Original Article

The Effect of Bilateral Uterine Artery Ligation after Intrapartum or Postpartum Hemorrhage on Ovarian Reserve Markers and Pregnancy Outcome

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ABSTRACT

Objectives: Postpartum hemorrhage (PPH) and intrapartum hemorrhage (IPH) are serious and life-threatening obstetric complications. The most common cause is uterine atony. We intended to determine the effect of uterine artery ligation (UAL (after intrapartum hemorrhage (IPH) or Postpartum Hemorrhage (PPH) on ovarian reserve markers and pregnancy outcome.

Materials and Methods: This prospective cohort research was conducted on 120 females aged from 20 to 35 years old with PPH or IPH after cesarean section, not responded to medical therapy and performed effective UAL for management of hemorrhage. Patients were classified into two equal groups, case group: cases who underwent bilateral uterine artery ligation after PPH or IPH after cesarean section, control group: who underwent normal cesarean section without PPH or IPH. Follow up of women seeking pregnancy at 6,12, and 24 months.

Results: Ovarian reserve (follicle size, FSH, pre antral follicle count (AFC) and anti-Müllerian Hormone) in females who underwent bilateral UAL after PPH or IPH (case group) were comparable between case group and control group at all follow up measurements after 6,12, and 24 months.

Conclusions: UAL does not seem to compromise the cases' consequent fertility (ovarian reserve markers) and pregnancy outcomes.

Key Words: Intrapartum hemorrhage, ovarian reserve, postpartum hemorrhage, pregnancy, uterine artery ligation.

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INTRODUCTION

Postpartum hemorrhage after delivery (PPH) is a potentially fatal condition. Considered to be the most frequent cause is uterine atony. The placenta accreta, placental abruption, retained placenta, genital tract injuries, uterine rupture, and coagulation problems are further established risk factors for PPH. With appropriate and prompt surgical therapy, PPH-related mortalities and morbidities can be avoided[1,2].

In PPH patients who were unresponsive to massage and uterotonic treatment, a variety of surgical methods have been documented. Although subtotal or total hysterectomy can be performed, it is a radical treatment, especially in young women. Other options include uterine compression sutures, bilateral uterine artery ligation (UAL), internal iliac artery (hypogastric artery) ligation (BIIAL), or uterine compression sutures[3,4].

One of the most common surgical methods for preserving fertility is UAL. It is simple to do and effective at reducing PPH. Additionally, it is rather safe and permits future childbearing for the patients. Furthermore, it has a success rate of above 90%[5,6].

The phrase "ovarian reserve" refers to the ovary's functional potential and indicates the quantity and quality of the oocytes contained therein[7]. The reserve of primordial follicles in the ovary is referred to as the ovarian reserve. It is a significant factor in determining human fertility potential. An appropriate indicator of ovarian function is a diminished ovarian reserve, which represents the process of follicular depletion and a drop in oocyte quality[8].

It is well known that the ovarian arteries, which are direct branches of the abdominal aorta, and the uterine arteries supply the ovaries with blood[9]. Of note, UAL has a hemostatic effect since it ligates or embolizes the uterine artery, blocking its blood supply[5].

Even when the ovaries are left in place, numerous studies have shown that hysterectomy might cause a diminished ovarian reserve and an early menopause[10-12]. FSH levels were shown to be increased in hysterectomy

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patients, even when just one ovary was removed[13]. Finally, diminished ovarian reserve was seen following embolization of the uterine artery (UAE)[11]. However, the effects of UAL on ovarian reserve have not been adequately studied. Therefore, the aim of this study was to investigate the possible negative effects of UAL on ovarian reserve markers and subsequent pregnancy outcomes.

MATERIAL AND METHODS

This prospective case-control study included 120 females aged from 20 to 35 years old. The research was performed with approval from the Ethical Committee of the Faculty of Medicine (36034/11/22) at Obstetrics and Gynecology department in Tanta University Hospital, Egypt, between June 2020 to October 2022. Informed consent was taken from every patient. The study was registered at clinicaltrials.gov (NCT05647538).

Exclusion criteria were the presence of male factor, tubal factor, hypertension, autoimmune disease, morbid obesity, absence of lactation diabetes millets, vascular disease, smoking or the use of alcohol, the presence of additional surgery or medical disease, detection of a uterine anomaly, history of intrauterine growth restriction in previous pregnancies, and usage of a hormonal therapy through the research.

