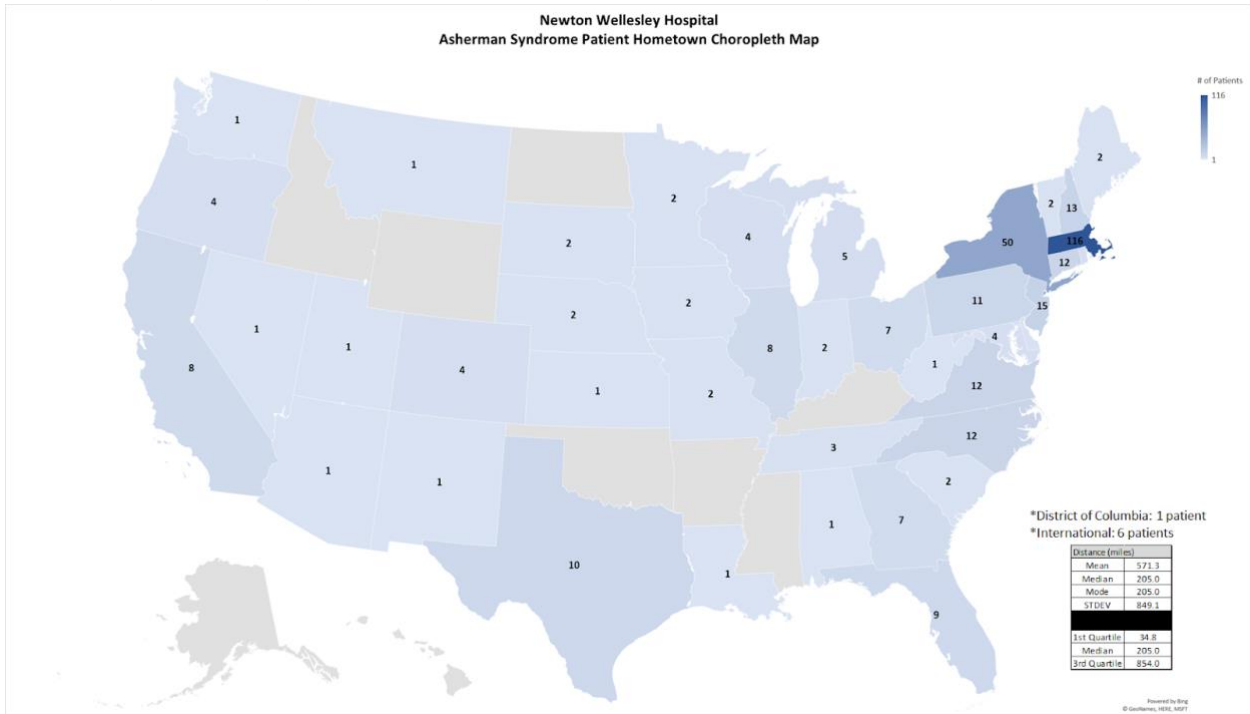


Figure 2: Asherman Syndrome Patient Contact Flow Chart

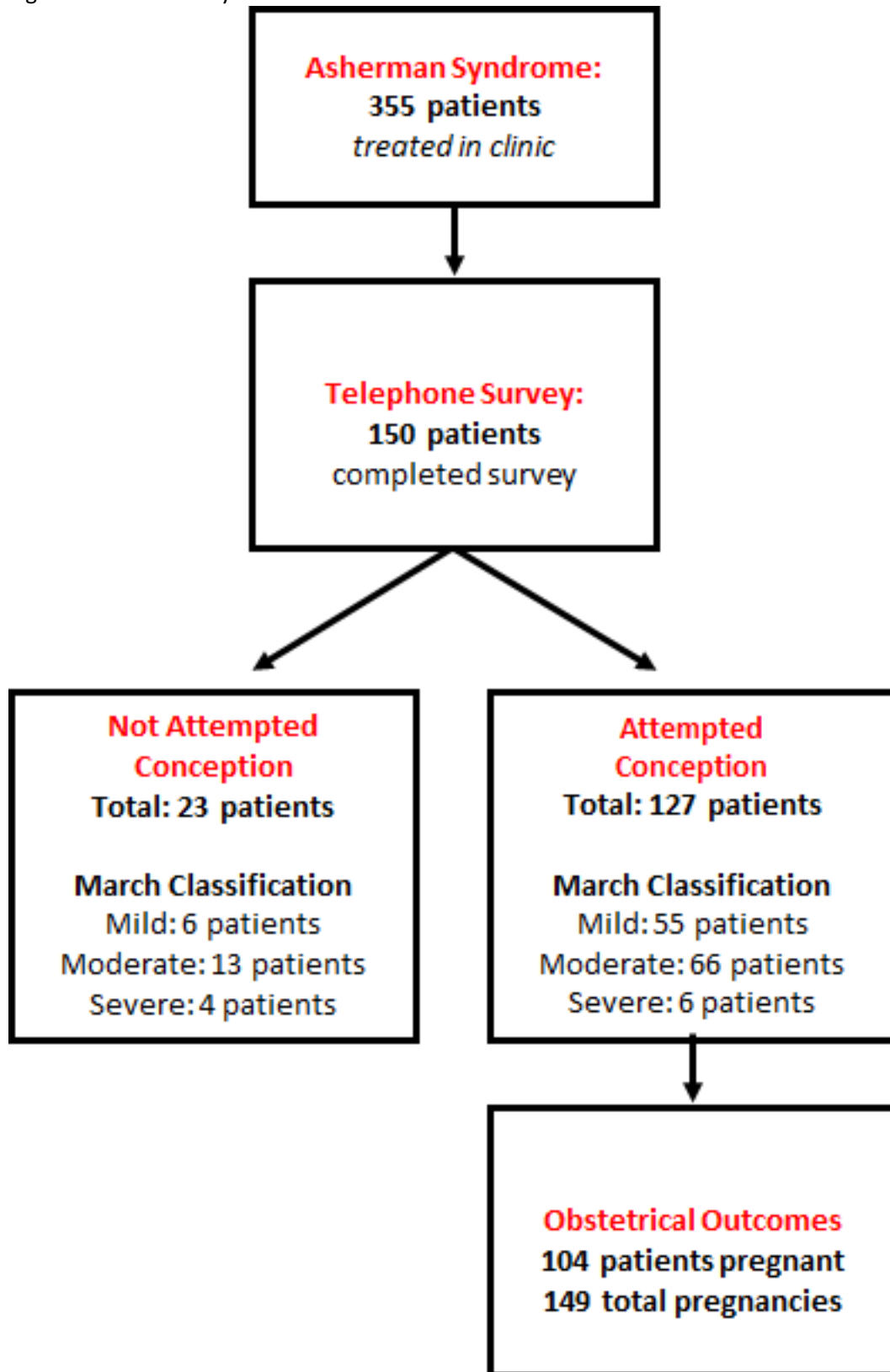


Table 1. Patient Characteristics (All clinic patients) by March Classification

	March Classification			p-value
	Mild (n=151)	Moderate (n=173)	Severe (n=31)	
Age**	35.9 (4.9)	35.1 (4.4)	35.6 (5.5)	0.329
Gravidity**	2.1 (1.6)	2.1 (1.8)	2.5 (1.7)	0.485
Parity**	0.6 (0.8)	1.0 (1.1)	1.7 (1.7)	<0.001
Chief Complaint†				0.579
Infertility	98 (64.9%)	113 (65.3%)	21 (67.7%)	
Recurrent Pregnancy Loss	17 (11.3%)	13 (7.5%)	1 (3.2%)	
Menstrual Irregularity	30 (19.9%)	40 (23.2%)	8 (25.8%)	
Dysmenorrhea	3 (2.0%)	1 (0.6%)	1 (3.2%)	
Non-cyclic pelvic pain	3 (2.0%)	6 (3.5%)	0	
Presenting Menstrual Pattern†				<0.001
Normal	66 (43.7%)	47 (27.2%)	3 (9.7%)	
Light	54 (35.8%)	83 (48.0%)	15 (48.4%)	
Absent	24 (15.9%)	40 (23.1%)	11 (35.5%)	
Heavy	7 (4.6%)	3 (1.7%)	2 (6.5%)	
Presumed Etiology†				<0.001
D&C/D&E - Early Pregnancy Loss or Elective Termination	86 (56.9%)	68 (39.3%)	5 (16.1%)	
D&C/D&E – Postpartum	29 (19.2%)	60 (34.7%)	12 (38.7%)	
Intrauterine Device Insertion	0	1 (0.6%)	0	
