

## Association of Emergency Salpingectomy with Ovarian Reserve

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### Abstract

**Objective(s):** The aim of this study was to explore the effect of salpingectomy due to ruptured ectopic pregnancy on ipsilateral ovarian reserve and function.

**Materials and methods:** This prospective observational study was conducted in Infertility Care and Research center, Dhaka, Bangladesh between January 2014 and December 2019. Seventy five (75) patients who had history of unilateral salpingectomy due to ruptured ectopic pregnancy and who needed ART were the target population of this study. Seventy-five (75) patients of same age group with history of bilateral tubal block on laparoscopy were taken as control. Both groups of patients underwent ART (IVF/ICSI) with standard protocol of ART. Ovarian reserve was compared between two groups with and without salpingectomy and response to stimulation during ART was compared between two groups and between two ovaries of salpingectomy group to see the difference of function between ipsilateral and contralateral ovary. Main outcome measures were ovarian volume, AFC, AMH, FSH, E2 on day10, number of egg retrieval, number of embryo and pregnancy rate between two groups and ovarian volume, AFC, number of egg retrieval in each ovary of study group.

Data are presented as mean  $\pm$  SD. Differences between groups were tested using the *t*-test and Chi square-test as appropriate. The Statistical Package for Social Sciences (SPSS 11.0, Chicago) was used for statistical analysis.. A p-value  $<0.5$  was considered as significant.

**Results:** Both groups were similar in age. There was significant difference in ovarian volume, AMH, FSH and number of follicle development in study and control group. But there was no difference in number of transferable embryo and pregnancy rate between the groups  $p>0.05$ . When ovarian volume, number of antral follicle, number of mature follicle and number of oocyte retrieved were compared between ipsilateral and contralateral ovaries of patient of salpingectomy group, it showed significant difference in each parameter. Ovary of operated side was smaller in size, having low number of follicles and produced less number of retrievable oocyte.

**Conclusion:** In conclusion according to our observation it can be said that salpingectomy in ectopic pregnancy may impair ovarian reserve and function. If there is bilateral salpingectomy it may shorten the reproductive life. Long term effect of unilateral and bilateral salpingectomy need to be evaluated.

**Keywords:** Salpingectomy, Ectopic pregnancy, Ovarian reserve.

### Introduction

Salpingectomy is a common operation for ruptured ectopic pregnancy and in unruptured ectopic pregnancy where other tube is found healthy. In unruptured ectopic pregnancy if other tube is not healthy salpingostomy is the choice of surgery. When ectopic pregnancy occurs in an infertile woman then in-spite of other healthy tube many surgeons do salpingostomy in unruptured tube. But to majority surgeons salpingectomy is the preferred option

to salpingostomy as recurrent ectopic pregnancy rate is higher after salpingostomy than after salpingectomy<sup>1</sup>. One of the important issue of salpingectomy is the possibility of losing of ovarian reserve of operated side due to impaired blood supply after salpingectomy. If the procedure is not performed properly particularly in an emergency situation of massive blood loss, it may disrupt the normal blood flow to the ovary. Till date number of studies were conducted to evaluate the impact of salpingectomy on ovarian reserve and ovarian function but all are not consistent<sup>2-6</sup>. All studies

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reported the overall ovarian response to stimulation in patients with unilateral or bilateral salpingectomy or before and after surgery except two<sup>3,4</sup> who compared the response of ipsilateral (ovary of operated side) and contralateral ovary of the patient.

Chan et al described that after salpingectomy ovarian stromal blood flow of the operated side seemed to be relatively impaired compared to the non-operated side and they speculated that the

less blood supply might result in the decreased ovarian function<sup>7</sup>. Gelbaya et al observed a significant increment of follicle stimulating hormone (FSH) level after salpingectomy of hydrosalpinx tube and reduced estrogen (E2) concentration on the day of hCG injection in the same group, which might suggest a compromised ovarian response to in-vitro fertilization (IVF) treatment after salpingectomy. But they concluded that prophylactic salpingectomy in women with hydrosalpinx may compromise ovarian response to stimulation without affecting pregnancy rates. Lass et al noted that salpingectomy had no detrimental effect on the total number of retrieved oocytes during the IVF performance although the retrieved oocytes from the operated ipsilateral ovary were fewer than that from the contralateral ovary<sup>3</sup>. Dar et al also concluded that the surgery did not alter ovarian response in IVF cycles<sup>8</sup>. Mode of surgery might have some difference in jeopardizing ovarian blood supply. Chan et al shown that reduction in antral follicle and ovarian blood flow were not observed in those patients whose salpingectomy was done by laparotomy<sup>7</sup>. Controversies exist whether salpingectomy either due to EP or hydrosalpinx reduces the ovarian reserve and ovarian function and surgical procedure like laparoscopy or open method laparotomy has any effect.

