A Seven-Year Histopathological Review of Malignant Ovarian Tumours Seen in Kano

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Abstract
Background: Ovarian malignancies are important causes of morbidity and mortality and understanding their pathology go a long way in proffering adequate clinical management.
Objective: To determine the pattern, frequency and age distribution of malignant ovarian tumours received in the Pathology department of Aminu Kano Teaching Hospital, (AKTH), Kano over a 7 year period (2001 2007).
Methods: A retrospective analysis of all malignant ovarian tumours received and processed at the Pathology Department of AKTH, Kano between 1st January 2001 and 31st December 2007.
Results: The ovarian tumours included 212 (66.2%) benign and 108 (33.8%) malignant cases. Serous cystadenocarcinoma was the most common malignant tumour representing 31.5% of all cases. Twenty eight cases of granulosa cell tumours accounting for 25.9% of the malignant tumours were next in frequency while dysgerminoma and Burkitt's lymphoma were the most common tumours seen in children in the first decade of life and constituted 5.5 and 2.8% of all malignant tumours respectively.
Conclusion: The study has shown that malignant tumours constitute about a third of all ovarian tumours seen in this North-Wesrtern part of Nigeria covered by Aminu Kano Teaching Hospital with serous cystadenocarcinoma being overall the most common malignant ovarian tumour and peak age range of occurrence being in the fifth decade.
Key Words: Ovarian Cancer; Histology, Epithelial Tumour

Introduction
Ovarian cancers are important causes of morbidity and mortality in women and this arises from observations that most produce non-specific symptomatology and in many cases would have reached advanced stages at the time of diagnosis.

Epidemiologically, amongst cancers of the female genital tract, malignant tumours of the ovary rank third after those of the endometrium and cervix in the developed countries.[1] At present ovarian cancer is the sixth most common cancer and seventh most common cancer related cause of death in women, with 204,000 new cases and 125,000 deaths worldwide in the year 2005.[2] It however remains the most common cause of gynaecological related deaths.[3] Developed countries report the highest incidence of the malignant tumours with rates in excess of 9 per 100,000 with the exception of Japan which has an incidence of 6.4 per 100,000.[2]

Available literature has shown that tumours of epithelial origin constitute 60-65%, germ cell tumours 15-20% and sex-cord stromal tumours 5-10% among Caucasians.[1] The preponderance of epithelial malignancies in the developed countries is similar to the scenario in several countries in the West African sub-region.[4] However, in Asians (including Indians and Japanese) and Ugandans, the incidence of malignant germ cell tumours in general is higher than that seen in the west.[5]

Several theories have been propounded to explain the aetiopathogenesis of ovarian cancers. First is the pelvic contamination theory which postulates that carcinogens, chemical or biological, that result in ovarian malignancies

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gain entry to the pelvis through sanitary products or surgical contamination.[6] The ovulation theory in the aetiopathogenesis of ovarian cancers has identified ovulation-related risk factors like low parity, early menarche, late menopause and breast feeding.[7] This has been hinged on the effect of uninterrupted cycles of ovulation resulting in continuous remodeling of the germinal epithelium with resultant tendency towards metaplasia and dysplastic changes.[8] Oral contraceptive pill use on the other hand has been shown to be protective against cancers of the ovary for as long as 20 years after discontinuation.[9] This may be due to their suppressive effect on follicle rupture and hence the decreased need for repeated repair of the ovarian surface epithelium

As with most other tumours, advancing age is an important risk factor, with risk increasing from 15.7 to 54 per 100,000 as age increases from 40 to 79 years.[8] The serous carcinomas are rare before the second decade of life while mucinous carcinomas have a mean age of 53 to 54 years.[10] Malignant ovarian germ cell tumours however are most common in the first two decades of life.[11] In more recent times the concept of Ovarian Intra-epithelial neoplasia (OIN) has been gaining increasing consideration. This concept is similar to the precursor lesions seen in the vagina, cervix and prostate, and is based on the observation that in patients that have ovarian cancer, tissues adjacent to the cancer or from the contralateral ovary often show areas of cellular and / or nuclear atypia believed to represent precursor lesions.[12] Other risk factors that have also been identified for ovarian malignancies include genetic factors, notable among which are the inheritable BRCA mutations and the Lynch 2 syndrome.[13] In terms of early diagnosis three-Dimensional (3-D) imaging, using trans-vaginal probes is presently being used to study tumour angiogenesis and is anticipated to enable prediction of tumour behaviour.[14]

Materials and Methods
This retrospective study comprised all cases of malignant ovarian tumours recorded in the Histopathology Department of Aminu Kano Teaching hospital between 1st January, 2001 and 31st December, 2007. Relevant information such as age and laterality of the neoplasms were obtained from accompanying pathology request cards followed by retrieval of the Haematoxylin and Eosin stained slides which had been produced from the biopsies of these cases. The slides were then reviewed and subsequently classified into major histogenetic groups based on the 2002 World Health Organization International Classification of Diseases-Oncology (WHO ICD-O) protocol.[15] The results were then analyzed using EPI INFO Database.

