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RESEARCH ARTICLE

BIRTH WEIGHT IN WOMEN WITH ASHERMAN'S SYNDROME POST HYSTEROSCOPIC ADHESIOLYSIS: CASE-CONTROL STUDY

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ABSTRACT

Introduction: Women with Asherman's syndrome (AS) have damaged endometrium and reduced blood flow to the uterus and placenta which may lead to low birth weight and several obstetric complications.

Objective: to determine the association between low birth weight and obstetrical complications in women with AS compared to women with normal intrauterine cavity.

Materials and Methods: A retrospective case-control study conducted in Women's Specialized Hospital, King Fahad Medical City, From December 2008 to December 2015. Pregnant women with AS undergone hysteroscopic adhesiolysis that presented to our clinic were matched for age, parity, body mass index, methods of conception and gestational age to pregnant women without AS based on a 1:3 ratio. The main outcome measure included birth weight and obstetrical complications.

Results: The study included 56 women with 14 cases and 42 controls. Pregnant women with AS had significantly lower birth weight (2.23 ± 0.28 kg) compared to pregnant women without AS (3.13 ± 0.383 kg) ($P < 0.001$ odds ratio [OR] 0.029, 95% confidence interval [CI] 0.006 to 0.148, $P = 0.001$). Complications of delivery including retained placenta, placenta previa and fetal death were significantly higher in patients with AS compared to controls 28.6% 7.1% and 7.1% compared to 4.8%, 0% and 0% , respectively. This was statistically significant ($P < 0.001$).

Conclusion: Pregnant women with AS delivered low birth weight newborns and had more obstetrical complications in compared to pregnant women with normal cavity.

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INTRODUCTION

Asherman's syndrome (AS) is defined by the presence of intrauterine permanent adhesions, obliterating the uterine cavity partially or completely. It usually occurs after trauma to the basalis layer of the endometrium after endometrial curettage [1]. It was first described by Heinrich Fritsch in 1894 after that Joseph G. Asherman who described the pathology and symptoms of this syndrome [2].

Patients with Asherman's syndrome may present with amenorrhea with or without severe dysmenorrhea, oligomenorrhea, infertility, or recurrent miscarriages [3]. The syndrome occurs most frequently after repeated curettage for incomplete abortion (50%), postpartum hemorrhage (24%), and elective abortion (17.5%). Others less common etiologic factors include myomectomy, hysterotomy, diagnostic curettage, cesarean section and tuberculosis [3-5].

Direct visualization of the uterus via hysteroscopy is the most reliable method for diagnosis. Other methods are sonohysterography (SHG), hysterosalpingogram (HSG) and MRI [6-8].

Hysteroscopic adhesiolysis is the treatment of choice for the management of intrauterine adhesions [9].

Several obstetric complications have been reported in women with corrected Asherman's syndrome like miscarriages [10-13], abnormal placentation [14-19], cervical incompetency [15, 20], IUGR (intrauterine growth retardation) [21], premature birth [22-24], uterine rupture [25-27], and preeclampsia may also be another complication after Asherman's syndrome.

This retrospective study has been designed to determine the associations between low birth weight in women with Asherman's syndrome post hysteroscopic adhesiolysis and women who had normal intrauterine cavity post hysteroscopy.

MATERIALS AND METHODS

An analytical retrospective case-control study was carried out, and it had included 56 pregnant women who attended Women's Specialized Hospital, King Fahad Medical City, in Riyadh, Saudi Arabia, between 2008 to December 2015. Fourteen women who had undergone hysteroscopic adhesiolysis for intrauterine adhesions and eventually became pregnant were considered cases. Three control subjects were matched to each study patient; a ratio of cases: controls of 1:3 (n=42).

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The birth weight of the infants of 42 pregnant women was examined and compared to pregnant women who had previous hysteroscopic adhesiolysis. Each pregnant case was matched to age, parity, body mass index, previous curettage, postpartum hemorrhage, abortion, myomectomy, cesarean section and endometritis, method of conception either spontaneous or assisted reproductive techniques (ovulation induction, intrauterine insemination (IUI) or In vitro fertilization (IVF) treatment), gestational age (either preterm, less than 37+0 weeks, or term delivery), the mode of delivery either cesarean sections or vaginal delivery. Other main outcome measures including birth weight and obstetrical complications (retained placenta, placenta previa, fetal death and postpartum hemorrhage) were analyzed.

