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A CLINICO-PATHOLOGICAL EVALUATION OF OVARIAN TERATOMAS IN UYO, NIGERIA DURING A 10 YEAR PERIOD

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ABSTRACT

Objective: To show the clinicopathologic pattern of ovarian teratomas (OT) in Uyo, Nigeria and how they compared to results from other parts of the world.

Design: This was a quantitative observational, descriptive study of all OT specimens that were histologically diagnosed in the Histopathology Department of University of Uyo Teaching Hospital, Uyo, Nigeria.

Results: Of the 149 ovarian specimens received, OT was seen in 54 cases accounting for 36.2% of all ovarian lesions. Most of the patients were between age groups 20-29 years (37%) and 30-39 years (29.6%). The youngest patient was aged 4.5 years, while the oldest was 68 years with a mean age of 33.7 years with a standard deviation of 13.8. The complaints at presentation were mainly abdominal pain (50%), abdominal swelling (42.6%), per vagina bleeding (7.4%). All the patients had laparotomy, which was a cystectomy (68.5%), oophorectomy (22.2%) or a hysterectomy (9.3%). In 46.3% of cases, the widest diameter of the mass was greater than 10cm, while in 37% of cases, the widest diameter was \leq 10cm. The contents were cheesy material admixed with tuft of hair (70.4%), sebum (37%), serous / mucinous fluid (18.5%), bone (7.4%), teeth (5.6%), cartilage (5.6%). Histologically majority of the OT were mature teratomas (MT) (88.9%). Malignant transformation of a MT (MTMT), immature teratoma and struma ovarii were seen in 5.6%, 3.7% and 1.9% of cases respectively.

Conclusion: The frequency and pattern (histologically) is same as known for OT globally. Very few asymptomatic patients presented, while no patient had laparoscopic surgery.

INTRODUCTION

Teratoma was derived from the Greek word "teraton" which means monster.¹ Teratoma usually occurs in midline structures like the gonads (testis and ovary), intracranial sites (pineal region and neurohypophysis), mediastinum, retroperitoneum and sacrococcygeal region.² Recently, teratomas have been reported to occur in nasal septum and gluteal region.³ Ovarian tumors can arise from, the surface epithelium derived from the coelomic epithelium, sex cord/stromal cells or germ cells.⁴ Ovarian teratoma (OT) is the most common ovarian germ cell neoplasm and can be mature type, immature or specialized type.^{4,9} In Europe and different parts of Asia, they were documented as the most common ovarian neoplasms.^{5-7,9,10} In few African studies that centred on OT, they were reported as the most common ovarian neoplasms.^{11,12}

No previous work has been done exclusively on the clinicopathological pattern of OT in the University of Uyo Teaching Hospital, Uyo, Nigeria. There is a need to have a comprehensive literature on OT in Africa which will help us reappraise our over dependence on western data. The aim of this study is to show the clinicopathologic pattern of OT in Uyo, to compare them with findings from other centres locally and outside Nigeria and to generate a baseline data for OT in this part of the country.

METHODS AND MATERIAL

This is a quantitative observational descriptive study of all OT specimens that were histologically diagnosed in the Histopathology Department of University of Uyo Teaching Hospital, Uyo, Nigeria over a 10-year period from 1st January 2007 to 31st December 2016. This histopathology laboratory is the only facility where histopathology services are rendered in

Akwa Ibom State and as such renders services to the host hospital and many privately owned hospitals within the State. These specimens were received in 10% buffered formalin and processed with auto processors. Paraffin embedded sections (at 2-3 μ m) were routinely stained with hematoxylin and eosin stains. Data were extracted from the departmental registers, patient request forms and duplicate copies of histology reports of all cases. Information extracted includes age, side/laterality of ovary affected, symptoms at presentation, operative procedure utilised, gross/microscopic morphology findings and histology diagnosis. The information extracted were analyzed using predictive analytical software, version 17 (IBM, SPSS Inc, Chicago, IL, USA). Simple frequencies were determined for categorical variables and mean was evaluated for continuous data. Correlation of variables was by using Pearson's chi-squared test, with a P value \leq 0.05 taken to be significant.