Pelvic Inflammatory Disease	0	2 (1.2%)	0	

Hysteroscopic Polypectomy	6 (4.0%)	2 (1.2%)	0	
Hysteroscopic Metroplasty	3 (2.0%)	0	0	
Hysteroscopic Myomectomy	5 (3.3%)	1 (0.6%)	1 (3.2%)	
Laparoscopic Myomectomy	2 (1.3%)	4 (2.3%)	0	
Abdominal Myomectomy	7 (4.6%)	6 (3.5%)	2 (6.5%)	
Cesarean Section	5 (3.3%)	19 (11.0%)	2 (6.5%)	
Endometrial Ablation	0	3 (1.7%)	8 (25.8%)	
Unclear	8 (5.3%)	7 (4.1%)	1 (3.2%)	
Medical History†				0.114
Yes	27 (17.9%)	18 (10.4%)	6 (19.4%)	
No	124 (82.1%)	155 (89.6%)	25 (60.7%)	
Previous Miscarriages **	1.3 (1.2)	1.0 (1.3)	0.6 (0.9)	<0.001
D&C/D&E - Early Pregnancy Loss or Elective Termination**	1.0 (0.9)	0.7 (1.0)	0.4 (0.8)	<0.05
D&C/D&E – Postpartum**	0.2 (0.5)	0.4 (0.6)	0.4 (0.6)	<0.05

*percentages may not add up to 100% because of rounding

† chi squared test

**f- test (ANOVA)

Table 2. Patients Characteristics (Completed Telephone Survey) by March Classification

	March Classification			p-value
	Mild (n=61)	Moderate (n=79)	Severe (n=10)	
Age**	36.2 (5.3)	34.2 (4.2)	36.0 (4.3)	<0.05
Gravidity**	1.8 (1.4)	2.2 (1.9)	2.8 (2.0)	0.14
Parity**	0.6 (0.9)	1.0 (1.2)	1.9 (2.4)	<0.05

