

Role of Tubal Ligation / Salpingectomy in Reducing the Risk of Ovarian Cancer

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Abstract

Introduction: Amongst the gynaecological malignancies, epithelial ovarian carcinoma is the most lethal. Early stage neoplasms in the fimbriated end of the fallopian tube could be the cause of development of ovarian carcinoma. We aim to correlate opportunistic tubal ligation / salpingectomy as an effective preventive strategy in the occurrence of epithelial ovarian carcinoma. **Material & Methods:** This is a prospective case-control study. Cases were patients who underwent total hysterectomy with bilateral salpingo-oophorectomy with a histologically verified epithelial ovarian cancer and controls were patients who underwent the same surgical procedure for benign gynaecological conditions specifically myoma uteri and adenomyosis with normal ovaries a final histology report. Using appropriate statistical methods the correlation between the occurrence of epithelial ovarian carcinoma and previous tubal ligation / salpingectomy was determined. **Results:** A total of 158 cases were included in the study amongst which 28 cases were post-surgical patients with histologically verified epithelial ovarian cancer and 130 post-surgical patients for benign gynaecologic conditions with normal ovaries a final histology report were

controls. The study showed that without previous tubal ligation / salpingectomy procedure the odds of developing epithelial ovarian carcinoma increased by 1.54 times in the subjects after adjusted for age, parity and obesity. **Conclusion:** Tubal ligation / salpingectomy reduces the risk of developing epithelial ovarian carcinoma. At the time of surgery and planning a hysterectomy for benign indications patients should be counselled regarding risk-reducing salpingectomy to conserve ovarian function and prevent ovarian epithelial carcinoma.

Keywords: Epithelial ovarian carcinoma, Tubal ligation, Salpingectomy.

Introduction

Epithelial ovarian carcinoma is of the most lethal gynaecological malignancies [1]. There has been no effective screening test and treatment for advanced stage ovarian carcinoma. Hence the need to develop preventive methods is important. The early stage neoplasm of fallopian tubes are called serous tubal intraepithelial carcinomas (STIC). They are found in the secretory type cells in fimbriated end of fallopian tubes. The pathogenesis of development of

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ovarian cancers is by shedding of this precursor lesions on the ovarian surface. This has been proven by histology.

STIC lesions in the fallopian tubes have not only been found in women with known breast carcinoma (BRCA) mutations but were also seen in 50% to 60% of sporadic serous ovarian cancers. Furthermore, STIC are known to harbour the same TP53 mutations found in concomitant ovarian carcinomas implicating a clonal relationship.

Epithelial ovarian carcinoma are categorised into Type I and Type II based on recent theories on the tumorigenesis of epithelial ovarian carcinoma supported by immunohistochemical, morphological and molecular studies.

Type I ovarian malignancies includes low-grade endometrioid, low-grade serous, Brenner tumours, Clear cell and Mucinous carcinomas. They start as a low grade lesion and later on develop into a malignancy. They are genetically stable and have specific mutations including KRAS, BRAF, CTNNB1, ERBB2, PTEN, ARID1A, PIK3CA, and PPP2R1A.

Type II ovarian malignancies present in an advanced stage and are highly unstable and are very aggressive tumours. They include high-grade endometrioid, high-grade serous, malignant mixed mesodermal tumours (carcinosarcomas) and undifferentiated carcinomas [2].

In view of the possible origin of ovarian carcinoma from fimbriated ends of fallopian tubes, opportunistic tubal ligation/salpingectomy may therefore be an effective preventive strategy. The aim of this study was to determine the association between the occurrence of epithelial ovarian carcinoma and a previous history of tubal ligation/salpingectomy.

Materials and methods

This prospective study was conducted at a tertiary care centre in Mangalore, Karnataka from January 2015-2018, with a sample size of 158. The cases included were patients who underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy along with a histologically confirmed epithelial ovarian cancer and controls were patients who underwent surgery for benign gynaecological conditions like uterine fibroids and adenomyosis with normal ovaries a final histology report.

The demographic data like age, height and weight of the patients were collected. Other patient

information like risk factors (gravidity, parity, obesity, pelvic endometriosis, and polycystic ovarian syndrome), history of tubal ligation / salpingectomy and age of the patient when it was performed were noted. The surgical procedures with indication were also documented. The histological diagnosis was obtained with the specific histology subtype of epithelial ovarian cancer. The association between the occurrence of epithelial ovarian carcinoma and a previous tubal ligation / salpingectomy was determined using appropriate statistical methods.

Inclusion criteria

- Histology confirmed ovarian tumours.
- Benign gynaecological conditions.

Exclusion criteria

- Borderline ovarian tumours.
- Other associated malignancies.