RESULTS

Six thousand four hundred and twenty seven (6427) specimens were received in the histopathology laboratory during the period of study. All reports with ambiguous conclusions were excluded. Also excluded were histopathology reports with any of the major identification parameters (like age and diagnosis) missing. In all five reports were excluded. One hundred and forty nine (2.3% of all histopathology specimens seen) of them were ovarian specimens, while OT were seen only in 54 cases accounting for 36.2% of all ovarian lesions and 0.8% of all specimens received. Most of the patients were between age groups 20-29 years (37%) and 30-39 years (29.6%), as shown in table 1. The youngest patient was aged 4.5 years, while the oldest was 68 years and a mean age of 33.9 years a standard deviation of 13.8.

Table 1
Age group distribution of cases

Age group	Frequency	Percentage
≤19	4	7.4
20-29	20	37
30-39	16	29.6
40-49	5	9.3
50-59	3	5.6
60-69	6	11.1
Total	54	100

Table 2 shows the patients presenting complaints, clinical diagnosis and operative procedures. The complaints at presentation were mainly abdominal pain (50%), abdominal swelling (42.6%), per vagina bleeding (7.4%), while 5.6% of the cases were asymptomatic. The clinical diagnosis was a dermoid cyst in 27.8%, ovarian cyst in 35.2%, not stated in 29.7% and meig

syndrome in 3.7% of cases. All the patients had laparotomy, which was a cystectomy (68.5%), oophorectomy (22.2%) or a hysterectomy (9.3%). The association of the symptoms at presentation with age, tumor size and histological diagnosis using Pearson's chi-squared test, each gave a P value > 0.05.

Table 2
Symptoms, clinical diagnosis and surgical procedure used

	Frequency	Percentage (%)
Symptoms at presentation		
Abdominal pain	27	50
Abdominal swelling/mass	23	42.6
Vaginal bleeding	4	7.4
Asymptomatic	3	5.6
Others	11	20.4
Clinical Diagnosis		
Ovarian cyst	19	35.2
Dermoid cyst	15	27.8
Meig syndrome	2	3.7
Ovarian torsion	1	1.9
Malignant ovarian lesion	1	1.9
Not stated	16	29.7
Laparotomy Procedure		
Cystectomy	37	68.5
Oophorectomy	12	22.2
Hysterectomy	5	9.3

Gross morphologic features and histologic diagnoses of the OT are as presented in table 3. Left sided lesions accounted for 35.2% of cases. Majority of the OT were uniloculated (66.7%). In 46.3% of cases, the widest diameter of the mass was greater than 10cm. The contents were cheesy material admixed

with tuft of hair (70.4%), sebum (37%), serous / mucinous fluid (18.5%), bone (7.4%), teeth (5.6%), cartilage (5.6%). Histologically majority of the OT were mature teratomas (MT) (88.9%). Malignant transformation of a MT (MTMT), immature teratoma (IT) and struma ovarii were seen in 5.6%, 3.7% and

1.9% of cases respectively. MTMT was seen in 5.6% (3) of cases and it significantly associated to their ages ($p = 0.000$), using Pearson's chi-squared test. They were all post-menopausal (aged 52, 52, 68; mean = 57years) and it did not correlate to the size of the ovary ($p = 0.329$) though they were all 11cm in diameter respectively.

Table 3
Gross and micro morphologic features

	Frequency	Percentage
Site		
Left	19	35.2
Right	18	33.3
Both sides	3	5.6
Not stated	14	26
Loculation		
Unilocular	36	66.7
Multilocular	18	33.3
Size		
≤ 10cm	25	46.3
> 10cm	20	37
Gross Content		
Cheesy material/hair	38	70.4
Sebum	20	37.0
Yellowish fluid	10	18.5
Bone	4	7.4
Teeth	3	5.6
Cartilage	3	5.6
Histologic Diagnosis		
Mature teratoma	48	88.9
Malignant transformation	3	5.6
Immature teratoma	2	3.7
Struma Ovarii	1	1.9

There was significant association between the clinical diagnosis and histologic diagnosis ($p = 0.006$), using Pearson's chi-squared test. The association between age and histologic diagnosis was significant ($p = 0.000$).