Hysteroscopic classification of AS (mild if filmy adhesion occupying less than one-quarter of uterine cavity and ostial areas and upper fundus minimally involved or clear, moderate if one-fourth to three fourth of cavity involved and ostial areas and upper fundus partially involved and no agglutination of uterine walls or severe if more than three fourth of cavity involved and occlusion of both ostial area and upper fundus and agglutination of uterine walls) were recorded [9].

We excluded women who had high blood pressure, heart diseases, infections such as rubella, cytomegalovirus, toxoplasmosis, syphilis, kidney disease, lung disease, sickle cell anemia, smoking, drinking alcohol, or abusing drugs. In addition, we excluded fetuses with chromosomal defects, previous history intrauterine growth retardation and multiple gestations (twins, triplets, or more) in both groups.

All Categorical variables age group, Marsh classification, curettage, postpartum hemorrhage (PPH) and previous Cesarean sections were presented as numbers and percentages. Continuous variables height, weight, BMI and weight of baby were expressed as Mean ± S.D. Chi-square /Fisher's exact test was applied according to whether the cell expected frequency is smaller than 5 and determine the significant relationship between Asherman's syndrome and study variables. Independent sample t-test was used to see the mean significant difference among Asherman's syndrome and birth weight and other study parameters. Binary logistic regression was applied to determine the significant predictors / risk factors which were associated with Asherman's Syndrome. P-value of less than 0.05 was considered statistically significant. All data was entered and analyzed through statistical package SPSS version 22. Institutional review board approval was granted for the study (15-440).

RESULTS

The study included 56 women (14 cases of AS and 42 control subjects). Their age ranged between 21 and 39 years with a mean of 30.5 years and (±SD) of (±5 years). Their body mass index ranged between 22.86 and 35.30 kg/m² with a mean of 29.77 kg/m² and (±SD) of (±3.17 kg/m²). Their parity ranged between zero and 5 with a median of 1. The weight of their babies ranged between 1.6 and 3.8 Kg with a mean of 2.91Kg and (±SD) of (±0.53 Kg).

Table 1 shows that according to March classification, cases of Asherman's syndrome were classified as minimal (57.1%), moderate (28.6%) and severe (14.3%). Curettage and postpartum hemorrhage due to retained placenta were reported

among twenty seven (48.2%) and nineteen (33.9%) of the participants, respectively. Open myomectomy and endometritis were observed separately among eleven (19.6%) of the participants. Previous cesarean section was reported among seventeen (30.4%) of the participants. Regarding the methods of conception; it was spontaneous among thirty two (57.2%) of the participants whereas IVF and IUI were reported among twenty (35.7%) and four (7.1%) of the participants, respectively. Nineteen (33.9%) of the participants had preterm delivery. Twenty six (46.4%) of the participants delivered through cesarean section. Obstetrical complications were encountered among thirteen (23.2%) of the participant, mainly retained placenta among six (10.7%) of the participant.

Table 1 Clinical characteristics of Patients (n = 56)

Characteristics	Categories	n (%)
AshrmanSyndrom (AS)	No Ashrman	42 (75)
	Ashraman	14 (25)
Marsh Classification of cases of AS	Minimal	8 (57.1)
	Moderate	4 (28.6)
	Severe	2 (14.3)
Curettage	No	29 (51.8)
	Yes	27 (48.2)
Post-partum hemorrhage	No	37 (66.1)
	Yes due to Retained Placenta	19 (33.9)
Open myomectomy	No	45 (80.4)
	Yes	11 (19.6)
Endometritis	No	45 (80.4)
	Yes	11 (19.6)
Previous cesarean sections	No	39 (69.6)
	Yes	17 (30.4)
Method of conception	Spontaneous	32 (57.2)
	In vitro fertilization "IVF"	20 (35.7)
	Intrauterine insemination "IUI"	4 (7.1)
Neonatal outcome	Pre term	19 (33.9)
	Term	37 (66.1)
Mode of Delivery	Vaginal	30 (53.6)
	Cesarean sections	26 (46.4)
	No Complications	43 (76.8)
Obstetrical complications	Retained Placenta	6 (10.7)
	Placenta Previa	1 (1.8)
	Fetal Death	1 (1.8)
	Post-partum hemorrhage	5 (8.9)

