

Annals of Health Research



IN THIS ISSUE

- Beta Lactamase-Producing Bacteria
- Insulin Resistance
- Cardiac Diseases in Pregnancy
- Antibiotic Prescription
- Antenatal Care Services
- Epithelial Ovarian Tumours
- Low Back Pain
- Regional Anaesthesia in Children
- Somatisation
- Nigella sativa and Essential Tremor
- Neonatal Conjunctivitis
- Long Term Non-Progressive HIV Infection

PUBLISHED BY THE MEDICAL AND DENTAL CONSULTANTS ASSOCIATION OF NIGERIA, OOUTH, SAGAMU, NIGERIA.

ORIGINAL RESEARCH

Clinicopathologic characteristics of epithelial ovarian tumours in Ile-Ife, Nigeria

Anjorin AO*1, Omoniyi-Esan GO2, Odujoko OO2, Anjorin AO3

¹Department of Histopathology, University of Medical Science Teaching Hospital /Hospitals Management Board, Akure, Ondo State, Nigeria.

²Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria.

³Department of Family Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria.

*Correspondence: Dr AO Anjorin, Department of Histopathology, University of Medical Science Teaching Hospital/Hospitals Management Board, Akure, Ondo State, Nigeria. Email: dranjie@gmail.com;

ORCID - https://orcid.org/0000-0002-0466-4731.

Abstract

Background: Epithelial ovarian tumours (EOT) have complex clinicopathologic characteristics and biological behaviours. There are benign, borderline and malignant ovarian tumours and the commonest ovarian tumours in many regions are of epithelial origin. Many studies have described the histomorphological characteristics of the tumours.

Objective: To describe the clinical and histopathological features of epithelial ovarian tumours.

Methods: This was a retrospective review of the histopathology reports of all epithelial ovarian tumours specimens submitted to the Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospital, Ile-Ife from January 2005 to December 2014. The EOT cases were described in terms of age, clinicopathological characteristics and distribution of histological types.

Results: The frequencies of benign, borderline and malignant EOTs were 41.2%, 3.9% and 54.9% respectively and the patients were aged 23 to 94 years (mean 46.5±2.6 years). The majority of cases were often asymptomatic.

Conclusion: Abdominal swelling was the most common presenting complaint while serous ovarian tumours were the most preponderant histological types.

Keywords: Clinico-pathology, Epithelial ovarian tumours, High-grade serous carcinoma, Ile-Ife, Ovarian neoplasm.

Introduction

Histological diagnosis of ovarian tumours is done by classification according to the most probable tissue of origin as follows: surface epithelial, germ cell, sex cord stromal, androblastoma, lipoid cell tumour, soft tissue tumours not specified to the ovary, metastatic tumours and tumour-like conditions. The most common types are the surface epithelial tumours which are followed by the germ cell and sex cord-stromal types as reported by many studies in Nigeria.

The epithelial ovarian tumours (EOT) have complex clinicopathologic characteristics and biological behaviours with a variety that includes benign, borderline and malignant ovarian tumours. The commonest ovarian tumours in many regions are of epithelial origin, accounting for about 40-60%.^[1,2] These tumours include serous, mucinous, endometroid, clear cell and Brenner subcategories.

Lately, mixed varieties of these groups were found to exist such as sero-mucinous ovarian tumours, [3-5] likewise metastatic tumours to the ovaries. [6-8] Therefore, the nature of the cells and cellular origin of EOTs should be assessed histologically and the differentiation determined diligently as it plays a significant role in determining the aggressiveness of these tumours and subsequent prognostic indices for patient management and survival. The clinical presentation of patients with these tumours also varies as most are asymptomatic with unpredictable aggressiveness. an Therefore, and prognosticating putting patients into treatment categories to identify those likely to respond to chemotherapeutic drugs becomes an almost impossible task without a proper histopathological appraisal of the tumours. [9,10]

In this study, the clinicopathological characteristics of epithelial ovarian tumours in a tertiary health institution were examined.

