Pregnancy Rate in Women with Normal Uterine Cavity and those with Corrected Uterine Cavitary Lesions in ICSI Cycles

Original Article

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ABSTRACT

Aim: To investigate the pregnancy rate in women with normal uterine cavity and those with previously corrected uterine cavitary lesions, assessed by hysteroscopy in ICSI cycles.

Study Design: A prospective cohort study**.**

Materials and Methods: The study included women undergoing ICSI cycles. Patients were allocated into two groups, patients with normal uterine cavity (group 1, n=122) and patients with previously corrected uterine cavitary lesions (group 2, n=122). Office hysteroscopy was performed post-menstrual. The main outcome measure was clinical pregnancy rate. Secondary outcomes were the implantation rate and the take home baby rate.

Results: In both groups the mean±SD of the total amount of gonadotrophins used, duration of stimulation, peak estradiol level, endometrial thickness and number of mature follicles, the implantation rate there was not statistically significant different in both groups (2.22 ± 0.84 vs. 2.46 ± 0.95, *p*=0.419). Also, the pregnancy rate showed no statistically significant difference between both groups (33.6% vs. 23.8%, *p*=0.089).

Conclusion: Correction of uterine cavitary lesions makes the implantation rate and pregnancy rate to be comparable to women with normal uterine cavity.

Key Words: Hysteroscopy; ICSI; pregnancy rate; uterine cavity.

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INTRODUCTION

Intrauterine pathology had been reported in up to 25% of infertile women having in-*vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI) treatment and in as many as 50% of women with recurrent implantation failure, leading to suggestion that correction of such pathology could improve treatment outcome[1,2]. Hysteroscopy allows visual assessment of the cervical canal and uterine cavity and provides the opportunity to operate in the same setting. Routine outpatient hysteroscopy before starting IVF has been postulated to diagnose and treat abnormalities of the cervix and uterine cavity and hence improve IVF outcome[3-5].

A systematic review of published studies suggested that outpatient hysteroscopy in the menstrual cycle preceding an IVF treatment cycle could significantly increase the clinical pregnancy rate in women who had previously had recurrent implantation failure, even when no hysteroscopic abnormality was detected[6].

However, the result of the TROPHY study - published in the Lancet in 2016 concluded that Outpatient hysteroscopy before IVF in women with a normal ultrasound of the uterine cavity and a history of unsuccessful IVF treatment cycles does not improve the livebirth rate and they recommended that further research into the effectiveness of surgical correction of specific uterine cavity abnormalities before IVF is warranted[7].

Different articles, working on the evaluation of the endometrial cavity in infertile patients and prior to IVF recommended that there is an urgent need to RCT to emphasize the benefit of removal of the detected intrauterine lesions before proceeding to IVF. Therefore, the aim of the current study is to investigate the pregnancy rate in women with normal uterine cavity and those with previously corrected uterine cavitary lesions, assessed by hysteroscopy in ICSI cycles.

PATIENTS AND METHODS

This prospective cohort study had been carried on 244 women undergoing ICSI trial in IVF center of women's Health Hospital, Assiut University, Assiut, Egypt. This study was started on October 2018 and follow up of the patients ended in December 2020.

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The confidentiality of all patients admitted to the study was protected. The study participants will not be identified by name in any report or publication resulting from data collected in the study.

All women had written consent to participate. Clear description to the women that her refusal for participation in the study do not affect by any mean the quality-of-care patient going to receive in our service.

Patients were allocated into 2 groups; group 1 included 122 women with normal uterine cavity documented by office hysteroscopy and considered the control group. Group 2 included 122 women with previously corrected Uterine lesions either by hysteroscopy or by open surgery and found to have normal cavity after correction as demonstrated by office hysteroscopy (OH).

All hysteroscopic procedures were performed to women in the cycle prior to ICSI cycles with vaginoscopic technique using 4mm outer hysteroscopy sheath and with 2.9mm optical lens. Office hysteroscopy was performed for all women in the outpatient clinic of Women's Health Hospital. All women received 400 micrograms misoprostol 6-12 hours before the procedure.