From table 2, it is evident that among studied factors that could be associated with AS, only obstetrical complications and birth weight of the baby were significantly associated with AS. Complications were reported among 50% of women with AS compared to 15% of those without AS, p=0.010. Patients with AS have a mean±SD low birth weight of 2.23± 0.280 kg of their babies compared with 3.13 ± 0.383 kg for babies of women who did not have AS. The difference was statistically significant, p<0.001. Similarly, birth weight was significantly lower among babies of women with AS either delivered preterm (2.735 ± 0.22 versus 1.97 ± 0.24 kg) or term (3.33 ± 0.27 versus 2.38 ± 0.18 kg), p<0.001.

Logistic regression analysis revealed that the only significant predictor for AS was the birth weight as an increase in the birth weight by one gram was associated with a decrease in the likelihood of AS by 2.9% (Adjusted OR=0.029; 95% CI: 0.006-0.148), p<0.001. All other studied variables were not significantly associated with AS. Table 3

DISCUSSION

Online search yielded very few studies analyzing the health of infants born to women with a history of AS or even the impact of the syndrome on pregnancies and these data were mainly

from case reports. Our study aims to determine the associations between low birth weight in women with Asherman's Syndrome post hysteroscopic adhesiolysis in comparison with women who had normal intrauterine cavity post hysteroscopy.

Table 2 Association between demographic characteristics and Asherman's Syndrome

		Normal cavity	Asherman's syndrome	P - value
Group Age	≤ 35	36 (85.7%)	10 (71.4%)	0.227
	> 35	6 (14.3%)	4 (28.6%)	
Group of Parity	≤ 3	39 (92.9%)	13 (92.9%)	0.989
	> 3	3 (7.1%)	1 (7.1%)	
Miscarriage		0.95 ± 0.193	1.43 ± 0.429	0.324
Height		164.10 ± 5.40	161.07 ± 6.36	0.126
Weight		79.89 ± 8.90	76.72 ± 10.01	0.305
BMI		29.80 ± 2.94	29.67 ± 3.92	0.912
Curettage	No	23 (54.8%)	6 (42.9%)	0.440
	Yes	19 (45.2%)	8 (57.1%)	
History of incomplete abortions	No	24 (57.1%)	6 (42.9%)	0.353
	Yes	18 (42.9%)	8 (57.1%)	
postpartum hemorrhage	No	28 (66.7%)	9 (64.3%)	0.871
	Yes	14 (33.3%)	5 (35.7%)	
Open Myomectomy	No	34 (81.0%)	11 (78.6%)	0.846
	Yes	8 (19.0%)	3 (21.4%)	
Endometritis	No	34 (81.0%)	11 (78.6%)	0.846
	Yes	8 (19.0%)	3 (21.4%)	
Previous Cesarean sections	No	29 (69.0%)	10 (71.4%)	0.867
	Yes	13 (31.0%)	4 (28.6%)	
Method of conception	Spontaneous	24 (57.1%)	8 (57.1%)	0.989
	IVF	15 (35.7%)	5 (35.7%)	
	IUI	3 (7.1%)	1 (7.1%)	
Neonatal outcome	Pre Term	14 (33.3%)	5 (35.7%)	0.871
	Term	28 (66.7%)	9 (64.3%)	
Mode of Delivery	Vaginal	23 (54.8%)	7 (50.0%)	0.757
	Cesarean sections	19 (45.2%)	7 (50.0%)	
	No Complications	36 (85.7%)	7 (50.0%)	
	Retained Placenta	2 (4.8%)	4 (28.6%)	
obstetrical complications	Placenta Previa	0 (0.0%)	1 (7.1%)	*0.010
	Uterine Rupture	0 (0.0%)	0 (0.0%)	
	Fetal Death	0 (0.0%)	1 (7.1%)	
	postpartum hemorrhage	4 (9.5%)	1 (7.1%)	
Birth Weight		3.13 ± 0.383	2.23 ± 0.28	* < 0.001
	Pre Term	2.735 ± 0.22	1.97 ± 0.24	
Birth Weight		3.33 ± 0.27	2.38 ± 0.18	* < 0.001
	Term			