Methods

This was a retrospective observational study of EOT cases managed at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria over ten years from January 2005 to December 2014. The original examination request cards were retrieved and studied. The biodata and the clinical details of the patients along with macroscopic and microscopic descriptions of the tumours were recorded. Formalin-fixed blocks paraffin-embedded (FFPE) previously diagnosed epithelial tumours from the departmental archive were reviewed. Non-epithelial primary ovarian cancer,

ovarian metastatic cancer and primary ovarian

epithelial neoplasm, in which slide sections were unsuitable, or tissue blocks were unavailable, were excluded from the study. Biopsies were obtained from patients who had total abdominal hysterectomy and salpingooophorectomy, bilateral and unilateral salpingo-oophorectomy and ovarian cystectomy. The retrieved tissue blocks were remounted and then serially sectioned by a manually operated microtome to 2-3µm thin slices. Thereafter, the slices were floated on a warm-water bath and set on adhesive coated slides. The slides were placed on a warmer set at 60°C for 1 hour and routine Haematoxylin and Eosin (H&E) staining was done. The newly prepared H&E slides were reviewed and diagnostic criteria for WHO classification of EOT by histological cell type and behaviour were used. Further histological grading was done using the WHO/Universal/Shimizu criteria (based on architectural pattern, nuclear pleomorphism and mitotic activity). They were also compared with the MD Anderson 2tier grading (based on nuclear pleomorphism and mitotic activity alone).

The data were analysed using the Statistical Package for Social Sciences software (SPSS), version 20. Descriptive statistics were carried out for socio-demographic variables such as age, size of tumour and laterality. The continuous variables were described in the form of mean, median, minimum and maximum and measures of variability.

Archival tissues were used in all cases, the names and identity of the patients were not used and there was no contact between the patients and the investigator at any time. Ethical clearance for the study was obtained from the Ethical Review Committee of the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife.

Results

Out of 51 cases of EOT examined, the frequency of benign, borderline and malignant EOTS were 21 (41.2%), 2 (3.9%) and 28(54.9%) respectively.

The age distribution of the patients ranged from 23 to 94 years (mean of 46.5±2.6 years) as shown in Figure 1. Most patients were in the 4th decade of life. Benign EOT occurred more frequently in the younger age groups; 68.4% of the patients were aged less than 40 years and 84% of the malignant cases occurred in

patients above the age of 40 years. The borderline tumours occurred at about the age of 50 years. The youngest of the benign EOT cases was 23 years, while the oldest patient with malignant EOT was 94 years. Majority of the cases were from two age groups 21 to 30 years and 41 to 50 years respectively. The mean age for benign EOTs was 37.4 years, while the mean age for borderline and malignant EOT was 50.5 years and 53.3 years respectively.

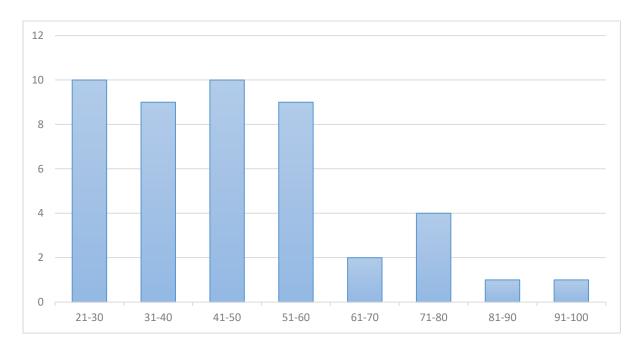


Figure 1: Age distribution of Epithelial Ovarian Tumours

Figure 2 shows that abdominal swelling was the most frequent presenting symptom (74.4%), 18.6% had abdominal pain with associated weight loss while vaginal bleeding occurred in 4.7%. One patient was 16 weeks pregnant and she presented with anorexia, generalized body weakness, easy fatigability and abdominal pain.

The histological diagnoses of the cases were put into sub-categories by histological cell type sub-category: 38 (74.5%) were serous tumours, 8 (15.7%) were mucinous tumour, 3 (5.9%) were Brenners tumours. There was one case (2.0%) each of signet ring cell carcinoma and

endometroid carcinoma. No case of clear cell was recorded. Out of 21 benign EOT cases, 14 (66.7%) were serous adenoma, 2 (9.5%) were serous adenofibroma, 2 (9.5%) were mucinous cystadenoma and 3 (14.3%) cases of Brenner tumours were recorded.