Figure 1 shows the ectodermal derivatives seen histologically. Skin and its appendages were the commonest (74.1%), distantly followed by neural elements (13%).

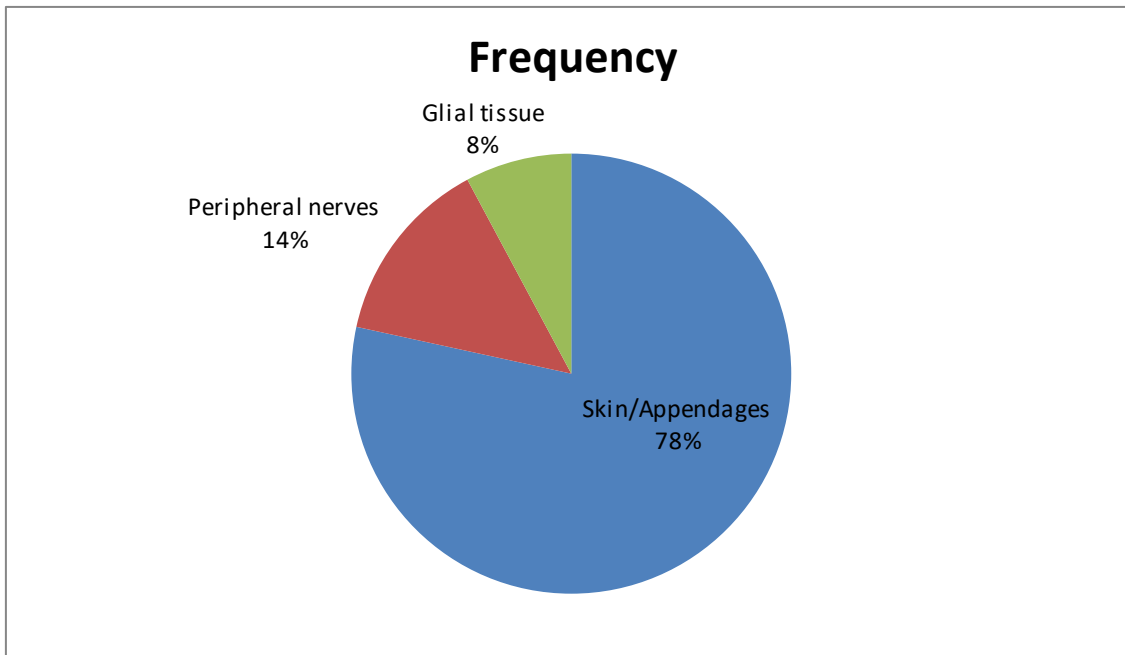


Figure 1: Microscopic composition of ectodermal components

Adipose tissue (24.1%), cartilage (18.5%), bone (14.8%) and smooth muscle (13%) in this descending order were the common mesodermal elements seen, as shown in figure 2.