After taking history and performing clinical and Gynecological examination all laboratory tests in couple were revised, including semen analysis of the husband. Ovarian reserve was assessed by AMH level. Prolactin and TSH levels were measured.

The eligibility criteria for all women in the study were women age between 18 – 38 years, with primary or secondary infertility with normal ovarian reserve and all women had BMI between 20-35.

All women in both groups were prepared for ICSI trial. The study protocol was to match women in both groups regarding age, BMI and AMH level, unfortunately this could only achieved for the BMI as women in the control group were found to be younger than those in the study group, especially in number of women with age between 35-38 years old.

The couple's infertility workup and all procedures performed were done according to the standard protocol in the IVF Unit in women's health hospital. All patients were examined by transvaginal ultrasound and all abnormal findings were recorded. All uterine cavity abnormalities were recorded. For any detected pathology an appropriate surgical management had been performed under general anesthesia in the endoscopy unit.

Assisted reproduction procedures were performed in all patients with controlled ovarian hyperstimulation as the standard protocol in the IVF unit in Women's Health Hospital.

Protocols of Controlled Ovarian Hyperstimulation (COH)

1- Long luteal agonist protocol

Pituitary down-regulation with the GnRH agonist triptorelin acetate (Decapeptyl, ferring, Germany) was started in the mid-luteal phase (on day 21) of the preceding cycle at a daily subcutaneous (SC) dose of 0.1 mg .The dose was subsequently reduced to (0.05 mg) once serum Estradiol (E2) reached less than 60 pg/mL. The lowered dose was continued till the day of hCG administration.

With the start of menstruation, transvaginal ultrasound was done and if no ovarian cyst, COH was commenced (on cycle day 2-3) using SC recombinant FSH (Gonal F; Serono, Egypt) or highly purified urinary FSH (Fostimon, IBSA, Italia) and HMG (Menogon, IBSA, Italia).

The dose and type of gonadotropin had been tailored in each case based on patient age, clinical characteristics, and ovarian reserve. Ovarian response was monitored by serial serum E2 levels and trans-vaginal ultrasound ovarian monitoring starting on day 2 or 3 of stimulation cycle.

Once at least two leading follicles reached a size of ≥18 mm in diameter or more, 10.000 IU of hCG intramuscularly were administered. Ovum pickup was performed under transvaginal ultrasound guide 36 hours after hCG administration. ICSI was done following the standardized techniques.

The number of embryos transferred was individualized to the patient and no more than three embryos were transferred after embryo grading. Women with cancelled cycle were excluded from the study. The luteal phase was supported using intramuscular progesterone 100mg once daily. Serum β-hCG was measured 14 days after embryo transfer.

2- Antagonist protocol

Women were instructed to use combined oral contraceptive pills (Genera, Bayer, Egypt) in the cycle preceding the stimulation cycle. When two or more follicle reached 14 mm in diameter or serum E2 became more than 850 pg/ml, GnRH antagonist was started using Cetrotide 0.25 mg SC daily (Cetrolerix , Serno , Egypt).

Number of the follicles with a diameter more than 14 mm was aspirated and recorded. Both agonist or antagonist protocol were used for the patients. The number of oocytes retrieved was recorded and after performing ICSI the numbers of embryos were recorded. The quality of embryos transferred has compared and tabulated in addition to the protocol for controlled ovarian hyperstimulation. Embryos

was transferred on day 3 according to the standard lab procedure. All embryo transfers had performed under abdominal ultrasound guidance. The number of transferred embryos (1 to 3) chosen according to embryo availability & quality.