There were 2 cases of borderline EOT, one was serous borderline and the other was a mucinous borderline tumour. Of the 28 malignant EOT cases, 21 (75%) were serous cystadenocarcinoma, 5 (17.9%) mucinous cystadenocarcinoma, and signet ring cell carcinoma and endometrioid carcinoma had 1 (3.6%)

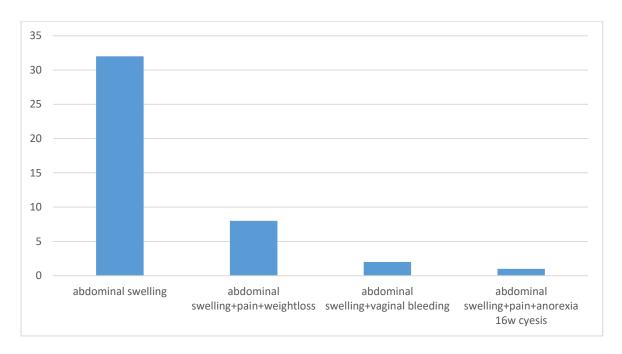


Figure 2: Clinical symptoms of patients with Epithelial Ovarian Tumours

There was a predominance of the serous histological subtypes constituting 74.5% of all EOT. There were 16 cases of benign serous tumours, 1 case of serous borderline tumour and 21 cases of malignant serous tumours. The benign serous tumours constituted 31.4% of all EOT. Out of the 16 cases of benign serous tumours, 2 cases were serous adenofibroma while 14 were serous cystadenomas (Table I).

On gross examination, the mean size of the tumour in the widest diameter was 16.4±1.3cm with a range of 5 to 30cm. The benign EOT had a mean size of 14.9±2cm, while the borderline and malignant EOTs had mean diameters of 27.0cm and 17.2±1.6cm respectively. The mucinous tumours were the largest of the EOT; the mean sizes of the mucinous cystadenoma, mucinous borderline tumours and mucinous carcinomas were 30.0cm, 27.0cm and 17.3cm respectively. The Brenner tumours were next in size with a mean of 23.0cm while the serous tumours were third with the mean sizes for benign, borderline and malignant serous tumours being 14.5cm, 17.0cm and 17.1cm respectively. Ten (10) of the malignant EOT displayed a solid and diffuse stromal infiltration by malignant tumour tissue while glandular and papillary growth pattern was present in three and 11 cases respectively. There were two cases of glandular expansile growth pattern due to intra-luminal mucin as shown in (Figure 3).

The degree of nuclear pleomorphism was determined by assessing the variation in nuclear sizes of cells of the malignant EOT. They were classified as mild in 6, moderate in 11 and marked in 10 cases. Also, the number of mitotic figures per 10 high power field (hpf) was counted and tissues were classified as follows: 8 cases were mild (0-9 per 10hpf), 15 were moderate (10-24 per hpf) and 4 were marked (>24 per hpf).

The histological grading of malignant EOT was done using the Shimizu/Silverberg grading system. Eight cases were graded 1, 14 cases were graded 2 and 5 cases were graded 3. The MD Anderson 2-tier grading system was also used for the same set of the malignant EOTs as follows: 8 cases were low grade and 19 were high-grade EOT as shown in Tables II and III.

Table I: Histological Diagnosis of Epithelial Ovarian tumours made within the study period

Histological diagnosis	Frequency	Percentage
Serous Cystadenoma	14	27.5
Serous adenofibroma	2	3.9
Serous borderline	1	2
Serous carcinoma	21	41.2
Mucinous cystadenoma	2	3.9
Mucinous borderline	1	2
Mucinous carcinoma	5	9.8
Brenners tumour	3	5.9
Signet ring carcinoma	1	2
Endometrioid carcinoma	1	2
Total	51	100

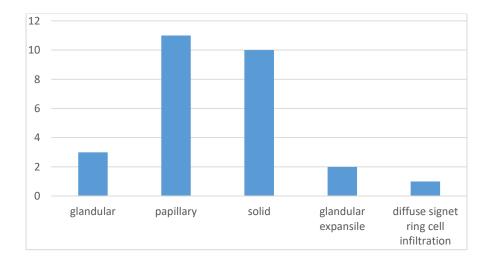


Figure 3: Architectural patterns of the malignant Epithelial Ovarian Tumours

Table II: Silverberg/Shimizu Grading system and MD Anderson Grading system

Histolo		MD Anderson		Total
systems	S	Low Grade	High Grade	
Silver	Grade 1	8	0	8
berg/ Shimi	Grade 2	0	14	14
zu	Grade 3	0	5	5
Total		8	19	27

