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Original Article

Pathology Section

Histopathological Study of Incidental or Opportunistic Salpingectomy Specimens and the Association of Tubal and Ovarian Lesions in South Eastern Nigeria

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ABSTRACT

Introduction: There is heightened interest on the fallopian tube in recent times. Most reports on the subject emanate from western countries thus data on fallopian tube is lacking in Nigerian and African populations.

Aim: To establish the histopathological status of grossly normal fallopian tube specimens and the pattern of gynaecological disease contributing to concomitant resection of normal fallopian tube and to determine if there are any association between tubal and uterine and or ovarian lesions.

Materials and Methods: The study was a prospective cross-sectional study of incidental fallopian tubes received at University of Nigeria Teaching Hospital and Enugu State University Teaching Hospital from 1st January 2012 to 31st December 2014. The Haematoxylin and Eosin (H&E) stained sections of the entire tube were examined. Statistical analysis was done using IBM SPSS software version 20.0. Measures of central tendency and variation were calculated for numerical variables while frequency and proportions were calculated for categorical variables. Fisher's-Exact and chi-square tests were done as appropriate.

Results: Fallopian tubes from 120 female subjects were studied. The mean age of the women was 48.7±10.1 (range: 26-79) years. Sixty one out of the 120 women (61/120, 50.8%) had fallopian tubes within normal limits. Eighty lesions were identified in fallopian tubes of 49.2% (59/120) of the women. No case of Serous Tubal Intraepithelial Carcinoma (STIC) was diagnosed. Statistically significant association was seen between ovarian sex cord stromal tumours and moderate to marked epithelial hyperplasia of the fallopian tube ($p<0.001$).

Conclusion: Extensive sampling protocol revealed identifiable pathological, mostly benign lesions in 49.2% of grossly normal fallopian tubes. Diseases of the uterine corpus, particularly uterine leiomyoma, were the commonest cause of incidental fallopian tube resection.

Keywords: African population, Fallopian tube, Gynaecological disease, SEEFIM protocol

INTRODUCTION

The fallopian tube is a part of the female gynaecological tract eponymously named after Gabriele Fallopius who in 1561 correctly described its anatomical course [1]. Its bland macroscopic appearance belies; the very crucial role it plays in the propagation of human species. It acts as conduit between the ovaries and the uterine cavity and also provides suitable microenvironment for final gamete maturation, fertilization and early embryonic development [2]. From the stand point of pathology, fallopian tube lived in the shadows of other segments of the female gynaecological tract before the year 2000. It contributed far less pathology in routine surgical pathology practice than the ovary, uterine corpus, endometrium or cervix. However, from around the year 2000 till date, the fallopian tube has remained a subject of intense study and scrutiny following the discovery that it could be the source of high grade epithelial ovarian cancer, the most lethal of all gynaecological malignancies.

The advent of fallopian tube as object of concerted research interest was perhaps serendipitous given that the focus of investigations which revealed its crucial importance was the ovary. The practice of risk-reducing prophylactic oophorectomy at 35 years or after childbearing for women genetically predisposed to ovarian cancer had evolved following the recognition of the ineffectiveness of ovarian cancer screening measures and the persistence of high ovarian cancer mortality [3]. Histopathologic study of prophylactically resected salpingo-oophorectomy tissue in this class of women, in search of precursors of ovarian cancer, found a preponderance of serous intraepithelial carcinoma in the fallopian tube rather than the ovary. Beginning with a 2001 paper by Piek JMJ et al., [4], through several subsequent works [5, 17], evidence were incrementally elaborated to the effect that majority of pelvic serous cancers arise from a lesion in the fallopian tube now called Serous Tubal Intraepithelial Carcinoma (STIC).