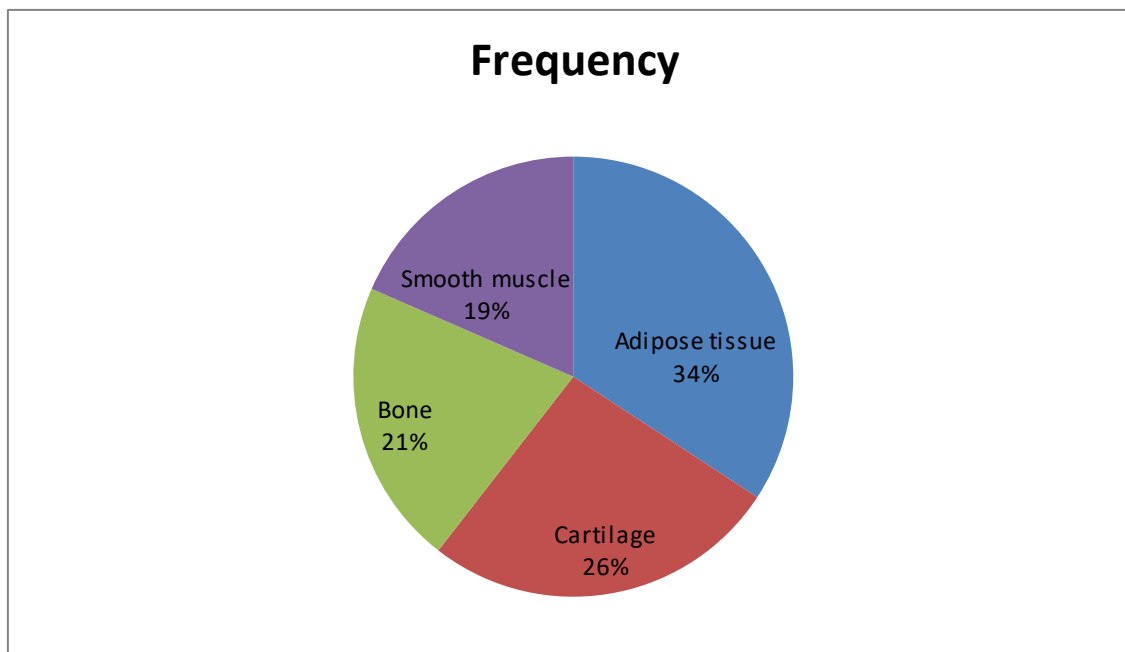


Figure 2: Microscopic composition of mesodermal components

Gastrointestinal epithelium distantly followed by thyroid follicles was the common endodermal derivatives as shown in figure 3. Figures 4-5 show gross and microscopic pictures of MTMT and IM.