Chief Complaint†				0.632
Infertility	43 (70.5%)	52 (65.8%)	21 (67.7%)	
Recurrent Pregnancy Loss	3 (4.9%)	5 (6.3%)	1 (3.2%)	
Menstrual Irregularity	12 (19.7%)	16 (20.3%)	8 (25.8%)	
Dysmenorrhea	1 (1.6%)	1 (1.3%)	1 (3.2%)	
Non-cyclic pelvic pain	2(3.3%)	5 (6.3%)	0	
Presenting Menstrual Pattern†				0.29
Normal	23 (37.7%)	22 (27.9%)	1 (10.0%)	
Light	19 (31.2%)	35 (44.3%)	7 (70.0%)	
Absent	16 (26.2%)	20 (25.3%)	2 (20.0%)	
Heavy	3 (4.9%)	2 (2.5%)	0	
Presumed Etiology†				<0.001
D&C/D&E - Early Pregnancy Loss or Elective Termination	32 (52.5%)	36 (45.6%)	2 (20.0%)	
D&C/D&E – Postpartum	15 (24.6%)	24 (30.4%)	3 (30.0%)	
Hysteroscopic Polypectomy	3 (4.9%)	1 (1.3%)	0	
Hysteroscopic Metroplasty	1 (1.6%)	0	0	
Hysteroscopic Myomectomy	1 (1.6%)	1 (1.3%)	1 (10.0%)	
Laparoscopic Myomectomy	1 (1.6%)	1 (1.3%)	0	

Abdominal Myomectomy	3 (4.9%)	3 (3.8%)	1 (10.0%)	
Cesarean Section	1 (1.6%)	10 (12.7%)	1 (10.0%)	
Endometrial Ablation	0	1 (1.3%)	2 (20.0%)	
Unclear	4 (6.6%)	2 (2.5%)	0	
Medical History				0.55
Yes	9 (14.8%)	8 (10.1%)	2 (20.0%)	
No	52 (85.3%)	71 (89.9%)	8 (80.0%)	
Previous Miscarriages **	1.0 (1.0)	1.1 (1.3)	0.6 (0.7)	0.39
D&C/D&E - Early Pregnancy Loss or Elective Termination**	0.8 (0.8)	0.8 (1.0)	0.6 (1.0)	0.75
D&C/D&E – Postpartum**	0.3 (0.6)	0.3 (0.5)	0.3 (0.5)	0.96
Attempting Pregnancy	55 (90.2%)	66 (83.5%)	6 (60.0%)	†
IVF Utilization	29 (52.7%)	35 (53.0%)	2 (33.3%)	0.645

*percentages may not add up to 100% because of rounding

† chi squared test

**f- test (ANOVA)

Table 3. Presenting Menstrual Pattern by March Classification

Presenting Menstrual Pattern	March Classification			P-value
	Mild	Moderate	Severe	
Normal	23 (37.7%)	22 (27.9%)	1 (10.0%)	0.286

Light	19 (31.2%)	35 (44.3%)	7 (70.0%)	
Absent	16 (26.2%)	20 (25.3%)	2 (20.0%)	
Heavy	3 (4.9%)	2 (2.5%)	0 (0.0%)	

Table 4. Follow-up Menstrual Pattern for Patients that Presented with Amenorrhea by March Classification

Absent Presenting Menstrual Pattern N = 38 patients	March Classification			P-value
	Mild	Moderate	Severe	
Follow Up Menstrual Pattern				
Normal	8 (50.0%)	12 (60.0%)	0 (0.0%)	<0.05
Light	7 (43.8%)	1 (5.0%)	1 (50.0%)	
Absent	1 (6.3%)	3 (15.0%)	1 (50.0%)	
Heavy	0 (0.0%)	4 (20.0%)	0 (0.0%)	

Table 5. Patient Reported Pregnancies Outcomes

Patient Outcomes All Patients Attempting Conception N = 127 patients	Mild	Moderate	Severe	p-value
	(n=55)	(n=66)	(n=6)	
>= 1 Pregnancy	47 (85.5%)	53 (80.3%)	4 (66.7%)	0.47
>= 1 Miscarriage	20 (36.4%)	12 (18.2%)	3 (50.0%)	<0.05
>= 1 Live Birth	28 (50.9%)	36 (54.6%)	1 (16.7%)	0.21
Pregnancy Outcomes All Pregnancies N = 149 pregnancies	Mild	Moderate	Severe	p-value
	(n=70)	(n=72)	(n=7)	

Pre-term & Full-Term Births	29 (41.4%)	39 (54.2%)	1 (14.3%)	x
SAB/TAB/Ectopic	32 (45.7%)	21 (29.2%)	5 (71.4%)	x
Active Pregnancies	9 (12.9%)	12 (16.7%)	1 (14.3%)	x
Trimester of Active Pregnancies				
First Trimester	5 (55.6%)	3 (25.0%)	0 (0.0%)	x
Second Trimester	4 (44.4%)	4 (33.3%)	1 (100.0%)	x
Third Trimester	0 (0.0%)	5 (41.7%)	0 (0.0%)	x

Table 6: Multivariable Analysis

Characteristic	Patient Reported Pregnancy Outcomes					
	Having one or more pregnancies		Having one or more miscarriages		Having one or more live births	
	Adjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
March Classification						
Mild	Ref.	-	Ref.	-	Ref.	-
Moderate	0.3 (0.1, 1.1)	0.06	0.3 (0.1, 0.8)	<0.05	1.0 (0.4, 2.1)	0.95