Patients were classified into two equal groups control group: underwent normal cesarean section without PPH, case group: cases underwent BUAL after PPH or IPH after cesarean section and did not respond to medical therapy and performed successful bilateral UAL for hemorrhage management.

IPH and PPH were described as a loss of blood more than 1L. Intractable PPH was described as PPH that continued despite standard medical therapy (methylergonovine maleate, oxytocin, and misoprostol), bimanual compression and fundal massage.

All patients underwent clinical parameters assessment (age, cycle history, BMI, parity, preceding treatment and/or surgery menstruation characteristics (more or less quantity of menstruation and dysmenorrhoea) and endometrial biopsy.

The ovarian reserve markers (AFC, AMH and FSH) were recorded at 6, 12 and 24 months after BUAL.

Finally, patients were asked about their desire for pregnancy in the future The data of subsequent pregnancy cases following bilateral UAL primary were recorded and follow-up was done at 6, 12 and 24 months after BUAL.

Intervention

Bilateral UAL was done 2 cm under the Kerr incision (lower segment transverse). A 2-Vicryl absorbable suture (Ethicon, Neuilly-surSeine, France) was introduced from the anterior to posterior views of the myometrium 2–3 cm medial to the descending part of the uterine vessels within an avascular area in the broad that was ligament and tied. Following the surgery, the uterine tone and hemorrhage were managed.

Blood sample collection

It was obtained at 9:00, and 11:00 AM after a fasting period of one night on days 3 to 5 of the menstrual cycle, then it was centrifuged two hours after collection and evaluated the same day. AMH levels were determined using a two-sided immunoassay that was enzymatically amplified (ELISA).

Sample size

The sample size was determined utilizing G. power 3.1.9.2 (Universitat Kiel, Germany). The sample size was determined to demonstrate ovarian reserve markers (AMH) (the primary outcome) with a mean (± SD) value 2.17±0.50 in BUAL group and a mean (± SD) value 2.48 ± 0.64 in control group according to a previous study[14] based on the following considerations: 0.05 α error and 80% power of the study, effect size: 0.53. four cases were added to each group to overcome dropout. Therefore, 60 cases were allocated in each group.

Statistical analysis

SPSS v26 was utilized to do statistical analysis (IBM Inc., Chicago, IL, USA). Comparing the two groups an unpaired Student's t- test was used for quantitative data provided as mean and standard deviation (SD). ANOVA was used to analyze repeated measurements. Qualitative variables were given as frequency and percentage (%) and examined using the Chi-square test. A two-tailed *P value* of 0.05 or less was considered statistically significant.

RESULTS

Demographic data were insignificantly different between both groups.

Regarding ovarian reserve markers (pre-AFC, Follicle size, AMH, FSH), there was an insignificant difference between both groups a 24 month (Table 1).

The mean value(±SD) of AFC 11.30 ±0.96 after 6 month, 11.42 ±1.22after 12m, and 11.67±1.16 after 24 m. The mean value (±SD) of follicle size 8.38±1.15 after 6 month, 8.42±1.12 after 12m, and 8.47±1.16 after 24m. The mean value(±SD) of AMH 2.13±0.50 after 6 month, 2.14 ± 0.49after 12m, and 2.19 ± 0.49after 24m. The mean value(±SD) of FSH 7.98±1.08after 6 month, 8.04±0.98after 12m, and 8.16±0.91after 24m (Table 2).

There was an insignificant difference at all measurements regarding ovarian reserve (pre-AFC, Follicle size, AMH and FSH) in case group (Table 3).

Women who needed to be pregnant was 58 in control group with success rate of (89.5%) and in case group was 50 with success rate of 86.20% no significant difference between both groups (Table 4).

Table 1: Patient characteristics of the studied groups

		Control group (n=60)	Case group (n=60)	*Pvalue*
Age (years)		27.15±4.44	26.93±5.16	0.806
Weight (Kg)		66.37±5.95	64.485.85 ±	0.083
Height(m)		1.60.07 ±	1.6±0.07	0.615
BMI(Kg/m^2)		25.443.5 ±	24.52±3.54	0.157
Gestational age (weeks)		37.57±1.13	37.38±1.08	0.363
Parity		1.90.71 ±	1.70.56 ±	0.089
Parity	Primipara	18 (30%)	21(35%)	0.697
	Multi para	42 (70%)	39 (65%)	

Data presented as mean ± SD, frequency (%), BMI: body mass index.