Outcome measures

The primary outcome was clinical pregnancy rate defined as fetal cardiac activity per single transfer on trans-vaginal ultrasound at 7 weeks by TVUS[8]. Secondary outcomes were chemical pregnancy rate (detect by B-HCG 14 days after embryo transfer), implantation rate (defined using ultrasound as the percentage of embryos implanting successfully relative to the total number of embryos transferred), abortion rate, preterm labor rate and Baby take home rate.

Sample size estimation

The 2008 Canadian ART Registry (CARTR) shows a clinical pregnancy rate of 38% for IVF cycles in Canada. This was used to estimate a 38% clinical pregnancy rate for the control group. A 17% decrease in clinical pregnancy rate would be clinically acceptable in the corrected group. The sample size calculation was performed using a one-sided Chi-square test with continuity correction and an alpha of 0.05 assuming a clinical pregnancy rate of 38% in the control group and 21% in the intervention group. A total of 244 subjects (122 in each group) are required to provide an 80% power and 5% probability of error to detect a clinically meaningful, 17% expected decrease in clinical pregnancy rate.

STATISTICAL ANALYSIS

Data entry and data analysis were done using SPSS version 22 (Statistical Package for Social Science). Data were presented as number, percentage, mean, standard deviation, median and range. Chi-square and Fisher Exact tests were used to compare between categorial variables. Independent samples t- test and Mann-Whitney test were used to compare between quantitative variables in both groups, *P-value* considered statistically significant when $P < 0.05$.

RESULTS

This study included 244 patients: 122 women in the control group with normal 2D US and normal hysteroscopic findings during examination with office hysteroscopy and 122 women with corrected uterine lesions. The personal and demographic data of women in both groups were presented in (Table 1) with corrected uterine lesions (Figure 1).

Table 1: Personal, infertility data and induction protocol of women in the study groups

	Control (n= 122)	Corrected lesion (n= 122)	*P-value*
Age: (years)			
Mean ± SD	29.57 ± 5.31	31.43 ± 5.1	0.006*
BMI: (Kg/m2)	29.75 ± 5.01	29.02+ 3.99	0.209
Mean ± SD			
Duration of infertility: (years) Mean ± SD	7.15 ± 4.69	7.72 ± 4.82	0.311
Type of infertility:			
Primary	92 75.4%	91 74.6%	0.882
Secondary	30 24.6%	31 25.4%	
AMH: (ng/ml)	2.66 ± 1.13	2.31 ± 1.50	0.043*
FSH: (IU/ml)	5.51 ± 2.57	5.30 ± 1.99	0.897
LH: (IU/ml)	4.27 ± 2.49	4.19 ± 3.49	0.883
TSH: (IU/ml)	2.15 ± 0.95	2.14 ± 1.59	0.661
Basal endometrial thickness (mm)	2.86 ± 1.27	2.82 ± 1.10	0.580
Induction protocol:			
Antagonist	83.6% (102 women)	79.5% (97 women)	0.409
Agonist	16.4% (20 women)	20.5% (25 women)	
Total days of stimulation:	11.50 ± 1.85	11.17 ± 1.46	0.126

* *P-value* is statistically significant <0.05

There were no statistically significant differences between these parameters in women in the two groups except for age which is statistically significant higher in the group of corrected lesions. There were no statistically significant difference in the baseline hormonal levels listed in the table except for AMH which is significantly lower in the corrected group. These two differences were mostly due to that more women in the corrected group (34=28%) were more than 35 years old compared to the control group (19=15.6%).

There was no statistically significant difference between groups regarding method of pituitary suppression, type of gonadotrophin used, or type of triggering agent.

There was no statistically significant difference in both groups in the total number of follicles in both ovaries, number of oocytes collected and injected as well as the total number of embryos. Women in corrected group had significantly thicker endometrium at the day of maximal follicular growth and more embryos transferred as shown in (Table 2).

The pregnancy outcome for both groups is shown in (Table 3). There was no statistically significant difference in implantation, chemical pregnancy, clinical, pregnancy, abortion, and baby take home rates between both groups. Multiple pregnancy and preterm labor rates were not significantly different in both groups. Clinical pregnancy rates in relation to type of corrected lesion are shown in (Table 4). All lesions were treated hysteroscopically except 11 cases of open myomectomy.

