Evaluation of Ovarian Reserve Following Bilateral Internal Iliac Artery Ligation for Severe Obstetric Hemorrhage

Abou Saeda M.R., Rabie N. H., Afify N.S. and El Taieb E. M.

Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, Cairo Egypt
Noha.rabei@yahoo.com

Abstract: **Objective*:*** The aim of the study was to assess the ovarian reserve by measuring the anti-Müllerian hormone (AMH) and assessing the antral follicular count (AFC) after bilateral internal iliac artery ligation (IIAL) for severe obstetric hemorrhage. **Methods:** It was a retrospective study which was carried out at Ain Shams Maternity Hospital in the period from February 2011 to April 2013. 17 matched pair of patients who delivered in the period from 2006 to 2010 were included in the study. The study group had bilateral IIAL for severe obstetric hemorrhage. AMH and AFC were assessed on the 3rd day of the menstrual cycle. **Results:** AMH and AFC were significantly decreased in the study group (P<0.001) than in the control group. **Conclusion:** Ovarian reserve was decreased after bilateral IIAL for severe obstetric hemorrhage.

Keywords: Ovarian reserve**,** anti-Müllerian hormone**,** antral follicular count , bilateral internal iliac artery ligation**.**

1. Introduction

Ovarian reserve is a term used to describe the functional potential of the ovary and reflects the number and quality of oocytes within it [1]. The term ovarian reserve denotes the available pool of primordial follicles in the ovary. It is a major determinant of human fertility potential. Diminished ovarian reserve reflects the process of follicular depletion and decline in oocyte quality and can be considered as an accurate measure for ovarian function [2].

Over the last two decades a number of ovarian reserve tests have been investigated. Methods used to predict prospectively response to ovarian stimulation have included mainly the measurement of serum FSH, estardiol, inhibins and AMH or ultrasonographic assessment of pretreatment ovarian volume and the number of early AFC [3]. It was reported that the AFC and AMH are the most significant predictors of poor ovarian response to stimulation in ART through a comparative analysis of AMH, inhibin B and three dimensional ultrasound determinants of ovarian reserve [4].

The number of antral follicles is indicative of the relative number of primordial follicles remaining in the ovary and therefore can be considered as a good index of ovarian reserve. The number of antral follicles is defined as the total number of follicles less than 10mm in diameter in both ovaries [5]. Analysis of histologically determined primordial follicles that count in human ovaries has demonstrated that there is indeed a relationship with serum AMH [6].

There is growing evidence that AMH is exclusively produced by granulosa cells of ovarian follicles in the adult female. It is a unique biomarker of ovarian follicular status [7]. AMH is a glycoprotein, a member of the transforming growth factor-β superfamily AMH levels represent the most sensitive marker for the inevitable decline in the number of primordial follicles related to aging [8]. AMH in healthy female is either just detectable or undetectable in cord blood at birth and demonstrates a marked rise by three months of age, while still detectable it falls until four years of age before rising linearly until eight years of age and then remains constant from mid-childhood to early adulthood. It does not change significantly during puberty, from twenty five years of age AMH declines to undetectable levels at menopause [9].

It was reported that, the AFC and AMH are the most significant predictors of poor response to ovarian stimulation during assisted reproductive techniques (ART) through a comparative analysis of AMH, inhibin-B and three-dimensional ultrasound determinants of ovarian reserve [10].

IIAL has been advocated in the management of intractable obstetric [11]. Postpartum hemorrhage accounts for 30% of maternal mortality worldwide. Uterine atony is the most common cause of post partum hemorrhage and accounts for 80% of cases [12]. Internal iliac artery ligation was found to be indicated if life-threatening pelvic hemorrhage could not be controlled by conservative methods; or in case of a prophylactic reduction of pelvic blood flow to prevent anticipated hemorrhage; or if preservation of reproductive function was desired [13]. The long-term

effects of that intervention on ovarian function remain unknown. It has not been possible to follow young patients for whom internal iliac artery ligation has been performed. While subsequent pregnancies clearly appear to be possible, they also appear to carry a high risk of recurrence for postpartum hemorrhage[14]. The incidence of post operative amenorrhea is not known. It is common for menses to resume after operation within three months. Although there has been reports of normal pregnancy and delivery occurring after IIAL but how frequently it occurred was not followed up[15]. It is reasonable to believe that reproductive capacity is not lost after internal iliac artery ligation provided that the patient has a normal uterus. The type of suture material used for internal iliac artery ligation does not seem to affect either effectiveness of the technique or subsequent fertility. However recananlization rates may be greater with absorbable suture material[16].