Table 2: Ovarian reserve markers between both groups at 24 months.

	Control group (n=58)	Case group (n=58)	*Pvalue*
Pre antral follicle count	11.95١٫٤9±	11.67١٫١6±	0.268
Follicle size	8.830.80 ±	8.47±١٫16	0.052
AMH (ng/ml)	2.250.51 ±	2.190.49 ±	0.527
FSH(IU/L)	8.290.95 ±	8.160.91 ±	0.437

Data presented as mean ± SD, AMH: Anti-Müllerian Hormone, FSH: Follicle-Stimulating Hormone.

Table 3: Ovarian reserve markers in case group during follow up.

	6 months (n=60)	12 months (n=59)	24 months (n=58)	*Pvalue*
Pre antral follicle count	11.30 ± 0.96	11.42 ±1.22	11.67±1.16	0.187
Follicle size	8.38±1.15	8.42±1.12	8.47±1.16	0.956
AMH (ng/ml)	2.13±0.50	2.14 ± 0.49	2.19 ± 0.49	0.770
FSH (IU/L)	7.98±1.08	8.04±0.98	8.16±0.91	0.608

Data presented as mean ± SD or frequency (%), AMH: Anti-Müllerian Hormone, FSH: Follicle-Stimulating Hormone

Table 4: Pregnancy outcome between groups during follow up.

	Control group (n=58)	Case group (n=58)	*Pvalue*
Pregnancy outcome	52(89.6%)	50 (86.20%)	0.775

Data presented as frequency (%).

DISCUSSION

UAL is one of the most common procedures for sustaining fertility. It is straightforward and successful in controlling PPH[14]. Diminished ovarian reserve is a major cause of infertility. Ovarian function was evaluated by more consistent ovarian reserve indicators as proxy for the possibility to conceive, such as anti-Müllerian hormone (AMH) level, age, AFC and FSH levels[15].

In our study, there was an insignificant difference at all measurements regarding ovarian reserve markers (pre-AFC, Follicle size, AMH and FSH) in case group. Also, ovarian reserve markers were insignificantly different between both groups at 24 months. In line with our results, McLucas *et al*.,[16] described that UAL possessed no impact on ovarian reserve in females <40 years old. Further, Singhal *et al*.,[17] suggested UAL is a preferable technique than bilateral HAL in uncontrolled PPH with a rate of success >90% and a relatively few complications.

In our current study, pregnancy outcome was insignificantly different between both groups. This agree with our results, Kaump *et al*., and Hu *et al*.,[18,19] who showed that UAL has no impact on ovarian reserve indicators in cases under 40–45 years old with insignificant changes in FSH and AMH concentrations were noticed in females under forty-five years old at twelve months following UAL.

In line with our results, Loïc Sentilhes *et al*.,[20] found that UAL, for IPH, PPH does not seem to compromise the cases' subsequent fertility and obstetrical result. Also, In Mohr-Sasson *et al*.,[21] study who revealed that UAE did not have impact on ovarian reserve indicators in cases under 40–45 years old, and insignificantly different in FSH and AMH were seen 12 months following treatment in females younger than 45 years. It was also reported that UAE did not influence ovarian reserve in women under the age of 40 and which ovarian reserve assessments did not reveal significantly different between these participants.

Women who needed to be pregnant was 58 in control group with success rate of (89.5%) and in case group was 50 with success rate of 86.20% no significant difference between both groups. Promising results were observed by Sentilhes *et al*.[20] who reported that woman who underwent stepwise uterine devascularization and B-Lynch compression suturing, became pregnant again.

Bilateral UAL is among the most essential fertility-preserving treatments in PPH cases with a high pregnancy rate, and based on our experiment, we can theorize that it has no impact ovarian reserve in these cases, recommending the use of UAL to avert hysterectomy in cases of IPH or PPH.

Our study had some limitation as insufficient sample size with short duration of follow up.

Future research with larger sample sizes is necessary to strengthen our conclusion and are needed to compare our UAL usage technique with other techniques. Therefore, to better understand the mechanism of effect on ovarian reserve during post-UAL period, results of longer follow-up periods excluding lactation periods are needed.

CONCLUSION

UAL is an effective and safe approach for managing life-threatening obstetrical hemorrhage such as intrapartum or postpartum atony and could be a fertility-sparing technique when done by a dependable skilled operator without any negative effects on ovarian reserve and pregnancy outcome.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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