We did subgroup analysis for women 35 years old or less in each group to correct this age difference. (Table 5) shows the pregnancy outcome for women 35 years or less in both groups. There were no statistically significant differences between all parameters as shown in the table.

Table 3: Primary and secondary outcomes in the study groups

	Control (n= 122)		Corrected lesion (n= 122)		*P-value*
	No.	%	No.	%	
Pregnancy test:					
Positive	41	33.6%	29	23.8%	0.089
Chemical pregnancy	3	7.3%	0	0.0	0.261
Clinical pregnancy	38	31.1%	29	23.8%	0.198
Type of pregnancy:					
Single	27	71.1%	22	75.9%	
Twins	11	28.9%	6	20.7%	0.406
Triples	0	.0%	1	3.4%	
Abortion:	10	24.3%	8	27.8	0.245
Implantation rate: Mean ± SD		15.80% (49/310)		10.2% (37/363)	0.419
Maturity:					
Pre-term	10	35.7%	10	45.5%	0.485
Full-term	18	64.3%	12	54.5%	
Take home baby rate:					
Yes	23	18.4%	20	16.4%	0.100

Table 4: Summary of the corrected uterine cavitary lesions

	No. (122)	%	CP	CPR	*p- value*
Polyp	56	45.9%	14	25%	
Septum	29	23.8%	6	20.7%	
Adhesion	12	9.8%	3	25%	
Hysteroscopic myomectomy	11	9.0%	2	18.2%	0.891
Open myomectomy	11	9.0%	4	36.4%	
Myomectomy+polypectomy	2	1.6%	0	0%	
Isthmocele (CS niche)	1	0.8%	0	0%	

Table 5: Comparison of data of women less than 35 year in both groups

	Control group (103)	Corrected group (88)	*P-value*
Age	28.16 ± 4.5	29.17 ± 4.2	0.11
AMH	2.72 ± 1.1	2.49 ± 1.5	0.22
Implantation rate	43/260 (16.53%)	31/257 (12.06%)	0.146
Clinical pregnancy	33 (32.03%)	24 (27.27%)	0.607
Abortion	9 (27.27%)	4 (16.66%)	0.122
Take home baby	23 (22.33%)	19 (21.6%)	0.531
PTL/Total deliveries	10/24 (41.66%)	8/19 (42.1%)	0.874