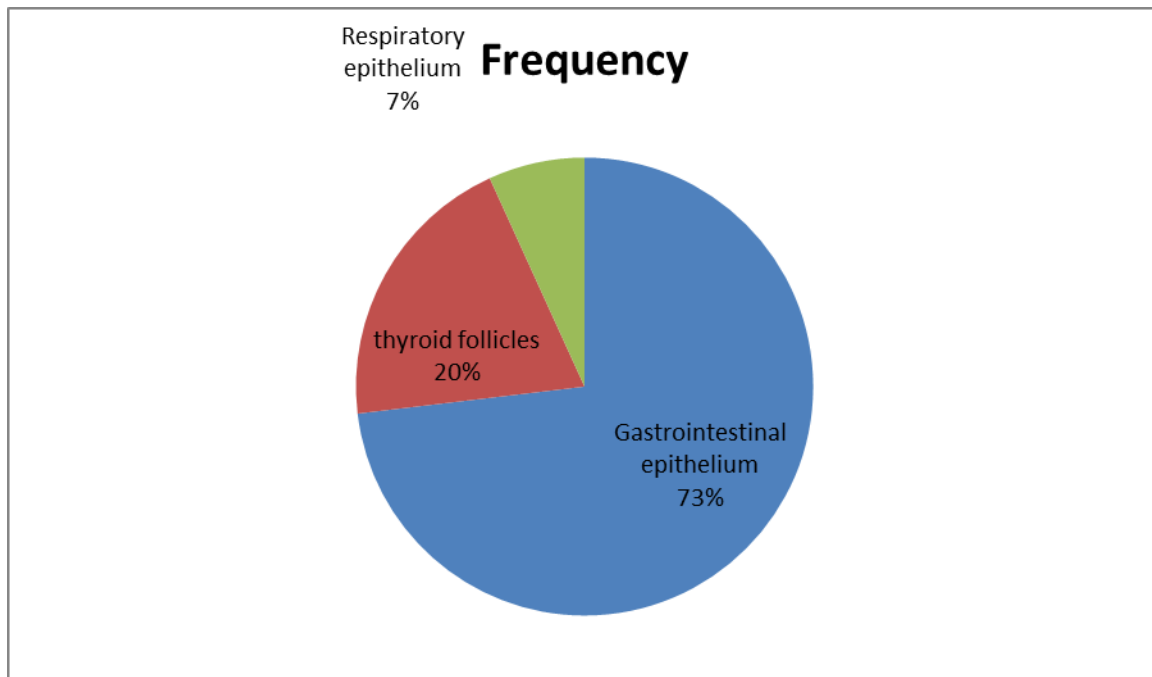


Figure 3: Microscopic composition of endodermal components

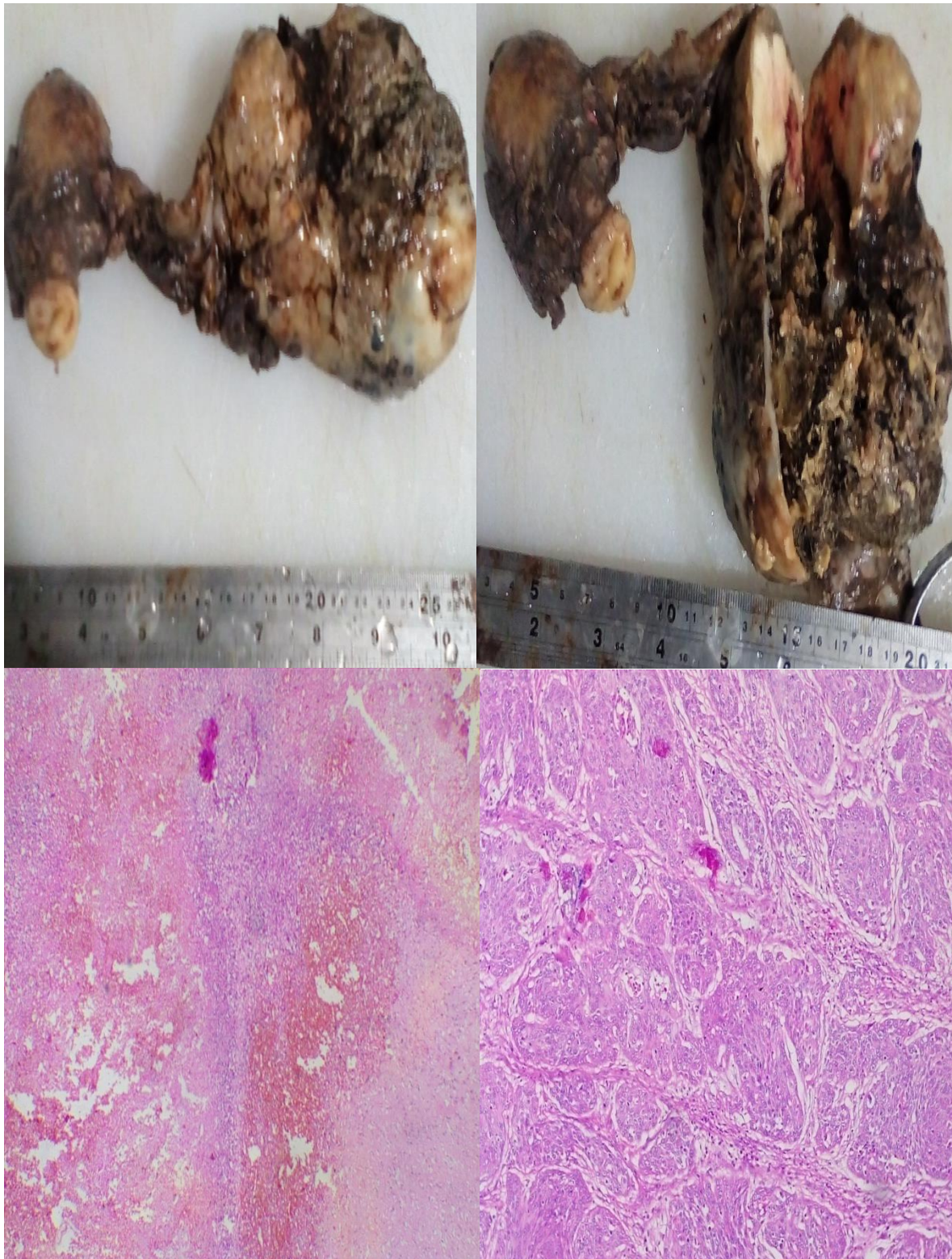


Figure 4: A case of MTMT in a 52-year-old woman: A) A left ovarian mass, B) Cut surface of the mass shows a fleshy solid mass on the apical section, while the lower pole shows tuft of hair. C) Histology of same mass showing extensive areas of necrosis, D) Showing clusters of atypical, pleomorphic squamous cells.

