Burden of Illness of Intrauterine Adhesions Following Intrauterine Procedures: A Retrospective Analysis of Real-World Data

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BACKGROUND

Intrauterine adhesions (IUAs) occur when scar tissue binds the surfaces of the uterine cavity, often due to surgical procedures or infections. UAs can have an adverse impact on a woman's health, as they are associated with menstrual abnormalities, periodic abdominal pain, infertility, recurrent abortion, and pregnancy-related complications.[1-3] These complications also lead to the consumption of significant health care resources and may impose substantial costs upon healthcare payers.[4] Therefore, the clinical and economic burden of IUAs appears to be immense, particularly when considering the high rates of recurrence of IUAs following surgical removal, as well as the relative lack of effective treatment and prevention strategies.

OBJECTIVE

- **Primary Objectives**: 1.) Evaluate the clinical and obstetrical outcomes among women undergoing adhesiolysis to compare results with those of women who did not undergo any uterine procedures/adhesiolysis. 2.) Determine the overall disease burden in terms of healthcare resource use, clinical outcomes, and healthcare costs.
- **Key Outcomes:** Rates of absent uterine bleeding, placenta accreta spectrum, postpartum hemorrhage, pregnancies, live births, miscarriages, pre-term deliveries, and cesarean deliveries.
- **Secondary Objectives**: 1.) Study the effectiveness of adhesiolysis as an IUA treatment strategy. 2.) Identify the unmet needs for effective treatment strategies in the IUA disease landscape.

DATA SOURCE

The study utilizes an anonymous database provided by **Health Verity® Marketplace™**. This database is the largest source of closed-payer medical claims available from health insurance companies. It covers over 150 distinct payers and includes data from over 120 million patients with commercial, Medicaid, or Medicare coverage.

METHODOLOGY

Study Design and Cohort Selection:

- This observational study adheres to the study design outlined in the flow diagram below.
- The study period includes **6 months of continuous enrollment** leading up to three distinct cohort selections until December 2019.
- **The three cohorts are as follows:**
  1. Adhesiolysis Cohort
  2. Procedure-free Non-IUA Cohort
  3. Procedure Experienced Non-IUA Cohort

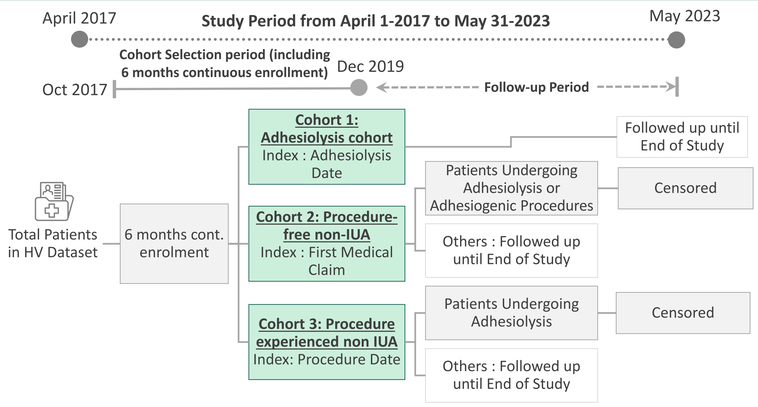
Follow-Up and Outcome Evaluation:

- All cohorts were followed through the end of the study (May 2023).
- The primary objective was to **evaluate and compare clinical and economic outcomes** across these groups.

Comparison of Study Groups:

- Propensity score matching techniques were employed for matching cohorts based on key baseline characteristics.
- Post matching, study groups were analyzed, and the results were compared using appropriate statistical tests.

STUDY FLOW DIAGRAM



RESULTS

Table 1. Patients with Adverse Events During The Follow-up Period

Pregnancy Outcomes	Adhesiolysis Cohort		Procedure-Free Non-IUA Cohort		Procedure-Experienced Non-IUA Cohort		P-Value
	N=2,768		N=2,768		N=2,768		
	#	%	#	%	#	%	
Uterine Bleeding and Pain							
Heavy Menstrual Bleeding	475	17.2%	261	9.4%	487	17.6%	<0.05
Absent Uterine Bleeding	495	17.9%	164	5.9%	386	13.9%	<0.05
Irregular Menstrual Bleeding	94	3.4%	25	0.9%	41	1.5%	<0.05
Other Abnormal Uterine Bleeding Conditions	552	19.9%	257	9.3%	647	23.4%	<0.05
Pelvic Pain	1,442	52.1%	930	33.6%	1,237	44.7%	<0.05

1. We used the student chi-squared-test to compare the proportions of the three cohorts. The difference between the two cohorts is considered statistically significant only when the p-value is less than 0.05 (i.e. <0.05), unless not significant (>0.05).