		Histological g	Histological grading of histologically diagnosed cases		
		Serous	Mucinous	Endometrioid	
		carcinoma	Carcinoma	carcinoma	
MD	Low grade	4	4	0	8
Anderson	High grade	17	1	1	19
Total		21	5	1	27

Table III: MD Anderson Grading of histologically diagnosed cases

There was a significant correlation between nuclear pleomorphism, histological grading p = 0.00001 as well as between mitotic activity of the malignant EOT and histological grading p = 0.00001. However, correlation of tumour architectural pattern with the histological grading showed no significant relationship (p = 0.664).

Discussion

The WHO's classification of tumours divided EOT into benign, borderline, and malignant (carcinoma), with the diagnosis of carcinoma based on the identification of infiltrative stromal invasion. [11] These tumours have various growth patterns such as glandular, papillary and solid architectural patterns for the serous carcinomas and expansile or infiltrative growth patterns for the mucinous carcinomas which are the key components in the histological grading of these tumours. [12].

In the present review of a 10-year period, the relative frequencies for benign, borderline and malignant EOTS were 41.2%, 3.9% and 54.9% respectively. These show that malignant cases were predominant during the study period as compared to an earlier study conducted at the same centre by Omoniyi-Esan *et al.* [13] that found benign tumours constituting the majority (66.7%) of EOT. At present, there is an active gynae-oncology unit in the institution after the study by Omoniyi-Esan *et*

al was reported. In addition, the institution presently receives more referrals from neighbouring peripheral health facilities and other surrounding hospitals. These factors may be the reason for the higher rate of malignant EOTs in the present study. The borderline tumours had low frequency compared to benign and malignant EOTs and this is similar to the findings in other studies from the same centre, and other centres within and outside Nigeria. [13-15]

It has been reported previously that benign EOT occur in younger age groups, the borderline tumours in the fourth to fifth decades and malignant in older ages beyond the sixth decade of life. [16] The findings from the present study confirmed this tendency and it appears that there is an age proportion for benign, borderline and malignant EOTs all over the world. The benign EOTS affect younger women with many cases diagnosed between the second and the third decades of life; the borderline tumours affect relatively older ages in the sixth decade while malignant cases occur in much older patients in this environment.

The histological sub-categories of the EOTs showed a predominance (74.5%) of the serous histological subtypes of all EOTs within the period. Benign serous tumours were the most common of the benign EOTs making up 31.4% of all EOTs and majority (75%) of the malignant EOTs were serous adenocarcinoma.