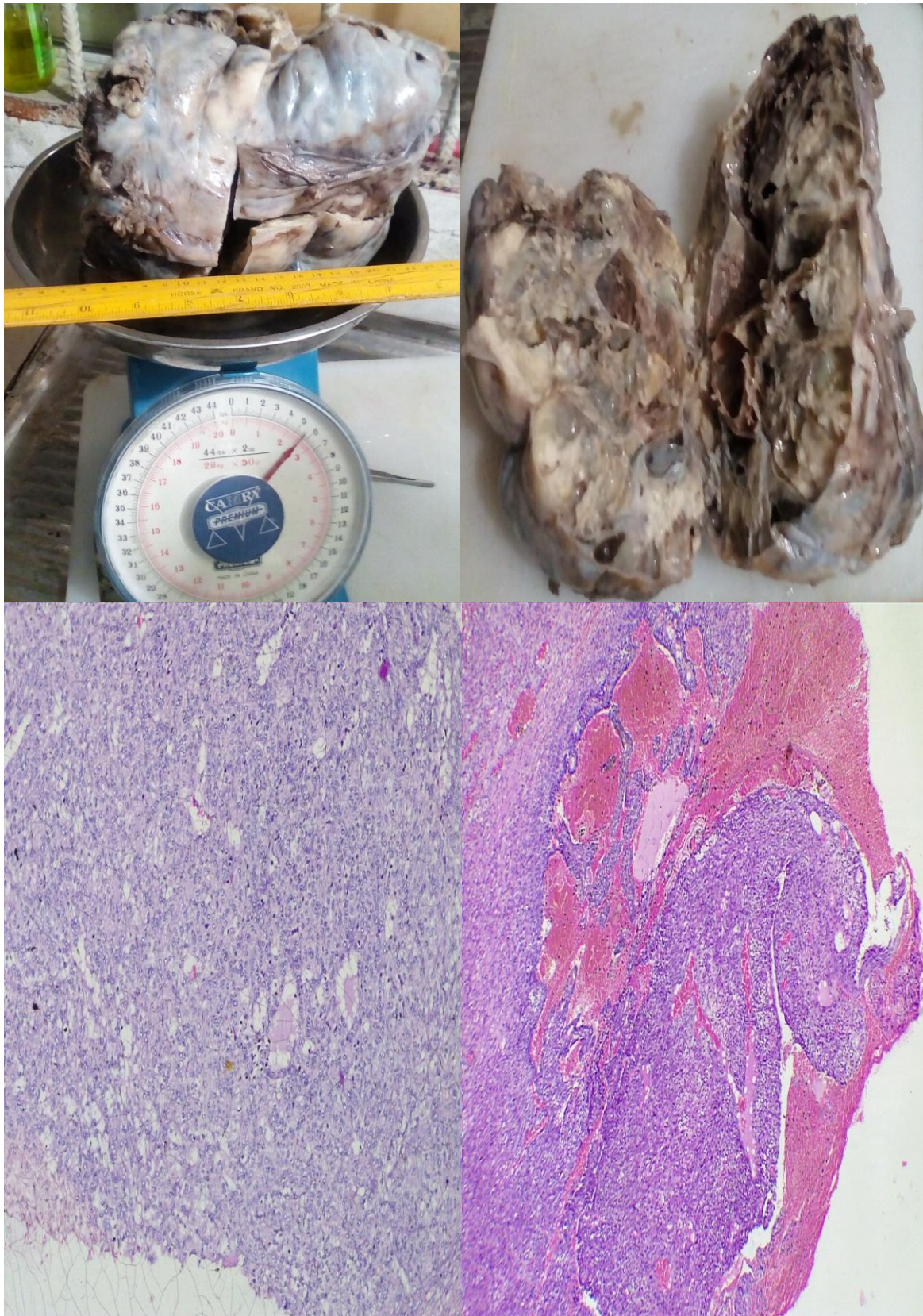


Figure 5: Immature teratoma in a 4.5 year old. (A) A huge irregular mass weighing 2.8kg, (B) Cut surface showing multicystic spaces a few solid areas, (C) Histology showing numerous blastema cells (immature cells), (D) Another section showing blastema cells and areas of necrosis.