The fallopian tube specimens we receive in our practice are usually in the form of segmental salpingectomy tissue from bilateral tubal ligation, tubal ectopic gestation and incidental salpingectomy tissues resected together with other diseased segments of gynaecological system. Authors do not yet have cases in the prophylactic category. This present study was carried out to generate and analyse data on the fallopian tube in a Nigerian population. It focused solely on tubes removed during surgery for other gynaecological conditions. These tubes are incidental fallopian tubes from women undergoing surgery for reasons other than tubal pathology. Because of the normal gross appearance of these tubes, their sampling and examination in routine practice are often perfunctory. This study was aimed at a more thorough assessment of the histopathological status of this category of fallopian tubes by the use of extensive sampling procedure, seeking to determine among other concerns, if STIC occurred with any meaningful frequency in them. Authors also sought to determine if there is any association between histopathological lesions of the fallopian tube and that of the other segments of the gynaecological tract as well as the pattern of gynaecological pathologies contributing to incidental salpingectomy.

MATERIALS AND METHODS

The study was a prospective cross-sectional study of all qualified fallopian tube specimen submitted to the histopathology laboratories of University of Nigeria Teaching Hospital (UNTH) Enugu and Enugu State University Teaching Hospital (ESUTH) from January 2012 to December 2014. In all, fallopian tubes from 120 subjects were studied. Seventy five cases were from UNTH and 45 came from ESUTH. Ethical clearance was obtained from University of Nigeria Teaching Hospital Health Research Ethics Committee (NHREC/05/01/2008B-FWA00002456-1RB00002323). All fallopian tubes resected in the course of surgery for gynaecological conditions of the cervix, uterine corpus or ovaries and obstetric emergencies like ruptured uterus were included as in these conditions the fallopian tube was not the primary site of the offending pathology and salpingectomy was thus incidental. Segmental salpingectomy tissues of bilateral tubal ligation and tubal ectopic pregnancies were excluded. Tubal ligation and ectopic pregnancy specimens fall outside the definition of incidental salpingectomy and were thus excluded. Also, tubal ligation specimens are incomplete segments of tubes which lack fimbriated end and so cannot be examined by the Sectioning and Extensively Examining the Fimbriated End (SEEFIM) sampling protocol adapted in this study.

Patient's biodata and clinical information were extracted from the requisition forms. The primary lesion which prompted the surgery was grossly examined and sampled according to routine histopathological gross examination procedures. The fallopian tubes were sampled using SEE FIM protocol in order to ensure optimal histological evaluation [18].

As per the protocol the distal 2 cm (the fimbrial end) of the fallopian tube was amputated from the rest of the tube and sectioned longitudinally. The remainder of the tube was cut in cross sections (bread loafed) at 2-3 mm interval. The entire specimen was submitted for processing.

This sampling technique ensured that the surface epithelium of the fimbria is extensively exposed since in situ/early neoplastic epithelial lesion was most often seen in the fimbriae.

All the sections were stained with Haematoxylin and Eosin and the slides were studied by three of the investigators to arrive at the diagnoses. Lesions were diagnosed and classified based on the criteria established in two reference texts [19,20].

STIC is defined as focal replacement of normal fallopian tube epithelium by cells with malignant features [13,15,21].

STATISTICAL ANALYSIS

Data obtained were analysed using frequency and cross tabulation procedures in IBM SPSS software version 20.0 for windows. Measures of central tendency and variation were calculated for numerical variables while frequency and proportions were calculated for categorical variables. The chi-square and Fisher's-Exact tests were done as appropriate. An alpha level of 0.05 was used for all statistical tests.

RESULTS

Fallopian tubes from 120 female subjects were studied. The mean age of the women was 48.7±10.1 (range: 26-79) years. Majority (71%) of the patients were within the age group of 40 to 59 years [Table/Fig-1].