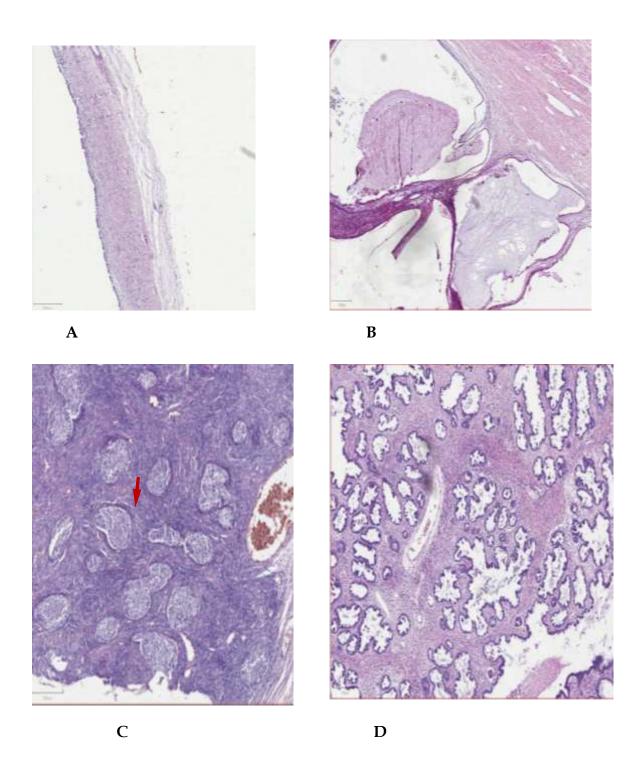


Figure 4: Serous cystadenoma cyst wall lined by simple epithelium. H&E x40 (A); Mucinous cystadenoma with abundant mucin pool. H&E x40 (B); Brenners Tumour: Diffuse solid epithelial nest (arrow) within dense fibrous stroma. H&E x40 (C); Serous borderline tumour.; Multiple epithelium-lined cystic spaces. H&E x40 (D).

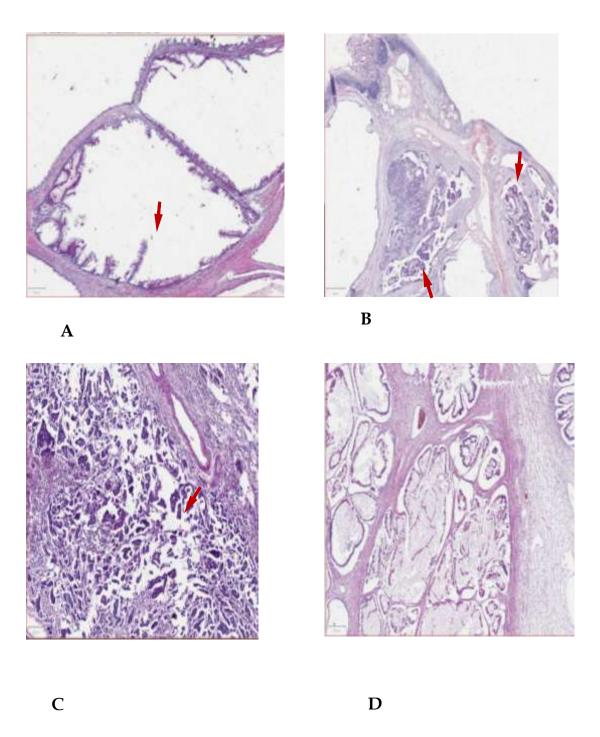


Figure 5: Mucinous borderline tumour: Cyst with micropapillary projection (red arrow) H&E x40 (A); High grade Serous cystadenocarcinoma. Cyst wall infiltration by papillary growth of malignant epithelium. H&E x40 (B); Low grade Serous cystadenocarcinoma: Papillary architectural growth pattern. H&E x40 (C); Mucinous carcinoma. Expansile glandular architectural growth pattern H&E x40 (D).

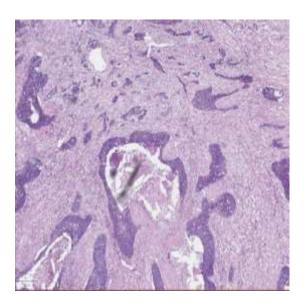


Figure 6: Endometrioid carcinoma: Infiltrating trabecules of malignant squamoid epithelium H&E x40

This is similar to the report of Ghartimagar et al [16] that found serous adenocarcinoma to be the predominant (72.7%) of all malignant EOTs seen in Nepal. The peak age for serous tumours was 27 years, 51 years and greater than 60 years for benign, borderline and malignant serous EOT respectively. This is similar to the findings by Yakasai et al in Kano where the mean age of occurrence for malignant ovarian cancer was 57±4.5years. [17] The epithelial ovarian tumours were bilateral in 9.8%, similar to the finding of Tuncer who 12.8% bilaterality for serous reported tumours. [18] This disagrees with the finding of Lee-Jones et al where 50% of all ovarian carcinoma was bilateral. [19] There was a case of borderline serous tumour in the present study; this relatively affects females in the sixth decades. These tumours generally are of low malignant potential exhibiting an atypical epithelial proliferation of serous type cells but without destructive stromal invasion.