DISCUSSION

OT accounted for 36.2% of all ovarian neoplasms in the index study, which is close to the rate of 38.6% observed in a neighbouring state and rates of 32.6% and 33% reported in Taiwan and India respectively.^{9,12,16} The reason for this cannot be readily explained. The index rate is less than 42.8% seen in Turkey, 49% and 57.6% seen in 2 different studies from Nepal.⁵⁻⁷ Studies from Pakistan had lower rate of 17%.¹³ Age groups 20-39 years accounted for 66.6% of cases and this agrees with all previous studies with a slight variation in the mean age of occurrence.^{5-9,12,16}

The commonest symptom at presentation was abdominal pain which is similar to observations in previous studies.^{5,7,9,12,16} Asymptomatic presentation of OT could be seen in as much as 16% -22.5% of cases.^{5,9} In this study, only 5.6% (3 cases) were asymptomatic. This may explain the health seeking behaviour of people in our setting, where hospital presentation is mostly based on symptomatology. No previous study reported bleeding per vagina in their symptoms at presentation. This was seen in 7.4% (4 cases) in our series. No significant association (using Pearson's chi-squared test) was seen between this symptom and their age, tumor size or histologic diagnosis. (They patients were aged 4.5 years: immature teratoma; 20 years: mature teratoma; 50 years: mature teratoma and 68 years: malignant transformation of a mature teratoma).

The observation that there was a significant association (using Pearson's chi-squared test) between clinical diagnoses and histologic diagnoses does not reduce the importance of tissue histology in OT management. The role of histopathology as the gold standard in making diagnosis was substantiated as it was only in 27.8% of cases that the gynaecologist predicted it was an OT and it turned out to be so.

Most of the OT specimens in the index study were from cystectomy and oophorectomy. There was no significant correlation between the surgical procedure and the size of the ovarian mass or the age of the patient. The small sample size may be the reason. No case was surgically operated using laparoscopic procedure. This is due to non-availability of the equipment. Based on recommendations by The Royal College of Obstetricians and Gynecologists (RCOG) in the UK, a laparoscopic surgery is generally considered to be the gold standard for the management of all benign ovarian masses (including MT). Its advantages include; been cost-effective due to its associated earlier patient discharge from hospital and return to work mainly due to less intra operative blood loss, reduced postoperative pain, fewer postoperative adhesions and better cosmetic values.^{15,17,18} The significant drawbacks for laparoscopic procedures are longer theatre/operating time and higher risk of spillage of tumor contents.¹⁷ In poor settings, both lack of trained personnel's and equipment or "trained but not practicing personnel" may also be important determinants/draw backs. Major indication for laparotomy in OT management is large ovarian masses, though there is no agreed consensus about the maximum cyst size at which it is indicated.¹⁵ Ovarian cystectomy is usually the technique of choice in younger women unless the patient chooses oophorectomy. The RCOG recommends that during counselling for surgery the possibility of removing an ovary should also be discussed with the patient because it could be either an expected or unexpected part of the procedure.¹⁵ For postmenopausal and perimenopausal women with multiple cysts in the same ovary or with large teratoma, where there is no much ovarian tissue to conserve, oophorectomy is the standard operation.^{15,18}

During gross examination, the mean diameter was 12cm which is greater than

7cm in Turkey, 7.4cm in India, 8cm in Nepal and <10cm in Pakistan.^{5,7,13,16} The reason for this observation may be because 73% of the index cases were aged 39 years or less. Previous report has it that the natural increasing levels of sex hormones (estrogen and progesterone) may explain the increase in size of MT after puberty, and their arrested growth after menopause.¹⁹ The predominant gross feature on sectioning was a cystic mass containing grumous/cheesy material mixed with tuft of hair. This is similar to previous findings.^{5,13} Studies have shown that no relationship exists between the clinical features of patients (mean age of patients, postmenopausal and pregnancy status, tumor size, symptoms), gross morphology and histopathological contents of MT.²⁰