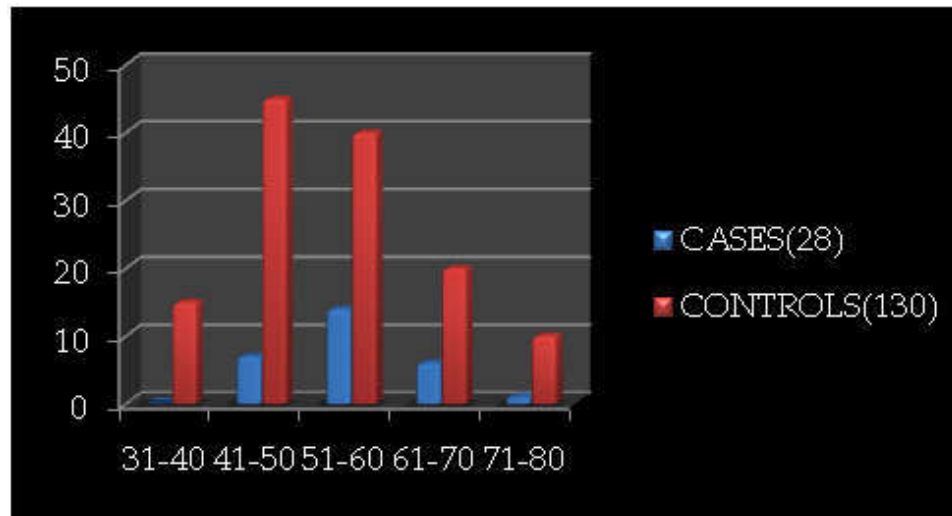
Statistical analysis

The data was collected and all the information was manually entered into an electronic spreadsheet file. Then the subsequent data processing and analysis was carried out. Descriptive statistics such as frequency and percentage were used for continuous variables such as age, Body Mass Index (BMI), gravidity and parity and categorical data variables were used such as disease status, presence of polycystic ovarian syndrome (PCOS), and obesity to provide an overview of the study population. Proportion per categories of the qualitative variable such as presence of PCOS, obesity, etc. was also described. Point and interval estimates of the proportion for those who underwent tubal ligation/salpingectomy was also determined. The exposure odds were computed to determine the association of the performance of said procedures among cases and controls. The odds ratio for the exposure and outcome of interest was determined.

Results

In our study a total of 28 cases and 130 controls were studied. The characteristics of both cases and controls are depicted in (Table 1). For cases majority of women at the time of diagnosis of the disease were aged between 51 to 60 and controls between 41 to 50 years as shown in (Graph 1).

Among all 28 cases, 10% were nulliparous,



Graph 1: Age groups of cases and controls

3% were uniparous and 87% were multiparous women. Among 130 controls 12% were nulliparous, 13% were uniparous and 75% were multiparous women. Among the benign conditions 14% had endometriosis, 9% had polycystic ovarian disease, 58% had fibroid and 19% had adenomyosis as depicted in (Table 1).

Table 1: Risk factors of both cases and controls

Risk Factors	Cases (28)	Controls (130)
31-40 Yrs	0	15 (11%)
41-50 Yrs	7 (25%)	45 (35%)
51-60 Yrs	14 (50%)	40 (31%)
61-70 Yrs	6 (21%)	20 (15%)
71-80 Yrs	1 (4%)	10 (8%)
Nulliparous	3 (10%)	16 (12%)
Uniparous	1 (3%)	17 (13%)
Multiparous	24 (87%)	97 (75%)
Tubal ligation	9 (32%)	55 (42%)
Obese	10	34
Endometriosis	-	18

PCOD	-	12
Fibroid	-	76
Adenomyosis	-	24

Of the eligible cases 9 (32%) out of 28 and 55 (42.3%) out of 130 controls had history of tubal ligation (Table 1). Among cases, epithelial subtypes most commonly identified were serous being 12, 8 cases of mucinous, 6 cases of endometroid and 2 cases had clear cell carcinoma. (Table 2).

Table 2: Histological subtypes of the cases studied.

Histological Subtypes	Cases	Percentage
Clear cell	2	7
Endometroid	6	21
Mucinous	8	29
Serous	12	43

The association of tubal ligation and subtype of epithelial ovarian carcinoma in patient's less than 35 years of age showed 1 out of 12 serous, 2 out of 8 mucinous and 1 out of 6 endometroid, whereas



Graph 2: Association of tubal ligation / salpingectomy and subtype of ovarian carcinoma

patient's with age more than 35 years showed 3 out of 12 serous, 1 out of 8 mucinous and 1 out of 6 endometrioid malignancy. (Table 3) & (Graph 2)

Table 3: Tubal ligation and subtype characteristics.

