A Study of Morphological Changes in the Cases of Fallopian Tubes in Ovarian Surface Epithelial Serous Tumours in Tertiary Care Hospital

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ABSTRACT

BACKGROUND AND AIMS

In the past decade origin of high grade serous carcinoma of ovaries has its origin from the clonal expansion of the secretory cells of the distal fallopian tube. We have tried to see the relationship based on morphological and immunohistochemically studies of the lesion known as "Serous Tubal Intraepithelial Carcinoma" (STIC), which resembled high grade serous carcinoma of ovary. To study the association between ovarian surface epithelial serous tumours and STIC.

MATERIALS AND METHODS

We studied 143 consecutive cases of ovarian surface epithelial serous tumours retrospective and prospective study from July 2009 to June 2019, which includes 99 cases of benign serous cyst adenomas, 8 were borderline and 36 were high grade serous carcinomas of ovary. Complete examination of the fallopian tubes from each case was done according to serial Sectioning and Extensive Examination of Fimbria (SEE-FIM) protocol from July 2009. Immuno-staining for p53 was done on sections from ovary and fallopian tube.

RESULTS

STIC lesions was identified in fallopian tubes from 9 cases of high grade serous group (25 %) while no STIC was identified in non-high grade serous group. Fimbrial end of fallopian tube were involved in all the cases. Results are compared using chi square test. A statistically significant association was found between high grade serous carcinoma group and STIC (p=0.003)

CONCLUSION

STIC coexists with a significant number of high-grade serous carcinoma of ovary cases and further studies are needed to detect STIC in early stages of high grade serous carcinoma of ovary.

KEYWORDS

High Grade Serous Carcinoma (HG-SC), Serous Tubal Intraepithelial Carcinoma (STIC), Fallopian tube, SEE-FIM, Tumours retrospective

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INTRODUCTION

Ovarian carcinomas are the most lethal cancers in female population. The presentation is usually in the stage III. The reason being no proper screening for the early detection and minimal symptoms to detect the disease.

Serous tumours of the ovary are the most common type of epithelial tumours. They account for 30 % of all ovarian neoplasm and more than 60 % of malignant epithelial tumours. Out of 30 %, 60 % are benign, 10 % are borderline and 30 % are malignant tumours. The average age of serous carcinomas is mid to late 50's.

It is clear that poor understanding the pathogenesis of surface epithelial serous tumours has led to difficulty in early detection. Although many theories have put forth for describing the how the mesothelium has undergo metaplasia and dysplasia, but there is poor understanding about the precursors of high grade serous carcinoma of ovaries. For decades research for high grade serous carcinoma of ovary was on ovary. In spite of early detection the survival has not improved. In recent years histopathological studies have proved beyond doubt that the sources of most high grade serous ovarian carcinomas are fallopian tube mucosa. The basis of this hypothesis was the finding of the Serous Tubal Intraepithelial Lesions (STIC) in the fimbrial part of the fallopian tubes. STIC lesions has morphological and immunohistochemical similarities with high grade serous ovarian carcinomas. To support this hypothesis, STIC was also detected in the fallopian tube mucosa of women who do not have genetic predisposition for ovarian carcinoma.[1-5]

MATERIALS AND METHODS

The study was conducted in the department of pathology, Sri Dharmasthala Manjunatheshawara college of medical sciences and hospital, Dharwad, India, during the year 1st July 2009 to 30th June 2019. Study period was 10 years. Of the total 143 cases of ovarian surface epithelial serous tumours, 99 cases were benign, 8 were borderline, and 36 were High grade serous carcinomas of ovary. The specimens received were fixed in 10 % formalin for histopathological examination. Specimens are sectioned and examined and processed according to standard guidelines. The fallopian tube is examined according to SEE-FIM protocol. Representative sections from fallopian tubes were processed for H and E and p53.[6]

SEE-FIM protocol was not applied to cases from July 2009 to June 2017.[7]

Tubal intra epithelial lesions were first studied by morphology followed by p53 immunostaining.[8]

RESULTS

Total of 143 ovarian serous epithelial tumours were studied out of these 99 benign tumours and 8 border line tumours didn't show any changes in fallopian tube. Total of 36 high grade serous carcinoma were studied. The age group of HGSC ranged from 23 years to 78 years. Common age group of HGSC is peri and post-menopausal age group. The lesions were seen in 5th decade followed by 4th and 6th decade. Tubal lesions were situated in the fimbrial end of the fallopian tube in 9 cases (25 %) with a p value of 0.003 which is significant (Tables 1-3).[9]

Age	No. of cases	Percentage
20-30	2	5.6
31-40	2	5.6
41-50	9	25
51-60	12	33.2
61-70	9	25
71-80	2	5.6
Total	36	100 %

Table 1. Distribution of HGSC of Ovary in Different Age Group.