	Severe	0.3 (0.02, 3.4)	0.31	1.8 (0.3, 11.2)	0.51	0.1 (0.01,1.2)	0.06
Age		0.8 (0.6, 0.9)	<0.001	1.0 (0.9, 1.1)	0.69	0.9 (0.8, 0.9)	<0.05
Gravidity		1.4 (0.3, 7.7)	0.71	1.5 (0.6, 3.6)	0.38	1.1 (0.4, 3.0)	0.71
Parity		0.6 (0.1, 3.7)	0.59	0.6 (0.2, 1.6)	0.33	1.2 (0.5, 3.2)	0.84
Presenting Menstrual Pattern							
Normal		Ref.	-	Ref.	-	Ref.	-
Light		2.3 (0.6, 8.6)	0.21	1.7 (0.6, 4.7)	0.31	0.6 (0.2, 1.5)	0.19
Absent		1.2 (0.2, 6.3)	0.8	1.4 (0.4, 4.8)	0.6	0.7 (0.2, 1.9)	0.28
Heavy		3.2 (0.2, 65.6)	0.45	2.2 (0.3, 17.0)	0.47	0.5 (0.1, 4.3)	0.58
Medical History		0.6 (0.1, 2.6)	0.48	0.8 (0.2, 3.1)	0.79	0.7 (0.2, 2.4)	0.63
Previous Miscarriages (Reported at time of clinic)		0.7 (0.1, 3.9)	0.67	1.0 (0.4, 2.4)	0.98	0.6 (0.3, 1.6)	0.4
D&C/D&E - Early Pregnancy Loss or Elective Termination		3.2 (1.0, 10.8)	0.06	0.7 (0.4, 1.5)	0.4	1.8 (0.9, 3.6)	0.12
D&C/D&E – Postpartum		1.4 (0.3, 6.3)	0.67	2.2 (0.7, 6.7)	0.15	0.7 (0.3, 1.9)	0.41
IVF Utilization		0.7 (0.2, 2.4)	0.6	1.3 (0.5, 3.4)	0.54	0.6 (0.2, 1.3)	0.19

Table 7- Asherman Syndrome - Obstetrical Outcomes Literature Review Summary

	Asherman Syndrome - Obstetrical Outcomes Literature Review					Follow Up	Pregnancy Rate (% All Patients)				Live Birth Rate (% All Patients)				Assisted Reproductive Technology (% All Patients)
	Primary Author	Publication Year	Country	Classification System	# Patients Attempting Conception		Mean Follow Up Time (Years)	Overall	Mild	Moderate	Severe	Overall	Mild	Moderate	Severe
1	Sugimoto	1978	Japan	Sugimoto	192	x	41.1% (79/192)	x	x	x	24.5% (47/192)	x	x	x	x
2	Fedele	1986	Italy	ND	31	x	70.9% (22/31)	x	x	x	29.0% (9/31)	x	x	x	x
3	Friedman	1986	USA	ND	33	x	72.7% (24/33)	x	x	x	69.7% (23/33)	x	x	x	x
4	Valle	1988	USA	Valle	187	x	79.7% (143/187)	93.0% (40/43)	78.3% (76/97)	57.4% (27/47)	60.9% (114/187)	81.4% (35/43)	66.0% (64/97)	31.9% (15/47)	x
5	Goldenberg	1995	Israel	March	36	1.76	55.6% (20/36)	x	x	x	22.2% (8/36)	x	x	x	x
6	Pistofidis	1996	Greece	Pistofidis	86	x	34.9% (30/86)	34.7% (17/49)	38.5% (10/26)	27.3% (3/11)	24.4% (21/86)	26.5% (13/49)	30.8% (8/26)	0.0% (0/11)	100.0% (86/86)
7	Roge	1997	France	AFS	50	2.03	56.0% (28/50)	x	x	x	48.0% (24/50)	x	x	x	4.0% (2/50)
8	McComb	1997	Canada	AFS	6	x	83.3% (5/6)	x	x	x	66.7% (4/6)	x	x	x	x
9	Pabuccu, Atay	1997	Turkey	March	40		85.0% (34/40)	x	x	x	57.5% (23/40)	x	x	x	x
10	Chen, Soong	1997	China	March	7	x	42.9% (3/7)	x	x	42.9% (3/7)	28.6% (2/7)	x	x	28.6% (2/7)	x
11	Protopapas	1998	United Kingdom	ESH	7	1.04	42.9% (3/7)	x	x	x	14.3% (1/7)	x	x	x	x
12	Capella-Alboue	1999	France	ESH	28	2.58	42.8% (12/28)	x	x	42.8% (12/28)	32.1% (9/28)	x	x	32.1% (9/28)	x
13	Preutthipan	2000	Thailand	ND	45	1	35.6% (16/45)	x	x	x	x	x	x	x	x
14	Feng	2001	China	Sugimoto	186	ND	83.9% (156/186)	x	x	x	78.0% (145/186)	x	x	x	x
15	Coccia	2001	Italy	March	3	x	66.7% (2/3)	x	x	x	33.3% (1/3)	x	x	x	x
16	Zikopoulos	2004	Belgium	AFS	46	3.27	x	x	x	x	43.5% (20/46)	33.3% (2/6)	44.4% (11/25)	46.7% (7/15)	54.3% (25/46)
17	Fernandez, Al-Najar	2005	France	ESH	64	x	43.8% (28/64)	x	x	x	32.8% (21/64)	x	x	x	x
18	Pabuccu, Onalan	2007	Turkey	AFS	71	3.17	39.4% (28/71)	x	x	x	23.9% (17/71)	x	x	x	33.8% (24/71)
19	Thompson	2007	United Kingdom	AFS	17	x	52.9% (9/17)	66.7% (2/3)	42.9% (3/7)	57.1% (4/7)	47.1% (8/17)	x	x	x	23.5% (4/17)
20	Yu	2007	China	ESGE	85	3.9	45.9% (39/85)	64.7% (11/17)	53.6% (15/28)	32.5% (13/40)	29.4% (25/85)	47.1% (8/17)	35.7% (10/28)	17.5% (7/40)	47.1% (4/85)
21	Roy	2009	India	ESGE	89	2.04	40.4% (36/89)	58.1% (18/31)	30.0% (12/40)	33.3% (6/18)	33.7% (30/89)	54.8% (17/31)	25.0% (10/40)	16.7% (3/18)	x
22	Deans	2010	Australia	ESH	124	x	79.0% (98/124)	x	x	x	23.4% (29/124)	x	x	x	32.3% (40/124)
23	Orozco	2012	Mexico	AFS	39	ND	71.7% (28/39)	x	x	x	28.2% (11/39)	x	x	x	x
24	Myers	2012	USA	AFS	12	x	50.0% (6/12)	x	x	x	33.3% (4/12)	x	x	x	x
25	Fernandez, Peyrelevalde	2012	France	AFS & ESHRE	22	2.17	40.9% (9/22)	x	x	x	27.3% (6/22)	x	x	x	x
26	Takai	2015	Nigeria	ND	78	2	32.1% (25/78)	x	x	x	x	x	x	x	x
27	Chen, Zhang	2017	China	AFS	332	2.25	48.2% (160/332)	60.7% (82/135)	53.4% (55/103)	25.0% (23/92)	42.2% (140/332)	55.6% (75/135)	46.6% (48/103)	18.5% (17/92)	x
28	Xu	2018	China	AFS	151	x	71.5% (108/151)	x	x	x	53.0% (80/151)	x	x	x	31.1% (47/151)
29	Chen, Xiao	2018	China	AFS	139	x	55.4% (77/139)	x	x	x	39.6% (55/139)	x	x	x	x
30	Hui	2018	Singapore	ESGE	44	x	56.8% (25/44)	54.5% (12/22)	52.9% (9/17)	80.0% (4/5)	40.9% (18/44)	45.5% (10/22)	41.2% (7/17)	20.0% (1/5)	x
31	Zhu	2019	China	AFS	232	2.05	38.1% (90/236)	x	45.0% (59/131)	29.5% (31/105)	x	x	x	x	x
32	Morales	2020	USA	March	127	2.26	81.9% (104/127)	85.5% (47/55)	80.3% (53/66)	66.7% (4/6)	51.2% (65/127)	50.9% (28/55)	54.6% (36/66)	16.7% (1/6)	52.0% (66/127)