Table 2. Pregnancy Outcomes Among Patients with Pregnancies During The Follow-up Period

Pregnancy Outcomes	Adhesiolysis Cohort		Procedure-Free Non-IUA Cohort		Procedure-Experienced Non-IUA Cohort		P-Value
	N = 863		N = 346		N = 874		
	#	%	#	%	#	%	
Live Births							
0	177	20.5%	39	11.3%	336	38.4%	<0.05
≥ 1	686	79.5%	307	88.7%	538	61.6%	<0.05
1	583	67.6%	246	71.1%	455	52.1%	<0.05
2	94	10.9%	56	16.2%	81	9.3%	<0.05
3+	9	1.0%	5	1.4%	2	0.2%	<0.05
Still Birth							
0	863	100.00%	346	100.00%	870	99.54%	0.062
1+	0	0.00%	0	0.00%	4	0.46%	0.062
Live Birth and Still Birth							
0	863	100.0%	346	100.0%	874	100.0%	NA
1+	0	0.0%	0	0.0%	0	0.0%	NA
Delivery Outcome Unspecified							
0	860	99.7%	345	99.7%	869	99.4%	0.702
1+	3	0.3%	1	0.3%	5	0.6%	0.702
Miscarriages							
0	624	72.3%	295	85.3%	505	57.8%	<0.05
≥ 1	239	27.7%	51	14.7%	369	42.2%	<0.05
1	196	22.7%	46	13.3%	292	33.4%	<0.05
2	36	4.2%	4	1.2%	66	7.6%	<0.05
3+	7	0.8%	1	0.3%	11	1.3%	0.253

1. We used the student chi-squared-test to compare the proportions of the three cohorts. The difference between the two cohorts is considered statistically significant only when the p-value is less than 0.05 (i.e. <0.05), unless not significant (>0.05).

Table 3. Delivery Outcomes Among Patients with Live Births During the Follow-Up Period

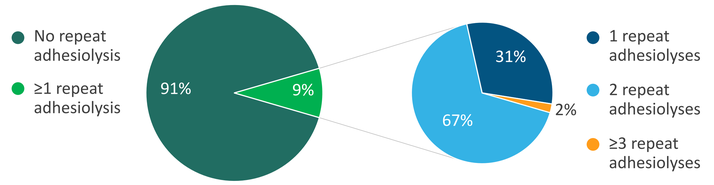
Outcomes	Adhesiolysis Cohort		Procedure-Free Non-IUA Cohort		Procedure-Experienced Non-IUA Cohort		P-Value
	N=689		N=308		N=543		
	#	%	#	%	#	%	
Gestational Length at Delivery							
Full Term Delivery	589	85.5%	282	91.6%	488	89.9%	<0.05
Preterm Delivery (Any Trimester)	100	14.5%	26	8.4%	55	10.1%	<0.05
Second Trimester Preterm	10	1.5%	1	0.3%	6	1.1%	0.290
Third Trimester Preterm	80	11.6%	22	7.1%	43	7.9%	<0.05
Unspecified (Preterm)	10	1.5%	3	1.0%	6	1.1%	0.774
Delivery Type							
Vaginal Delivery	211	30.6%	176	57.1%	296	54.5%	<0.05
Cesarean Delivery	312	45.3%	68	22.1%	145	26.7%	<0.05
Unknown Delivery Type	166	24.1%	64	20.8%	102	18.8%	0.074
Placenta Related Outcomes							
Placenta Accreta	24	3.5%	0	0.0%	4	0.7%	<0.05
Placenta Percreta	4	0.6%	0	0.0%	0	0.0%	0.084
Placenta Increta	4	0.6%	0	0.0%	1	0.2%	0.255
Placenta Previa	93	13.5%	12	3.9%	55	10.1%	<0.05
Post Partum Hemorrhage	122	17.7%	24	7.8%	136	25.0%	<0.05

1. We used the student chi-squared-test to compare the proportions of the three cohorts. The difference between the two cohorts is considered as statistically significant only when the p value is less than 0.05 (i.e. <0.05),unless not significant (>0.05)

RESULTS – CONT.