The mucinous EOTS are less common than their serous counterparts and in this study, they made up 15.7% of all the EOT; these were

further sub-classified into benign, borderline and malignant tumours in 2, 1 and 5 cases respectively. Malignant mucinous EOTs are less common in this environment and this corroborates previous findings with a slight increase in Ile-Ife by Sabageh et al who reported a frequency of 4.3%. [2] However, this is in contrast with findings from Sokoto northern Nigeria, were mucinous tumour constituted 35% of all malignant ovarian tumours. [20] There is often difficulty differentiating primary malignant mucinous EOT from metastatic mucinous tumours. Once metastatic ovarian tumours are excluded by morphological features and ancillary methods, primary mucinous EOT tend to have a low occurrence of between 2% and 8% of epithelial carcinoma. [21,22] These tumours are often larger than the serous tumours, the largest size in this study was a 30cm mucinous cystadenoma which was bigger than the largest serous cystadenoma of 26cm size. The largest mucinous carcinoma was 27cm compared with the largest serous carcinoma which was 26cm, likewise, the mucinous borderline tumour was 27cm in the widest diameter. This is due to the enormous amount of mucin secretion within the cystic mass. A similar finding was reported in Nnewi, Nigeria where a case of giant mucinous cystadenoma was reported. [23] Other studies also corroborated these findings. [16,23,24] The age of occurrence for the benign mucinous tumours was in the third decade and the mucinous carcinoma occurred between the fourth and the ninth decades of life. This finding corroborates earlier reports by Onyegbule and Lerwill. [23,25]

The Brenners tumour sub-category formed 5.9% of all the EOT in the present study. All the cases were benign Brenner tumour and the age of occurrence in this study was between 33 and 94, consistent with findings stating that this group is often diagnosed in peri- and post-menopausal women. [26,27] The average tumour size in this study was 23cm in the widest diameter. There was a case of a bilateral tumour and the patient also had endometrial hyperplasia; this observation suggests that Brenner tumour can elaborate oestrogen. [28]

Ovarian carcinoma has been classified into low grade and high-grade types based on histopathological nuclear features and mitotic activity present (MD Anderson grading systems). [29,30] In this study, the distribution of the types of ovarian carcinoma showed 29.6% as low-grade ovarian carcinoma and 70.4% as high-grade ovarian carcinoma. The majority (63%) of the ovarian carcinoma were highgrade serous carcinoma (HGSC). This finding is consistent with other studies that reported HGSC as the most common and by far, the deadliest ovarian carcinoma. [31] The single case of endometrioid carcinoma in this study was also high grade histologically. Therefore, HGSC is still the most common malignant EOT. These groups have varied epidemiological and genetic risk factors, as well as precursor lesions and molecular events oncogenesis, response chemotherapy, and prognosis.

Endometrioid carcinoma is the least common and can often be misdiagnosed if strict adherence to the WHO classification of EOTs is not taken because there may be many squamous metaplastic (squamoid) areas mimicking adenosquamous carcinoma. [32,33] EOT are primarily tumours of the ovary and they develop from the Mullerian epithelium. However, studies have expressed doubts about the origin of the tumour, that just like the testes (a germ cell organ) the ovary rarely has epithelial tumours but mostly, the germ cell tumours and stroma neoplasia. Therefore, the question arises: "is there any true primary epithelial tumour of the ovary or the observed epithelial tumours are secondaries from drop-off from the fallopian tube, endometriosis and endocervical epithelium and recently, for the Brenners tumour that they arise from the wathered cell nest of the mesovarium, mesosalpinx and ovarian hilum"? 34,35 This question makes the histological characteristics of EOT insufficient for diagnosis and hence, the emphasis on the need for a phenotypic and genotyping characterization to prove their origin as a primary ovarian tumour or metastatic epithelial tumour deposits.

Conclusion

The majority of the ovarian tumours studied in Ile-Ife are the serous type and the serous carcinomas are the commonest malignant type. These are mostly high grade with potential aggressive behaviour, hence the patients present with worsened clinical features which may contribute to poor survival.

Acknowledgement: The entire members of the Department of Morbid Anatomy and Forensic Medicine, OAUTHC, Ile-Ife are appreciated for the technical aspect of the study.

Authors' Contributions: AAO1 conceived and designed the study. AAO1, OOO and AAO2 participated in data analysis and interpretation.

AAO1 and OOO drafted the manuscript. O-EGO reviewed the manuscript for sound intellectual contents. All the authors approved the final version of the manuscript.