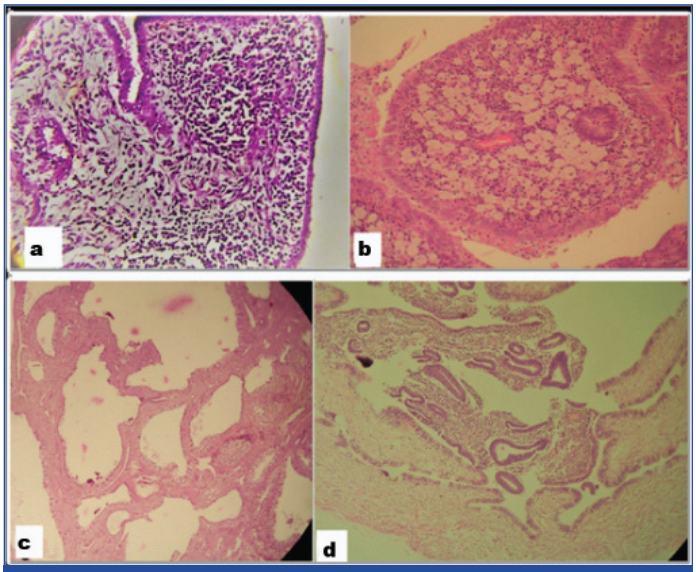
[Table/Fig-2] show the spectrum of histopathological diagnoses in the fallopian tubes. Sixty one out of the 120 women (61/120, 50.8%) had fallopian tubes within normal limits. Eighty pathological lesions were diagnosed in fallopian tubes of 59 women. This number represented 49.2% (59/120) of all cases studied. Mucosal epithelial proliferations consisting of moderate to marked epithelial hyperplasia together with atypical epithelial hyperplasia constituted 43.7% (35/80) of the lesions diagnosed. Fifteen cases of chronic salpingitis were seen representing 18.8% (15/80) of all lesions. The histo-morphological forms of salpingitis diagnosed included salpingitis with prominent lymphoid follicles as well as chronic follicular salpingitis [Table/Fig-3]. One case of Invasive serous adenocarcinoma of the fallopian tube was seen [Table/Fig-4]. This case clearly showed a point of transition from benign to malignant epithelium and associated small tumour deposits on the ovarian surface. Secondary involvement of the fallopian tube by carcinoma was detected in 3.3% (4/120) of the women studied. Reckoned as percentage of lesions diagnosed, secondary involvement or metastases constitutes 5% (4/80). The primary tumour in two of these cases was endometrial carcinoma and the remaining 2 cases

Age group (years)	Frequency	Percent
≤29	4	3.3
30-39	15	12.5
40-49	41	34.2
50-59	44	36.7
60-69	12	10.0
70+	4	3.3
Total	120	100.0

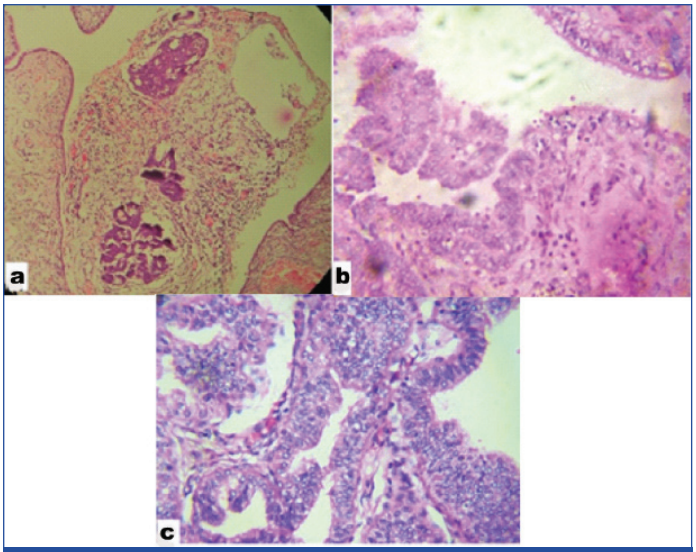
[Table/Fig-1]: Age group distribution of women undergoing total abdominal hysterectomy with salpingectomy.