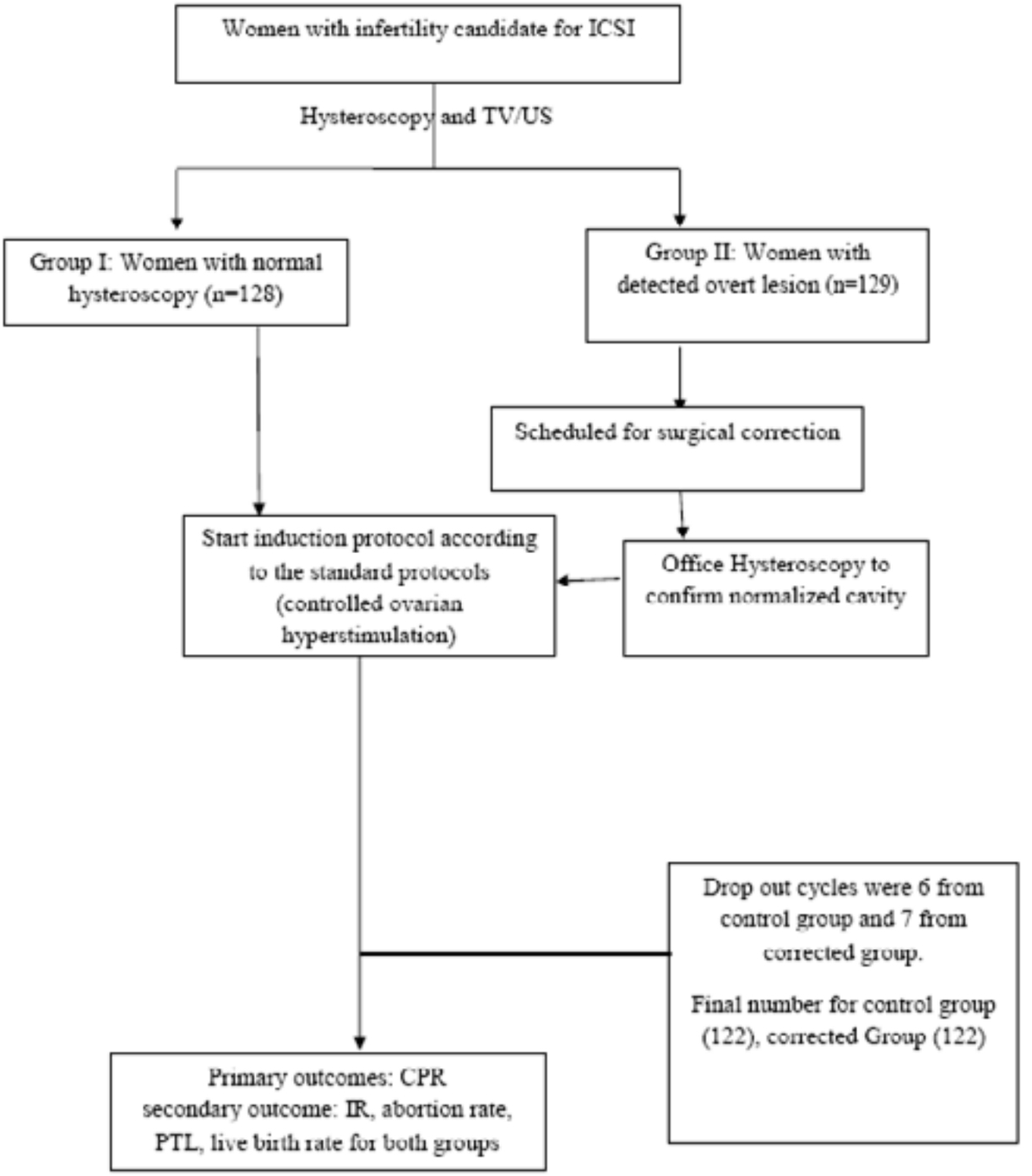

Fig. 1: Flow chart of the study and follow up methods

DISCUSSION

Hysteroscopy is considered for several years the gold standard for assessment of the uterine cavity and for detection of intracavitary lesion (ICL) that might affect implantation and reduces the chance of achieving pregnancy in both natural and IVF/ICSI cycles. Office hysteroscopy (OH) enables the gynecologist to visualize and detect ICL without anesthesia. The assessment of intrauterine abnormality is a core part of infertility evaluation as it impacts the complex process of embryo implantation[9].

Different ICL were diagnosed and described in infertile women with normal 2DUS or 3DUS. A Cochrane review for treating subfertility associated with suspected major uterine cavity abnormalities recommended that more research is needed to measure the effectiveness of the hysteroscopic treatment of suspected major uterine cavity abnormalities prior of IVF or ICSI

The results of our study showed that the uterine cavity after removal or correction of different ICLs behaves like a denovo normal cavity. There was no statistically significant difference between the take home baby rate in women in both groups. We couldn't match women in the control group with those in the corrected group regarding age as women between 35-38 in the corrected group were more than those in the control group during the study period.

This could be explained partly that women in the corrected group needed much time in their infertility evaluation and decision making for undergoing corrective surgery ,specially that many of them do the surgical correction on their own expenses ,moreover many of those women have waited for some time for spontaneous pregnancy after the surgical correction and those who decide to have assisted conception after that time need more time to save money for the ICSI trail as there is no governmental health insurance coverage for such procedures in Egypt.