- Live birth rates were the highest among the procedure-free cohort (88.7%), followed by the adhesiolysis cohort (79.5%) and procedure-experienced non-IUA cohort (61.6%). (Table2)
- Miscarriage rates were significantly higher in the adhesiolysis cohort (27%) as compared to the procedure-free cohort (14.7%). (Table2)
- Pre-term delivery rates were highest among women who underwent adhesiolysis (14.5%). These rates dropped to 8.4% for women who did not undergo any adhesiogenic procedure. (Table 3)
- Cesarean deliveries were most prevalent among the adhesiolysis cohort. (Table 3)
- Among the adhesiolysis cohort, 9% of women underwent repeat adhesiolysis procedures, and 2.3% of women underwent up to 4 repeat adhesiolysis procedures.

Figure 2. Patients with Occurrence Of IUAs During The Follow-up Period



- The costs of live births were highest among the adhesiolysis cohort ($1,295) as compared to procedure-free cohort ($1,160).
- Cost of miscarriage among adhesiolysis cohort and procedure experienced cohort was $2,122 and $2,265 respectively, significantly higher than women who did not undergo any procedures ($1,171).

Table 5.Healthcare Costs Outcomes During Follow-up Among Patient Cohorts

Cost Category	Adhesiolysis Cohort		Procedure-Free Non-IUA Cohort			Procedure-Experienced Non-IUA Cohort		
	Mean	SD	Mean	SD	P-Value	Mean	SD	P-Value
Procedural Costs (Adhesiolysis)	$2,959	2,344	NA	NA	NA	NA	NA	NA
Diagnostics Costs (Hysteroscopy, HSG or SHG)	$ 506	$ 620	$ 623	$ 788	0.184	$ 471	$ 515	0.375
Induced Abortions	$ 1,778	$ 1,527	NA	NA	NA	$ 1,063	$ 1,017	<0.05
Live Births	$ 1,295	$ 537	$ 1,160	$ 353	<0.05	$ 1,171	$ 415	<0.05
Miscarriage	$ 2,122	$ 1,377	$ 2,523	$ 1,140	0.369	$ 2,265	$ 1,509	0.380
Ectopic Termination	$ 2,886	$ 2,764	$ 1,023	$ 51	0.409	$ 6,535	NA	NA
Cesarean Delivery	$ 1,334	$ 499	$ 1,303	$ 432	0.647	$ 1,295	$ 452	0.435
Vaginal Delivery	$ 1,465	$ 650	$ 1,146	$ 419	<0.05	$ 1,175	$ 519	<0.05

1.These costs are calculated on a per-event basis, considering only the line charges specific to the mentioned line items.
2."N" represents the number of occurrences of each outcome (ie, the number of times that cost item appears in each cohort).
3.Here, to compare the means of two cohorts, we have used student t-test . The difference between the two cohorts are considered as statistically significant only when the p value is less than 0.05 (i.e. <0.05),unless not significant (>0.05)
4.In this table, Adhesiolysis cohort is being compared with Procedure-Free Non-IUA Cohort and Procedure-Experienced Non-IUA Cohort separately, and respective p-values are reported accordingly.

CONCLUSIONS

- The results demonstrate that adhesiolysis tend to marginally improve the patient outcomes which underscores that adhesiolysis is not an effective treatment strategy to prevent IUAs and other adverse outcomes.
- Among the adhesiolysis cohort, significant rates of adverse events and pregnancy complication were observed which demonstrates that women undergoing adhesiolysis tend to cause significant health burden on the health care payers. As a result, we observe greater healthcare resource and costs involved for such patients.
- Patients who undergo adhesiogenic procedures but have not undergone adhesiolysis have the worst patient outcomes in general when compared to the three cohorts. This could be due to un-diagnosed adhesions present in these women. Therefore, the IUAs tend to be underdiagnosed and may have even greater healthcare disease burden.

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DISCLOSURES

DS, CM, MP, NR, LS, AM, RW, JM, and JK are employees of Axtria. MGM and IF are consultants for Rejoni Inc.

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