Microscopically the predominant feature in MT was skin and its appendages (74.1%), distantly followed by adipose tissue and gastrointestinal glands. This is similar to findings by Ikimalo et al but different from findings by Ayhan et al and Khan et al that reported 100% presence of skin and its appendages in all OT specimens seen.^{7,12,13} However all studies agree that ectodermal derivatives mainly skin is the most common microscopic feature.

MTMT is a very rare complication of MT. Ayhan et al in Turkey reported 4 cases at a rate of 1.4%. Similar to our finding, they were all squamous cell carcinoma, cases had a mean age of 50 years and a tumor size of 9.2cm.⁷ No case was reported in the studies from Nepal, Taiwan, Port Harcourt and India.^{5,9,12,16} Risk factors for MTMT include older age, large tumor masses, postmenopausal status and elevated tumor markers like (CA-125, squamous cell carcinoma antigen, carcinoembryonic antigen, CA 125, CA19-9)²¹ The role of tumor markers in MTMT is not clearly understood because their high concentration have been noticed also in patients with benign tumors.²² These in conjunction with its cost

are the reasons why it is not routinely used in our setting. Also, in our hospital routine evaluation of adnexal masses does not always include high imaging studies such as computed tomography (CT) and magnetic resonance imaging, thereby reducing the preoperative diagnosis. Of all the listed risk factors, age in conjunction with magnetic resonance imaging (MRI) citing of a solid component is the most consistent risk factors of MTMT (though no feature is specific).²³ Since most MT may be detected many years (close to 2 decades) prior to malignant transformation, it is postulated that prolonged exposure to various carcinogens in the pelvic cavity might be the predisposing factor to cytogenetic abnormalities which precede histological changes in a mature tissue.²⁴ Hence for early detection and prevention of MTMT, regular pelvic ultra sound scan examinations are needed and once MT is diagnosed during the childbearing years, operation should not be delayed.^{21,24} As an institution, when a MT is observed during abdomino-pelvic scan for other procedures, such a patient should be counselled on the need for elective surgery to remove it. Great emphasis should be placed on this especially if the female is menopausal. Other malignant tumors that can arise from MT aside squamous cell carcinoma include; adenocarcinoma, thyroid carcinoma, malignant melanoma, transitional cell carcinoma, sarcoma, carcinoid tumor, and neuroectodermal tumor.²⁵

Immature teratomas (IT) was seen in 3.7% (n = 2) of cases in our series. Both were the only patients less than 20 years (aged 18 and 4.5 years) and it was statistically significant. Both had a diameter of 22cm and 16cm and weights of 1.8kg and 3kg respectively. IT are generally rare ovarian tumors, occur mainly in adolescence, has never been reported in menopausal women, and are almost always unilateral and usually solid. In IT, the tissues that originate from the 3 germ layers are

mostly mature tissues however there are usually the presence of immature or embryonal structures.^{26,27} The index rate and patient features are within the previously observed range and clinical features.^{5-7,12,16,26,27} In both IT, the common immature elements were mostly of ectodermal origin (neuroepithelial rosettes).

The major limitation of this study is the small sample size, hence some of the inconclusive findings may simply be due to limited statistical power. Also the follow up of the patients post laparotomy were not done. There should be proper advocacy by the hospital management on the need for the government to provide laparoscopic surgery equipment and train the necessary manpower, so that its OT patients will benefit from the great advantages of laparoscopic procedures as obtainable in developed and developing nations.

In conclusion the clinicopathological pattern of OT seen in Uyo, Nigeria has been documented and findings show that the frequency and pattern (histologically) is same as known for OT. Histopathology still remains the mainstay for diagnosis of OT. Adequate sampling is essential in OT especially in peri and menopausal women to establish any malignant transformation so as to avoid an erroneous diagnosis. Very few asymptomatic patients presented, while no patient had laparoscopic surgery.

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