Table 3 Independent Risk Factors Associated with Asherman's Syndrome

Characteristics	OR	95% C.I	P-value
Age	2.40	0.565 – 10.193	0.235
Parity	1.0	0.096 – 10.471	0.989
BMI	0.98	0.815 – 1.196	0.895
Curettage	1.61	0.476 – 5.47	0.442
Open Myomectomy	1.15	0.261 – 5.148	0.846
Endometritis	1.15	0.261 – 5.148	0.846
Previous Cesarean sections	0.892	0.236 – 3.378	0.867
Method of conception	1.0	0.381 – 2.625	0.998
Neonatal outcome	0.9	0.253 – 3.197	0.871
Delivery Outcome	1.21	0.361 – 4.064	0.757
Low Birth Weight	0.029	0.006 – 0.148	* < 0.001

Among women with a past history of AS, the rate of preterm delivery ranged between 17.9 and 50% [24, 14, 28]. In accordance with that, the present study reported a rate of 35.7%.

In the present study, the spontaneous conception rate with AS was 57.1% (8 out of 14). It has been reported in an earlier study that the rate was 45.5% (133 out of 292) [29].

In pregnant women with Asherman's syndrome, the defective placentation may lead to intrauterine growth restriction

(IUGR)[23,30]. Women with a previous history of AS, have damaged endometrium, and therefore a reduced blood flow to the uterus and placenta. This will eventually lead to poor placental perfusion [23]. The current study revealed a significant association between AS and low birth weight. A previous retrospective case-control study found no difference in pregnancy outcome aside from low birth weight in pregnancies with and without intrauterine adhesions [31].

The defective uterine endometrium and the obliterated uterine cavity may also predispose women to ectopic tubal and cervical pregnancies [32]. In the current study, the reported complications were retained placenta, placenta previa, fetal death and post-partum hemorrhage. Retained placenta and placenta previa were also reported by Feng *et al.* [33] in their study as outcomes of intrauterine adhesions.

Women who have had previous intrauterine surgeries or procedures particularly surgical curettage are at higher risk for AS [29]. This was also found in our present study where the rate of curettage was higher, although not significant as a result of the relatively small sample size, among cases with AS compared to their matched control subjects (57.1% versus 45.2%).

There are three stages of AS, Stage I (mild), Stage II (moderate) and Stage III (severe), which indicates the higher the extent of endometrial cavity involvement, the higher the stage [9]. According to March classification, cases of Asherman's syndrome in the present study were classified as minimal (57.1%), moderate (28.6%) and severe (14.3%). Outcome of AS depends mainly on the degree of Intra-uterine adhesions. Klatsky *et al* [34] reported that if intra-uterine adhesions are only mild and filmy they can stretch with uterine growth during pregnancy. They also documented that the prediction of the outcome of AS is challenging, and thus close monitoring of the pregnancy by an obstetrician is essential in order to screen for potential complications in patients with previous history of Asherman's syndrome.

Everett [35] reported that, in the general population, in 550 women who conceived, 67 pregnancies (12%) ended in miscarriage. The spontaneous miscarriage rate after treatment of intrauterine adhesions was around 20%. It is unclear whether this represents an increase in the risk of early miscarriage after treatment of Asherman's syndrome. In the present study, we matched controls for the miscarriage to explore the influence of infant birth weight regardless of the miscarriage.

Among the limitations of this study is the fact that the study sample was relatively small as it was limited to Women's Specialized Hospital, which could affect the generalize ability of results. We relied on records in the current study out of which some were incomplete particularly regarding babies' information (NICU admission, early neonatal death, developmental assessment) and umbilical artery Doppler during pregnancy. Despite these limitations, we found a relationship between AS and low birth weight as well as the presence of obstetrical complications, and thus close monitoring of the pregnancy is essential in order to screen for potential complications in patients of AS. In the light of the study's results, we recommended conducting a study with adequate sample size to increase the study's power and thus more generalizable results.

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