Conflicts of Interest: None.

Funding: Self-funded **Publication History:** Submitted 21 September; Accepted 10 April 2020.

References

- Khatri R. Clinicopathological analysis of ovarian tumours at Birendra Military Hospital. Med J Shree Birendra Hosp 2010; 10: 26–31.
- Sabageh D, Olaofe OO, Sabageh A. An analysis of the clinicopathologic characteristics of ovarian tumors in Ile-Ife, Nigeria. Ann Trop Pathol 2012; 3: 97–104.
- 3. Karpathiou G, Chauleur C, Corsini T, Venet M, Habougit C, Honeyman F, et al. Seromucinous ovarian tumor. A comparison with the rest of ovarian epithelial tumors. Ann Diagn Pathol 2017; 27: 28–33.
- 4. Nakamura E, Sato Y, Moriguchi S, Yamashita A, Higo T, Asada Y. Ovarian Seromucinous Borderline Tumor and Clear Cell Carcinoma: An Unusual Combination. Case Rep Obstet Gynecol 2015; 2015: 1–5.
- Taylor J, Glenn McCluggage W. Ovarian seromucinous carcinoma: Report of a series of newly categorized and uncommon neoplasm. Am J Surg Pathol 2015; 39: 983–992.
- Kubeček O, Laco J, Špaček J, Petera J, Kopecký J, Kubečková A, et al. The pathogenesis, diagnosis, and management of metastatic tumors to the ovary: a comprehensive review. Clin Exp Metastasis 2017; 34: 295–307.
- 7. Kakushima N, Kamoshida T, Hirai S, Hotta S, Hirayama T, Yamada J, et al. Early gastric cancer with Krukenberg tumor and review of cases of intramucosal gastric

- cancers with Krukenberg tumor. J Gastroenterol 2003; 38: 1176–180.
- 8. Leen SLS, Singh N. Pathology of primary and metastatic mucinous ovarian neoplasms. J Clin Pathol 2012; 65: 591–595.
- 9. Hauptmann S, Friedrich K, Redline R, Avril S. Ovarian borderline tumors in the 2014 WHO classification: evolving concepts and diagnostic criteria. Virchows Arch 2017; 470: 125–142.
- 10. Avril S. Histopathological markers of treatment response and recurrence risk in ovarian cancers and borderline tumors. Pathologe 2017; 38: 180–191.
- 11. Meinhold-Heerlein I, Fotopoulou C, Harter P, Kurzeder C, Mustea A, Wimberger P, et al. The new WHO classification of ovarian, fallopian tube, and primary peritoneal cancer and its clinical implications. Arch Gynecol Obstet 2016; 293: 695–700.
- 12. Brown J, Frumovitz M. Mucinous tumors of the ovary: Current thoughts on diagnosis and management. Curr Oncol Rep 2014; 16: 389.
- 13. Omoniyi-Esan GO, Olaofe OO, Omonisi AE, Komolafe AO, Fadahunsi O. Histopathological Analysis of ovarian Cancer In Ile-Ife southwest, Nigeria. Niger J Postgrad Med 2011; 4: 15–19.
- 14. Buowari D. Ovarian cyst at general hospital Aliero, Nigeria: A one-year review. Trop J Med Res 2009; 13: 433-434.
- 15. Tropé CG, Kaern J, Davidson B. Borderline ovarian tumours. Best Pract Res Clin Obstet Gynaecol 2012; 26: 325–336.
- Ghartimagar D, Ghosh A, KC G, Ranabhat S, Talwar O. Surface epithelial tumors of ovary - an analysis in a tertiary referral hospital. J Pathol Nepal 2013; 3: 397–402.