	Fallopian tube - UR (UR-unremarkable)	Fallopian tube - STIC	Total
HGSC	27	9	36
%	75	25	100

Table 2. STIC Lesions in HGSC of Ovary.

Surface Epithelial Serous Tumours	Cases	%
Benign	99	69.2
Borderline	8	5.6
High grade serous carcinoma	36	25.2
Total	143	100

Table 3. Surface Epithelial Serous Tumours of Ovary.

DISCUSSION

Emergence of clinical pathological and molecular findings there is a strong evidence supporting HGSC arise from the clonal expansion of secretory cells in the fallopian tubes.

Examinations of prophylactically removed fallopian tubes showed salphingo-oophorectomy specimens from BRCA mutations carrier showed STIC lesions in the fimbrial part of the fallopian tube.[10]

Pick et al., were the first to describe "dysplastic changes or tubal dysplasia" in BRCA mutated carriers later these lesions were called STIC lesions.[11]

Many later studies confirmed the presence of STIC in the fallopian tube mucosa of BRCA mutation carriers underwent prophylactic salphingo-oophorectomy procedures. Incidence of STIC in these studies was between 2 % to 17 % and STIC was typically located in fimbrial part of the fallopian tube. Kindelberger et al., conducted the study on serous carcinoma he studied 55 cases of serous carcinomas in which they found 53 % of STIC lesions in the fallopian tubes. They correlated TP53 mutation in STIC lesions and ovarian serous carcinomas which showed both same mutations confirming the fallopian tube origin etiology.[12]

Another study by Roh et al., examined 85 high grade serous carcinomas of ovary and found 36 % of STIC correlations.

In a study done by Przybycin et al., 47 high grade serous carcinomas of ovary and found 60 % showed STIC lesions.

In a study done by Diniz et al., 32 ovarian serous carcinomas of ovary and found 13 % of STIC correlations.

In a study done by Tang et al., from Canada 39 ovarian serous carcinomas and found 31 % of STIC lesion in fallopian tubes.

In a study done by Koc et al., 34 ovarian serous carcinomas

and found 38 % STIC correlations.[13]
In study done by Howitt et al., 58 cases of High grade serous carcinomas were studied in that 50 % of STIC lesions were reported.[14]
In study done by Seidman et al., 64 High grade serous carcinomas were studied and showed 40 % of STIC correlations.
In a study done by Munakata et al., 55 serous tumours out of which 23 were High grade serous carcinoma, 8 were borderline, 23 were adenoma are studied in which showed 21 % STIC lesions in the fallopian tubes.[15]
In a study done by Malmberg et al., 18 serous ovarian carcinomas were studied in which showed 33 % of STIC lesions.
From the above findings and many other similar findings give strong evidence to the hypothesis that STIC which is always present in the fimbria, may be the origin site of high grade serous ovarian carcinoma in both BRCA mutation as well as sporadic ovarian cancer.[16]
In our study we examined 36 cases of ovarian carcinoma for which bilateral Salpingo-oophorectomy was done.
Intra epithelial lesions are first assessed by morphology, followed by immunohistochemistry for p53 (Figures 1-4).

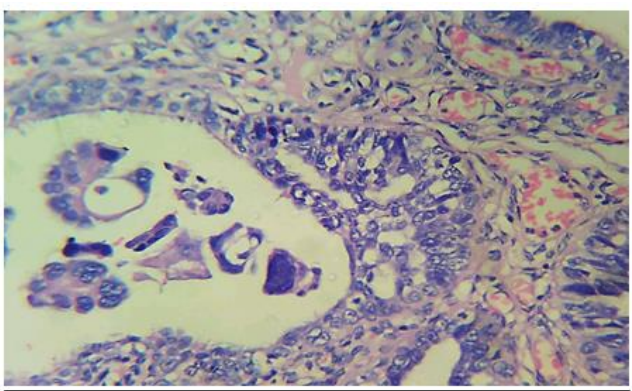

Figure 1. STIC Cells with Increased N: C Ratio with Prominent Nucleoli. Tumour Cells in Lumen. H and E 40x

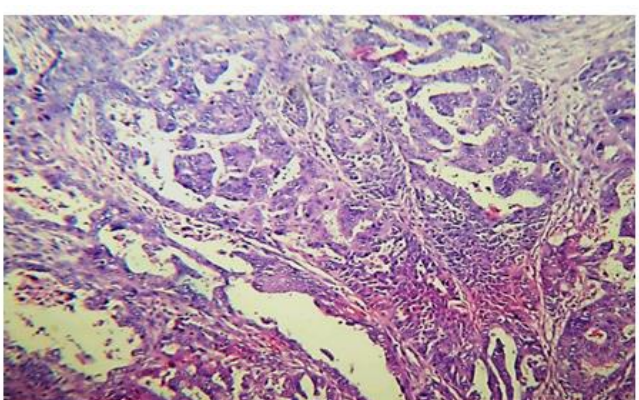

Figure 2. STIC Lesion in Fallopian Tube. H and E 10x.