Pathology	Frequency (%)
Atypical epithelial hyperplasia	6 (7.5)
Marked epithelial hyperplasia	11 (13.6)
Moderate epithelial hyperplasia	18 (22.5)
Chronic salpingitis	15 (18.8)
Invasive serous adenocarcinoma	1 (1.3)
Metastatic carcinoma	4 (5.0)
Endometriosis	2 (2.5)
Squamous metaplasia	2 (2.5)
Wolffian remnant	6 (7.5)
Paramesonephric cyst	14 (17.5)
Walthard nest	1 (1.3)
TOTAL	80 (100)

[Table/Fig-2]: Histopathologic lesions diagnosed in the fallopian tubes*.
*Eighty (80) lesions were diagnosed in the fallopian tube of 59 women because two different classifiable histologic lesions were present in 21 women.



[Table/Fig-3]: a) A photomicrograph of chronic salpingitis. The stroma of the fallopian tube is infiltrated with chronic inflammatory cells predominantly lymphocytes; b) A photomicrograph showing chronic xanthogranulomatous salpingitis. The stroma is infiltrated with foamy macrophages and plasma cells; c) A photomicrograph showing chronic follicular salpingitis. The plicae are fused to form a pseudoglandular pattern; d) A photomicrograph showing endometriosis in the fallopian tube. (H&E; original magnification 100X).



[Table/Fig-4]: a) A photomicrograph showing secondary involvement of the fallopian tube by metastatic carcinoma; b) A high power photomicrograph showing primary high grade serous adenocarcinoma of the fallopian tube; c) A high power photomicrograph showing marked epithelial hyperplasia of the fallopian tube. Marked epithelial stratification is present but ciliation is retained precluding the diagnosis of serous tubal intraepithelial carcinoma (H&E stain; original magnification x400).

had high grade serous adenocarcinoma of the ovary. The secondary involvement was present as tubal serosal implants or luminal tumour. Atypical epithelial hyperplasia was diagnosed in 6 (5%) of women studied. It constituted 7.5% (6/80) of all lesions diagnosed. None of the cases of atypical hyperplasia met the criteria for diagnosis of serous tubal intraepithelial carcinoma thus no case of STIC was diagnosed in this series.

[Table/Fig-5,6] show the gynaecological tract lesions which prompted the surgical procedure in which the fallopian tubes were incidentally removed. A total of 154 pathologic lesions were seen in the 120 cases. Overall, 75.3% (116/154) of the gynaecological tract lesions were benign while 24.7% (38/154) were malignant. Categorisation of these lesions according to specific gynaecological organs shows that 103 (66.9%) were lesions of uterine corpus, 38 (24.7%) were lesions of the ovary and 13 (8.4%) were lesions of the cervix. Uterine leiomyoma was by far the most common disease leading to hysterectomy, accounting for majority (63/154, 41%) of the lesions provoking total abdominal hysterectomy with salpingo-oophorectomy.

	Frequency
Leiomyoma	63
Endometrial carcinoma	6
UV prolapse	5
Endometrial hyperplasia	9
Adenomyosis	4
Chronic endometritis	4
Leiomyosarcoma	3
Clear cell carcinoma	2
Uterine rupture	2
Malignant mullerian mixed tumour	1
High grade serous carcinoma	1
Low grade serous carcinoma	1
Endometrial polyp	1
Endometrial stromal sarcoma	1
TOTAL	103

[Table/Fig-5]: Diseases of uterine corpus contributing to incidental salpingectomy.

Statistically significant association (Fisher's-exact test; p<0.001) was demonstrated between sex cord stromal tumours of the ovary and moderate to marked epithelial hyperplasia of the fallopian tube. Out of 13 cases of sex cord stromal tumours of the ovary, moderate to marked epithelial hyperplasia was present in the accompanying fallopian tubes of 11 cases. Similarly, statistically significant relationship was seen to exist between endometrial hyperplasia and moderate to marked epithelial hyperplasia (Fisher's-exact test; p=0.006). No statistically significant relationship existed between uterine leiomyoma and moderate to marked epithelial hyperplasia (chi-square: χ^2 (1)=0.27, p=0.60) or uterine leiomyoma and chronic salpingitis (chi-square: χ^2 (1)=0.39, p=0.53).