Results
One hundred and eight cases of malignant ovarian tumours were recorded during the study period and these represented 33.8% of all ovarian tumours received. The ages ranged from 8 to 75 years with a mean of 38.8 ± 17.7years.

Table 1 shows the age distribution of the various histogenetic groups. Surface epithelial tumours accounted for 48 (44.5%) cases and sex-cord stromal tumours 30 (27.8%) cases. Twenty two cases of germ cell tumours were recorded representing 20.3% of the cases while Burkitt's lymphoma and metastatic tumours represented 3 (2.8%) and 5(4.6%) cases respectively.
Serous cystadenocarcinoma was the most frequent malignant histological subtype representing 31.5% of all the malignant tumours, with a modal age range in the fifth decade, but no statistically significant laterality.

These tumours were followed in frequency by granulosa cell tumours, a subtype of sex-cord stromal tumour, accounting for 25.9% of malignant tumours recorded. In general the granulose cell tumours were largely uncommon before the third decade while majority 80% (24 cases) were seen from the fourth decade and beyond. Malignant germ cell tumours were the least common major histogenetic group with 22 cases accounting for 20.3% of all the malignancies and showing a peak age frequency in the second decade (10 19 years). The malignant germ cell tumour variant most commonly seen was the yolk sac tumour (40.9%). Other uncommon types of malignant tumours seen were two cases of arrhenoblastoma, both in the fourth decade of life, 3 cases of Burkitt's lymphoma (two in the

Table 1: Histogenetic classification and age distribution of the malignant ovarian tumours.

Key:IMT=immature teratoma, YST= yolk sac tumour. DYSG= dysgerminoma, SCA=serous cystadenocarcinoma, MCA=mucinous cystadenocarcinoma, END=endometrioid carcinoma,

Age (yrs) Histogenetic Type		0-9	10-19	20-29	30-39	40-49	50-59	60-69	..	Total	%
Germ cell tumours	IMT		6	1						7	**6.5**
	YST		5	2	1		1			9	**8.3**
	DYSG	1	3	1				1		6	**5.5**
Surface epithelial tumours	SCA		1	3	2	19	6	3		34	**31.5**
	MCA			1		3			1	5	**4.6**
	END					2	1		1	4	**3.7**
	CCA			1	1					2	**1.9**
	BT				1	1		1		3	**2.8**
Sex cord stromal tumours	GCT	1	1	4	5	4	8	3	2	28	**25.9**
	ARRH					2				2	**1.9**
Others	MET			2	1		2			5	**4.6**
	BURK	2	1							3	**2.8**
Subtotal		**4**	**17**	**15**	**11**	**31**	**18**	**8**	**4**	**108**	**100**
(%)		**(3.7)**	**(15.7)**	**(13.9)**	**(10.2)**	**(28.7)**	**(16.7)**	**(7.4)**	**(3.7)**	**(100)**	

cystadenocarcinoma, MCA=mucinous cystadenocarcinoma, END=endometrioid carcinoma, GCT= granulosa cell tumour, ARRH = arrhenoblastoma, BURK= Burkitt's lymphoma, BT= Brenner tumour, MET= metastasis. CCA = clear cell carcinoma.

first decade of life) and 5 metastatic tumours.

Discussion

The true incidence of ovarian cancer in Africa is not known largely due to absence of population based Cancer Registries. However, available literature suggest that the incidence is relatively low compared to those in Northern and Eastern Europe and the Middle East where comparative studies among Negroid and Caucasian races have been carried out.[15-17]

The proportion of malignant ovarian tumours relative to all malignant gynaecological tumours has been documented to show variation in various regions of Nigeria. In Sokoto it was 18.2%, Maiduguri 16.3%, Lagos 14.1%, Ibadan 9.8%, Zaria 8.9% but as high as 24.1% in this study.[18-22]Among female in developed countries frequency rates of about 30% are reported.[16]

The observed proportion of 33.8% of malignant ovarian tumours relative to all ovarian tumours in this study is greater than findings from Benin City and Maiduguri, Nigeria where 19% and 20.7% respectively of ovarian tumours were reported to be malignant.[23, 24] It is however closer to reports from sub-Saharan Africa which have indicated that malignant tumours represent 28 to 33% of all ovarian tumours.[25, 26] It also agrees with findings of investigations in Kuala Lumpur, Malaysia where 31% of the reported cases of ovarian tumours were malignant and similar with findings in Karachi (40.81%) and other studies from Europe and America.[27-29]