In clinical practice, evaluation of the uterine cavity is usually done with a transvaginal ultrasound scan (TVS) prior to IVF. Due to the perceived advantages of hysteroscopy over TVS, such as the potential for simultaneous detection and treatment of intrauterine pathologies, use of a pre-IVF screening hysteroscopy has gained widespread acceptance [5]. It is now considered the gold standard for the diagnosis of uterine cavity pathology[10,11].

Singla *et al*., studied the role of pre-IVF hysteroscopy in women with unexplained infertility for detecting unsuspected intrauterine lesions and effect on pregnancy outcome [9]. They concluded that there was high prevalence rate of unsuspected intrauterine lesions in women with unexplained infertility. Clinical pregnancy rates were not significantly higher in patients who underwent pre-IVF hysteroscopy. Further larger studies and randomized controlled trials are needed to verify the positive outcome of use of hysteroscopy prior to IVF[12].

All women included in the study were with normal ovarian reserve test results and had no other endocrinopathy or endometriosis other confounding factors that may affect the results of patients in the groups. Women both all groups were comparable with their personal, demographic data, type and duration of infertility except for age and AMH which is significantly lower in this group, which were statistically significant higher in the group of patients with corrected lesions. This difference is explained to some extent by the time needed for diagnosis of the abnormality in the group with corrected lesion. As well as to the time needed to take the decision after the operation and the postoperative period allowed for the patients to have a chance to conceive or referred to assisted conception.

Although there was no statistically significant difference in the basal endometrial thickness in the group of women with corrected uterine lesions and those with control of normal uterine cavity; there was a statistically increased thickness in the endometrium of corrected lesions at day of maximum follicular growth.

Screening hysteroscopy in woman prior to IVF may reveal intrauterine pathology that may not be detected by routine TVS. The reported rate of intrauterine pathology is 12% in women undergoing first IVF[7,13,14], while in our study we found endometrial polypi in 45.9% of the corrected group.

It is assumed that uterine cavity abnormalities may interfere with factors that regulate the embryo-endometrium interplay for example, hormones and cytokines, reducing the possibility of pregnancy. Many hypotheses have been formulated in the literature as to how endometrial polyps, submucous fibroids, intrauterine adhesions, and uterine septa may impair implantation of the human embryo; nevertheless, the precise mechanisms of the action through which each one of these cavity abnormalities affects this essential reproductive process are poorly understood. Different intracavitary lesions can affect implantation and subsequently ICSI outcomes. Endometrial polyps are the most frequently observed pathological finding in the uterus and are usually benign lesions. The exact prevalence of endometrial polyps is not known. Nevertheless, endometrial polyps have been implicated in about 50% of cases of abnormal uterine bleeding and 35% of infertility[15].

Post polypectomy, pregnancy rates improved two-fold in intrauterine inseminated patients[16]. Stamatellos *et al*. conducted a retrospective study and reported that hysteroscopic polypectomies appeared to increase pregnancy rates and ultimately improved fertility in women

who were previously infertile with no known cause[17]. The hysteroscopic removal of polyps prior to intrauterine insemination (IUI) can increase the chance of a clinical pregnancy compared with simple diagnostic hysteroscopy and polyp biopsy[10]. This clearly explain the comparable pregnancy and baby take home rate in both groups in our present study with CPR of 25% in patients underwent ICSI after polypectomy versus 31% clinical pregnancy rate in the control group with no statistically significant difference.

Based on that, if an endometrial polyp is detected during an ART cycle and less than 20 mm in size, it can be managed expectantly without compromising clinical pregnancy or live birth rates. Also, when polyp 10 mm in size are found in symptom-free patients prior to ART, expectant management may be considered, given that spontaneous regression following the menstrual cycle has been observed in 27% of cases[18]. On the other hand, some authors claim that; the lack of predictive characteristics for spontaneous regression and duration of time needed to achieve this phenomenon would make expectant management undesirable in an infertile patient, in whom time factor is important[19].