Aim of the Work

The aim of this work is to assess ovarian reserve both hormonally by measuring AMH and sonographically by assessing AFC after bilateral IIAL for severe obstetric hemorrhage.

2.Patients and Methods

The current study was carried out at Ain Shams Maternity hospital in the period from February 2011 to April 2013. It was a retrospective study. Patients were included in this study after informed consent. Patients were divided in two groups:

Group A: Included patients who had internal iliac artery ligation for severe obstetric hemorrhage in the past five years starting from 2006 till 2010.
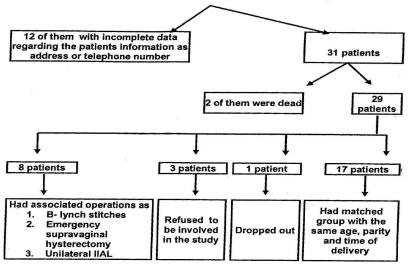
Group B: Included women of the same age, parity and time after delivery who had no internal iliac artery ligation procedure.

The inclusion criteria were: age between 18-40 years and the presence of no medical disorders. The exclusion criteria were age less than 18 years and more than 40 years, smokers, history of infertility, previous history of induction of ovulation, family history of premature menopause, associated ovarian pathology, performance of bilateral tubal ligation, and endocrinal disease affecting fertility.

Patients were subjected to history taking, physical examination, assessment of serum AMH and transvaginal ultrasound to assess AFC. Serum AMH and AFC were assessed on the third day of the menstrual cycle. 5 ml of blood were withdrawn, the blood was centrifuged at the 3500 rpm for 10 minutes and the serum was stored in polypropylene tubes at 2-8 °C for hormonal assay which was performed by technician who was blinded to the patients data. Serum AMH level was measured using enzyme-linked immunosorbent assays (ELISA) (Beckman-coulter). Ultrasound scanner Medison: sono Ace X4 Korea vaginal probe of multifrequency ranging from 4 to 9 MHz was used for AFC assessment.

3.Results

The total number of patient who had IIAL in the period from 2006 to 2010 was 43 patients. The recruited study group and control group (seventeen matched pairs) were included in the study as shown in figure (1): 17 patients who had IIAL were included as the study group. The mean age in both groups was 33.2±6 years ranging from 21-40 years. The mean time after delivery was 4.4 ±1.4 years ranging from 3-7 years.

Fig (1): Study recruitment group. 17 patients who had IIAL were included as the study group.

Table (1) shows that there was no correlation between time post IIAL/delivery and both AMH and AFC. AMH was significantly higher in the control group as shown in table (2). AFC was significantly higher in the control group as shown in table (3). The number of pregnancies was significantly higher in the control group as shown in table (4).

Table (1): Correlation between time post-IIAL/delivery and both AMH and AFC in the study group.

	Study group		Control group	
	r	*p*	r	*p*
AMH	0.095	0.717	0.062	0.814
AFC	-0.143	0.583	-0.015	0.954

r: Pearsons' correlation test
There was no significant correlation between time after parturition and both AMH and AFC in the study group.

Table (2): Comparison between both groups as regards AMH (ng/ml).

	Mean±SD	Range	Difference
Study group	0.7±0.4	0.1-1.7	-0.7±0.5
Control group	1.4±0.8	0.2-3.0	
t	6.042	*P*	<0.001 HS

T: Paired t-test,
HS: highly significant
AMH was significantly higher in the control group than the study group.

Table (3): Comparison between both groups as regards AFC.