Pregnancy rate is defined as patients conceived/patients attempting conception
 Live birth rate is defined as live birth/patients attempting conception
 ND = Not Disclosed

Classification Systems:
 March
 AFS: American Fertility Society
 ESH: European Society of Hysteroscopy
 ESGE: European Society of Gynecological Endoscopy
 ESHRE: European Society of Human Reproduction and Endocrinology
 Valle
 Sugimoto
 Pistofidis

Supplemental Table 1. Patient Characteristics (Telephone Survey Completion)

	Telephone Survey		p-value
	Completed (n=150)	Did Not Complete (n=205)	
Age**	35.2 (4.8)	35.7 (4.7)	0.289
Gravidity**	0.9 (1.2)	0.9 (1.0)	0.439
Parity**	1.0 (1.1)	1.1 (1.3)	0.884
Chief Complaint†			<0.05
Infertility	103 (68.7%)	129 (62.9%)	
Recurrent Pregnancy Loss	8 (5.3%)	23 (11.2%)	
Menstrual Irregularity	29 (19.3%)	49 (23.9%)	
Dysmenorrhea	3 (2.0%)	2 (1.0%)	
Non-cyclic pelvic pain	7 (4.7%)	2 (1.0%)	
Presenting Menstrual Pattern†			0.427
Normal	46 (30.7%)	70 (34.2%)	
Light	61 (40.7%)	91 (44.4%)	
Absent	38 (25.3%)	37 (18.1%)	
Heavy	5 (3.3%)	7 (3.4%)	

Presumed Etiology†			0.959
D&C/D&E - Early Pregnancy Loss or Elective Termination	70 (46.7%)	89 (43.4%)	
D&C/D&E – Postpartum	42 (28.0%)	59 (28.8%)	
Intrauterine Device Insertion	0	1 (0.5%)	
Pelvic Inflammatory Disease	0	2 (1.0%)	
Hysteroscopic Polypectomy	4 (2.7%)	4 (2.0%)	
Hysteroscopic Metroplasty	1 (0.7%)	2 (1.0%)	
Hysteroscopic Myomectomy	3 (2.0%)	4 (2.0%)	
Laparoscopic Myomectomy	2 (1.3%)	4 (2.0%)	
Abdominal Myomectomy	7 (4.6%)	8 (3.9%)	
Cesarean Section	12 (8.0%)	14 (6.8%)	
Endometrial Ablation	3 (2.0%)	8 (3.9%)	
Unclear	6 (4.0%)	10 (4.9%)	
Medical History†			0.435
Yes	19 (12.7%)	32 (15.6%)	
No	131 (87.3%)	173 (84.4%)	
Previous Miscarriages **	1.0 (1.1)	1.1 (1.3)	0.482