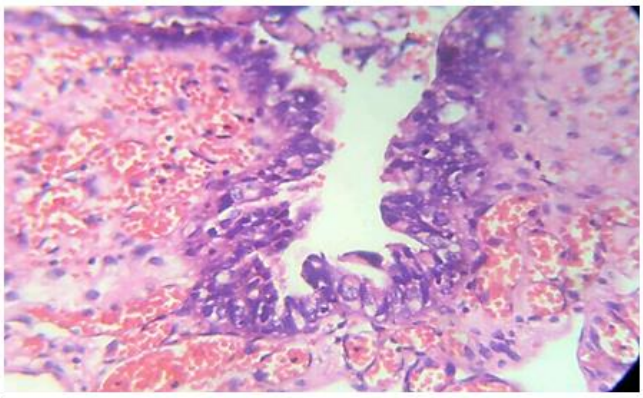

Figure 3. STIC Cells with Increased N: C Ratio with Prominent Nucleoli. H and E 40x.

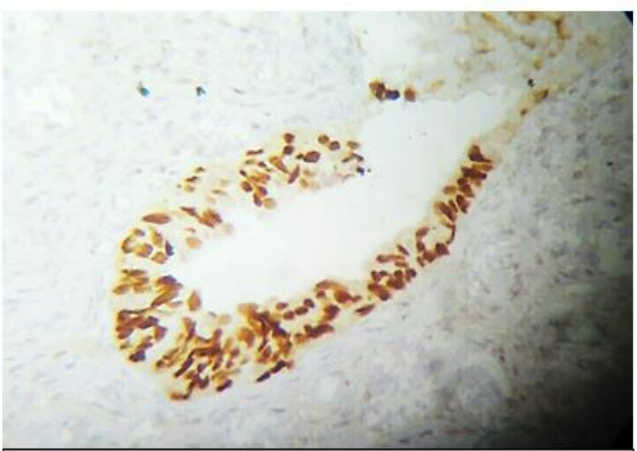

Figure 4. STIC Lesion in Fallopian Tube. IHC P53. 40x.

The approach in our study was proposed by Vang and Bogaerts et al., as described below
For morphological interpretation of STIC following cytological abnormalities were noted.[17]

- Increased nuclear cytoplasmic ratio.
- Nuclear pleomorphism.
- Disordered growth.
- Increased mitosis.
- Absence of ciliated epithelium.
- Presence of large nucleoli.

If these abnormalities in the fallopian tubes are found they are taken as STIC lesions. If these are not present they are considered as no STIC lesions.[18]
On performing IHC two patterns are considered as positive for nuclear stain.

- More than 75 % cells in the lesion show diffuse strong positivity for p53 (Nuclear stain).
- Total absence of staining (0 % labelling index) which is due to mutated abnormal protein.

Both the above pattern of p53 staining were considered positive, while lesion showing weak nuclear staining or cytoplasmic staining considered negative.
For the foci that is morphologically not suspicious for STIC is considered p53 positivity are called p53 signatures having

- Strong nuclear staining-darkening from nuclear detail.
- More than 12 adjacent nucleus.

- Morphologically normal epithelium.

If the above criteria are met (morphology and p53) tubal lesions are diagnosed as STIC and if only p53 positivity they are diagnosed as p53 signatures.
A statistically significant association of STIC with high grade serous carcinoma of ovary was seen in our study indicating that "STIC represent an exclusive feature of high grade serous carcinoma of ovaries".[19]
Further study is required for early detection of STIC lesions for preventing High grade serous carcinomas of ovaries and also for treatment.

For STIC detection, no methods are available apart from surgical resection, in future screening of epithelial ovarian carcinoma may come by biomarker identification and newer screening methods for STIC. That's why more and more studies are needed to understand better about the pathogenesis of high grade serous carcinomas.
BRCA related carcinomas of ovary originate in fallopian tube. Risk reducing salpingectomy in young patients should be regularly followed up for management purpose.[20-22]

CONCLUSION

Serous tubal intraepithelial carcinoma was identified in the fallopian tubal epithelium of an established high grade serous ovarian carcinoma. However accurate estimate of the fraction remains to be detected.
Our study supports the hypothesis of fallopian tube being the origin of fraction of high grade serous ovarian carcinomas.

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