More recently (Mouhayar *et al*., 2017) concluded that performing either office or operative hysteroscopic polypectomy prior to infertility treatment was cost-effective for both IUI and IVF/ICSI treated women[20]. Sensitivity analysis showed that hysteroscopic polypectomy was cost-effective over a range of plausible pregnancy rates and polypectomy costs. Polypectomy prior to IUI is recommended from a clinical and cost standpoint, as the procedure doubles the pregnancy rate, shortens time to pregnancy, and is cost-effective across a range of polyp sizes.

Bosteels *et al*., 2018 in a Cochrane Review concluded that there is a large benefit with the hysteroscopic removal of submucous fibroids for improving the chance of clinical pregnancy in women with otherwise unexplained subfertility cannot be excluded. The hysteroscopic removal of endometrial polyps suspected on ultrasound in women prior to IUI may increase the clinical pregnancy rate. More randomized studies are needed to substantiate the effectiveness of the hysteroscopic removal of suspected endometrial polyps, submucous fibroids, uterine septum or intrauterine adhesions in women with unexplained subfertility or prior to IUI, IVF or ICSI[10].

Recent study concluded that there is consensus that submucosal fibroids have a detrimental impact on the chances of success with IVF/ ICSI. Furthermore, there is some evidence of the benefit of myomectomy for submucosal fibroids to improve ART outcomes. For this reason, every effort should be made to remove all submucosal fibroids[21].

Wang Z, 2020, studied Reproductive outcome of a complete septate uterus after hysteroscopic metroplasty. They concluded that Hysteroscopic uterine metroplasty may improve the reproductive performance of a septate uterus. Resection of the cervical septum may increase the probability of a live-birth pregnancy for patients with a cervical septum, and this procedure could be recommended for cases of a complete uterine septum[22]. Results of our study are in favor of hysteroscopic adhesolysis for cases with mild to moderate intrauterine synechia with improved CPR of 25% comparable to the control group with 31%.

CONCLUSION

In conclusion, our current study demonstrated that correction of intrauterine cavitary lesions makes the implantation rate and pregnancy rate to be comparable to women with normal uterine cavity.

CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCES

1. Moini A, Kiani K, Ghaffari F and Hosseini F. Hysteroscopic findings in patients with a history of two implantation failures following in *vitro* fertilization. Int J Fertil Steril. 2012 Apr; 6(1): 27.

2. Cenksoy P, Ficicioglu C, Yıldırım G and Yesiladali M. Hysteroscopic findings in women with recurrent IVF failures and the effect of correction of hysteroscopic findings on subsequent pregnancy rates. Arch Gynecol Obstet. 2013 Feb; 287(2): 357-60.

3. Golan A, Ron-El R, Herman A, Soffer Y, Bukovsky I and Caspi E. Diagnostic hysteroscopy: its value in an in-*vitro* fertilization/embryo transfer unit. Hum Reprod. 1992 Nov 1; 7(10): 1433-4.

4. Carneiro MM. What is the role of hysteroscopic surgery in the management of female infertility? A review of the literature. Surg Res Pract. 2014 Mar 3; 2014.

5. Campo R, Meier R, Dhont N, Mestdagh G and Ombelet W. Implementation of hysteroscopy in an infertility clinic: The one-stop uterine diagnosis and treatment. Facts, Views Vis ObGyn. 2014; 6(4): 235.

6. El-Toukhy T, Sunkara SK, Coomarasamy A, Grace J and Khalaf Y. Outpatient hysteroscopy and subsequent IVF cycle outcome: a systematic review and meta-analysis. Reprod Biomed Online. 2008; 16: 712-19.