Gynaecologic organ	Histological diagnosis	Frequency
Ovary	Follicular cyst	14
	Granulosa cell tumour	9
	High grade serous adenocarcinoma	4
	Corpus luteum cyst	3
	Transitional cell carcinoma	1
	Mucinous cystadenocarcinoma	1
	Sertoli-Leydig cell tumour	1
	Sclerosing stromal tumour	1
	Fibrothecoma	1
	Cellular fibroma	1
	Serous cystadenoma	1
	Embryonal carcinoma	1
Cervix	CERVIX	
	Squamous cell carcinoma	4
	CIN*	3
	Chronic cervicitis	3
	Clear cell carcinoma	1
	Lymphoepithelioma-like carcinoma	1
	Endocervical gland hyperplasia	1
Total		51

[Table/Fig-6]: Diseases of the Ovary and Cervix contributing to incidental salpingectomy.

DISCUSSION

This present study was undertaken in a Nigerian population to ascertain the histopathological status of a common group or subset of fallopian tube specimen (incidental salpingectomies) in a histopathology laboratory and determine, among other concerns, if (STIC) occurred with any reasonable frequency in these tubes. The report by Piek JMJ et al., was crucial in its recommendation for closer scrutiny of the fallopian tube in ovarian cancer research [4]. In their study of occurrence of (pre)neoplastic lesions in overtly normal fallopian tubes from women predisposed to developing ovarian carcinoma, they found preponderance of dysplasia in the fallopian tubes and thus recommended that the fallopian tube should attract closer attention [4].

A major contributor to identification of dysplasia or STIC in the fallopian tube has been the SEE-FIM (Sectioning and Extensively Examining the Fimbriated End) protocol [18]. Authors do not know of any study emanating from Nigeria or Sub-Saharan Africa which utilised the SEE-FIM protocol. The only histopathological study of the fallopian tube in an African population, to the best of our knowledge, is by Izegbu MC et al., who retrospectively reviewed the slides of all fallopian tube specimens received at the Lagos State University Teaching Hospital over a 4 year period [22]. The tissues had been sampled by conventional method which entails examination of 1-3 sections per tube.

As shown in the result of our study, there were pathologic lesions in 49% (59/120) of the cases. Fifty one percent of the tubes were histologically within normal limits on H&E. This finding stands in sharp contrast to the report by Izegbu MC et al., who in a retrospective analysis of all fallopian tubes submitted to a teaching hospital over a 4-year period observed no pathologic lesion in the fallopian tubes

of total abdominal hysterectomy with salpingectomy specimens (the category of specimen investigated in this present study) [22]. The disparity in finding may be explained by differences in study and sampling methods-theirs was a retrospective review of conventionally sampled fallopian tubes while ours is a prospective study employing extensive (SEE-FIM) sampling protocol. The findings of this current study thus, suggest that extensive sampling will reveal some identifiable pathological process in a good number of the incidental salpingectomy tissues. Fortunately, most of the identified lesions are not of malignant nature suggesting that the cost of such elaborate sampling protocol should be weighed against clinical benefit in any future institutional change in gross examination policy. However, we identified for cases of metastatic carcinoma of the fallopian tube which translated to fallopian tube involvement in 23.5% (4/17) of endometrial and ovarian carcinoma. This finding seems to reinforce an earlier recommendation that all tissues of both fallopian tubes in cases of ovarian, peritoneal and endometrial serous carcinomas be routinely submitted for histopathological analysis [19].