We observed 75 patients of unilateral salpingectomy whose surgery was done in an emergency situation due to ruptured ectopic pregnancy with heavy blood loss. So, laparotomy was the procedure of choice. Purpose of this study was to observe whether salpingectomy has an impact on reducing ovarian reserve and ovarian function and negative impact on subsequent reproductive outcome.

## Methodology

This prospective observational study was conducted in Infertility Care and Research center, Dhaka, Bangladesh between January 2014 and December 2019. The patient who came for fertility treatment were the target population for this study. The aim of the study was to observe whether there is any compromise of ovarian reserve and function after emergency salpingectomy or not. Seventy five (75) patients who had history of unilateral salpingectomy due to ruptured ectopic pregnancy and who needed ART were the target population of this study. All patients passed at least one year after surgery. Ovarian reserve was tested by antral follicle count (AFC), serum AMH, FSH. As advanced age is associated with reduced ovarian reserve<sup>9</sup> we selected only the patients of young age group ranging from 20-34 years. To compare function of ipsilateral ovary (operated side) with that of contralateral ovary (non-operated side) we included only unilateral salpingectomy patients. Patients with endometrioma and with history of

adhesiolysis and other ovarian surgery were excluded from this study as endometrioma itself and any ovarian surgery reduces ovarian reserve<sup>10</sup>. Patients with PCOS were also excluded as their AMH level is high, which may not shed any impact after slight reduction after surgery. Seventy-five (75) patients of same age group with same exclusion criteria with history of bilateral tubal block on laparoscopy were taken as control. Both group of patients underwent ART (IVF/ICSI) with standard protocol. Ovarian reserve parameters like AMH and AFC and response to stimulation were compared between two groups with and without salpingectomy. As AMH secreted from both ovaries cannot be estimated separately, excluding AMH, ovarian volume, AFC, and response to stimulation were compared between two ovaries of salpingectomy group to see the difference of function between ipsilateral and contralateral ovary. Main outcome measures were ovarian volume, AFC, AMH, FSH, E2 on day10, number of egg retrieval, number of embryo and pregnancy rate between two groups and ovarian volume, AFC, number of egg retrieval in each ovary of study group. Ovarian volume is measured by using transvaginal sonographic measurement and applying the formula  $0.5 \times \text{length} \times \text{width} \times \text{thickness}$  of the ovary. AMH, FSH and E2 was done on D2/D3 of the cycle. Though AMH can be done at any day but for patients' convenience all samples took at a time.

Data are presented as mean  $\pm$  SD. Differences between groups were tested using the *t*-test and Chi square-test as appropriate. The Statistical Package for Social Sciences (SPSS 11.0, Chicago) was used for statistical analysis.. A *p*-value  $<0.5$  was considered as significant.

Ethical permission was not sought for as there was no intervention other than day to day standard IVF procedure for which the clinic is licensed.

## Results

A total 75 patients were recruited as study who had history of unilateral salpingectomy due to ruptured ectopic pregnancy. Seventy-five patients who had bilateral tubal block or who were patients of unexplained infertility were the control group. Both groups were similar in age. There was significant difference in ovarian volume, AMH, FSH and number of follicle development in study and control group. But there was no difference in number of transferable embryo and pregnancy rate between the groups  $p>0.05$  (Table 1).

When ovarian volume, number of antral follicle, number of mature follicle and number of oocyte retrieved were compared between ipsilateral and contralateral ovaries of patient of salpingectomy group, it shown significant difference in each parameter (Table 2). Ovary of operated side was smaller in size, having low number of follicles and produced less number of retrievable oocyte.