	Mean±SD	Range	Difference
Study group	5.8±3.0	2-12	-15.0±3.6
Control group	20.8±5.2	14-30	
t	17.236	*P*	<0.001 HS

T: Paired t-test,
HS: highly significant
AFC was significantly higher in the control group than in the study group.

Table (4):Comparison between both groups as regards number of pregnancies post-IIAL/parturition

	Median (IQR)	Range	Difference
Study group	0(0-1)	0-1	0(0-1)
Control group	1(0-2)	0-4	
z	-2.588	*P*	<0.010 S

IQR: Inter-Quartile range, Z: Wilcoxon signed rank, S: Significant
The number of pregnancies was significantly higher in the control group than the study group.

4.Discussion

In the current study 17 matched pair of patients were included AMH was significantly higher in the control group than in the study group (*p*-value <0.001). The study group had lower AMH level (0.7±0.4ng/ml) compared to the control group (1.4±0.8ng/ml). AFC was significantly lower in the study group with mean (5.8±3.0) than the control group with mean AFC (20.8±5.2). Overall findings of the present study showed that the ovarian reserve was decreased in women who had IIAL.

Raba (2010) reported that IIAL in the treatment of obstetric hemorrhage leads to dilation of the ovarian arteries and reversed flow in the ovarian branches of the uterine arteries. These change the blood supply to the ovaries and impair ovarian

reserve. Results of **Raba (2010)** were following angio-CT scan, in the study group reversed blood flow in the ovarian branches of the uterine arteries was observed: contrast medium flowed from the ovarian arteries towards the ovaries and from the ovarian branches of the uterine arteries to the uterine arteries. In the control group, there was no contrast medium flow from the ovaries towards the ovarian branches of the uterine arteries. Quantitative digital angiography of the ovarian arteries showed that, in the study group, the mean ovarian artery diameter was significantly/dilated ($p < 0.05$). Also, AMH levels were significantly lower ($p < 0.05$), while there were no significant differences in FSH levels between groups ($p < 0.05$)[17].

Raba and Baran (2009) reported that IIAL as a way of treating intrapartum hemorrhage, causes the decrease of pulsatility index and systolic/diastolic ratio in ovarian arteries. Characteristic changes of pulsatility index, resistivity index and systolic/diastolic ratio parameters in uterine arteries after IIAL have not been observed. Changes of ovarian flow velocity parameters suggest the possibility of changes in the ovarian function[18].

Simsek et al. (2012) reported that ovarian reserves of patients were not adversely affected by the surgical procedure. FSH and estradiol concentrations and the mean volume of the ovaries were similar between the study (n: 10) and control (n: 56) groups[19].

Also, **Yildirim et al. (2009)** reported that pelvic circulation was not compromised after bilateral internal iliac artery ligation, comparing doppler blood flow characteristics of the uterine, arcuate, and ovarian arteries of women who had bilateral internal iliac artery ligation with those of the controls [20].

Nizard et al. (2003) stated that IIAL for postpartum hemorrhage is not responsible for secondary infertility, uterine contractility disorders, placental perfusion insufficiency, fetal anomalies or IUGR. They reported 21 pregnancies, 13 term deliveries and one ectopic pregnancy after performing IIAL in 68 patients with intractable postpartum hemorrhage[14].

In conclusion of the current study, AMH and AFC were significantly reduced in the group of patients who had IIAL. Thus AMH and AFC can be used for assessment of ovarian reserve especially if future pregnancy is desired.