7. El-Toukhy T, Campo R, Khalaf Y, Tabanelli C, Gianaroli L, *et al*. Hysteroscopy in recurrent in-*vitro* fertilisation failure (TROPHY): a multicentre, randomised controlled trial. Lancet. 2016; 387(100382): 2614-2621.

8. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, *et al*. The international committee for monitoring assisted reproductive technology (ICMART) and the world health organization (WHO) revised glossary on ART terminology, 2009. Hum Reprod. 2009 Nov; 24(11): 2683-7.

9. Singla S, Gupta S, Munjal R, Chawla S and Dash BB. Role of pre IVF hysteroscopy in women with unexplained infertility for detecting unsuspected intrauterine lesions and effect on pregnancy outcome. Fertil Sci Res. 2020 Jan; 7(1): 105.

10. Bosteels J, van Wessel S, Weyers S, Broekmans FJ, D'Hooghe TM, *et al*. Hysteroscopy for treating subfertility associated with suspected major uterine cavity abnormalities. Cochrane Database Syst Rev. 2018 Dec; 12(12): CD009461.

11. Taylor E and Gomel V. The uterus and fertility. Fertil Steril. 2008; 89: 1-16.

12. Palshetkar N, Pai H and Pisat S. Role of hysteroscopy prior to assisted reproductive techniques. J Gynecol Endoscopy Surg. 2009 Jan; 1(1): 27.

13. Smit JG, Kasius JC, Eijkemans MJ, Koks CA, van Golde R, *et al*. Hysteroscopy before in-*vitro* fertilisation (inSIGHT): a multicentre, randomised controlled trial. Lancet 2016; 387(10038): 2622-9.

14. Oliveira FG, Abdelmassih VG, Diamond MP, Dozortsev D, Nagy ZP, *et al*. Uterine cavity findings and hysteroscopic interventions in patients undergoing in *vitro* fertilization-embryo transfer who repeatedly cannot conceive. Fertil Steril. 2003; 80(6): 1371-5.

15. Check JH, Bostick-Smith CA, Choe JK, Amui J and Brasile D. Matched controlled study to evaluate the effect of endometrial polyps on pregnancy and implantation rates following in *vitro* fertilization-embryo transfer (IVF-ET). Clin Experiment Obstet Gynecol. 2011 Sep; 38(3): 206-8.

16. Pérez-Medina T, Bajo-Arenas J, Salazar F, Redondo T, Sanfrutos L, *et al*. Endometrial polyps and their implication in the pregnancy rates of patients undergoing intrauterine insemination: a prospective, randomized study. Hum Reprod. 2005 Jun; 20(6): 1632-5.

17. Stamatellos I, Apostolides A, Stamatopoulos P and Bontis J. Pregnancy rates after hysteroscopic polypectomy depending on the size or number of the polyps. Arch Gynecol Obstet. 2008 May; 277(5): 395-9.

18. Galliano D, Bellver J, Díaz-García C, Simón C and Pellicer A. ART and uterine pathology: how relevant is the maternal side for implantation?. Human Reprod update. 2015 Jan; 21(1): 13-38.

19. Surrey ES. Should diagnostic hysteroscopy be performed before in *vitro* fertilization-embryo transfer?. J Minimal Inv Gynecol. 2012 Sep; 19(5): 643-6.

20. Mouhayar Y, Yin O, Mumford SL and Segars JH. Hysteroscopic polypectomy prior to infertility treatment: A cost analysis and systematic review. Eur J Obstet Gynecol Reprod Biol. 2017 Jun; 213: 107-15.

21. Sarıdoğan E and Sarıdoğan E. Management of fibroids prior to in *vitro* fertilization/intracytoplasmic sperm injection: A pragmatic approach. J Turk Ger Gynecol Ass. 2019 Mar; 20(1): 55.

22. Wang Z, An J, Su Y, Liu C, Lin S, *et al*. Reproductive outcome of a complete septate uterus after hysteroscopic metroplasty. J Int Med Res. 2020 Oct; 48(3): 0300060519893836.