- 17. Yakasai IA UE, Otubu J, Yakasai IA, Ugwa EA. Gynecological malignancies in Aminu Kano Teaching Hospital Kano: A 3-year review. Niger J Clin Pract 2013; 16: 63–66.
- 18. Tuncer ZS, Gunalp S, Aksu T, Ayhan A. Benign epithelial ovarian tumors. Eur J Gynaecol Oncol 1998; 19: 391–393.
- 19. Lee-Jones L. Ovary: Epithelial tumors. Atlas Genet Cytogenet Oncol Haematol 2004; 8: 120–138.
- Nnadi D. C, Nwobodo E., Tunau K., Malami S. Histo-Pathological features of primary ovarian tumours managed in A Tertiary Hospital, Sokoto. Sahel Med J 2009; 12: 171–174.
- 21. Hu A, Li H, Zhang L, Ren C, Wang Y, Liu Y, *et al.* Differentiating primary and extragenital metastatic mucinous ovarian tumours: an algorithm combining PAX8 with tumour size and laterality. J Clin Pathol 2015; 68: 522–528.
- Ackroyd SA, Goetsch L, Brown J, Houck K, Wang C, Hernandez E. Pancreaticobiliary metastasis presenting as primary mucinous ovarian neoplasm: A systematic literature review. Gynecol Oncol Rep 2019; 28: 109–115.
- 23. Onyegbule O, Etigbue J, Uyoh I, Ezenri U, Okafor C. Giant mucinous cystadenoma in Nnewi, Nigeria. Ann Med Health Sci Res 2015; 5: 222-225.
- 24. Pilone V, Tramontano S, Picarelli P, Monda A, Romano M, Renzulli M, et al. Giant mucinous ovarian borderline tumor. A good lesson from an asymptomatic case. Int J Surg Case Rep 2018; 50: 25–27.
- 25. Lerwill MF, Young RH. Mucinous tumours of the ovary. Diagnostic Histopathol 2008; 14: 366–387.
- Sangwaiya A, Garg S, Kalhan S, Satarkar R, Singh P, Gill M. Malignant Brenner tumor of ovary: A rare entity. Clin Cancer Investig J 2015; 4: 584-586.

- 27. Brenner Tumor B, Zheng R, Heller DS. Resident Short Reviews A Review of the Literature. Arch Pathol Lab Med 2019; 143: 1278–180.
- 28. Hiroi H, Osuga Y, Tarumoto Y, Shimokama T, Yano T, Yokota H, et al. A case of estrogen-producing Brenner tumor with a stromal component as a potential source for estrogen. Oncology 2002; 63: 201–204.
- Bodurka DC, Deavers MT, Tian C, Sun CC, Malpica A, Coleman RL, et al. Reclassification of serous ovarian carcinoma by a 2-tier system. Cancer 2012; 118: 3087–3094.
- 30. Matsuno RK, Sherman ME, Visvanathan K, Goodman MT, Hernandez BY, Lynch CF, *et al.* Agreement for tumor grade of ovarian carcinoma: analysis of archival tissues from the surveillance, epidemiology, and end results residual tissue repository. Cancer Causes Control 2013; 24: 749–757.
- 31. Lisio M-A, Fu L, Goyeneche A, Gao Z, Telleria C. High-Grade Serous Ovarian Cancer: Basic Sciences, Clinical and Therapeutic Standpoints. Int J Mol Sci 2019; 20: E952. doi: 10.3390/ijms20040952.
- 32. Shoji T, Takatori E, Murakami K, Kaido Y, Takeuchi S, Kikuchi A, et al. A case of ovarian adenosquamous carcinoma arising from endometrioid adenocarcinoma: a case report and systematic review. J Ovarian Res 2016; 9: 48: 2-7.
- 33. Fu YS, Stock RJ, Reagan JW, Storaasli JP, Budd Wentz W. Significance of squamous components in endometrioid carcinoma of the ovary. Cancer 1979; 44: 614–621.

- 34. Gilks CB, Irving J, Köbel M, Lee C, Singh N, Wilkinson N, *et al.* Incidental nonuterine high-grade serous carcinomas arise in the fallopian tube in most cases: Further evidence for the tubal origin of high-grade serous carcinomas. Am J Surg Pathol 2015; 39: 357–364.
- 35. Kuhn E, Ayhan A, Shih IM, Seidman JD, Kurman RJ. Ovarian Brenner tumour: A morphologic and immunohistochemical analysis suggesting an origin from fallopian tube epithelium. Eur J Cancer 2013; 49: 3839–349.



This is an Open Access document licensed for distribution under the terms and conditions of the Creative Commons Attribution License (http://creativecommons.org/licenses/by-nc/4.0). This permits unrestricted, non-commercial use, reproduction and distribution in any medium provided the original source is adequately cited and credited.