References
1. Macklon NS, Fauser BC. Ovarian reserve. Semin Reprod Med. 2005;23(3):248-56.
2. Scott RT, Jr., Hofmann GE. Prognostic assessment of ovarian reserve. Fertil Steril. 1995;63(1):1-11.
3. Fawzy M, Lambert A, Harrison RF, Knight PG, Groome N, Hennelly B, *et al.* Day 5 inhibin B levels in a treatment cycle are predictive of IVF outcome. Hum Reprod. 2002;17(6):1535-43.
4. Jayaprakasan K, Chan Y, Islam R, Haoula Z, Hopkisson J, Coomarasamy A, *et al.* Prediction of *in vitro* fertilization outcome at different antral follicle count thresholds in a prospective cohort of 1,012 women. Fertil Steril. 2012;98(3):657-63.
5. Lambalk CB, de Koning CH, Flett A, Van Kasteren Y, Gosden R, Homburg R. Assessment of ovarian reserve. Ovarian biopsy is not a valid method for the prediction of ovarian reserve. Hum Reprod. 2004;19(5):1055-9.
6. Hansen KR, Hodnett GM, Knowlton N, Craig LB. Correlation of ovarian reserve tests with histologically determined primordial follicle number. Fertil Steril. 2011;95(1):170-5.
7. Appasamy M, Muttukrishna S, Pizzey AR, Ozturk O, Groome NP, *et al.* Relationship between male reproductive hormones, sperm DNA damage and E. Relationship between male reproductive hormones, sperm DNA damage and markers of oxidative stress in infertility. Reprod Biomed Online 2008; 14: 159-165.
8. Artemis Karkanaki, Christos Vosnakis, Dimitrios Pandidis. The clinical significance of anti-Müllerian hormone evalautionin gynecological endocrinology Hormones, 10(2): 95-103.
9. Hagen CP, Aksglaede L, Sorensen K, Main KM, Boas M, Cleemann L, *et al.* Serum levels of anti-Müllerian hormone as a marker of ovarian function in 926 healthy females from birth to adulthood and in 172 Turner syndrome patients. J Clin Endocrinol Metab. 2010;95(11):5003-10.
10. Jayaprakasan K, Campbell B, Hopkisson J, Johnson I, Raine-Fenning N. A prospective, comparative analysis of anti-Müllerian hormone, inhibin-B, and three-dimensional ultrasound determinants of ovarian reserve in the prediction of poor response to controlled ovarian stimulation. Fertil Steril. 2010;93(3):855-64.
11. Ledee N, Ville Y, Musset D, Mercier F, Frydman R, Fernandez H. Management in intractable obstetric hemorrhage: an audit study on 61 cases. Eur J Obstet Gynecol Reprod Biol. 2001;94(2):189-96.
12. Soltan MH, Faragallah MF, Mosabah MH, Al-Adawy AR. External aortic compression device: the first aid for postpartum hemorrhage control. J Obstet Gynaecol Res. 2009;35(3):453-8.
13. Wagaarachchi PT, Fernando L. Fertility following ligation of internal iliac arteries for life-threatening obstetric hemorrhage: case report. Hum Reprod. 2000;15(6):1311-3.

14. Nizard J, Barrinque L, Frydman R, Fernandez H. Fertility and pregnancy outcomes following hypogastric artery ligation for severe post-partum hemorrhage. Hum Reprod. 2003;18(4):844-8.
15. Dildy GA, 3rd. Postpartum hemorrhage: new management options. Clin Obstet Gynecol. 2002;45(2):330-44.
16. Papp Z, Sztanyik L, Szabo I, Inovay J. Successful pregnancy after bilateral internal iliac artery ligation monitored by color Doppler imaging. Ultrasound Obstet Gynecol. 1996;7(3):211-2.
17. Raba G. Effect of internal iliac artery ligation on ovarian blood supply and ovarian reserve. Climacteric. 2011;14(1):54-7.
18. Raba G, Baran P. Hemodynamic parameters following bilateral internal iliac arteries ligation as a treatment of intrapartum hemorrhage. Ginekol Pol. 2009; 80(3):179-83.
19. Simsek Y, Yilmaz E, Celik E, Turkcuoglu I, Karaer A, *et al.* Efficacy of internal iliac artery ligation on the management of postpartum hemorrhage and its impact on the ovarian reserve. J Turk Soc Obstet Gynecol 2012; 9(3): 153-8.
20. Yildirim Y, Gultekin E, Kocyigit A, Yilmaz C, Ertopcu K, Arioz DT. Color Doppler analysis of pelvic arteries following bilateral internal iliac artery ligation for severe postpartum hemorrhage. Int J Gynaecol Obstet. 2009; 104(1):22-4.

11/12/2013