Epithelial hyperplasia (mucosal epithelial proliferation) of the fallopian tube which was a common finding in the present study had been the subject of a number of previous studies in the past and till date its clinical significance has remained unsettled with various researchers expressing varying opinions. An earlier work [23] concluded that it is a frequent finding of no clinical significance. Robey and Siva [24] found it to be associated with ovarian serous tumours of low malignant potential, a finding which could not be sustained by the work of Yanai I et al., [25]. However, Kurman RJ et al., identified a variant of tubal epithelial hyperplasia designated papillary tubal hyperplasia which showed strong association with borderline serous tumours of the ovary being present in 91% of fallopian tubes resected with such borderline tumours [26].

The studies by Yanai I et al., tried to standardise the diagnosis of epithelial proliferation of the fallopian tube, grading it into mild, moderate and marked (severe) categories by well-defined criteria [25]. They observed that mucosal epithelial proliferation of moderate to marked degree occurred in 25-40% of the tubes and with this came their recommendation that 'only moderate to marked mucosal epithelial proliferation should be considered a diagnosable lesion in the future'.

The current study identified moderate to marked epithelial hyperplasia of the fallopian tube in 24.2% of the tubes, a figure which is close to that of Yanai I et al. Tubal epithelial proliferation has been anecdotally associated with salpingitis as well as endogenous and exogenous oestrogen [25]. However, none of the patient in our study had any history of hormonal drug intake. Further studies on the role of oestrogen and even multi-parity in the genesis of proliferative epithelial lesions of the fallopian tube is warranted as this is currently not well covered in literature.

Six cases of atypical epithelial hyperplasia were seen in the 120 subjects studied. In these cases, the tubal epithelium had some cytological atypia but did not meet the strict criteria required for diagnosis of STIC. Thus, no STIC was diagnosed in this study. This is not entirely surprising as STIC is more frequently seen in women at high risk for serous ovarian cancer. These are women with family history of breast and/or ovarian cancer or germline mutations of BRCA1 and BRCA2 genes. A systematic review of studies found that coexistence of STIC with high grade serous cancers ranged from 11% to 61% (mean: 31%, 95% CI: 17-46%) [27]. Meserve EEK et al., and Rabban JT et al., reported on the prevalence of serous tubal intraepithelial carcinoma in women without a genetic risk or history of high grade serous carcinoma [28,29]. In the two studies, the prevalence of STIC among this category of subjects was 0.1% (2/1747) and 0.8% (4/522) respectively. Present finding of no STIC was in the general population as our subjects were not stratified by presence or otherwise of increased risk of hereditary breast or ovarian cancer. Tang S et al., studied association of STIC with various conditions and reported no STIC in any of 74 cases of non-serous endometrial malignancies, 15 non-gynaecologic malignancies and 90 cases of benign conditions [12]. The small size of our study may have contributed to non-diagnosis of any STIC in our study. Also noteworthy is the report by Mahe E et al., that multiple deeper level sections of SEE-FIM blocks increased detection of STIC by 25% [30].

LIMITATION

The study is limited by size. A larger sample size would have improved the study's precision and external validity. Another limitation is that of denudation of focal areas of tubal epithelium, a known sequel of surgical and histopathological handling. This might have led to some degree of under diagnosis. In spite of these limitations, the study is relevant as it has started the process of filling the knowledge gap on histopathological profile of apparently normal fallopian tubes among Nigerian women and SSA population in general. The strength of this study, however, lies in its prospective design, with reduced likelihood of missing or incomplete data. Furthermore, the study utilized the SEE-FIM protocol which is a more extensive technique with higher sensitivity and specificity than the traditional or conventional sampling approach.

CONCLUSION

This study has shown that uterine leiomyoma is responsible for over half of the incidental salpingectomies in Enugu, Nigeria. With extensive sampling, an identifiable pathological process could be found in up to 49% of cases. Most of the lesions detected were mostly inconsequential. STIC, a lesion described in subjects at high risk of developing ovarian cancer seems to be of low prevalence in the general population, though studies employing larger sample size are needed to arrive at a more certain conclusion. Sex cord stromal tumour of the ovary showed strong association with epithelial hyperplasia of the fallopian tube.

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