D&C/D&E - Early Pregnancy Loss or Elective Termination**	0.8 (1.0)	0.8 (0.9)	0.81
D&C/D&E – Postpartum**	0.3 (0.5)	0.3 (0.5)	0.5
March Classification			0.315
Mild	61 (40.7%)	90 (43.8)	
Moderate	79 (52.7%)	94 (45.9)	
Severe	10 (6.7%)	21 (10.2)	

*percentages may not add up to 100% because of rounding

† chi squared test

**t-test

Supplemental Table 2. Telephone Survey Results for All Obstetrical Outcomes.

Number of patients (with 0, 1, 2, 3, 4, 5, >5) full term births, preterm births, miscarriages, terminations, ectopics, currently pregnant since last treatment at Newton Wellesley Hospital based on telephone survey results.

March Classification	Obstetrical Outcomes							
	All	%	Mild	%	Moderate	%	Severe	%
All Patients Attempting Pregnancy								
N	127	100.0%	55	43.3%	66	52.0%	6	4.7%
Full Term Births								
0	78	61.4%	33	60.0%	40	60.6%	5	83.3%
1	47	37.0%	21	38.2%	25	37.9%	1	16.7%
2	2	1.6%	1	1.8%	1	1.5%	0	0.0%
3	0	0.0%	0	0.0%	0	0.0%	0	0.0%
4	0	0.0%	0	0.0%	0	0.0%	0	0.0%
5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
>5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Preterm Births								
0	109	85.8%	49	89.1%	54	81.8%	6	100.0%
1	18	14.2%	6	10.9%	12	18.2%	0	0.0%
2	0	0.0%	0	0.0%	0	0.0%	0	0.0%
3	0	0.0%	0	0.0%	0	0.0%	0	0.0%
4	0	0.0%	0	0.0%	0	0.0%	0	0.0%
5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
>5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Miscarriages								
0	92	72.4%	35	63.6%	54	81.8%	3	50.0%
1	21	16.5%	12	21.8%	7	10.6%	2	33.3%
2	10	7.9%	6	10.9%	3	4.5%	1	16.7%
3	4	3.1%	2	3.6%	2	3.0%	0	0.0%
4	0	0.0%	0	0.0%	0	0.0%	0	0.0%
5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
>5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Terminations								
0	127	100.0%	55	100.0%	66	100.0%	6	100.0%
1	0	0.0%	0	0.0%	0	0.0%	0	0.0%
2	0	0.0%	0	0.0%	0	0.0%	0	0.0%
3	0	0.0%	0	0.0%	0	0.0%	0	0.0%
4	0	0.0%	0	0.0%	0	0.0%	0	0.0%
5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
>5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Ectopics								
0	122	96.1%	53	96.4%	64	97.0%	5	83.3%
1	5	3.9%	2	3.6%	2	3.0%	1	16.7%
2	0	0.0%	0	0.0%	0	0.0%	0	0.0%
3	0	0.0%	0	0.0%	0	0.0%	0	0.0%
4	0	0.0%	0	0.0%	0	0.0%	0	0.0%
5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
>5	0	0.0%	0	0.0%	0	0.0%	0	0.0%
Currently Pregnant								
Pregnant	22	17.3%	9	16.4%	12	18.2%	1	16.7%

Citations:

1. Yu D, Wong YM, Cheong Y, Xia E, Li TC. Asherman syndrome-one century later. *Fertil Steril* 2008;89:759–79, doi:http://dx.doi.org/10.1016/j.fertn- stert.2008.02.096.
2. Khan Z, Goldberg JM; Hysteroscopic Management of Asherman's Syndrome. *J Minim Invasive Gynecol*. 2018 Feb;25(2):218-228. doi: 10.1016/j.jmig.2017.09.020. Epub 2017 Oct 9.
3. Schenker JG, Margalioth EJ. Intrauterine adhesions: an updated appraisal. *Fertil Steril* 1982;37:593–610.
4. Salazar CA, Isaacson K, Morris S; A comprehensive review of Asherman's syndrome: causes, symptoms and treatment options. *Curr Opin Obstet Gynecol*. 2017 Aug;29(4):249-256. doi: 10.1097/GCO.0000000000000378.
5. Gargett CE, Nguyen HP, Ye L. Endometrial regeneration and endometrial stem/progenitor cells. *Rev Endocr Metab Disord* 2012; 13:235–251.
6. Friedler S, Margalioth EJ, Kafka I, Yaffe H. Incidence of post-abortion intra-uterine adhesions evaluated by hysteroscopy—a prospective study. *Hum Reprod* 1993;8:442–4.
7. Takai IU, Kwayabura AS, Ugwa EA; et all. A 10-year Review of the Clinical Presentation and Treatment Outcome of Asherman's Syndrome at a Center with Limited Resources. *Ann Med Health Sci Res*. 2015 Nov-Dec;5(6):442-6. doi: 10.4103/2141-9248.177984.
8. Badawy SZ, Orbuch L, Khurana KK. Secondary amenorrhea with severe intrauterine adhesions and chronic uterine torsion after cesarean section in a teenage girl. *J Pediatr Adolesc Gynecol* 1998;11:93–6.
9. Capmas P, Pourcelot AG, Fernandez H; Are synechiae a complication of laparotomic myomectomy? *Reprod Biomed Online*. 2018 Apr;36(4):450-454. doi: 10.1016/j.rbmo.2018.01.010. Epub 2018 Feb 2. PMID: 29454580
10. Riaz A, Zil-E-Ali A; Hysteroscopic Myomectomy can lead to intrauterine adhesions and infertility. *J Pak Med Assoc*. 2017 Jun;67(6):964-965.
11. Papoutsis D, Georgantzis D, Daccò MD, et all; A rare case of Asherman's syndrome after open myomectomy: sonographic investigations and possible underlying mechanisms. *Gynecol Obstet Invest*. 2014;77(3):194-200. doi: 10.1159/000357489. Epub 2014 Feb 15.
12. Saiga A, Yokota H, Higashide T, Takishima H, Omoto A, Kubota Y, Horikoshi T, Uno T; The Relationship Between Gelatin Sponge Preparation Methods and the Incidence of Intrauterine Synechia Following Uterine Artery Embolization for Postpartum Hemorrhage. *Cardiovasc Intervent Radiol*. 2019 Feb;42(2):195-204. doi: 10.1007/s00270-018-2078-x. Epub 2018 Sep 20. PMID: 30238332.
13. Buttram Jr., V.C., Turati, G., 1977. Uterine synechiae: variations in severity and some conditions which may be conducive to severe adhesions. *Int. J. Fertil*. 22, 98–103.
14. Gilman AR, Dewar KM, Rhone SA, Fluker MR. Intrauterine adhesions following miscarriage: look and learn. *J Obstet Gynaecol Can* 2016;38:453–457.
15. Hooker AB, Lemmers M, Thurkow AL, et al. Systematic review and metaanalysis of intrauterine adhesions after miscarriage: prevalence, risk factors and long-term reproductive outcome. *Hum Reprod Update* 2014; 20:262–278.
16. Hooker A, Fraenk D, Bro Imann H, Huirne J. Prevalence of intrauterine adhesions after termination of pregnancy: a systematic review. *Eur J Contracept Reprod Health Care* 2016; 21:329–335.
17. Smorgick N, Barel O, Fuchs N, et al. Hysteroscopic management of retained products of conception: meta-analysis and literature review. *Eur J Obstet Gynecol Reprod Biol* 2014; 173:19–22.

18. Hooker AB, Aydin H, Bro Imann HAM, Huirne JAF. Long-term complications and reproductive outcome after the management of retained products of conception: a systematic review. *Fertil Steril* 2016; 105:156–164.
19. Barel O, Krakov A, Pansky M, et al. Intrauterine adhesions after hysteroscopic treatment for retained products of conception: what are the risk factors? *Fertil Steril* 2015; 103:775–779.
20. Yu X, Yuhan L, Dongmei S, et al. The incidence of postoperative adhesion following transection of uterine septum: a cohort study comparing three different adjuvant therapies. *Eur J Obstet Gynecol Reprod Biol* 2016;201:61–64.
21. Touboul C, Fernandez H, Deffieux X, et al. Uterine synechiae after bipolar hysteroscopic resection of submucosal myomas in patients with infertility. *Fertil Steril* 2009; 92:1690–1693.
22. Bhandari S, Ganguly I, Agarwal P, et al. Effect of myomectomy on endometrial cavity: a prospective study of 51 cases. *J Hum Reprod Sci* 2016; 9:107–111.
23. Valle RF, Sciarra JJ. Intrauterine adhesions: hysteroscopic diagnosis, classification, treatment, and reproductive outcome. *Am J Obstet Gynecol*. 1988;158(6 Pt 1):1459–1470.
24. Pabuccu R, Atay V, Orhon E, Urman B, Ergun A. Hysteroscopic treatment of intrauterine adhesions is safe and effective in the restoration of normal menstruation and fertility. *Fertil Steril*. 1997;68:1141–1143.
25. Duffy S, Reid PC, Sharp F. In-vivo studies of uterine electrosurgery. *Br J Obstet Gynaecol*. 1992;99:579–582.
26. Bougie O, Lortie K, Shenassa H, et al; Treatment of Asherman's syndrome in an outpatient hysteroscopy setting. *J Minim Invasive Gynecol*. 2015 Mar-Apr;22(3):446-50. doi: 10.1016/j.jmig.2014.12.006. Epub 2014 Dec 10.
27. March CM. Management of Asherman's syndrome. *Reprod Biomed Online* 2011; 23:63–76.
28. Myers EM, Hurst BS; Comprehensive management of severe Asherman syndrome and amenorrhea. *Fertil Steril*. 2012 Jan;97(1):160-4. doi: 10.1016/j.fertnstert.2011.10.036. Epub 2011 Nov 17.
29. Guo J, Li TC, Liu Y, et al; A prospective, randomized, controlled trial comparing two doses of oestrogen therapy after hysteroscopic adhesiolysis to prevent intrauterine adhesion recurrence. *Reprod Biomed Online*. 2017 Nov;35(5):555-561. doi: 10.1016/j.rbmo.2017.07.011. Epub 2017 Jul 29.
30. Chen L, Zhang H, Wang Q; Reproductive Outcomes in Patients With Intrauterine Adhesions Following Hysteroscopic Adhesiolysis: Experience From the Largest Women's Hospital in China. *J Minim Invasive Gynecol*. 2017 Feb;24(2):299-304. doi: 10.1016/j.jmig.2016.10.018. Epub 2016 Nov 14.
31. Zhu R, Gan L, Wang S, Duan H; A cohort study comparing the severity and outcome of intrauterine adhesiolysis for Asherman syndrome after first- or second-trimester termination of pregnancy. *Eur J Obstet Gynecol Reprod Biol*. 2019 Jul;238:49-53. doi: 10.1016/j.ejogrb.2019.02.030. Epub 2019 May 4.
32. Deans R, Vancaillie T, Ledger W, et al; Live birth rate and obstetric complications following the hysteroscopic management of intrauterine adhesions including Asherman syndrome. *Hum Reprod*. 2018 Oct 1;33(10):1847-1853. doi: 10.1093/humrep/dey237.
33. Capella-Allouc S, Morsad F, Rongieres-Bertrand C, Taylor S, Fernandez H. Hysteroscopic treatment of severe Asherman's syndrome and subsequent fertility. *Hum Reprod*. 1999;14:1230–1233.
34. Roy KK, Baruah J, Sharma JB, et al; Reproductive outcome following hysteroscopic adhesiolysis in patients with infertility due to Asherman's syndrome. *Arch Gynecol Obstet*. 2010 Feb;281(2):355-61. doi: 10.1007/s00404-009-1117-x. Epub 2009 May 20.