## Discussion

Salpingectomy is the choice of surgery in ruptured ectopic pregnancy<sup>11-13</sup>. Whether this salpingectomy have any effect

**Table 1: Comparison of baseline characteristics and response to IVF-ET treatment between study and control group**

Variable	Study group (n=75)		Control group (n=75)		Significance
	Mean	SD	Mean	SD	
Age (Yrs)	32	±4.9	33	±4.1	0.1773
Ovarian volume (cm <sup>3</sup> )	6.17	±2.1	7.5	±2.5	0.0001
AFC	7.5	±1.51	8.1	± 1.61	0.0199
AMH (ng/ml)	2.12	±1.2	2.89	±1.9	0.0035
FSH (IU/L)	8.9	±2.1	8.1	± 1.98	0.0176
E2 on day of triggering (pg/ml)	2056	±221.1	2100	±198.4	0.2016
Unit of FSH needed	2809.21	±978.25	2615.45	±954.23	0.2214
Days of stimulation	10.89	±2.34	10.32	±2.52	0.1533
No of follicle	12.7	±2.35	13.9	±2.12	0.0013
No of oocytes retrieved	11.8	±3.1	12.2	±2.91	0.4165
No of embryo	9.5	±2.21	10.2	±2.67	0.0824
No of pregnancy N (%)	23 (30.66)		25 (33.33)		0.726

**Table 2: Comparison of ovarian volume, antral follicle count and response to ovarian stimulation between ipsilateral and contralateral ovaries of patients who underwent salpingectomy**

Variable	Ipsilateral ovary		Contralateral ovary		Significance
	Mean	SD	Mean	SD	
Ovarian volume	5.01	±1.2	7.32	±2.1	0.0001
AFC	6	±1.23	8.9	±1.71	0.001
No of follicle	4.5	±1.1	8.2	±2.1	0.0001
No of retrieved oocyte	3.9	±1.5	7.9	± 1.98	0.0001

on ovarian reserve or ovarian function is a controversial issue. Some authors shown lower AMH<sup>3</sup>, higher dose of gonadotropin requirement during stimulation<sup>14</sup>, and fewer follicle and lower number of egg retrieval<sup>15</sup> during IVF after salpingectomy due to ectopic pregnancy. If so, should we take any extra precaution during surgery or afterwards is a matter of concern. One of the concerns of salpingectomy is that there is possibility of impairing the ovarian function after the procedure. The most important blood supply to the fallopian tube is the medial tubal artery, which originates at the same point as the median ovarian artery. The blood supply of the ovary is very closely related to the fallopian tube. During salpingectomy due to cutting, tying or cauterization, it may disrupt the normal blood flow to the ovary. Animal study proved that any surgery around the tube carries a potential risk of damaging the ovarian blood supply leading to risk of impairment of the ipsilateral ovarian function<sup>16,17</sup>. Sezik et al examined 24 patients who had history of hysterectomy with or without bilateral salpingectomy and reported that complete removal of fallopian tubes had a deleterious effect on ovarian blood supply<sup>18</sup>. Lass et al<sup>3</sup> described that a degree of blood flow impairment to the ovary occurred after salpingectomy, which impaired follicular development but not significantly to cause ovarian shrinkage. Beyth and Winston<sup>16</sup> observed fewer oocyte in operated side after fimbriectomy in rabbit. McComb and Delbeke<sup>17</sup> shown the effect of surgical division of anastomatic vessels between ovary and fallopian

tube in rabbit's ovary. A significant reduction of number of ovulation in operated side compared with contralateral side suggests the impairment of tubo-ovarian blood supply.

In a meta-analysis Luo J et al<sup>19</sup> compared the ovarian reserve, volume and ovarian response to treatment between pre and post salpingectomy patients. They concluded that salpingectomy did not impact the ovarian reserve in ectopic pregnancy patients. Ovarian reserve in terms of AMH, AFC, basal FSH and all parameters of ovarian response like dose and duration of gonadotropin, E2 level on the day of triggering and number of retrieved oocytes were of no significant differences between pre and postsurgical group. Compensatory blood supply of the contralateral artery in the mesosalpinx might be responsible to recover the damage of vessels during salpingectomy<sup>20</sup>. Venturella et al<sup>21</sup> reported the same that wide excision of the mesosalpinx in salpingectomy did not alter blood supply and ovarian reserve and salpingectomy might not compromise ovarian function.