Parameters	Serous	Mucinous	Endometrioid	Clear Cell
H/o salpingectomy	4	3	2	0
No H/o salpingectomy	8	5	4	0
Age during procedure				
Less than 35 yrs	1	2	1	0
More than 35 yrs	3	1	1	0
Time since tubal ligation				
1-10 yrs	0	0	0	0
10-19 yrs	2	0	1	2
20 yrs & above	2	3	1	0

The incidence of various histological ovarian carcinomas after the tubal ligation 10 years post procedure was nil, between 10-19 years 2 cases were serous, 1 was endometrioid and 2 were clear cell carcinoma. After 20 years post procedure 2 cases were serous and 3 cases were mucinous carcinoma (Table 3). The odds ratio of developing epithelial ovarian carcinoma increases by 1.54 times in the absence of previous tubal ligation.

Discussion

Epithelial ovarian carcinoma is the most lethal of the gynaecological malignancies. Despite better surgical techniques, and chemotherapy and other innovative techniques in the field of oncology there was no significant improvement in survival rate over recent decades. Hence it was necessary to determine a strategy to prevent ovarian tumours and detect cancer in early stage to reduce the burden of ovarian cancer on women's health and society. They are called 'silent abdominal tumors' as symptoms such as abdominal distension, early satiety due to the presence of ascites, and peritoneal / omental metastases occur late in the course of the disease. Periodic clinical examination, estimation of serum CA-125 level and transvaginal sonography are of significance in detecting ovarian cancers but these are not found to be perfectly effective [3].

1 to 6% of high-risk women undergoing risk reducing bilateral salpingo-oophorectomy (BSO) have pre-invasive lesions in the distal fallopian tubes. Hence removal of the fallopian tubes or cutting a segment of it may be a risk-reducing strategy as some of the ovarian cancers arise in the fallopian tubes [4].

'Pelvic serous carcinomas' are fallopian tubal, serous ovarian and peritoneal carcinomas. Tubal neoplasia is the primary lesion in high-grade serous pelvic carcinomas. These tumours originate in tubal fimbria as STIC and may spread to peritoneum and ovaries giving rise to serous ovarian and peritoneal carcinomas.

A meta-analysis study conducted by Cibula et al. in 2011 inferred that previous tubal ligation in women at average risk for ovarian cancer was associated with a 34% overall risk reduction; however, no significant risk reduction was seen in women with mucinous or borderline tumours [5].

A cohort study by Falconer et al in 2015, involving 2,51,465 Swedish women resulted in lower risk for ovarian cancer among women with previous salpingectomy (HR=0.65, 95% CI=0.52) compared to the unexposed population. With bilateral salpingectomy a 50% decrease in risk of ovarian cancer was found when compared with unilateral salpingectomy (HR= 0.35, 95% CI= 0.17 to 0.73) [6].

Several studies have shown that tubal ligation /salpingectomy reduces the risk of developing epithelial ovarian carcinoma. In a study by Madsen et al. in 2015, the procedure of tubal ligation decreased the overall cancer risk (odds ratios 0.87; 95% confidence interval 0.78-0.98) of epithelial ovarian tumours with the highest risk reduction associated with endometrioid cancer [7].

Two meta-analysis studies showed that tubal ligation reduces the risk of epithelial ovarian carcinoma. A meta-analysis was done by Rice et al. on 30 studies in 2012, on tubal ligation and 24 studies on hysterectomy from the year 1969 to 2011. It was found that tubal ligation decreases the risk of ovarian carcinoma with a relative risk of 0.70 (95% CI: 0.64, 0.75). The association between the tubal ligation and the ovarian cancer risk was stronger for endometrioid tumours (RR= 0.45, 95% CI: 0.33, 0.61) compared to serous tumours in secondary analysis of the study [8].

Our study also showed that without previous tubal ligation/salpingectomy procedure the odds of developing epithelial ovarian carcinoma increased by 1.54 times in the study subjects and the highest risk reduction for endometrioid tumours.

Conclusion

Amongst the gynaecological malignancies, epithelial ovarian carcinoma is the most lethal. Early stage neoplasms in the fimbriated end of the

fallopian tube could be the cause of development of ovarian carcinoma. Hence, the risk of development of ovarian carcinoma can be reduced by tubal ligation/salpingectomy. While planning an hysterectomy for benign lesions and in patients who are at average risk of ovarian cancer, tubal ligation/risk-reducing salpingectomy should be counselled regarding this option at the time of abdominal or pelvic surgery. Additional studies with a larger sample size over a period of at least 10 yrs will help find out the role of tubal ligation/risk-reducing salpingectomy procedure as a primary preventive strategy for women against ovarian cancer.

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