35. Fernandez H, Al-Najjar F, Chauveaud-Lambling A, et al; Fertility after treatment of Asherman's syndrome stage 3 and 4. *J Minim Invasive Gynecol*. 2006 Sep-Oct;13(5):398-402
36. Fernandez H, Peyrelevade S, Legendre G, et al; Total adhesions treated by hysteroscopy: must we stop at two procedures? *Fertil Steril*. 2012 Oct;98(4):980-5. doi: 10.1016/j.fertnstert.2012.06.032. Epub 2012 Jul 15.
37. Hui CY¹, Lau MS, Ng GY, Tan HH. Clinical and Reproductive Outcomes Following Hysteroscopic Adhesiolysis for Asherman Syndrome in an Asian Population. *Ann Acad Med Singapore*. 2018 Jan;47(1):36-39.
38. Baradwan S, Baradwan A, Bashir M, Al-Jaroudi D. The birth weight in pregnant women with Asherman syndrome compared to normal intrauterine cavity: A case-control study. *Medicine (Baltimore)*. 2018 Aug;97(32):e11797.
39. Cruz Orozco OP¹, Castellanos Barroso G, Gaviño Gaviño F, et al; Future reproductive ability in post-treatment Asherman's syndrome patients. *Ginecol Obstet Mex*. 2012 Jun;80(6):389-93.
40. Xu W, Zhang Y, Yang Y, et al; Effect of early second-look hysteroscopy on reproductive outcomes after hysteroscopic adhesiolysis in patients with intrauterine adhesion, a retrospective study in China. *Int J Surg*. 2018 Feb;50:49-54. doi: 10.1016/j.ijisu.2017.11.040. Epub 2017 Dec 1.
41. Chen L, Xiao S, He S, et al; Factors That Impact Fertility after Hysteroscopic Adhesiolysis for Intrauterine Adhesions and Amenorrhea: A Retrospective Cohort Study. *J Minim Invasive Gynecol*. 2019 Mar 14. pii: S1553-4650(19)30125-6. doi: 10.1016/j.jmig.2018.12.023.
42. Feng ZC, Yang B, Shao J, Liu S. Diagnostic and therapeutic hysteroscopy for traumatic intrauterine adhesions after induced abortions: clinical analysis of 365 cases. *Gynaecol Endosc* 1999;8:95–8.
43. Fedele L, Vercellini P, Viezzoli T, Ricciardiello O, Zamberletti D. Intrauterine adhesions: current diagnostic and therapeutic trends. *Acta Eur Fert*. 1986;17:31–37.
44. Liu L, Huang X, Xia E, Zhang X, Li TC, Liu Y; A cohort study comparing 4 mg and 10 mg daily doses of postoperative estradiol therapy to prevent adhesion reformation after hysteroscopic adhesiolysis. *Hum Fert (Camb)*. 2019 Sep;22(3):191-197. doi: 10.1080/14647273.2018.1444798. Epub 2018 Mar 5. PMID: 29504823.
45. Pistofidis GA, Dimitropoulos K, Mastrominas M. Comparison of operative and fertility outcome between groups of women with intrauterine adhesions after adhesiolysis. *J Am Assoc Gynecol Laparosc* 1996;3(Suppl):S40.
46. Preutthipan S, Linasmita V. Reproductive outcome following hysteroscopic lysis of intrauterine adhesions: a result of 65 cases at Ramathibodi Hospital. *J Med Assoc Thai* 2000;83:42–6.
47. Zikopoulos KA, Kolibianakis EM, Platteau P, de Munck L, Tournaye H, Devroey P, Camus M. Live delivery rates in subfertile women with Asherman's syndrome after hysteroscopic adhesiolysis using the resectoscope or theVersapoint system. *Reprod Biomed Online* 2004;8:720–5.