In current study we observed that ovarian volume and number of AFC of operated side reduced significantly in comparison to contralateral side (Table 2). As a result, though average ovarian volume, number of follicle and AMH level was within normal range they were significantly lower when we compared with control group who had no salpingectomy (Table1). All cases were laparotomy and were done in an emergency situation. The close

anatomical association of the vascular and nervous supply to the fallopian tubes and ovaries constitutes the rationale for the risk of impaired ovarian function after surgery. Chan et al<sup>22</sup> described that AFC and ovarian blood flow were significantly reduced when salpingectomy was done by laparoscopy. They did not find any reduction of AFC and ovarian blood flow when salpingectomy was done by laparotomy. They explained that during open surgery it was easy to place the surgical clamp very close to the mesenteric border of the affected fallopian tube and hence limit any damage to the blood vessels in mesosalpinx. On the other hand during laparoscopy use of diathermy causes heat damage, which could be extensive as depth of the damage cannot be limited to the excision site.

But this theory is not applicable for our series where laparotomy was the method of surgery. Though chances of cauterization was less in laparotomy, clamping of mesosalpinx in an emergency situation might involve major tributary of ovarian artery during entry through suspensory ligament. Regarding ovarian volume no study shown reduction of ovarian volume. It may require years to become clinically evident low volume of ovary. We examined the patients who already passed at least one year after surgery. Mean interval of salpingectomy and ART was  $4.09 \pm 1.74$  years with a range of 1-7 years. As this parameter is not applicable for control group, this data was not presented in the table. This long duration may be a cause of slowly decreasing size of the ovary. Though mean ovarian volume reduced, in 16 cases volume was normal in operated side.

Regarding outcome of IVF-ET Luo J et al<sup>19</sup> shown that salpingectomy had no effect on duration of gonadotropin, number of egg retrieval, number of transferable embryo and pregnancy rate, but amount of gonadotropin used was higher in post-salpingectomy group. In another two retrospective case controlled studies shown no difference in ovarian response after gonadotropin stimulation during IVF treatment in patients with or without salpingectomy<sup>23,24</sup>. In order to avoid bias another two researchers used same patient as control and compared the ovarian response before and after salpingectomy and found no difference<sup>25,26</sup>. Same was also observed by Xi et al<sup>20</sup> that initial and total dose of gonadotropin was higher in salpingectomy group. But finally controlled group also needed higher dose. However, Lass et al<sup>3</sup> showed a reduced number of follicle and less number of retrieved oocyte in operated side in comparison to non-operated side. We also observed that number of follicle and egg retrieval was lower in operated side than non operated side (Table 2). In our series we observed ovarian volume was reduced and AFC was also lower in ipsilateral side. Though egg retrieval was lower in ipsilateral side in comparison to contralateral side, there was no significant difference in egg retrieval between control and study group. Net outcome of treatment was compensated by other unaffected ovary. Sumiala et al and Chan et al<sup>27,22</sup> reported that antral follicle count and ovarian blood flow were significantly reduced in operated side due to interruption of blood supply. Ovarian volume was not reduced in their series and they explained that it needs years for such difference to be clinically evident. Reduction

of ovarian volume is a late phenomenon and can only be shown years after salpingectomy, which is applicable for our series.

The response to treatment was not altered in many studies including the current one as any subtle reduction in ovarian blood flow and antral follicle count may be overcome by the hyperstimulation induced by high dose of gonadotropin. Strandell et al<sup>26</sup> described that due to application of high dose of gonadotropin ovarian response was not altered even after bilateral salpingectomy. However, the long-term implication of impaired ovarian function cannot be ignored. There is a possibility of shortening of reproductive life due to impairment of function particularly if the procedure is performed in both sides. There might be early menopause in this group of patient and fertility specialists need to treat these patients as priority basis.

In conclusion according to our observation it can be said that salpingectomy in ectopic pregnancy may impair ovarian function and if there is bilateral salpingectomy it may shorten the reproductive life. Long term effect of unilateral and bilateral salpingectomy need to be evaluated. Moreover, care should be taken during surgery to avoid accidental involvement of the part of the infundibulo pelvic ligament during clamping.

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