Recent studies have indicated a steady rise in the incidence of malignant surface epithelial tumours in areas with previously low rates even though not to the levels seen in North Americans and Europeans.[30, 31] A 25-year review of ovarian cancers in Osaka, Japan, showed an increase in the incidence of carcinomas, particularly the serous and mucinous varieties, with the incidence of germ cell tumours remaining stable, while that for sex-cord stromal tumours showed a decline.[30] While a multi-centre study is required to evaluate the trend in Nigeria, a three and a half-year longitudinal study by Odukogbe et al reported that tumours of epithelial origin constituted as high as 76.2% of all the malignant ovarian tumours seen at the University College Hospital, Ibadan, Nigeria.[21] The authors suggested declining fertility and increasing use

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of ovulation inducing drugs as likely responsible factors for these changes. This is corroborated by the findings of a British study which showed that age specific incidence rates have remained stable in the younger population, while increasing among the older population above 65 years of age.[32] The disparity was also attributed to the widespread use of contraceptive pills in the younger generation, thus contributing to their relative protection from ovarian carcinomas.

Findings from the present study show serous cystadenocarcinoma to be the most common malignant ovarian tumour, accounting for 31.5% of all the malignant cases seen. This is comparable to findings in Zaria, Nigeria (23.9%), and Karachi, Pakistan (33.3%).[22, 33] It contrasts however with a study by Okonofua et al in Ile-Ife, Nigeria where of 31 consecutive cases of ovarian carcinomas they found mucinous cystadenocarcinoma (52% of cases) to be the most common epithelial malignancy.[34]
The serous and mucinous cystadenocarcinomas were predominantly seen in women in the fifth decade of life which concurs with observations on the predilection of these epithelial tumours for older age groups. However while the Surveilance Epidemiology and End Results (SEERS) cancer statistics review[35] has revealed that only about 13% of ovarian cancer bearing women are 45 years or younger this study shows that 43.5% of the cases are younger than 40 years. Similarly Kyari et al in Maiduguri also documented that 23% of cases were below 40 years of age.[19] A comparative population based study in Israel reported that not only did the Afro-Asian immigrants have a lower incidence rate for epithelial cancers, the peak age at diagnosis was about a decade earlier than those of European and North American descent.[36] In addition while the reported median age in the SEERS data is 63 years, it was 49 years in this study. The lower average life expectancy in developing countries has been suggested for this variance,[37] thus the women may not live long into the age range where these tumours are more frequently seen as among Caucasians. Other suggestions for this difference include possible genetic differences in metabolism of female sex hormones, and higher parity among Africans has also been adduced for this.[37,38]

Malignant sex-cord stromal tumours were next in frequency to the surface epithelial tumours in this study constituting 27.8% of the cases seen. This is comparable with findings in South Africa (22.9%) and India (21.4%).[26, 39] The malignant sex cord stromal tumours were predominantly represented by granulosa cell tumours, accounting for 25.9% of all the ovarian tumours in this study and in concordance with other studies in Nigeria, Africa and Asia.[22, 23, 25, 39]Adult granulosa cell tumours were the more common variety and the majority, 14 (50%) of cases, occurred between 30-59 years. This age distribution is about a decade earlier than that reported by an Israeli study (age range 40-59 years) which also showed a higher incidence of these tumours amongst women of European and American origin compared to those of African and Asian descent.[40]

Malignant germ cell tumours were the least frequent histogenetic group and constituted 6.9% of all ovarian neoplasms seen over the study period. This is consistent with observations in the literature that have documented the incidence to be about 35%.[1] The endemicity of Burkitt's lymphoma in Africa has long been established but worldwide the incidence has varied.[41] The rarity of adult ovarian Burkitt's lymphoma is supported by the finding of only 10 cases over a 27-year period in a review by Konje et al in Ibadan, representing a frequency of only 1.3%.[42] In this study two out of the three cases of ovarian Burkitt's lymphoma seen were bilateral. All three cases were below the age of 20 years with a mean age of about ten years, a finding comparable to reports from Zaria, Northern Nigeria, where the only case documented was below the age of ten years.[22]

Three (75%) of the 5 metastatic tumours to the ovaries seen in this study were well differentiated adenocarcinomas that were established clinically to be of gastrointestinal tract origin. This is consistent with findings by Yada-Hashimoto et al in a Japanese study reporting non-gynaecological primaries (59.3%) to be more common in their series of 64 women.[43] Various histochemical and

immunohistochemical stains are employable to differentiate primary and secondary ovarian tumours from one another. For example positive mucicarmine, PAS with diastase and cytokeratin 7 and 20 help in diagnosing the Krukenberg tumours.[15] We were however constrained by the by the absence of such facilities at out centre to enable more accurate histological categorization.

In conclusion this 7-year histopathological review of malignant ovarian tumours in AKTH has shown that they constitute about a third of all ovarian tumours, were predominantly serous cystadenocarcinomas and have peak age range of occurrence in the fifth decade similar to most African and Asian studies but earlier than observed from Caucasian populations.

There is need for establishment of immunohistochemical techniques in hospital laboratories and up to date radiological equipment to facilitate prompt and reliable diagnosis. This is second only to the need to establish local and national Cancer Registries to enable comprehensive epidemiological data collection.

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